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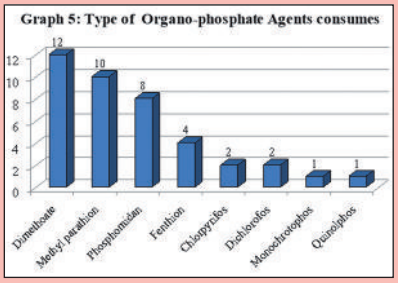

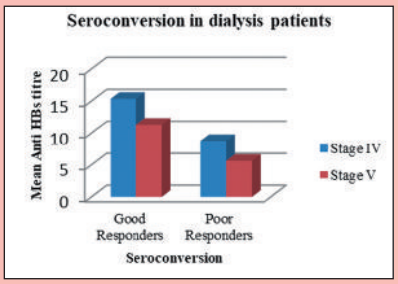

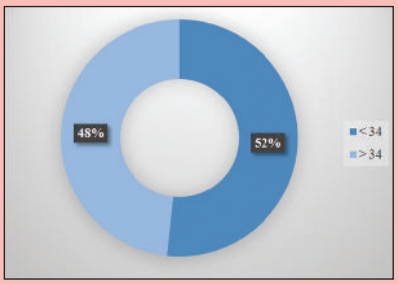

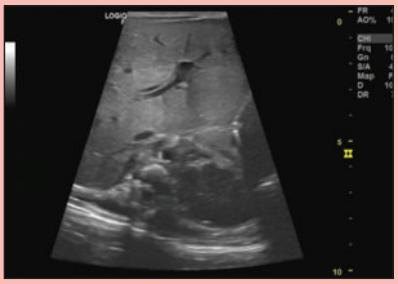

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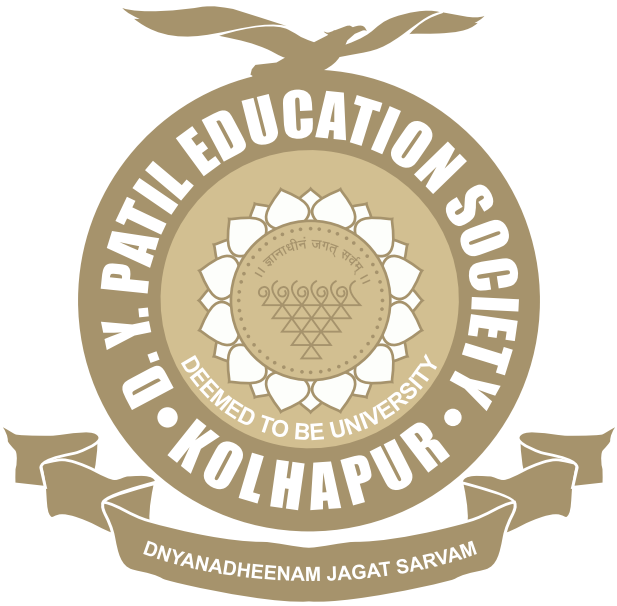

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Cochlear Implant

A cochlear implant (CI) is a medical device that uses electricity to stimulate the spiral ganglion cells of the cochlear nerve to restore sensorineural hearing loss. The purpose of this device is to convert sound to an electrical signal and deliver this to the cochlear nerve. Thus a cochlear implant transmits sound from the external world to the cochlear nerve bypassing the external ear, the middle ear, and a portion of the inner ear. These devices are surgically inserted by otolaryngologists who work closely with audiologists to make this device effective for patients. Cochlear implantation has become a routine procedure worldwide for the management of severe-to-profound sensorineural hearing loss. It is a remarkable example of successful collaboration between engineers, surgeons, scientists and the medical community and the technique is evolving rapidly. This device is the most successful device to replace sensory deprivation.

The appropriate selection of patients who will benefit from this technology is a challenge. Cochlear implant surgery is indicated in individuals with bilateral severe to profound hearing loss (pre lingual or post lingual) and limited benefit from binaural amplification (hearing aids).

In India, approximately 400,000 children, under the age of 4 are having severe to profound hearing loss. Approximately 100,000 additional children are born each year with severe to profound hearing loss. Children use their hearing to learn about the world around them and develop communication skills. The most important period for speech and language development occurs in the first 6 months of life. If the baby has a hearing loss, the process of developing language can be delayed. Unaddressed hearing loss will lead to Cognition issues, problems with Education and Employment, Social Isolation and Loneliness. So early identification and intervention is necessary. The best time to screen hearing is before the discharge of a newborn baby and mother from the hospital. The best time to confirm hearing loss is before 3 months and to start intervention is before 6 months. The earlier we take action, the easier it becomes for the brain to accept, adapt and learn.

We, at our D.Y. Patil Hospital and research institute, have started Universal Screening of newborn. Under this programme all the newborn babies are screened for hearing by performing OAE (Oto acoustic emission test) before discharge. We have also started the Cochlear Implant programme in our otolaryngology department. In this we operate

babies under the age of 5 years for insertion of cochlear implant and rehabilitation of these babies is done in our audiology department. This is done totally free of cost as the hospital is empaneled in RBSK (Rashtriya Bal Swasthya Karyakram) of Ministry of Health & Family Welfare, Government of India and also in ADIP (Assistance to Disabled Persons for purchase/fitting of Aids and Appliances) department of Empowerment of Persons with Disabilities (Divyangjan), Ministry of Justice & amp; Empowerment, Government of India

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REVIEW ARTICLE

RECENT TRENDS IN CARBON QUANTUM DOTS AND THEIR BIOLOGICAL APPLICATION

Anuja Vibhute, **Arpita Pandey Tiwari*****

INTRODUCTION

Synthesis of CQD's

Many methods have been proposed to prepare CQDs during the last decade, which can be roughly classified into "Top-down" and "Bottom-up" approaches, and they are shown in (Fig. 1*). Three problems facing CQDs preparation got to be noticed: (i) carbonaceous aggregation during carbonization, which may be avoided by using electrochemical synthesis, confined pyrolysis or solution chemistry methods, (ii) size control and uniformity, which is vital for uniform properties and mechanistic study, and may be optimized via post-treatment, like gel electrophoresis, centrifugation, and dialysis and (iii) surfaceproperties that are critical for solubility and selected applications, which may be tuned during preparation or post-treatment. We will discuss the most methods for CQDs synthesis.

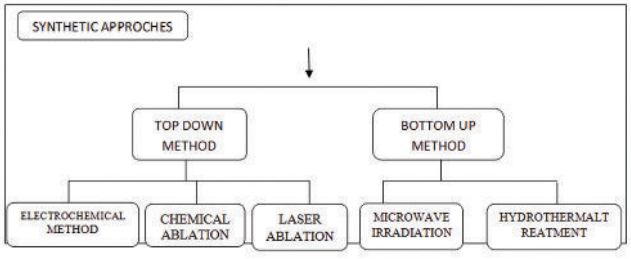

Fig. 1* : Shows the synthetic methods of Carbon Quantum Dots.

Synthetic methods – Top down synthesis methods

Electrochemical Method - Lu et al.[1] used high-virtue bars of graphite and significantly arranged pyrolytic graphite was utilized as an anode, with a parcel of 2 cm, platinum wire as a counter terminal, trailed by their establishment into ionic liquid/water arrangement. The peeling of carbon matter was started by the utilization of static possibilities. The procedure of peeling was led because of the mind boggling trade of anionic intercalation from the ionic liquid and anodic oxidative cleavage of water. Until the pH of shedding items was impartial, they were washed with ethanol and water. After partition by filtration and ultracentrifugation at 15,000 rpm at 20 °C, C-spots of 6-8 nm size were gotten with the QY of 2.8-5.2%. Yao

et al. [2] settled an anode of range unadulterated graphite ring and a cathode of a titanium tube at the center of the electrolyzer. A protected O-ring was utilized to isolate the cathode and anode. Cleaned water was utilized for an electrolyte medium. Ultrasonic force and electrolytic voltage were applied at once, and unadulterated blue fluorescent C-spots of 2-3 nm size were immediately delivered with no intricate decontamination. The QY of the got C-dabs was found as 8.9%. The resultant C-dabs had a brilliant fluorescence impact and thermodynamic soundness in fluid solution. [3] The degree of C-dabs can be overseen by changing the present thickness. Bigger C-specks with longer emanation frequency can be shaped by bringing down the flow density. [4]

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Photoluminescent C-dabs 3 nm in size are explicitly fabricated by electrochemical staggering of multi-walled carbon nanotubes. [5] Water-solvent C-spots can likewise be set up by the concoction oxidation treatment of flour. [6]

Chemical Ablation - Solid oxidizing acids carbonize little natural particles to carbonaceous materials, which can be additionally cut into little sheets by controlled oxidation. [7-12] This technique may experience the ill effects of brutal conditions and radical procedures. Peng and Travas-Sejdic announced a basic course to plan luminescent CQDs in a watery arrangement by drying out starches with concentrated H_2SO_4, trailed by breaking the carbonaceous materials into individual CQDs with HNO_3, lastly passivating with amine-ended mixes (4,7,10-trioxa-1,13-tridecanediamine). [11] The surface passivation was fundamental for the photoluminescence (PL) of these CQDs. The emanation frequency of these CQDs can be tuned by contrasting the beginning material and the span of the nitric corrosive treatment. The multi-color emanation capacities and nontoxic nature of these CQDs empower them to be applied in life science look into. Photoluminescent CQDs were incorporated in one-pot utilizing polyethylenimine (PEI), a cationic stretched polyelectrolyte, as both a carbon source and passivating operator by means of HNO_3 oxidation. [12]

Rather than the ordinarily detailed pH-uncaring CQDs, the PL of these CQDs was exceptionally pH-touchy, i.e., the PL power diminished with expanding pH from pH 2 to 12. What's more, the pH reaction of the PL conduct was reversible. This property blesses them the possibility to fill in as proton sensors in observing cell utilization forms with proton discharge. When hatched with HeLa cells, the CQDs could promptly infiltrate the cell layer and show low cytotoxicity and ideal biocompatibility, which is fundamental for HeLa cell imaging.

Laser Ablation - The laser removal strategy [13] utilizes a high-vitality laser heartbeat to illuminate the outside of the objective to a thermodynamic state in which high temperature and high weight are produced, quickly warms up and vanishes into a plasma state, and afterward the fume takes shape to frame nanoparticles.[14] Li et al. (2011) announced an easy way to deal with integrate CQDs through laser illumination of carbon forerunner, which was scattered in various common natural solvents. The as-got CQDs showed obvious and tunable photoluminescence (PL). [15] Moreover, Hu et al. (2009) exhibited the surface condition of the CQDs can be changed by choosing appropriate natural dissolvable during the laser illumination process so as to tune the PL properties of the incorporated CQDs. [16] Laser removal is a powerful strategy to get ready CQDs with tight size appropriation, great water solvency, and fluorescence qualities. Nonetheless, its convoluted activity and significant expense limit its application.

BOTTUM UP -METHODS

Microwave Irradiation-This system has been a critical methodology in manufactured science and offers various favorable circumstances, for example, being non-lethal, easy, adaptable and ease. Notwithstanding, poor authority over size of got particles is one of its fundamental disservices.[17] one-advance green microwave-helped blend of fleece inferred fluorescent CQDs is accounted for by Wang et al.[18] In this work, an answer of modest bits of fleece (0.3 g) and 40 ml DI water was readied, at that point filled a microwave absorption tank and warmed at 200˚ C for 60 min by microwave illumination. This technique isn't just basic and effortless, yet additionally unnecessary to

any added substances, for example, acids, bases or salts for additional complex post-treatment procedure to refine the CQDs. Yang et al. built up an ease and one-advance microwave approach for blend of water-dissolvable CQDs with normal width of 4 nm, in which folate receptor (FR) and folic corrosive (FA) filled in as carbon forerunners.[19] A legitimate measure of FA and FR were added to refined water and warmed for 8 min in 500 W microwave. The arrangement shading changed from yellow to brown lastly dim earthy colored grouped strong, during the procedure, which showed the development of CQDs. The arrangement was then centrifuged and separated through a 0.22 mm layer to dispose of agglomerated particles. The readied particles indicated exceptional PL and had high QY of about 25%. Moreover, FA atoms in the CQDs let them to be taken by FA-receptor-positive malignancy cells, which renders them as another biocompatible test to recognize FA-receptor-positive disease cells from typical cells in natural imaging and malignancy determination. [19] Another basic method to plan CQDs (under 5 nm) from glucose or dynamic carbon by utilizing a one-advance salt or corrosive helped ultrasonic treatment system was investigated by Li et al. [20] In this strategy, they previously arranged 1 mol/l arrangement of glucose in deionized water and afterward included HCl (50 ml, 36–38 wt.%) into the arrangement of glucose. From that point onward, the blended arrangement was ultrasonicated for 4 h. At long last, the unadulterated arrangement of CQDs procured from glucose/HCl was broiler dried at 80 C for 6 h. A splendid and brilliant PL could be radiated from such mono-scattered water-dissolvable fluorescent CQDs, which covers the entire noticeable to (close to infrared) N-IR phantom range (Figure 1). Specifically, the N-IR outflow of CQDs can be accomplished by N-IR excitation. Furthermore, the CQDs had incredible up-change fluorescent properties and the outcomes indicated that the molecule surfaces were wealthy in hydroxyl gatherings, that gave them high hydrophilicity. [20]

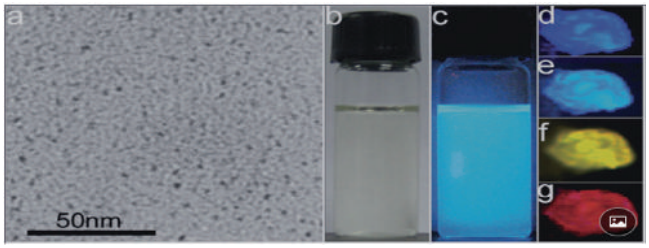


Fig. 1 : (a) TEM image of 5 nm-CQDS obtained from glucose; (b, c) photographs of CQDs dispersals in water with visible light and UV (365 nm, centre) illumination, respectively; (d–g) fluorescent microscope images of CQDs under diverse excitation: d, e, f and g for 360, 390, 470 and 540 nm, respectively. (Reprinted from Ref. [20] Copyright 2011, with permission from Elsevier).

Hydrothermal/solvothermal treatment- A green, modest and basic way to deal with combine excellent fluorescent CQDs by aqueous treatment of business gelatin with no added substance and convoluted post-treatment. As follows 0.8 g gelatin was added to 40 mL water and was broken down at 40 C under tumult. Along these lines, the above admixture was filled a tempered steel autoclave with a Teflon liner of 50 mL limit and warmed at 200 C for 3 h. At long last, the reactor was consequently cooled to room temperature. The subsequent light yellow arrangement was centrifuged at 16,000 rpm for 30 min to expel weight accelerate and agglomerated particles and afterward yielded a light earthy colored fluid arrangement of CQDs for additional portrayal. The yield controlled by freeze-dried technique was determined to be estimated 38.6%. [21] Carbon quantum specks (CQDs) were incorporated from oil palm - based actuated carbon through aqueous carbonisation with low temperature process. To sum things up, 6 g of oil palm - enacted carbon powder was added to 150 mL of deionised water. The blend was then moved into a 200 mL Teflon - lined autoclave

and fixed firmly to keep up the inbuilt weight. The autoclave was warmed at 200 °C for 3 h. The response vessel was permitted to cool to room temperature, and the arrangement was centrifuged at 1000 rpm for 30 minutes. The arrangement was sifted through 0.2 µm channel to expel micron - estimated particles. The last arrangement was lyophilised to acquire strong CQDs. The CQDs were scattered in DI water at a centralization of 7.6 mg/mL and put away at 4 °C for additional characterisation .[22]

Fluorescent NS-CQDs from banana juice was inferred through a basic one-advance aqueous technique. In a commonplace investigation, 80 gm of banana was cut into little pieces and transformed into a glue with 100 mL of deionized water. At that point 20 mL of the banana juice (mash free) was blended in with 20 mL of ethanol utilizing constant mixing. The above arrangement was moved in Teflon connected treated steel aqueous pot and put in the suppress heater at 150 °C for 4 h. The acquired dim earthy colored item was additionally disintegrated in the 20 mL of water and sonicate for 1 h, and the build-up was isolated by filtration. From that point onward, 50 mL of ethanol was included into the watery filtrate and mixed for 30 minutes, trailed by centrifugation (7000 rpm) for 15 min multiple times under encompassing conditions to isolate the huge particles. The water-solvent carbon dabs with ethanol were kept in a vacuum desiccator for vanishing of ethanol at room temperature. [23] The schematic portrayal of NS-CQDs creation from banana juice is appeared in Fig. 2.

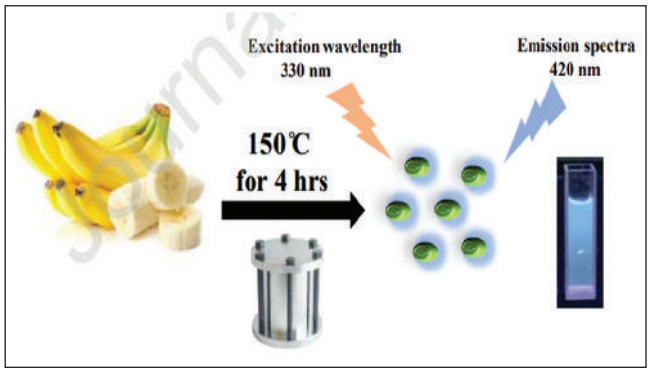


Fig. 2 : Schematic representation of synthesizing NS-CQDs from banana juice.

Table 1 : Different synthesis routes of CQDs from different precursors, their optical properties and applications

No.	Precursors	Synthesis route	Photocatalysis	Application	Ref.	Reference
1	graphite rods Ti(OBu)4 and TEOS	an electrochemical method, a sol-gel method	TiO2/CQDs, SiO2/CQDs	degradation of MB, Photocatalysis	24	1
2	mate herb, KNO3, L-lysine and FeSO4	pyrolysis, drying-vacuum, ultrasonic treatment	Fe-NF/CND	degradation of MO, Photocatalysis	25	2
3	chitosan, TiO2, HQC and Fe(HQC)3	hydrothermal treatment	HQC/TiO2, CQDs/HQC/TiO2, Fe(HQC)3/TiO2	degradation of phenol	26	3
4	graphite rods and P25	an electrochemical method, hydrothermal treatment	CQDs/P25	water splitting	27	4
5	graphite rods, NH3 and urea	an electrochemical method, hydrothermal treatment, pyrolysis	C-dots/g-C3N4	water splitting	28	5
6	CA and NiP	thermolysis	CQD-NiP	water splitting	29	6

7	graphite rods, BiVO4 and cyclohexane	an electrochemical method, hydrothermal treatment, reflux	CDs/BiVO4 QDs	water splitting	30	7
8	glucose, CuSO4 and PVP	ultrasonic treatment	CQDs/Cu2O	conversion of CO2	31	8
9	glucose and urea	ultrasonic treatment, hydrothermal treatment	CND/pCN	conversion of CO2	32	9
10	graphite rods	an electrochemical method	CQDs	acid catalysis	33	10
11	L-cysteine, CdCl2 and Na2S	pyrolysis, electrophoretic and sequential chemical bath deposition	C dot/CdS Sensing QY %	reduction of nitro-benzene derivatives	34	11
12	Citric acid and guanidinium	Solid-phase pyrolysis	19.2	Fe3+ Sensing	35	12
13	2,5-diaminobenzenesulfonic acid and 4-aminophenylboronic acid hydrochloride	Hydrothermal	5.44	Fe3+ Sensing	36	13
14	Folic acid, 3-aminopropyl trimethoxy silane, glycerol	Hydrothermal	46	Fe3+ Sensing	37	14
15	Citric acid, diammonium hydrogen phosphate	Hydrothermal	59	Fe3+ Sensing	38	15
16	Adenosine 50 triphosphate	Hydrothermal	43.2	Fe3+ Sensing	39	16
17	L-glutamic acid	Solid-phase microwave assisted pyrolysis	41.2	Fe3+ Sensing	40	17
18	DL-malic acid, ethanolamine, ethane-sulfonic acid	Microwave-assisted pyrolysis	15.13	Fe3+ Sensing	41	18
19	Chitosan, acetic acid and 1,2-ethylenediamine	Microwave-assisted pyrolysis	20.10	Fe3+ Sensing	42	19
20	Anhydrous citric acid, 1–10 phenanthroline	Pyrolysis	10	Sensing	43	20
21	Aminosalicylic acid	Solvothermal	16.4	Sensing	44	21
22	Mangosteen pulp	Pyrolysis	-	Sensing	45	22
23	Coffee ground	Hydrothermal	5	Sensing	46	23
24	Jujubesx	Hydrothermal	-	Sensing	47	24
25	Sweet potatoes	Hydrothermal	8.64	Sensing	48	25
26	Jinhua bergamot	Hydrothermal	50.78	Sensing	49	26
27	Rose-heard radish	Hydrothermal	13.6	Sensing	50	27
28	N-Methyl-2-pyrrolidone, dimethyl-imidazolidinone	Pyrolysis	11.6%	Bioimaging, electrocatalysts	51	28
29	Citric acid monohydrate, L-cysteine	Hydrothermal	73%	Bioimaging	52	29

30	Diammonium hydrogen citrate, urea	Solid state reaction	46.4%	Sensor, bioimaging,	53	30
31	Citric acid, diethylenetriamine, gadolinium chloride	Hydrothermal	69.86%	Bioimaging	54	31
32	Hair	Carbonization-microwave	86.06%	Bioimaging	55	32
33	Gelatin	Hydrothermal	31.6%	Bioimaging, fluorescent Ink	56	33
34	Citric acid, cysteamine	Hydrothermal	81%	Composites, bioimaging	57	34
35	Alanine, ethylenediamine	Hydrothermal	46.2%	Biosensing, bioimaging	58	35
36	Amino acids	Electrochemical/ electroanalytical	46.2%	Bioimaging	59	36
37	Orange juice	Hydrothermal treatment at 120°C	26	Bioimaging	60	37
38	Watermelon peels	Carbonization at 220°C	7.1	Bioimaging	61	38
39	Glucose	Hydrothermal treatment at 200°C	1.1–2.4	Bioimaging	62	39
40	L-Glutamic acid x	Pyrolysis	28	Biological detection	63	40
41	Citric acid, branched polyethyleneimine	Microwave pyrolysis	12–13%	In vivo gene delivery	64	41
42	Citric acid, urea, H2SO4, H3PO4	Microwave	-	Screening of oxygen-states in CQDs	65	42
43	Activated carbon, KOH	High-energy ball milling	7.6%	Electrochemi-luminescence	66	43
44	Sweet pepper		19.3	ClO− detection	67	44
45	Ginger juice		13.4	Inhibit the growth of tumors	68	

Drug Delivery

No.	Carbon Nanoparticles	Drug Loaded	Ligand Attached	Cell Targeted	Application	Ref
46	C-dots	Dox	Nuclear localization signal peptide	A549	Drug delivery	69
47	C-dots	Dox	-	HeLa	Drug delivery	70
48	C-dots	Dox	-	HeLa	Drug delivery	71
49	C-dots	Dox	Transferrin CHLA-266,	SJGBM2	Drug delivery	72
50	C-dots	Dox	Folic acid	HeLa	Drug delivery	73
51	C-dots	-	Folic acid	HeLa, NIH3T	Drug delivery	74

Gene delivery

No.	Precursors	Synthesis route	Quantum Yield(%)	Application	Ref
52	bPEI, 1 M ammonium persulfate (APS)	Hydrothermal	54.3	Gene Delivery	75
53	Sodium alginate, hydrogen peroxide, Plasmid TGF-b1	Hydrothermal	54	Gene Delivery	76
54	citric acid, bPEI25k, HCl 0.1, DNA complexes	microwave-assisted pyrolysis	31.5-48.1	Gene Delivery	77
55	arginine and glucose (0.1 g), pSOX9	microwave- assisted pyrolysis	12.7	non-viral gene delivery	78
56	Polyethylene glycol, Chitosan NP-dsRNA complex	Microwave assisted method	-	Gene Delivery	79

Applications of carbon quantum dots

The CQDs possess special physicochemical and catalytic properties which will make them as candidates for a few biomedical applications. Two characteristics of CQDs i.e. their small size, also as biocompatibility, can give them great opportunity to be used as drug delivery vehicles while are often monitored within the body thanks to their PL characteristics. The CQDs with minor toxicity, high hydrophilicity and water solubility, excitation wavelength-dependent PL emission, and chemical stability have versatile potential applications within the biomedical fields. Here after, we specialise in the most bio-applications of the CQDs and up to date advances in each area are going to be discussed. Fig. 2* shows various applications of CQDs in biomedical field.

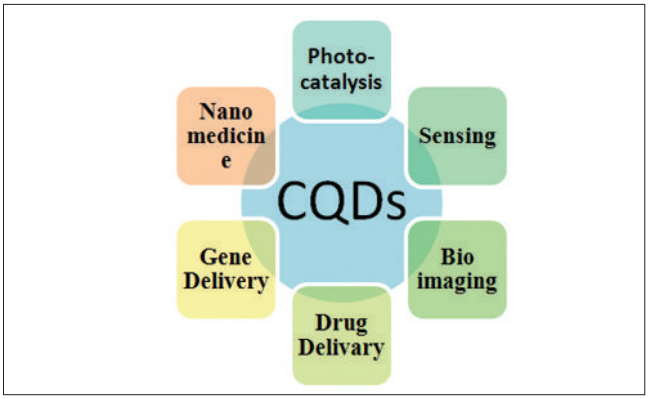


Fig. 2* : biomedical applications of CQDs

Photocatalysis - CQDs can show potential in photocatalysis applications due to the features as follows. Primarily, CQDs show superiority in water solubility, chemical stability and low toxicity to other common photocatalysts (e.g., ZnO, TiO2, CdS). CQDs exhibit excellent and tunable optical properties of absorbance and PL after specific surface modification. especially, Up-converted photoluminescence (UCPL) of CQDs, known to be an physical phenomenon wherein materials emit shorter wavelength light than the excitation source, can considerably extend the daylight absorption of wide bandgap semiconductors into the visible region and even the near infrared region. Moreover, photoinduced CQDs are both excellent electron donors and acceptors, leading to efficient separation of electrons and holes. Therefore, CQDs can function a flexible component in photocatalyst design, like electron mediators, photosensitizers, spectral converter and sole photocatalyst. CQDs are ready to play multifaceted roles in photocatalysis, like electron mediators, photosensitizers, spectral converter and sole photocatalyst.

Electron Mediators - Photocatalytic activity is strongly hooked in to the transport and separation efficiencies of photogenerated electrons and holes within the photocatalysts. However, free charge carriers

(electrons and holes) are often trapped or scattered by various sorts of random defects, leading to increased recombination probability. [80,81] Therefore, promoting the separation of photogenerated electrons and holes will facilitate the photocatalytic process. it's been demonstrated that carbon nanostructures have an outsized electron-storage capacity[82] thus, the photo excited electrons from semiconductors or other forms of photocatalysts are often shuttled within the conducting network of CQDs, retarding the recombination of photogenerated carriers at the junction interface. In fact, CQDs with their simple synthesis and low toxicity have attracted considerable interest in serving as electron mediators.[83,84]

Photosensitizers- aside from performing as an electron mediator, CQDs display PL and UCPL rendering them as promising photosensitizers in photocatalytic systems.[85-87] Meanwhile, CQDs show remarkable merits on multiple aspects compared to other photosensitizers. Firstly, CQDs are typically terminated by acid groups at their surface, which impart high solubility in aqueous solutions and supply potential for further functionalization. Besides, unlike graphene materials. [88,89] and organic dyes, [90] CQDs are often cost-effectively synthesized on an outsized scale via environmentally friendly methods. Furthermore, due to their low-toxicity, CQDs might be adopted to exchange toxic CdS/CdSe quantum dots. [91] The CQDs show good photostability and therefore the NiP is that the limiting factor for the steadiness during this system.[92]

Spectral converters- Many conventional photocatalysts are wide-bandgap semiconductors (e.g., TiO2, ZnO) which will only be excited by UV light. This greatly limits their wide practical applications because the UV light only accounts for 4% of the entire solar power. [93] Generally, narrow-bandgap semiconductors like CdS and CdSe are employed to couple with conventional TiO2-based photocatalyst systems to utilize the complete spectrum of sunlight. However, they're restricted in practical applications due to their toxicity and instability. to increase the sunshine absorption range from the UV to the light region, more robust approaches are desirable. CQDs are employed as a spectral converter in CQD-based composite photocatalysts, taking advantages of their UCPL properties.[94]

Solephotocatalyst-Theabovementionedphotocatalytic applications of CQDs are beat conjunction with other inorganic materials, while it's been found that CQDs also can directly act as photocatalysts alone.[100] Hu et al. have proposed the mechanism of CQDs as a sole photocatalyst and highlighted that surface oxygenated functional groups are the many factor affecting the photocatalytic activities of CQDs. [98] As shown in **Fig. 3**, the photocatalytic mechanism of CQDs is proposed. CQDs are beat conjunction with other inorganic materials, while it's been found that CQDs also can directly act as photocatalysts CQDs are alone. [95,96] Hu et al. have proposed the mechanism of CQDs as a sole photocatalyst and highlighted that surface oxygenated functional groups are the many factor after the photocatalytic activities of CQDs. [97]

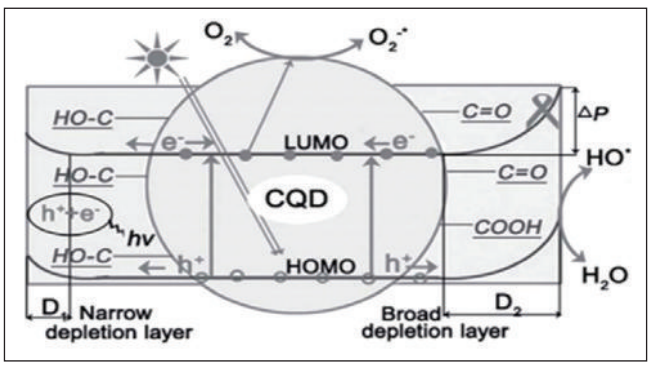


Fig. 3 : The photocatalytic mechanism of CQDs with oxygen containing surface groups. Reprinted with permission from ref. 100. Copyright 2009 John Wiley and Sons.

Sensing- CDs are widely used in the field of fluorescence analysis because of their adjustable fluorescence, superior stability and good water solubility. The fluorescence of CDs is closely related to the surrounding environment. The interaction between CDs and chemicals leads to the quenching/enhancement of CD fluorescence. [98] Compared with inorganic semiconductor quantum dots and fluorescent dyes, CDs display low toxicity and good biocompatibility. In addition, the synthesis of CDs is relatively simple and easy. Due to the gradual development of green synthesis methods, the production cost of CDs has been greatly reduced and the yield has been increased, making CDs a very promising fluorescent probe. The constructed fluorescence sensing systems can be roughly divided into two types: solution phase sensing and solid phase sensing. The solution phase sensing by using CDs can be well applied to sense various analytes, such as cations and anions, small molecules and macromolecules, cells and bacteria and so on. In comparison, solid phase sensing usually includes the application in fingerprint sensing, test paper sensing, electrospun nanofibrous film sensing, etc. Lai et al. [99] developed fluorescent CDs capable of detecting E. coli and tumor cells.

The CQDs that were synthesized by sodium hydroxide-assisted reflux method from poly (ethylene glycol) (PEG), were used for the detection of Hg^{2+} with excellent sensitivity and selectivity. It was observed that the strong fluorescent emission of the CQDs (at 450 nm) decreased by an increase in the Hg^{2+} ions concentration in the solution. This phenomenon has been attributed to the quenching effect of the Hg^{2+} ions on the CQDs through electron or energy transfer. The low value of LOD of 1 fM has been reported for this sensor (100). The CQDs synthesized by solid-state reaction of diammonium hydrogen citrate and urea with a QY of 46.4% showed a low value of LOD of 19 μM and linear relationship with the concentration in the range of 25 to 300 μM for Fe^{3+} ions. [101] The CQDs fluorescence sensors have also the advantage of having a good selectivity that means these sensors could detect specific ions or chemical compounds in a mixture of different ions or chemical species. It has been reported that N-doped CQDs that were obtained from a hydrothermal method of isoleucine and citric acid with the sizes in the range of 6-15 nm were used for selective detection of Fe^{3+} ions in a solution. By the addition of Fe^{3+} ions to the medium at concentrations in the range of 0-60 μM, the fluorescence intensity of the CQDs quenched up to 93%, and the color of the solutions changed from blue to colorless (under UV). It was speculated that the interaction of Fe^{3+} ions with the oxygen functional groups on the CQDs surface caused the CQDs emission to be quenched. These conditions were also repeated while other ions such as Fe^{2+}, Ag^{+}, Mn^{2+}, Cd^{2+}, Pb^{2+}, Cu^{2+}, Co^{2+}, Ni^{2+}, Hg^{2+}, Na^{+}, K^{+} Zn^{2+}, and Al^{3+} were added to the solution. The difference in the quenching behavior of the CQDs in the presence of different ions confirmed that the synthesized CQDs have excellent selectivity toward Fe^{3+} ions in the solution. [102]

The CQDs can also be used for designing of sensor nanoswitches. In recent years, several types of research have been focused on designing and application of nanoswitches with the aid of various molecules for different purposes. Molecular nanoswitches can respond to some stimuli to perform an action such as chemical sensing or reaction control. [103] Many of the researches on the nanoswitches focus on the switches that are based on molecular DNA. [104-106] During recent years some nanoswitches have been reported that

work based on the CQDs. For example, fluorescent nanoswitch by the aid of the CQDs that were synthesized from 2,2′-(ethylenedioxy)- bis(ethylamine) and malic acid through a hydrothermal method were quenched by Cr(VI) (turnoff), and the fluorescence emission was recovered (turn-on) by sensing Ascorbic Acid (AA) in the environment (compared to other biomolecules or metal ions tested) **(Fig. 4)**. [107]

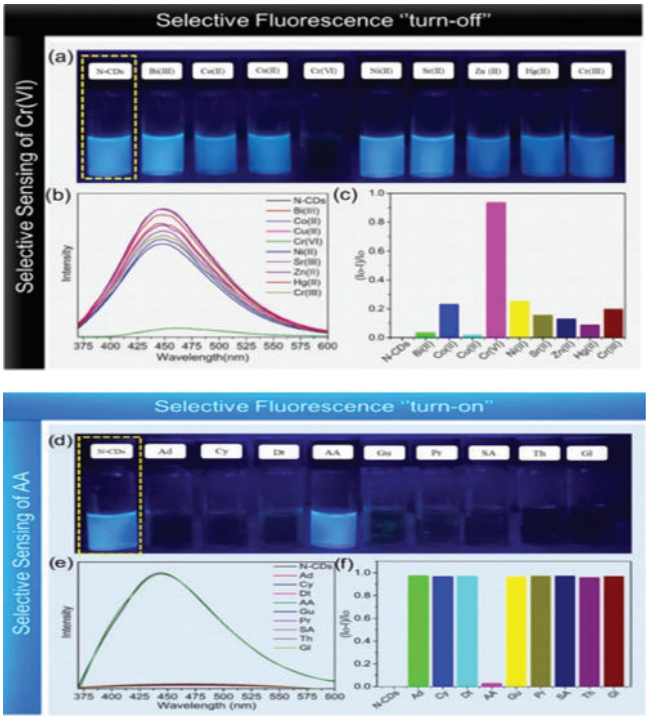


Fig. 4 : a) the CQDs in aqueous solution with several metal ions (under UV light) which illustrated selective detection of Cr(VI) (turn-off), b) fluorescence spectra of the CQDs after addition of several metal ions (excitation wavelength: 320 nm), c) fluorescence intensity ratio, ((I0-I)/I0 where I and I0 are fluorescence intensities of CQDs with and without metal ions, respectively) of CQDs solution with different ions, d) the solutions which shows the fluorescence emission of the CQDs that had been quenched by formation of CQDs-Cr(VI) complex, recovers selectively by ascorbic acid among other common interfering biomolecules (adenine (Ad), L-cysteine (Cy), dextrose (Dt), L-ascorbic acid (AA), guanine (Gu), L-proline (Pr), sulphonilic acid (SA), thymine (Th), and glycine (Gl)), e) fluorescence spectra of the CQDs-Cr(VI) complex which shows the fluorescence intensity recovers selectively by addition of AA (excitation wavelength: 320 nm) among other common interfering biomolecules (under UV light), f) fluorescence intensity ratio (I0 − I)/I0 of CQDsCr (VI) complex with different biomolecules. Reprinted with permission from ref. [107] Copyright 2019 American Chemical Society.

Bio-imaging - The three different vital kinds of *in vitro* CD-based cell imaging including cancer cell imaging, (108,109,110) stem cell imaging, [111] and neuron imaging, [112] which provide the possibility of using CDs for *in vivo* applications, especially being helpful in exploring the development, diagnosis and treatment of cancers and neurological diseases, discussed in the section of *in vivo* biomedical applications of CDs. In addition, the imaging of organelles including nucleus imaging, [113,114] mitochondrial and endoplasmic reticulum imaging *etc.*[115]

In vitro imaging

Cancer cell imaging Cancer, like ghosts, is obsessed with human health, devouring the lives of millions of people each year. Therefore, advanced methods for early cancer diagnosis are becoming more and more significant for preventing tumor development. Specifically, functionalized CDs can penetrate many kinds of cancer cells and probe them more efficiently by FL imaging. [116,109,117] The special recognition mechanism is primarily dependent on the interaction between functional CDs and the surface groups of cancer cells. As shown in the study of Ruan *et al.*, PEGylated CDs were developed by using glucose and glutamic acid as precursors, and the as-prepared CDs could specifically anchor glioma cells through recognizing the surface group of angiopep-2, resulting in higher sensitivity for glioma imaging over normal brain tissues. [118] Wang *et al.* developed dual-element CDs with nitrogen and chloride. Such CDs exhibited strong pH-sensitive fluorescent emission for sensing intracellular pH and cytochrome *c* by multi-color imaging in HeLa cells. [119]

The Liang group developed natural biomass carbon dots for near-infrared fluorescence imaging-guided PDT of cancer cells and mouse tumors. [120] Also, Ramanan and co-workers synthesized photoluminescent CDs from eutrophic algal blooms, which acted as a potential biomarker in the imaging of MCF-7 cells. [110] These research studies showed that fluorescent CDs provide a new potentiality in biological studies of cancer cell identification. Folic acid conjugated CDs were used for imaging of cancer cells, but the folate receptor occurred not only in hepatoma cells or breast cancer cells. Thus, improving the specificity and targeting capability of fluorescent CDs is much more significant for tracing cancer cells. [121]

Stem cell imaging - Labelling strategies for stem cells are urgently needed for regeneration medicine in order to understand the natural organ development process [122-124] and the contribution of stem cells to various tissue regeneration including bone repair,[125] skin renewal[126] and neurorepair.[127] Due to their small size and outstanding biocompatibility, CDs can effortlessly penetrate stem cells for imaging *via* the endocytosis mechanism in a concentration- and time-dependent manner as other carbon nanoparticles.[128]

Zhang and co-workers developed yellow-emission CDs to label three different kinds of stem cells without any obvious impact on their proliferation or differentiation capacity during long-term imaging.[129] Meanwhile, as depicted in **Fig.5A and B,** Liu *et al.* synthesized green emission CDs for successfully probing the live stem cell.[130] However, the interaction between CD probes and stem cells has not yet been studied carefully. Recently, the Yang group employed citric acid-based CDs and their derivatives for labelling and tracking of rat bone marrow mesenchymal stem cells (rBMSCs).[131] The authors found that these CDs could facilitate high-efficiency osteogenic differentiation of rBMSCs toward osteoblasts by boosting osteogenic transcription and increasing matrix mineralization **(Fig. 5C).** Afterwards, Chen *et al.* reported the promoting effects of multifunctional photoluminescent CDs for neuronal differentiation of EMSCs through a non-viral gene delivery mode, because the as-prepared CDs possessed admirable properties to condense macromolecules of the plasmid DNA.[112] As displayed in **(Fig. 5D),** the synthesized porphyra polysaccharide-derived CDs exhibited not only significantly high transfection efficiency, but also high performance in neuronal differentiation of EMSCs. These findings showed that CDs would be applied as both safe and effective gene carriers to guide the differentiation of adult neuronal stem cells.

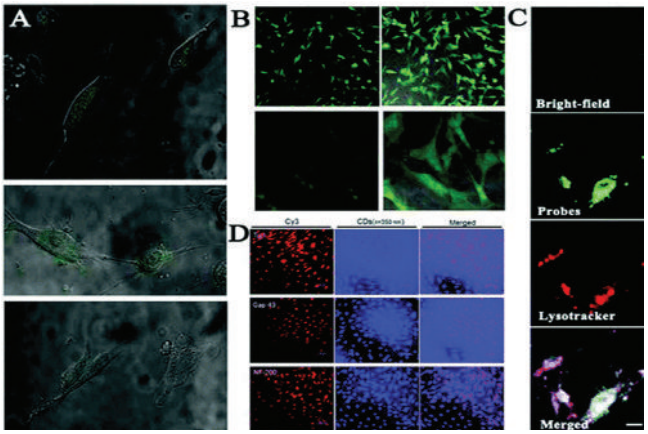


Fig. 5 : (A) Fluorescence (fluorescence + bright-field) images of the live stem cells and (B) the fixed stem cells labelled with the EDA-CDs (130). (C) Long-term rBMSClabeling and tracking by CDs (green) co-located with Lyso Tracker (red) (131) (D) Immunofluorescence staining using a Cy3-conjugated secondary antibody (red) for neuronal markers including proteins of Tuj1, Map2 and Tau. The converted cells were also visualized with the bright blue fluorescence of CDs when excited at a wavelength of 350 nm. (112)

Neural cell imaging - To further improve our understanding of the properties and functions of the nervous system, development of new imaging methods

to visualize the relationships among the brain structure, neuron activity and neurochemistry is in great demand. Advances in nanomaterials may help overcome the current imaging challenge in neurosciences. Some research has been done *in vitro* to investigate the interaction between neurons and CDs based on assessing the cytotoxicity of CDs, the application of CDs as gene carriers for drug delivery and their use in electric activity sensing and tracking. For example, Gao *et al.* found that the red emission CDs did not affect the PC12 cell viability with a gradual increase of CD concentration. [132] However, CDs probes in neuron cells and the central nervous system (CNS) have been less investigated in terms of their potential value in the diagnosis and therapy of human CNS diseases. The Lu group developed a direct and more economical fluorescent neural tracer based on cholera toxin B-carbon dot conjugates (CTB-CDs), which could be taken up and retrogradely transported by neurons in the peripheral nervous system of rats. This tracer can be used in *in vitro* and *in vivo* bioimaging of neuron cells or tissues based on the special binding ability to gangliosides from the nerve cell membrane and nervous tissues **(Fig. 6A)**.[112] As illustrated in Fig. 6B, Khan and co-workers used dopamine (DA), an important inotropic vasopressor agent in neurological diseases, to anchor the biocompatible CDs for controlling drug release under physiological conditions.[132] The tenure of DA anchored on CDs released at pH 7.4 was greatly extended to 60 h, which exhibited great biocompatibility to Neuro-2A cells and non-infliction of any anatomical distortions or hostile effects on tissues *in vivo*, additionally as shown in Fig. 6C. More interestingly, Nissan *et al.* synthesized Ga-CDs-Ga-coated substrates, which showed a 97% increase in branch number originating from the soma and played an important role in neural growth **(Fig. 6D).**[133]

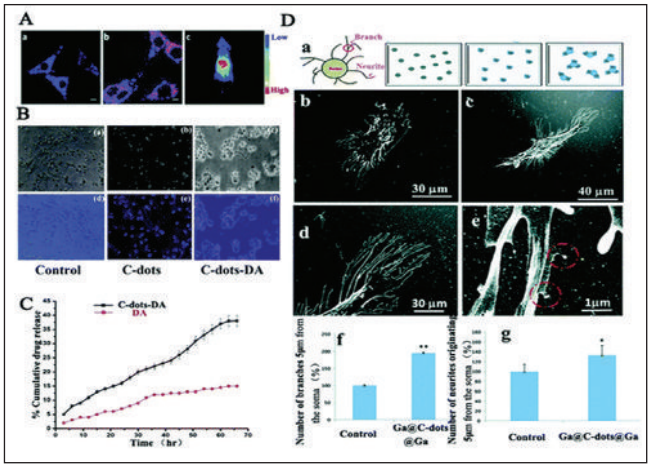


Fig. 6 : (A) Bio-imaging of cholera toxin B-CDs in PC12 cells and in nude mice (112). (B) Fluorescence microscopy of Neuro 2A cells treated respectively with CDs-DA, DA, PBS and (C) the release rates of CDs-DA and DA with respect to time (132). (D) SH-SY5Y cell morphology demonstrating branch and neurite counting on the modified substrate, on glass, Ga-CDs-Ga coated substrates, and the HRSEM images of neurite branches and branch numbers. [133]

Nucleus imaging - Staining of nuclei is crucial to reveal their morphology and their roles in cell metabolism, growth, differentiation and heredity. [134] Due to their small nanometre sizes (<10 nm), highly positive charge obtained from precursors with a quaternary ammonium group, and strong absorption capability on the membrane, CDs as newly developed nanomaterials may be incorporated into a cell nucleus for binding to the DNA and RNA. Datta *et al.* proved the uptake of CDs into the nucleus for the first time. [113] In their study, the authors combined cationic quaternized CDs with anionic graphene oxide sheets to form biocompatible hybrid nanomaterials. Owing to the electrostatic interactions with the negatively charged components of the lipid membrane, the hybrid nanomaterials as the bio probe could easily internalize into the nucleus of NIH/3T3 cells. After that Yin's group prepared dopamine-mimicking nitrogen-doped CDs as a nucleus-staining agent for cell imaging. The great

performances of the nitrogen-doped CDs in nucleus staining, which is attributed to their small sizes, surface positive charges and dopamine-mimicking properties, were validated within four different types of cancer model cells, including rat PC12, A549, HepG2 and MD-MBA-231 **(Fig. 7A)**.[114] In addition, Khan *et al.* discovered yellow-orange emissive CDs localizing in the nucleolus of HeLa cells for specifically binding to RNA, which was confirmed by an RNase digestion test **(Fig. 7B)**.[135] Recently, in our research, the as-prepared CDs showed a hydrogen-bonding-induced emission (HBIE) phenomenon with good biocompatibility, ultrasmall sizes, and strong affinity for nucleic acid, facilitating the *in situ* imaging of nuclei in living cells .[136]

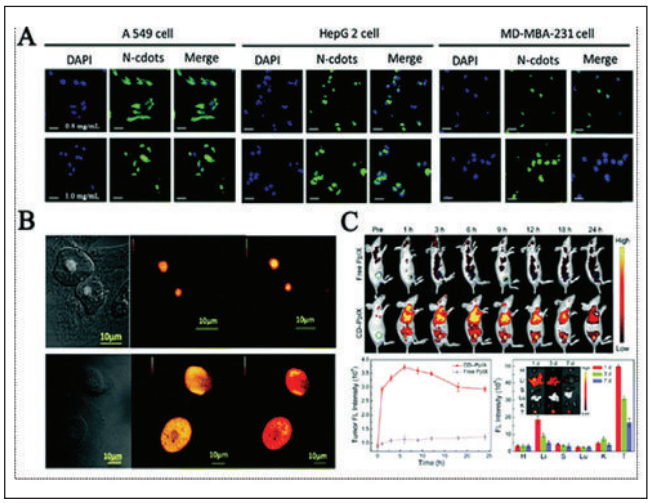


Fig. 7 : (A) Fluorescence images of A549, HepG 2 and MD-MBA-231 cells after incubation with medium containing different concentrations of the N-CDs for 12 h. [114] (B) RNase digestion results confirmed that the carbon dots mainly bind to RNA in the nucleolus, in which CDs localized specifically in the nucleolus (a) and after digestion with RNase enzyme CDs localized all over the nucleus of native HeLa cells (b).[135] (C) Fluorescence images *in vivo*, quantitative fluorescence analysis of the tumors after intravenous injection, and bio-distribution of CD-PpIX in tumor-bearing mice for different time periods in key tissues and tumor of the mice. [138]

Furthermore, nucleus-targeting CDs could be exploited to facilitate drug transportation or mediate gene transfection. Yang *et al.* employed functionalized CDs with a nuclear localization signal peptide to transport doxorubicin (DOX-CDs) into cancer cells. Cell imaging results confirmed that DOX-CDs were mainly located in the nucleus and could efficiently cause apoptosis in human lung adenocarcinoma A549 cells.[137] These results firstly demonstrated the potential applications of CDs in gene-target delivery.

The *in vivo* studies showed that these CDs possessed a negatively charged surface. Conjugating with protoporphyrin IX (PpIX) enabled the CDs to obtain tumor-targeting ability. Therefore, applying such CDs in cancer therapy can result in effective tumor ablation with little toxicity effects after laser irradiation, as shown in **(Fig. 7C).**[138]

As a summary of this section, a CD-based nanoplatform for nucleus imaging is very important for real-time live-cell tracking and drug delivery. The fast uptake and nuclear entry mechanism of CDs could be attributed to their small size and good biocompatibility. However, the reason behind the ability of multifunctional CDs to avoid lysosomal/endosomal entrapment and selectively target nucleus is not clear.

Imaging of other organelles - Although the fluorescence imaging technique for monitoring cellular biological processes has become more and more mature, further efforts should be made towards subcellular imaging and organelle analysis for long-term tracking of the changes in cell morphology and cell function. These studies will be conducive to further understanding the direct relationship between organelles and major diseases.

As one of the vital subcellular organelles, mitochondria is the powerhouse producing ATP and metabolic center in cells. The dysfunction of mitochondria is responsible for many diseases including inflammation, neurodegenerative diseases, diabetes and cardiac dysfunction.[139-141] CDs that have great cellular permeability, photostability, great water solubility and long tracking time have been reported as new mitochondrial-imaging probes in many investigated cell lines.[115,142] Du *et al.* fabricated multifunctional FL nanoprobes based on mitochondria-targeting ligand-linked CDs for imaging the mitochondrial H_2O_2 in Raw 264.7 cells.[143] Then, in order to reduce the cost and improve the photostability, Hua *et al.* ingeniously prepared intrinsic mitochondria targeting CDs without any further modifications of mitochondrial tropic ligands.[115] As depicted in (**Fig. 8A)**, the as-produced CDs could quickly penetrate cells and specifically anchor on mitochondria *via* temperature-dependent transport and caveolae-mediated endocytosis, which provided great promise in mitochondrial imaging and mitochondria-targeted photodynamic cancer therapy. Wu *et al.* developed a fluorescent CDs based mitochondria-targetable nanoprobe (CDs-TPP) for FL imaging of peroxynitrite in mitochondria.[142] The image staining with both nanoprobe and Mito-tracker showed that CDs-TPP had excellent mitochondria-targeting ability and great imaging contrast in MCF-7 cells **(Fig. 8B)**.

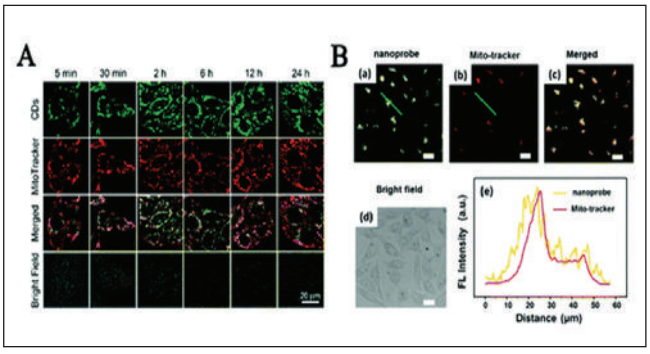


Fig. 8 : (A) Co-localization of CDs and mitochondria for MCF-7 cells. [115] (B) Confocal images of MCF-7 cells co-stained with both CDs and Mito-tracker, and the fluorescence intensity profile of the linear region of interest across a selected single cell.[142] Fluorescence images about CD co-location with lysosome probes

These potential applications for *in vitro* imaging reflect that CDs are highly promising to open new opportunities in biomedical applications, serving as competent nanocarriers for fabricating drug delivery systems to cancer cells and organelle-targetable nanoprobes. However, current CD-based probes still have drawbacks in some respects and much more efforts should be made in the development of multifunctional CDs with better properties, such as excellent targeting capability, easy surface functionalization, non-cytotoxicity, high quantum yield and high fluorescence stability for *in vitro* imaging.

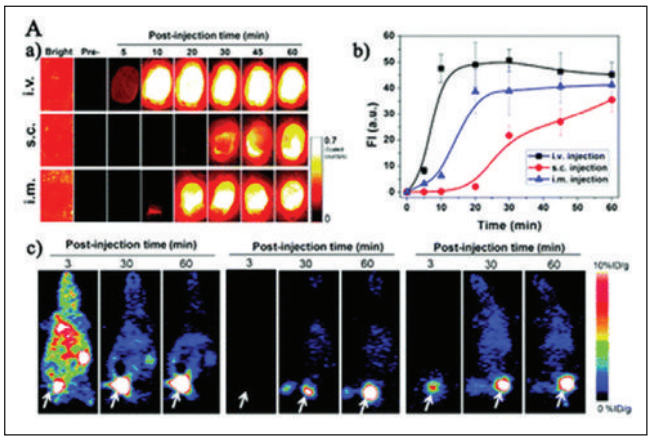
In vivo biomedical applications

On basis of *in vitro* studies, lots of endeavours have contributed to *in vivo* biomedical applications based on FL CDs for future clinical diagnosis and treatment in recent years.[143-145] Yang *et al.*, for the first time, reported the *in vivo* imaging of CDs by adopting three injection avenues in mice. [146] Subsequently, more and more studies have been carefully performed to explore the *in vivo* application of CDs by animal models.

Biodistribution and uptake of CDs in mice and zebrafish- CDs play a vital role in current biomedical research, they may possess chronic toxicity, low stability, and potential undesired accumulation in organs/tissues. So, CDs' biodistribution and uptake *in vivo* must be evaluated. Tao *et al.* for the first time performed a systematic investigation of the performance of near infrared (NIR) FL CDs under *in vivo* conditions and analyzed the bio-distribution of

CDs in mice using a radio labelling method. The results showed that the CDs first heavily accumulated in the reticuloendothelial system and kidneys, and then they were gradually cleared *via* renal and fecal pathways with low toxic effects in mice.[147]

According to the study of Huang *et al.*, the CDs could be quickly excreted from the body after three different injection routes in mice, and its clearance rate was ranked as intravenous (tail vein) > intramuscular (muscle of left leg) > subcutaneous (under the skin of left leg),[148] as shown in (**Fig. 9A)**. In addition, as indicated in (**Fig. 9B),** Wang and co-workers observed that the polymer-coated nitrogen-doped CDs were accumulated within the glioma based on the enhanced permeability and retention effect (EPR), and then mainly administrated to the brain, liver and kidneys after 90 min post-injection for *in vivo* glioma targeting FL imaging. [149] After being injected into mice, the CDs were mainly taken up by the cells in the bladder and tumor, while the liver cells showed negligible uptake of CDs.



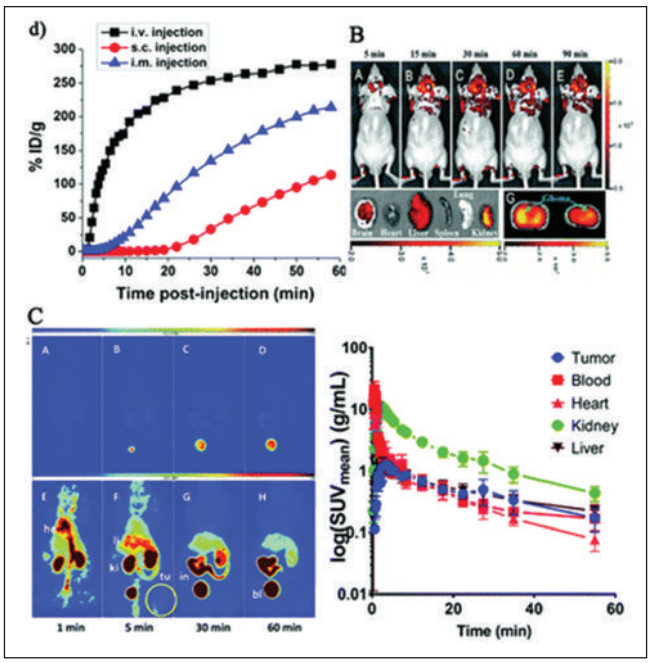


Fig. 9 : (A) Representative imaging of ^{64}Cu-CDs after injection through three routes in mice (intravenous injection, subcutaneous injection, intramuscular injection [148]. (B) *In vivo* imaging of glioma-bearing mice intravenously administered with the pN-CDs at various time points post-injection and after pN-CD administration for 90 min (F) [149]. (C) Maximum intensity projections obtained from a PET study after a single intravenous injection of [^{64}Cu] Cu-NOTA-CDs in A431 tumor-bearing mice. [150]

Recently, Nadia *et al.* investigated the biodistribution and uptake of CDs in rats and tumor mice through radioelement labelling and dynamic experiments of positron emission tomography, which showed a rapid renal clearance of CDs from the *in vivo* systems. But the biodistribution and pharmacokinetic properties of CDs are strongly affected by the surface charge, positive zeta potentials and hydrophilicity of the CDs, [150] which were significantly accumulated in the liver and intestine. **(Fig. 9C)**

Red fluorescence imaging-guided cancer theranostics - As we all know, biocompatible CDs possess great potential as a nanoplatform for clinical biomedical

applications, especially in 1optical cancer theranostics. Moreover, the spontaneous FL emission of biological molecules and the background light scattering of biological samples in the short-wavelength region strongly interfere with the excitation and emission of CDs in both near-infrared (NIR-I and NIR-II) windows, and therefore, providing deeper FL penetration into the tissue sample and achieving the efficient imaging contrast still remain a great challenge.[147,151] Ge and co-workers first developed novel red-emissive CDs with a strong photoacoustic response and high photothermal conversion efficiency ($\eta \approx 38.5\%$). These CDs were used for living mice imaging through intravenous injection. [152] The results showed that the CDs exhibited the enhanced permeability and retention (EPR) effect and accumulated in the HeLa tumor area. A significant FL signal was observed in the tumor area in comparison with other tissues after being treated with intravenous injections of CDs in tumor-bearing nude mice. Soon after, Ge *et al.* prepared red emitting CDs by utilizing polythiophene benzoic acid as the carbon source. [153] The synthesized CDs emitted bright FL in the red region and possessed dual photodynamic and photothermal effects with singlet oxygen ($^1O_2$) generation and high photothermal conversion efficiency under 635 nm laser irradiation. As shown in **(Fig. 10A),** these unique characteristics made CDs a red-light-triggered theranostic agent for imaging-guided photodynamic–photothermal combination therapy within the therapeutic window (600–1000 nm).Alternatively, doping of nitrogen atoms into CDs is propitious to obtain the red-shifted PL emission which is due to the electron-doping effect of the doped graphitic nitrogen atoms. [154,155]

Zheng *et al.* prepared new NIR CDs (CyCD) from a hydrophobic cyanine dye and poly (ethylene glycol) *via* a solvothermal process, which showed preferential uptake of tumor cells and high photo thermal conversion efficiency.[156] The results demonstrated that the CyCD was an outstanding candidate for efficient NIR FL cancer imaging and therapy *in vivo* as shown in **(Fig. 10B).**

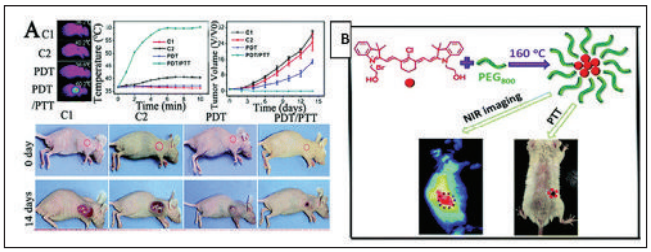


Fig. 10 : (A) Photothermal imaging and treatment effects of PDT/PTT in HeLa bearing tumor mice after being injected with CDs *via* the tail vein (154). (B) Synthesis of new CDs with intrinsic theranostic abilities, imaging in model mouse bearing tumors after the intravenous injection of CDs and the tumor-bearing mouse after PTT .[152]

Imaging probes to brain tissues and tumors - Delivering fluorescent probes to brain tumors and normal nerve terminals presents one of the most challenging issues in neuroscience applications due to the blocking effect of the blood brain barrier (BBB). BBB penetration of CDs strongly depends on their small particle sizes and hydrophilic surface properties, which extend the circulation time and promote passive targeting *via* enhancing the permeability and retention effect. [157,158]

In vivo imaging showed that high-contrast biodistribution fluorescent signals of the Asp-functional CDs were detected in the glioma mass 20 min after tail vein injection **(Fig. 11A),** indicating that the ability of these CDs to freely penetrate the BBB and accurately target the glioma site rather than normal brain tissues (the hippocampus and cortical layer 24 h after injection) **(Fig. 11B)**. Therefore, Asp-modified

CDs as a FL probe had the guided targeting potential for diagnosis of glioma, one of the important intracranial primary tumors.

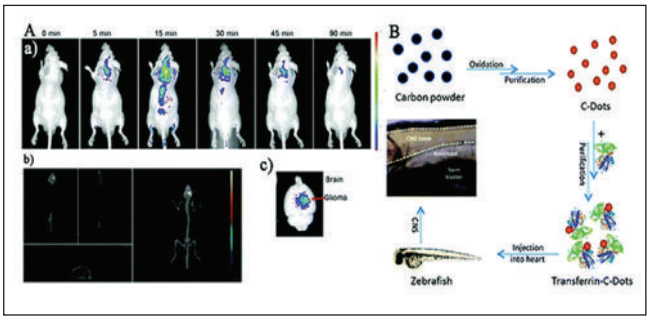


Fig. 11 : (A) The imaging of glioma-bearing mice after tail intravenous injection of CDs-Asp at different times and the CDs-Asp distribution in the brain 20 min after injection. (B) Distribution of CDs-Asp in glioma, hippocampus and cortical layer 24 h after injection as the green fluorescence.[158]

Borisova *et al.* analyzed the neuroactive effects of fluorescent CDs on the key characteristics of both GABA (glutamate and γ-aminobutyric acid) and glutamatergic neurotransmission in isolated rat brain nerve terminals.[159] The results indicated that CDs in a dose-dependent manner decreased exocytotic release of [^{3}H] GABA and L-[^{14}C] glutamate, attenuated the initial velocity of Na^+-dependent transporter-mediated uptake of [^{3}H] GABA and L-[^{14}C] glutamate, and increased the neurotransmitter ambient level of nerve terminals. The combination of the fluorescent and neuromodulatory features of CDs enables their potential usage in probing and visualization of key processes in nerve terminals and related neurological processes in theranostics.

Drug Delivery - Recent advances in nanomedicine have resulted in drug delivery systems that are capable of targeting and delivery of the drug to the specific parts of the body. The drug delivery systems are sometimes conjugated with fluorescent nanomaterials for imaging. The QDs with small sizes, various surface chemistry, and at the same time fluorescence properties have been used in therapeutic applications as an effective drug delivery vehicle. The nanovehicle localization can be done in vitro or in vivo using methods such as high-performance liquid chromatography (HPLC) and by the aid of fluorescence emission properties of some of the drugs which are time consuming methods. [160] QDs have been used for developing numerous drug delivery systems in recent years. [161,162] The CQDs which are mainly composed of C, N, O and H atoms are excellent candidates for drug delivery systems as well. The DOX is one of the most used model anticancer drugs in drug delivery systems. The DOX has also been loaded on CQDs for drug delivery. The possible mechanism for DOX loading on the CQDs is functional groups that make bonding between the CQDs and DOX. On the other hand, the electrostatic interaction between positively-charged DOX and negatively-charged CQDs as well as hydrophilicity of the CQDs which promotes hydrogen bonding between DOX and CQDs are the main proposed mechanisms for observed enhanced drug loading on the CQDs. [163]

Different steps of the drug delivery of CQDs-DOX include a) CQDs-DOX entry into the cells (through endocytosis) and forming vesicles, b) transporting CQDs-DOX vesicles into the lysosomes and c) release of the protonated DOX (in lysosomes acidic environment) and entry into the cell nuclei.[164] The application of CQDs in drug delivery systems could result in a more localized drug-loaded CQDs in tumor cells compared to the using drug alone. CQDs that were synthesized hydrothermally from milk were used for DOX delivery to cancer cells. It was observed that DOX-loaded CQDs were more toxic to the adenoid cystic carcinoma cell line (ACC-2) compared to the mouse fibroblast cell line (L929).[165]

The CQDs used in DDSs can become magnetic to be used for magnetic resonance imaging (MRI) while having the benefit of drug delivery and fluorescence imaging. The MRI combined with fluorescence imaging would have the benefit of superior tissue penetration and spatial resolution of MRI and easy microscopic tissue examination of the fluorescent imaging. [166]

The CQDs have been used in multifunctional platforms for drug delivery and magnetic delivery and/or MRI agents and/or simultaneous co-delivery of two or more drugs, including multi-functional DDS of CQDs and DOX and heparin as an auxiliary medicine for delivery to the A549 cells. [167] The CQDs have also been used for drug delivery in other researches, including passivated CQDs with polyamine containing organosilane molecules for delivery of DOX. [168]

Gene Delivery - Gene therapy which has received considerable attention in biotechnological and medical fields is based on the correction of the origin of diseases through delivery and expression of exogenous DNA encoding for the missing or defective gene product. Therefore, a key factor for gene therapy is the application of proper gene vectors. [169] The different kinds of nanoparticles [170,171] and QDs [172] have been used for gene delivery. The CQDs could also be used as a platform for gene delivery due to their biocompatibility, low toxicity, strong fluorescence emission, broad excitation spectra, and stable PL. It is shown that the CQDs have a superior capacity to condense plasmid DNA with excellent transfection efficiency. The CQDs have been used as a gene vector for chondrogenesis from fibroblasts. By application of CQDs, the plasmid SOX9 could be condensed to form nanoparticles in the range of 10–30 nm. The formed nanoparticles have excellent properties such as high solubility, low cytotoxicity and fluorescence emission. [169]

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ORIGINAL ARTICLE

DIAGNOSING A BREAST MALIGNANCY IN FEMALE IN A TERTIARY CARE CENTRE : A PROSPECTIVE STUDY

Chandrakala Singh Rajput*, *Basavraj Kadalage**, Rekha Khyalappa****

ABSTRACT

Introduction- With changing lifestyle, dietary pattern there is a surge in the breast malignancy. Breast lumps are one of the most common health problems women confront. These tumours are common in younger to middle-aged women and for a variety of reasons, they frequently go undetected. The stigma around it causes females to hide their complaints. There are numerous etiologic causes for these tumours, which may be benign or malignant. Breast cancer is the most common type of cancer and the second leading cause of cancer-related deaths in women, second only to lung cancer in Asian and black women, while it is the leading cause of death in Hispanic women. A prompt diagnosis and early treatment can improving survival rates. **Methodology-** 60 female patients who presenting to the outpatient and inpatient departments of the Department of General Surgery, at tertiary care hospital, with complaints of a palpable breast tumour were included in the study. A detailed history and thorough clinical examination done in all cases. The physical examination of the bilateral breasts with bilateral axillae is done followed by USG guided Core Needle Biopsy. **Result-** In our study, we evaluated the diagnostic accuracy and predictability of the modified triple test for palpable breast lump. Of all the three components Clinical examination, Core Needle Biopsy (CNB) and Ultrasonography (USG) had 100% specificity,100% sensitivity, 100%positive predictive value and 100% negative predictive value in diagnosing malignancy. **Conclusion-** Modified triple test is very accurate, reproducible, cost effective method in diagnosing the breast lumps in a tertiary care centre.

Keywords : Breast, tumour, Core Needle Biopsy cancer, disease, females.

INTRODUCTION

In the current world people are now more aware about their health. With increasing education and improving financial conditions of young females, they are willing to invest in their health. Young female with breast swelling constitute a major share of input at any surgical Out-patient department (OPD). A female can present with a variety of symptoms such as breast soreness, nipple discharge, cystic lesions, and, more typically, a lump. Not to our surprise majority of them are benign, but there always a possibility of malignancy. In any sort of breast lump, diligent and meticulous investigation, arriving at a precise diagnosis, and timely treatment are required. Until recently, most people thought that any lump or tumour in the breast should be taken out and looked at under a microscope to be sure of what it was. This was because a preoperative clinical assessment alone

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was not clear enough. Most of the time, breast disease shows up as a lump in the mammary gland that doesn't hurt, a discharge or erosion of the nipple, puckering or pulling back of the skin around the breast, or swelling in the armpit. It always had been challenge for the treating surgeon to make clinically a provisional diagnosis of a lump in the breast. One has to use all the arrows in his quiver to arrive at conclusion viz. thorough and detailed clinical examination[1], breast imaging (mammography, thermography, ultrasonogram[2-5] and tissue or cytology based test (Fine Needle Aspiration cytology(FNAC), Core Needle Biopsy (CNB) or excision biopsy).[6-10] When these test are used individually the results or the diagnostic yield was not that promising. These dismal results of solitary test lead to combining the various test systematically. At the moment, a combination of tests is used to screen people with lumps in their breasts for early signs of a cancerous condition. This combination improves both sensitivity and specificity, which cuts down on time and money spent diagnosing and makes patients more likely to follow instructions.

"Triple Test" which comprises of three individual tests physical examination, mammography and Fine Needle Aspiration cytology(FNAC) [7-10] has now become the gold standard for judging breast lumps. "Modified Triple Test" is the modification of triple test which a combination of physical examination, ultrasonography (in place of mammography) and core needle biopsy in place of Fine Needle Aspiration cytology(FNAC).[10-13] With the development of Triple assessment, surgeons now have a diagnostic technique that is conveniently accessible, cost effective, minimally invasive, quick, and patient friendly. This proved to be a watershed moment in the detection of a breast lump. With the development of mammography, surgeons were eventually able to use a radiological tool to make a reasonable pre-operative diagnostic of the breast. However, the emergence of fine needle aspiration cytology (Fine Needle Aspiration cytology) changed the game. The combination of physical examination, mammography, and Fine Needle Aspiration cytology (FNAC) began to be referred to as the "triple test" for the evaluation of breast masses and has since become the gold standard for such evaluations. The Modified triple assessment is used to diagnose breast cancer in patients who have symptoms that could be caused by the disease, according to National Institute for Health and Clinical Excellence (NICE) guidelines. The "Modified Triple Test" refers to the combination of physical examination, sono-mammography, and Core Needle Biopsy (CNB).[8-10.]

The purpose of this study is to investigate the method used in establishing the diagnosis of breast malignancy. We evaluated the role of modified triple assessment in the diagnosis of breast lumps, as well as the sensitivity and specificity of modified triple assessment in terms of histology. Also, to provide an easily available, cost effective, least invasive, rapid and patient compliant diagnostic tool for breast lump along with the study of the effectiveness of the test to differentiate benign lesion from malignant breast lesion.

MATERIALS AND METHODS

This prospective observational study was conducted at Tertiary care hospital after all the necessary ethical permissions were taken from the Institutional Ethics Committee. The time period of the study was from 2020 to 2022. This study included 60 patients who presented to the outpatient and inpatient departments of the respective hospital, with complaints of a palpable breast tumour. Written informed consent was taken from the patients. Female patients with palpable Breast

lump were included in the study, whereas Patients who refuse lump excision/biopsy/Fine Needle Aspiration cytology(FNAC), who had previously irradiated breast and lactating mothers were excluded from the study. A detailed history and thorough clinical examination done in all cases. The physical examination of the breast is separated into three parts: inspection, palpation, and lymph node examination. During the breast examination, look for any asymmetry findings, particularly, misalignments in the overall contour of the breast, skin colour changes - Dimpling / retractions of the skin, nipple discharge on its own. While the patient is sitting upright, examine the breasts first. Ask the patient to gently place her hands on her thighs to relax both upper extremities. Some motions can be performed to tension the skin covering the breasts, making it easier to notice anomalies, particularly the presence of dimpling or skin retractions. In the first manoeuvre, instruct the patient to raise both arms over the head and hold this position for a few seconds before proceeding with the inspection. In the second movement, have the patient press both hands firmly against their hips. Continue to monitor any irregularities in the breasts that may become more visible as a result of this manoeuvre.[14,15] Breast palpation begins with the patient sitting straight on the examination table. This is the identical posture that was used throughout the examination. On the patient's lap, both hands are relaxed. The patient should then lie supine on the examination table with both hands behind his or her head, and the palpation should be repeated on both sides. In this posture, the examiner can press any lesions against the chest wall, making it simpler to discover anomalies that could have gone undetected in the upright position. For the same reason, it makes it easier to examine the nipple area for nodules and discharges. When palpating the breasts, it is critical to look for the following characteristics of any discovered masses.

Shape : most benign lesions, such as a cyst or fibroadenoma, have extremely uniform boundaries, but malignant nodules are usually invariably irregular in shape.

Consistency : A lump that feels rock hard or otherwise very stiff is most likely cancerous, whereas a rubbery or elastic consistency is most likely benign.

Skin attachment : a lesion that is very attached to the skin is frequently malignant. o Changes over time: fast changes in a lesion over weeks to months boost the possibility of cancer.

Tenderness : Cancerous nodules are typically non-tender, whereas benign lesions are frequently especially painful. A benign lump that fluctuates in tenderness during the menstrual period.

After a complete clinical breast examination, the patient receives an ultrasound evaluation. A linear 12.5 MHz-17.5 MHz transducer is ideal for research. After a thorough evaluation, bilateral breast USG is performed11.

Methods and equipment for Core Needle biopsy [8-11]

Preparation of biopsies using Ultrasonography equipment. The ultrasonography equipment should have a high-frequency, linear array transducer (7.5 MHz or higher). It was recently recommended that utilizing a high-frequency, appropriately focused 10- to 12-MHz transducer increases breast lesion resolution and contrast.[10] Following sonographic discovery of a breast lesion in the supine position with the ipsilateral arm lifted above the head, the breast must be washed with antiseptic soap and local analgesia administered

as part of the cutting-edge biopsy preparation. Various types of needles such as Automated large-core needle biopsy (LCNB), Directional vacuum-assisted biopsy device (VAB) are used to get accurate and reliable results.

Fig. 1 : steps of USG guided Core Needle Biopsy

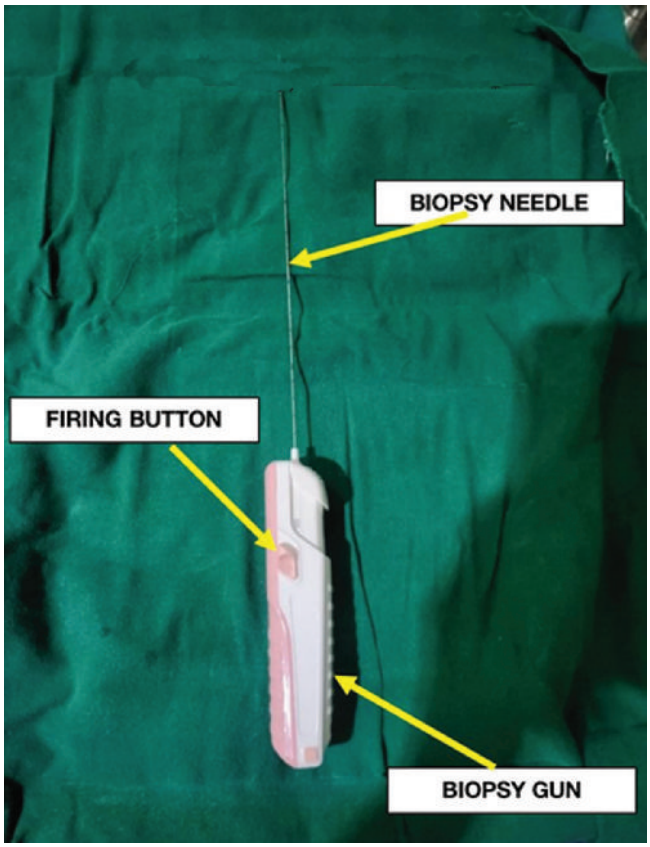

Fig. 2 : Core Needle Biopsy Gun

RESULTS

The study comprised 60 female patients after applying inclusion and exclusion criteria.

AGE DISTRIBUTION

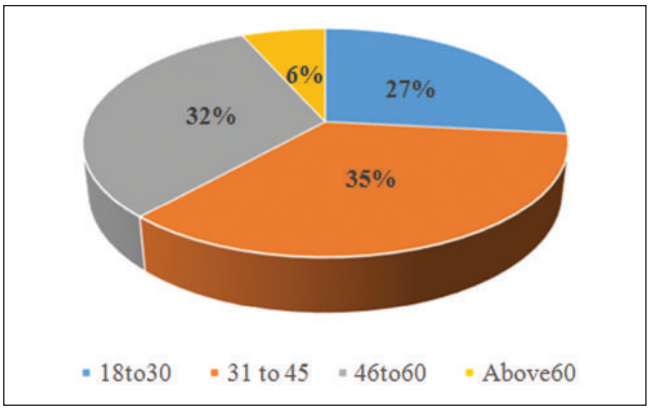

Fig. 3 : Age Group (in Year)

Out of the 60 patients, 16 were between the ages of 18 and 30 (27%), 21 were between the ages of 31 and 45 (35%), 19 were between the ages of 46 and 60 (32%), and patients were over the age of 60 (6%).

1. SYMPTOMS DURATION

Symptoms Duration (in Months)	No. of patients	Percentage
0 to 6	39	65%
7 to 12	16	27%
13 to 18	4	7%
19 to 24	1	1%
Total	60	100%

The majority of the patients 39 patients (65%) had symptoms for 0 to 6 months, 16 patients (16%) had symptoms for 7 to 12 months, patients (65%) had symptoms for 0 to 6 months, 4 patients (7%) had symptoms for 13 to 18 months, and only 1 patient (1%) had symptoms for 19 to 24 months.

2. PAIN OVER LUMP

Pain over lump	Benign	Malignant	Grand Total	Chi Square Value	P Value
Painful	34 (77.27%)	12(75%)	46(76.67%)	0.034	0.85
Painless	10 (22.73%)	4(25%)	14(23.33%)		
Total	44 (100%)	16(100%)	60(100%)		

P-Value = 0.85 (> 0.05)

46 of the 60 patients felt pain over the lump, and 12 of them (75%) were confirmed to have malignant disease. Four patients out of 14 (23.33%) had painless lumps.

There is no correlation between Pain over lump and Histopathology report (HPR).

1. NIPPLE DISCHARGE

Nipple Discharge	Benign	Malignant	Total	Chi Square Value	P Value
Absent	44 (100%)	14 (87.5%)	58 (96.67%)	5.69	0.02
Present	0 (0%)	2 (12.5%)	2 (3.33%)		
Total	44 (100%)	16 (100%)	60 (100%)		

P-Value = 0.02 (< 0.05)

Two patients out of a total of 60 presented with nipple discharge (3.33%), and two of them were discovered to have malignancy (3.33%).

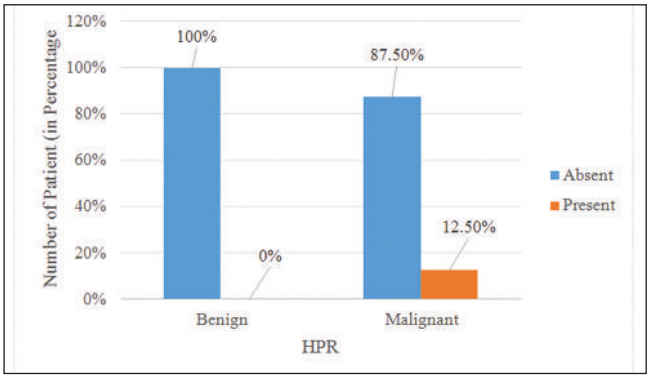

Fig. 4 : Nipple Discharge

Nipple Discharge and Histopathology report (HPR) have a substantial relationship.

2. QUADRANT INVOLVEMENT

Quadrat involvement	Benign	Malignant	Grand Total	Chi Square Value	P Value
LI	3(7%)	1(6.25%)	4(7%)	3.69	0.3
LO	11(25%)	3(18.75%)	14(23%)		
UI	14(32%)	2(12.50%)	16(27%)		
UO	16(36%)	10(62.50%)	26(43%)		
Grand Total	44(100%)	15(100%)	60(100%)		

P Value = 0.00 (< 0.05)

Out of the 60 patients, most commonly involved quadrant is upper outer 26(43%) and least commonly involved quadrant is lower inner 4(7%).

Quadrat involvement and Histopathology report (HPR) have a substantial relationship.

3. AXILLARY LYMPH NODE INVOLVEMENT

Axillary lymph Node involvement	Benign	Malignant	Total	Chi Square Value	P Value
No	44(100%)	10(62.5%)	54(90%)	18.33	0.00*
Yes	0 (0%)	6(37.5%)	6(10%)		
Total	44(100%)	16(100%)	60(100%)		

P Value = 0.00 (< 0.05)

Patients Six patients out of a total of 60 (ten percent) were determined to have malignancy (37.5 percent).

Axillary node involvement is associated with Histopathology report (HPR).

4. INCIDENCE OF BENIGN DISEASE

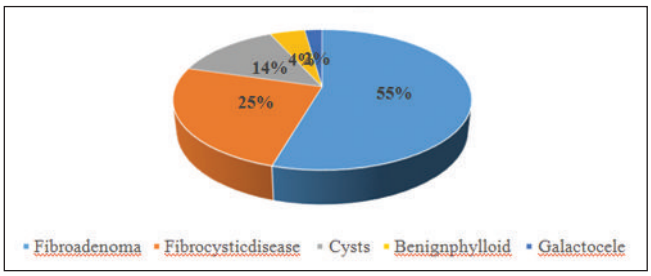

Fig. 5 : Incidence of Benign Disease

44 of 60 individuals had benign breast disease. Twenty-four patients had Fibroadenoma, eleven patients had Fibrocystic disease, six patients had Cysts, two patients had Benign phylloid, one patients had Galactocele.

5. INCIDENCE OF MALIGNANT DISEASE

Disease	No. of patients
Invasive ductal carcinoma	6 (37.5%)
Malignant phylloid	2 (12.5%)
Ductal carcinoma insitu	3 (18.75%)
Lobular carcinoma insitu	2 (12.5 %)
Invasive papillary carcinoma	2 (12.5 %)
Inflammatory breast cancer	1 (6.25 %)
Total	**16 (26.67%)**

16 of 60 individuals had biopsy-proven malignancy. Six patients had Invasive ductal carcinoma, two patients had malignant phylloid, three patients had ductal carcinoma in situ, two patients had lobular carcinoma in situ, two patients had invasive papillary neoplasm, two patients had invasive lobular carcinoma and one patient had inflammatory cancer of the breast.

6. SURGICAL METHOD

Excision biopsy, Breast conservation surgery (BCS), or Modified Radical Mastectomy were all performed on all 60 individuals in the study (MRM). Excision biopsy was performed on 44 individuals. Four patients were treated with BCS because they were eligible. Modified Radical Mastectomy was performed on 12 individuals.

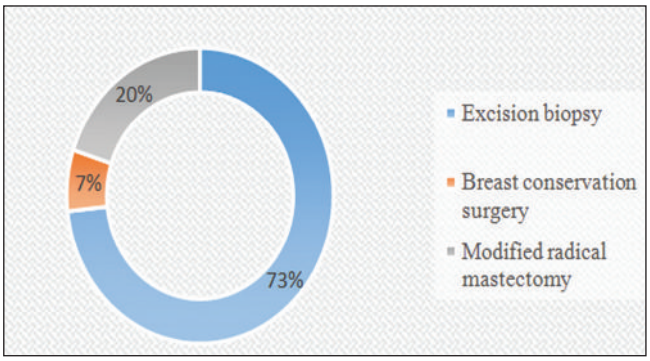

Fig. 6 : Type of Surgery

7. Sensitivity and Specificity of Clinical Examination as compared with Histopathology report (HPR)

		Histopathology report (HPR)		
		Malignant	Benign	Total
Clinical examination	Malignant	10	0	10
	Benign	6	44	50
	Total	16	44	60

P-Value = 0.00 (< 0.05). There is significant association between Clinical examination and Histopathology report (HPR)

8. Sensitivity and Specificity of Ultrasonography (USG) as compared with Histopathology report (HPR)

Sensitivity - 68.75 % Specificity -100 %

Positive Predictive Value (positive predictive value (PPV)) - 100 % Negative Predictive Value (negative predictive value (NPV)) -89.80 %

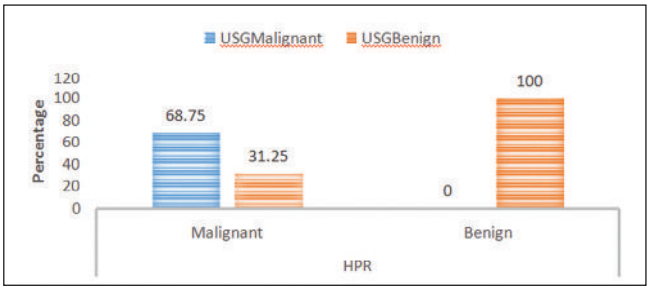

Fig. 7 : Results of USG Against HPR

P-Value = 0.00 {< 0.05} There is significant association between Ultra-sonography (Ultrasonography (USG)) test and Histopathology report (Histopathology report (HPR)

9. Sensitivity and specificity of Core Needle biopsy as compared with Histopathology report (HPR)

		Histopathology report (HPR)		
		Malignant	Benign	Total
Core needle biopsy	Malignant	14	0	14
	Benign	2	44	46
	Total	16	44	60

P-Value = 0.00 (< 0.05)

There is significant association between Core needle biopsy test and Histopathology report (HPR)

10. Combined Result of Modified triple test (Clinical Examination, Ultrasonography and Core Needle biopsy)

Modality	Clinical	Ultrasonography (USG)	Core needle Biopsy	MTT
Sensitivity (%)	62.5	68.75	87.5	100
Specificity (%)	100	100	100	100
positive predictive value (PPV) (%)	100	100	100	100
negative predictive value (NPV) (%)	88	89.8	95.65	100

DISCUSSION

Our study is evaluating the modified triple test, which is currently extensively used for early and quick identification of breast cancer[14,15]. The modified triple test aims to make a fairly good pre-operative diagnosis of a breast lump, hence preventing procedures on benign breast lumps.

In our study, we are evaluating the modified triple test's efficiency as isolated test viz. Clinical breast examination, ultra-sonogram of breast and Fine Needle Aspiration cytology (FNAC) and as a combination of these three components for detection of breast malignancy. Final definitive histopathological examination of the breast lump was used as reference for comparison. **Gobbler et al** concluded that if the 3 components of the triple test were concordant, the combined evaluation of all three had a diagnostic accuracy of 100%, whereas in the case of discordant results, the diagnostic accuracy dropped to 75%. He came to the conclusion that a preceding surgical biopsy and frozen section may not be required when triple tests conclusively confirm cancer.[16] In a systemic review of about fifteen studies of triple test as main diagnostic tool for palpable lump in the breast, a conclusion was derived that, when all the three components are taken together it is consistently more sensitive as compared to the single test or component. Accuracy of diagnosing malignancy is about 95-100% when at least one of the three components is positive. When all the three tests of the triple test are concordant, whether negative or positive, the diagnosis is almost 99% accurate. In 55 young females with palpable breast tumours, Vetto et al. utilised a modified triple test to detect the lesion. He discovered that the modified triple test had a rather good diagnostic accuracy for detecting and distinguishing cancers. According to his assessment, the modified triple test is a cost-effective way to avoid unnecessary surgery. We would like to discuss the result of our study in the light of these above information. Our is a prospective study and 60 patients included in the study.[17] Breast lumps were most common between the ages of 18 and 60 in our study, and they were least common after the age of 60, which is consistent with other studies. Younger females with higher educational position and knowledge are more likely to present early

in the disease's progression.

One of the presenting symptom was pain over the lump and almost 25% of patients with painless lumps turned to be malignant on HPE. in contrast to 75% painful lumps. Kaire Innos et al (BMC public health 2013) also published similar results and the common presentation of malignancy being painless lump.[18] 77 In our clinical examination discharge from nipple was a significant finding. Among the patients with discharge 12.5% turned out to be malignant on definitive histopathological results. We can imply that a nipple discharge can be an important clue in the diagnosis of malignancy, but it had been usually benign and less than 10-15% tend to be malignant as shown by Van Zee K J et al. [19]A bigger cohort with a larger study group may probably correct the skewed result in our study. Upper outer quadrant was the commonly involved location in our study Khemka et al, hussain.et al, and Khoda et al also presented similar results in their individual studies. As there is more amount of epithelial tissue in the outer upper quadrant this leads to be the reason for more lesion in this site.[20] 62.5% of patients with breast lump had involvement of axillary lymph node out of which 37.5% had malignancy proven by biopsy. We can conclude that it a strong predictor of malignancy. Same results had been shown by Voss M et al [21]He concluded that axillary metastasis is more in stage 3 malignancy and there is less and slower incidence of metastasis with well differentiated tumors. Nodal involvement is a strong indicator for advanced or fast growing malignancy which warrant urgent attention.

The clinical examination exhibited a sensitivity of 62.5% and a specificity of 100% in diagnosing breast cancer, according to a comprehensive analysis of the clinical examination data. Positive predictive value was 100% for the clinical examination (positive predictive value (PPV)). We determined that the clinical examination's sensitivity ranges from 21% to 100% and its specificity extends from 50% to 97.8% by comparing our findings to those of previous studies. Only patients with confirmed palpable lumps were included in the analysis, attributing to the high sensitivity of our sample. Our findings align with those of a large number of other studies. Crystal et al., Susan et al, Corsetti et al, and Sahiner et al all have recommended the ultrasonography of breast in young females who have dense breast tissue, and they found 89% sensitivity in diagnosing symptomatic and palpable breast abnormality.[22-25] In our study, 11 of 60 participants exhibited sonographic data suggestive of cancer. Histopathology report (HPR) was positive in 16 of 60 patients. Ultrasonography has a sensitivity of 68.75% and a specificity of 100% in detecting cancer in our investigation. The Positive Predictive Value (positive predictive value (PPV)) for detecting cancer was 100%, while the Negative Predictive Value (negative predictive value (NPV)) for ruling out breast cancer was 89.80%.

When we compared our findings to the available literature, we found a reasonable correlation. Khoda et al [20] 80 patients achieved an Ultrasonography (USG) sensitivity of 91.6% and specificity of 100%, with a 100% positive predictive value and a 97.3% negative predictive value. Pande et al. summarised his results for sensitivity (95%), specificity (94.1%), positive predictive value (95.5%), and negative predictive value (93.7%) in another investigation. [26]

Jan et al. reported comparable findings with a sensitivity of 68.75%, a larger proportion of positive patients are overlooked. [27] So, while diagnosing a benign lump does not always imply that it is benign, a combination of tests is recommended to confirm the diagnosis, but

Ultrasonography (USG) is a very essential and helpful tool for screening and detection of breast malignancy. In our study core needle biopsy classified 46 out of 60(66.6) patients as benign and 14 out of 60(23.4%) as malignant. Out of 14 patients which were reported as malignant on Core Niddle Biopsy (CNB) turned to be positive on Histopathology report (HPR) whereas 2 patients out of 46 reported benign turned out to be malignant on final Histopathology report (HPR). In our investigation, the sensitivity and specificity of core needle biopsy to identify cancer were 87.5% and100%, respectively. Having a Positive Predictive Value (PPV) of 100 percent and a Negative Predictive Value (NPV) of 95.65 percent. The results of our core needle biopsy study are comparable to those of other investigations. HM Verkoijen et al. in his meta-analysis of 5 cohort studies analyzing Sensitivity rate, histological agreement between needle biopsy and subsequent surgery or long-term mammographic follow-up and clinical consequences for different disease prevalence. He reported sensitivity rate of (97%). In his analysis they reported a concordance between the Core Niddle Biopsy (CNB) and later surgical biopsy or long-term mammographic follow-up was also high (94%). He concluded that core needle biopsy is a promising alternative. However, additional research is needed to explore the limiting factors of the technique.[28] Wendy Bruening et al in their study comprising of review of 83 studies comprising of different techniques of core needle biopsy concluded after a detailed analysis of the data from all the studies conducted during the period of 1990 to 2008 that Stereotactic- and ultrasonography-guided core-needle biopsy procedures seem to be almost as accurate as open surgical biopsy, with lower complication rates. They derived the conclusion that irrespective of the technique of Core Needle Biopsy (CNB), the results are promising[29] R Gruber et al. in his review9 studies over a period of Jan 1994 to Dec 2006 comprising of the German speaking countries, evaluated for the cost effectiveness of Core Needle Biopsy (CNB) against open surgical biopsies. He estimated a phenomenal cost reduction of 50-96% when Core Needle Biopsy (CNB) is used in place of Open surgical biopsy. [30] Homesh NA et al in their Prospective RCT with a cohort of 296 patients with breast lumps during the period of May 1998 -- May 2002. The patients were randomized with Fine Needle Aspiration cytology(FNAC) or Core Needle Biopsy (CNB) as diagnostic modality. The results were then compared with the final diagnosis by histopathology. They summarized their result with the Fine Needle Aspiration cytology(FNAC) sensitivity was 66.66%, 81.8% specificity, 75.7% accuracy, positive predictive value (PPV) 100% and negative predictive value (NPV) 90%, while in core needle breast biopsy sensitivity was 92.3%, 94.8% specificity, 93.4% accuracy, positive predictive value (PPV) 100% and negative predictive value (NPV) 100%. The diagnostic accuracy of Core Niddle Biopsy (CNB) was higher than the Fine Needle Aspiration cytology (FNAC), which was statistically significant ($p<0.05$).[31] In our study, 16 individuals (12.5%) tested positive for malignant disease, whereas 44 patients (87.5%) were found to have benign lesion using the modified triple test. All patients who tested positive for malignancy on the modified triple test also tested positive for malignancy on the final Histopathology report (HPR), whereas patients initially labelled as benign turned out to be malignant. In our investigation, the sensitivity, specificity, positive predictive value, and negative predictive value of the modified triple test are each 100%.

COMPARISON OF STUDIES USING MODIFIED TRIPLE TEST

Study	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value%
Our study	100	100	100	100
Baykara et al	100	92.01	53.16	100
Khoda et al	100	100	100	100
Jan et al	100	99.3	93.3	100
Vaithyanathan et al	100	82	76.9	100

This comparison of our results with those of other studies demonstrates that the modified triple test can be used as a very reliable, valuable test for the rapid diagnosis of malignancy, and that the results aid in differentiating benign from malignant lesions, facilitate the initiation of early, accurate surgical treatment, and prevent unnecessary surgeries.

CONCLUSION

In our study, we evaluated the diagnostic accuracy and predictability of the modified triple test for palpable breast masses. After summarizing the results and analyzing the data statistically we would like to conclude that, modified triple test is very accurate, reproducible, cheap method in diagnosing the breast lumps. We can safely conclude that at a tertiary care centre like ours modified triple test is a excellent method of establishing the diagnosis of breast malignancy. Clinical test alone is least sensitive in making the diagnosis of breast malignancy. Ultrasonography (USG) had the highest specificity (100%).Core Needle Biopsy (CNB) is most accurate in sensitivity specificity positive predictive value (PPV) and negative predictive value (NPV) when all the component are taken together. The results of our study are comparable with other studies available in literature. The sample size (N=60) was the limitation of our study.

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ORIGINAL ARTICLE

A STUDY ELECTROPHYSIOLOGICAL AND ECG CHANGES IN ORGANO PHOSPHATE POISONING (OPP) PATIENTS AND CORRELATE FOR PROGNOSTICATION USING THE PERADENIYA SCALE.

Himanshu Rao,* ***Sushma Jotkar*****

ABSTRACT

Background : OPP (organophosphate poisoning) induced delayed polyneuropathy (OPIDP) is a sensory-motor distal axonopathy that usually occurs after the ingestion of large doses of certain OP insecticides. The present research was conducted to study electrophysiological and ECG changes in OPP patients and correlate for Prognostication using the Peradeniya scale. **Material and Methods :** The present Cross-Sectional study was conducted on 40 patients presenting with organophosphate poisoning in the medical ICU under the Dept. of Medicine, tertiary care center. ECG was recorded at the time of admission and after every 12 hrs, till 3 days & findings was noted in the proforma. Nerve conduction velocity (NCV) was conducted on the patients after 24 hrs. Of exposure of poison (and till 72 hrs. if a patient on a ventilator) and findings were noted. **Results :** More than half, 25 (52.5%) patients belong to middle age group 21 to 40 years. Male to female ratio was 4:1. Most common OP consumed was Dimethoate by 12 (30%), Methyl parathion by 10 (25%) patients. Most common ECG abnormality was QTc Prolongation in 24 (60%), Low Voltage in 6 (15%). Sensory neuropathy was observed in 12 (30%), Demyelination in 12 (30%) and 8 (20%) patients were found to have Axonopathy. The majority, 29 (72.5%) had a POP scale 0 to 3 followed by 9 (22.5%) patients had a score 4 to 7. **Conclusion:** Common ECG abnormalities are QTc Prolongation, low voltage, and ST elevation. Sensory neuropathy, Demyelination, and Axonopathy were common. The association of the POP scale with Nerve conduction abnormalities was not significant. The association between a higher POP scale and mortality was statistically significant. The majority of the NC abnormalities were seen in poisoning by Dimethoate and Phosphomidan.

Keywords: Organophosphorus poisoning, POP scale, ECG abnormalities, Nerve Conduction abnormalities

INTRODUCTION

Organophosphorus (OP) insecticides are one of the commonest causes of morbidity and mortality due to poisoning worldwide, especially in developing countries like India due to their easy availability. The morbidity and mortality outcomes depend on the time lag between exposure and the initiation of management. So, it is cardinal to recognize the entire spectrum of the symptoms early and clinically categorize them according to their severity. Hence quick clinical diagnosis and affordable prognostication tool is the need of the hour.

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Organophosphorus compounds have assumed considerable importance in most parts of the world particularly developing countries but also in western countries. [1] Hospital-based statistics suggest that nearly half of the admissions in an emergency with acute poisoning are due to organophosphorus compound poisoning. [2] The toxicity of those compounds and the paucity of appropriate medical facilities lead on to a high fatality rate. These compounds first discovered more than 100 years ago are at present the predominant group of insecticides employed globally for pest control [3]. Organophosphorus compound poisonings are found to be a leading cause of death in agricultural countries globally. [4-5]

Organophosphate-induced delayed polyneuropathy (OPIDP) is an uncommon clinical condition. It occurs in association with the ingestion of large amounts of organophosphate after the stimulation of cholinergic receptors [6] It is characterized by distal degeneration of some axons of both the peripheral and central nervous systems occurring one to four weeks after single or short-term exposures. [7] The prevalence of OPIDP in patients with organophosphate poisoning is nearly 22%**.** [8]

The clinical sequence can be of three types: Type I syndrome (acute poisoning) is characterized by acute cholinergic effects appearing within a day of exposure to opc, often within hours. Cholinergic symptoms include tachycardia or bradycardia, diarrhea, vomiting, fasciculations, sweating, salivation and micturition, which are treatable with atropine.[9] Type II or Intermediate syndrome follows the intense cholinergic crises of organophosphate poisoning and occurs in up to 20 to 50% of cases depending on the severity of poisoning, its duration and the type of organophosphate compound. Their symptoms manifest 24 - 96 hrs after the poisoning on recovery from the cholinergic crises and include muscular weakness, affecting predominantly proximal limb muscles and neck flexors. Unlike delayed polyneuropathy, this syndrome carries a death risk due to respiratory depression. The clinical course may last from 5 to 18 day. [10] Type III syndrome (OPIDP) is induced by many organophosphate esters (ops), may cause a distal dying back axonopathy characterized by cramping muscle pain in the legs, paresthesia and motor shortcoming beginning 10 days to three weeks after the initial exposure. Associated signs include high stepping gait associated with bilateral foot drop, absent ankle jerks, weakness of intrinsic hand muscles and wrist drop. Sensory symptoms may be present but it is predominantly a motor neuropathy. Pyramidal tract involvement may also be present. Diagnosis is based on history of organophosphate poisoning, clinical findings, electromyography, and nerve conduction studies which show typical denervation patterns.

Organophosphate-induced delayed neuropathy (OPIDN) is a sensorymotor distal axonopathy that usually occurs after the ingestion of large doses of certain organophosphate insecticides. Most of the patients developed a mixed polyneuropathy, mainly motor. [11] The neurotoxic effects of organophosphates have been well known since the dramatic outbreak of "Ginger Jake Paralysis", which crippled as many as 50 000 in the USA in the 1930s. [12] Since then several other epidemics have occurred in different regions such as in Sri Lanka. [13]

In this epidemic area, adolescent girls attaining menarche or women right after childbirth were affected and developed polyneuropathy between

fourteen and thirty days after gingili oil ingestion, following local customs and tradition. Recovery from OPIDN is considered to be generally poor. It is possible that several other factors such as the age of the patients, the difference in the chemical structure of the organophosphate, and the duration of initial intoxication in some way contribute towards a favourable outcome. [14]

So, there is a need of easy, quick and reliable parameter to assess the severity of organophosphorus poison on admission for prognostication. In this regard Peradeniya Organophosphorus Poisoning scale can be applied as a relatively easy, bed side and quick method to categorise the patients with OP poison on admission and also a reasonably reliable method to assess the outcome. The present research was conducted to study electrophysiological and ECG changes in OPP patients and correlate for Prognostication using Peradeniya scale.

AIMS AND OBJECTIVES

Aim: To study electrophysiological and ECG changes in OPP patients and correlate for Prognostication using the Peradeniya scale.

Objectives: To determine prognostication of OPP patients using the Peradeniya scale, to study ECG (Q-T interval, ST changes, P-wave changes) changes in acute OPP patients, to study NCV in OPP patients, and to correlate electrophysiological changes & Peradeniya scale in OPP patients.

MATERIAL AND METHODS

Study Area: Dept. of Medicine, a tertiary care center for a duration of 18 months.

Study design: Observational Cross-Sectional Study.
Study setting: ICU Patients of tertiary care center.
Study Subjects: All patients presenting with organophosphate poisoning in the medical ICU are subjects.

Inclusion Criteria: All adult males/females/other genders (> 18 years) with a history of exposure to organophosphorus compound during the study period are included.

Exclusion Criteria:

Patients who received treatment with atropine before admission, mixed poisoning with other substances, known cases of cardiac illness, known cases of long QT syndromes, patients known to be taking drugs recently which are likely to prolong QT interval, patients with other causes of neuropathy, and those who couldn't give consent for study were not be added.

SAMPLE SIZE : 40 Cases

Sample size calculation : The sample size (n) was calculated using the Slovin formula which is as follows. Therefore, **40 cases** of COVID-19 Pneumonia were studied considering significance and error.

METHODOLOGY : The study was started after approval of the Research & Ethics committee. Data collection was done till June 2022.

Method of Collection of Data :

All patients in this study were informed about the procedure and informed valid written consent were taken Detailed history with general physical examination and neurological examination was done

according to proforma. ECG was recorded at the time of admission and after every 12 hrs. till 3 days & findings were noted in the proforma. NCV was conducted on the patients after 24 hrs. Of exposure of poison (and till 72 hrs. if a patient on ventilator) and findings were noted. (Median nerve, ulnar nerve, ant. tibial nerve, common peroneal nerve is included) Basic routine tests like CBC, BSL, Urea Creatinine, Serum Electrolytes, and LFT were done.

STATISTICAL / DATA ANALYSIS

Data was entered into a Microsoft Excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test, and Fisher Exact tests were used as a test of significance for qualitative data continuous data was represented as mean and standard deviation. Unpaired t-test was used as a test of significance to identify the mean difference between two quantitative variables for comparison.

Graphical representation of data: MS Excel and MS Word were used to obtain various types of graphs such as bar diagrams. p-value (Probability that the result is true) of 0.05 was considered as statistically significant after assuming all the rules of statistical tests.

ETHICAL CONCERN :

Written informed valid consent was taken from the patients in English and local language (Marathi) as performed and approved by IEC. Consent for study participation from next of kin was taken for unconscious patients. All patients were given Standard of Care during their participation in the study.

RESULTS

Table 1 : Age group of the patients:

Age group	Frequency	Percent
≤ 20 Years	6	15.0
21 to 40 Years	25	62.5
41 to 60 Years	7	17.5
> 60 years	2	5.0
Total	40	100.0

In the present study, out of 40 patients with organophosphate poisoning, more than half, 25 (52.5%) patients belong to middle age group 21 to 40 years. Mean age was 33.68±11.99 years ranging from 17 to 61 years.

Table 2 : Gender distribution of the patients:

Gender	Frequency	Percent
Male	32	80.0
Female	8	20.0
Total	40	100.0

Out of 40 patients, the majority, 32 (80%) were male and 8 (20%) were females. Male to female ratio was 4:1.

Out of 40 patients, the majority, 9 (22.5%) were farmers, 8 (20%) were housewives, 6 (15%) unemployed. 4 (10%) were labourer and 4 (10%) were student. (Fig. 1)

Table 3 : Comorbidities among patients:

Comorbidities	Frequency	Percent
Hypertension	10	25.0
Diabetes Mellitus	3	7.5
Obesity	3	7.5
IHD	2	5.0
CKD	1	2.5
No Comorbidities	23	57.5

Out of 40 patients, 17 (42.5%) had one or other comorbidities most common being Hypertension 10 (25%), Diabetes Mellitus in 3 (7.5%) and Obesity in 3 (7.5%) patients. 23 (57.5%) patients didn't have any comorbidities.

Out of 40 patients, most common OP consumed was Dimethoate by 12 (30%), Methyl parathion by 10 (25%) patients. 8 (20%) patients consumed Phosphomidan and 4 (10%) patients consumed Fenthion.

Out of 40 patients, 25 (62.5%) patients presented within 6 hours of consumption of chemical agent, 12 (30%) presented between 6 to 12 hours. Late presentation (> 12 hours) was seen in 3 (7.5%) patients. Mean Time between consumption to hospital admission 5.54±3.26 hours

Most common presentation was oral Secretions in 35 (87.5%) and Fasciculations in 22 (55%) patients. Depressed Mental Status 13 (32.5%) and Pin Point Pupils in 6 (15%) patients.

Most common ECG abnormality was QTc Prolongation in 24 (60%), Low Voltage in 6 (15%) and ST elevation in 6 (15%) patients. Inverted T wave and Extrasystole seen in 5 (12.5%) patients each.

Majority, 28 (70%) stayed in hospital for ≤ 5 Days and 10 (25%) stayed for 6 to 10 Days. Only 2 patients stayed for > 2 days. Mean duration of Hospital Stay 4.95±2.94 days.

Half of the patients were found to have one or other Nerve conduction abnormalities.

Sensory neuropathy was observed in 12 (30%), Demyelination in 12 (30%) and 8 (20%) patients were found to have Axonopathy.

33 (82.5%) patients recovered completely and discharged and 7 (17.55%) died during the course of treatment.

Majority, 29 (72.5%) had POP scale 0 to 3 followed by 9 (22.5%) patients had score 4 to 7 and only 2 patients had scale 8 to 11.

Table 4 : Association between Peradeniya (POP) Scale and Nerve conduction abnormalities:

Nerve conduction abnormalities		**Peradeniya Scale**			**Total (n=40)**	**P value**
		0 to 3	**4 to 7**	**8 to 11**		
NC abnormalities	Present	13 (44.8%)	5 (55.6%)	2 (100%)	20 (50%)	0.298
	Absent	16 (55.2%)	4 (45.4%)	0 (0%)	20 (50%)	
Axonopathy	Present	7 (24.14%)	1 (11.1%)	0 (0.0%)	8 (20%)	0.534
	Absent	22 (75.86%)	8 (88.9%)	2 (100%)	32 (80%)	
Demyelination	Present	7 (24.14%)	3 (33.3%)	2 (100%)	12 (30%)	0.075
	Absent	22 (75.86%)	6 (66.7%)	0 (0%)	28 (70%)	
Sensory neuropathy	Present	7 (24.14%)	3 (33.3%)	2 (100%)	12 (30%)	0.075
	Absent	22 (75.86%)	6 (66.7%)	0 (0%)	28 (70%)	
Total		29 (100%)	9 (100%)	2 (100%)	40 (100%)	

Out of 29 patients with POP scale 0 to 3, only 44% had Nerve conduction abnormalities, Axonopathy, Demyelination and Sensory neuropathy was seen in 24.14% patients each. Out of 9 patients with POP scale 4 to 7, only 55.5%% had Nerve conduction abnormalities, 11.1% had Axonopathy, 33.3% had Demyelination and Sensory neuropathy was seen in 33.3% patients. Out of 2 patients with POP scale 8 to 11, both had Nerve conduction abnormalities, Demyelination and Sensory neuropathy but none had Axonopathy.

Association of POP scale with Nerve conduction abnormalities, Axonopathy, Demyelination and Sensory neuropathy was not significant (all p values >0.05).

Table 5 : Peradeniya (POP) scale grade and duration of hospital-stay:

POP Scale Grade	Duration of hospital-stay			Total	Chi-Square & p-value
	≤ 5 Days	6 to 10 Days	> 10 Days		
0 to 3	21 (75%)	6 (60%)	2 (100%)	29 (72.5%)	7.004, 0.136
4 to 7	7 (25%)	2 (20%)	0 (0%)	9 (22.5%)	
8 to 11	0 (0%)	2 (20%)	0 (0%)	2 (5%)	
Total	28 (100%)	10 (100%)	2 (100%)	40 (100%)	

75% of the patients with duration of stay ≤ 5 Days had POP scale 0 to 3. 60% of the patients with duration of stay 6 to 10 Days had POP scale 4 to 7 and both patients with duration of stay >10 Days had POP scale 0 to 3. Association of POP scale and duration of hospital-stay was not significant (p value 0.136).

Table 6: POP Scale Grade and outcome:

POP Scale Grade	Outcome		Total	Chi-Square & p-value
	Death	Discharged		
0 to 3	0 (0%)	29 (87.87%)	29 (72.5%)	24.608, 0.000
4 to 7	5 (71.43%)	4 (12.12%)	9 (22.5%)	
8 to 11	2 (28.57%)	0 (0%)	2 (5%)	
Total	7 (100%)	33 (100%)	40 (100%)	

71.43% of the patients who died Days had POP scale 4 to 7 and 28.57% had 8 to 11. 87.87% of the discharged patients had POP scale 0 to 3. Association of POP scale and mortality was statistically significant (p value <0.05).

Majority of the NC abnormalities were seen in poisoning by Dimethoate (30%) and Phosphomidan (30%) but difference not significant (p value 0.587) Majority of the Axonopathy were seen in poisoning by Dimethoate (25%) and Methyl parathion (25%) but difference not significant (p value 0.223) Majority of the Demyelination were seen in poisoning by Phosphomidan (33.3%) and Dimethoate (25%) and but difference not significant (p value 0.518) Majority of the Sensory neuropathy were seen in poisoning by Phosphomidan (33.3%) and Fenthion and Methyl parathion (16.7% each) but difference not significant (p value 0.124)

Majority of the patients with hospital ≤ 5days had Dimethoate (35.71%) poisoning. Patients who stayed 6 to 10 Days had Phosphomidan (30%) poisoning and out of 2 patients who stayed >10 days one consumed Dichlorofos and one had Dimethoate poisoning. Association of type of agent consumed with duration of stay was statistically significant (p value <0.05).

Above table shows out of 7 deaths, Maximum mortality was seen in Fenthion (50%) followed by Phosphomidan, 37.5% mortality and in Dimethoate 16.7% mortality seen.

DISCUSSION

The present observational cross-sectional research was conducted on ICU Patients of Dept. of Medicine, tertiary care center to study electrophysiological and ECG changes in OPP patients and correlate for Prognostication using Peradeniya scale.

Age group of the patients:

In the present study, out of 40 patients with organophosphate poisoning, more than half, 25 (52.5%) patients belong to middle age group 21 to 40 years. Mean age was 33.68±11.99 years ranging from 17 to 61 years. **Murat Sungur et al.** [62] observed the mean age group of OP exposure was 30±15 years. **Karalliedde L et al.** [63] of documented 91% of their cases were under the age of 30. In Kashmir valley **Malik et al.** [64] revealed that 33.5% of the cases of OP were under the age of 25. In Mangalore, Karnataka, India the most common age group to be affected was 20-30 tears (36.6%) [(65)]. The series reported in this research had the similar pattern of age group affection. The reason could be that this age group, by all probability, is vulnerable to various emotional conflicts that occur during this phase of life. This young age group affected by exposure form the viable entity of any population both in terms of procurement and productivity.

Gender distribution of the patients:

Out of 40 patients, majority, 32 (80%) were male and 8 (20%) were females. Male to female ratio was 4:1. **S. Shivakumar and K Raghavan et al.** [66] of Tamilnadu reported 165 cases of organophosphorus poisoning and sex distribution was similar to the case series (male n=122, female n=45). On the contrary to the series in **Murat Sungur** et al. [62] study of 47 cases of OP in Turkey [(female n=25, male=22)] and **Malik et al.** [64], observation of 122 cases in Kashmir valley [(female n=114, male=50)] female intoxication was more. [64] This variation was due to handling of poison by the respective sex in their respective locality. In Kashmir the female populations are predominantly employed in apple orchards and they are involved in pesticide control. In southern part of India males are actively involved in spraying fertilizers and pesticides.

Occupation of the patients:

Out of 40 patients, majority, 9 (22.5%) were farmers, 8 (20%) were housewife, 6 (15%) unemployed. 4 (10%) were labourer and 4 (10%) were student. **Wesselling C et al.** [67] reported that large worker populations were exposed to increasing amounts of pesticides. In Kashmir valley, 2/3rd third of the population who had exposure were engaged in apple orchard [(64)].

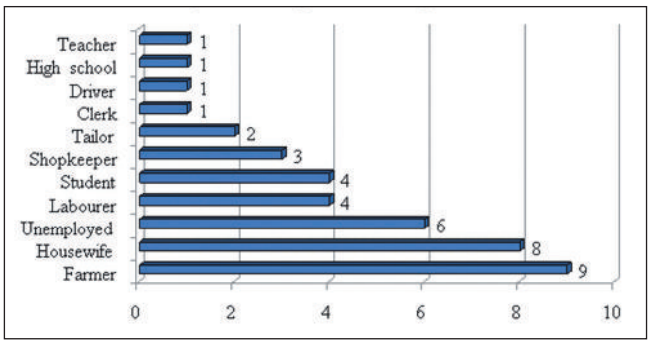


Fig. 1 Occupation of the patients

Presenting Symptoms / Signs :

Most common presentation was oral Secretions in 35 (87.5%) and Fasciculations in 22 (55%) patients. Depressed Mental Status 13 (32.5%) and Pin Point Pupils in 6 (15%) patients. **Murat Sungurb et al.** [62] in Turkey reported that the CNS symptoms such as depressed mental status, confusion and muscle weakness were the common presentation. **Kenneth D. Ketz et.al.** [68] from Pittsburg reported neuro psychiatric manifestations, ototoxity, Guillain-Barré – like syndrome and isolated bilateral recurrent laryngeal nerve palsy in OP compound poisoning.

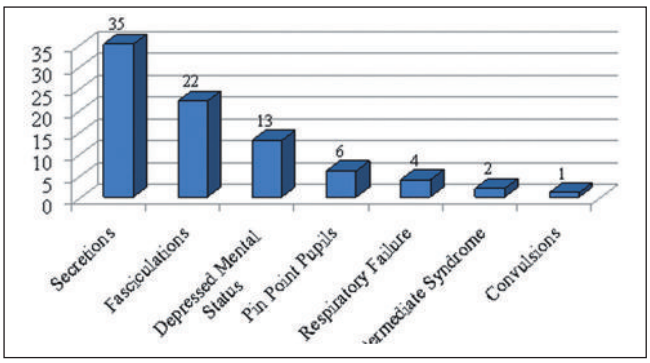


Fig. 2 : Presenting Symptoms/Signs

Type of organo-phosphate agents consumes :

Out of 40 patients, most common OP compound consumed was Dimethoate by 12 (30%), Methyl parathion by 10 (25%) patie wwnts. 8 (20%) patients consumed Phosphomidan and 4 (10%) patients consumed Fenthion. **Murat Sungurb et al.** [62] in turkey observed the three common type of OP were: Dichlorvas 24 (51.1%), Ethyl-Parathion 5 (10.6%), Fenthion 4 (8.5%). In sub urban West Bengal **Arup Kumar Kundu et al.** [69] showed that mortality was high in poisoning with monocrotophos and dimethoate (31%) and nil with Malathion. In the Mangalore study methyl parathion was the most common poison consumed.

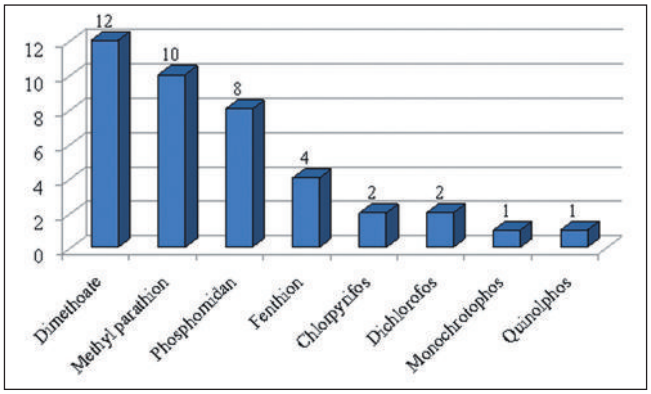


Fig. 3 : Type of Organo-phosphate Agents Consumes

ECG Abnormalities:

Most common ECG abnormality was QTc Prolongation in 24 (60%), Low Voltage in 6 (15%) and ST elevation in 6 (15%) patients. Inverted T wave and Extrasystole seen in 5 (12.5%) patients each. This is similar to that observed by **A M Saadeh et al** [70], **P. Karki et al** [71], **Chuang et al** [72] and **Kiss and Fazekas.** [73]

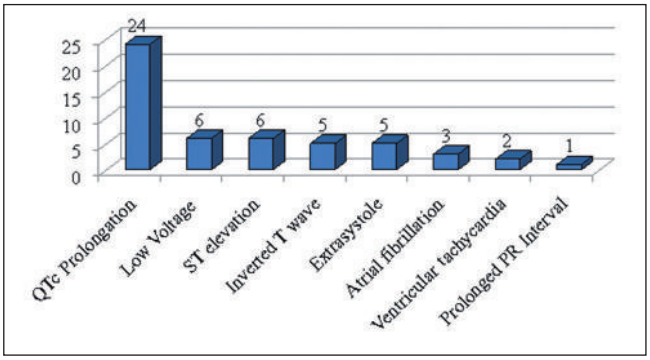


Fig. 4 : ECG Abnormalities

Nerve conduction abnormalities:

All patients underwent nerve conduction studies according to the clinical severity. In the nerve conduction study, compound muscle action potential, sensory nerve action potential and nerve conduction velocities were measured in all four limbs. The normal values of these parameters were taken as controls. Half of the patients were found to have one or other Nerve conduction abnormalities. Sensory neuropathy was observed in 12 (30%), Demyelination in 12 (30%) and 8 (20%) patients were found to have Axonopathy.

Peradeniya Organophosphorus Poisoning (POP) Scale Grading:

Majority, 29 (72.5%) had POP scale 0 to 3 followed by 9 (22.5%) patients had score 4 to 7 and only 2 patients had scale 8 to 11. **Arup Kumar Kundu et al** [69] reported**,** mild 15 (14%), moderate 55 (50.9%), and severe 32 (29.6%) in his study based on OP poisoning in sub-urban West Bengal. In that study, the severe grade of poisoning was associated with increased ventilatory support and poor outcome. Similarly, in this case series, clinical severity association with need of ventilatory support and mortality was statistically significant.

Association between Peradeniya (POP) Scale and Nerve conduction abnormalities:

Out of 29 patients with POP scale 0 to 3, only 44% had Nerve conduction abnormalities, Axonopathy, Demyelination and Sensory neuropathy was seen in 24.14% patients each. Out of 9 patients with POP scale 4 to 7, only 55.5%% had Nerve conduction abnormalities, 11.1% had Axonopathy, 33.3% had Demyelination and Sensory neuropathy was seen in 33.3% patients. Out of 2 patients with POP scale 8 to 11, both had Nerve conduction abnormalities, Demyelination and Sensory neuropathy but none had Axonopathy. Association of POP scale with Nerve conduction abnormalities, Axonopathy, Demyelination and Sensory neuropathy was not significant (all p values >0.05).

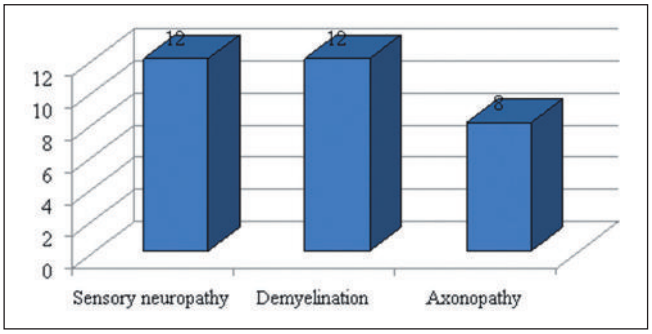
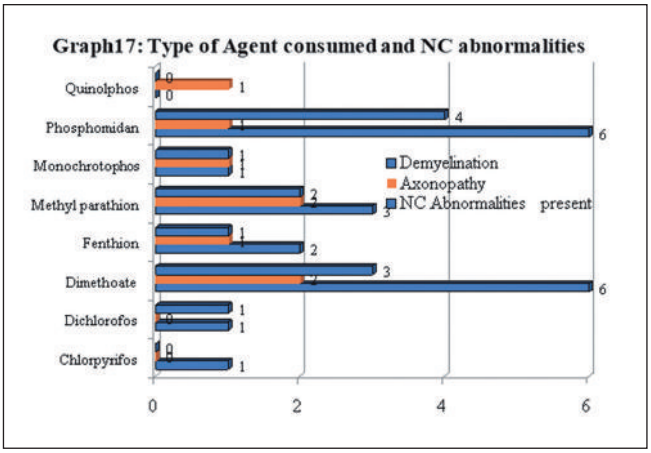


Fig. 5 : Different Nerve condition abnormalities



Peradeniya (POP) scale grade and duration of hospital-stay:

75% of the patients with duration of stay ≤ 5 Days had POP scale 0 to 3. 60% of the patients with duration of stay 6 to 10 Days had POP scale 4 to 7 and both patients with duration of stay >10 Days had POP scale 0 to 3. Association of POP scale and duration of hospital-stay was not significant (p value 0.136).

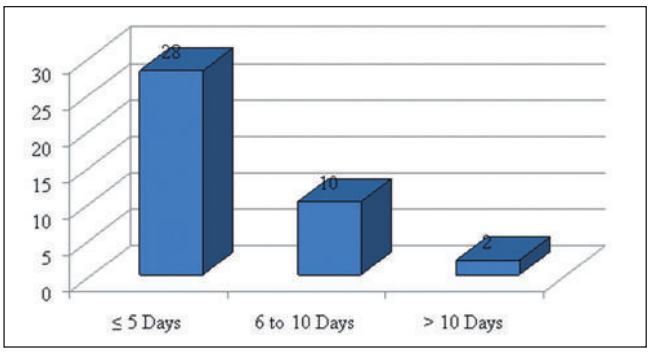
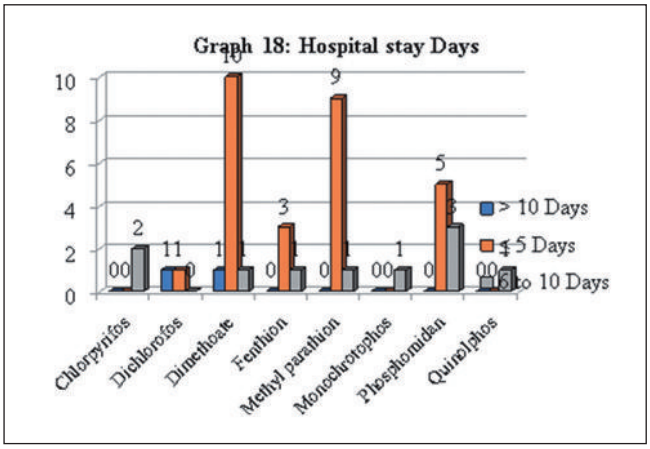


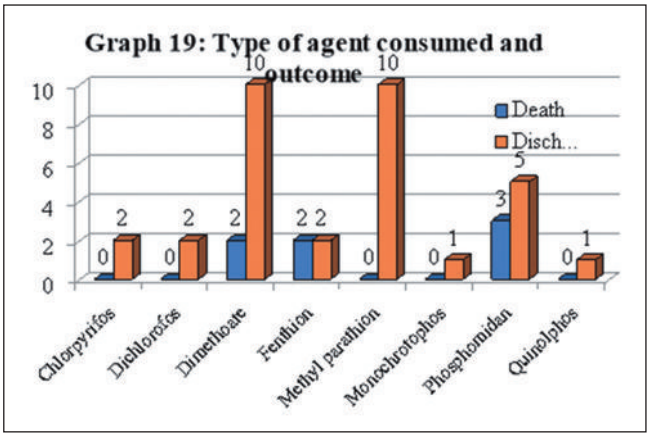
Fig. 6 : Hospital Stay (days)



Outcome of the patients:

33 (82.5%) patients recovered completely and discharged and 7 (17.55%) died during the course of treatment. In all cases primary cause of death was respiratory failure with secondary cardiac arrest. It has resulted from central respiratory depression, respiratory muscle weakness, increased bronchial secretions, broncho spasm and acute pulmonary oedema.

71.43% of the patients who died Days had POP scale 4 to 7 and 28.57% had 8 to 11. 87.87% of the discharged patients had POP scale 0 to 3. Association of POP scale and mortality was statistically significant (p value <0.05). Out of 7 deaths, Maximum mortality was seen in Fenthion (50%) followed by Phosphomidan, 37.5% mortality and in Dimethoate 16.7% mortality seen. **Karalliedde L et al** [63] reported mortality rate of 18% in their study of 92 cases of OP consumption in Sri Lanka. **Arup Kumar Kundu et al** [69] **(West Bengal)** analysed that increased time interval before initial atropinisation, higher clinical grading, type of poison (e.g., monocrotophos and dimethoate) were associated with increased mortality. In Kashmir valley a study of 164 patients of OP poisoning, the mortality rate was 5.5% [(64)]. In the **Mangalore study** [65]**,** the mortality was 26.2%. **Murat Sungur** and **Muhammed Güven** [62] of Turkey reported the mortality rate of 32%.



SUMMARY

In the present study, out of 40 patients with organophosphate poisoning, more than half, 25 (52.5%) patients belong to middle age group 21 to 40 years. Mean age was 33.68±11.99 years ranging from 17 to 61 years. Majority, 32 (80%) were male and 8 (20%) were females. Male to female ratio was 4:1. Majority, 9 (22.5%) were farmers, 8 (20%) were housewife, 6 (15%) unemployed. 4 (10%) were labourer and 4 (10%) were student. 17 (42.5%) had one or other comorbidities most common being Hypertension 10 (25%), Diabetes Mellitus in 3 (7.5%) and Obesity in 3 (7.5%) patients. 23 (57.5%) patients didn't have any comorbidities. Most common OP consumed was Dimethoate by 12 (30%), Methyl parathion by 10 (25%) patients. 8 (20%) patients consumed Phosphomidan

and 4 (10%) patients consumed Fenthion. 25 (62.5%) patients presented within 6 hours of consumption of chemical agent, 12 (30%) presented between 6 to 12 hours. Late presentation (> 12 hours) was seen in 3 (7.5%) patients. Mean Time between consumption to hospital admission5.54±3.26 hours Most common presentation was oral Secretions in 35 (87.5%) and Fasciculations in 22 (55%) patients. Depressed Mental Status 13 (32.5%) and Pin Point Pupils in 6 (15%) patients. Most common ECG abnormality was QTc Prolongation in 24 (60%), Low Voltage in 6 (15%) and ST elevation in 6 (15%) patients. Inverted T wave and Extrasystole seen in 5 (12.5%) patients each. Majority, 28 (70%) stayed in hospital for ≤ 5 Days and 10 (25%) stayed for 6 to 10 Days. Only 2 patients stayed for > 2 days. Mean duration of Hospital Stay 4.95±2.94 days. Half of the patients were found to have one or other Nerve conduction abnormalities. Sensory neuropathy was observed in 12 (30%), Demyelination in 12 (30%) and 8 (20%) patients were found to have Axonopathy. 33 (82.5%) patients recovered completely and discharged and 7 (17.55%) died during the course of treatment. Majority, 29 (72.5%) had POP scale 0 to 3 followed by 9 (22.5%) patients had score 4 to 7 and only 2 patients had scale 8 to 11. Out of 29 patients with POP scale 0 to 3, only 44% had Nerve conduction abnormalities, Axonopathy, Demyelination and Sensory neuropathy was seen in 24.14% patients each. Association of POP scale with Nerve conduction abnormalities, Axonopathy, Demyelination and Sensory neuropathy was not significant (all p values >0.05). 75% of the patients with duration of stay ≤ 5 Days had POP scale 0 to 3. 60% of the patients with duration of stay 6 to 10 Days had POP scale 4 to 7 and both patients with duration of stay >10 Days had POP scale 0 to 3. Association of POP scale and duration of hospital-stay was not significant (p value 0.136). 71.43% of the patients who died Days had POP scale 4 to 7 and 28.57% had 8 to 11. 87.87% of the discharged patients had POP scale 0 to 3. Association of POP scale and mortality was statistically significant (p value <0.05). Majority of the NC abnormalities were seen in poisoning by Dimethoate (30%) and Phosphomidan (30%) but difference not significant (p value 0.587) Majority of the Axonopathy were seen in poisoning by Dimethoate (25%) and Methyl parathion (25%) but difference not significant (p value 0.223) Majority of the Demyelination were seen in poisoning by Phosphomidan (33.3%) and Dimethoate (25%) and but difference not significant (p value 0.518) Majority of the Sensory neuropathy were seen in poisoning by Phosphomidan (33.3%) and Fenthion and Methyl parathion (16.7% each) but difference not significant (p value 0.124) Majority of the patients with hospital ≤ 5days had Dimethoate (35.71%) poisoning. Patients who stayed 6 to 10 Days had Phosphomidan (30%) poisoning; out of 2 patients who stayed >10 days, one consumed Dichlorofos and one had Dimethoate poisoning. Association of type of agent consumed with duration of stay was statistically significant (p value <0.05). Out of 7 deaths, Maximum mortality was seen in Fenthion (50%) followed by Phosphomidan, 37.5% mortality and in Dimethoate 16.7% mortality seen.

CONCLUSION

Most common OP consumed is Dimethoate and Methyl parathion. Common presentation are oral secretions and Fasciculations. ECG abnormalities are QTc Prolongation, low voltage and ST elevation. Half of the patients were found to have one or other Nerve conduction abnormalities. Sensory neuropathy, Demyelination and Axonopathy were common. Recovery rate was 82.5%. Patients with POP scale 0

to 3, only 44% had Nerve conduction abnormalities. Association of POP scale with Nerve conduction abnormalities, Axonopathy, Demyelination and Sensory neuropathy was not significant (all p values >0.05). 71.43% of the patients who died Days had POP scale 4 to 7. Association of POP scale and mortality was statistically significant (p value <0.05). Majority of the NC abnormalities were seen in poisoning by Dimethoate and Phosphomidan. Intensive supportive care, early POP scale measurement, respiratory support is due course of treatment are also emphasized.

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STUDY THE ROLE OF ABPM IN IDENTIFYING PRE-DIALYSIS BP CHANGES IN PATIENTS ON HAEMODIALYSIS

Rohan Katta*, *Ajit Joshi*****

ABSTRACT

INTRODUCTION : ABPM has been used to define the relationship between BP, target organ damage, and outcomes in patients with chronic and end-stage renal disease (ESRD). Hypertension in these patients shows some distinguishing features on ABPM. First, the prevalence of non-dipping (elevated nocturnal BP) is very high. Second, in patients on dialysis, changes in intravascular volume in the intra- and interdialytic period may result in marked swings of BP. Third, as in patients without CKD, discrepancies between clinic and home BP readings are common. The traditional methods of measuring BP intermittently in the medical setting may thus fail to provide an accurate picture of BP load, and hence result in sub-optimal treatment. The aim of the study is to assess the role of ABPM and monitoring pre-dialysis BP changes to decide antihypertensive medication. **METHODOLOGY :** Ambulatory BP of 84 patients on regular haemodialysis for more than 3 months, was assessed. ABPM machine was attached to the patient 24 hours before the appointment for haemodialysis. Observations noted and conclusions drawn. Necessary clearances were taken from the Institutional Ethics Committee. **OBSERVATIONS :** Out of total of 84 CKD patients, mean Ambulatory Blood Pressure were observed for all. The mean average pre-dialysis BP was 154.51/98.31. Mean average BP during dialysis 153.26/100.79. Mean average post-dialysis BP 152.86/94.76. A statistically significant difference was not observed between mean blood pressure values. (P value = 0.172, P value= 0.209) **CONCLUSION :** As observed from the results of the study, it is important to continue the usual dose of antihypertensives even pre-dialysis to provide optimal treatment.

INTRODUCTION

Hypertension (HT) is a common and challenging problem in patients on chronic hemodialysis (HD). HT in dialysis has several unique features. First, the prevalence is very high with 75% to 90% of patients on HD being hypertensive. [1] Second, young HD patients have higher average systolic blood pressure (SBP) than the elderly, perhaps because arterial stiffening occurs at a younger age, and the elderly HD patient has an increased risk for cardiomyopathy, unlike the general population in which SBP increases with age. [2] The relationship between elevated BP recorded in the interdialytic period and mortality is direct and linear as in the general population.[3] Compared with peri-dialytic and home BP recordings, 24-hour ambulatory BP displays closer associations with indices of target organ damage and is a stronger predictor of mortality. [4] Interdialytic BP measurement is superior for diagnosing masked HT. [5] and nocturnal

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HT, which is associated with target organ damage and increased cardiovascular (CV) events.[6]

Therefore, ambulatory blood pressure monitoring (ABPM) is considered the "gold standard" approach for the management of HT among patients on dialysis.[7] The ABPM protocol involves application of an appropriate-sized cuff to the nondominant arm and measurement of blood pressure(BP) every 30 min during the day and night for a 24-h period. BP should be appreciated as a continuous variable that variates throughout the day and night following a circadian rhythm with levels rising during daytime and falling during sleep. [8] ABPM over clinic BP measurements makes an accurate diagnosis of masked hypertension, assessing target organ damage, predicting outcomes, and evaluating response to therapy in chronic kidney disease (CKD) patients. Nocturnal BP is superior to day time BP in predicting cardiovascular disease (CVD) outcomes. This shows both systolic and diastolic pressure variability over 24 hrs maximum during night hours (nocturnal hypertension) and non-dipping of early morning BP. Both non-dipping status and nocturnal hypertension are associated with target organ damage and cardiovascular (CV) risk.[9] ABPM has been used to define the relationship between BP, target organ damage, and outcomes in patients with chronic and end-stage renal disease (ESRD). Hypertension in these patients shows some distinguishing features on ABPM. First, the prevalence of non-dipping (elevated nocturnal BP) is very high. Second, in patients on dialysis, changes in intravascular volume in the intra- and interdialytic periods may result in marked swings of BP. Third, as in patients without CKD, discrepancies between clinic and home BP readings are common. [10] The dialysis unit BP have poor agreement with ABPM. Pre-dialysis BP were biased estimates of SBP and DBP by a variable amount. Higher pre-dialysis measurements are possible because of increased intravascular volume, withholding of antihypertensive medications just before treatment, white coat effect, and lack of standardized measurements. Whereas post-dialysis BP seems to be less biased, the poor agreement with ABPM precludes their use to predict ABPM with any precision. Accordingly, current techniques for recording BP in the dialysis unit are insufficient to predict ABPM. [11] The home and ambulatory BP measurements from the interdialytic time period are better predictors of mortality than individual pre or post haemodialysis (HD) BP measurements. Interdialytic BP measurements are considered the gold standard for assessing overall BP burden and risk for catastrophic outcomes in HD patients. [12] Interdialytic weight gain (IDWG) is an easily measurable parameter in the dialysis unit, routinely assessed at the beginning of the dialysis session. It is used along with clinical symptoms and signs and predialysis blood pressure readings to make decisions regarding the amount of fluid removal during a dialysis session. IDWG is also used as a basis for fluid and salt intake recommendations. [13] A greater IDWG is directly associated with a better nutritional status, although it is also associated with higher predialysis blood pressure. The greater the IDWG%, the better the long-term prognosis of the patients. The beneficial effects of IDWG on the nutritional status and prognosis are greater than the negative aspects that depend on its effects on blood pressure. [14] The large variations of blood pressure (BP) during each hemodialysis (HD) and the fluctuation of BP levels in the interdialytic period suggest that more frequent interdialytic blood pressure measurement

may be necessary to obtain a reliable blood pressure profile, and interdialytic ambulatory blood pressure monitoring (ABPM) may be the best method to evaluate the blood pressure profile. Since interdialytic and intradialytic blood pressure changes are associated with morbidity and mortality, the early detection of such changes are required to prevent any unfortunate outcome. This can be done only by ambulatory BP monitoring pre-dialysis, during dialysis, and post-dialysis. Dialysis is associated with large changes in the hemodynamic status of the patients and often results in hemodynamic instability. Early detection of such changes are required to reduce the morbidity and mortality of patients undergoing dialysis. This is possible to some extent by ambulatory BP monitoring before, during, and after dialysis. In this study, we aim to study the BP variation using ABPM for 24 hours before haemodialysis in order to aid in the adjustment of antihypertensives and ultrafiltration according to BP changes.

METHODOLOGY

The study was done on all stable chronic kidney disease patients undergoing regular hemodialysis for more than three months at tertiary care center Kolhapur, over 18 months. It was designed as a prospective observational study. Eliminating dropouts and non-consenting individuals, 84 patients were studied and followed up till completion of the study, for completeness of data.

All stable chronic kidney disease patients on regular hemodialysis for more than three months, patients willing to come to the hospital 24 hours before hemodialysis, and age groups of more than 18 years, of both male and female genders were included in the study.

However, patients with acute renal failure, unstable patients with malignant hypertension or on life support like a ventilator, and patients on initiation of hemodialysis were excluded from our study.

The entire procedure was explained to the patient and clear instructions for handling the machine while it is at home with the patient were provided verbally and in a written format in a language of the patient's understanding. Valid, Written, Informed Consent was taken in the patient's own language. All the study participants underwent ambulatory BP monitoring. ABPM was put on 24 hours before the appointment for haemodialysis.

Data were entered into a Microsoft Excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test and Fisher Exact tests were used as tests of significance for qualitative data continuous data was represented as mean and standard deviation. unpaired t-test was used as a test of significance to identify the mean difference between two quantitative variables for comparison. MS Excel and MS Word were used to obtain various types of graphs such as bar diagrams. p-value (Probability that the result is true) of 0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Standard of care treatment was provided to the patient; ABPM was done by the machine owned by me. Since the patient need to visit 24 hours before haemodialysis, transport, and other logistic expenses were borne by me.

RESULTS

84 stable chronic kidney disease patients undergoing regular haemodialysis for more than three months at tertiary care centers fulfilling the inclusion criteria were included in the study. In the present study, the Maximum number of patients belonging to the 61 to 80 years age group i.e 39 (46.4%), followed by 41 to 60 years 30 (30.5%), 18 to 40 years 11 (13.1%) and more than 80 years 4 (4.8%) respectively. The mean age was 58.54±15.72 years. Among a total of 84 patients, 51 (60.7%) were male, and 33 (39.3%) females. The percentage of male patients was more.

From the below graph out of a total of 84 patients on haemodialysis, 43 (51.2%) were on Nifedipine, 36 (42.95%) were on Clonidine, 16 were (19%) on Furosemide, 15 were (17.9%) on metoprolol, 8 (9.5%) were on Telmisartan, 6 (7.1%) were on Chlorthalidone and 1 (1.2%) was on Amlodipine anti-hypertensive drugs respectively. From the below graph, it was observed that 82 (97.6%) patients were not on pre-dialysis anti-hypertensive drug treatment.

From the below graph out of total 84 CKD patients, mean Ambulatory Blood Pressure were observed. Mean average systolic pre-dialysis BP (154.51± 15.34), Mean average Diastolic pre-dialysis BP (98.31 ±9.97), Mean average systolic during dialysis BP (153.26±15.09), Mean average Diastolic during dialysis BP (100.79±20.25), Mean average systolic post-dialysis BP (152.86±15.72), Mean average Diastolic post-dialysis BP (94.76 ±8.98). A statistically significant difference was not observed between mean blood pressure values. (P value = 0.172, P value= 0.209 which is > 0.05)

From the below graph, Inter-dialysis weight gain and interdialytic blood pressure rise were observed in 75 (85.71%), and 69 (82.14%) patients on haemodialysis. Night blood pressure dipping was absent in the maximum number of haemodialysis patients i.e. 62 (73.81%)

DISCUSSION

This study was undertaken to determine the role of Ambulatory Blood Pressure Monitoring in the management of Hypertension in patients with chronic kidney disease undergoing regular haemodialysis and to assess the correlation between intradialytic blood pressure with ambulatory blood pressure monitoring. Dialysis is associated with large changes in haemodynamic status of the patients and often results in haemodynamic instability. Early detection of such changes are required to reduce the morbidity and mortality of patients undergoing dialysis. This is possible to some extent by ambulatory BP monitoring before, during, and after dialysis. The large variations of blood pressure (BP) during each haemodialysis (HD) and the fluctuation of BP levels in the interdialytic period suggest that more frequent interdialytic blood pressure measurement may be necessary to obtain a reliable blood pressure profile, and interdialytic ambulatory blood pressure monitoring (ABPM) may be the best method to evaluate the blood pressure profile.

Distribution of patients according to Duration on Hemodialysis : (Fig. 1)

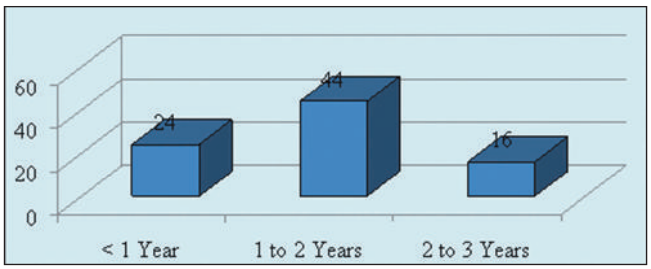

Fig. 1 : Duration of Haemodialysis

In my study out of a total of 84 patients, 44(52.4%) since 1 to 2 years, 24 (28.6%) since less than 1 year, and 16 (19%) had since 2 to 3 years on hemodialysis. Mean duration on maintenance hemodialysis was1.47±0.72 years. **In the Jong Hyun Jhee et al study,** [19] mean dialysis vintage (dialysis duration in years) observed was 8.7±4.5 years. In **Indhumathi, et al study,** [17] mean dialysis vintage in months were 24.64. the findings were consistent with our study. In the **Mogal Vajed et al study,** [16] mean haemodialysis vintage in Group 1 and Group 2 was 9.75±8.87 and 15.19±16.96 years respectively. Frequency of dialysis per week was studied in Group I and group 2 percentage of twice a week, thrice a week haemodialysis was (64%, 51%), (36%, 49%) respectively.

However, in my study mean duration was 1.47 ± 0.72 years and was due to late presentation of patients with symptoms.

Distribution of patients according to Type of anti-hypertensive Drugs, Number of Anti-hypertensive drugs, Pre-dialysis Anti-Hypertensive Treatment: (Fig. 2, 3)

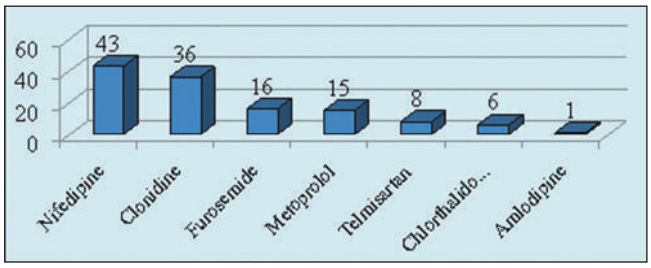

Fig. 2 : Drug Treatment

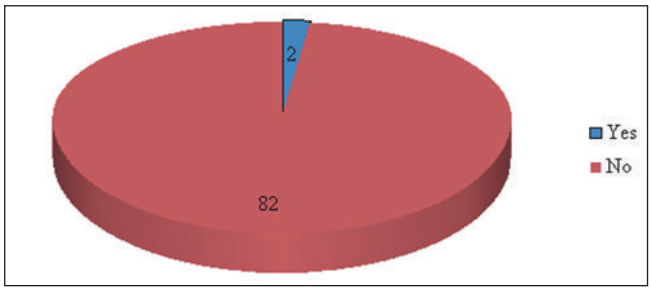

Fig. 3 : Anti-HTN Treatment

In my study out of total 84 patients on haemodialysis, 43 (51.2%) on Nifedipine anti-hypertensive drug, 36 (42.95%) on Clonidine, 16 (19%) on Furosemide, 15 (17.9%) on metoprolol, 8 (9.5%) on Telmisartan, 6 (7.1%) on Chlorthalidone and 1 (1.2%) on Amlodipine anti-hypertensive drug respectively. 38 patients were on multiple anti-hypertensive drugs. 82 (97.6%) patients were not on pre-dialysis anti-hypertensive drug treatment. **In Jong Hyun Jhee et al study,** [19] 1,271 (55.3%) ACE inhibitors, 1,167 (50.8%) calcium channel blockers, 1,085 (47.2%) beta-blockers and 246 (10.7%) alpha-blockers group of anti-hypertensive drugs. **In the Ambreen Gul et al study,** [20] Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) are first line therapy due to the high prevalence of cardiomyopathy among dialysis patients and β-adrenergic blocking agents in participants with recent myocardial infarction. **Heerspink et al**. [21] assessed eight RCTs. Administration of AHT agents was associated with significant decreases in cardiovascular events, cardiovascular mortality, and all-cause mortality although the mean decrease in SBP was only 4.5 mm Hg. **Agarwal et al.** [21] assessed five RCTs. Administration of AHT drugs was associated with a decrease in CVD events.

Distribution of patients according to Mean Duration of Dialysis and UF (Fig. 4)

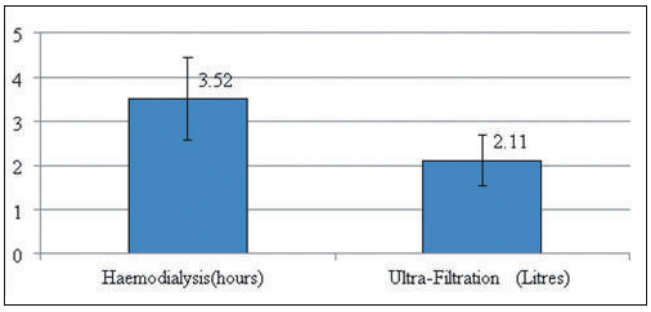

Fig. 4 : Mean Duration of Dialysis and UF

In my study, it was observed that the Mean duration of dialysis (hours) and ultra-filtration (litres) were 3.53± 0.73 and 2.11± 0.58 respectively **In Aldo J. Peixoto et al,** [15] Ultrafiltration (kg) Patient Characteristics in the Two Monitoring Periods were in study 1 (2.3 ± 1.4), in study 2 (2.6 ± 1.3) and difference between two studies was (0.5 ± 0.4). Findings similar and consistent with our study.

Distribution of patients according to Occurrence of Hypertension: (Fig. 5)

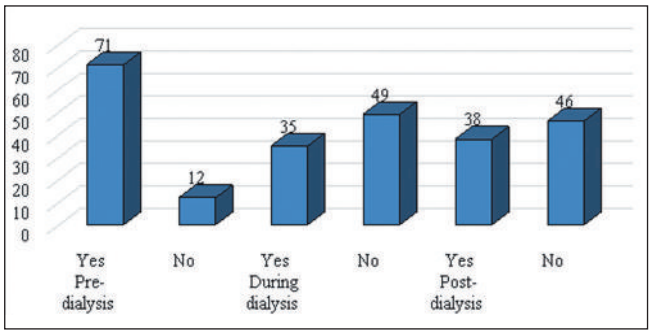

Fig. 5 : Occurrence of Hypertension

In my study, it was observed that 71 (85.5%) had occurrence of Hypertension before starting dialysis, 35 (41.6%) during dialysis, 38 (45.2%) developed Hypertension post-dialysis. **In Indumati et al study,**[17] hypertensions was found in all patients (100%), and uncontrolled hypertension was noted in 30 (81%) patients by ABPM thus unmasking HT in nine (24.3%). There is a high prevalence of uncontrolled HT in study cohort (n=30, 81%). Findings are similar and consistent with our study. **In AM Thompson et al study,** [23] Of 71 dialysis patients in whom 44-h interdialytic BP monitoring was compared with dialysis center measurements taken by a nurse, 43% of patients classified as hypertensive by pr-edialysis systolic BP were normotensive on ABPM, while 25% of patients classified as normotensive by pre-dialysis systolic BP were hypertensive. Whereas pre-dialysis BP measurements tend to overestimate BP load, the relationship between post-dialysis readings and BP control appears to be more variable.

Distribution of patients according to Mean Ambulatory Blood Pressure (Fig. 6)

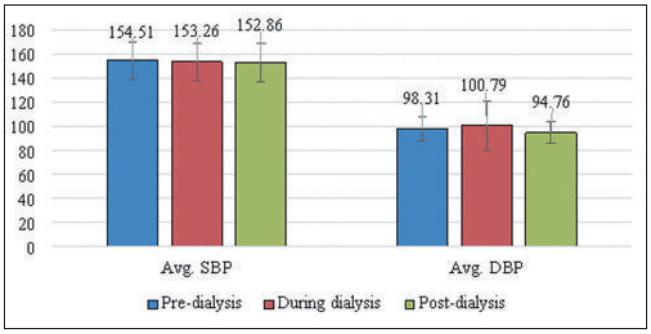

Fig. 6 : Mean Ambulatory Blood Pressure

In my study out of total of 84 CKD patients, mean Ambulatory Blood Pressure were observed. Mean average systolic BP and Diastolic BP pre-dialysis, during dialysis and post-dialysis were (154.51 ± 15.34, 98.31 ± 9.97), (153.26 ± 15.09, 100.79±20.25), (152.86 ± 15.72, 94.76 ± 8.98). A statistical significant difference was not observed between mean blood pressure values. (P value=0.172, P value=0.209 which is > 0.05) **In AM Thompson et al study,**[23] many BP measurements were made during dialysis, studies have attempted to determine if one reading in particular or an average of readings can provide a more accurate assessment of interdialytic BP. **Mitra et al.** compared [24] measurements made on arrival, 10 min after resting in a quiet room, at the onset of dialysis, end of dialysis, and 20 min post-dialysis, with average 48-h ABP readings in a group of 40 stable dialysis patients and found that the 20 min post-dialysis BP reading was most representative of BP control in the interdialytic period. **Conlon et al.** averaged dialysis [(25)] center readings from multiple visits and showed that predialysis BPs averaged over 12 treatment sessions showed a strong correlation with ABPM. **Aldo J. Peixoto et al,** [15] BP was analyzed

according to three different methods: isolated, pre-HD and post-HD values, average pre-HD and post-HD values for the five HD sessions surrounding each monitoring period, and 48-hour interdialytic ABPM. Reproducibility was determined by analysis of the SD of the differences (SDD) between the two monitoring periods and the coefficient of variation of each method of BP determination. Results showed better reproducibility of ABPM (SDD, 10.6/6.6 mm Hg; coefficient of variation, 7.5%/8.1%) compared with isolated pre-HD BP (SDD, 24.4/11.3 mm Hg; coefficient of variation, 16.7%/14.1%) or post-HD BP (SDD, 16.8/14.5 mm Hg; coefficient of variation, 11.7%/17.8%), and averaged pre-HD BP (SDD, 14.7/7.2 mm Hg; coefficient of variation, 10.1%/9.1%) or post-HD BP (SDD, 12.4/8.7 mm Hg; coefficient of variation, 8.9%/11.1%).

Distribution of patients according to Inter dialysis weight gain and Blood pressure changes: (Fig. 7)

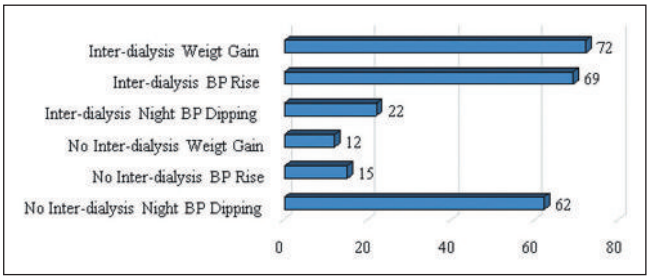

Fig. 7 : Inter dialysis weight gain and Blood pressure changes

In my study, Inter-dialysis weight gain and interdialytic blood pressure rise were observed in 75 (85.71%), and 69(82.14%) patients on haemodialysis. Night blood pressure dipping was absent in a maximum number of haemodialysis patients i.e. 62(73.81%). **In AM Thompson et al study, [23] t**he poor correlation between dialysis and ABPM readings is explained in part by changes in BP that occur in the interdialytic period, which cannot be captured by measurements made in the dialysis center. A loss of diurnal variation in BP has been associated with a poor renal prognosis. In a 3-year longitudinal study of 28 non-dippers and 20 dippers with hypertension and CKD, non-dipping at baseline was predictive of a faster decline in renal function and a greater increase in proteinuria. **Santos et al. [88]** studied BP in the interdialytic period in 71 stable haemodialysis patients and found a statistically significant increase in average daytime and night time BPs from the first to the second day of the interdialytic period. In a study of 20 mostly black haemodialysis patients, **Agarwal et al [27]** reported a similar pattern of BP changes and also observed a decrease in BP in the period after dialysis, a finding that has been described by others. **In Indumati et al study, [17]** 81% of elderly patients in dialysis unit were non-dippers. Nine patients with normal peri-dialytic BP were found to have uncontrolled HT by ABPM as well as non-dippers of nocturnal BP (P = 0.000). **In Jordana B. et al study, [28]** Mean pre-dialysis SBP was 146 ± 19 mm Hg, 44-hour ambulatory SBP was 140 ± 21 mm Hg, daytime SBP was 141 ± 20 mm Hg, and nighttime SBP was 134 ± 25 mm Hg. Twenty-four (77%) participants did not experience an appropriate 10% nocturnal BP decline (non-dippers), including 7 (23%) who experienced an increase in nocturnal BP (reverse dippers). The mean number of successful ambulatory BP readings was 67 ± 16 over 44 hours. In **Mogal Vajed et al study, [16]** Inter dialysis weight gain was observed between group 1 (1.65 ± 0.73) and group 2 (2.14 ±0.83). the difference between two was statistically significant (P value = 0.004). From various literature discussed it was seen that ambulatory BP monitoring plays an

important role in the management of Hypertension in patients with chronic kidney disease undergoing regular hemodialysis and non-dipping denotes the worst prognosis of renal disease.

SUMMARY

In present study, Maximum number of patients belonging to 61to 80years age group i.e 46.4%(39), followed by 41 to 60 years 30.5%(30), 18 to 40 years, 13.1% (11) and more than 80 years 4.8% (4) respectively. The mean age was 58.54±15.72 years. Among total 84 patients, 60.7% (51) were male and 39.3% (33) females. The percentage of male patients was more. 55.9% (47) had anorexia, 52.3% (44) had facial puffiness, 48.8% (41) had itching, 45.2% (38) had generalized weakness, 39.29% (33) had breathlessness, 36.90% (31) B/L pedal oedema, 5.95% (5) had irritability, and 1 (1.19%) had palpitations and 19% (16) no any fresh symptoms. 52.4% (44) since 1 to 2 years, 28.6% (24) since less than 1 year and 19% (16) since 2 to 3 years on haemodialysis.Mean duration on maintenance haemodialysis was1.47±0.72 years. Hypertension was observed in 98.85% (83) patients, 35.7% (30) Type-2 Diabetes Mellitus, 23.8% (20) ischemic heart disease, 9.5% (8) COPD, 4.8% (4) and Cerebro-vascular accident. 51.2% (43) on Nifedipine anti-hypertensive drug, 42.95% (36) on Clonidine, 19% (16) on Furosemide, 17.9% (15) on metoprolol, 9.5% (8) on Telmisartan, 7.1% (6) on Chlorthalidone and 1.2% (1) on Amlodipine anti-hypertensive drug respectively. 97.6% (82) of patients were not on pre-dialysis anti-hypertensive drug treatment. Pre-dialysis mean body weight was 60.25 ± 8.61 and post-dialysis mean body weight was 58.95±26.024 respectively. There was a significant difference observed between Pre-dialysis and Post-dialysis mean body weight. (t-value = 26.024. p value <0.05). Mean dry Weight was 58.96±8.51 Kg and Mean BMI was 21.77±2.17 Kg/m^2. The mean duration of dialysis (hours) and ultra-filtration (liters) were 3.53±0.73 and 2.11± 0.58 respectively.

The mean HB value (mg/dl) was 8.19 ±1.87, the mean total leucocyte count (per micro litre) was 10787.95±5176.81 and the mean platelet count (per micro litre) was 61199.25±25754.56 respectively. Mean laboratory parameters during Pre-dialysis and post-dialysis were serum urea (132.39±47.55, 87.13± 45.97), serum creatinine (5.78±2.64, 3.79 ±1.74), serum sodium (139.56± 7.72, 140.38±7.14), serum potassium (4.67±1.03, 4.31±0.88), and blood sugar levels (141.59±36.50, 129.90±31.44). a significant difference was observed between serum urea, serum Creatinine, Serum Potassium, and Blood Sugar Levels (p value<0.05) 85.5% (71) had occurrence of Hypertension before starting dialysis, 35(41.6%) during dialysis, 38 (45.2%) developed Hypertension post-dialysis. Mean Ambulatory Blood Pressure was observed. Mean average systolic BP and Diastolic BP pre-dialysis, during dialysis and post-dialysis, were (154.51±15.34, 98.31±9.97), (153.26±15.09, 100.79±20.25), (152.86±15.72, 94.76±8.98). A statistically significant difference was not observed between mean blood pressure values. (P value=0.172, P value=0.209 which is > 0.05) Inter-dialysis weight gain and interdialytic blood pressure rise were observed in 75 (85.71%), and 69 (82.14%) patients on haemodialysis. Night blood pressure dipping was absent in the maximum number of haemodialysis patients i.e. 62 (73.81%)

CONCLUSION

ABPM is useful in identifying pre-dialysis BP changes in patients on haemodialysis. During ABPM it was found that there was not much difference between pre-dialysis, intra-dialytic and post-dialysis, this could be because of the proper selection of ultrafiltrate value and repeated BP monitoring. Inter-dialytic weight gain has a positive corealtion with pre-dialysis BP changes. There was no night dipping on ABPM in most of the patients on dialysis, so there is an increased possibility of cardiovascular morbidity and mortality.

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ORIGINAL ARTICLE

IDENTIFICATION OF THE PATTERN OF IMPAIRMENT OF SPIROMETRIC PARAMETERS IN HYPOTHYROID PATIENTS

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ABSTRACT

Introduction- Hypothyroidism is a clinical condition characterized by decrease in thyroid hormone production. It causes the metabolism to slow down, affecting the entire body. It is mostly prevalent in older women. It can be treated with hormone replacement therapy. **Methodology-** The present study was conducted in the Department of General Medicine at tertiary care hospital, on diagnosed hypothyroidism patients. The time period of the study was for 2 years. All the patients fulfilling the inclusion and exclusion criteria were selected for the study. Anthropometric measurements and clinical findings were recorded. Relevant care was provided. All the study participants underwent spirometry. Spirometric parameters were recorded for analysis. **Result-** The correlation between the patient's serum T3 levels and grade of restriction has been assessed. With decrease in serum T3 values there was worsening in grade of restriction. Correlation between patient's serum T4 levels and grade of restriction has been assessed. With decrease in serum T4 values there was worsening in grade of restriction. Correlation between patient's serum TSH levels and grade of restriction has been assessed. With increase in serum TSH values there was worsening in grade of restriction **Conclusion-** All the patients of hypothyroidism should undergo spirometry to prevent complications and all patients with impaired spirometry should undergo thyroid function tests for early diagnosis and treatment.

Keywords - Hypothyroidism, hormones, spirometry, parameters, women

INTRODUCTION

Hypothyroidism is a clinical condition characterised by a decrease in thyroid hormone production. Despite proper pituitary stimulation, primary hypothyroidism happens when the thyroid is unable to create enough thyroid hormones. [1-2] It might be mild or severe. Serum thyroid stimulating hormone (TSH) levels over the upper reference limit in the presence of normal free thyroxin levels defines subclinical hypothyroidism (fT4). Overt primary hypothyroidism was characterised by a high TSH and a subnormal fT4.[1] Contrarily, central or secondary hypothyroidism results from diseases of the hypothalamus or pituitary gland or flaws in the TSH molecule and is brought on by inadequate stimulation of the normal thyroid gland. It is predicted that there will be 4.1 new cases of overt hypothyroidism for every 1000 women and 0.6 new cases for every 1000 males per year. [3] TSH values that were more than 10 mIU/L, which are indicative of severe hypothyroidism, were found in 4.4 percent of the population among those who were elderly (having an age >60 years).[4] Researches conducted in India indicated that hypothyroidism was the most prevalent type of thyroid malfunction there.[5,6]

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It has been found that the prevalence of hypothyroidism in people in India ranges from 3.9 percent to 10.95 percent. The frequency of hypothyroidism that had not been discovered in the patient population was 3.47 percent.[6] In patients with hypothyroidism, abnormalities in spirometry indices were found in comparison to those seen in controls.[8-9] These were indicative of a restrictive pathology rather than an obstructive one, and they may have been caused by interstitial oedema as a symptom of myxoedema itself, in addition to the respiratory muscle weakness that was previously stated. Since the influence of hypothyroidism on the respiratory system was controversial, with studies revealing both obstructive and restrictive patterns, further research was required to comprehend how the respiratory system is involved in hypothyroid individuals. Consequently, evaluation of the patient's pulmonary function using spirometry was seen as being of utmost significance in hypothyroid patients. Whether hypothyroid patients had any impairment in lung function parameters or not is determined by this study. And if such impairment was found, to determine the type of respiratory disease pattern that was present. By carrying out this research, we were able to highlight changes in the pattern of impairment of spirometry parameters (obstructive, restrictive, and mixed).

MATERIALS AND METHODS

The present study was conducted in the Department of General Medicine at tertiary care hospital after getting all the necessary ethical permissions from the Institutional Research Committee. It was a Prospective Observational study. The sample size taken for the study was 100 patients. The duration for the study was of 2 years from December 2020 to December 2022. Valid, written, informed consent was obtained from the patients in their own language. Patients aged from 18 to 80 years, ready to give informed consent, diagnosed patient with hypothyroidism, and on thyroxine for 2 or more years were included in the study. Whereas, patients previously diagnosed with cardiac disorders for e.g. LVF, PAH, CCF, with co-existing or treated Chronic Pulmonary Disease, those with significant smoking history and diagnosed case of occupational lung disease, patients with CVA, neuromuscular and skeletal conditions, drugs known to interfere with pulmonary function like Amphotericin B, Isoniazid, Amiodarone, Nitrofurantoin, Methotrexate, Aspirin, ACE inhibitors and chemotherapeutic drugs, and pregnant ladies were excluded from the study. All the necessary investigations were done including the Thyroid profile and CBC. Hypothyroidism patients were diagnosed by TSH> 4 IU/L & T4 < 0.7ng/dl & T3 < 77ng/dl. Anthropometric measurements and Clinical findings were recorded. All the study participants underwent spirometry. Standard care of treatment was given to the patients. Spirometry was done at free of charges. Spirometric parameters recorded for analysis were Forced vital capacity (FVC), Forced expiratory volume in 1st second (FEV1), FEV1/FVC, Peak expiratory flow rate (PEFR), Forced expiratory flow 25%-75% (FEF25%-75%).

Interpretation of spirometry data:

PFT Parameters	Obstructive Pattern	Restrictive Pattern	Mixed Pattern
FEV1	Diminished	Diminished / Normal	Diminished
FVC	Diminished / Normal	Diminished	Diminished
FEV1 / FVC	Diminished	Normal / Increased	Diminished

RESULTS

Table 1 : Frequency distribution of study participants according to impairment pattern

Impairment pattern	Frequency	Percentage
normal	37	37.0
mild restriction	32	32.0
moderate restriction	25	25.0
severe obstruction	1	1.0
severe restriction	5	5.0
Total	100	100.0

Table 2 : Distribution of study participants according to impairment pattern and T3 levels

T3 levels	Impairment pattern					P value
	normal	mild restriction	moderate restriction	severe obstruction	Severe Restriction	
Normal	33(89.2%)	22(68.8%)	20(80%)	1(100%)	5(100%)	0.00
abnormal	4(10.8%)	10(31.3%)	5(20%)	0	0	0.001
Total	37(100%)	32(100%)	25(100%)	1(100%)	5(100%)	

Chi square test is used. P values are significant

Table 3 : Distribution of study participants according to impairment pattern and T4 levels

T4 levels	Impairment pattern					P-value
	normal	mild restriction	moderate restriction	severe obstruction	Severe Restriction	
Normal	21(56.8%)	21(65.6%)	9(36%)	0	3(60%)	0.00
abnormal	16(43.2%)	11(34.4%)	16(64%)	1(100%)	2(40%)	0.0001
Total	37(100%)	32(100%)	25(100%)	1(100%)	5(100%)	

Chi square test is used. P values are significant

Table 4 : Distribution of study participants according to impairment pattern and TSH levels

TSH levels	Impairment pattern					P value
	normal	mild restriction	moderate restriction	severe obstruction	Severe Restriction	
Normal	20(54.1%)	14(43.8%)	6(24%)	0	2(40%)	0.00
abnormal	17(45.9%)	18(56.3%)	19(76%)	1(100%)	4(80%)	0.0002
Total	37(100%)	32(100%)	25(100%)	1(100%)	5(100%)	

Chi square test is used. P values are significant

DISCUSSION

In our present study, normal findings were present in 37(37%), mild restriction was among 32(32%), moderate restriction was among 25(25%), severe restriction was among 5(5%) and severe obstruction was among 1(1%). In a study done by Jagdale et al55, obstructive pattern (32%), followed by mixed pattern and restrictive pattern (28%, 22% respectively). Hypothyroidism causes respiratory depression, interference of neuromuscular transmission to respiratory muscles, alveolar hypoventilation and deposition of mucopolysaccharides in muscles. All these factors lead to impaired lung functions in hypothyroidism. There was a statistically significant difference between normal pattern patients, mild restriction patients, moderate restriction patients, severe restriction patients and severe obstruction patients in regards to T3, T4, TSH levels. (Table 1)

Among normal pattern patients, majority had normal T3 levels followed by abnormal T3 levels, among mild restriction pattern patients, majority had normal T3 levels followed abnormal T3 levels. Among moderate restriction patients, majority had normal T3 levels followed abnormal T3 levels, Severe obstruction and severe restriction patients all had normal T3 levels.

There was statistically significant difference between groups in regards to T3 levels. (Table 2)

Among normal pattern patients, majority had normal T4 levels followed abnormal T4 levels, among mild restriction pattern patients, majority had normal T4 levels followed abnormal T4 levels. Among moderate restriction patients, majority had abnormal T4 levels followed normal T4 levels, Severe obstruction patients had abnormal T4 levels and severe restriction patients majority had abnormal T4 levels followed normal T4 levels. There was statistically significant difference between groups in regards to T4 levels. (Table 3)

Among normal pattern patients, majority had normal TSH levels followed by abnormal TSH levels, among mild restriction pattern patients, majority had abnormal TSH levels followed by normal TSH levels. Among moderate restriction patients, majority had abnormal TSH levels followed normal TSH levels. Severe obstruction patients had abnormal TSH levels, and severe restriction patients, the majority had abnormal TSH levels followed by normal TSH levels, there was statistically significant difference between groups in regards to TSH levels. (Table 4)

The results of a study that was carried out by Maiti SR et al showed a substantial positive link with FEF 25-75 percent and FEV1/FVC. However, a significant negative correlation was found between TSH and FVC and FEV1. In restrictive lung disease, a normal or increasing value was diagnostic, as opposed to a decreased value, which was observed in obstructive lung illnesses. FT4 was shown to have a substantial positive connection with FVC, FEV1, and FEV1/FVC in research that was carried out by Maiti SR et al[7]. There was not a significant link found between TSH or fT4 and FVC, FEV1, or FEV1/FVC, according to the findings of research carried out by Jagdale et al.[10]

The correlation between patient's serum T3 levels and grade of restriction has been assessed. With decrease in serum T3 values there was a worsening in grade of restriction. The correlation between patient's serum T4 levels and grade of restriction has been assessed. With decrease in serum T4 values there was a worsening in grade of restriction. Correlation between patient's serum TSH levels and the grade of restriction has been assessed. With increase in serum TSH values there was worsening in grade of restriction.

CONCLUSIONS

The present study was conducted in the Department of General Medicine, at Tertiary care centre, Kolhapur on diagnosed hypothyroidism patients. This study was aimed at evaluating the pattern of impairment of spirometric parameters in hypothyroid patients. From the above study we come to the conclusion that, a restrictive pattern is observed among most of the hypothyroid patients. Higher TSH levels and low fT4 levels leads to greater fall in spirometry parameters. Hence, all the patients with hypothyroidism should undergo spirometry to prevent complications and all patients with impaired spirometry should undergo thyroid function tests for early diagnosis and treatment.

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ORIGINAL ARTICLE

SEROCONVERSION OF HEPATITIS B VACCINATION IN CHRONIC KIDNEY DISEASE : A HOSPITAL BASED OBSERVATIONAL STUDY

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ABSTRACT

Background : Hepatitis B infection is a constant threat despite availability of effective vaccine. Patients with Chronic Kidney Disease (CKD) have higher risk of acquiring Hepatitis B infection and further progressing to become chronic carrier. Present research aims to study seroconversion rates of Hepatitis B vaccination in pre-dialysis and dialysis patients. Also it aims to correlate seroconversion with the nutritional status of the patients. **Methods :** This is a hospital based observational study conducted in tertiary healthcare facility. Total 110 participants were enrolled for the study after obtaining written informed consent. Demographic information was captured using standardized questionnaire. Nutritional assessment was done by calculating BMI, Lean body mass and Mid Arm Circumference (MAC). Anti HBsAb estimation has been done before beginning of schedule and 1 month after last dose. Data entry and analysis done using statistical software SPSS version 20.0 **Results :** Out of total 110 patients 69 (62.7%) were males and 41 (37.3%) were females. The mean age[€]of the patients was 46.6±11.85 years Seroconversion rates were significantly higher (p=0.014) in the pre-dialysis group (89.4%) than the dialysis group (69.8%). There were significant higher seroconversion rates ($p < 0.05$) among subjects who have better BMI, Lean Body Mass and MAC. **Conclusion :** Vaccination with HBV in early CKD gives a chance for higher seroconversion. Patients can be screened for CKD and should be immunized at the earliest for better antibody titre.

Keywords *:* CKD, ESRD, Hepatitis B Vaccination, Seroconversion rate, Dialysis

INTRODUCTION

Hepatitis B infection is a public health problem and continues to threat even though effective vaccination is available. Chronic diseases have become a major cause of global morbidity & mortality. In India, the projected number of deaths due to chronic diseases will rise from 3.78 million in 1990 (40.4% of all deaths) to an expected 7.63 million in 2020 (66.7% of all deaths). [1-2]

The increase in the prevalence of Chronic Kidney Disease (CKD) & its progression to ESRD (End Stage Renal Disease) has highlighted the importance of CKD & its risk factors in developed as well as developing countries. [3] The average incidence of ESRD in developing countries is 150 per million populations which is lower than the developed countries. [4] One of the common and most serious infectious diseases

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encountered in Chronic kidney diseases during hemodialysis is Hepatitis B-Virus (HBV). [5]

Patients with CKD have a higher risk of acquiring Hepatitis B infection during dialysis sessions & subsequently may become chronically infected to become Hepatitis B carriers. [6-7] Hepatitis B infection is difficult to treat, which is why prevention of the Hepatitis B vaccine (HB vaccine) is the most efficient way to tackle the problem. So, as a measure of prevention, Hepatitis B vaccine is recommended for all patients on maintenance hemodialysis& for all pre-end stage renal disease patients before they become dialysis dependent.[8-9]

However, Patients with CKD have a reduced response to vaccination because of the general immune suppression associated with uremia and thus seroconversion to HBV is lower in patients undergoing hemodialysis than general population.[10]. The present research aims to study seroconversion rates of Hepatitis B vaccination in the pre-dialysis and dialysis patients. Also, it aims to correlate seroconversion with the nutritional status of the patients.

METHODOLOGY

The present study is a Hospital based observational prospective study. It was carried out at a tertiary care center. Ethical clearance was sought from Institutional Ethics Committee prior to the commencement of the study.

Patients attending OPD & IPD in the institute diagnosed as Chronic kidney disease (CKD) from e-GFR during the period September 2016 to August 2018 were included only after obtaining written informed consent from them. The subjects with age 18 years or more with Laboratory confirmed negative serology results to HbsAg and those on renal dialysis or a pre-dialysis patient with e-GFR less than 60 ml/min for more than 3 months were included in the study. Stages of CKD were categorized from stage 0 to 5 according to Cockcroft - Gault formula [e-GFR= (140-age) x weight/72 x serum creatinine x 0.85 (if female)]. The subjects with previous hepatitis B infection, HBV vaccination, immuno-compromised patients, those on systemic immune-modulatory medications, and haemoglobin <7 g/dl were excluded from the study.

Total of 110 patients including 69 males and 41 females were part of the study. Demographic information was captured using a standardized questionnaire. Nutritional assessment was done by calculating BMI, Lean body mass, and Mid Arm Circumference (MAC) with standardized formula and procedure. All patients received vaccination according to vaccination protocol for CKD in Indian Journal Nephrology,2016 guidelines with Energix at intervals of 0,1,2 and 6 months. Anti-HBsAb estimation has been done before the beginning of the schedule and 1 month after the last dose. Anti-HBs titer>10 mIU/ml were defined as good responders while Antibody titer <10 mIU/ml were considered as poor responders.

Data entry and analysis were done using the statistical software SPSS 20.0. demographic and clinical profile of the participants is represented as frequency and percentage. The chi-square test was applied to study the correlation between Hepatitis B vaccination seroconversion rates among pre-dialysis and dialysis patients and also a correlation of seroconversion rates with the nutritional status of the subjects. p-value of

statistical tests less than 0.05 was considered to be significant.

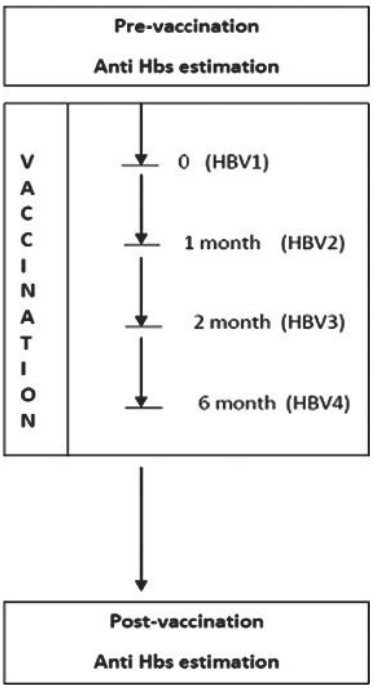

Fig 1 : Sequence of events in the present research

RESULTS

Out of total 110 patients 69 (62.7%) were males and 41 (37.3%) were females. The mean age[e]of the patients was 46.6±11.85 years. As per Cockcroft - Gault formula, 10.1% belonged to CKD stage 1, 15.4% belonged to CKD stage 2, 16.3% belonged to CKD stage 3, 22.7% belonged to stage 4 and rest 34.5% belonged to CKD stage 5. Majority of the patients presented with breathlessness (69%) followed by generalised weakness (63.6%), oedema (59%), anorexia (56.3%), decreased urine output (39%), abdominal pain (7.2%) & altered sensorium (2.7%). Hypertension & Diabetes Mellitus were the most prevalent co-morbidities present in 81.1% & 56.3% patients respectively while 37.2% patients had associated cardiovascular diseases & 11.8% had renal disease. Nutritional assessment was done using BMI, Lean Body Mass and Mid Arm Circumference values. The Mean Mid Arm Circumference, Lean Body Mass & BMI values of patients were 21.62±2.19cm, 38.07±2.23kg & 22.64±1.91kg/m^2 respectively.

Table 1 : Demographic and clinical profile of the study participants

	Categorization	N	Percent
Age (years)	21-30	12	10.9%
	31-40	25	22.7%
	41-50	38	34.5%
	51-60	17	15.4%
	>60	18	16.3%
Sex	Male	69	62.7%
	Female	41	37.3%
Symptoms	Breathlessness	76	69%
	Generalised weakness	70	63.6%
	Oedema	65	59%
	Anorexia	62	56.3%
	Decreased urine output	43	39%
	Abdominal pain	8	7.2%
	Altered sensorium	3	2.7%
Stages of CKD	CKD1	12	10.9%
	CKD2	17	15.5%
	CKD3	18	16.4%
	CKD4	25	22.7%
	CKD5	38	34.5%
Associated Co-morbidities	Hypertension	90	81.1%
	Diabetes Mellitus	62	56.3%
	Cardiovascular disease	41	37.2%
Addiction	Smoking/ tobacco chewers	42	38%
	Alcohol	27	24.5%

Mean HbsAbtitre for CKD stage I, stage II, stage III, stage IV and stage V were observed to be 30.58+2.58, 25.26+2.18, 19.26+2.56, 15.35+2.46, 11.29+1.45 among good responders. Among the poor responders antibody titre in stage II, stage III, stage IV, stage V were 8.62+1.03, 6.26+2.23, 8.75+1.23, 5.62+1.36. Pre-dialysis patients i.e. Stage I, II and III of CKD and dialysis patients i.e. Stage IV andV of CKD are plotted against their mean HBsAbtitre as shown in the Fig. no. 1 and Fig no.2

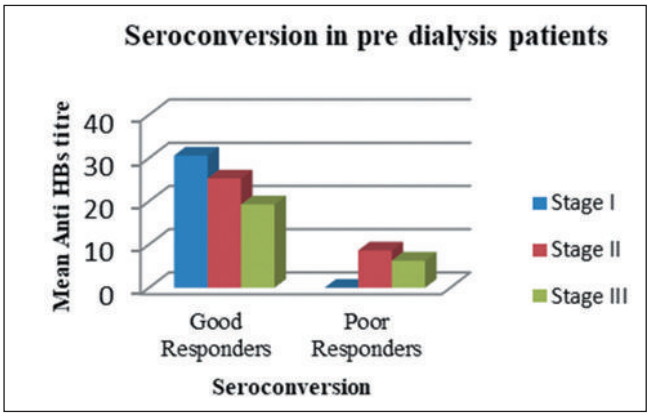

Fig. 2 : Anti HBsAb titre in pre-dialysis patients

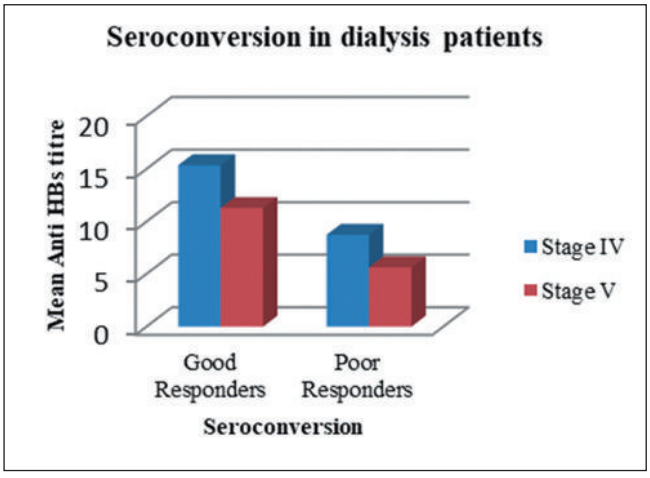

Fig. 3 : Anti HBsAb titre in dialysis patients

Seroconversion rates of pre-dialysis patients were compared with that of dialysis patients. It was observed that seroconversion rates were significantly higher (pvalue=0.014) in the pre-dialysis group (89.4%) than in the dialysis group (69.8%) implicating role of early vaccination. The same is represented in tabular form in table no.2.

Table 2 : Seroconversion rates in pre-dialysis and dialysis patients

	Good Responders	Poor Responders	Total
Pre-dialysis	42 (89.4%)	5 (10.6%)	47 (100%)
Dialysis	44 (69.8%)	19 (30.2%)	63 (100%)
P value	0.014		

Nutritional status of the subjects were done using the anthropometric parameters i.e. Body Mass Index (BMI), Lean Body Mass and Mid-Arm Circumference (MAC). There were significant higher seroconversion rates among subjects who have better BMI, Lean Body Mass and MACi.e. higher the anthropometric parameters better is the seroconversion (Table no.3).

Table 3 : Anthropometric parameters according to CKD stages & its correlation with seroconversion

Anthropometric parameters	CKD Stages	Good Responders	Poor Responders	P value
BMI (kg/m2)	I	25.6 ± 1.4	-	-
	II	24.2 ± 2.0	23.2 ± 2.0	<0.01
	III	22.1 ± 2.4	21.5 ± 3.1	<0.01
	IV	20.2 ± 1.5	19.2 ± 1.7	<0.01
	V	18.1 ± 2.0	16.9 ± 1.9	<0.01
Lean Body Mass (kg)	I	40.0 ± 3.8	-	-
	II	39.1 ± 1.9	38.2 ± 2.0	<0.01
	III	36.0 ± 2.3	34.1 ± 3.0	<0.01
	IV	35.0 ± 1.6	32.9 ± 2.7	<0.01
	V	33.9 ± 1.6	31.0 ± 1.9	<0.01
MAC (cm)	I	26.6 ± 2.7		-
	II	25.9 ± 1.9	24.1 ± 2.0	<0.01
	III	23.9 ± 2.3	21.2 ± 2.0	<0.01
	IV	21.5 ± 1.6	20.0 ± 2.6	<0.01
	V	20.6 ± 1.4	18.9 ± 1.9	<0.01

DISCUSSION

A hospital-based observational, prospective study was conducted with 110 patients to study the pattern of seroconversion of Hepatitis B vaccination in CKD patients.

The seroconversion rates reported in various studies range from 78% to 83%. Gomthy S et al reported 82.6% was the overall seroconversion rate and the rest 17.4% with low antibody titer had to be re-vaccinated. [11] Hashemi B et al reported 78% oveall seroconversion rate to HBV vaccination. [8] In the present study, we found the overall seroconversion rate to be 78.18% which is consistent with the above studies.

With regard to seroconversion rates among different stages of CKD there are variations in different studies. In one of study by Ghadiani MH et al [12] studies comparing the response€rate to the HB vaccine observed CKD stages 3-4 patients had higher response rates than dialysis patients (P <0.001). In another study by Hashemi et al, there was no statistically significant difference in seroconversion rates among different stages of CKD. In the present study, we found seroconversion rates were significantly higher (pvalue=0.014) in the pre-dialysis group (89.4%) than in the dialysis group (69.8%).

There is a significant correlation between BMI **(p<0.01),** lean body mass **(p<0.01)** & MAC **(p<0.01)** with seroconversion. Similar observations were noted in the studies of Vanitha-Rani N et al [13], Pearson et al. [14]and Yigit IP et al. [15]

CONCLUSION

Immunization in the early stages of CKD has a good chance for higher seroconversion i.e. if patients are vaccinated early, pre-dialysis HBV infection may be avoided. Nutritional status also has an impact on the seroconversion of the Hepatitis B vaccine, the better the nutritional status better is the seroconversion.

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ORIGINAL ARTICLE

COMPARISON OF THE ENDOTHELIAL CELL LOSS IN MANUAL SMALL INCISION CATARACT SURGERY WITH VISCOEXPRESSION & MODIFIED BLUEMENTHAL TECHNIQUE

Vaidehi A. Jethwa, **Milind M. Sabnis*****

ABSTRACT

Introduction : Cataract is the most common cause of reversible blindness worldwide. Although it cannot be prevented, normal visual function can be restored with the help of a cataract surgery. Various factors like developmental abnormalities, trauma, metabolic disorders and drug induced changes and significantly age factor, can cause the formation of cataract. This prospective study is conducted to assess the endothelial cell density loss in Manual Small Incision Cataract Surgery (MSICS) with viscoexpression and in Modified Blumenthal technique(MB) post operatively. **Methodology :** The study was conducted in the Department of Ophthalmology at Tertiary care centre, Kolhapur. The duration of the study was from March 2021 to August 2022 and the sample size taken for this study was 122 patients. All patients coming to the ophthalmology OPD, who met the inclusion criteria, were taken up for the study. Specular microscopy was done to assess the corneal endothelial cell count 1 day prior to surgery and 1st,3rd& 5th week post operatively. The corneal endothelial cell loss in 61 patients for MSICS with viscoexpression and 61 patients for Modified Blumenthal technique was done. Cases were age matched and divided into age groups of ten years. Every alternate patient was taken for MSICS with viscoexpression and modified Blumenthal technique respectively. Each group was compared based on the variables mentioned above and results was analyzed. **Results :** At one month of postoperative period there is no statistically significant difference in endothelial cell loss between pre-operative and post-operative assessments. **Conclusions :** Our study suggests that there is a considerable Corneal Endothelial cell loss in regular follow ups on 1st,3rd and 5th week postoperatively, in both the techniques of cataract Surgeries named Manual Small Incision Cataract surgery with viscoexpression and Modified Blumenthal Technique. When compared to their age matched groups, the endothelial cell loss after cataract surgery is more pronounced as the age increases, in both the techniques. At one- month postoperative period there was no statistically significant difference in endothelial cell loss between MSICS with viscoexpression and Modified Blumenthal Technique.

Keywords : Cataract, surgery, endothelial cell loss, MSICS, blindness

INTRODUCTION

In worldwide, the most common cause of reversible blindness is Cataract.[1] There is no method to prevent cataract, but with the help of cataract surgery we can restore normal visual function. Cataracts may cause due to various causes like developmental abnormalities, trauma, metabolic disorders and drug induced

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changes.[2] Age is the main cause of visually significant cataract. So with increasing age, as the lens becomes compact and thicker and also it will lose its optical clarity for any reason, this is called **"senile cataract"**.[2-3] The endothelial cell layer of cornea is a single layer of flat polygonal (hexagonal) epithelial cells having "active-pump" mechanism which appear as a mosaic pattern on slit lamp. The cell density of endothelium is around 3000 cell/mm^2 in young adults which decrease in advanced age. The corneal endothelial cells do not proliferate and the cell loss is compensated by the enlargement, migration of neighboring cells. Corneal decompensation occurs when there is >75% cells are lost. [4] The change in corneal endothelial cell density and morphology occur after cataract surgery and seen more in diabetic patients.

Specular microscopy is a non-invasive photographic technique that allows to visualize and analyze the corneal endothelial cell morphology. Shabtay Dikstein produced a classic paper showing how the specular microscope can be used to investigate corneal endothelium morphology.[5] The instrument projects light onto the cornea and captures the image which is reflected from the optical interface between the corneal endothelium and aqueous humour. At birth, normal cornea has an endothelial cell density of 4500-6000 cells/mm^2, but these cells do not have capacity to regenerate. As the eyes ages, cells enlarge to compensate for the cell loss and to maintain the endothelial cell monolayer that is essential for transparency.[4] Assuming cell loss in range of 0% to 30% after any intraocular surgery, a patient who is having at least 1000-1200 cells/mm^2, will undergo the procedure without an increased risk of corneal oedema postoperatively. The endothelial cell density ranging from 300 to 400 cells/mm^2 is more prone to develop corneal oedema. If the endothelial cell density reaches a critical lower limit, due to surgical interventions like small incision cataract surgery with viscoexpression and modified Blumenthal technique, the transparency can no longer maintained and vision is severely compromised.

Corneal endothelial cell count and morphology can be altered after cataract surgery. It can be measured by specular microscopy. This study was conducted for endothelial cell density loss post-operatively in patients who have been undergone through Manual Small Incision Cataract Surgery (MSICS) with viscoexpression and Modified Blumenthal technique of cataract surgery.

MATERIALS & METHODS

The study was conducted in the Department of Ophthalmology at Tertiary care centre, Kolhapur after getting all the necessary ethical permissions from the Institutional Research Committee. It was a Prospective comparative study. The duration of the study was from March 2021 to August 2022 and the sample size taken for this study was 122 patients. Written informed consent was taken from the patients in their local language. All the patients having senile cataract coming to ophthalmology OPD, belonging to the age group of 51 – 70 years and both the genders were included in the study. Patients having diabetes, glaucoma and uveitis, corneal pathologies, history of previous ocular trauma, ocular surgeries, operative complications like vitreous loss, nucleus drop were excluded from the study. Vision was tested on the standard Snellen's chart. Intraocular pressure management was done by Applanation tonometry under topical anaesthesia. Detailed anterior segment examination was done on slit lamp, before and after pupillary dilatation. Specular microscopy was done to assess the corneal endothelial

cell count 1 day prior to surgery and 1st,3rd& 5th week post operatively. The corneal endothelial cell loss in 61 patients for MSICS with viscoexpression and 61 patients for Modified Blumenthal technique was done. Cases were age matched and divided into age groups of ten years each viz.

51 years – up to 60 years of age
Above 60 years – upto 70 years of age

Every alternate patient was taken for MSICS with viscoexpression and modified Blumenthal technique respective. Each group was compared based on the variables mentioned above and results was analysed.

STATISTICAL ANALYSIS

Master chart was prepared by using MS-EXCEL sheet 200/ and data analysis was done on SPSS Software version 23.0. The recorded data was analysed by unpaired t test.

RESULTS

1. Age distribution in MSICS with Viscoexpression and Modified Blumenthal technique.

In the present study, there were total of 122 eyes of 122 cases were examined and age matched analysis was done. Out of 122 cases, 61 cases had undergone MSICS with viscoexpression and 61 cases had undergone modified Blumenthal technique. In MSICS with viscoexpression, 29 patients (48%) were of the age group 51 years – upto 60 years, 32 patients (52%) were of the age group above 60 years– upto 70 years of age. In modified Blumenthal technique, 28 patients (46%) were of the age group 51 years – upto 60 years, 33 patients (54%) were of the age group above 60 years– upto 70 years of age.

Table 1 : Age distribution in MSICS with Viscoexpression and Modified Blumenthal technique.

Age Group (in Years)	Technique	
	MSICS with Viscoexpression	Modified Blumenthal Technique
51 years – upto 60 years	29 (48%)	28 (46%)
Above 60 years– upto 70 years	32 (52%)	33 (54%)
Grand Total	61	61

2. Sex distribution in MSICS with Viscoexpression and Modified Blumenthal technique.

Table 2 : Sex distribution in MSICS with Viscoexpression and Modified Blumenthal technique

Technique		Modified Blumenthal Technique		MICS with Viscoexpression	
Age Group (in Years)		51 years – upto 60 years	above 60 years - upto 70 years	51 years – upto 60 years	above 60 years - upto 70 years
Sex	Female	19 (68%)	12 (36%)	18 (62%)	13 (41%)
	Male	9 (32%)	21 (64%)	11 (38%)	19 (59%)
Grand Total		28	33	29	32

The following depicts age matched endothelial cell density loss between age group of 51years – up to 60 years and above 60 years – up to 70 years in our study. In both age groups, endothelial cell density was evidently lower in regular follow up as compared to pre-operative values and is statistically significant in both age groups as P value is < 0.05.

Table 3 : Endothelial cell loss (CD) in MSICS with Viscoexpression

Age Group (in Years)	Pre Op (Mean ± SD)	1st F/U (1st week) (Mean ± SD)	2nd F/U (3rd week) (Mean ± SD)	3rd F/U (5th week) (Mean ± SD)	P-Value
51 years– upto 60 years	2565.63 ± 359.10	2500.59 ± 360.07	2408.94 ± 371.01	2322.31 ± 368.35	0.04*
P-values using Paired t test		0.00*	0.00*	0.00*	
above 60 years – upto 70 years	2523.07 ± 318.44	2449.24 ± 315.33	2349.90 ± 314.47	2250.38 ± 332.90	0.01*
P-values using Paired t test		0.00*	0.00*	0.00*	

*indicates significant P value (<0.05)

4. Endothelial cell loss (CD) in Modified Blumenthal technique

The following depicts age matched endothelial cell density loss between age group of 51years – upto 60 years and above 60 years - upto 70 years in our study. In both age groups, endothelial cell density was evidently lower in regular follow up as compared to pre-operative values and is statistically significant in both age groups as P value is < 0.05.

Table 4 : Endothelial cell loss (CD) in Modified Blumenthal technique

Age Group (in Years)	Pre Op (Mean ± SD)	1st F/U (1st week) (Mean ± SD)	2nd F/U (3rd week) (Mean ± SD)	3rd F/U (5th week) (Mean ± SD)	P-Value
51 years – upto 60 years	2608.28 ± 259.58	2519.25 ± 285.52	2410.17 ± 276.36	2285.60 ± 255.47	0.0001*
P -values using Paired t test		0.01*	0.00*	0.00*	
above 60 years – upto /0 years	2657.36 ± 283.44	2548.48 ± 262.80	2445.90 ± 253.27	2315.72 ± 238.12	0.0000*
P-values using Paired t test		0.00*	0.00*	0.00*	

*indicates significant P value (<0.05)

5. Endothelial Cell Loss Comparison In The Age Group 51 Years– Upto 60-Years

As depicted below, the comparison of the endothelial cell loss in MSICS with Viscoexpression and modified Blumenthal technique in age group of 51years – upto 60 years of age, there is no statistical significant difference in endothelial cell loss in both techniques in regular follow ups compared to pre-operative values as p-value is more than 0.05.

Table 5 : Endothelial Cell Loss Comparison In The Age Group 51 Years– Upto 60 Years

Technique	Pre Op (Mean ± SD)	1st F/U (1st week) (Mean ± SD)	2nd F/U (3rd week) (Mean ± SD)	3rd F/U (5th week) (Mean ± SD)
MSICS with Viscoexpression	2565.63 ± 359.10	2500.59 ± 360.07	2408.94 ± 371.01	2322.31 ± 368.35
MB	2608.29 ± 259.59	2519.25 ± 285.53	2410.18 ± 276.37	2285.61 ± 255.48
P- value	0.16	0.19	0.22	0.33

6. Endothelial Cell Loss Comparison In The Age Group Above 60 Years - Upto 70-Years

As depicted below, the comparison of the endothelial cell loss in MSICS with Viscoexpression and modified Blumenthal technique and in age group of above 60 years - upto 70 years of age, there is no statistical significant difference in endothelial cell loss in both techniques in regular follow ups compared to pre-operative values as P value is more than 0.05.

Table 6 : Endothelial Cell Loss Comparison In The Age Group Above 60 Years - Upto 70 -Years

Technique	Pre Op (Mean ± SD)	1st F/U (1st week) (Mean ± SD)	2nd F/U (3rd week) (Mean ± SD)	3rd F/U (5th- week) (Mean ± SD)
MSICS with Viscoexpression	2523.07 ± 318.44	2449.24 ± 315.33	2349.90 ± 314.47	2250.38 ± 332.90
MB	2657.36 ± 283.45	2548.48 ± 262.81	2445.91 ± 253.28	2315.73 ± 238.13
p-value	0.13	0.27	0.32	0.47

DISCUSSION

In the developing world, Manual Small Incision Cataract Surgery-technique is gaining popularity as quick, relatively inexpensive techniques for high volume cataract management. After cataract surgery, change in corneal endothelial cell density and morphology are observed and seen more in diabetic patients. This prospective study was conducted to assess the endothelial cell density loss in two different techniques of cataract surgery. Specular microscopy is non-invasive photographic technique that allows to visualise and analyse the Corneal endothelial cell morphology. The instrument projects light on cornea and captures the image which is reflected from optical interface between corneal endothelium and aqueous humour. So that, we can use specular microscopy in order to compare various variables of the corneal endothelium among different age groups and also analysis the same between two different techniques of cataract surgery.These patients were operated using two techniques namely, Manual Small Incision Cataract Surgery(MSICS) with Viscoexpression and Modified Blumenthal technique.

The operated patients were later classified based on the age group 51 years – upto 60 years and above 60 years - upto 70 years to prove the main aim of the study. Among the patients who underwent cataract surgery, **57** patients (46.72%) were from age group of 51 years – upto 60 years and 65 patients (53.28%) were from age group above 60 years - upto 70 years. Both male and female patients were included in this study.

MSICS WITH VISCOEXPRESSION

In our current study, Mean ECD count

For age group of 51 years upto 60 years,

Pre-op: 2565.63 ± 359.10
1st follow up: 2500.59 ± 360.07
2nd follow up: 2408.94 ± 371.01
3rd follow up: 2322.31 ± 368.35

As depicted above, Corneal endothelial cell loss in MSICS with viscoexpression in age group of 51 years upto 60 years is about 2.53% on 1st follow up, 6.11% on 2nd follow up and 9.48% on 3rd follow up.

As compared to pre-operative values, there is statistically significant difference in endothelial cell loss when assessed on regular follow ups(p=0.04).

For age group of above 60 years – upto 70 years,

Pre-op: 2523.07 ± 318.44
1st follow up: 2449.24 ± 315.33
2nd follow up: 2349.90 ± 314.47
3rd follow up: 2250.38 ± 332.90

As depicted above, Corneal endothelial cell loss in MSICS with viscoexpression in age group above 60 years – upto 70 years is about 2.93% on 1st follow up, 6.86% on 2nd follow up and 10.81% on 3rd follow up as compared to pre-operative values.

As compared to pre-operative values, there is statistically significant difference in endothelial cell loss when assessed on regular follow ups(p=0.01).

This was comparable to a study by Jagani SN et.al (2015)[6], Jagani had done randomized prospective observational study of 100 patients (above the age of 45 years) and study was done at Dr. D. Y. Patil Hospital and Research Center, Pune. He studied the loss of endothelial cell density in the patients underwent

MSICS with viscoexpression.

In previous study, Corneal endothelial cell loss was about 10.63% on 1st follow up, 15.12% on 2nd follow up and 16.24% on 3rd follow up compared to pre-operative values.

As we compared endothelial cell loss with previous study, we see same endothelial cell density loss in both the age groups after examination done on subsequent follow ups who underwent MSICS with viscoexpression cataract surgery and a clear cut reduction in the corneal ECD has been observed with increasing age when correlated with age matched groups.

MODIFIED BLUMENTHAL TECHNIQUE

In our current study, Mean ECD count

For age group of 51 years upto 60 years,

Pre-op: 2608.28 ± 259.58
1st follow up: 2519.25 ± 285.52
2nd follow up: 2410.17 ± 276.36
3rd follow up: 2285.60 ± 255.47

As depicted above, Corneal endothelial cell loss in Modified Blumenthal Technique in age group of 51 years upto 60 years is about 3.41% on 1st follow up, 7.60% on 2nd follow up and 12.37% on 3rd follow up.

As compared to pre-operative values, there is statistically significant difference in endothelial cell loss when assessed on regular follow ups (p=0.0001).

For age group of above 60 years – upto 70 years,

Pre-op: 2657.36 ± 283.44
1st follow up: 2548.48 ± 262.80
2nd follow up: 2445.90 ± 253.27
3rd follow up: 2315.72 ± 238.12

As depicted above, Corneal endothelial cell loss in Modified Blumenthal Technique in age group above 60 years – upto 70 years is about 4.10% on 1st follow up, 7.96% on 2nd follow up and 12.86% on 3rd follow up as compared to pre-operative values.

As compared to pre-operative values, there is statistically significant difference in endothelial cell loss when assessed on regular follow ups(p=0.0000).

This was comparable to a study by Jain K. et al (2015) [7], Jain K had done randomized prospective observational study of 25 patients (51 years to 80 years of age). He studied the loss of endothelial cell density in the patients underwent Modified Blumenthal technique.

In previous study, Corneal endothelial cell loss was about 6.6% on 1st follow up, 6.32% on 2nd follow up and 5.7% on 3rd follow up compared to pre-operative values

As we compared endothelial cell loss with previous study, we see progressive endothelial cell density loss in both the age groups after examination done on subsequent follow ups who underwent Modified Blumenthal Technique cataract surgery and a clear cut reduction in the corneal ECD has been observed with increasing age when correlated with age matched groups.

In age group of 51 years upto 60 years

In MSICS with viscoexpression, the corneal endothelial cell loss is about 2.53% on 1st follow up , 6.11% on 2nd follow up and 9.48% on 3rd follow up and is Modified

Blumenthal Technique, the corneal endothelial cell loss is about 3.41% on 1st follow up, 7.60% on 2nd follow up and 12.37% on 3rd follow up as compared to pre-operative values.

In age group above 60 years upto 70 years

In MSICS with viscoexpression, the corneal endothelial cell loss is about 2.93% on 1st follow up, 6.86% on 2nd follow up and 10.81% on 3rd follow up and in Modified Blumenthal Technique, the corneal endothelial cell loss is about 4.10% on 1st follow up, 7.96% on 2nd follow up and 12.86% on 3rd follow up as compared to pre-operative values.

In our current study, there is no statistically significant difference in endothelial cell loss between pre-operative and post-operative assessments on regular follow ups when compared to age matched groups in both the cataract surgery techniques.

CONCLUSION

The results in our study suggest that there is a considerable Corneal Endothelial cell loss in regular follow ups on 1st, 3rd and 5th week postoperatively, in both the techniques of cataract Surgeries named Manual Small Incision Cataract surgery with viscoexpression and Modified Blumenthal Technique. When compared to their age matched groups, the endothelial cell loss after cataract surgery is more pronounced as the age increases, in both the techniques. At one-month postoperative period there was no statistically significant difference in endothelial cell loss between MSICS with viscoexpression and Modified Blumenthal Technique. As MISCS with viscoexpression and modified Blumenthal technique are economical and less dependent on technology, it may be the appropriate surgical procedure for treatment of Cataract surgery in the developing countries. Also the Modified Blumenthal Technique of MSICS is also highly effective, safe in hard cataracts, involving minimal intraocular manipulation by experienced hands.

Pre-operative evaluation of patients with cataract using specular microscopy. Analysis of endothelial Cell count and morphology can help to determine adequate surgical technique in patients with gross endothelial cell loss and necessary precautions can be taken intra-operatively.

Proper case selection, diligent surgery and adequate post-operative care use essential to maintain a clear cornea. Patient counselling, awareness of the condition and proper care should be taken along with the ocular manifestation.

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ORIGINAL ARTICLE

PROSPECTIVE ANALYSIS OF SPINE SURGERIES IN D. Y. PATIL MEDICAL COLLEGE AND RESEARCH INSTITUTE KOLHAPUR

Vrashab Prabhu, Uday Ghate**, **S. A. Lad******

ABSTRACT

Introduction : The spine is one of the appealing areas in orthopedics where there has been appreciable debate about how to treat its pathologies. Previously the non-operative treatment was used for spine injuries the outcomes of non-operative therapy, neurological recovery remained largely unchanged. A variety of surgical methods and equipment have been developed to enhance the reduction and alignment of the spinal column. **Material and Method :** In this study, all spine cases which were admitted under the Orthopaedic department & cases treated with spine surgeries will be studied for a period of one year from August 2020 to July 2022 selection done in the criteria of all the spine patients who were admitted. The inclusion criteria for this study are all spine-operated cases including traumatic, infective, tumours, and degenerative. Patients with congenital spine pathologies, revision surgery were excluded from this study. **Results :** In the present study, a total of 72 patients were studied, the maximum number of patients belonging to 41 to 60 years' age group, maximum are Hypertensive. 28 (38.89%). Mean Duration of Surgery was 2.63±0.93 hours. Mean Intra-Operative Blood Loss was 305.97±96.23 ml All 72 (100%) patients had minimal disability at 6 weeks and at 3 weeks respectively. The mean VAS score after 6 weeks was 3.53 ± 0.64 and after 3 months 1.34 ± 0.48. In 40 (55.6%) spine patients Post-Operative Neurology was same as pre-operative and in 32 (44.5%) improved neurology. Discussion: In the present study, the Maximum number of patients belonging to 41 to 60years age out of total 72 spine patients, 51 (70.9%) had degenerative, 16 (22.2%) trauma and 5 (6.9%) infective cases, also lumbar region was affected in majority of patients, and total 72 spine patients, 28 (38.89%) Decompression, 11 (15.28%) Decompression with Instrumentation, 9 (12.50%) Decompression with Discectomy, 5 (6.94%) Debridement with Decompression and Instrumentation, 4 (5.56%) Discectomy, 2 (2.78%) Microdiscectomy, 1 (1.39%) Posterior Foraminotomy and Posterior Cervical laminar wiring operations were performed, in this study 40 (55.6%) spine patient's Post-Operative Neurology was same as pre-operative and in 32 (44.5%) improved neurology. **Conclusion:** Degenerative spinal stenosis is a condition that can be safely treated with surgical decompression. It can give long-term postoperative relief of symptoms and return of function, which is independent of the age, severity of radiologic findings, and persistence of neurologic deficit.

Keywords : Spine Surgeries, Degenerative spinal stenosis, Spinal Injuries

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INTRODUCTION

The spine is one of the fascinating areas of orthopaedics where there has been considerable debate about how to treat its pathologies. Before the turn of the 20th century, non-operative treatment was used for spine injuries. However, compared to the outcomes of non-operative therapy, neurological recovery remained largely unchanged. With the advent of posterior instrumentation later, Harrington changed spinal treatment and rehabilitation. Since then, a variety of surgical methods and equipment have been developed to enhance the reduction and alignment of the spinal column. However, with the right surgery, some individuals' root function and spinal cord function may be improved.

The final surgical choice is based on a balance of the projected risks and benefits and is affected by the patient's values and the surgeon's expertise. This is a collaborative process between patients and surgeons. The most frequent reason for doing spinal surgery is to treat degenerative spinal diseases. These ailments include spondylolisthesis, disc herniations, and deformities including scoliosis and spinal stenosis. The choice to continue with spinal surgery is based on the patient's values and knowledge of the particular risks and advantages of the suggested technique. It is crucial that patients understand the risks associated with surgery and how their individual spinal diagnosis and overall medical profile may affect those risks. To fully comprehend and adequately communicate risks to patients, it is crucial to precisely document adverse effects or problems after spine surgery. The dorsolumbar region is the most common location for spine fractures, and 60% of these fractures are burst fractures. TB spine is the other significant spine pathology for which anterior decompression and stabilisation surgery is currently preferred. There are roughly 10 million tuberculosis cases in India. One to three percent of the 10 million people have bone and joint issues. The vertebral lesion, which makes up 50% of all cases of bone and joint tuberculosis, is the most frequent skeletal lesion.

Data examining radiological and clinical variables for the functional outcomes of various spine surgeries are scarce. A lack of research has also been done on the connection between patient survival and functional outcomes. As a result, it is worthwhile to report on the analysis of functional outcomes as well as survival and their relationship in a patient population that may be homogeneous. The present study was conducted to assess the functional outcomes of various spine surgeries conducted in the tertiary care center Kolhapur from August 2020 to July 2022.

AIMS AND OBJECTIVE

Aim : To assess functional outcomes of various spine surgeries conducted in a tertiary care center, from August 2020 to July 2022

Objectives : To study epidemiology - age, sex, and incidence of Spine surgeries in our geographical area. To study functional outcome and patient satisfaction following spine surgeries using VAS analog and Oswestry Disability Index.

MATERIAL AND METHOD

The study was intended in a tertiary care center in this study, all spine cases which were admitted under the Orthopaedic department & treated with spine surgeries will be studied.

Study Period : 2 years (August 2020 to July 2022)
Study design : Prospective analysis.
Sample Size : 30

Collection of data : Study setting: IPD of the tertiary care center is an institutional database to identify all patients who underwent various spine surgeries between August 2020 to July 2022. Demographic data as well as preoperative and postoperative medical conditions. Radiological findings confirmed on the electronic archive. Case selection was done in the criteria of all the spine patients who were admitted in the tertiary care center and undergo surgery.

The diagnosis is based on clinical examination and supported by radiological (X-ray) examination.

In all the cases, primarily routine investigation and radiological examinations were carried out.

On admission, the primary line of management, investigations, and hence surgical procedure is planned and executed.

Patient were examined at 6 weeks and at 3 months post-surgery to evaluate the functional outcome of the patient and patient satisfaction.

DATA ANALYSIS

Continuous data was categorized for statistical purposes, was analyzed using the Chi-square test. Continuous data was analyzed using mean standard deviation, standard error of the mean, student t-test & ANOVA (if more than 2 groups). The association of categorical data was done using the Chi-square test. Independent and paired t-tests and bivariate/ partial correlation of continuous data were done. Linear regression was done if a significant correlation of continuous data is found. Multinomial logistic regression was performed on those risk factors/that show significance between normal and deranged TSH.

Graphical representation of data : MS Excel and MS Word were used to obtain various types of graphs such as bar diagrams.

Statistical software : MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyse data.

INCLUSION CRITERIA : The inclusion criteria include all spine-operated cases in DY Patil Kolhapur between August 2012 to July 2022. It includes Traumatic, Infective, Tumours, and Degenerative.

EXCLUSION CRITERIA : Congenital spine pathologies, Revision surgery.

POST-OPERATIVE EVALUATION:

Postoperatively patients were assessed by the Scoring system at 6 weeks and at 3 months, the functional outcome would be calculated.

SCORING SYSTEM : A concerned generalized scoring system has been included which would evaluate the functional outcome and cover all the inclusion criteria accordingly.

VISUAL ANALOGUE SCALE : It is a measurement instrument for subjective characteristics or attitudes that cannot be directly measured. When responding to a VAS item, respondents specify their level of agreement with a statement by indicating a position along a continuous line between two endpoints.

Oswestry Disability Index (ODI)

0% –20%: Minimal disability, 21%–40%: Moderate Disability, 41%–60%: Severe Disability

61%–80%: Crippling back pain, 81%–100%: These

patients are either bed-bound or have an exaggeration of their symptoms

RESULTS

Table 1 : Distribution of patients according to Age group.

Age group	Frequency	Percent
> 60 Years	16	22.2
21 to 40 Years	24	33.3
41 to 60 Years	32	44.4
Total	72	100.0

Table no. 1 In present study, the Maximum number of patients belonging to 41 to 60 years age group i.e. 32 (44.4%), followed by 21 to 40 Years 24 (33.3%), and more than 60 years 16 (22.2%) respectively. The mean age was 48.60±14.58 years.

Table 2 : Distribution of patients according to Gender.

Gender	Frequency	Percent
Male	39	54.2
Female	33	45.8
Total	72	100.0

Table no. 2 Among total 72 patients, 39 (54.2%) were male, and 33 (45.8%) females. The percentage of male patients was more.

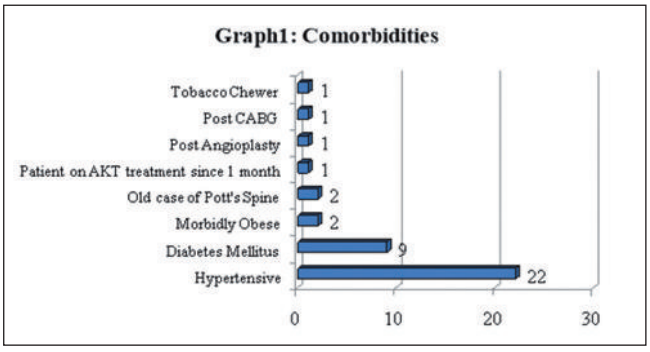

Fig. 1 : Distribution of patients according to comorbidities

Fig. 1 shows out of total 72 patients, maximum number of patients were Hypertensive i.e 22 (20.8%), 9 (6.9%) Diabetes Mellitus, 2 (2.8%) morbidly obese, 2 (2.8%) Old case of Pott's Spine, 1 (1.4%) Patients on AKT treatment (since1 month), post angioplasty, post CABG, tobacco chewer and 40 (55.6%) with no any co-morbidities.

Table 3 : Distribution according to Classification of the patients

Classification	Frequency	Percent
Degenerative	51	70.9
Trauma	16	22.2
Infective	5	6.9
Total	72	100.0

From table no. 3 it was observed that out of total 72 spine patients, 51 (70.9%) had degenerative, 16 (22.2%) trauma and 5 (6.9%) infective cases.

Table 4 : Distribution of patients according to Duration of symptoms

Symptoms	Frequency	Percent
< 1 months	23	31.9
1 month to 6 months	24	33.3
6 months to 1 Year	10	13.9
> 1 Years	15	20.8
Total	72	100.0

From Table no. 4 it was observed that out of a total of 72 spine patients, 24 (33.3%) had symptoms from 1 month to 6 months, 23 (31.9%) since < 1 month, 15 (20.8%) since > 1 year and 10 (13.9%) 6 months to 1 Year. Mean Duration of symptoms was 13.53±24.75 months.

Table 5 : Distribution of patients according to Etiology

Etiology	Frequency	Percent
Canal Stenosis	25	34.72
Fracture	13	18.06
Canal Stenosis + Listhesis	13	18.06
PIVD	10	13.89
Canal Stenosis + PIVD	6	8.33
Spondylodiscitis	5	6.94
Total	72	100.00

From table no. 5 etiology of total 72 spine patients was observed, 25 (34.72%) had Canal Stenosis, 13 (18.06%) fracture and Canal Stenosis + Listhesis, 10 (13.89%) PIVD, 6 (8.33%) Canal Stenosis + PIVD and 5 (6.94%) Spondylodiscitis etiology

Table 6 : Distribution of patients according to Diagnosis

Diagnosis	Frequency	Percent
Canal Stenosis	25	34.72
Spondylolisthesis	13	18.06
Wedge Compression Fracture	13	18.06
PIVD	10	13.89
Canal stenosis with PIVD	6	8.33
Koch spine	5	6.94
Total	72	100.0

From Table no. 6 diagnosis of a total of 72 spine patients were observed, 25 (34.72%) had Canal Stenosis, 13 (18.06%) Spondylodiscitis and Wedge Compression fracture, 10 (13.89%) PIVD, 6 (8.33%) Canal Stenosis with PIVD and 5 (6.94%) Koch spine diagnosis.

Table 7 : Distribution of patients according to Regions of Spinal Cord involved

Regions of Spinal Cord	Frequency	Percent
Upper cervical	0	0.00
Lower cervical	11	15.28
Upper Thoracic	1	1.39
Lower Thoracic	1	1.39
Thoracolumbar	3	4.17
Lumbar	38	52.78
Lumbosacral	18	25.00
Total	72	100.0

In table no. 7 Regions of Spinal Cord involved studied in total 72 spine patients, 38 (52.78%) had Lumbar, 18 (25%), 11 (15.28%) lower cervical, 1 (1.39%) Upper Thoracic and Lower Thoracic, 3 (4.17%) Thoracolumbar regions involved.

Table 8 : Distribution of patients according to Operation performed

Operation Performed	Frequency	Percent
Decompression	28	38.89
Decompression with Instrumentation	11	15.28
Decompression with Discectomy	9	12.50
Debridement + Decompression + Instrumentation	5	6.94
Discectomy	4	5.56
Microdiscectomy	2	2.78
Posterior Foraminotomy	1	1.39
Posterior Cervical laminar wiring	1	1.39
Total	72	100.0

Table no. 8 shows on total 72 spine patients, 28 (38.89%) Decompression, 11 (15.28%) Decompression with Instrumentation, 9 (12.50%) Decompression with Discectomy, 5 (6.94%) Debridement with Decompression and Instrumentation, 4 (5.56%) Discectomy, 2 (2.78%) Microdiscectomy, 1 (1.39%) Posterior Foraminotomy and Posterior Cervical laminar wiring operations were performed

Table 9 : Distribution of patients according to Duration of the surgery

Duration of surgery	Frequency	Percent
< 1 Hour	5	6.9
1 to 2 hours	21	29.2
2 to 3 Hours	29	40.3
3 to 4 hours	12	16.7
> 4 hours	5	6.9
Total	72	100.0

Table no. 9 showed duration of surgery in total 72 patients, maximum duration of surgery was 2 to 3 hours i.e 29 (40.3%), followed by 1 to 2 hours 21 (29.2%), 3 to 4 hours 12 (16.7%), 5 (6.9%) had <1 hour and >4 hour. Mean Duration of Surgery was 2.63±0.93 hours. Mean Intra-Operative Blood Loss was 305.97±96.23 ml

Table 10 : Distribution of patients according to ODS score

ODS score		Frequency	Percent
At 6 weeks	Minimal Disability	72	100
At 3 months	Minimal Disability	72	100

Table no.10 ODS score assessed, it was observed that all 72 (100%) patients had minimal disability at 6 weeks and at 3 weeks respectively.

Table 11 : Distribution of patients according to Mean VAS Score

Mean VAS Score	Mean	Std. Dev.
VAS after 6 Weeks	3.53	0.64
VAS after 3 Months	1.34	0.48

Table no. 11 VAS score was assessed, it was observed that mean VAS score after 6 weeks was 3.53 ± 0.64 and after 3 months 1.34 ± 0.48.

Table 12 : Distribution of patients according to Post-Operative Neurology

Neurology	Frequency	Percent
Improved	32	44.5
Same as Pre-operative	40	55.6
Total	72	100.0

Table no. 12 showed that in 40 (55.6%) spine patients Post-Operative Neurology was same as pre-operative and in 32 (44.5%) improved neurology

DISCUSSION

Distribution of patients according to Age group and Gender (Table 1, 2)

In present study, the Maximum number of patients belonging to the 41 to 60 years age group i.e. 32 (44.4%), followed by 21 to 40 Years 24 (33.3%), and more than 60 years 16 (22.2%) respectively. The mean age was 48.60±14.58 years. 39 (54.2%) were male and 33 (45.8%) females. The percentage of male patients was more.

Studies	Mean age (in years)	Gender
Yoon Jae Seong et al [1]	57.9 ± 6.1 in group 1 59.7 ± 5.2 in group 2	Female/Male (35/10) in group 1, (32/10) in group 2
Suratwala, Sanjeev J. et al [2]	57 years (range, 27–81).	-
Panel Andrew N et al [3]	59.2 years (range 22–91)	52.8% male patients 47.2% female patients
Sara Khor et al [4]	, 61.3 [12.5] years	Female 944 (59.6%)

All the above-mentioned studies had similar and consistent findings with the present study. From various literature and present study findings, it was seen that percentage of male patients was more

Distribution of patients according to comorbidities : (Fig. 1)

Above table shows out of total 72 patients, a maximum number of patients were Hypertensive i.e 22 (20.8%), 9 (6.9%) Diabetes Mellitus, 2 (2.8%) morbidly obese, 2 (2.8%) Old cases of Pott's Spine, 1 (1.4%) Patients on AKT treatment (since1 month), post angioplasty, post CABG, tobacco chewer and 40 (55.6%) with no any co-morbidities.

In Sara Khor et al study, [4] 727 (46.0%) were obese, Rheumatoid arthritis 31 (2%) Hypertension 919 (58%) Diabetes 285 (18%) Asthma 219 (14%) Sleep apnea 245 (15%) coronary artery disease 148 (9%) Prior spine surgery 395 (25%).

Yoon Jae Seong et al study, [1] in Group1, Group 2 patients with cardiovascular diseases (13, 14), Patients with diabetes (06, 05), and with other comorbidities were (2 ,1) (ref 13)

Distribution according to Classification of the patients. (Table 3)

In the present study out of total 72 spine patients, 51 (70.9%) had degenerative, 16 (22.2%) trauma, and 5 (6.9%) infective cases.

In N. Rath et al study [5] it was seen that there were different types of Cord injury patterns The most common pattern is Central Cord syndrome,9 where the central tracts are injured due to shearing and compressive demyelination in the center of the spinal cord. Other injury patterns are anterior cord syndrome where motor pyramidal and spinothalamic tracts are affected or Brown-Sequard lesions where one half of the cord is affected. Some of the injuries

Studies	Mean age (in years)	Gender
Yoon Jae Seong et al [1]	57.9 ± 6.1 in group 1 59.7 ± 5.2 in group 2	Female/Male (35/10) in group 1, (32/10) in group 2
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to the cord occur without any major radiological damage to the spinal column, described as SCIWORA (Spinal Cord Injury without radiological abnormality). section of the adult population where the spinal canal is congenitally narrow, resulting in a reduction of the protective space around the spinal cord by the cerebrospinal fluid column. Similarly, others have a variety of degenerative spinal disorders that result in a narrowing of the space available for the cord, like multiple-level disc protrusions, calcified ligamentum flavum lesions and hypertrophy or Ossification of Posterior Longitudinal Ligaments (OPLL)

Distribution of patients according to Duration of symptoms. (Table 4)

From above table it was observed that out of total 72 spine patients, 24 (33.3%) had symptoms since 1 month to 6 months, 23 (31.9%) since < 1 months, 15 (20.8%) since > 1years and 10 (13.9%) 6 months to 1 Year. Mean Duration of symptoms was 13.53±24.75 month.

In Kristen Radcliff et al study, [6] An as-treated analysis was performed on patients enrolled in the Spine Patient Outcomes Research Trial (SPORT) for the treatment of spinal stenosis or degenerative spondylolisthesis, it was seen that Patients with spinal stenosis with fewer than twelve months of symptoms experienced significantly better outcomes with surgical and nonsurgical treatment relative to those with symptom duration greater than twelve months. There was no difference in outcome of patients with degenerative spondylolisthesis according to symptom duration.

Distribution of patients according to Etiology and diagnosis. (Table 5, 6)

In present study, etiology of total 72 spine patients was observed, 25 (34.72%) had Canal Stenosis, 13 (18.06%) fracture and Canal Stenosis + Listhesis, 10 (13.89%) PIVD, 6 (8.33%) Canal Stenosis + PIVD and 5 (6.94%) Spondylodiscitis etiology ref4

Diagnosis of total 72 spine patients was observed in the study, 25 (34.72%) had Canal Stenosis, 13 (18.06%) spondylodiscitis and Wedge Compression fracture, 10 (13.89%) PIVD, 6 (8.33%) Canal Stenosis with PIVD and 5 (6.94%) Koch spine diagnosis.

In Sara Khor et al study, [4] 1583 (80.6%) patients underwent elective lumbar fusion procedures; the diagnosis of patients was Degenerative disc 473 (30%), Disc herniation 220 (14%), Post laminectomy / failed back syndrome 238 (15%), Instability 274 (17%), Spondylosis 281 (18%), Spondylolisthesis 1033 (65%), Stenosis 1223 (77%), Pseudarthrosis 75 (5%), Other spine problems 264 (17%), Radiculopathy 1461 (92%), Myelopathy 55 (3%).

Distribution of patients according to Regions of Spinal Cord involved. (Table 7)

In present study, regions of spinal cord involved studies in total 72 spine patients, 38 (52.78%) had Lumbar, 18 (25%) Lumbosacral, 11 (15.28%) lower cervical, 1 (1.39%) Upper Thoracic and Lower Thoracic, 3 (4.17%) Thoracolumbar regions involved.

In Andreas G. Tsantes et al study, [7] it was stated that the most frequently involved spinal segment is the lumbar spine (58%), followed by the thoracic spine (30%), and the cervical spine (11%). Hematogenous sacral infection is rare. In most cases, sacral osteomyelitis results from pressure ulcers, trauma, surgery, or through contiguous spread from a pelvic infection.

In present study, also lumbar region was affected in majority of patients.

Distribution of patients according to Operation performed. (Table 8)

In present study on total 72 spine patients, 28 (38.89%) Decompression, 11 (15.28%) Decompression with Instrumentation, 9 (12.50%) Decompression with Discectomy, 5 (6.94%) Debridement with Decompression and Instrumentation, 4 (5.56%) Discectomy, 2 (2.78%) Microdiscectomy, 1 (1.39%) Posterior Foraminotomy and Posterior Cervical laminar wiring operations were performed

In Suratwala, Sanjeev J. et al study,[2] Solid arthrodesis at the first surgery was achieved in 65/80 (81%). Adjacent segment degeneration was noted in 11 patients. Of these, 5 had undergone an extension of their fusion within the study period.

Jacobs et al. [8] reviewed single or double-level anterior inter-body fusion techniques for cervical degenerative disc disease.) They collected 33 studies (2,267 patients) and compared different surgery techniques; anterior cervical discectomy, ACDF using autograft or allograft, or a cage. There was no evidence that one technique was better than another for clinically significant pain relief for patients with chronic cervical degenerative disc disease.

Taku Sugawara et al study,[9] for the treatment of cervical spondylotic myelopathy, widely utilized techniques including ACDF, ACCF, laminoplasty, and laminectomy with fusion improved functional outcome (Class III).

Distribution of patients according to Duration of the surgery. (Table 9)

Duration of surgery in total 72 patients, the maximum duration of surgery was 2 to 3 hours i.e 29 (40.3%), followed by 1 to 2 hours 21 (29.2%), 3 to 4 hours 12 (16.7%), 5 (6.9%) had <1hour and >4 hour. Mean Duration of Surgery was 2.63±0.93 hours. Mean Intra-Operative Blood Loss was 305.97±96.23 ml

Distribution of patients according to ODS score and Mean VAS Score. (Table 10, 11)

In present study, ODS score and VAS score of patients was assessed, it was observed that all 72 (100%) patients had minimal disability at 6 weeks and at 3 weeks respectively. And mean VAS score after 6 weeks was 3.53 ± 0.64 and after 3 months 1.34 ± 0.48.

In Yoon Jae Seong et al study, [1] the level of pain was measured using a 10-point visual analog scale (VAS), and functional disability was assessed with the Oswestry Disability Questionnaire. The VAS score ranged from 0 to 10 (maximum pain), and the Oswestry score ranged from 0 to 100 (maximum severity). Repeated ANOVA was used to calculate the differences within each group during the follow-up. Significant differences between the preoperative and postoperative scores were found in each group ($p < 0.05$). A t-test was used to calculate the differences between the groups. No significant differences were found between the groups.

In Suratwala, Sanjeev J. et al study, [2] the Oswestry Disability Index scores improved from 49.8 to 35.1 (29.5%) ($P < 0.001$). The Roland Morris scores improved from 17.6 to 12.2 (30.7%) ($P < 0.001$). For the SF-36 scales, significant ($P < 0.001$) improvement was seen in all scales except Role Emotional scores and Mental Composite Scales.

In Sara Khor et al study, [4] the median baseline ODI, NRS back pain, and NRS leg pain scores were 46 of 100, 6 of 10, and 6 of 10, respectively. On average, PRO scores improved over time after surgery, with

most of the improvements observed in the first 2 months. The PRO scores were significantly improved at 12 months compared with baseline scores at a population level, but large variations were observed at the individual level.

Distribution of patients according to Post-Operative Neurology. (Table 12)

In the present study, 40 (55.6%) spine patient's Post-Operative Neurology was same as pre-operative and in 32 (44.5%) improved neurology.

In Benzel, Edward C.et al study, [10] the patients were evaluated postoperatively for both stability and neurologic outcome using a modification of the Japanese Orthopaedic Association Assessment Scale. Functional improvement occurred in all but one patient in the laminectomy plus DLS group. The average improvement was 3.1 ± 1.5 points in this group; whereas the average improvement in the laminectomy and the ACDF groups was 2.7 ± 2.0 and 3.0 ± 2.0 points respectively. All of the patients who improved substantially (≥6 points) in the laminectomy plus DLS and the laminectomy alone groups had normal cervical spine contours (lordosis).

In Sara Khor et al study, [4] in the surgical group, leg pain improvement rate was the highest, with 198 of 410 patients (48.3%) achieving MCID at 2 months, and 53 of 83 patients (63.9%) achieving this level of improvement in 12 months. At both 2 and 12 months, patients who had undergone operations had a significantly higher rate of response compared with those who had not had an operation.

SUMMARY

In present study, the maximum number of patients belonging to 41 to 60 years age group i.e 32 (44.4%), followed by 21 to 40 Years 24 (33.3%), and more than 60 years 16 (22.2%) respectively. The mean age was 48.60±14.58 years. Among the total 72 patients, 39 (54.2%) were male and 33 (45.8%) female. The percentage of male patients was more. Maximum number of patients were Hypertensive i.e 22 (20.8%), 9 (6.9%) Diabetes Mellitus, 2 (2.8%) morbidly obese, 2 (2.8%) Old case of Pott's Spine, 1 (1.4%) Patients on AKT treatment (since1 month), post angioplasty, post CABG, tobacco chewer and 40 (55.6%) with no any co-morbidities. 51 (70.9%) had degenerative, 16 (22.2%) trauma and 5 (6.9%) infective cases. 24 (33.3%) had symptoms since 1 month to 6 months, 23 (31.9%) since < 1 months, 15 (20.8%) since > 1years and 10 (13.9%) 6 months to 1 Year. Mean Duration of symptoms was 13.53±24.75 months. 25 (34.72%) had Canal Stenosis, 13 (18.06%) fracture and Canal Stenosis + Listhesis, 10 (13.89%) PIVD, 6 (8.33%) Canal Stenosis +PIVD and 5 (6.94%) Spondylodiscitis etiology. 25 (34.72%) had Canal Stenosis, 13 (18.06%) Spondylodiscitis and Wedge Compression fracture, 10 (13.89%) PIVD, 6 (8.33%) Canal Stenosis with PIVD, and 5 (6.94%) Koch spine diagnosis. 38 (52.78%) had Lumbar, 18 (25%), 11 (15.28%) lower cervical, 1 (1.39%) Upper thoracic and Lower thoracic, 3 (4.17%) Thoracolumbar regions involved. 28 (38.89%) Decompression, 11 (15.28%) Decompression with instrumentation, 9 (12.50%) Decompression with Discectomy, 5 (6.94%) Debridement with Decompression and Instrumentation, 4 (5.56%) Discectomy, 2 (2.78%) Microdiscectomy, 1 (1.39%) Posterior Foraminotomy and Posterior Cervical laminar wiring operations were performed Maximum duration of surgery was 2 to 3 hours i.e 29 (40.3%), followed by 1 to 2 hours 21(29.2%), 3 to 4 hours 12 (16.7%), 5 (6.9%) had <1hour and >4 hour. Mean Duration of Surgery was 2.63±0.93 hours. Mean Intra-Operative Blood Loss was 305.97±96.23

ml All 72 (100%) patients had minimal disability at 6 weeks and at 3 weeks respectively. The mean VAS score after 6 weeks was 3.53 ± 0.64 and after 3 months 1.34 ± 0.48. In 40 (55.6%) spine patients Post-Operative Neurology was same as pre-operative and in 32 (44.5%) improved neurology.

CONCLUSION

Surgical management of symptomatic low- and mid-grade non-dysplastic spondylolisthesis had shown better functional clinical outcomes and more control of pain. Degenerative spinal stenosis is a condition that can be safely treated with surgical decompression. It can give long-term postoperative relief of symptoms and return of function, which is independent of the age, severity of radiologic findings, and persistence of neurologic deficit. These patients often have associated pathology that causes similar symptoms. In our experience, the presence of associated pathology with residual back symptoms may result in poor medium-term (<5 years) functional outcomes. These coexistent conditions have to be addressed, if possible, to maximize the outcome of the surgical procedure. The association of poor outcome with comorbid pathology should be used to council the patient preoperatively as regards expectations from the surgical procedure. Pedicle screw fixation is an excellent treatment for spine fractures. Pedicle screw fixation should be done as early as possible in order to facilitate neurological recovery, help in good nursing care and mobilization of the patient, and prevent deterioration of the neurological status. Pedicle screw instrumentation provides less surgical exposure, correction of deformity and better stabilization of one motion segment above and below the fracture. Surgery remains the preferred mode of treatment, especially for managing complicated spinal tuberculosis. Functional outcomes among those with spinal tuberculosis are affected by pain, spinal cord compression, and rehabilitative intervention. Future works on exploring the functional outcomes of patients with spinal tuberculosis may wish to focus on utilizing an outcome measure that is more specific to spinal cord-related disorders, considering initial functional outcome as a prognostic tool, and measuring the effectiveness of specific rehabilitative regimens in the functional outcome.

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ORIGINAL ARTICLE

THE STUDY OF PROPHYLACTIC ADMINISTRATION OF INTRAVENOUS TRANEXAMIC ACID & ITS EFFECTIVENESS IN REDUCING THE BLOOD LOSS DURING LOWER SEGMENT CAESAREAN SECTION

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ABSTRACT

INTRODUCTION : Obstetric blood loss is a significant factor in maternal mortality and is consistently underestimated, leading to insufficient blood replacement. Caesarean delivery is particularly linked to varying levels of blood loss. This present study was aimed to find whether prophylactic administration of intravenous Tranexamic acid is effective in reducing the blood loss during lower segment caesarean section. **METHODOLOGY :** The present study was conducted on 150 (75 in Study Group and 75 controls) primi and second gravida patients with term gestation and singleton pregnancy who were selected for emergency and elective caesarean section, admitted to tertiary care hospital during the study duration. Patient in study group received injection Tranexamic acid 15mg /kg dose infusion in 100 ml Ringer lactate solution over 10 - 15 minutes prior to the skin incision. Patient in control group will be given plain Ringer lactate. Intraoperative amount of blood loss was measured by gravimetric method. **RESULTS :** Patients who had received tranexamic acid had 105.33 ml less blood loss than patients who did not receive tranexamic acid. Mean blood loss 2 hours after surgery, was 42.63 ml in the study group and it was 76.33 ml in the control group (P= 0.00), suggesting that there was statistically highly significant difference in blood loss. Fall of Hb was more in control group. The mean difference in fall of Hb is 0.25 gm% which is highly significant (P=0.001) **CONCLUSION :** The lower segment caesarean section blood loss may be greatly reduced using tranexamic acid, both during and after the procedure. The frequency of postpartum haemorrhage among the tranexamic acid group is low since use of the drug has not led to excessive blood loss.

Key Words : Tranexamic Acid, Blood Loss, Caesarean Section, Post-partum haemorrhage.

INTRODUCTION

Obstetric blood loss is a significant factor in maternal mortality and is consistently underestimated, leading to insufficient blood replacement. The prevalence of Caesarean sections has been rising recently [1]. Caesarean delivery is particularly linked to varying levels of blood loss. Tranexamic acid is significant because it lessens blood loss and the requirement for blood transfusions. Patients who receive blood are at risk of transfusion-related side effects like febrile non-hemolytic transfusion reactions and blood-borne infections. Blood is a precious commodity. [2] Tranexamic acid is a synthetic lysine derivative that inhibits the lysine binding sites on plasminogen molecules in order to have an anti-fibrinolytic effect.[3-4] Since tranexamic acid

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is an anti-fibrinolytic agent, it strengthens the blood coagulation mechanism. Rapid fibrinogen and fibrin breakdown also takes place after placental delivery, along with an increase in plasminogen activity and fibrin degradation products as a result of the fibrinolytic system being activated. This activation occurs 6 to 10 hours after delivery and might lead to further bleeding. When used as an adjuvant to another regimen or as a safe and effective alternative during the third stage of labour to avoid postpartum haemorrhage, tranexamic acid has an anti-fibrinolytic effect. [5]

MATERIALS & METHODS

The present study was conducted at tertiary care hospital after receiving all the necessary ethical permissions from the Institutional Research Committee. It was Comparative prospective study The sample size taken for this study was 150 patients (75 in Study Group and 75 controls). Patients with primi and second gravida with term gestation, singleton pregnancy, emergency and elective cases for caesarean section were included in this study. Whereas, patients allergic to tranexamic acid, underlying medical illness like cardiac, renal and liver diseases, patients with past history of thromboembolic disorders, PIH, preeclampsia, HELLP, abnormal placenta –abruptio placenta, placenta previa, polyhydramnios, multiple pregnancy, estimated fetal weight > 4kgs (Macrosomia), myoma uterus with pregnancy, and prolonged labour were excluded from the study.

All patients were counselled and informed about the study and the effects of drug Tranexamic acid. Written informed consent was obtained from patients in their local language. Detailed obstetric and medical history was taken in all patients. Weight and height were recorded. Vital parameters were checked. General, systemic and obstetric examination done. USG done to confirm gestational age, fetal well-being, and liquor status. Complete blood count, bleeding time, clotting time at the time of admission, renal and liver function test, urine examination for albumin, sugar and deposit sat the time of admission were done. Half of the Antenatal women were placed in STUDY GROUP (Group A) and half of the antenatal women were placed in CONTROL GROUP (GROUP B). Patient in STUDY group (Group A) received injection Tranexamic acid 15mg /kg dose infusion in 100 ml Ringer lactate solution over 10 - 15 minutes prior to the skin incision. After delivery of baby during Caesarean Section, they received Injection oxytocin 10 units intramuscularly. Patient in CONTROL GROUP (GROUP B) did not receive injection Tranexamic acid. They were given plain Ringer lactate. Lower segment caesarean section done under spinal anaesthesia. After the delivery of the baby, Injection oxytocin 10 units intramuscularly given. Both groups received parenteral Antibiotics just prior to surgery.

Intraoperative amount of blood loss was measured by gravimetric method. Blood collected in the suction container was noted and soaked mops was weighed before and after the surgery. Amniotic fluid and volume of blood loss before placental delivery was included in the study. Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software.

RESULTS

1) In both groups, majority were from 21 to 25 years and the difference between groups was not significant (p value 0.511).
2) In both groups, majority had normal BMI and the difference between groups was not significant (p value 0.348)

3) Mean weight, height and BMI were comparable in both groups and the difference was not significant.

4) Maximum patients were primi gravida in both groups. The difference was not significant (p value 0.614)

5) In both groups, most common indication of LSCS was Foetal distress followed by Cephalo-pelvic Disproportion.

6) The mean duration of surgery in both groups was not statistically significant.

7) Comparison of Birth weight of Baby between study and control groups revealed that there is no statistical difference in birth weight of baby in both the groups.

Table 1 : Pre-op and post-op vitals of patients

Group	Tx Group		Control		P -value
	Mean	Std. Dev.	Mean	Std. Dev.	
SBP before surgery	116.05	7.49	116.72	7.71	0.592
SBP after surgery	114.32	7.21	114.99	7.53	0.581
DBP before surgery	75.84	5.08	78.19	4.93	**0.005**
DBP after surgery	74.64	4.65	77.52	5.06	**0.000**
HR before surgery	84.19	4.15	82.64	4.80	**0.036**
HR after surgery	83.00	8.95	82.93	5.06	0.955
RR before surgery	16.85	0.78	17.03	0.77	0.174
RR after surgery	16.99	0.71	17.15	0.69	0.163

8) Pre-Op and Post-Op Vital Parameters: Heart Rate Systolic BP Diastolic BP Respiratory Rate There was no statistically significant difference in the vital signs before and 2 hours after delivery in both the groups. Only DBP was mildly raised in control group.

Table 2 : Blood Loss in Both Groups

Group	Tx Group		Control		P -value
	Mean	Std. Dev.	Mean	Std. Dev.	
Blood Loss at end of surgery	272.87	61.06	378.20	69.39	**0.000**
Blood Loss 2 hours after end of surgery	42.63	8.15	76.33	12.80	**0.000**
Total Blood Loss	315.49	65.57	454.53	73.00	**0.000**

9) Mean blood loss at end of the surgery was 272.87 ml in the Study Group and it was 378.20 ml in the Control Group (P= 0.00), suggesting that there was statistically highly significant difference in blood loss in both the groups. Patients who had received tranexamic acid had 105.33 ml less blood loss than patients who did not receive tranexamic acid.

Mean blood loss 2 hours after surgery, was 42.63 ml in the Study Group and it was 76.33 ml in the Control Group (P= 0.00), suggesting that there was statistically highly significant difference in blood loss in both the groups. Patients who received tranexamic acid had 33.7 ml less blood loss than patients who did not receive tranexamic acid.

Mean total blood loss 315.49 ml in the Study Group and it was 454.5 ml in the Control Group (p=0.00) suggesting that there was statistically highly significant difference in blood loss in both the groups.

Table 3 : Fall in haemoglobin

Group	Tx Group		Control		P -value
	Mean	Std. Dev.	Mean	Std. Dev.	
Hb (on Admission)	10.40	0.62	10.65	1.37	0.146
Hb (3rd post-operative day)	9.57	0.62	9.68	0.81	0.366
Fall in Hb	0.75	0.36	1.00	0.36	0.000

10) Pre-operative Hb% was compared to Hb% in 3rd postoperative day in both study and control group. There was a fall of 0.75 gm% in study group while the fall in control group was much higher at 1.00 gm%. The mean difference is 0.25 gm% which is highly significant (P=0.001)

11) Need for additional uterotonics: There was no statistical significance (p=0.30) between two groups.

Table 4 : APGAR Score

Group	Tx Group		Control		P -value
	Mean	Std. Dev.	Mean	Std. Dev.	
APGAR at 1 min	7.20	0.55	6.65	0.63	0.000
APGAR at 5 min	8.20	0.55	7.65	0.63	0.000

12) Comparison of Apgar between study and control groups at 1 and 5 minutes showed Study Group had mean Apgar score of 7.20 at 1min & 8.20 at 5 min, while new-borns born to subjects in Control Group had mean Apgar score of 6.65 at 1 min & 7.65 at 5 min. There was significant difference in Apgar score in both the groups. (Mean and Median are same at 1 min & at 5 min in both groups).

Table 5 : Side Effects

Side effects	Group		Total	Chi-Square & p-value
	Tx Group	Control		
Nausea	4(5.33%)	1(1.33%)	5(3.33%)	2.0291, 0.362
Vomiting	5(6.67%)	4(5.33%)	9(6%)	
No side effects	66(88%)	70(93.33%)	136(90.67%)	
Total	75(100%)	75(100%)	150(100%)	

Table shows that incidence of drug side effects like nausea, vomiting was not increased in study group as compared to control group. Thus, suggesting that the use of Tranexamic acid had no significant adverse reactions. Also, there was no incidence of thrombosis in Tx group.

DISCUSSION

Blood Loss during and following Caesarean Section

Mean blood loss at end of the surgery was 272.87 ml in the Study Group and it was 378.20 ml in the Control Group (P= 0.00), suggesting that there was statistically highly significant difference in blood loss in both the groups. Patients who had received tranexamic acid had 105.33 ml less blood loss than patients who did not receive tranexamic acid. Mean blood loss 2 hours after surgery, was 42.63 ml in the Study Group and it was 76.33 ml in the Control Group (P= 0.00), suggesting that there was statistically highly significant difference in blood loss in both the groups. Patients who received tranexamic acid had 33.7 ml less blood loss than patients who did not receive tranexamic acid.

Mean total blood loss 315.49 ml in the Study Group and it was 454.5 ml in the Control Group (p=0.00) suggesting that there was statistically highly significant difference in blood loss in both the groups. Hence from the above result it is obvious that tranexamic acid is a potent antifibrinolytic drug that influences the blood loss in caesarean section and its therapeutic efficacy can be used in minimizing caesarean section blood loss.

Incidence of side effects

Patients in study group and 1 patient in Control Group had nausea. 5 patients in Study Group and 4 in control group had vomiting. The incidence of drug side effects like Nausea, vomiting was not increased in study group as compared to control group. Thus, suggesting that

the use of Tranexamic acid had no significant adverse reactions. Also, there was no incidence of thrombosis in Tx group. They didn't observe any complications caused by TX such as venous thromboembolism, gastrointestinal problems and hypersensitivity.

Also, Mayur et al[8], concluded in their study that not even a single patient in Study Group developed thrombosis and the incidence of side effects like nausea, vomiting and diarrhoea were found to be not statistically significant by difference in both groups. These results were corroborated by Yang H et al[9] and Lind-off C et al[13] 60, Gai MY et al [14].

CONCLUSION

The lower segment caesarean section blood loss may be greatly reduced using tranexamic acid, both during and after the procedure. The frequency of postpartum haemorrhage among the tranexamic acid group is low since use of the drug has not led to excessive blood loss. The use of tranexamic acid has no effect on foetal outcome as shown by the APGAR score. Adverse medication responses are not connected to the administration of tranexamic acid. There is no thrombosis risk among tranexamic acid users.

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ORIGINAL ARTICLE

EVALUATION OF PROGNOSIS AND OUTCOME OF ACUTE INTESTINAL OBSTRUCTION IN ADULTS USING AGESS SBO SCORE

Khan Omar Ali Khan Mukhtader Ali* , *Abhinandan M. Kadiyal**, Aniket Patil****

ABSTRACT

Introduction - Intestinal obstruction is a blockage that keeps food or liquid from passing through your small intestine or large intestine (colon). Various factors like hernias, colon cancer, certain medications, adhesions in the abdomen after surgery etc. are responsible for it. It is observed in all age groups and mostly males are affected by it. If not treated early, sometimes the patient might need to go undergo emergency surgery. **Methodology-** The study was carried out at tertiary care hospital from November 2020 to November 2022. 60 patients were included in this study. Patients fulfilling the inclusion and exclusion criteria were included. **Results-** This AGESS SBO (Acute general emergency surgical severity small bowel obstruction) score can be used in a straightforward and easily visible manner. In most of the patients (23.33%) the AGESS SBO score was 5, followed by AGESS SBO score of 3, and 6 was observed in 13.33% of patients respectively. In this study, The AGESS SBO score was significantly more in patients who died compared to cured patients. A remarkable association was found amongst AGESS score and mortality. **Conclusion-** AGESS SBO score was observed to be considerably more in non-surviving patients compared to cured subjects. A significant correlation was found between AGESS score and mortality.

Keywords - Acute Intestinal Obstruction, abdomen, hernia, AGESS SBO, mortality.

INTRODUCTION

Acute intestinal obstruction (AIO) is the emergency condition developed because of impairment or disruption in the forwarding movement of intestinal materials. The incidence of AIO was found to be 2% to 8% with declining mortality and morbidity.[1] It is observed in all age groups. It is one of the most frequent reasons for patients to undergo emergency surgery.[2] AIO results due to various etiological factors such as adhesions, neoplasm, and herniation. However, adhesions obtained from prior abdominal surgery account for 60% to 75% of cases of small bowel obstruction (SBO). An increased incidence of SBO is associated with lower abdominal and pelvic surgeries (such as hernia repairs, appendiceal, colorectal, and gynecologic surgery). Further conditions contributing to the development of AIO involves inflammatory bowel disease (5% to 7%), intestinal invagination, volvulus, (<5%) intra-abdominal collection, gallstones, and foreign contents.[3-7] Management of AIO involves the correction of physiologic imbalances, providing bowel relaxation and decompression, and removal of the cause of impediment. The two major management techniques available for the treatment of AIO are non-operative (medical) and operative management (surgical).

The clinical variety of presentation and early postoperative consequences of subjects treated

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surgically for AIO are important for understanding the current strategies and their adequacy in the management of this important condition. The current study was commenced to access the clinical presentations, etiological factors, and outcomes after surgical management of AIO in adults.

MATERIALS AND METHOD

The present prospective observational study was carried out at tertiary care hospital from November 2020 to November 2022 after institutional ethical committee approval. The sample size taken for the study was 60 patients. Patients who fulfilled the inclusion criteria such as those aged above 18 years presenting to the emergency department with characteristics of intestinal obstruction were recruited in the study. Intraoperative and postoperative outcomes were noted in predesigned proforma. AGESS SBO score was calculated in all the included subjects.

STATISTICAL ANALYSIS

A master chart of all the outcomes of each patient was prepared using MS Excel. Data were evaluated using SPSS V 1.2.5001 software. Continuous variables were shown in mean±SD whereas, categorical variables were presented in percentage and frequency. Paired T-Test and Wilcoxon signed-rank test were used to compare the variables. The Chi-square test was used to find the association between the variables. P<0.05 was considered statistically significant.

RESULT

Distribution of age

The mean age of the subject was 56.2±17.02 years. The large number of subjects were of age between 61-70 years (28.33%) followed by the patients aged between 51-60 years (18.33%), 41 to 50 years (15%), 71 to 80 years (15%), 21 to 30 years (8.33%), 31 to 40 years (8.33%), >80 years (5%), and <20 years (1.67%) respectively. (Fig.1)

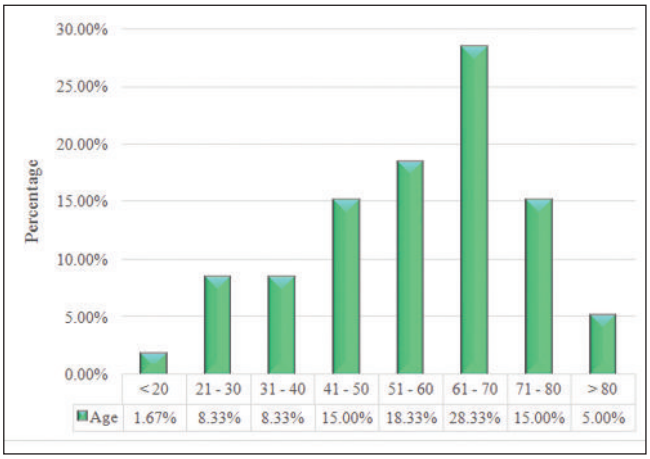

Fig. 1 : Distribution of Age

Distribution of gender

In this study, the percentage of males and females was found to be 71.67% (n=43) and 28.33% (n=17) respectively which indicates that males were predominantly present as compared to females. (Table 1.)

Table 1 : Distribution of Gender

Gender	Frequency	%
Female	17	28.33%
Male	43	71.67%

Distribution of Presenting Symptoms

In this study, the most commonly observed symptom was abdominal pain (n=55, 91.67%) followed by vomiting (n=29, 48.33%), constipation (n=16, 26.67%), abdominal distension (n=8, 13.33%), loose motion followed by constipation (n=8, 13.33%), abdominal swelling (n=4, 6.67%) swelling inguinal region (n=1, 1.67%), and swelling over the umbilical region (n=3, 5%) (Fig.2)

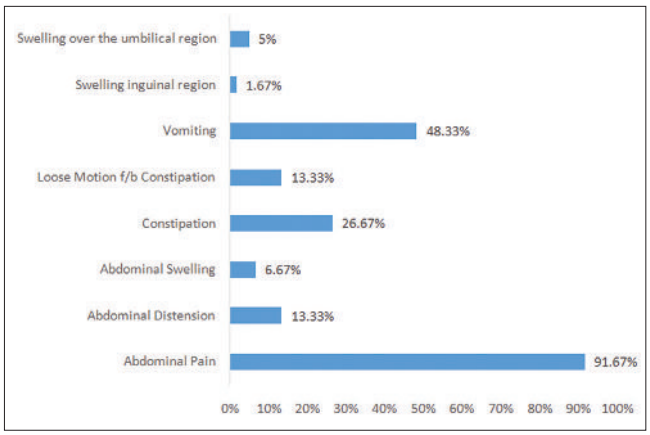

Fig. 2 : Distribution of Presenting Symptoms.

Distribution of past surgical history

A total of 16 patients had past surgical history among which 2 patients had an open appendectomy (3.33%), 1 had exploratory laparotomy (1.67%), 3 subjects had a hysterectomy (5%), 4 had Laproscopic appendectomy (6.67%), 4 had Lower Segment Caesarean Section (6.67%), and 2 had an open tubal ligation (3.33%) (Table 2)

Table 2 : Distribution of past surgical history

Past Surgical History	Frequency	%
Open Appendicectomy	2	3.33%
Exploratory Laparotomy	1	1.67%
Hysterectomy	3	5.00%
Lap appendectomy	4	6.67%
LSCS	4	6.67%
Open tubal ligation	2	3.33%

Distribution of surgical management with exploratory laparotomy

In this study, 8 (13.33%) subjects underwent adhesiolysis surgical management with exploratory laparotomy, followed by adhesiolysis and ileostomy (n=1, 1.67%), Hartman's procedure (n=1, 1.67%), underwent ileostomy (n=7, 11.67%), primary repair of perforation (n=12, 23.33%), resection and anastomosis (n=16, 26.67%), resection and anastomosis + adhesiolysis (n=1, 1.67%), and derotation volvular surgery (n=1, 1.67%) were the surgical management with exploratory laparotomy. (Fig.4)

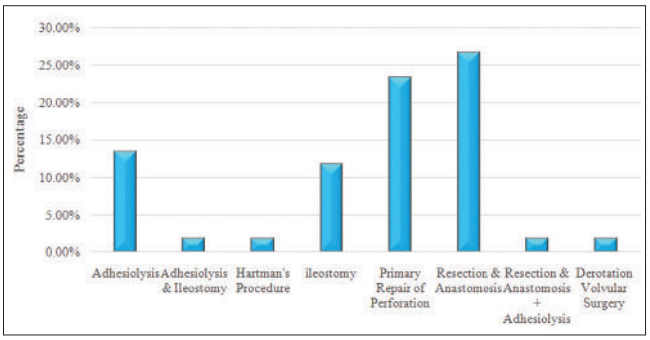

Fig. 3 : Distribution of exploratory laparotomy

Distribution of surgical management with hernia repair.

In 6.67% of patients, hernia repair was performed followed by umbilical hernia repair and inguinal hernia repair performed in 5.01% and 1.67% of patients respectively. (Table 3)

Table 3 : Distribution of surgical management with hernia repair

Hernia Repair	Frequency	%
Inguinal hernia repair	1	1.67%
Incisional hernia repair	4	6.67%
Umbilical hernia repair	2	5.01%

Distribution of intraoperative findings

In this study, perforation (n=13, 23.64%) was the most commonly observed intraoperative finding followed by other operative findings such as adhesions (n=9, 16.36%), bowel ischemia (n=8, 14.54%), bowel gangrene (n=7, 12.73%), obstructed hernia (n=7, 12.73%), perforation and bowel ischemia (n=4, 7.27%), ileal stricture (n=3, 5.45%), adhesions and bowel

ischemia (n=1, 1.82%), rectal mass (n=1, 1.84%), strangulated hernia (n=1, 1.84%), and volvulus (n=1, 1.84%) (Fig.5)

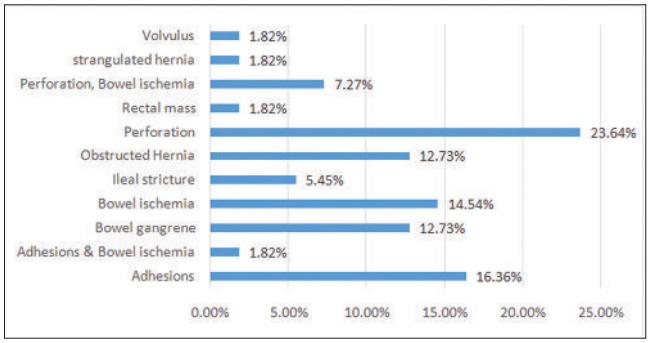

Fig. 5 : Distribution of intraoperative findings

Distribution of mortality

Mortality was noted in 13.33% (n=8) of patients whereas, 86.67% of patients recovered uneventfully. The detailed distribution of subjects according to mortality is depicted in Fig.6

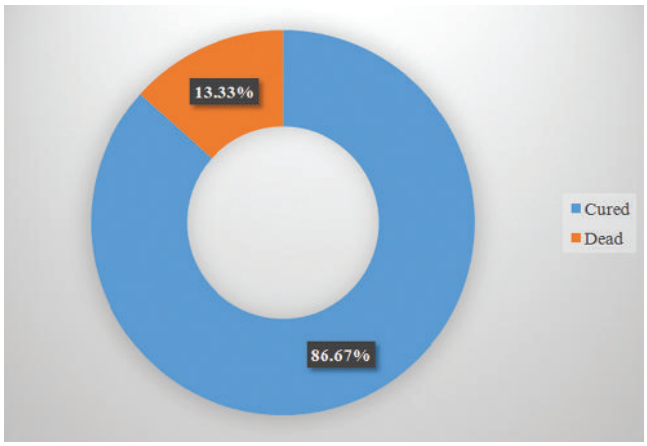

Fig. 6 : Distribution of Mortality

Distribution of surgical complications

In this study, wound infection (13.33%) was found to be the most common surgical complication followed by the anastomotic leak (6.67%), burst abdomen (3.33%), ileus (3.33%), and fecal fistula (1.67%). (Table 4)

Table 4 : Distribution of Surgical Complications

Surgical Complications	Frequency	%
Anastomotic leak	4	6.67%
Burst Abdomen,	2	3.33%
Ileus	2	3.33%
Fecal Fistula	1	1.67%
Wound infection	8	13.33%

Distribution of AGESS SBO score

In most of the patients (23.33%, n=14) the AGESS SBO score was 5, followed by AGESS SBO score of 3, and 6 was observed in 13.33% (n=8) of patients respectively. The detailed distribution of subjects according to AGESS SBO score is depicted in Table 5.

Table 5 : Distribution of AGESS SBO Score

AGESS SBO Score	Frequency	%
0	2	3.33%
1	1	1.67%
2	7	11.67%
3	8	13.33%
4	7	11.67%
5	14	23.33%
6	8	13.33%
7	2	3.33%
8	1	1.67%
9	8	13.33%
11	2	3.33%

Comparison of AGESS SBO score with mortality

In this study, The AGESS SBO score was significantly more in patients who died compared to cured patients (8.375±2.21 vs 4.5±2.32, P=0.00166). A significant correlation was found between AGESS score and mortality (Table 6)

Table 6 : Comparison of AGESS SBO score with Mortality

Mortality	AGESS SBO Score		P-Value
	Mean	SD	
Yes	8.375	2.21	0.00166
No	4.5	2.32	

DISCUSSION

The current study was undertaken to study various ways of clinical presentation, results, interpretation of investigation and surgical management, and early complications of surgical treatment in subjects with AIO.

In the present research, we involved subjects >18 years of age, the mean age of the patients was 56.2±17.02 years. The peak incidence was seen in the 61-70 year's age group (28.33%) followed by 51-60 years (18.33%), 41 to 50 years (15%), 71 to 80 years (15%), 21 to 30 years (8.33%), 31 to 40 years (8.33%), >80 years (5%), and <20 years (1.67%). Various studies have reported different findings which are illustrated in Table 1. The variance in the results may be because of the variation in the inclusion criteria.

Table 7 : Comparison between studies

Studies	Age (years)	Predominant incidence at age group (%)
Bargaje P. et al.[2]	46±15.4	40-50 (23.3%)
Patnaik SK et al.[9]	51.9	51-60 (21%)
Present study	56.2±17.02	61-70 (28.33%)

We found male predominance in patients with AIO than in females (71.67% vs 28.33%). A similar trend is also reported by the various previous reports (Table 2). The possible explanation of male predominance may be a lifestyle, occupation, and socio-economical status.

Table 8 : Comparison between studies

Studies	Male (%)	Female (%)
Shivakumar CR. Et al[8]	66	44
Present study	71.67	28.33

Comparison between studies

In this study, the most commonly observed symptom was abdominal pain (n=55, 91.67%) followed by vomiting (n=29, 48.33%), constipation (n=16, 26.67%), abdominal distension (n=8, 13.33%), loose motion followed by constipation (n=8, 13.33%), abdominal swelling (n=4, 6.67%) swelling inguinal region (n=1, 1.67%), and swelling over the umbilical region (n=3, 5%). In the study of Bargaje P. et al. reported abdominal pain vomiting and constipation as predominant patients presenting characteristics.[2] While, Patanaik SK et al. colicky abdominal pain, nausea and vomiting, distension of the abdomen, and cessation of flatus and bowel. [9]

Here, we found the previous history of surgery in 26.67% of the patients. This includes open appendectomy (3.33%), exploratory laparotomy (1.67%), hysterectomy (5%), laparoscopic appendectomy (6.67%), LSCS (6.67%), and open tubal ligation (3.33%). The study by Alam J. et al. reported the previous history of surgery in 8.74% of the patients that including the closure of ileal perforation, appendectomy, closure of gastro-duodenal, perforation, LSCS, and salpingectomy. [10]

Surgical complications such as wound infection (13.33%) were found to be the most common surgical complication followed by the anastomotic leak (6.67%), burst abdomen (3.33%), ileus (3.33%), and fecal fistula (1.67%). We observed mortality in 13.33% of cases while the uneventful recovery was noted in

86.67% of the patients.[2] Patanaik SK et al. reported no incidence of mortality.[9] Whereas, Shivakumar CR. et al. reported mortality in 6% of the patients.[8]

This AGESS SBO score can be used in the acute abdomen for SBO in a straightforward and easily visible manner. This study, to the best of our knowledge, is among one of few studies assessing participants using AGESS SBO. In most of the patients (23.33%) the AGESS SBO score was 5, followed by AGESS SBO score of 3, and 6 was observed in 13.33% of patients respectively. In this study, The AGESS SBO score was significantly more in patients who died compared to cured patients (8.375±2.21 vs 4.5±2.32, P=0.00166). A remarkable association was found amongst AGESS score and mortality.

LIMITATION OF THE STUDY

Investigator was not blind and the study was single centered all together could have led to some bias. Generalization could be better if a large sample size was included. A multicentre single-blind study with a large sample size involving all the variables is the further recommendation of the study.

CONCLUSION

The study aimed to study the various ways of clinical presentation, results, interpretation of investigation and surgical management, and early complications of surgical treatment in patients with AIO and evaluate the prognosis and outcome of acute intestinal obstruction using AGESS SBO Score [Acute General Emergency & Surgical Severity small bowel obstruction score]. AIO is more common in males at >50 years of age than in females. We observed abdominal pain, vomiting, and constipation were the most common presenting characteristics of AIO. A previous history of abdominal surgery can also affect AIO outcomes. The mortality was seen in 13.33% (n=8) of patients whereas, uneventful recovery was noted in 86.67% of patients. AGESS SBO score was observed to be considerably more in non-surviving patients compared to cured subjects. A significant correlation was found between AGESS score and mortality. Prompt diagnosis and early surgical treatment after resuscitation is the key to favourable treatment outcomes. Further studies are warranted to confirm the present study findings.

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NEWBORN WITH TYPE IV-A CHOLEDOCHAL CYST

Bandi Babita Goud, Prathamesh Kotawadekar*,* ***Pradeep S. Patil*****

ABSTRACT

Choledochal cysts are congenital cystic dilatation of the bile duct that may affect the extrahepatic, intrahepatic, or both biliary radicles. In developing countries, people are more likely to contract this rare illness. We present a highly uncommon case of a male newborn with a Type IV-A choledochal cyst. The definitive diagnosis was made based on magnetic resonance cholangiopancreatography (MRCP) which showed left sided dilated intrahepatic biliary radicals with fusiform dilatation of common bile duct (CBD) and common hepatic duct (CHD). The decision to follow up with a subsequent surgical plan was taken because there were no complications and the bilirubin level returned to normal after conservative treatment.

Keywords : Type IV-A; Choledochal Cyst; Rare; Newborn

INTRODUCTION

A choledochal cyst is an aneurysmal dilatation of the bile duct affecting the extrahepatic, intrahepatic, or both biliary radicles. It is a rare disorder that is more common in developing countries than in the west. [1,5] Although choledochal cysts are typically thought to affect children and infants, cases have been recorded in newborn as well as 80 years old patients; however, 60 percent of such cysts are diagnosed in patients less than 10 years old. The classical triad of symptoms is abdominal mass, pain, and jaundice, present in 19-60 percent of cases.[1,4-5]

The Todani classification (1977) was developed from the earlier Alonso-Lej classification (1959). Todani classified choledochal cysts into 5 types in 1977 based on the cyst's location or degree of dilatation. Type IV-A is a special type as there are multiple cystic intrahepatic dilatations along with the extrahepatic dilatation of biliary system, whereas type IV-B is characterized by multiple dilatations of only the extrahepatic bile ducts.[2,7-8]

The best initial method for assessing intrahepatic and extrahepatic bile duct dilatation is ultrasound. The intrahepatic biliary tree can be more precisely identified using computed tomography. Magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiography and intraoperative cholangiography are definitive studies that demonstrate anatomic details of the biliary tree and the pancreaticobiliary ductal junction.

CASE PRESENTATION

A male newborn was intubated and admitted to the NICU after being delivered by emergency c-section

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at 39 weeks of gestation due to meconium-stained liquor. Additional clinical evaluation revealed a mild yellow discoloration of the skin and sclera as well as intermittent fever. The baby was found to be anaemic and icteric. Investigations revealed haemoglobin of 8.1 gm/dl, total leucocyte count of 14000/ul, and platelets count of 25,000/dl.

Liver function test showed serum bilirubin of 9.6 mg/dl, direct bilirubin 5.1 md/dl and indirect bilirubin 4.5mg/dl.

Ultrasound showed mild dilated intrahepatic biliary radicals and gross dilated common bile duct (CBD) and common hepatic duct (CHD) of diameter 6.3 mm with intraluminal sludge, suggesting type IV-A choledochal cyst. (Fig. 1,2,3)

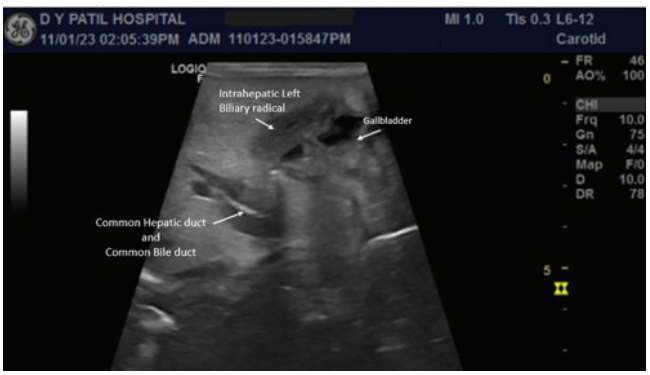

Fig. 1 : USG image showing mild dilated intrahepatic biliary radicals and gross dilated common bile duct (CBD) and common hepatic duct (CHD) with intraluminal sludge.

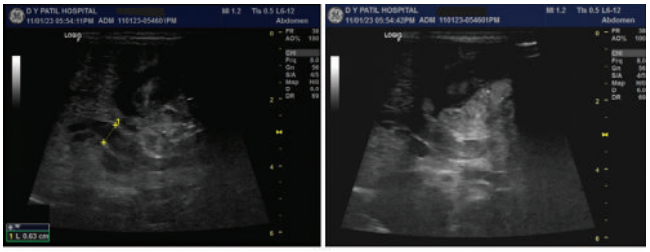

Fig. 2 : USG image showing gross dilated common bile duct (CBD) and common hepatic duct (CHD) of diameter 6.3 mm with intraluminal sludge.

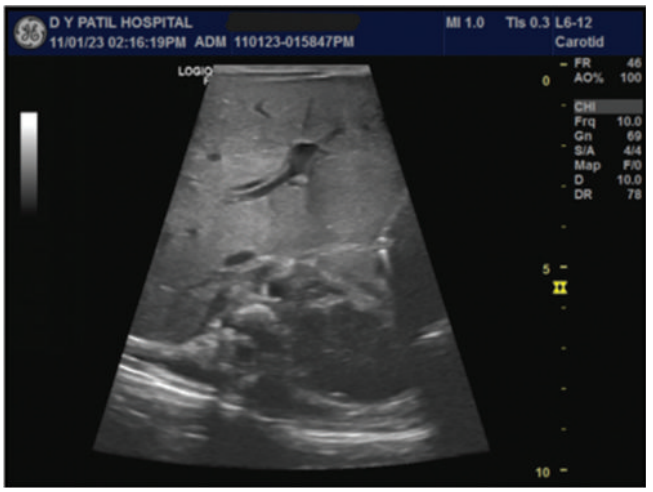

Fig. 3 : USG image showing mild dilated intrahepatic biliary radicals

The definitive diagnosis was made based on magnetic resonance cholangiopancreatography (MRCP) which showed left sided mildly dilated Intrahepatic biliary radicals and right sided intrahepatic biliary radicals were mildly prominent. Fusiform dilatation of common bile duct (CBD) and common hepatic duct (CHD) was seen, measuring 8.2 mm with intraluminal sludge. There was abrupt tapering of distal CBD, 4.5mm proximal to ampulla. The diameter of distal most CBD was 1.4mm. Gall bladder was contracted with intraluminal sludge. (Fig. A, B)

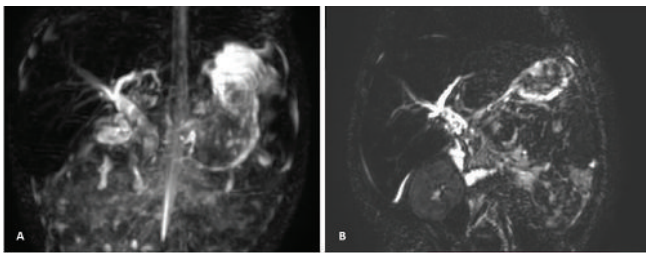

Fig. 4 : 3D MRCP & Fig. B : MRI MRCP PLAIN : Image showing left sided mildly dilated intrahepatic biliary radicals and right sided intrahepatic biliary radicals were mildly prominent. Fusiform dilatation of common bile duct (CBD) and common hepatic duct (CHD) with intraluminal sludge. Abrupt tapering of distal CBD. 4.5 mm proximal to ampulla. Gall bladder was contracted with intraluminal sludge.

The newborn was maintained on conservative treatment initially. After few days bilirubin levels returned to normal and there were no other complications. Hence a follow up was suggested for subsequent surgical plan if required.

DISCUSSION

Choledochal cysts are rare abnormalities of the bile ducts that are distinguished by excessive biliary ductal system enlargement. Vater was the first to describe them in 1723, and Todani et al. classified them in 1977. Even though they might manifest later in life, most cases are usually discovered in the first ten years of life. Many explanations have been put forth, but the Babbitt Theory is the one that is generally accepted, which contends that an irregularity at the junction of the pancreatic duct and the common bile duct outside of the Vater ampulla is the main cause of cyst formation. As a result, a long, shared canal is formed that allows pancreatic juice to enter the bile duct. [6] A long common channel (more than 15 mm) is formed when the pancreatic duct and common bile duct abnormally join together outside of the duodenum wall. This condition is referred to as an aberrant pancreaticobiliary junction, or pancreaticobiliary malfunction.

People who have significant biliary tract expansions are more likely to experience biliary stagnation, which can lead to frequent cholangitis, development of calculi and in the end secondary biliary cirrhosis and malignant transformations.

Surgery involving complete cyst removal and bile duct reconstruction is the best course of action for treating cysts.

Choledochal cysts are traditionally divided into five types according to the Todani classification of bile duct cysts.

TYPE	SUBTYPE	TREATMENT
Type I	Ia: dilatation of extrahepatic bile duct (entire) Ib: dilatation of extrahepatic bile duct (focal segment) Ic: dilatation of the common bile duct portion of extrahepatic bile duct	Cysts are excised and the biliary system is reconstructed with a hepatic-jejunostomy with a Roux-en-Y segment of the jejunum.
Type II	Saccular dilatations from the intrahepatic or supraduodenal extrahepatic bile ducts suggesting a true diverticulum.	The cyst can be removed by making a separate incision in the duct and closing it over the over a T-tube with sutures.
Type III (choledochocele)	A focally dilated segment of distal common bile duct protrudes into the duodenum.	Type III cysts are accessed through the duodenum using both an endoscopic sphincterotomy and a trans-duodenal sphincteroplasty.
Type IV	type IV a: fusiform dilation of the entire extrahepatic bile duct with extension of dilation to the intrahepatic bile ducts type IV b: multiple cystic dilations involving only the extrahepatic bile duct	Extra hepatic cyst excision and bilioenteric anastomosis, which significantly lowers the risk of cholangiocarcinoma. Left hepatectomy is an option if only the left lobe is affected. Roux-en-Y hepatico-jejunostomy is used to achieve the bilioenteric anastomosis.
Type V (Caroli disease)	Rare form of congenital biliary cystic disease manifested by cystic dilations of intrahepatic bile ducts in association with benign renal tubular ectasia and other forms of renal cystic disease.	Localised: segmentectomy or lobectomy. Diffuse: conservative measures.

The choledochal cyst is treated surgically once it has been identified. The pancreatic duct opening must be carefully identified and protected. The most effective surgical approach to treating choledochal cysts entails completely removing the cyst before joining the small intestine to the bile duct.

In our patient there were mildly dilated intrahepatic biliary radicals and fusiform dilatation of CBD and CHD. As such there were no complications and bilirubin level came to normal after conservative treatment so decision was made of follow up for further surgical plan.

CONCLUSION

Choledochal cysts present in their typical form very infrequently. The Type IV-A is a unique type because it is uncommon and has multiple cystic intrahepatic dilatations in addition to extrahepatic biliary system dilatations. The best initial method for assessing biliary duct system dilatation is ultrasound, and the gold standard for further evaluation is MRCP. Cyst excision surgery is performed in conjunction with a partial hepatectomy. Most patients with extra hepatic bile duct cysts who have had them properly removed and rebuilt have excellent prognosis.

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