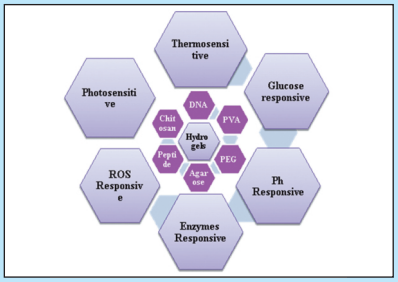
ISSN 0974-2743

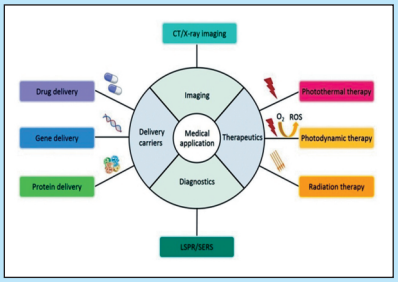
MJDYPU

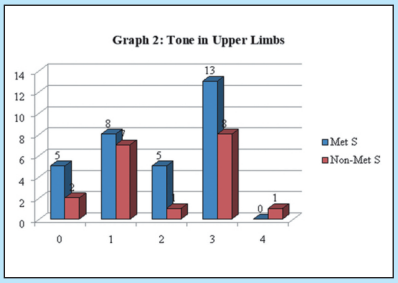
DNYANSHODH

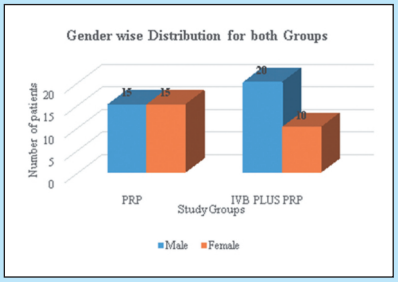
Medical Journal D.Y. Patil University, Kolhapur

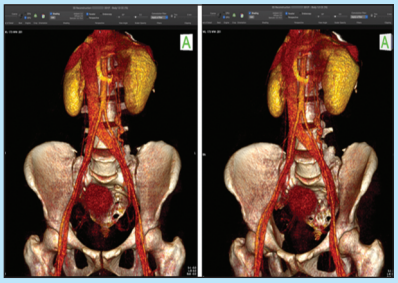
Vol. XV | Issue - I | September - 2022

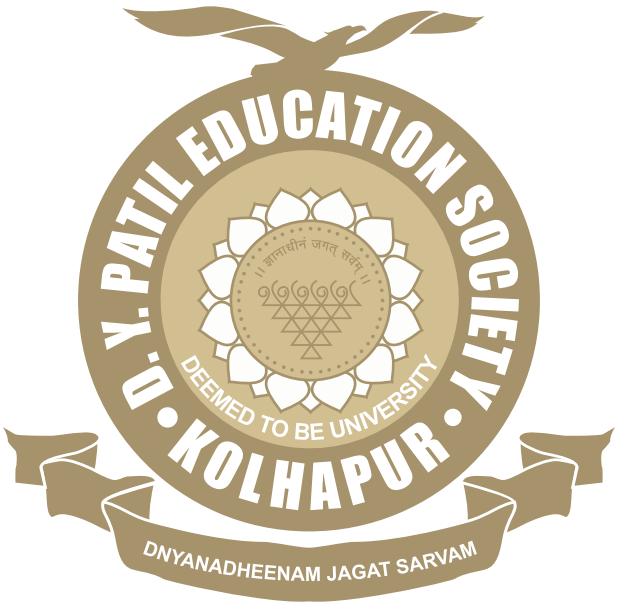












MJDYPU
is published biannually by

Registrar,
D. Y. Patil University,
Kolhapur - 416 006.
Maharashtra (INDIA)
www.dypatilkolhapur.org
ISSN 0974 - 2743
Index to Proquest Medical Library

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Artificial Intelligene (AI) : A Game Change is Health Care and Medicine

The amalgamation of Artificial Intelligence (AI) into healthcare and medicine has steered in a new era of possibilities and advancements. This union of cutting-edge technology and the field of medicine holds huge potential to revolutionize patient care, diagnosis, treatment, and overall healthcare management. In the current scenario of the complex landscape of modern healthcare, it becomes increasingly evident that AI is not just a tool but a game-changer that demands our attention.

One of the most noteworthy contributions of AI in healthcare lies in its ability to process and analyse vast amounts of medical data in a very less time when compared to a human. This analytical expertise is evident in diagnostic imaging, where AI algorithms can promptly identify anomalies in medical images, aiding radiologists in making accurate diagnoses. By doing so, AI minimizes human error, enhances efficiency, and ultimately improves patient outcomes.

Furthermore, AI-driven predictive analytics have demonstrated their potential to forecast disease outbreaks, patient admission rates, and even individual patient deterioration. These insights empower healthcare professionals to allocate resources effectively, proactively manage patient conditions, and prevent adverse events. This shift from reactive to proactive care not only saves lives but also reduces the burden on healthcare systems.

The application of AI extends beyond diagnostics to the realm of personalized medicine. By analysing an individual's genetic makeup and medical history, AI algorithms can predict patient responses to specific treatments, leading to tailored interventions that maximize therapeutic success. This individualized approach minimizes adverse effects and accelerates recovery, heralding a new era of patient-centric care.

However, the integration of AI in medicine is not without its challenges. Ethical concerns surrounding data privacy, bias in algorithms, and the fear of replacing human expertise persist. Striking a balance between technological innovations and maintaining the human touch in medicine is crucial. It is imperative that medical professionals remain at the forefront of AI development, guiding its implementation and ensuring that the human aspect of patient care remains paramount.

Incorporating AI education into medical curricula is essential to equip future healthcare professionals

with the skills needed to collaborate seamlessly with AI technologies. This partnership between human expertise and AI intelligence will undoubtedly yield the best outcomes for patients.

In conclusion, the integration of AI into healthcare and medicine presents a turning point moment in the history of medicine. Its capacity to enhance diagnostics, enable proactive care, and usher in personalized treatments highlights its transformative potential. As a responsible healthcare professionals, it is our responsibility to harness AI's capabilities while upholding the ethical standards and human connection that define the practice of medicine. By embracing AI, we stand on the cusp of a healthier, more efficient, and patient-centric healthcare landscape.

Dr. Arpita Pandey Tiwari
Associate Professor,
Department of Medical Biotechnology & Stem Cell and
Regenerative Medicine Centre for Interdisciplinary Research

REVIEW ARTICLE

APPLICATIONS OF BIOCOMPATIBLE AND BIODEGRADABLE SODIUM ALGINATE HYDROGELS

Mahima Choudhary, Kajal Gaikwad**,* ***Shivaji Kashte******

ABSTRACT

Ionotropic alginate hydrogels are flexible substances for an extensive variety of programs. Their biocompatibility and biodegradability have made them the best applicants for biomedical programs along with tissue engineering and drug delivery. Most of the studies associated with ionotropic alginate hydrogels have been performed on Ca_2^+-cross-connected alginate. However, alginate can produce hydrogels with a big variety of divalent and trivalent cations. In current years, the cross-linking of alginate with Fe_3^+ cations has attracted a growing hobby because of its splendid homes. The specific coordination of Fe^{3+} cations has been located to be important for mechanical strength, porosity, swelling, and different physicochemical homes of the cloth not often visible in different ionotropic alginate hydrogels. In addition, the wealthy redox chemistry of Fe_3^+ cations has been exploited for an extensive variety of programs, along with drug delivery, tissue engineering, and environmental remediation. In this overview we spotlight the latest that worries Fe_3^+-cross-connected alginate hydrogels, encompassing from homes and synthesis to programs and destiny perspectives. We consider that this overview could stimulate revolutionary thoughts and sell the studies of this cloth, mainly to novel practical substances with the new and rising program.

Keywords : Biomaterials, Hydrogels, Biocompatibility, Biodegradability.

INTRODUCTION

Biomaterials have historically been designed to be inert and now no longer engage with organic structures withinside the host. Materials derived from herbal sources (e.g., wood) have an extended record as biomaterials and feature regularly been used to update tissues misplaced to disorder or trauma (e.g., prosthetics). Since the early 20th century, however, those substances started out to get replaced through artificial polymers, ceramics, and metallic alloys, because of their higher overall performance and greater reproducible properties, compared to clearly derived substances [1-2] The greater latest evolution in this discipline has now caused the definition of a biomaterial as a fabric supposed to interface with organic structures to evaluate, treat, increase, or update any tissue, organ, feature of the frame [3] and barriers for the usage of biomaterials is nevertheless expanding. The layout of recent biomaterials is now centered on mimicking many capabilities of the extracellular matrices of frame tissues, as those can adjust host responses in a well-described manner, and clearly-derived substances have recently been

*Junior Resident, **Ph.D. Student, ***Ph. D. Assistant Professor, Department of Stem Cell and Regenerative Medicine, Centre for Interdisciplinary Research, D. Y. Patil Education Society (Deemed to be University), Kolhapur- 416006 (MS), India
Corresponding E-mail : shivajikashte.cir@dypgroup.edu.in

regaining plenty of interest due to their inherent biocompatibility**.**

Alginate is a certainly going-on anionic polymer normally acquired from brown seaweed and has been notably investigated and used for lots of biomedical packages, because of its biocompatibility, low toxicity, distinctly low cost, and moderate gelation with the aid of using the addition of divalent cations including Ca_2^+. [4] Alginate hydrogels may be organized with the aid of using diverse cross-linking methods, and their structural similarity to extracellular matrices of residing tissues permits extensive packages in wound healing, shipping of bioactive marketers including small chemical pills and proteins and molecular transplantation. Alginate wound dressings preserve a physiologically wet microenvironment, decrease bacterial contamination on the wound site, and facilitate wound healing. Drug molecules, from small chemical pills to macromolecular proteins, may be launched from alginate gels in a managed manner, relying at the cross-linker sorts and cross-linking methods. In addition, alginate gels may be orally administrated or injected into the frame in a minimally invasive manner, which permits significant packages withinside the pharmaceutical arena. Alginate gels are also promising for molecular transplantation in tissue engineering. Tissue engineering goal to offer man-made tissue and organ replacements to sufferers who are suffering the loss or failure of an organ or tissue. [5] Hydrogels are used to supply cells to the preferred site, offer an area for new tissue formation, and manipulate the shape and characteristics of the engineered tissue. In this review, the overall residences of alginate and its cutting-edge and potential programs in biomedical technological know-how and engineering will be discussed.

Classification of Hydrogel :

Hydrogels can be divided into two categories by the forming molecule types, natural polymer, and synthetic polymer. Commonly, naturally derived hydrogels including cellulose, chitosan, alginate, and agarose are common in the natural environment. They keep their biochemical and biocompatible properties with the host tissue, although with relatively weak mechanical strength, difficulty in reproducing accurate formulation and drug loading, and potential immunogenic risks. Synthetic polymers are man-made polymers derived from polymerized monomers. Hydrogels made of synthetic polymers like poly (ethylene glycol) (PEG), poly (vinyl alcohol) (PVA), and synthetic biopolymers including peptide and DNA possess high water absorption capacity, well-defined structure, wide varieties of raw chemical resources, intelligent reply to different stimuli. By far, hydrogels can be formulated with various polymers to endow them with diverse functionality in biomedical applications. Based on the responsive stimuli, smart hydrogels could be divided into physical, chemical, and biochemical responsive hydrogels. They are extensively applied in biomedical fields, including therapeutic delivery contact lenses, corneal prostheses, wound healing, bone regeneration, and tissue engineering. [6]

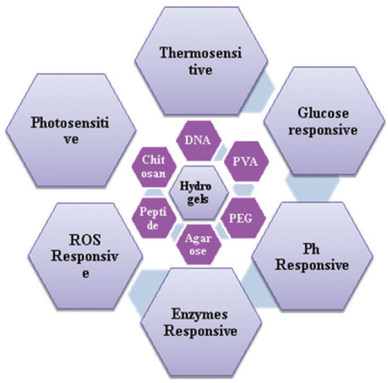

Fig. 1 : Schematic diagrams showing the rational design of smart hydrogels.

Hydrogels have been investigated extensively by researchers all over the world due to their outstanding physical/chemical/biological features and potential applications in many different fields. Hydrogels are generally soft and semi-solid matters that possess a polymeric three-dimensional hydrophilic networks with the ability to maintain large amounts of water with tunable biocompatibility, biodegradability, and mechanical properties. Hydrogels play a significant role in the biomedical fields due to their biocompatibility and low toxicity. They can be divided in two categories, natural polymer, and synthetic polymer. They act as a framework to support the structure of hydrogels. Commonly, naturally derived hydrogels including cellulose, chitosan, alginate, and agarose are common in the natural environment. They keep their biochemical and biocompatible properties with low toxicity, although with relatively weak mechanical strength. Hydrogel made of synthetic polymers are chemically strong but cell toxic like polyethylene glycol (PEG), polyvinyl alcohol (PVA), and synthetic biopolymers including peptide and DNA possess high water absorption capacity and well-defined structure. They are extensively applied in biomedical fields, including therapeutic delivery, contact lenses, corneal prosthesis, wound repair and regeneration, bone regeneration and tissue engineering, skeletal muscle regeneration, and spinal cord injury.

Alginate : general properties

Commercially available alginate is typically extracted from brown algae (Phaeophyceae), including *Laminaria hyperborea, Laminaria digitata, Laminaria japonica, Ascophyllum nodosum, and Macrocystis pyrifera*.[7] by treatment with aqueous alkali solutions, typically with NaOH.[8] The extract is filtered, and either sodium or calcium chloride is added to the filtrate in order to precipitate alginate. This alginate salt can be transformed into alginic acid by treatment with dilute HCl. After further purification and conversion, water-soluble sodium alginate powder is produced.[9] On a dry weight basis, the alginate contents are 22–30% for *A. nodosum* and 25–44% for *L. digitata*.[10] Bacterial biosynthesis may provide alginate with more defined chemical structures and physical properties than can be obtained from seaweed-derived alginate. Bacterial alginate can be produced from *Azotobacter and Pseudomonas*. The pathway of alginate biosynthesis is generally divided into (i) synthesis of precursor substrate, (ii) polymerization and cytoplasmic membrane transfer, (iii) periplasmic transfer and modification, and (iv) export through the outer membrane.[11] Recent progress in the regulation of alginate biosynthesis in bacteria, and the relative ease of bacteria modification may enable the production of alginate with tailor-made features and wide applications in biomedical applications.

Biocompatibility of Sodium Alginate

Although the biocompatibility of alginate has been notably evaluated in vitro in addition to in vivo, there is nonetheless debate concerning the effect of the alginate composition. Much of this confusion, though, probably pertains to various stages of purity withinside the alginate studied in diverse reports. For example, it has been said that excessive content material alginates have been immunogenic and about 10 instances stronger in inducing cytokine manufacturing as compared with excessive G alginates. However, others discovered very little immune reaction around alginate implants S. The immunogenic reaction on the injection or implantation web websites is probably attributed to impurities last withinside the alginate. Since alginate is acquired from herbal sources, diverse impurities along with

heavy metals, endotoxins, proteins, and polyphenolic compounds may want to probably be present. Importantly, alginate purified with the aid of using a multi-step extraction technique to a totally excessive purity did now no longer result in any good-sized overseas frame response while implanted into animals. Similarly, no good-sized inflammatory reaction become discovered while gels fashioned from commercially available, fantastically purified alginate were subcutaneously injected into mice.

Alginate is a polysaccharide of natural origin that exhibits exceptional qualities such as biocompatibility, gel-forming capacity, non-toxicity, and processing ease. Sodium alginate, a hydrogel form of alginate, oxidized alginate, and other alginate-based polymers are employed in different biomedical sectors, particularly in drug delivery, wound healing, and tissue engineering, because of the exceptional capabilities of alginate. Alginate is readily processed into a variety of 3D scaffolding materials, such as hydrogels, microcapsules, microspheres, foams, sponges, and fibers. These alginate-based bio-polymeric materials are used in particular for tissue healing, scar healing, wound healing, cartilage repair and treatment, new bone regeneration, and the creation of scaffolds for cell growth. Although alginate and its composites are more effectively used in a variety of organs and tissues, including bone, teeth, cartilage, skin, and liver, at the moment they are unable to simultaneously meet all of the strategy parameters (mechanical strength, degradation, or bioactivities) necessary for tissue engineering. By using certain physical and chemical procedures, alginate may be easily transformed and blended, and the new alginate derivative materials that are produced have varied structures, functions, and qualities with better mechanical strength, cell affinity, and gelation properties. All things considered, it was determined that alginate gel and alginate composites are presently going to be promising biomaterials in the field of various tissue engineering. Tissue engineering is a novel medical regenerative approach that promises the regeneration of damaged tissues. Tissue engineering employs both synthetic and natural biomaterials to promote tissue or organ growth outside of the body. An anionic polysaccharide like alginate played a significant role in a hydrogel formulation due to its ideal deflocculating, gelling, protein absorption potential, biocompatibility, moisture retention, biodegradability, and visco elastic characteristics. The wound healing process is one of the most complex biological mechanisms, resulting in the formation of fibrotic tissue masses in the absence of hormone activity for skin tissue defects caused by trauma and burns. As a result, Wang et al. created a benlysta-loaded sodium alginate hydrogel with excellent anti-inflammatory and skin tissue regeneration properties. Furthermore, the characterization studies revealed that the benlysta loaded sodium alginate hydrogel has an ideal swelling rate, sustained rate of drug release, biodegradability, and excellent fibroblast and epidermal cellular proliferation. This benlysta-loaded sodium alginate hydrogel will eventually provide new ideas for the treatment and management of skin tissue defects.

HYDROGEL FORMATION AND ITS PROPERTIES

Methods of gelling

Alginate is typically used in the form of a hydrogel in biomedicine, including wound healing, drug delivery, and tissue engineering applications. Hydrogels are three-dimensionally cross-linked networks composed of hydrophilic polymers with high water content. Hydrogels are often biocompatible, as they are structurally like the macromolecular-based components in the body, and can often be delivered into the body

via minimally invasive administration. Chemical and physical cross-linking of hydrophilic polymers are typical approaches to forming hydrogels, and their physicochemical properties are highly dependent on the cross-linking type and cross-linking density, in addition to the molecular weight and chemical composition of the polymers. Here, we summarize various approaches to cross-link alginate chains to prepare gels, and how these approaches alter the hydrogel properties relevant to biomedical applications.

Ionic cross-linking

The most common method to prepare hydrogels from an aqueous alginate solution is to combine the solution with ionic cross-linking agents, such as divalent cations (i.e., Ca^{+2}). The divalent cations are believed to bind solely to guluronate blocks of the alginate chains, as the structure of the guluronate blocks allows a high degree of coordination of the divalent ions. The guluronate blocks of one polymer then form junctions with the guluronate blocks of adjacent polymer chains in what is termed the egg-box model of cross-linking, resulting in a gel structure (Fig. 4). Calcium chloride ($CaCl_2$) is one of the most frequently used agents to ionically cross-link alginate. However, it typically leads to rapid and poorly controlled gelation due to its high solubility in aqueous solutions. One approach to slow and control gelation is to utilize a buffer containing phosphate (e.g., sodium hexametaphosphate), as phosphate groups in the buffer compete with carboxylate groups of alginates in the reaction with calcium ions, and retard gelation. Calcium sulfate ($CaSO_4$) and calcium carbonate ($CaCO_3$), due to their lower solubilities, can also slow the gelation rate and widen the working time for alginate gels. For example, an alginate solution can be mixed with $CaCO_3$, which is not soluble in water at neutral pH. Glucono-δ-lactone is then added to the alginate/$CaCO_3$ mixture in order to dissociate Ca^{+2} from the $CaCO_3$ by lowering the pH. The released Ca^{+2} subsequently initiates the gelation of the alginate solution in a more gradual manner.

Biodegradation of alginate and its hydrogels

Alginate is inherently non-degradable in mammals, as they lack the enzyme (i.e., alginase) that can cleave the polymer chains, however ionically cross-connected alginate gels may be dissolved through the discharge of the divalent ions cross-linking the gel into the encircling media because of alternate reactions with monovalent cations consisting of sodium ions. Even if the gel dissolves, though, the common molecular weights of many commercially to be had alginates are better than the renal clearance threshold of the kidneys, and possibly will now no longer be absolutely eliminated from the body. An appealing method to make alginate degradable in physiological situations consists of partial oxidation of alginate chains. Slightly oxidized alginate can degrade in aqueous media, and these materials have demonstrated potential as a delivery vehicle of drugs and cells for various applications.

BIOMEDICAL APPLICATION

Pharmaceutical applications

The traditional function of alginate in pharmaceutics consists of serving as a thickening, gel-forming, and stabilizing agent, as alginate can play an extensive function in controlled-release drug products. Oral dosage paperwork is presently the maximum common use of alginate in pharmaceutical applications, however, the use of alginate hydrogels as depots for tissue-localized drug transport is growing. Here, we in

short describe the latest development in managed drug transport the use of alginate and/or its derivatives.

Delivery of small chemical drugs

Delivery of small chemical capsules Alginate gels had been investigated for the transport of quite a few low molecular weight capsules, and are likely maximum beneficial while a number one or secondary bond among the drug and the alginate may be exploited to adjust the kinetics of drug release. Alginate gels are commonly nanoporous (pore size ~5 nm).[12], main to the fast diffusion of small molecules via the gel. For example, the discharge of flurbiprofen from ionically cross-linked, partly oxidized alginate gels is nearly entire in 1.5 h. However, incorporation into beads shaped from partly oxidized alginate withinside the presence of each calcium ions and adipic acid dihydrazide (mixture of ionic and covalent cross-linking) brought about a extent because of the multiplied variety of cross-hyperlinks and resultant decreased swelling.[13-14] The managed and localized transport of antineoplastic marketers has additionally been done the use of partly oxidized alginate gels. Multiple capsules may be loaded into alginate-primarily based totally gels for simultaneous or sequential transport, because the chemical shape of the drug and mode of incorporation will dramatically regulate the discharge kinetics. For example, methotrexate (non-interactive with alginate) changed into hastily launched via way of means of diffusion, whilst doxorubicin, covalently connected to the alginate, changed into launched thru chemical hydrolysis of the cross-linker. Mitoxantrone, ionically complexed to alginate, changed into simplest launched after the dissociation of the gel.[14]

Protein Delivery

The protein-drug market place is hastily growing, and diverse protein capsules are to be had due to the improvement of recombinant DNA technology. Alginate is a first-rate candidate for the transport of protein capsules, considering proteins may be integrated into alginate-primarily based totally formulations below enormously moderate situations that decrease their denaturation, and the gels can guard them against degradation till their launch. A style of techniques was investigated to manipulate the fee of protein launch from alginate gels. In general, the discharge fee of proteins from alginate gels is rapid, because of the inherent porosity and hydrophilic nature of the gels. However, heparin-binding growth factors consisting of vascular endothelial increase factor (VEGF) or simple fibroblast increase factor (bFGF) show off similar, reversible binding to alginate hydrogels, allowing a sustained and localized launch.[14-15] The launch in this situation may be conveniently manipulated by changing the degradation fee of the gels (e.g., use of in-part oxidized alginate), to make protein launch as a minimum in part depending on the degradation reaction.[15]

Wound dressing

The remedy of acute and persistent wounds is an urgent want in lots of sides of medicine, and alginate-primarily based totally wound dressings provide many tremendous features. Traditional wound dressings (e.g., gauze) have supplied particularly a barrier function – retaining the wound dry by permitting evaporation of wound exudates even as stopping access of pathogens into the wound. [16] In contrast, cutting-edge dressings (e.g., alginate dressings) offer wet wound surroundings and facilitate wound healing.[17] Alginate dressings are normally produced through ionic cross-linking of an alginate answer with calcium ions to shape a gel, observed through processing to shape

freeze-dried porous sheets (i.e., foam), and fibrous non-woven dressings. Alginate dressings withinside the dry shape soaks up wound fluid to re-gel, and the gels then can deliver water to a dry wound, keeping a physiologically wet microenvironment and minimizing bacterial contamination on the wound site. These features also can sell granulation tissue formation, speedy epithelialization, and healing. Various alginate dressings along with AlgicellTM (Derma Sciences) AlgiSite MTM (Smith & Nephew), Comfeel PlusTM (Coloplast), KaltostatTM (ConvaTec), SorbsanTM (UDL Laboratories), and TegagenTM (3M Healthcare) are commercially available.

Tissue regeneration with protein and cell delivery

Alginate gels were broadly explored over the past numerous many years as a car to supply proteins or cell populations that could direct the regeneration or engineering of diverse tissues and organs withinside the body. The diverse programs of alginate gels have exploited the extensive variety of gelling approaches, bodily properties, cellular adhesion, and degradation conduct of this own circle of relatives of materials. There are limits to the dimensions of a regenerative agent that can be released from alginate hydrogels with diffusion, because of the pore length of 5 nm. Most proteins without difficulty diffuse out from alginate gels, even with inside the absence of gel degradation, although degradation can pace release.[16-17] DNA (size -100 nm) can be released from degrading alginate gels, and antibodies might be released from alginate gels by the same mechanism. Cells must migrate out of alginate hydrogels, and/or be released as the gel degrades. There have been several qualitative studies of cell migration in various nanoporous alginate gels, in which migration occurred but was not quantitatively analyzed. The number of cells migrating outward as a function of the porosity and RGD presentation in macroporous alginate gels has been quantified, as has the migration speed of cells both within a microporous RGD-alginate gel and in the surrounding ECM gel. [18]

Muscle, nerve, pancreas, and liver

Alginate gels also are being actively investigated for his or her capacity to mediate the regeneration and engineering of a few different tissues and organs, inclusive of skeletal muscle, nerve, pancreas, and liver.[18-19] Current techniques for skeletal muscle regeneration encompass mobile transplantation, increased issue transport, or an aggregate of each approach, and alginate gels have determined capacity in those techniques. A mixed transport of VEGF and insulin-like increase issue-1 (IGF-1) from alginate gels turned into used to modulate each angiogenesis and myogenesis. The localized and sustained transport of each increased element brought about great muscle regeneration and purposeful muscle formation, because of satellite tv for pc mobile activation and proliferation, and cell safety from apoptosis through the launched elements. Long-time period survival and outward migration of number one myoblasts into broken muscle groups in vivo from RGD-alginate gels had been dramatically better through the sustained transport of hepatocyte increase issue (HGF) and fibroblast increase issue 2 (FGF 2) from the gels. This brought about widespread re-population of host muscle tissue and multiplied the regeneration of muscle fibers on the wound site. [19-20] Alginate gels have additionally been investigated for the restoration of the relevant and peripheral nerve systems. Alginate primarily based totally notably anisotropic capillary gels, brought into acute cervical spinal wire lesions in grownup rats, had been incorporated into the spinal wire parenchyma without most important

inflammatory responses and directed axonal re-growth.[21-22] Alginate gels, covalently cross-related with ethylenediamine, had been beneficial to repair a 50-mm hole in cat sciatic nerves and promoted the outgrowth of regenerating axons and astrocyte reactions on the stump of transected spinal cords in younger rats. Alginate gels had been extensively utilized as glue for restore of peripheral nerve gaps that could not be sutured.

Conclusions and future perspectives

Depending at the residences of unique polymeric materials, the hydrogels can reply to exclusive enter signals, bodily or chemical, triggering gel–sol transition and freeing preloaded shipment molecules or nano species. On the opposite hand, the alternative process, the sol-gel transition, may be brought about withinside the presence of unique cross-linkers or upon converting the environment (e.g., temperature, pH, etc.). While many man-made polymers had been notably studied for reversible sign-brought about sol–gel transformations, herbal polymers, and amongst them, alginate, have confirmed mechanical, bodily, chemical features, that are mainly crucial for biomedical packages, such as sign-brought about drug release. While biocompatibility of alginate is specifically crucial for biomedical packages, 33 running as implantable or externally wearable materials, lots broader packages in generation have emerged. For example, sign switchable hydrogels (artificial or herbal, such as alginate), had been notably used for the introduction of sign-switchable interfaces and changed electrodes. Novel uncommon packages in biocomputing have become feasible because of sign-brought-about adjustments withinside the alginate shape and residences. The crucial part of the sign-managed hydrogel shape is a cross-linker this is liable for the sol–gel transformation. Notably, exclusive metallic cations can perform as cross-linkers, every form of the cation with exclusive functionality.

Alginate has confirmed exquisite software and capacity as a biomaterial for plenty of biomedical programs, mainly withinside the regions of wound recuperation, drug delivery, in vitro cell culture, and tissue engineering. The most appealing functions of alginate for those programs consist of biocompatibility, moderate gelation conditions, and simple adjustments to put together alginate derivatives with new houses. Alginate has a musical document of secure medical makes use of as a wound recuperation dressing fabric and pharmaceutical component, and has been correctly implanted in a whole lot of programs, together with islet transplantation for remedy of kind 1 diabetes and chondrocyte transplantation for remedy of urinary incontinence and vesicoureteral reflux. A chemically changed alginate has additionally been widely used as a service to promote periodontal regeneration. Like different hydrogels, however, alginate gels have very constrained mechanical stiffness and greater normal bodily houses. A continuing venture is matching the bodily houses of alginate gels to the want in a specific application. Consideration of the variety of variables to be had cross linking strategies, the use of molecules with diverse chemical structures, molecular weights, and cross-linking capability will frequently yield gels appropriate for every application. Although now no longer a focal point here, many of the ideas reviewed in this newsletter are without delay applicable to molecular encapsulation strategies. However, covalent cross-linking reactions can purpose toxicity to the cells to be encapsulated, and the suitable desire of molecular-like-minded chemical reagents (e.g., initiator), and thorough elimination of unreacted reagents and by-merchandise will probably be wished in the one's programs.

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REVIEW ARTICLE

GOLD NANOPARTICLES SYNTHESIS METHODS AND APPLICATION

*Radhika Jadhav**, **Deepak Sawant****

ABSTRACT

Nanotechnology has vast applications in almost all fields of science and technology. Metal nanoparticles are being extensively used in biomedical fields due to their small size-to-volume ratio and extensive thermal stability. Gold nanoparticles (AuNPs) are one of the prominent metal nanoparticles (NPs) with a broad range of applications in various fields of science and technology. AuNPs are biocompatible, amenable to desired functionalization, non-corroding, and exhibit size and shape-dependent optical and electronic properties. These excellent properties of AuNPs exhibit their tremendous potential for use in diverse biomedical applications. Herein, we have evaluated the recent advancements of AuNPs to highlight their exceptional potential in the biomedical field. Special focus has been given to emerging biomedical applications including bio-imaging, site-specific drug/gene delivery, nano-sensing, diagnostics, photon-induced therapeutics, and theranostics.

INTRODUCTION

Nanomaterial with diameter 1-100 nm is defined as nanoparticles. [1] Nanotechnology has contributed to significant scientific and technological advances in biotechnology, diagnostics, and therapeutics. In particular, nanotechnology is increasingly being used to develop new and improved drug delivery systems. [2] Recently, metal nanoparticles (MNPs) are broadly applied in biomedicine field because of their unique and novel physicochemical properties such as large surface area, small sizes. [3]

AuNPs are the most biocompatible metal nanoparticles having relatively nontoxic behavior in biological media and owing to their high surface area, different chemicals including drug molecules, targeting ligands, and imaging probes can be conjugated to their surface, making AuNPs as ideal candidates for different therapeutic functions. [4]

1. Properties of gold nanoparticles:

Gold is a yellow solid and it is inert in nature while AuNPs are wine red solution. AuNPs exhibit different sizes ranging from 1 nm to 8 μm and also they show various shapes including nanosphere, nanorod, nanoshell, nanocube, nanocage, and branched. The AuNPs optical properties are defined through their plasmon resonance that is related to collective excitation of conduction electrons and concentrated in visible to infrared regions, depending on the structure, shape, and size of particle. All these specific properties make AuNPs the most potential nanomaterial for different applications in biomolecular ultrasensitive detection, chemical and biological sensing, labeling for proteins and cells, molecular imaging, and delivering drugs, genes, antigens, and antibodies into cells. [3]

*Ph.D. Student, **Tutor, D. Y. Patil Medical College, Kolhapur
Corresponding E-mail : sawantlab@gmail.com

2. Synthesis methods of AuNPs:

Generally, there are different techniques to synthesis AuNPs by dividing them into chemical, physical, and biological techniques.

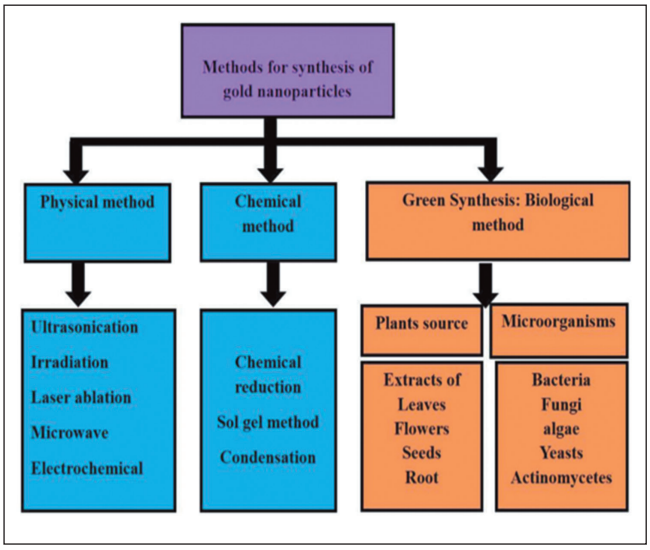

Fig 1: Different methods for synthesis of AuNPs

2.1. Chemical synthesis methods:

The citrate reduction synthesis technique is most common technique used in the synthesis of AuNPs. This technique introduced by Turkevitch in 1951, includes chloroauric acid reduction with trisodium citrate, resulting in formation of AuNPs with a size distribution from 10-20 nm. The basic principle of this technique involves the reduction of gold ions (Au^{3+}) to produce gold atoms (Au^{0}) by using some reducing agents like amino acids, ascorbic acid, UV light, or citrate. [5] The size of AuNPs can be controlled by varying salt concentration, rate of addition of reactants, and temperature. In this technique, citrate functions as a stabilizing and reducing agent that causes a colloidal suspension which stops aggregation of nanoparticles. [3]

Schiffrin– Brust method was first reported in 1994, which is based on a two-phase procedure that is favorable for preparing AuNPs in organic solution with high stability. This method employs tetrabutylammonium bromide (TOAB) as a transfer agent from organic to inorganic solution and the size of particles can be obtained from 2 to 6 nm in diameter. [4]

The previous two methods can synthesize only spherical AuNPs; however, they can also be formulated in a number of geometries and shape such as rods. The most commonly used technique to synthesize rod shaped AuNPs is seed-mediated growth. [5] In the seed-mediated growth method, the first small seeds serve as nucleation centers. In the next step, the very reactive sites on these centers can grow further to achieve a required shape of particles with a predicted size under controlled conditions. Two reducing agents, hydroxylamine and ascorbic acid, are usually used in this technique. The size of the prepared AuNPs can be varied from 5 to 40 nm by control of [HAuCl4]: [seeds] ratio. [3]

2.2. Physical methods:

Methods such as UV radiation, thermolytic, photochemical, microwaves, and sonochemical are categorized as physical techniques. UV radiation and high temperature are major reducing agents in UV radiation and thermolytic techniques. The desired sizes of AuNPs can be obtained by optimizing of synthesis condition. The photochemical process produces gold nanorods that have self-assembly and complex physical properties than spherical AuNPs. In microwave irradiation techniques, to prepare AuNPs, photochemical reduction method or heating are used. The sonochemical technique has the ability to provide AuNPs within pores of the silica and Au/Pd bimetallic nanoparticles. [3]

2.3. Biological methods:

The cost of reducing agents and stabilizing agents limits their applications. Furthermore, the prepared nanoparticles by chemical methods may have toxic consequences in biomedical applications. So, there is a requirement to develop easy and cost-effective procedures for the synthesis of nanoparticles that do not consume any toxic chemicals. The synthesis of nanoparticles by biological methods in current years has become the center of attention as green and eco-friendly methods. In biological methods, the synthesis of nanoparticles usually carried out by microorganisms, plants or plant extracts and enzymes. [6]

The biological synthesis of nanoparticles by using plants such as *Azadirachta indica*, *Aloe Vera*, *Medicago sativ*a, *Coriandrum sativum and lemongrass*.[7] is a safe, dynamic, and energy efficient method. Metabolites (flavonoids, proteins, fatty acids, sugars, enzymes, and phenolic compounds) found in these sources play a significant role in both the bioreduction of metallic ions to NPs and their stability. Solvent medium, reducing and stabilizer agents should be nontoxic and safe. [8]

Microorganisms have been reported to be an excellent candidate for the synthesis of both intracellular and extracellular AuNPs. The negatively charged cell wall of bacteria can electrostatically interact with positively charged Au (III) ions. Certain materials produced by microbial cells like proteins, enzymes, and organic substances can act as capping agents to stabilize nanoparticles and, hence, prevent their agglomeration. Microorganisms possess certain reductase enzymes which can reduce metal salts to metal nanoparticles with narrow size distributions and monodispersity. [5] These methods involve microbes such as fungi, bacteria, algae, and viruses as reducing agents. They are environmentally friendly because the toxic chemicals produced during the biosynthesis of the nanoparticles can be degraded with the help of enzymes present in the microbes. [9]

3. Biomedical applications:

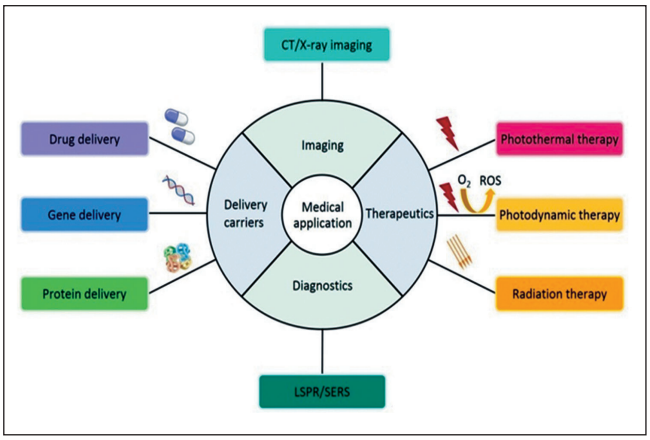

Fig. 2 : Various biomedical applications of AuNPs

3.1 Biosensing:

Polymer chain reaction (PCR) and enzyme-linked immune-sorbent assay (ELISA) are the two most popular bio-molecular sensing methods. However, these methods are expensive and complicated. The use of AuNPs-based sensing techniques could be a game changes in the biosensing applications. Till now AuNPs have also been used for efficient colorimetric, electrochemical, enzymatic, fluorescence resonance energy transfer (FRET), surface enhanced Raman scattering, and optical sensing applications. [20] The utilization of AuNPs in biological and chemical sensing is because of their intrinsic properties. The sensors of AuNPs can be colorimetric, fluorescence, and electrochemical. [3]

3.1.1. Electrochemical Sensing

AuNPs are perfect candidate for electrochemical detection of a broad range of molecules including, oligonucleotides, proteins, and organic small molecules because they remarkably improve the sensitivity of the electrochemical biosensors. The sequence-specific DNA detection has high importance in early detection of cancers, precise identification of pathogens, and clinical diagnostics of genetic diseases. [3]

3.1.2. Colorimetric sensing:

The colorimetric sensing based on AuNPs supplies a fast, low-price, and simple technique for the detection of various analytes like metal ions, heavy metal ions, alkaline and alkali earth metal ions, and molecules like anions, small organic molecules, proteins, and oligonucleotides. This technique is based on color change of suspension that permits the detection by naked eyes. AuNPs are introduced as interest candidates for colorimetric sensors because of their intense absorption in the visible region and intense dependency of SPR peaks on the immediate environment. In these sensors, AuNPs aggregation causes surface Plasmon coupling between nanoparticles leading to a visible color change from red to blue. [3]

3.2 Computed Tomography (CT) :

Imaging in medicine is an important tool for a number of procedures including the localization and diagnosis of cancers. The optical properties of gold make it very attractive for use as a contrast agent in imaging. [10]

CT is a potent molecular imaging tool for the diagnosis of cancer, that can give precious anatomical information associated with the location and size of tumors. The principle of CT imaging is based on an electron-density difference between targeted tissue and its surrounding. [3] The basis of CT imaging is the fact that healthy and diseased tissues or cells have different densities, which can generate in a contrast between normal and abnormal cells by using contrasting agents. Iodinated molecules are usually used as a contrasting agent, due to their unique X-ray absorption coefficient. [11] However, their usage has its own limitations, such as short imaging times, rapid renal clearance, reduced sensitivity and specificity, toxicity, and vascular permeation. [13] AuNPs with great electron density and atomic number possess a high X-ray attenuation coefficient and therefore can be applied as CT contrast agents. [3]

3.3 Therapeutic application:

3.3.1. Photothermal Therapy (PTT)

PTT is a novel type of hyperthermia that induced cell death in cancer cells by generating localized heat, particularly in early tumor stages. PTT is the main application of AuNPs in biomedicine. AuNPs have the ability to absorb light with high efficiency in a specific wavelength (visible or near-infrared (NIR) region) and convert it to heat through phonon-electron interaction. AuNPs are promising candidates for PTT of cancer due to easy conjugation with targeting drugs and molecules, high solubility, and high absorption cross-sections bon. The shape and size of AuNPs are key factors in PTT. In general, nanorods, nanocages, and nanoshells due to their intensive light absorption in the NIR region are beneficial in PTT. [3]

3.3.2. Radiotherapy (RT) :

Radiotherapy is the main therapy and is valuable to cure around 50% of all types of cancer infected. The cure depends on the deposition of drug dose in cancer cells, usually by the bombardment of either gamma radiations or high energy X-rays or by a

beam of high energy ions which may enough to irradiate the tumor cells or either their cell membrane and finally cause their death. [9] RT is insufficient to eradicate radioresistant hypoxic tumors; therefore, there is a need to improve the efficiency of RT. This improvement can be obtained by using the radiation sensitizers that enhance the radiation sensitivity of the tumors and thereby increasing the radiation-induced damage to the tumor. AuNPs have been widely applied as suitable radio sensitizer agents, because of their advantages, including high X-ray absorption, facility of synthetic manipulation, and ease of exact control of physicochemical properties. [3]

3.4 Drug Delivery

Gold nanoparticles have lately been exploited as an excellent applicant for delivering numerous drugs to their target sites. These payloads range from small drug molecules to bigger biomolecules such as RNA, DNA, and proteins. Effective discharge of these payloads is an essential factor to be considered for efficient therapy. The release of therapeutic agent from gold nanoparticles can be achieved by using internal stimuli such as glutathione, pH etc., and as well as external stimuli such as light. Chemotherapy is a common approach for cancer treatment that results in destructive side effects, like anemia and weight and hair loss. Targeted drug delivery system (TDDS) is a practicable new technique in cancer therapy that delivers drugs to targeted cells, thereby reducing the therapeutic dosage by increasing the drug concentration in desired tissue and alleviating damage to healthy tissues. AuNPs with low toxicity and high biocompatibility are excellent candidates for TDDS. In addition, surface chemical properties of AuNPs/ GNPs allow them to be attached to various molecules such as peptides, antibodies, and antigens in order to actively target the desired cell, which was discussed in the previous sections. [4]

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ORIGINAL ARTICLE

A STUDY THE SHORT-TERM OUTCOME IN ACUTE ISCHEMIC STROKE AND ITS ASSOCIATION WITH THE COMPONENTS OF METABOLIC SYNDROME

Mahesh Patil, Rajesh Khyalappa**, **Shailendra Mane***.***

ABSTRACT

Introduction : Stroke is the third leading cause of death worldwide each year, most frequent types of stroke are related to Small or large artery thrombus causing about 45% of ischemic strokes, emboli account for 20%, and the remaining cases are having unknown origins. Metabolic abnormalities raise the risk of cerebrovascular diseases, which include obesity, hypertension, dyslipidemia, and insulin resistance, diabetes. Metabolic Syndrome constituents are typically correlated to the risk of ischemic stroke incidence. **Material and Method :** This study was done at Dept. of Medicine, in the time period of October 2020 to August 2022 of 50 patients admitted with clinical findings suggestive of Acute ischaemic stroke. In this study patients included are with intracranial hemorrhage, and patients excluded are with the source of embolus like atrial fibrillation, severe valvular heart disease, previous stroke, and Severe Cardiorenal and nutritional disorder. **Results :** In both groups, majority of the stroke patients were from age group 61 to 80 years (45.16% and 57.89%) respectively. Significantly more males were seen with Metabolic Syndrome (87.09%) compared to patients without Metabolic Syndrome (63.16%). The majority of the stroke patients with Metabolic Syndrome had a disability (71%) and Mortality (19%) compared to non-Metabolic Syndrome patients (47% and 16%). **Conclusion :** Metabolic Syndrome among patients with acute ischemic stroke in our study is 62 %. Ischemic stroke affects most commonly males in the age group > 60 years. High BMI, High BSL and low HDL levels are the most important risk factors for stroke in patients with metabolic syndrome. There is A need to develop preventive strategies directed to the control of Metabolic Syndrome and each of its component conditions for future stroke.

Keywords : Ischemic Stroke, Metabolic syndrome, cerebrovascular diseases,

INTRODUCTION

The metabolic syndrome, also known as syndrome X or insulin resistance syndrome, is a collection of metabolic abnormalities that increase the risk of diabetes mellitus and cardiovascular disease (CVD). Since the World Health Organization (WHO) first defined metabolic syndrome in 1998, the criteria have evolved to reflect growing clinical evidence and analysis by a variety of consensus conferences and professional organizations that have contributed to a greater understanding of this syndrome. Central obesity, elevated triglycerides, low levels of high-density lipoprotein (HDL) cholesterol, hyperglycemia, and hypertension are the main characteristics of metabolic syndrome. [1]

*Junior Resident, ** Professor and Head, ***Associate Professor, Department of Medicine, D. Y. Patil Medical College Kolhapur.
Corresponding E-mail : hospitalvenkateshwara@gmail.com

Stroke is the third leading cause of death worldwide each year, accounting for more than 700,000 cases of disability. [1] The most frequent type of stroke, accounting for 80% of all strokes, is an ischemic stroke. Small or large artery thrombus causes about 45% of ischemic strokes, emboli account for 20%, and the remaining cases have unknown origins. [2] Risk factors for atherothrombotic ischemic stroke include arterial hypertension, diabetes, dyslipidemia, smoking, alcohol use, age, and male gender. [3] Stroke risk is increased by two to four times in people with metabolic syndrome. [4-5]

As a collection of connected metabolic abnormalities that raises the risk of cerebrovascular diseases, Metabolic Syndrome can be referred to. It includes obesity, hypertension, dyslipidemia, and insulin resistance/diabetes. [6] According to World Health Organization diagnostic criteria, the primary pathomechanism of Metabolic Syndrome is considered to be insulin resistance. [7] Numerous epidemiological and clinical studies showed a strong correlation between Metabolic Syndrome and the likelihood of stroke. [8], including recurrence. [9]

People with Metabolic Syndrome are much more likely to experience an incident ischemic stroke than people without Metabolic Syndrome. After adjusting for other risk factors, the number of Metabolic Syndrome components is highly correlated to the risk of ischemic stroke incidence. [10] To varying degrees, each element of the metabolic syndrome is linked to an increased risk of stroke. The purpose of this study is to evaluate the association between the elements of metabolic syndrome and the immediate effects of acute ischemic stroke. According to the diagnostic criteria of the Trial of Org 10172 in Acute Stroke therapy (TOAST), patients under 40 years old with a diagnosis of the first-ever symptomatic atherothrombotic ischemic stroke were enrolled. [11]

Stroke is the third leading cause of mortality worldwide each year, accounting for more than 700,000 cases of disability. Although the majority of patients tend to recover in the first few days following a stroke, a small but significant percentage actually worsens, a condition known as early neurological deterioration (END). It is noteworthy that between 5% and 40% of individuals with acute ischemic stroke have END. Additionally, END is crucial for the prognosis of stroke since it may indicate a higher probability of mortality and more dependent on others for daily activities. As a result, in order to enhance the outcomes of strokes, it is crucial to identify and address END-related variables.

Therefore, the short-term fate of individuals who have had an acute ischemic stroke is correlated with metabolic syndrome and its components. Thus, the present study aims to investigate the effects of Metabolic Syndrome and its individual components on ischemic stroke, and their impact on the short-term outcomes of acute ischemic stroke among our hospitalized patients.

AIM AND OBJECTIVES

AIM : To study the short-term outcome in acute ischemic stroke and its association with the components of metabolic syndrome

OBJECTIVES : To study clinical profile of Acute ischemic stroke by neurological examination & imaging, to study the parameters to determine presence of metabolic syndrome, follow the patient after 3 months for detailed neurology examination

and disability by modified Rankin scale, correlate neurological recovery, disability, mortality of patients with Metabolic syndrome to decide outcome.

MATERIALS AND METHODS

Study Area : Dept. of Medicine, a tertiary care center.

Study Duration: October 2020 to August 2022

Study Design : Longitudinal Prospective observational study

Study Setting : 50 patients admitted with clinical findings suggestive of Acute ischaemic stroke at the Department of General Medicine tertiary care center were included in the study.

Inclusion Criteria : Patients with first-ever atherothrombotic ischemic stroke, less than twenty-four hours' duration were admitted to the Medicine ward. Those who are willing to come for follow-up after 3 months.

Exclusion Criteria : Age less than 16 years, patients with intracranial hemorrhage, patients with known source of embolus like atrial fibrillation (AF), moderate to severe valvular heart disease, history of previous stroke and Severe Cardio-renal or nutritional disorder.

METHODOLOGY

This is a longitudinal prospective observational study, which was conducted in the Department of Medicine, the study subjects are constituting patients with first-ever atherothrombotic ischemic stroke who are going to be admitted to the Medicine department. Study will begin after approval of Research and Ethics Committee. Diagnosis of the first-ever symptomatic atherothrombotic ischemic stroke according to the diagnostic criteria of Trial of Org 10172 in Acute Stroke treatment (TOAST). Diagnosis of metabolic syndrome according to the NCEP ATP III definition, metabolic syndrome is present if three or more of the following five criteria are met: waist circumference over 40 inches (men) or 35 inches (women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women) and fasting blood sugar over 100 mg/dl. [8] General information, previous medication history (including hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, and coronary heart disease) will be taken. The data of physical examination, detailed neurological assessment will be done on admission and after 3 months. After 3months disability assessed by modified rankin scale. After 3months outcomes are Death, Recovery, Disability. Laboratory data including fasting plasma glucose (FPG), Lipid profile and imaging results will be recorded. Standard of care treatment will be given to all patients.

Sample Size : 50

Sample size Calculation : In a study by **Liu et al (2015)** on Metabolic syndrome and the short-term prognosis of acute ischemic stroke, the prevalence of Metabolic Syndrome among the patients with acute ischemic stroke in the study was 58.3%.

Though our calculated sample size was 43, in the given study period we included 50 diagnosed cases of first-ever atherothrombotic ischemic stroke, less than twenty-four hours' duration who were admitted to the Medicine ward.

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. An 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. A 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 ISSUES : The study will begin after approval by the Ethical Research Committee Written informed consent will be taken from all participants to enroll study. Standard of care treatment will be given to all patients. Any other additional expenses will be borne by me.

RESULTS

In the present study we found that out of 50 patients with ischemic stroke, 31 (62%) were found to have metabolic syndrome (Met S).

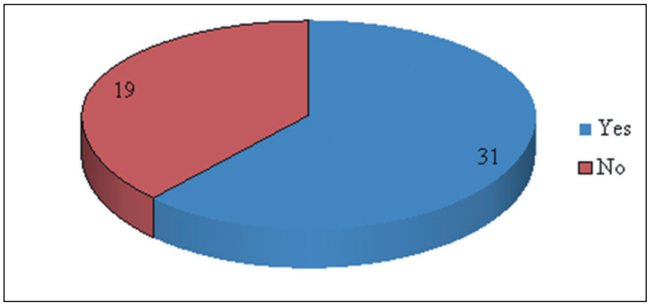

Fig. 1 : Prevalence of Metabolic Syndrome

In both groups, the majority of the stroke patients were from the age group 61 to 80 years (45.16% and 57.89%) respectively from Met S and non-Met S groups and the difference was not significance.

Mean age of the stroke patients with metabolic Syndrome was 56.52±14.59 years and 60.05±13.01 years for the patient without metabolic syndrome. The difference was not significant (p-value 0.391).

More males were seen with Metabolic Syndrome (87.09%) compared to patients without Metabolic Syndrome (63.16%) and the difference between the groups was significant **(p-value 0.047)**.

Table 1 : Presenting Symptoms:

Presenting Symptoms	Groups		Total	P value
	Met S	Non-Met S		
Weakness	30 (96.77%)	18 (94.74%)	48 (96%)	0.721
DOAM*	17 (54.84%)	9 (47.37%)	26 (52%)	0.608
Loss of consciousness	4 (12.90%)	2 (10.53%)	6 (12%)	0.802
Aphasia	4 (12.90%)	1 (5.26%)	5 (10%)	0.382

*Deviation of the angle of mouth Stroke patients showed the most common symptoms being weakness (96.77%) followed by deviation of angle of the mouth (54.84%), Loss of consciousness (12.90%), and Aphasia (12.90%) which were more common in Metabolic Syndrome as compared to non-Metabolic Syndrome (94.74%, 47.37%, 10.53%, 5.26% respectively) but the difference between the groups was not significant for none of the symptoms (all p-value>0.05).

Table 2 : Co-morbidities and Body Mass Index

Co-morbidities	Met S (n=31)		Non-Met S (n=19)		Total	P-value
	Freq.	Percent	Freq.	Percent		
Diabetes Mellitus	13	41.9	6	20.7	19 (38%)	0.464
Hypertension	19	61.3	8	27.6	27 (54%)	0.186
BMI ≥25Kg/m^2	19	61.3	5	26.3	24 (48%)	**0.035**

Diabetes Mellitus (41.9%) and Hypertension (61.3%) were more common in Metabolic Syndrome as

compared to non-Metabolic Syndrome (20.7% and 27.6% respectively) but the difference between the groups was not significant for none of the co-morbidities (all p value >0.05).

BMI >25Kg/m^2 was seen in 19 (61.3%) patients with Metabolic Syndrome but in only 5 (26.3%) normal patients. The difference was statistically significant (p value 0.035)

Table 3 : Addictions among Patients

Addictions	Groups		Total	P -value
	Met S	Non-Met S		
Alcohol intake	7 (22.58%)	4 (21.05%)	11(22%)	0.899
Smoking	9 (29.03%)	3 (15.79%)	12(24%)	0.287

History of alcohol intake (22.58%) and Smoking (29.03%) were more common in Metabolic Syndrome as compared to non-Metabolic Syndrome (21.05% and 15.79% respectively) but the difference between the groups was not significant for none of the addictions (both p-value>0.05).

Table 4 : ECG Findings

Major ECG Findings	Group		Total	Chi-Square & p- value
	Met S	Non-Met S		
Left Ventricular Hypertrophy	16 (51.61%)	2 (10.53%)	18 (36%)	6.94, **0.008**
Normal ECG	15 (48.39%)	17 (89.47%)	32 (64%)	
Total	31 (100%)	19 (100%)	50 (100%)	

Almost half of the stroke patients with Metabolic Syndrome had LVH on ECG, but only 10.53% of patients with non-metabolic Syndrome had LVH. The difference between the groups was statistically significant **(p-value 0.008)**.

Neurological Examination :

The majority of the stroke patients with Metabolic Syndrome as well as non-Metabolic Syndrome had upper limb tone of grade 3 (41.93% and 42.11%) and the difference between the groups was not significant (p-value 0.473).

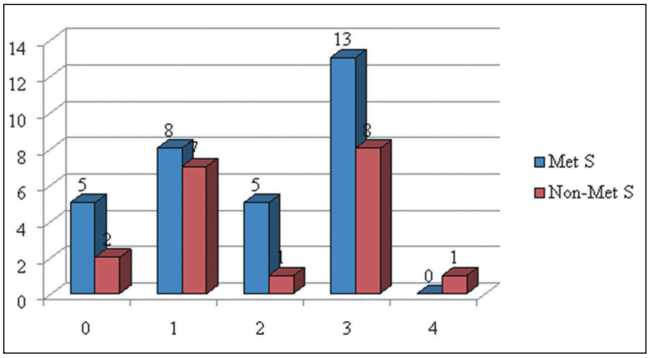

Fig. 2 : Tone in Upper Limbs

Table 5 : Tone in Lower Limbs

Tone	Group		Total	Chi-Square& p- value
	Met S	Non-Met S		
0.0	4 (12.09%)	3 (15.79%)	7 (14%)	2.886, 0.577
1.0	9 (29.03%)	6 (31.58%)	15 (30%)	
2.0	5 (16.13%)	1 (5.26%)	6 (12%)	
3.0	13 (41.93%)	8 (42.11%)	21 (42%)	
4.0	0 (0%)	1 (5.26%)	1 (2%)	
Total	31 (100%)	19 (100%)	50 (100%)	

The majority of the stroke patients with Metabolic Syndrome as well as non-Metabolic Syndrome had lower limb tone of grade 3 (41.93% and 42.11%) and the difference between the groups was not significant (p-value 0.577).

Table 6 : Power of Upper Limb

Power Grade	Group		Total	Chi-Square & p- value
	Met S	Non-Met S		
0.0	13(41.93%)	10(52.63%)	23(46%)	6.148, 0.292
1.0	4(12.90%)	1(5.26%)	5(10%)	
2.0	4(12.90%)	1(5.26%)	5(10%)	
3.0	4(12.90%)	5(26.32%)	9(18%)	
4.0	6(19.35%)	1(5.26%)	7(14%)	
5.0	0(0%)	1(5.26%)	1(2%)	
Total	31(100%)	19(%)	50(%)	

The majority of the stroke patients with Metabolic Syndrome as well as non-Metabolic Syndrome had upper limb power grade 0 (41.93% and 52.63%) and the difference between the groups was not significant (p-value 0.292).

Table 7 : Power of Lower Limb

Power Grade	Group		Total	Chi-Square & p- value
	Met S	Non-Met S		
0.0	9(29.03%)	5(26.32%)	14(28%)	1.529, 0.958
1.0	8(25.81%)	5(26.32%)	13(26%)	
2.0	3(9.68%)	2(10.53%)	5(10%)	
3.0	4(12.90%)	4(21.05%)	8(16%)	
4.0	5(16.13%)	2(10.53%)	7(14%)	
5.0	2(6.46%)	1(5.26%)	3(6%)	
Total	31(100%)	19(100%)	50(100%)	

The majority of the stroke patients with Metabolic Syndrome as well as non-Metabolic Syndrome had lower limb power grade 0 (29.03% and 26.32%) and the difference between the groups was not significant (p-value 0.958).

Mean Waist circumference was significantly high in Metabolic Syndrome patients compared to non-Metabolic Syndrome Patients (p value 0.000).

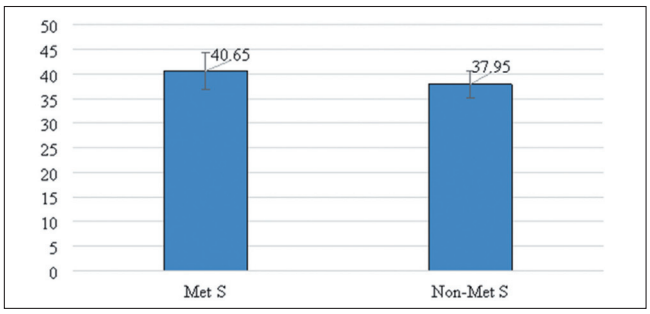

Fig. 3 : Mean Waist Circumference of the patients

In the present study, majority of the patients, 22% had MRS score of 4 followed by 18% had score as 9.

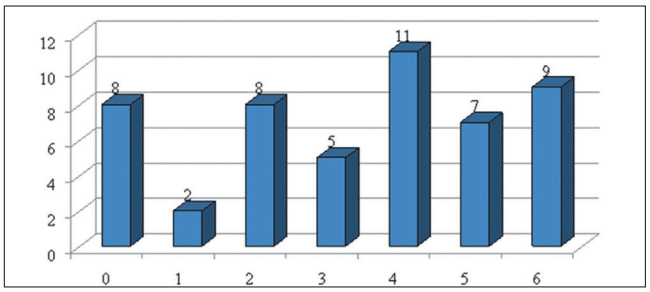

Fig. 4 : Modified Rankin Scale

The majority of the patients with Metabolic Syndrome had a Modified Rankin Scale score (MRS score) > 3 (67.74%) compared to non-Metabolic Syndrome patients, 31.58% had MRS score >3. Higher MRS was significantly associated with Metabolic Syndrome (p-value 0.013).

Mean MRS score of Metabolic Syndrome patients was also significantly high (3.90±1.78) compared to non-Metabolic Syndrome patients (2.37±2.11) p value 0.008).

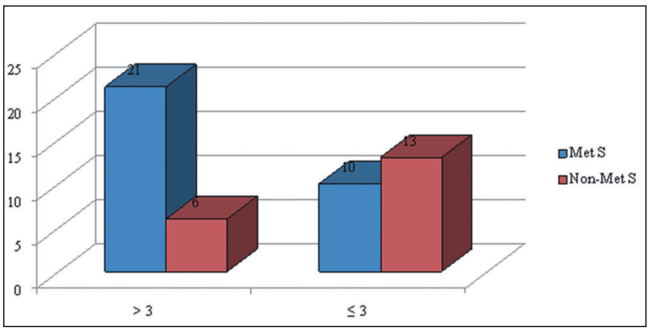

Fig. 5 : Modified Rankin Scale

Table 8: Mean Laboratory value of the patients:

Laboratory Parameters	Met S		Non-Met S		P value
	Mean	Std. Deviation	Mean	Std. Deviation	
Hemoglobin	13.44	2.12	12.92	2.09	0.396
Serum Urea	30.41	14.29	37.43	32.02	0.293
Serum Creatinine	1.08	0.40	1.26	0.80	0.294
Fasting BSL	141.26	42.20	108.13	40.94	0.009
Fasting Triglyceride	168.37	52.55	113.08	24.10	0.000
Fasting HDL	34.90	4.89	51.09	11.16	0.000

Mean fasting Blood Sugar levels (141.26±42.20 and 108.13±40.94mg/dL) and Fasting Triglyceride (168.37±52.55 and 113.08±24.10 mg/dL) were significantly high in patients with Metabolic Syndrome as compared to non-Metabolic Syndrome (p-value <0.05) Mean fasting HDL level (34.90±4.89 and 51.09±11.16 mg/dL) was significantly low in patients with Metabolic Syndrome as compared to non-Metabolic Syndrome (p-value <0.05) Other laboratory parameters like hemoglobin, Serum Urea, and Serum Creatinine were similar in both groups and difference was not significant. Majority of the stroke patients with high BSL had higher score of MRS (score 5 and 6 for 21% patients each) compared to patients with normal BSL (score 0 and 2 for 29% patients each). Higher BSL was significantly associated with high MRS score (p value 0.017)

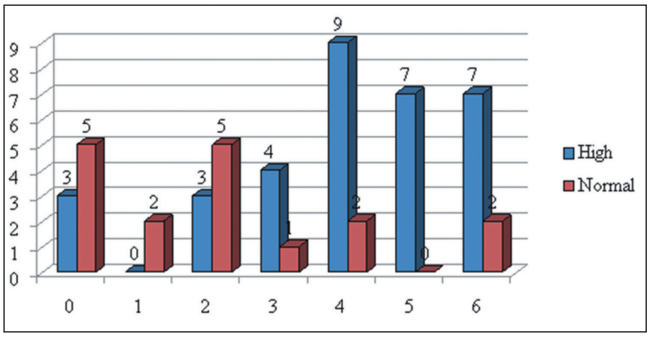

Fig. 6 : Modified Rankin Scale

Majority of the stroke patients with high TGs had higher score of MRS (score 4 and 5 for 33% and 21% patients) compared to patients with normal TGs (score 0 and 2 for 23% and 27% patients). Higher TGs was seen with high MRS score but lacks statistical significance (p value 0.055)

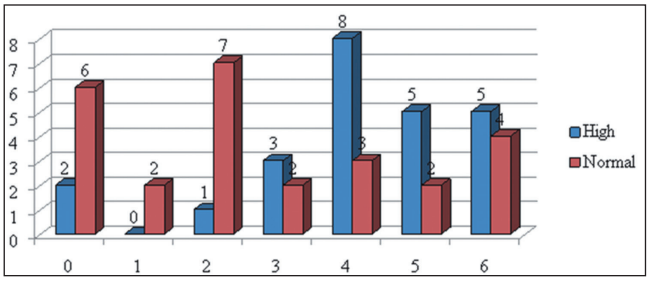

Fig. 7 : Modified Rankin Scale

Majority of the stroke patients with low fasting HDL had higher score of MRS (score 4 and 5 for 24% and 21% of patients) compared to patients with normal Fasting HDL (score 0 and 4 for 17.65% of patients each). Low fasting HDL was significantly associated with high MRS score (p-value 0.018)

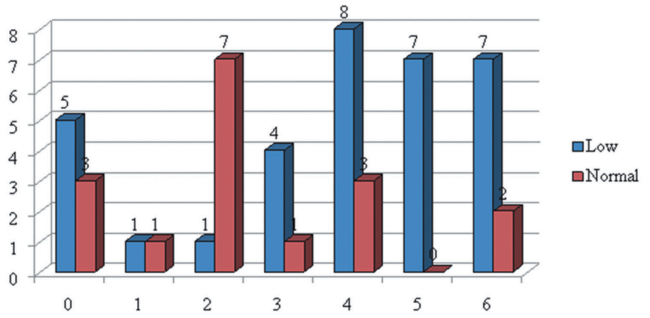

Fig. 8 : Fasting HDL Level

Majority of the stroke patients with high WC had higher score of MRS (score 4 and 6 for 23% patients each) compared to patients with normal WC (score 2 and 4 for 20.83% patients each). Higher WC is seen observed with high MRS score but lacks statistical significance (p value 0.311).

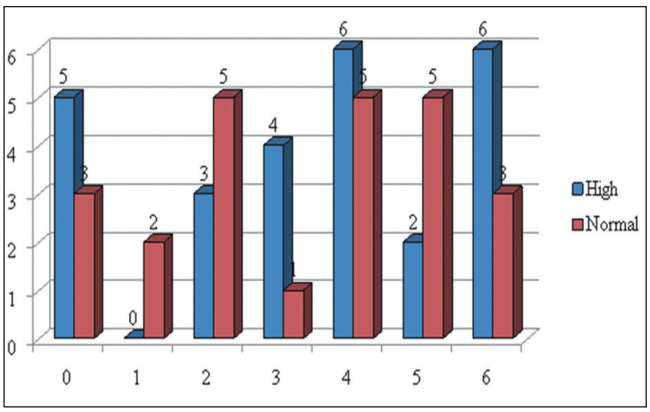

Fig. 9 : Waist Circumference

Majority of the stroke patients with high Blood Pressure (BP) had higher score of MRS (score 4 and 6 for 22% patients each) compared to patients with normal BP (score 0 and 2 for 21% and 28% patients). Higher BP observed with high MRS score but lacks statistical significance (p value 0.564)

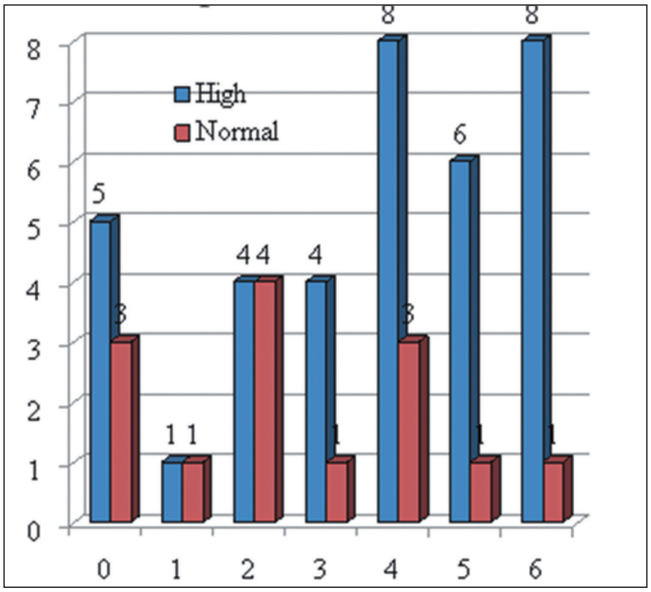

Fig. 10 : Blood Pressure

Based on MRS, outcome was assessed. 10 stroke patients were Recovery with full recovery, 31 discharged with disability and 9 patients died during the course in the hospital.

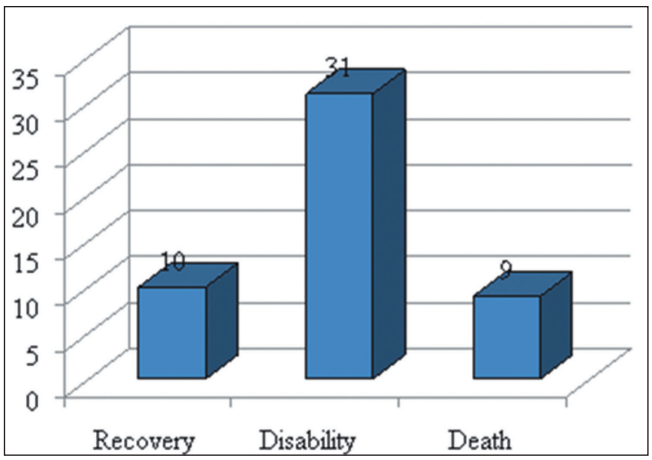

Fig. 11 : Outcome of patients as based on Modified Rankin Scale

Majority of the stroke patients with Metabolic Syndrome had disability (71%) compared to non-Metabolic Syndrome patients (47%). Mortality was 19% in Metabolic Syndrome patients compared to non-Metabolic Syndrome patients (16%)

Recovery rate was higher in non-Metabolic Syndrome patients (37%) compared to patients with Metabolic Syndrome (10%). But difference of outcomes between 2 groups was not statistically significant (p value 0.064)

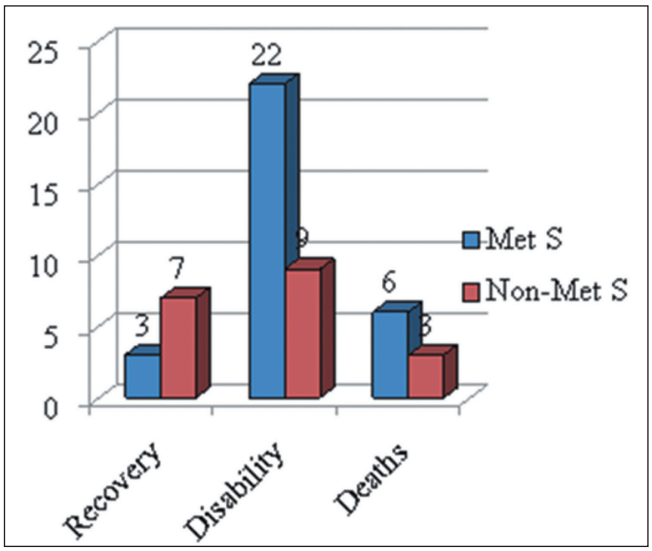

Fig. 12 : Outcome of the Patients

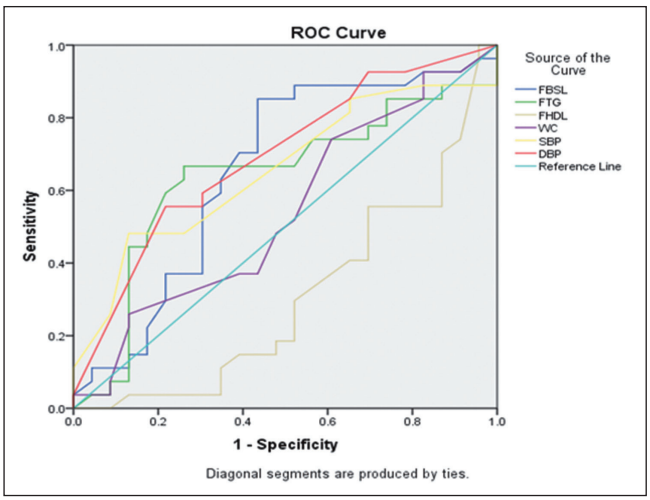

Fig. 13 : ROV Curve

Table 9 : Area Under the Curve for ROC curve

Test Result Variable(s)	Area	Asymptotic 95% CI		Std. Error	P value
		Lower Bound	Upper Bound		
WC	0.540	0.377	0.703	0.083	0.627
FBSL	0.655	0.496	0.815	0.082	0.060
FTG	0.637	0.475	0.798	0.082	0.098
FHDL	0.308	0.158	0.457	0.076	**0.020**
SBP	0.655	0.502	0.808	0.078	0.062
DBP	0.692	0.546	0.839	0.075	**0.020**

Above ROC is between MRS score > 3 and components of Metabolic Syndrome. Table shows AUC was maximum for Diastolic blood pressure for systolic BP and fasting BSL but statistical significance was seen only with DBP **(p value 0.020)**. HDL had significant inverse relation with higher MRS score with AUC 0.308 and **p value 0.020**.

DISCUSSION

A separate risk factor for vascular disorders including coronary artery disease and stroke has been identified called metabolic syndrome. Stroke is the third leading cause of mortality worldwide each year, accounting for more than 700,000 cases of disability. Although the majority of patients tend to recover in the first few days following a stroke, a small but significant percentage actually worsens, a condition known as early neurological deterioration (END). It is noteworthy that between 5% and 40% of individuals with acute ischemic stroke have END. Additionally, END is crucial for the prognosis of stroke since it may indicate a higher probability of mortality and more dependent on others for daily activities. As a result, it's critical to identify and treat END risk factors in order to enhance stroke. The goal of the current study was to examine the relationship between the elements of the metabolic syndrome and the short-term prognosis of acute ischemic stroke. We examined neurological measures that define the existence of the metabolic syndrome and characterized the clinical profile of acute ischemic stroke. Following the patient for a thorough neurology exam and disability assessment using the modified Rankin scale was done. The existence of metabolic syndrome was associated with neurological recovery, disability, and death to determine the patient's prognosis.

Prevalence of Metabolic Syndrome:

In the current study, 31 (62%) patients of 50 patients with ischemic stroke were confirmed to have metabolic syndrome (Met S). This outcome is in line with what **Ashtari et al. (2012)** [12] discovered, which was that 62% of the patients. The prevalence of Metabolic Syndrome was 51.4 and 57.29%, respectively, in the Chinese investigations on acute ischemic stroke. [13] The prevalence of Metabolic Syndrome was ound to be 46% in investigations **by Milionis HJ et al & others.** [14] In studies by **Shrestha et al** [15] **and E.I. Sorkhou et al** [16]**,** prevalence was lower at 32% and 34%, respectively.

There were also comparatively larger proportions of patients with Metabolic Syndrome in several other trials **(Mi et al., 2012; Liu et al., 2011; Iqbal et al., 2010; Kabir et al., 2008)** [17,18, 19]**.** In a cohort of study participants, metabolic syndrome was discovered in 50% of cases, according to **Mi et al. (2012)** [17]**,** with a hazard ratio for stroke recurrence (metabolic syndrome versus no metabolic syndrome) close to two. There are many people at risk of cardiovascular disorders including stroke and ischemic heart disease globally, and metabolic syndrome is becoming more prevalent and common **(Khang et al., 2010)** [20]**.** The comparatively high incidence of Metabolic Syndrome in this research may thus be attributable to the high prevalence of its associated risk factors, particularly high fasting blood glucose, high blood pressure, and high waist circumference or obesity.

Age distribution of the patients:

The majority of the stroke patients in both groups were between the ages of 61 and 80 (45.16% and 57.89%, respectively), from the Met S and non-Met S groups, and the difference was not statistically significant. The average age of stroke patients who also had metabolic syndrome was 60.05 13.01 years old, compared to 56.52 14.59 for those who did not. There was no discernible difference (p value 0.391).

Given that the modal age group had the highest prevalence of Metabolic Syndrome, these facts provide validity to earlier study findings. Similar to this, **Jia et al** [21]. demonstrated that middle-aged and elderly people with metabolic syndrome were more likely to get their first stroke. According to **Akpalu et al** [22]**,** the prevalence of metabolic syndrome rose with age and was reported to be 54% in patients with cardiovascular illnesses and 18% in healthy controls, respectively. This study thus supports the claim that the prevalence of metabolic syndrome tends to grow with age and is highest in the middle-aged population **(Akpalu et al., 2011; Jia et al., 2011)** [21-22]**.**

One significant risk factor for stroke is age. Instead than being a result of ageing, stroke can be brought on by a number of bad lifestyle choices, such using drugs or smoking **(Mohammad, 2014)** [23]**.**

Gender of the Patients:

Patients with Metabolic Syndrome were significantly more likely to be men (87.09%) than patients without Metabolic Syndrome (63.16%). (p value 0.047). Men are more likely than women to experience a stroke globally, according to a systematic assessment of the subject [24]. Additionally, recent research has consistently shown that there was a greater prevalence and incidence of smoking and heavy drinking in male patients compared to female patients [25]. These most likely emphasize the necessity of altering bad lifestyle habits and adopting sensible ones that can significantly reduce the risk of stroke. A mechanism that appears to stop working with menopause [(26)] has been hypothesized to explain why women do have a lower incidence of stroke than men. Physiologically, the beneficial effect of estrogen on cerebral circulation has been postulated to reduce the incidence of stroke in women. As a result, the gender distribution of the results might be anticipated given the study's mean age. In contrast to our investigation, Hillier TA et al [27] demonstrated that metabolic syndrome was linked to a two- to three-fold greater mortality risk from CVD in older women (> 65 years) with diabetes. According to this study, 64% of women over 60 who met the stroke criterion were female. This is comparable to studies on stroke and metabolic syndrome conducted in other

populations [12, 17]. Despite the fact that the difference was not statistically significant, **Ashtari et al. (2012)** [12] found that women (52%) had a higher prevalence of Metabolic Syndrome than men (44%).

Addictions among Patients:

Patients with Metabolic Syndrome were more likely to have a history of alcohol consumption (22.58%) and smoking (29.03%) than non-Metabolic Syndrome (21.05% and 15.79%, respectively), although there was no statistically significant difference between the groups for any of the addictions (both p values >0.05). Previous investigations have shown a causal relationship between Metabolic Syndrome and smoking and binge drinking [28]

Mean Waist Circumference and Laboratory Value of the patients :

When compared to non-Metabolic Syndrome patients, the mean waist circumference in Metabolic Syndrome patients was considerably higher (p-value 0.000). Patients with Metabolic Syndrome had substantially higher mean fasting blood sugar and fasting triglyceride levels than non-Metabolic Syndrome patients (p-value 0.05). Patients with Metabolic Syndrome had substantially lower mean fasting HDL levels than those without Metabolic Syndrome (p 0.05). These results are consistent with **Ashtari et al (2012)** [12].'s study, which discovered that 85% of its subjects had excessive waist circumference. According **to Mi et al. (2012)** [17]**,** elevated blood pressure and high fasting blood glucose are more common. Additionally, **Ashtari et al. (2012)** [12] noted increased percentages of study participants with high blood pressure and high fasting blood glucose. **Iqbal et al. (2010)** [19] discovered similar results in their research participants, including reduced high-density lipoprotein (DHDL) and increased triglyceride levels. The high prevalence of Metabolic Syndrome in the study participants may have been caused by the high prevalence of Metabolic Syndrome components found in this investigation.

Modified Rankin Scale of the patients :

In comparison to non-Metabolic Syndrome patients, the majority of Metabolic Syndrome patients (67.74%) had Modified Rankin Scale scores (MRS scores) > 3 (31.58%). Metabolic Syndrome was substantially correlated with higher MRS (p-value 0.013). The mean MRS score of patients with Metabolic Syndrome was likewise noticeably higher (3.901.78) than that of patients without Metabolic Syndrome (2.372.11) (p-value 0.008). Patients with the metabolic syndrome had a 2.05-fold risk for all strokes and a 2.41-fold risk for ischemic stroke, according to a cohort study by **Kurl S et al** [29] on 1131 males. In a cross-sectional investigation conducted by **V. Athyros et al. and others** [30] in 9669 Greek adults, CVD prevalence was compared in patients with metabolic syndrome. The results demonstrate that regardless of the criterion employed, CVD prevalence increased in the presence of metabolic syndrome.

Association between Modified Rankin Scale and Components of Metabolic Syndrome:

High MRS score was strongly correlated with higher BSL and lower fasting HDL (p 0.05). High MRS score was associated with higher TGs, higher WC, and higher BP, however this association is not statistically significant (p value >0.05). Cerebrovascular atherosclerosis, particularly occlusive big artery disorders, would be accelerated by central obesity and dyslipidemia (elevated TG, reduced HDL-C, and increased LDL-C) [31]. All stroke subtypes have

hypertension as their primary risk factor [32].

Association between occurrence of Metabolic Syndrome and Outcome of the patients:

Compared to non-Metabolic Syndrome patients (47%), the majority of stroke patients reported impairment (71%). Compared to non-Metabolic Syndrome patients (16%), those with Metabolic Syndrome had a mortality rate of 19%. Individuals without Metabolic Syndrome had a discharge rate that was greater (37%) than that of patients with Metabolic Syndrome (10%). However, the results difference between the two groups was not statistically significant (p value 0.064)

Area Under the Curve for ROC curve :

Diastolic blood pressure had the highest AUC compared to systolic blood pressure and fasting blood sugar levels on the ROC curve between MRS score > 3 and components of the metabolic syndrome, but only DBP showed statistical significance (p value 0.020). With an AUC of 0.308 and a p value of 0.020, HDL demonstrated a significant adverse relationship with higher MRS scores. Data accumulated over time supported the hypothesis that dyslipidaemia (low HDL-C and high TG) was directly associated with the poor outcomes of individuals with ischemic stroke [33]. In particular, when there is a persistent systemic inflammatory response, HDL-C particles might be presumed to exhibit pro-inflammatory and pro-atherogenic features [34]. Additionally, in individuals with a history of coronary heart disease, HDL-C enhances the generation of lipid peroxide and the oxidation of LDL-C and phospholipids [(35)]. Hypertension and yperglycemia were independent risk factors for cardiovascular illnesses, according to **Liu et al. (2011)** [18]. According **to Hwang et al. (2011)** [36]**,** metabolic syndrome and/or high fasting blood glucose were the best predictors of cardiovascular disease. The two best predictors of a first stroke or transient ischemic attack were found to be impaired fasting glucose and hypertension. Further, **Mozaffarian et al. (2008)** [37] showed that Metabolic Syndrome is linked to an increased risk of stroke and that the risk is larger in the absence of either hypertension or elevated fasting blood glucose alone. In the realm of stroke prevention, several research on the Metabolic Syndrome and ischemic stroke have been analysed; nevertheless, there is a paucity of information about the effect of the Metabolic Syndrome and its individual components on acute stroke prognosis. Our findings support recent studies that show that elements of the Metabolic Syndrome, namely hyperglycemia, are linked to poor short-term outcomes [38].

SUMMARY

In the present study we found that out of 50 patients with ischemic stroke, 31 (62%) found to have metabolic syndrome (Met S). In both groups, majority of the stroke patients were from age group 61 to 80 years (45.16% and 57.89%) respectively. Significantly more males were seen with Metabolic Syndrome (87.09%) compared to patients without Metabolic Syndrome (63.16%). Stroke patients showed most common symptoms being weakness (96.77%) followed by deviation of angle of mouth (54.84%). Diabetes Mellitus (41.9%), Hypertension (61.3%), History of alcohol intake (22.58%) and Smoking (29.03%) were more common in Metabolic Syndrome as compared to non-Metabolic Syndrome. Majority of the stroke patients with Metabolic Syndrome as well as non-Metabolic Syndrome had upper limb, lower limb tone of grade 3 and power grade 0 power. Mean Waist circumference was significantly high in Metabolic Syndrome patients compared to non-Metabolic

Syndrome Patients. Majority of the patients with Metabolic Syndrome had a Modified Rankin Scale score (MRS score) > 3 (67.74%) compared to non-Metabolic Syndrome patients, 31.58% had MRS score >3. Higher MRS was significantly associated with Metabolic Syndrome (p value 0.013). Mean MRS score of Metabolic Syndrome patients was also significantly high (3.90±1.78) compared to non-Metabolic Syndrome patients (2.37±2.11) (p value 0.008). Mean fasting Blood Sugar level (141.26±42.20 and 108.13±40.94mg/dL) and Fasting Triglyceride (168.37±52.55 and 113.08±24.10 mg/dL) were significantly high in patients with Metabolic Syndrome as compared to non-Metabolic Syndrome (p value <0.05) Mean fasting HDL level (34.90±4.89 and 51.09±11.16 mg/dL) was significantly low in patients with Metabolic Syndrome as compared to non-Metabolic Syndrome (p value <0.05) Majority of the stroke patients with high BSL and low fasting HDL had higher score of MRS compared to patients with normal BSL and normal fasting HDL (p value <0.05). Majority of the stroke patients with high TGs, high WC and high Blood Pressure had higher score of MRS compared to patients with normal parameters but lacks statistical significance (p value >0.05) Majority of the stroke patients with Metabolic Syndrome had disability (71%) and Mortality (19%) compared to non-Metabolic Syndrome patients (47% and 16%). Discharge rate was higher in non-Metabolic Syndrome patients (37%) compared to patients with Metabolic Syndrome (10%).

As per ROC curve, Diastolic blood pressure, for systolic BP and fasting BSL but statistical significance was seen only with DBP **(p value 0.020)**. HDL had significant inverse relation with higher MRS score with AUC 0.308 and **p value 0.020**.

CONCLUSION

The occurrence of Metabolic Syndrome among patients with acute ischemic stroke in our study is 62 %. Ischemic stroke affects most commonly males in the age group > 60 years. High BMI, High BSL, and low HDL levels are the most important risk factors for stroke in patients with metabolic syndrome. Metabolic Syndrome is associated with more severe neurological features as per MRS. Individually, high BSL and low fasting HDL had higher MRS scores. Higher diastolic pressure and hyperglycemia is a significant predictor for poor functional outcomes. Our data provided valuable information toward a better understanding of the risk factors of ischemic stroke. Fasting blood glucose, HDL, and body weight should be well monitored to reduce risk of stroke. There is a need to develop preventive strategies directed to the control of Metabolic Syndrome and each of its component conditions for future stroke.

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RENAL MORBIDITY IN TYPE2 DIABETES MELLITUS PATIENTS WITH & WITHOUT NAFLD

Tanuku Vivek *, ***Shimpa R. Sharma*****

ABSTRACT

Introduction : Non-alcoholic fatty liver disease (NAFLD) is independently associated with prevalent as well as incident Cardiovascular Diseases (CVD), Type 2 Diabetes Mellitus(T2DM), Chronic Kidney Disease (CKD) and Metabolic syndrome (MetS). Awareness of Renal Morbidity and full understanding is work at progress. Hence it was determined to assess the Renal morbidity as measured by eGFR in Patients of T2DM with and without NAFLD. **Methods :** Patients with type 2 Diabetes Mellitus (ICMR 2018 criteria) with proper informed and valid consent and satisfying essential inclusion and exclusion criteria were screened for presence of Fatty liver by Ultrasound and were divided into two groups; those with NAFLD and without NAFLD. All patients were investigated for Renal morbidity in terms of eGFR using MDRD formula. Result- Diabetic patients with NAFLD had lower eGFR levels compared to Diabetics without NAFLD. ($P<0.05$) Patients with Diabetes and NAFLD has significantly higher BMI, WHR, Duration of Diabetes compared to Diabetes patients without NAFLD. **Conclusion :** Group of Diabetics with NAFLD have to be closely monitoring for serum creatinine levels and BMI is required for early intervention and optimisation of treatment. Elderly patients required more prompt monitoring.

Keywords : NAFLD, Type 2 Diabetes Mellitus, Renal diseases, alcohol, obesity.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is an emerging condition that currently affects about 25 out of every 100 adults world-wide.[1] Type 2 diabetes (T2DM), Metabolic syndrome (MetS) and Obesity are all associated with Non-alcoholic fatty liver disease (NAFLD), which increases the risk of Cardiovascular disease and Renal diseases.[2] NAFLD is a multifaceted illness. Patients with progressive NAFLD have an increased risk of both hepatic and extra-hepatic pathologies apart from increased overall morbidity and mortality. Recently there is increased evidence showing that the risk, clinical profile, and the burden of NAFLD disease is being altered by genetic, epigenetic differences and life-style changes along with environmental factors, inflammatory states, the well-being of the intestinal microbes and hormonal balance.[3]

The entity NAFLD has been identified long time ago as a liver related feature in the spectrum of MetS. Steatosis a part of spectrum of NAFLD. Non-alcoholic steatohepatitis (NASH) results due to elevated Triglycerides (TG) and their accumulation in the hepatocytes.[4] This may progress to cause hepatic fibrosis followed by cirrhosis and even hepatocellular carcinoma if not treated in time.[5] NAFLD is also considered an independent risk factor for Renal morbidity especially

*Junior resident **Professor , Department of General Medicine, D.Y Patil Medical College, Kolhapur.
Corresponding E-mail : shimpasharma@gmail.com

in diabetic patients. [6] Liver is the main organ that is responsible for the regulation of carbohydrate and lipid metabolism and is the main source of inflammatory mediators and cytokines that result in cardiovascular and renal morbidity. A high-fat, low-nutrition, high-sodium diet and a sedentary way of life are also regarded as risk factors for NAFLD. Additionally, CKD can be induced by the use of nephrotoxic medications, glomerular, infectious, and other disorders, in addition to diabetes mellitus and hypertension. [10] The prevalence of CKD is also influenced by age and sex. Age >65 years and female gender were the two groups with the highest prevalence of CKD, suggesting that elderly women should concentrate on early diagnosis of renal function impairment. The risk of CKD in NAFLD patients is typically predicted by markers of NAFLD severity, elements of metabolic syndrome, and few renal function related markers. Additionally, the risk factors that are each separately linked to the development of CKD and NAFLD should not be disregarded. A thorough analysis of these variables has some influence on how clinical practice should be performed. [11] It has also been suggested that stimulation of the RAAS contributes to the decline in renal function in patients with NAFLD. All RAAS components are produced by fat cells, which also contribute up to 30% of the circulatory angiotensin II levels, which encourages the creation of pro-inflammatory molecules and lipogenesis.[12] On the one hand, it can accelerate the advancement of NAFLD; on the other hand, it can cause ectopic lipid deposition to constrict the glomerular efferent arteriole, which in turn triggers inflammatory and oxidative stress, which in turn eventually results in the formation of glomerular sclerosis.

The complex biochemical interactions between the fat tissue (i.e., adipose tissue), kidney and the liver makes it challenging to differentiate and understand the particular process of chronic kidney disease seen in patients with NAFLD. Alterations in activation of renin-angiotensin system and deranged anti-oxidant defence mechanisms and deranged lipogenesis provide increasing evidence of liver and kidney interactions and highlight the scope and need for research in this area. Knowing about these mechanisms helps us to identify modifiable risk factors and therapeutic targets for the occurrence and management of NAFLD and chronic kidney disease.[7] Prevalence of Chronic kidney disease (CKD) (eGFR <90ml/min/1.73 m^2) reportedly ranges from 20% to 55% in case of NAFLD whereas it is 5% to 30% in case of non-NAFLD population as reported by Mantovani A et al.[8] Cardiovascular morbidities in the same study was put at 21% in patients with Type2 DM (T2DM) and 40% in type 2 DM (T2DM) with NAFLD.[9] Presence of NAFLD in T2DM patients has been independently linked to occurrence of CKD and also to higher Cardiovascular morbidity (CV morbidity), as above.

The present study was conducted to evaluate kidney function using Estimated Glomerular filtration rate (eGFR) using MDRD formula, in patients of Type2 Diabetes mellitus (T2DM) with and without NAFLD.

MATERIALS AND METHODS

The study was conducted at out-patient as well as in-patient Department of Medicine at tertiary care hospital after attaining approval from the Institutional Ethical Committee. It was a comparative, Observational, and Cross sectional study. Data collection was done over 18 months. Total 160 patients with T2DM - 80 T2DM with NAFLD and 80 T2DM without NAFLD were included in the study. Patients who had T2DM (ICMR guidelines 2018), belonging to both the genders, who had alcohol consumption < 10 gm/day for females and 20 gm/day for males and those who revealed fatty

liver on ultrasonography. (for diagnosis of NAFLD) were included for the study. While, the patients who were known case of Acute or Chronic Kidney disease, Obstructive Kidney diseases, Cardiovascular diseases, Peripheral vascular disease were excluded from the study. Also, patients who had no other liver disease in past 6 months, conditions with accelerated atherosclerosis, autoimmune diseases, those on anti-cancer drugs, immune suppressants, steroids, COX 2 NSAIDS, known malignancy patients, patients with oliguria and polyuria of any etiology other than T2DM, and patient on nephrotoxic drugs were also excluded from this study. Proper valid written informed consent was taken from the patients in their local language. All the study Participants were screened for presence of Fatty liver by Ultrasound and were divided into two groups those; T2DM with NAFLD and T2DM without NAFLD. Renal morbidity was assessed using serum creatinine and estimated Glomerular filtration rate (eGFR). eGFR was calculated using automated calculation based on equation for Modification of Diet in Renal Disease (MDRD) study.

Also the demographic data like age, sex, gender and Anthropometric data like height, weight, waist-hip ratio, Body Mass Index (BMI) were collected and compiled using Microsoft Excel worksheet for analysis.

Reference Values (cut-off values)

S/NO	Parameters	Reference Values
1	Body Mass Index (Kg/m^2)	>24.99
2	Hypertension	>140/90 mm Hg
3	Random Blood Sugar*	>200 mg/dl
4	Fasting Blood sugar*	>126 mg/dl
5	Post prandial Blood sugar*	>200 mg/dl
6	HbA1c (gm%)*	>6.5 gm%
7	estimated Glomerular Filtration Rate (eGFR)	90 ml to 120 ml

* According to the ICMR guidelines for management of Type 2 Diabetes 2018.

RESULTS

AGE :

Table 1 : presents mean age of both genders in two groups (with and without NAFLD).

	NAFLD	Non-NAFLD	P-value
Male	57.71 ± 11.23	54.18 ± 12.80	< 0.05
Female	57.64 ± 15.11	57.48 ± 12.59	

Table 2 presents Anthropometric and Demographic data of total study participants and also of the two groups (with and without NAFLD).

Table 2 : Demographic and Anthropometric data of study population

PARAMETERS	TOTAL	NAFLD	NON-NAFLD	P-VALUES
AGE (Mean ± SD)	55.90± 13.80	57.68± 12.80	54.11± 14.58	0.10
Duration of Diabetes (Mean ± SD)	6.96± 4.95	7.88± 5.21	6.02± 4.49	0.02*
Duration of HTN (Mean ± SD)	3.75± 1.71	7.82± 4.88	6.16± 3.46	0.13
SBP (Mean ± SD)	122.5± 12.74	121.5± 12.93	123.5± 12.53	0.32
DBP (Mean ± SD)	77.00± 9.70	77.12± 12.93	76.87± 9.22	0.87
BMI (Mean ± SD)	26.85± 3.11	27.75± 3.35	25.95± 2.55	0.00*
WHR (Mean ± SD)	89.09± 9.18	1.05± 0.06	1.03± 0.05	0.03*
HBA1C (Mean ± SD)	7.84± 1.46	8.06± 1.50	7.62± 1.39	0.06

*indicates significant "P" value (<0.05)

Significantly higher duration of DM, BMI and WHR was noted in participants with NAFLD as compared to those without NAFLD (all p<0.05).

Comparison analysis

Table 3 presents the eGFR of the study participants with and without NAFLD in three groups; with reduced filtration(<90 ml/kg/1.73m^2), normal filtration(90-120 ml/kg/1.73m^2) and hyper filtration(>120 ml/kg/1.73m^2) groups.

Table 3 : Correlation of eGFR category with presence of NAFLD

	eGFR				P Value
	< 90	90 to 120	> 120	Grand Total	
Non NAFLD	13	62	5	80	0.00*
NAFLD	70	10	0	80	
Grand Total	83	72	5	160	

*indicate significant P- Value (< 0.05)

Significant correlation was noted between the presence of NAFLD and the presence of reduced eGFR below 90 ml/min/1.73m2 (p=0.00). All patients in the study population with hyper filtration did not have NAFLD.

DISCUSSION

The prevalence of spectrum of NAFLD in type 2 Diabetes mellitus patients is increasing over the period of time. The common risk factors like sedentary life style, metabolic syndrome and overweight (obesity) might be the reason for the association. There is a greater need for study about these two progressive entities to prevent morbidity and resultant mortality, by finding proper association in order to pave way for early diagnosis and management. The prevalence of NAFLD among patients with type 2 diabetes is 59.67% according to the meta-analysis conducted by Wenjie Dai et al. [13] This study was done by analysing the results of twenty-four studies involving 35,599 Type 2 Diabetes Mellitus patients. The usage of ultrasonography modality for diagnosis of NAFLD has been supported in studies conducted by Gomercić M et al and Hamaguchi et al in western population with 60 to 94% sensitivity and 84 to 95% specificity.[14] In this study USG was used for detection of fatty liver.

In the present study the patients with T2DM and NAFLD had higher body-mass index than the T2DM patients without NAFLD (Table 1) which was seen in the study of Fan R et al conducted in 3203 individuals of Zhejiang city of China who stated that increased BMI is an independent risk factor NAFLD.[15] According to study of Khan A et al there is significant correlation between obesity and occurrence of NAFLD.[16]

In this study the Waist-Hip ratio (WHR) is higher in the patients with Diabetes and NAFLD whereas it is slightly lower in patients with Diabetes without NAFLD (Table 1). Similar results were seen in the study of Lin Ms et al conducted in Japan, in 14,125 population taken from a health programme called “health dock”.[17]

The T2DM patients in this study with NAFLD had significantly lower values of eGFR implicating increased renal morbidity compared to patients without NAFLD. This was similarly shown by Chinnadurai R et al in 1419 European population with prevalence of 24-69.5%.[18] A study conducted by Hsieh MH et al in 96 Hispanic patients provides that there is association of impaired eGFR with increased fibrosis score in patients with NAFLD.[19]

The study which was conducted in the Middle-East by Al-Ozairi et al in 2020 showed that there is 44% of prevalence of chronic kidney disease in Diabetic patients.[20] It was suggested in study conducted by Byrne CD et al that the NAFLD itself is a non-dependent factor that contributes to the prevalence

of Chronic Kidney disease.[21] In that study, the T2DM was taken as a confounding factor. In this study the prevalence of renal morbidity in Diabetes with NAFLD patients is 87.5% (Table 2). Hence it suggests that renal morbidity is contributed by presence of both Diabetes and NAFLD.

It is evident that there is higher risk for Renal morbidity in patients those who have both, Diabetes and NAFLD. This study emphasises in need for close monitoring, prevention strategies, early diagnosis and management of the risk factors so that the progression of renal morbidity can be controlled preventing the mortality.

CONCLUSION

Present study has following conclusions:

- There is significant association between the Renal morbidity in Diabetic patients with NAFLD compared to those without NAFLD.
- The results of this study support stricter implementation of prevention and monitoring efforts to pre-empt Renal morbidity in T2DM patients with NAFLD as compared to those T2DM patients without NAFLD.

Conflict of Interest - The authors declare no conflict of interest.

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EVALUATION OF ARTERIAL STIFFNESS IN DIFFERENT STAGES OF CKD PATIENTS

Rajesh Khyalappa, **Syeda Kousar** ***

ABSTRACT

Introduction : Chronic kidney disease (CKD) generates vascular structure and function changes, with significant hemodynamic effects. The early arterial stiffening in CKD patients is a consequence of the interaction between oxidative stress and chronic vascular inflammation, leading to an accelerated deterioration of left ventricular function and alteration in tissue perfusion. Compared to the general population, CKD patientshave CV events twice as often. Increased conduit artery stiffness, especially of the elastic thoracic aorta, is a significant factor in cardiovascular disease, the primary cause of mortality in people with CKD. **Methodology :** The study was conducted at the OPD & IPD department of Dr. D.Y. Patil Hospital & Research Institute, Kolhapur. As per inclusion and exclusion criteria 150 patients were included in the study after counselling and written informed consent was taken in their own language. CKD classification was done based on KDIGO classification (2012) based on eGFR. Arterial stiffness was assessed by using the parameters of diabetic risk profiler and recorded on case record form (CRF). For evidence of early or asymptomatic cardiovascular changes, Carotid Intima Media thickness & Ankle Brachial index (ABI), Augmentation Index (AIX), and Pulse Wave Velocity (PWV) was performed. Data compiled and analysed using MS excel and SPSS. Results- The difference between GFR and ABI, AIX, PWV, C-F PWV, Bra ASI, AnkleASI, CIMT was statistically significant (P value is < 0.05) PWV and CIMT has a signification correlation with the fall in GFR. Higher measures of PWV, IMT, ABI and AIX were seen as the stage of CKD advancesfrom stage 3 to stage 5. **Conclusion :** There is increased risk of arterial stiffness as the stage of CKD advances. CIMT, ABI and PWV are the stiffness indices to assess CV morbidity. Arterial stiffness is a marker of CV morbidity. Hence, this study is useful to assess cardiovascular risk at an early stage and todelay CV morbidity by early intervention.

Keywords : CKD, arterial stiffness, cardiovascular, diabetic risk

INTRODUCTION

Chronic kidney disease (CKD) is becoming more widely recognized as a serious public health problem on a global scale. With chronic kidney disease (CKD), which affects more than 11% of adults worldwide, there is a higher-than-average risk of developing end-stage renal disease (ESRD), cardiovascular disease (CVD), and mortality. Cardiovascular disease is the main source of morbidity and mortality in CKD patients[1]. When the glomerular filtration rate (GFR) drops below 60 ml/min/1.73 m2, there is a graded and negative relationship between kidney function and cardiovascular morbidity and mortality. The prevalence of CKD, which is defined as kidney structural and/or functional abnormalities noticeable for at least

*Professor & Head of Department, **Junior Resident, Department of Medicine, D.Y. Patil Medical College, Kolhapur
Corresponding E-mail : reach.kousar@gmail.com

three months, is anticipated to fall between 8 and 16% globally [2]. Compared to the general population, CKD patients have CV events twice as often. Increased conduit artery stiffness, especially of the elastic thoracic aorta, is a significant factor in cardiovascular disease, the primary cause of mortality in people with CKD. Segmental pulse wave velocity (PWV), which measures the carotid-femoral aortic stiffness, is a potent, independent predictor of cardiovascular mortality in this population[2]. The non-invasive gold standard for evaluating arterial stiffness is the carotid-femoral PWV, and clinical investigations have shown that monitoring changes in vascular stiffness is a reliable substitute for cardiovascular endpoints[3,4]. Atheromomatosis, which may cause intermittent claudication and need surgery, is often indicated by peripheral artery disease (PAD), which is a common symptom. One of the most popular tests used to identify subclinical PAD is the ankle-brachial index (ABI), which is the ratio between the highest humeral systolic blood pressure and the systolic blood pressure of the lower limbs. A usual ABI is 1 or somewhat higher due to the impact of gravity on the cardiovascular system while standing. An indicator of systemic atherosclerosis, the ankle-brachial blood pressure index (ABI) is substantially correlated with mortality and may help identify those at high risk.[5,6] CIMT is commonly used in research studies as a surrogate endpoint to assess atherosclerosis.[7] It has been shown that CIMT is an independent predictor of future myocardial infarction and stroke risk and that it correlates with cardiac risk factors, improves with treatment known to lower atherosclerotic events, and is related to cardiac risk variables. The incidence of coronary heart disease and stroke is closely correlated with carotid artery intimal-medialthickness (CIMT), a well-established measure of systemic atherosclerosis in the CKDpopulation.[8] A greater augmentation index is linked to damage to the target organ and is a predictor of unfavorable cardiovascular events in a range of patient populations.[9] While upper arm blood pressure and pulse wave velocity cannot, augmentation index may distinguish between a variety of vasoactive. This study is aimed to evaluate the arterial stiffness in different stages of CKD patients, along-with estimation of cardiovascular risk.

MATERIALS AND METHODS

The study was conducted at the OPD & IPD department of Tertiary care center, Kolhapur after all the necessary ethical approval. Data collection was done until august end 2022. The sample size taken for the study was 150 patients. Patients were counselled and written informed consent was taken in their own language. Patients belonging to both the genders, above 18 years of age and CKD patients were included for the study. Whereas, patients with known CV diseases Malignancy, Pregnant or lactating mothers, known case of Peripheral vascular disease- Berger's disease, Raynaud'sdisease, Polycystic Kidney Disease, Drug induced hypertension (amphetamines, MAO inhibitors, SNRI, TCA, sympathomimetic, OCPs, systemic corticosteroids) were excluded from the study. All the necessary investigations were done like blood urea & serum creatinine. Arterial stiffness was assessed by using diabetic risk profiler and recorded on case record form (CRF). For evidence of early or asymptomatic cardiovascular changes, Carotid Intima Media thickness & Ankle Brachial index (ABI), Augmentation Index (AIX), and Pulse Wave Velocity (PWV) were performed.

Carotid to femoral PWV measurements

Measured in the supine position after at least 5 mins of rest. Pulse wave forms from Right Carotid & Right Femoral arteries are capturedfor 10 seconds.

The mechanism by which high PWV leads to CKD progression is likely attributable to an increment in propagation of energy in pulsatile flow wave into the low resistance kidneys. Loss of autoregulation on blood flow which results in exacerbation of pulsatile energy transmission; damage of glomerularvasculature as progressive loss of kidney function

CIMT Measurement -

Max CIMT was defined as the mean of the two max values, one of each carotid artery and divided into groups.

High > 0.86 or low <= 0.86mm

eGFR, BMI and gender remain significant predictors of CIMT

>= 0.86 – High Cardiovascular mortality and Morbidity

<= 0.86 Low Cardiovascular mortality and Morbidity

ABI Measurement

ABI =**Highest SBP Posterior tibial artery or Dorsalis pedis artery**

Highest Brachial SBP

ABI	Interpretation
> 1.4	Calcification/ Vessel hardening
1.0-1.4	Normal
0.9-1.0	Acceptable
0.8-0.9	Some Arterial Disease
0.5-0.8	Moderate Arterial Disease
<0.5	Severe Arterial Disease

GFR Cockcroft-Gault formula = (140- age) * weight (kg) * 0.85

Serum Creatinine * 72 Female

RESULTS

Table 1 : Mean Carotid Intima-Media Thickness in different stages of CKD

Parameter	Stage III		Stage V		Stage VI		P value
	Mean	SD	Mean	SD	Mean	SD	
Right CIMT	1.01	0.09	1.02	0.09	1.02	0.09	0.00*
Left CIMT	1.09	0.06	1.10	0.07	1.09	0.06	0.00*
Mean CIMT	1.16	0.09	1.17	0.08	1.16	0.08	0.00*

Table 2 : Mean of Pulse wave velocity in different stages of CKD

Parameter	Stage III		Stage V		Stage VI		P value
	Mean	SD	Mean	SD	Mean	SD	
Right Brachia PWV	1921.20	1389.63	2474.69	2468.59	2164.73	1824.93	0.00*
Left BrachiaPWV	1816.92	476.81	1855.03	1137.87	1835.97	670.79	0.00*
Mean PWV	2551.91	919.25	2596.76	1473.63	2574.34	1150.67	0.00*

*indicate statistically significant "P" value (P<0.05).

The mean values of Right, left and Mean PWV are significantly different in all stages (stage III, IV and V) (all P<0.01).

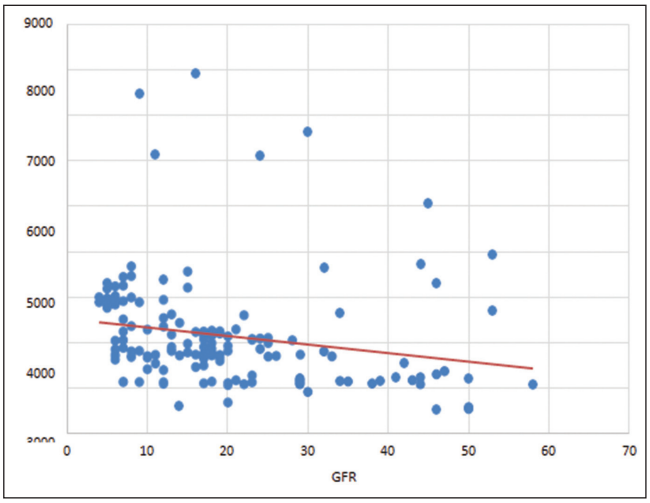

Fig. 1 : Correlation between GFR and PWV

In the above scatter diagram, all the points show the downward trend, from left upper corner to right lower corner which indicates a negative correlation between eGFR and PWV having Karl- Pearsons correlation coefficient r=-0.20 with 'p' value 0.01 (<0.05) indicates a significant negative correlation between eGFR and ABI (i.e PWV increases with the fall in GFR).

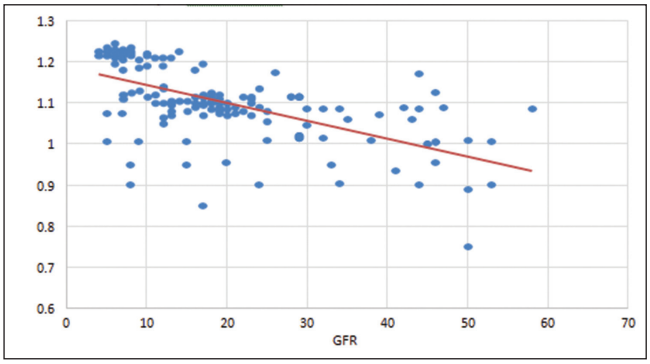

Fig. 2 : Correlation between GFR and CIMT

In the above scatter diagram, all the points show the downward trend, from left- upper corner to right lower corner which indicates a negative correlation between eGFR and CIMT having Karl- Pearsons correlation coefficient r=-0.61 with 'p' value 0.00 (<0.05) indicates a significant negative correlation between eGFR and CIMT (i.e CIMT increases with the fall in GFR).

DISCUSSION

In the above mentioned **Table no 1**. we have compared the Mean Carotid Intima- Media Thickness in different stages of CKD.As per the table, the mean value of right CIMT in stage III of CKD patients is 1.01 and SD is 0.09. In stage IV, the mean value is 1.02 and SD is 0.09 whereas in stage V the mean value is 1.02 and SD is 0.09. Means of right CIMT are significantly different in various stages of CKD (P value < 0.05). The mean value of Left CIMT in stage III of CKD patients is 1.09 and SD is 0.06. In stage IV, the mean value is 1.10 and SD is 0.07 whereas in stage V the mean value is 1.09 and SD is 0.06. Means of left CIMT are significantly different in various stages of CKD (P value < 0.05). The mean value of mean CIMT in stage III CKD patients is 1.16 with SD 0.09. In stage IV, the mean and SD value is 1.17 and 0.08. In stage V, the mean value is 1.16 with SD 0.08. Means of mean CIMT are significantly different in various stages of CKD (P value <0.05).

In Table no.2 we have compared the Mean of Pulse wave velocity in different stages of CKD. As per the above table, the mean value of PWV in right brachia is 1921.20 and SD is 1389.63 in stage III of CKD patients. In stage IV, the mean value is 2474.69 with SD 2468.59 whereas in stage V the mean value is 2164.73 and SD is 1824.93 which are significantly different in various stages of CKD (P value <0.05). The mean of PWV (left brachia) in stage III CKD patients is 1816.92 with SD as 476.81. In stage IV, the mean value is 1855.03 and SD is 1137.87 whereas in stage V the mean value is 1835.97 with SD 670.79 which are significantly different in various stages of CKD (P value <0.05). The mean value of Mean PMV in stage III CKD patients is 2551.91 and SD is 919.25. In stage IV, the mean and SD value are 2596.76 and 1473.63 respectively. In stage V, the mean value is 2574.34 with SD as 1150.67 which is significantly different in various stages of CKD (P value <0.05).From present study, it was observed that the association between arterial stiffness and CKD outcomes remained significant after those risk factors were taken into consideration in analysis, arterial stiffness can result in or result from CKD arterial stiffening, especially in the aortic vasculature, facilitates the transmission of excessive pressure and flow pulsatility into the microvascular beds of the kidneys, Hemodynamic stress on the kidney vasculature may result in endothelial dysfunction and

microvascular ischemia, leading to kidney damage. **Natalia G. Vallianou et al study**[10], CKD had been recognized as an independent CVD risk equivalent, and it is strongly recommended that the CKD population be considered the highest risk group for subsequent development of CVD. Mild to moderate CKD is robustly associated with increased cardiovascular morbidity and mortality, independently from classical cardiovascular risk factors, such as hypertension and diabetes. Novel risk factors such as inflammation, oxidative stress, bone and mineral disorders; hyperphosphatemia, hypercalcemia, secondary hyperparathyroidism - that are attributed to compromised renal function-, are highly associated with elevated cardiovascular risk in patients with kidney disease. Accounting for these various risk factors, we may be able to postulate that the pathophysiology involved in the development of CVD is common in the CKD and non CKD population. However, renal dysfunction alone, through novel risk factors, plays an important role in the worsening of CVD. Hence, treatment should target not only in slowing the progression of renal disease, but in modifying the additional CV factors early in the course of the disease, as well. Lifestyle modifications are known to counteract the development of CVD, such as decreased consumption of salt, glucose, protein, and free fatty acids, in addition to non-dietary factors like, smoking cessation, regular exercise, and weight loss. PWV and CIMT has a signification correlation with the GFR. Higher values of PWV and CIMT were seen as the stage of CKD advances from stage 3 to stage 5.

CONCLUSION

There is increased risk of arterial stiffness as the stage of CKD advances. CIMT, and PWV are the stiffness indices to assess CV morbidity. Arterial stiffness is a marker of CV morbidity. Hence, this study is useful to assess cardiovascular risk at an early stage and todelay CV morbidity by early intervention. Therefore, CKD patients are advised for serial measurement of stiffness indices to halt the progression of the disease. Several novel therapies to decrease the risk of cardiovascular diseases in CKD are to be made available in particular in those with advanced CKD, thus paving the way toward a more evidence-based approach to reduce cardiovascular risk in CKD.

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COMPARISION OF PAN-RETINAL PHOTOCOAGULATION WITH AND WITHOUT ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR IN THE TREATMENT OF HIGH-RISK PROLIFERATIVE DIABETIC RETINOPATHY

Bobbiti Linga Sai Greeshma Reddy, Milind M. Sabnis**,* ***Chintamani Khare******

ABSTRACT

Purpose : To compare PRP with and without intravitreal injection of bevacizumab (Anti-vascular endothelial growth factor) in patients of high-risk proliferative diabetic retinopathy. **Methods** : A prospective, interventional study was conducted in 60 patients with high-risk proliferative diabetic retinopathy, of which 30 were treated with pan-retinal photocoagulation and 30 with intravitreal bevacizumab followed by pan-retinal photocoagulation. Patients underwent complete ophthalmic evaluation, including IOP, BCVA, and fluoresce in angiography at 4,12,16 weeks post-treatment. The main outcome measures included the IOP changes, serial changes in BCVA, regression, and reactivation of neovascularization. **Results** : At each follow-up in this study, no significant difference was found in IOP in the 2 groups. Although there is an increase in mean BCVA in both groups at the 16th week of follow-up, there is no significant difference in best corrected visual acuity between the 2 groups at any follow-ups. Regression is not statistically different in the 2 groups however it is more in individuals who underwent IVB+PRP. But when combined with PRP, intravitreal bevacizumab led to a greater reduction in neovascularization than PRP alone. There was no statistically significant recurrence observed in both groups, but reactivation is seen more in PRP alone group. The total number of patients who had developed complications and had to undergo surgery in the PRP group is 3(10%) patients and in IVB+PRP are 2(6.6%) patients. However, there is no significant difference found between the two groups in our study. The mean sittings of PRP required in the PRP group is 3.83± 0.38 and in IVB PLUS PRP is 3.1 ± 0.31. The statistically significant difference is found in the sittings required for both groups. Patients who were given intravitreal bevacizumab required fewer sittings of PRP. **Conclusion** : In the short term, the adjunctive use of intravitreal bevacizumab with PRP showed no greater regression in neovascularization compared to PRP alone but required lesser sittings of PRP when combined with intravitreal bevacizumab.

INTRODUCTION

Diabetic retinopathy is a silent disease and calls for early detection and timely intervention. DR, also called diabetic eye disease is an entity occurring in patients of diabetes mellitus and there occurs degeneration of the retina causing gradual progressive painless deterioration of vision over 20 years or more. Diabetic retinopathy constitutes 4.8 percent of the global causes of blindness throughout the world. DR, a very specific

*Junior Resident, **M.S. Ophthalmology, ***M.S.(Oph), D.N.B.(Oph) F.M.R.F, F.I.C.O.(UK) Assistant Professor, Department of Ophthalmology, D. Y. Patil Medical College, Kolhapur. **Corresponding E-mail :** kharecm@gmail.com

repercussion of type 2 DM, is substantially correlated with the scale of sugar control and disease duration. Compared with the general population, patients with diabetes have a 20–25 fold higher risk of becoming blind. After the affliction has persisted for ten years, retinopathy is common but not always present, and the majority of patients are affected after twenty years. Thus, it has an impact on both young and old since the key factor is the diabetes age rather than the chronological age.[1] The primary long-term cause of diabetic retinopathy is chronic hyperglycemia, which is influenced to varying extents by inherited and acquired systemic determinants. Therefore, smoking can stop or slow the development of diabetes if there is strict long-term diabetic control combined with control of hypertension. Retinal neovascularization is an important risk factor for serious vision loss in diabetics. In these patients, retinal neovascularization development and progression[2] whether on disc or elsewhere, is a significant risk factor for irreversible vision loss. Since the signal protein VEGF factor plays a significant role in the pathologic mechanism of PDR, neovascularization is the main characteristic of the condition. VEGF is crucial for the development of PDR and has been linked to neovascularization of the human eye. When microvascular blockage causes ischemia in the retina, VEGF is released into the ocular fluid, which promotes the development of new blood vessels. Additionally, VEGF causes diabetic macular edema by making capillaries more permeable. Better visual rehabilitation can be facilitated by effective treatment in PDR. PRP has been the accepted management of high-risk PDR for the past 40 years.[1] It significantly slows down neovascularization in the retina. When PRP was administered to high-risk PDR patients, likelihood of the severe loss of vision was shown to be reduced by over 50%. 60% of PDR patients react to PRP within 3 months with the regression of new vessels. [2] Within three months, neovascularization in sixty percent of individuals with PDR responds to PRP. Despite PRP, many patients also need laser therapy, and 4.5% eventually need a pars plana vitrectomy. The current trend in DME treatment is anti-VEGF pharmacotherapy. It is yet unclear if anti-VEGF medications could be used as a substitute for PRP in high-risk PDR cases or as a supplementary therapy. According to the ETDRS study, laser therapy be lessening the likelihood of irreversible vision reduction and can reduce the course of the illness. Pan retinal photocoagulation is the preferred form of treatment for PDR because it reduces the chance of developing high-risk PDR by fifty percent over the course of three months. However, for patients having a thick cataract or vitreous hemorrhage, [3] photocoagulations might not be an option. Despite pan-retinal photocoagulation, there may develop complications such as vitreous hemorrhage, rubeosis, and secondary glaucoma in situations with persistent new arteries. [4] According to recent studies, VEGF is a major factor in the neovascularization of the eye, and intravitreal anti-Vascular endothelial growth factor injections can cause PDR neovascularization to regress. [5] Studying this comparison could also aid in selecting the surgical procedure and PDR's prognosis. The visual outcomes of pan-retinal photocoagulation in PDR are extremely positive. But continuous photocoagulation over the long term is necessary for successful visual outcomes. VEGF can be inhibited in addition to intravitreal anti-VEGF medications to assist limit neovascularization.[6] This intrusive, frequently painful procedure of laser may also be in reduced peripheral vision and more risk of diabetic macular oedema, despite the fact that severe loss of central vision caused by Proliferative

diabetic retinopathy can typically be prevented with Pan retinal photocoagulation.[7] Blocking VEGF has been linked to the reduction of neovascularization over the iris and the suppression of retinal, new vessel development in primates and humans. VEGF has been involved in the aetiology of human eye illnesses defined by new vessels.[8] With positive first results, many trials are presently examining the effectiveness of anti-VEGF medications in the management of patients with macular oedema due to diabetes and retinal Neovascularization. In the case of DR, regression of Neovascularization on the disc was recently shown following intravitreal injection of the antiangiogenic drug bevacizumab. [9-10] Although retinal Neovascularization tended to return within twelve weeks after one intravitreal bevacizumab injection, this impact seemed to be temporary. Therefore, the purpose of this current study is to examine any potential additional effects of intravitreal injection of bevacizumab when coupled with PRP in the treatment of Proliferative diabetic retinopathy. [11]

AIMS, OBJECTIVES AND HYPOTHESIS

AIM : To compare PRP with and without intravitreal injection of bevacizumab (Anti-vascular endothelial growth factor) in patients of high-risk proliferative diabetic retinopathy.

OBJECTIVES : To measure changes in Intraocular pressure after PRP with and without Intravitreal Bevacizumab, to compare the visual outcome (Best corrected visual acuity) after PRP with and without Intravitreal Bevacizumab. to evaluate effects of PRP with and without Intravitreal Bevacizumab on regression of neovascularization. to evaluate effects of PRP with and without Intravitreal Bevacizumab on reactivation of neovascularization.

HYPOTHESIS : There is no significant difference in IOP, BCVA, Regression of neovascularization and Reactivation of neovascularization after pan-retinal photocoagulation with and without Anti VEGF in the treatment of high risk proliferative diabetic retinopathy.

MATERIALS AND METHODS

TYPE OF STUDY : Comparative and Interventional study.

STUDY PERIOD : On receipt of the Institutional Ethics Committee's approval letter for the study under the subject, a study has been conducted during the period of March 2021 to July 2022

SAMPLE SELECTION AND SAMPLE SIZE : Patients were selected from tertiary care centers, who were diagnosed with high-risk PDR.

Considering the prevalence of High-risk PDR as 2% in our hospital, the total sample size calculated is 60.

The formula $N=4pq/e^2$ is used to determine sample size.

N is the size of the sample,

p is the prevalence

q = 100-p

e = allowable error (5-20% of p)

SAMPLING DESIGN : A simple Consecutive Sampling Method was followed, and samples were grouped into two, first group underwent pan-retinal photocoagulation, the second group underwent Intravitreal Bevacizumab followed by pan-retinal photocoagulation.

RESEARCH DESIGN AND DETAILED METHODOLOGY : After meeting inclusion and exclusion criteria, all patients coming to Ophthalmology OPD at a tertiary care center were included in this study. Informed written consent was taken from the patient before the study.

The vision was tested on a standard Snellen's chart. Intraocular pressure measurement was done by applanation tonometry under topical anesthesia. Detailed anterior segment examination was done on a slit lamp, before and after pupillary dilatation. Direct and indirect ophthalmoscopy was done after pupillary dilatation for fundus evaluation and diagnosis of High-risk PDR.

Retinal evaluation was performed by fundus photography and fluorescein angiography was done if needed. The cases were grouped into – GROUP A and GROUP B by simple consecutive method. The cases of group A underwent pan-retinal photocoagulation and cases of group B underwent Intravitreal bevacizumab followed by pan-retinal photocoagulation as treatment in Khare Eye Hospital and Laser Clinic by Dr. Chintamani Madhav Khare (vitreoretinal surgeon). The patients were scheduled for follow-up examination on 4 weeks, 12 weeks and 16 weeks and the baseline factors like IOP, BCVA, regression of retinal new vessels, were evaluated in 2 groups. Reactivation of neovascularization was evaluated in the two groups and results were analyzed.

THE OBJECTIVE METHODS INCLUDE

Technique of Intravitreal bevacizumab injection:

In the operating room, injection was carried out via pars plana under aseptic settings. Topical anaesthetic eye drops were injected at least three times prior to injection. The povidine-iodine solution was applied onto the eyelid borders and conjunctival sac. A lid speculum was inserted after a sterile drape had been placed. Using a tuberculin syringe, inject 2.5 milli gram (0.1 milli litre) of bevacizumab 4 milli metre away limbus in phakic eyes and 3.5 milli metre away limbus in pseudophakic eyes. to maintain a sufficient postoperative IOP, AC paracentesis was done before giving injection. To avoid reflux, the needle is carefully removed using sterile cotton swab. Following injection, topical corticosteroid and antibacterial eye drops were used four times per day for a week.

Pan Retinal Photocoagulation Procedure:

PRP is commonly administered via a laser indirect ophthalmoscope or a slit lamp device.

Slit lamp Biomicroscopy: The laser is connected to a standard slit lamp used in ophthalmology, and laser energy is administered in a coaxial manner. The patient is positioned in a seated position with a chin rest under it. Contact lens is used to focus on the retina. Headlamp: The patient could be sitting or lying down. The laser is coaxially linked to the doctor's usual indirect light. The retina is viewed using a handheld lens, and the laser is focused on the retina. The aiming beam is moved by the doctor's head motions. Apply topical anaesthesia to both eyes in both settings, either proparacaine or tetracaine. Over the course of one to four treatment sessions, both techniques produce burns that range in size from 1500 to 5000. The usual argon-type laser PRP is used in accordance with the DRS procedure, with burns that range in size from 200 to 500, pulse durations of 100 milliseconds, and power levels of 200 to 250 mW. Grey burns are ideal, but burns that are densely white are to be avoided.

INCLUSION CRITERIA

Patients with Type 2 diabetes mellitus, gender- male and female, all patients diagnosed with high-risk. Proliferative diabetic retinopathy according to ETDRS classification requiring management.

EXCLUSION CRITERIA

Hypertension, Insulin-dependent Diabetes mellitus, any history of other vitreoretinal diseases like vitreous degeneration, retinal detachment, and previous laser treatment, intravitreal injections or vitrectomy, active ocular inflammatory conditions like uveitis, scleritis, and Associated glaucoma. intraocular surgeries (cataract, ND YAG capsulotomy) in the last 3 months.

METHODS OF DATA COLLECTION

The patients examined in ophthalmology OPD at a tertiary care center, External ocular examination by torch, BCVA, examination by Slit lamp, Iop check-up by applanation tonometry (Goldmann's), Direct and indirect, ophthalmoscopy after pupillary dilatation.

INSTRUMENTS USED

Torch – 3 celled, Slit lamp Bio- microscope (Haag streit 5 step model), Goldmann applanation tonometer, Direct ophthalmoscope (Heine beta 200 LED), Indirect ophthalmoscope (Appasamy model AAIO WIRELESS) with 20D lens, Fundus camera (Topcon TRC NW 8F), Laser details: IRIDEX OCULIGHT GREEN LASER

METHODS OF DATA ANALYSIS Data analysis and a master chart was prepared by using Microsoft Office 365 Excel 2016 was used for data analysis.

OBSERVATION AND RESULTS

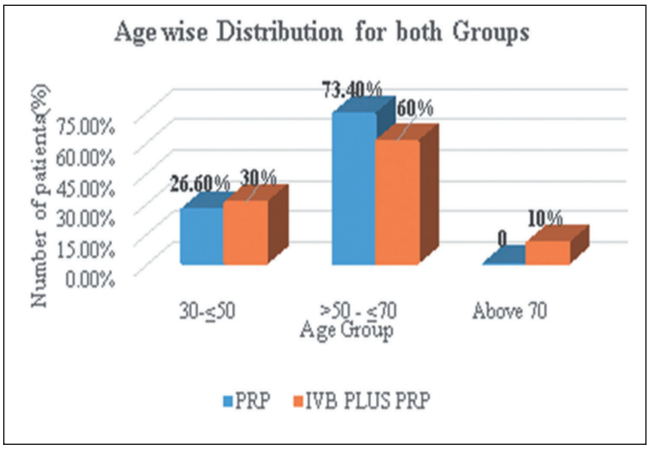

Fig. 1 : Distribution of patients according to Age.

With total of 60 Patients in our study, 8 (26.6%) patients of PRP and 9 (30%) patients of IVB+PRP were in 30-49 group, 22 (73.4%) patients of PRP and 18 (60%) patients of IVB+PRP were in 50-69 group, 3 patients of IVB+PRP were in above 70 group.

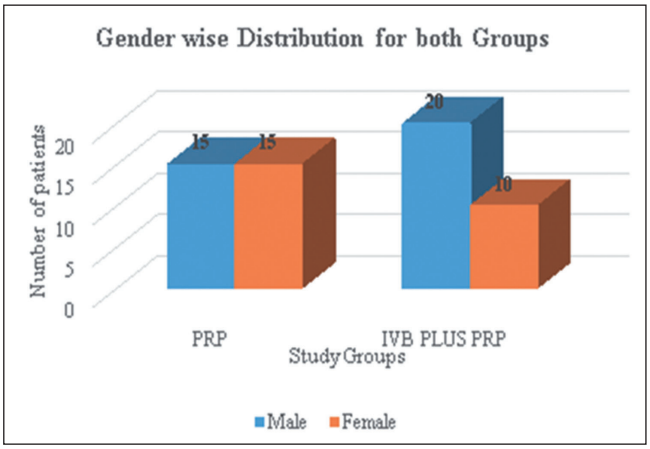

Fig. 2 : Gender wise distribution of patients.

Out of total of 60 Patients in our study, 35 patients were males and 25 patients were females. In which 15 of males were of PRP and 20 were of IVB + PRP, 15 of females were of PRP and 10 were of IVB + PRP.

Table 1 : Estimation of IOP in Both the Groups Before Procedure and in Follow ups

	IOP			
	Pre Procedure	4th week F/U	12th week F/u	16th week F/u
PRP	16.7 ± 2.22	17.83 ± 1.93	16.87 ± 2.18	16.77 ± 2.06
IVB PLUS PRP	16.03 ± 2.3	16.6 ± 2.44	16 ± 2.08	15.8 ± 2.14
P value	0.25	0.03	0.12	0.07

IOP was assessed in both groups in our study both before and after the procedure.

Mean IOP of patients who underwent PRP before procedure is 16.7 ± 2.2 and on 4th week f/u is 17.83 ± 1.93, on 12th week f/u 16.87 ± 2.18 and on 16th week f/u is 16.77 ± 2.06.

Mean IOP of patients who underwent IVB+PRP before procedure is 16.03 ± 2.3 and on 4th week f/u is 16.6 ± 2.44, on 12th week f/u 16 ± 2.08 and on 16th week f/u is 15.8 ± 2.14

There is no significant difference in IOP in both groups at each follow up.

Table 2 : Estimation of BCVA in Both the Groups Before Procedure and in Followups.

	BCVA			
	Pre Procedure	4th week F/U	12th week F/U	16th week F/U
PRP	0.47 ± 0.25	0.44 ± 0.24	0.42 ± 0.23	0.4 ± 0.23
IVB PLUS PRP	0.6 ± 0.27	0.55 ± 0.23	0.46 ± 0.21	0.44 ± 0.2
P value	0.06	0.08	0.48	0.48

The mean BCVA (according to the log Mar chart) of patients who underwent PRP before the procedure is 0.47 ± 0.25 and on the 4th week f/u is 0.44 ± 0.24, on the 12th week f/u 0.42 ± 0.23 and on 16th week f/u is 0.4 ± 0.23.

Mean BCVA of patients who underwent IVB+PRP before the procedure is 0.6 ± 0.27 and on the 4th week f/u is 0.55 ± 0.23, on the 12th week f/u 0.46 ± 0.21 and on the 16th week f/u is 0.44 ± 0.2.

There is no significant difference in BCVA in both groups at each follow-up, but there is an increase in mean BCVA at the 16th-week follow-up in both groups.

Table 3 : Distribution of Regression of Neovascularization in Both the Groups.

REGRESSION OF NV	4th week F/U	12th week F/U	16th week F/U
PRP	23 (76.7%)	27 (90 %)	27 (90 %)
IVB PLUS PRP	27 (90 %)	27 (90 %)	28 (93.3%)
P value	0.17	1	0.67

In our study, Regression of Neovascularization at 4th-week follow-up in the PRP group is seen in 23 (76.7%) patients, whereas, in the IVB+PRP group, it is seen in 27 (90%) patients.

At the end of the 12th week regression in both groups is 90%, and in the 16th week regression in the PRP group is seen in 27 (90%) patients but in the IVB+PRP group, it is seen in 28 (93.3%) patients.

There is no statistically significant difference in regression in both groups but regression is seen more in patients who underwent IVB+PRP.

Table 4 : Distribution of Reactivation of Neovascularization in Both the Groups

	PRP	IVB+PRP	P VALUE
REACTIVATION	3 (10%)	2 (6.6%)	0.63

In our study reactivation of neovascularization in the PRP group is seen in 3 (10%) patients and in the IVB+PRP group it is seen in 2 (6.6%) patients.

Table 5 : Distribution of Patients who had to undergo surgery (developed complications)

	PRP	IVB PLUS PRP	P value
Patients underwent surgery	3 (10%)	2 (6.6%)	0.63

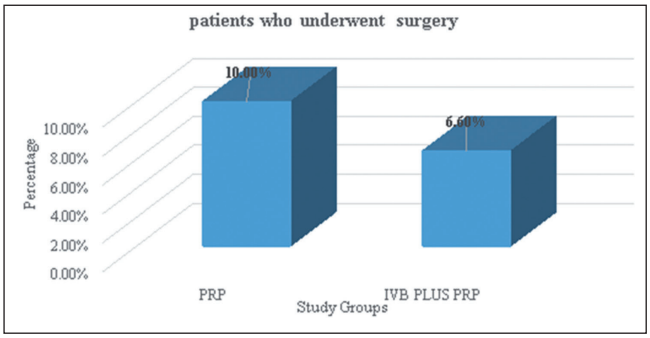

Fig. 3: Distribution of patients who had to undergo surgery (vitrectomy)

In our study total patients who had developed complications and had to undergo surgery in PRP group are 3 (10%) patients and in IVB+PRP are 2 (6.6%) patients.

Table 6 : Mean Sittings of PRP Required in Both Groups.

	PRP	IVB PLUS PRP	P value
SITTINGS OF PRP	3.83 ±0.38	3.1 ± 0.31	0.001

In our study, mean sittings of PRP required in PRP group is 3.83 ± 0.38 and in IVB PLUS PRP is 3.1 ± 0.31.

Statistically significant difference found in sittings required for both groups.

Patients who were given intravitreal bevacizumab required less sittings of PRP.

DISCUSSION

Our study was designed with a sample size of 60 considering the incidence of High-risk PDR as 2%. All high-risk PDR cases that meet the inclusion and exclusion criteria during the research period from March 2021 to July 2022 are included in our study and grouped into group A and group B by random sampling method. Group A patients underwent PRP and group B patients underwent Intravitreal Bevacizumab followed by PRP. In our study, we have defined the null hypothesis as there is no significant difference in IOP, Best corrected visual acuity, regression of neovascularization, and reactivation of neovascularization after pan-retinal photocoagulation with and without Anti VEGF in the treatment of high-risk PDR.

Total out of total 60 patients in our study, 8 (26.6%) patients of PRP and 9 (30%) patients of IVB+PRP were in 30-49 group, 22 (73.4%) patients of PRP and 18 (60%) patients of VB+PRP were in 50-69 group, 3 patients of IVB+PRP were in above 70 group. Out of total 60 patients, 25 patients were females and 35 patients were males. In which 15 of males were of PRP and 20 were of IVB+PRP, 15 of females were of PRP and 10 were of IVB+PRP.

IOP was measured before the procedure and at every follow-up in both groups. Before the procedure means IOP of patients in the PRP group is 16.7 ± 2.2 and on the 4th week f/u is 17.83 ± 1.93, on the 12th week

f/u 16.87 ± 2.18 and on the 16th week f/u is 16.77 ± 2.06. Before the procedure means IOP of patients in the IVB+PRP group is 16.03 ± 2.3 and on 4th week f/u is 16.6 ± 2.44, on the 12th week f/u 16 ± 2.08 and on the 16th week f/u is 15.8 ± 2.14. There is no significant difference in IOP in both groups at each follow-up. The mean BCVA (according to the log Mar chart) of patients who underwent PRP before the procedure is 0.47 ± 0.25 and on 4th week f/u is 0.44 ± 0.24, on 12th week f/u 0.42 ± 0.23 and on 16th week f/u is 0.4 ± 0.23. Mean BCVA of patients who underwent IVB+PRP before the procedure is 0.6 ± 0.27 and on the 4th week f/u is 0.55 ± 0.23, on the 12th week f/u 0.46 ± 0.21 and on the 16th week f/u is 0.44 ± 0.2. There is no significant difference in BCVA in both groups at each follow-up, but there is an increase in mean BCVA at the 16th-week follow-up in both groups. Regression of Neovascularization at 4th week follow-up in the PRP group is seen in 23 (76.7%) patients, whereas in the IVB+PRP group, it is seen in 27 (90%) patients. At the end of the 12th week, regression in both groups is 90%, and in the 16th week regression in the PRP group is seen in 27 (90%) patients but in the IVB+PRP group, it is seen in 28 (93.3%) patients. There is no statistically significant difference in regression in both groups but regression is seen more in patients who underwent IVB+PRP. Reactivation of neovascularization in the PRP group is seen in 3 (10%) patients and in the IVB+PRP group it is seen in 2 (6.6%) patients. The total number of patients who had developed complications and had to undergo surgery in the PRP group is 3 (10%) patients and in IVB+PRP 2 (6.6%) patients.

The mean sittings of PRP required in the PRP group is 3.83 ± 0.38 and in IVB PLUS PRP is 3.1 ± 0.31. There is a statistically significant difference in sittings required for both groups.

Patients who were given intravitreal bevacizumab required fewer sittings of PRP.

Patients diagnosed with high-risk Proliferative diabetic retinopathy who underwent complete PRP but who did not have fibrosis or regression of retinal new vasculature are at great risk of suffering a significant reduction in vision. The Macugen Diabetic Study Group discovered a decrease in retinal neovascularization in 62 percent of treated eyes compared to 0 percent of the untreated eyes when anti-VEGF medication was used in these cases. [12] According to Adamis et al. retinal new vessel reduction is more in patients who were given intravitreal injection compared to those who underwent pan-retinal photocoagulation alone. Arevalo et al. and Avery et al. state that the availability of bevacizumab and its use in ARMD patients, it's been propagated for patients diagnosed with DME and PDR. [13] Jorge e al. prospective, non-randomized research, a single 1.5 mg injection of bevacizumab resulted in a significant decrease in retinal neovascularization and showed improvement in BCVA in the group of 15 eyes who were followed up for 12th weeks.[14] In our study we investigated the effect of PRP with and without intravitreal bevacizumab patients diagnosed with high risk Proliferative diabetic retinopathy. From all patients after being told the nature of the disease and visual prognosis, informed consent was taken. Objectives investigated in this study are IOP, BCVA, Regression and reactivation of neovascularization in the 4th week, 12th week and 16th week follow-up. IOP: Mean IOP of patients who underwent PRP before the procedure is 16.7 ± 2.2 and on the 4th week f/u is 17.83 ± 1.93, on the 12th week f/u 16.87 ± 2.18, and on the 16th week f/u is 16.77 ± 2.06. The mean IOP of patients who underwent IVB+PRP before the procedure is 16.03 ± 2.3 and on the 4th-week f/u is

16.6 ± 2.44, on the 12th week f/u 16 ± 2.08, and on the 16th week f/u is 15.8 ± 2.14. No significant difference was noticed in IOP in both groups at each follow-up in this study. This result is comparable to that of the Chun et al. study, which found no significant difference between 2 groups in IOP. The result of this study is similar with the data which was taken from other studies (Chun et al; Iturralde et al; Mason et al.) which showed no apparent association between intravitreal bevacizumab injection and raised IOP. [15]

BCVA: Mean BCVA (according to logMar chart) of patients who underwent PRP before the procedure is 0.47 ± 0.25 and on 4th week f/u is 0.44 ± 0.24, on 12th week f/u 0.42 ± 0.23 and on 16th week f/u is 0.4 ± 0.23.

Mean BCVA of patients who underwent IVB+PRP before the procedure is 0.6 ± 0.27 and on the 4th week f/u is 0.55 ± 0.23, on the 12th week f/u 0.46 ± 0.21 and on the 16th week f/u is 0.44 ± 0.2.

There is no significant difference in BCVA in both groups at each follow-up, but there is an increase in mean BCVA at the 16th-week follow-up in both groups.

In contrast, earlier studies by Avery et al. and Haritoglou et al. showed that intravitreal anti-angiogenic therapy significantly improved BCVA.[13,16]

The disappearance of previously existing pre-retinal or pre-vitreous hemorrhage may account for this variation.

REGRESSION OF NEOVASCULARIZATION

Regression of Neovascularization at 4th week follow-up in the PRP group is seen in 23 (76.7%) patients, whereas in the IVB+PRP group, it is seen in 27 (90%) patients. At the end of the 12th week regression in both groups is 90%, and in the 16th week regression in the PRP group is seen in 27 (90%) patients but in the IVB+PRP group it is seen in 28 (93.3%) patients. There is no statistically significant difference in regression in both groups but regression is seen more in patients who underwent IVB+PRP. Although the use of intravitreal bevacizumab with PRP was linked to show a higher decrease of neovascularization than Pan retinal photocoagulation alone, results of the current investigation indicate that both therapies are related to regression of retinal new vessels in patients diagnosed with high-risk Proliferative diabetic retinopathy. (Manson et al; spaide and fisher).

When combined with PRP, intra-vitreal bevacizumab shows synergistic effects in treating high-risk Proliferative diabetic retinopathy with extensive disc neovascularization. Tonello et al. study showed that in high-risk PDR patients undergoing short-term observation, intravitreal bevacizumab injection was used adjuvantly with PRP and led to more neovascularization regression than PRP alone. [17]

REACTIVATION OF NEOVASCULARIZATION

Reactivation of neovascularization in the PRP group is seen in 3 (10%) patients and in the IVB+PRP group it is seen in 2 (6.6%) patients. There was no statistically significant recurrence observed in both groups, but reactivation is seen more in PRP alone group. Jorge et al; Bakri et al; Avery et al. studies state that a highly significant reduction of neovascularization was found at a one-month follow-up visit, in the majority of patients, reperfusion of retinal neovascularization was observed post 3 months after follow-up and necessitated further therapy. [13-14] According to studies by Arevalo et al. and Schmidinger et al., a significant number of high-risk PDR patients displayed a

recurrence of neovascularization starting at 3 months. Therefore, we decided to observe patients for at least 4 months following their initial treatment. [18]

PATIENTS UNDERWENT SURGERY

The total number of patients who had developed complications and had to undergo surgery in PRP group are 3 (10%) patients and in IVB+PRP are 2 (6.6%) patients. According to Chun et al. study patients who were given intra vitreal bevacizumab developed lesser complications and the requirement of surgery was less.

However, between the two groups in our investigation, there was no significant difference.

SITTINGS OF PRP REQUIRED

The mean sittings of PRP required in the PRP group is 3.83 ± 0.38 and in IVB PLUS PRP is 3.1 ± 0.31.

A statistically significant difference was found in the sittings required for both groups.

Patients who were given intravitreal bevacizumab required less sittings of PRP.

SUMMARY

In the study period from March 2021 to July 2022 at the tertiary care center all cases that satisfied inclusion and exclusion criteria were enrolled. This study comprised 60 patients diagnosed with high-risk Proliferative diabetic retinopathy, who were divided into 2: A and B groups. Group A patients underwent pan-retinal photocoagulation and group B patients underwent intra-vitreal bevacizumab followed by pan-retinal photocoagulation. In this study, we compared PRP with and without intravitreal injection of bevacizumab (Anti Vascular Endothelial Growth Factor) in patients diagnosed with high-risk PDR. Out of a total of 60 patients, 25 patients were females and 35 patients were males. Of which 15 males were of PRP and 20 were of IVB+PRP, 15 females were of PRP and 10 were of IVB+PRP.

At each follow-up in this study, no significant difference was found in IOP in the 2 groups.

Although there is an increase in mean BCVA in both groups at the 16th week of follow-up, there is no significant difference in best corrected visual acuity between the 2 groups at any follow-ups.

Regression is not statistically different in the 2 groups however it is more in individuals who underwent IVB+PRP. But when combined with PRP, intravitreal bevacizumab led to a greater reduction in neovascularization than PRP alone. There was no statistically significant recurrence observed in both groups, but reactivation is seen more in PRP alone group. The total number of patients who had developed complications and had to undergo surgery in the PRP group is 3 (10%) patients and in IVB+PRP 2 (6.6%) patients. However, there is no significant difference found in the two groups in our study. The mean sittings of PRP required in the PRP group is 3.83± 0.38 and in IVB PLUS PRP is 3.1 ± 0.31. The statistically significant difference is found in sittings required for both groups. Patients who were given intravitreal bevacizumab required fewer sittings of PRP.

CONCLUSION

In our study, we observed that there was no change in IOP in the group at any point of follow-up. The

findings of our study, which showed no correlation between PRP and a rise in IOP, were in line with those of other studies. There was no difference found in baseline BCVA compared between the two groups. The rate of neovascularization regression was found similar in the two groups, although it was higher when PRP and intravitreal bevacizumab were combined together. Reactivation was seen in both groups but more in PRP alone group. The number of PRP sessions needed for the two groups showed a significant difference. PRP alone group required more sittings of PRP than when compared to intravitreal bevacizumab. Although no difference in BCVA, regression was observed, from our results it might be assumed that giving intra-vitreal bevacizumab prior to pan retinal photocoagulation decreases the sittings of PRP required.

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ORIGINAL ARTICLE

THE PREVALENCE OF THYROID DISORDER IN PREGNANCY

Vyshnavi Namala, Prashant Shah**, Deepannita Roy Chowdhary***, **Neelima Shah*******

ABSTRACT

Introduction : The development of maternal thyroid disorders during early pregnancy can influence the pregnancy outcome and fetal development. The present study was conducted to know the prevalence of thyroid disorders in the Indian pregnant population and to know the obstetric outcomes of those pregnant women suffering from thyroid disorders. **Methodology :** The present study was conducted on 100 women who came for an antenatal check-up in the first trimester, with Singleton Pregnancy. A detailed history was taken followed by a thorough general physical examination. Patients were sent for TSH (Thyroid Stimulating Hormone) testing. If TSH (Thyroid Stimulating Hormone) was deranged, then FT3 and FT4 levels were checked. Depending upon the FT3 and FT4 values they are grouped as subclinical/overt hypothyroidism or hyperthyroidism. **Results :** Most of the patients in the present study were from the age group 21 to 30 years. The prevalence of thyroid disorders in the present study was 38%, including hypo and hyperthyroidism. 28% of patients were found to be hypothyroid; 10% of patients were hyperthyroid. **Conclusion :** The prevalence of thyroid disorders, especially hypothyroidism (28%) was high. Further studies are needed to assess adverse effects on maternal and fetal outcomes. Routine antenatal thyroid screening should be done.

Keywords : Thyroid Disorders, Hyperthyroidism, Hypothyroidism, Thyroid profile.

INTRODUCTION

The thyroid gland is the gland that comes under the endocrine gland. The thyroid gland Enlargement is called goiter. Toxic goiter secretes excess thyroid hormones. Nontoxic goiter secretes normal or even subnormal levels of hormones.[1-2] Mutation in developmental transcription factors or their downstream target genes are rare causes of thyroid agenesis or dyshormonogenesis and cause congenital hypothyroidism.[1] Maternal thyroid disorders during early pregnancy can impact the pregnancy outcome and fetal development. Thyroid dysfunction can lead to premature birth, pregnancy-induced hypertension, low birth weight in infants, IUGR (Intrauterine growth retardation), abruptio placenta, and increased fetal mortality.[3] Maternal hypothyroidism in the first trimester may be harmful to fetal brain development and can lead to mental retardation. In view of potential adverse outcomes associated with maternal thyroid disorders and the obvious benefits of treatment, some expert panels have suggested routine thyroid function screening in all pregnant women. The third week of gestation allows the thyroid gland to develop from the floor of the primitive pharynx. The gland migrates from the foramen cecum, at the base of the tongue,

*Junior resident, **Associate Professor, ***Intern, ****Associate Professor
Department of OBST & GYN, D. Y. Patil Medical College, Kolhapur **Corresponidng E-mail :** neelimapshah@gmail.com

along the thyroglossal duct to reach its final location in the neck.[4] This type of feature accounts for the rare ectopic location of thyroid tissue at the base of the tongue (lingual thyroid), and for the presence of thyroglossal duct cysts along the developmental tract.[1] The present study is being undertaken to know the prevalence of thyroid disorders in the Indian pregnant population and to know the obstetric outcomes of those pregnant women suffering from thyroid disorders.

OBJECTIVE

To study the prevalence of thyroid disorders in pregnant women.

MATERIAL AND METHODS

The present study was conducted at a tertiary care center. 100 women, who came for an antenatal check-up in the first trimester, with Singleton Pregnancy were included in the study. Patients with multifetal gestation, known chronic disorders (Diabetes or HTN), or with previous bad obstetric history with known causes were excluded from the study.

A proper history was taken regarding the signs and symptoms of thyroid disorders. Menstrual history, obstetric history, past history medical history, family history, and personal history were also taken. A thorough general physical examination with reference to pulse, blood pressure, body temperature, and respiratory rate was noted followed by CVS (Cardiovascular System), CNS (Central Nervous System), RS (Respiratory System), and Local thyroid examination. Patients are sent for TSH (Thyroid Stimulating Hormone) testing. If TSH (Thyroid Stimulating Hormone) comes deranged, then the free thyroid profile (FT3 and FT4 levels) are checked. Depending upon the FT3 and FT4 values they are grouped as hypothyroidism or hyperthyroidism.

RESULTS

In the present study, we included 100 antenatal women from the first trimester with a singleton pregnancy. Their TSH (Thyroid Stimulating Hormone) levels were assessed followed by testing of FT3 and FT4 levels.

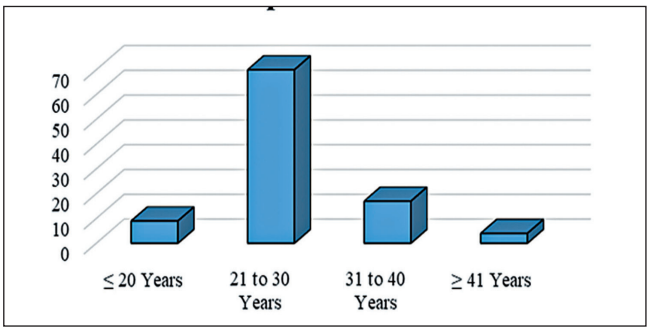

Fig. 1 : Age Distribution of the Patients

The above graph shows, that most of the patients in the present study were from the age group 21 to 30 years followed by 17% from 31 to 40 years. The mean of the patients was 26.82±5.84 years ranging from 19 to 45 years. (Fig. 1)

The prevalence of thyroid disorders in the present study was 38%, including hypo and hyperthyroidism. The remaining 62% of patients were normo-thyroid and their further thyroid testing was not done. (Table 1)

Table 1 : prevalence of thyroid disorders among patients

No. of persons screened	No. with Thyroid Disorders	% Prevalence	95% CI
100	38	38%	32.5 to 43.5

Our study shows that 28% of patients were found to be hypothyroid, and 10% patients were hyperthyroid. (Fig. 2)

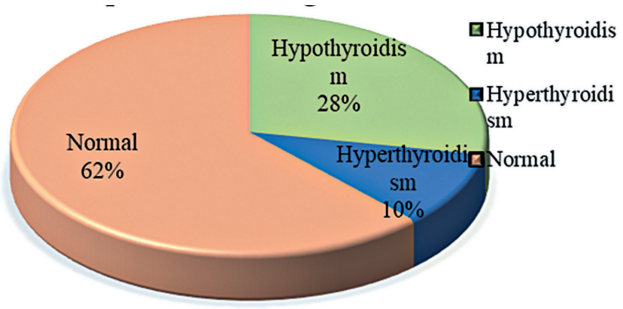

Fig. 2 : Percentage of Cases

Table 2 shows that mean TSH (Thyroid Stimulating Hormone) level of the hyperthyroid patients (2.39±1.93 mg/dL) was significantly less and the TSH (Thyroid Stimulating Hormone) levels of the hypothyroid patients (8.56±5.76 mg/dL) were significantly more than that of the normo-thyroid patients. The mean T3 level of the hyperthyroid patients (15.47±3.13 mg/dL) was significantly more and the T3 levels of the hypothyroid patients (8.18±4.32 mg/dL) were significantly less than that of normo-thyroid patients.

Also, the Mean T4 level of the hyperthyroid patients (1.85±0.56 mg/dL) was more and the T4 levels of the hypothyroid patients (1.32±0.781 mg/dL) were less than that of normal-thyroid patients but the difference was not significant.

Table 2. Thyroid profile of the patients (mg/dL)

Diagnosis		**TSH**	**T3**	**T4**	**FT3**	**FT4**
Hyperthyroid	Mean	2.39	15.47	1.85	--	--
	Std. Dev.	1.93	3.134	0.562	--	--
Hypothyroid	Mean	8.56	8.18	1.32	1.29	2.03
	Std. Dev.	5.76	4.32	0.781	0.141	0.707
Normo-thyroid	Mean	2.27	10.10	1.36	1.11	2.84
	Std. Dev.	1.19	2.57	0.341	0.232	0.392
P value		<0.01	<0.01	0.060	0.324	0.026

DISCUSSION

The present study was done in a tertiary care center. A total of 100 patients were screened for thyroid disorders in this prospective study. To know the prevalence of thyroid disorders in pregnancy is the principal aim of this study. The prevalence of thyroid disorders in our study was 38%. The prevalence in our study was higher as compared to the study by Sahu MT et al [5], who studied 633 women in the second trimester. The prevalence of thyroid disorders was 12.7% in their study. The prevalence of Hypothyroidism in our study was 28%. In the study of Casey BM et al [6] the prevalence was 23%, which is comparable to our study. In a study done by, Sahu MT et al [5] the prevalence was 6.47% which is very low and not consistent with our study. The prevalence of hyperthyroidism in our study was 10%. In a study done by Tuija manifesto et al [7], the prevalence was 3.5% for hyperthyroidism. In a study done by Sahu MT et al [5], the prevalence was 0.9% for hyperthyroidism. The prevalence of Hyperthyroidism was 0.5 % in a study done by Stagnaro Green A study.[8] The prevalence of hyperthyroidism in our study is higher compared to these studies.

CONCLUSION

Prevalence of thyroid disorders, especially hypothyroidism (28%) was high than hyperthyroidism (10%). It's important to follow up on the cases till pregnancy. Further studies are needed to assess adverse effects on maternal and fetal outcomes. Routine antenatal thyroid screening should also be done.

FUNDING - The authors declare that no funds, grants, or other support were received during the preparation of this manuscript."

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ORIGINAL ARTICLE

THE USE OF INTENSE PULSED LIGHT ON THE OUTCOME OF SCARS

Rakshit Jatla*, *Basavraj Kadalge*****, *Uddhav Patil******

ABSTRACT

INTRODUCTION : Laser therapy alters wound healing and scar formation. Intervention through laser therapy has been displayed to alter the wound healing process and influence the scar formation. **OBJECTIVE:** The objective of this study is to determine safety, efficacy of a single intense pulsed light treatment administered within 3 days pre operatively on the outcome of scar. **METHODS AND MATERIALS:** This is a randomised, controlled, split-scar pilot research with blinded assessments of treated versus untreated intended incision locations. One half of each intended scar is treated with 645nm IPL at 10-25 joules 3 days before surgery. The other half serves as a control. At 1, 2, and 3 months after surgery, clinical evaluations and POSAS scale measurements were done. **RESULTS**: 60 patients completed the study and are included in the analyses. Intense pulsed light pre- treatment showed beneficial effect as compared with no treatment. Both the patient and physician mean POSAS scores were significantly lower for the Intense pulsed light treated half of the scars compared with the control side. **CONCLUSION:** From the above data, there is proved evidence that a single pre-treatment of intense pulsed light can result in achievement of cosmetically better scar.

Keywords : Laser pre-treatment, Intense pulsed light, post-operative scar, POSAS score

INTRODUCTION

A scar is a permanent mark left on the skin following a cut or wound. Abnormal scarring can cause itching, movement restrictions, and deformities. Scar improvement involves plastic surgery, dermatology, and physical therapy.[1] Dysregulation in any of the three wound healing phases causes unusual scarring.[2-3] Unbalanced cytokines and growth factors may also cause it.[4] Surgical and non-surgical scar modification techniques exist during wound healing.[5] To reduce aberrant healing, surgeons use different surgical devices, materials, and procedures. Pressure garments, silicone gel, intra-lesional medication treatment, laser, radiation, and light therapies are non-surgical options.[6] HSPs, MMPs, and TGF-beta are the most researched laser-induced particles. These elements assist protein scaffolding, procollagen production, scar tissue fibre alignment, fibroblast chemotaxis, and procollagen organisation. Lasers aid scar treatment. Q-switched lasers can heal hyper-pigmented scars (e.g., Nd: YAG, alexandrite, ruby).[7] Pulsed ablative lasers (CO2, Er: YAG) heal atrophic acne scars and keloids, however keloids persist.[8] This laser heals erythematous, hypertrophic, and keloid scars. Vascularity-targeting lowers erythema, symptoms, and scar size.[9] Pulsed dye laser prevents scarring, according to study.[10] IPL is a cosmetic skin treatment that can reduce ageing signs

*Junior resident **Assistant Professor, ***Associate Professor, Department of General Surgery, D.Y. Patil Medical College, Kolhapur.
Corresponding E-mail : rakshitjatla@gmail.com

and unwanted hair. IPL's wide-band light emission gives it the nickname "false laser." IPL removes damaged or pigmented skin using light. Pulsed light sources emit non-coherent, wideband light to treat vascular and pigmented lesions. In most situations, patients were satisfied with IPL treatment, and it worked best with other medications. IPL devices can cure acne, pigmentation, vascular lesions, hirsutism, UV-damaged skin, scars, and melasma. [11-13] More recently, pilot research demonstrated that intense pulsed light (IPL) used after suture removal was beneficial on surgically produced scars.[14-15] IPL can restore hyper-pigmented scars by altering melanin on scar pigmentation due to blocking filters at 515, 550, 570, 590, 615, 645, and 755 nm. Scars, skin patches, and arachnid veins can be reduced. IPL mimics laser therapy. This study aimed to evaluate if a single intense pulsed light treatment of the intended incision area will show any effect on the quality of the postoperative scar. The objective of this study was to determine the safety, and efficacy of a single intense pulsed light treatment administered within 3 days pre-operatively on the outcome of the scar.

MATERIALS AND METHODS

This prospective, randomised, controlled, intra-individual split scar investigation was undertaken at tertiary care hospital. After receiving institutional ethics approval, the study lasted 2 years (October 2020-October 2022). 18-to-70-year-olds scheduled for elective surgery and willing to participate were included. Laparoscopic operations, emergency surgery, pregnancy, current or recent malignancy, systemic disease, and laser treatment excluded. Written, informed consent was obtained from the included patients before the initiation of the study. Study covered 60 patients. Subjects were marked 3 days before surgery. Before IPL, the incision site was divided into two halves and randomised for laser treatment (irradiation site) or control site. One of the two randomised sites received 645nm IPL at 10-25 Joules. Maximum IPL energy was established by skin type, colour, body area, and thickness. All subjects were exposed 30ms. Post-administration, patient told to apply cool compress if needed. Post-operative scar appearance was assessed at 1-month, 2-month, and 3-month intervals. The scar appearance was evaluated using the patient and observer scar assessment scale (POSAS).[16] For the observer scar assessment scale (OSAS), 1 blinded medical qualified observer scored scar based on parameters of the treated and control halves including vascularization, pigmentation, thickness, relief, and pliability. The scar on a scale ranging from 1 (normal skin) to 10 (worst scar imaginable). The total score on the OSAS is the sum of the scores of each item, yielding a total score ranging from 6 (best) to 60 (worst). Whereas, on the patient scar assessment scale (PSAS), the patients scored 1 to 10 to answer questions relating to pain, itching, colour, stiffness, irregularity, and thickness. The total score on the PSAS was the sum of the scores of each item, yielding a total score ranging from 6 (best) to 60 (worst). The patients were also asked to rate their overall satisfaction for each scar half using a quartile grading scale (0-not satisfied, 1-slightly satisfied, 2-satisfied, 3–very satisfied) 3 months post-operatively. Data was collected and entered into a Microsoft excel sheet using the SPSS IBM 20 version.

RESULTS

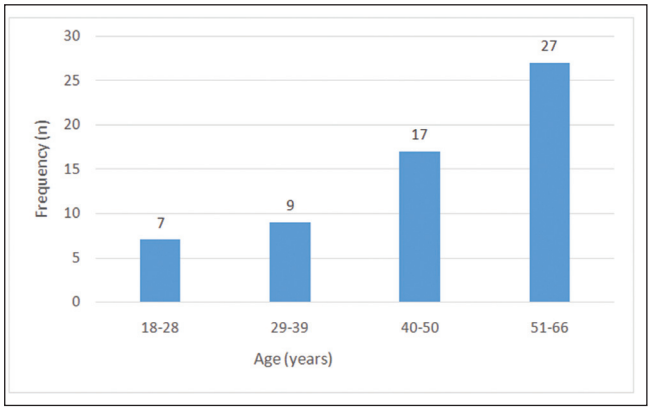

Fig. 1 : Distribution of subjects according to age groups

Age distribution-The average of the study participants was 46.15±12.92 years. Majority of patients belongs to 51-66 years age group (n=27, 45%) followed by 40-50 years (n=17, 28.33%), 29-39 years (n=9, 15%), and 18-28 years (n=7, 11.67%). The detailed distribution of subjects according to age categories is shown in Fig. 1.

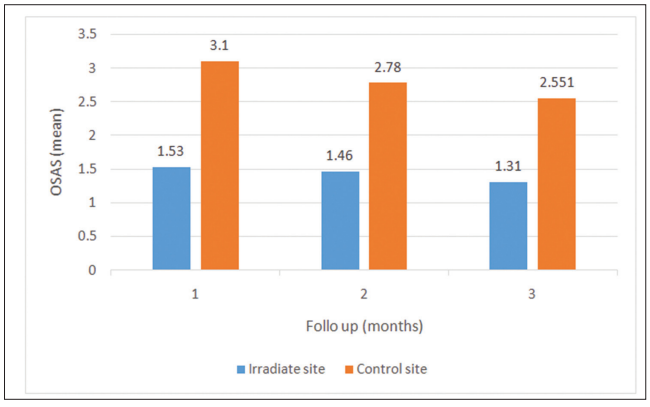

Fig. 2 : Distribution of OSAS score at different time intervals

OSAS scores at different time intervals- At postoperative one month, two months, and three months, the mean OSAS score was significantly less in the irradiate site compared to the control site (P=0.0000). OSAS at various time intervals is depicted in Fig. 3.

Table 1 : Distribution of PSAS scores at different time intervals

Follow-up (months)	PSAS score (mean±SD)		P value
	Irradiate site	Control site	
1	2.38±0.82	4.38±1.12	0.0000
2	1.98±0.70	3.28±1.04	0.0000
3	1.45±0.53	2.36±0.58	0.0000

PSAS scores at different time Intervals-Irradiate and control site PSAS scores at one (2.38±0.82 vs 4.38±1.12, P=0.0000) two (1.98±0.70 vs 3.28±1.04, P=0.0000) and three months (1.45±0.53 vs 2.36±0.58, P=0.0000) postoperative period was significantly less in irradiated site compared to control site. PSAS at various time intervals is depicted in Table 1.

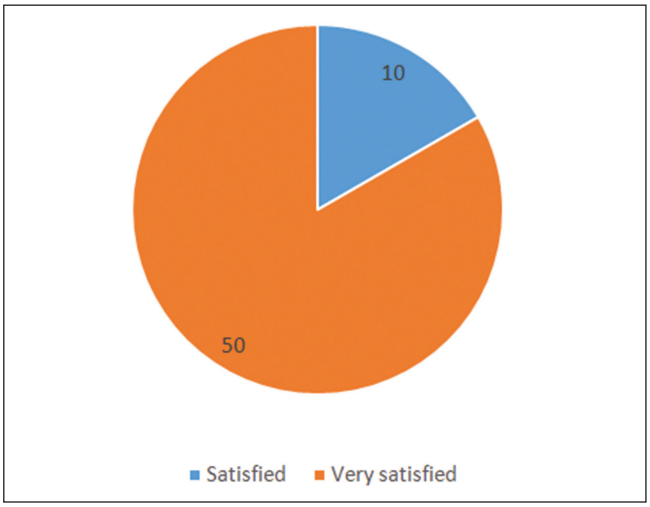

Fig. 3 : Distribution of subjects according to satisfaction scale

Patient satisfaction- Patient satisfaction assessed by a four-point grading scale showed more satisfaction in 83.33% of subjects whereas 16.67% of the subjects were found to be satisfied. The distribution of subjects according to the satisfaction scale is shown in Fig. 3.

DISCUSSION

The present study aimed to evaluate if a single intense pulsed light treatment of the intended incision area will show any effect on the quality of the postoperative scar. OSAS and PSAS scores were considerably lower in irradiated sites at 1-, 2-, and 3-month follow-up (P<0.0000). Most patients were satisfied with the irradiated area. No study participants had side effects. These findings imply that single preoperative IPL treatment improves scar appearance.

In this study, the average age of the participants was 46.15±12.92 years and among included subjects, most of the participants were male. These findings are comparable to the previous report.[17] Lifestyle, work profile, etc. may explain male predominance. Dysregulated wound healing causes abnormal scarring. [2-3, 18] Post-surgery pain, itching, and an abnormal appearance can cause psychological stress and reduce patient satisfaction. Here we administered IPL on the half site of the surgery and another half was considered as the control site. Postoperative 1 month, 2 months, and 3-month scars were appraised using POSAS scores, which showed improved aesthetic appearance and better likeness with surrounding unaffected skin compared to the control site. Laser treatment had no side effects. Most patients were satisfied with the laser treatment. Similarly, Friedman O. et al. conducted a study to assess the safety, efficacy, and final cosmesis of single pre-surgical laser treatment on surgical scar formation. They said preoperative laser treatment improves scars.[18] Reports imply a similar effect of post-operative laser.[14-15] One trial included a therapy 24 hours before surgery and two postoperative treatments with good results. [1]

Sample size and technique were study strengths. The irradiation scar looked better than the control scar. These findings suggest that a single intense pulsed light treatment administered within 3 days preoperatively is safe, and effective in postoperative scar management. The study's unblinded researchers and single-center design could have introduced bias. Inability to blind patients to treatment site may affect outcome evaluation. This study monitored patients for 3 months, but the literature suggests 12 months. Clinical endpoints preclude scar-prevention judgements. A double-blind study with a large sample size comparing the effect of laser administered pre-operatively and post-operatively on scar outcome is the further recommendation of the study.

CONCLUSION

The study aimed to evaluate if a single intense pulsed light treatment of the intended incision area will show any effect on the quality of the postoperative scar. OSAS score was lower in the irradiated site at 1-, 2-, and 3-month intervals. At all assessment points, irradiated site PSAS was lower than control site. No patient had laser-related side effects. The laser-treated scar pleased most participants. Administration of a single IPL 3 days before the surgery is safe and effective in postoperative scar management. Further studies are warranted to confirm the present study findings.

Conflict of Interest- The author declares no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975 as revised in 2000.

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ORIGINAL ARTICLE

UMBILICAL MICROFLORA, ANTISEPTIC SKIN PREPARATION, AND SURGICAL SITE INFECTION IN ABDOMINAL SURGERY

*Jineshwar Nyamagoud**, Uday Ghate**, **Sheetal Murchite** *

ABSTRACT

Introduction : Following abdominal surgery, surgical site infections (SSI) are common and a significant contributor to postoperative morbidity and extended hospital stays. Antiseptic skin preparation is a crucial step in the prevention of SSI in addition to antibiotic prophylaxis. In light of this, we carried out a study to evaluate the umbilical microflora in connection to the emergence of SSI after abdominal surgery. **Materials and Methods :** The study was conducted at Dr.D.Y. Patil Hospital & Research Institute, Kolhapur, on the patients receiving abdominal surgery. A sample of 160 patients were enrolled in the study. Before the procedure, an umbilical site swab was collected for culture and sensitivity testing. The surgical site was checked up to three days after the procedure. Swab of the infection site will be sent again if SSI is discovered. **Results :** Numerous resident (mainly staphylococci species and corynebacteria) and transient germs were present in the umbilicus' microflora (including enterococci species). In the current study, the total prevalence of SSI was 15%. Bacteria could still be cultured from 24.7% of the patients' umbilicus after antiseptic skin preparation. In the current study, the incidence of SSI was significantly increased by low albumin levels before to surgery, low haemoglobin levels, and related co-morbidities. Conclusions: In 25% of patients, antiseptic skin preparation fails to entirely remove the microflora of the umbilical region. However, the vast majority of SSI, at least in abdominal surgery, are brought on by intra-abdominal contamination rather than the skin microflora.

Keywords : abdominal, surgery, surgical site infection(SSI), microflora, antiseptic.

INTRODUCTION

Up to 15% of all nosocomial infections are caused by postoperative surgical site infections (SSI), a severe health concern.[1] SSI rates range from 10% to more than 30% depending on the type of procedure and the degree of contamination, especially in abdominal surgery. There is plenty of proof that postoperative SSI leads to higher rates of morbidity and death as well as an average week-long hospital stay extension.[2] When added to the indirect costs like lost income and insurance costs, the direct costs that arise seriously damage the health care system. In addition, patient-related factors such as age, nutritional status, smoking, diabetes mellitus, and concurrent medication are risk factors for developing SSI. Therefore, many strategies have been put forth to lower the rate of SSI.[3] For instance, the proper application of preoperative antibiotic medication can reduce SSI. Additionally, it has been demonstrated that SSI rates are decreased by shorter operation times, average body temperatures during the procedure, minimum blood loss, and

*Junior resident **Assistant professor, *Head of Department, Department of Surgery, D.Y. Patil Medical College, Kolhapur
Corresponding E-mail : sheetalmurchite@gmail.com

avoidance of intra-operative contamination with intestinal contents.[2,3] Since the 19th century, antiseptic skin preparations have played a significant role in the arsenal against SSI. There is some disagreement about whether preoperative antiseptic showering or bathing should be used, as well as the exact antiseptic and technique, even if there is no disagreement over the use of antiseptic skin preparation. A resident microflora, such as different staphylococcus species, and a transitory microflora, including both harmful and non-pathogenic microorganisms, are physiologically present on human skin.[4,5] The umbilicus is particularly susceptible to micro bacterial colonization, partly because it is frequently neglected during body cleansing and can house a humid milieu and occasionally foreign objects.[6,7] The umbilicus was selected because it stands in for the most polluted area and is challenging to clean during antiseptic skin preparation. It has been proposed that stomach hair serves as a collection point for clothing fibers, which then gather alongside skin scales, fat, and proteins in the umbilicus, where they are compressed. With this background, we conducted the study to analyze the microflora of the umbilicus in relation to the development of SSI following abdominal surgery along-with the comparison of the organism encountered in culture sensitivity of SSI and organism from umbilical microflora swab.

MATERIALS & METHODS

The study was conducted at Dr.D.Y. Patil Hospital & Research Institute, Kolhapur after receiving all the ethical permissions from the Institutional Ethical Committee. It was a prospective observational type of study. The time period for the study was of 2 years. All the procedure was explained and written informed consent was taken from the patients in their local language. Total 160 patients were included for the study. Patients more than 18 years planned for open abdominal surgery, who had clean, clean-contaminated or contaminated wound as per CDC criteria were included for the study. Patients with liver and renal failure cases, less than 18 years, and pre-existing infections were excluded from the study.

According to the CDC recommendations for preventing surgical site infections, post-operative surgical site infections were divided into three categories: superficial incisional SSI, deep incisional SSI, and deep/organ space SSI. The main outcome was the SSI, which was measured every day from the time of surgery until discharge and at the end of the 30-day follow-up. Secondary factors included post-operative problems that were rated using the Dindo-Clavien system, umbilical bacterial culture results before and after antiseptic skin preparation, and bacterial culture results of surgical site infections. Age, gender, BMI, ASA score, diabetes mellitus, hypertension, ischemic heart disease, previous laparotomies, and the reason for the surgery were also noted. In the surgery room, the first culture swab was collected right before skin prep. Standard procedures and povidone-iodine were used to prepare the skin as directed by the manufacturer. The second culture sample was obtained just prior to skin incision. The Medical Microbiology Department conducted all of the analyses. Another culture swab was collected and examined in the SSI case.

STATISTICAL ANALYSIS

The data was collected, compiled, and analyzed using EPI info (version 7.2). The qualitative variables were expressed in terms of percentages. The variables which are quantitative, were categorized and expressed in percentages or in terms of mean and standard deviations percentages. The difference between the

two proportions was analyzed using the chi-square or Fisher exact test. All analysis was two-tailed, and the significance level was set at 0.05.

RESULTS

Distribution of the subjects based on age and gender- The mean age of the subjects was 37.94 years. Majority of the cases were in the age group of 21 to 30 years in the present study (Fig. 1). Gender wise, Majority of the cases were 65.63% (Fig. 2)

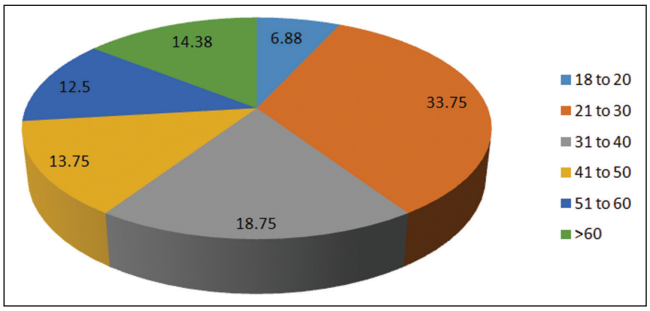

Fig. 1 : Distribution of the subjects based on the age

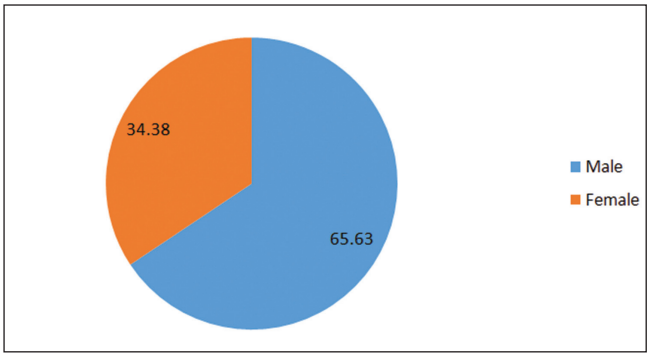

Fig. 2 : Distribution of the subjects based on the gender

Table 1 : Distribution of the subjects based on the ASA grades

ASA	Frequency	Percentage
Grade 1	9	5.63
Grade 2	108	67.50
Grade 3	35	21.88
Grade 4	8	5.00
Total	160	100.00

Majority of the cases were ASA grade 2 in the present study (67.50%).

Table 2 : Distribution of the subjects based on the comorbidities (n=160)

Co-morbidity	Frequency	Percentage
Diabetes mellitus	47	29.38
Hypertension	39	24.38
Ischemic heart disease	8	5.00
Previous laparotomy	11	6.88

Among 160 cases studied, 29.38% had Diabetes, 24.98% had hypertension, 5% had IHD and 6.88% had previous history of laparotomy.

Table 3 : Distribution of the subjects based on type of surgery

Type of surgery	Frequency	Percentage
Exploratory Laparotomy	43	26.88
Inguinal Hernioplasty	13	8.13
Lap Appendicectomy	84	52.50
Lap Cholecystectomy	12	7.50
Open Cholecystectomy	4	2.50
Other Organ resection	1	0.63
Total extra-peritoneal repair	3	1.88

Of the 160 cases studied, majority of them were laparoscopic appendix resection (52.50%) and exploratory laparotomy (26.88%) in the present study.

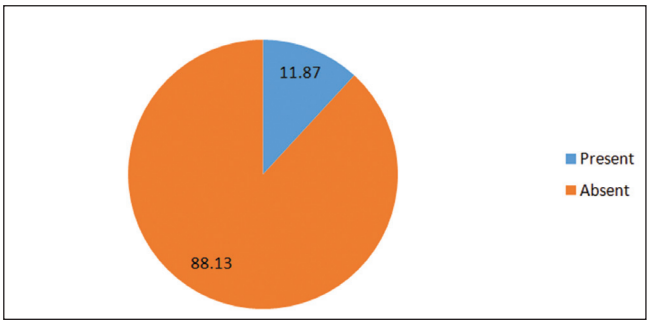

Fig. 3 : Distribution of the subjects based on the surgical site infection

The prevalence of surgical site infection was 11.87% in the present study.

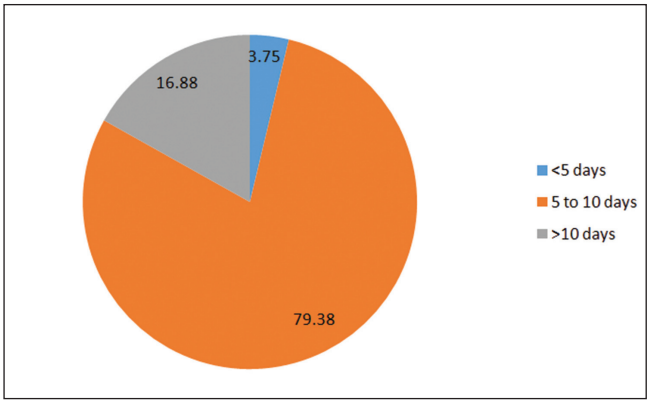

Fig. 4 : Distribution of the subjects based on hosptial stay

The average hospital stay was 8.06 days. Majority of them stayed between 5 to 10 days.

Table 4 : Distribution of the subjects based on resident umbilical microflora before and after antiseptic skin preparation

Micro-organism	Before	After
Coagulase-negative staphylococci, not specified	21	8
Staphylococcus hominis	40	4
Staphylococcus epidermidis	11	1
Staphylococcus haemolyticus	5	0
Staphylococcus capitis	4	1
Staphylococcus pasteuri	3	0
Corynebacterium spp., not specified	21	1
Corynebacterium amycolatum	2	1
Corynebacterium minutissimum	4	0
Corynebacterium mucifaciens	1	0
Corynebacterium tuberculostearicum	1	0
Micrococcus luteus	2	0
Arthrobacter cumminsii	2	0
Propionibacterium spp., not specified	1	0

Staphylococcus hominis, Corynebacterium spp- not specified, Coagulase-negative staphylococci not specified and Staphylococcus epidermidis were the most common organisms before the antiseptic skin preparation was done in the umbilical area.

Table 5 : Distribution of the subjects based on transient umbilical microflora before and after antiseptic skin preparation

Micro-organism	Before	After
Enterococci, not specified	1	0
Enterococcus faecalis	5	1
Enterococcus avium	2	0
apathogenic streptococci	3	1
Streptococcus viridans	1	1
Streptococci, not specified	1	0
Escherichia coli	1	0
Klebsiella pneumoniae	3	0
Klebsiella oxytoca	2	0
Citrobacter koseri	2	0
Citrobacter diversus	2	0
Citrobacter amalonaticus	1	1
Lactobacillus species	1	1
Spore-forming bacteria	1	0
Peptostreptococcus species	1	0
Bacteroides species Not specified	1	0

Enterococcus faecalis, apathogenic streptococci and Klebsiella pneumonia were the most common transient organisms before antiseptic skin preparation.

Table 6 : Distribution of the subjects based on microflora in SSI cases (n=19)

Case	Before	After	SSI
1	Sho, Sh, SP, Strept	Sepi	Klesbsiella
2	Spis, Sepi, Der	Sterile	Sterile
3	Spis, Sepi	Sepi	Sepi
4	S homi, Sepi, Shemo	Shomi	Klesbsiella
5	Spis, Sepi	Shomi, Spi	E Coli
6	Spis, Sepi	Shomi	Sterile
7	Spis, Sepi	Sterile	E Coli
8	Spis, Sepi	Sepi	Sepi
9	Sho, Sh, SP, Ctub	Sterile	Sterile
10	S homi	Coagulase negative Stap	E Coli

11	Spis, Sepi, Strept	Sepi	E Coli
12	Spis, Sepi	Shomi	E Fae
13	Spis, Sepi	Sepi	Ent Fae
14	Spis, Sepi	Shomi	Klesbsiella
15	Sho, Sh, SP, Ctub	Shomi	E Fae
16	Sho, Sh, SP, Ctub	Sepi	Pseudo
17	S homi, Sepi, Shemo	Sepi	Klesbsiella
18	Sho, Sh, SP, Ctub	Shomi, Spi	E Fae
19	Shemo, S capitis	Sepi	E coli

A total of 19 cases of surgical site infections were studied in detail. Of them, 2 cases had infections due to Staph Epidermidis which was present pre antisepsis and post anti-sepsis also. Rest all were caused by the different organism than when compared to micro profile before anti-sepsis preparation.

Table 7 : Association of different factors with surgical site infection

Variable	SSI				P value
	Present (n=19)		Absent (n=19)		
	Number	%	Number	%	
Gender					
Male	13	68.42	92	65.25	0.7842
Female	6	31.58	49	34.75	
Co-morbidity					
Diabetes mellitus	3	15.79	44	31.21	0.1660
Hypertension	7	36.84	32	22.70	0.1775
Ischemic heart disease	2	10.53	6	4.26	0.2390
Previous laparotomy	1	5.26	10	7.09	0.7672
Age (Mean)	57.97	7.97	37.67	15.90	0.5666
Hospital stay (Mean)	12.78	3.45	7.41	2.05	<0.001
Type of surgery					
Exploratory Laparotomy	6	31.58	37	26.24	0.1222
Inguinal Hernioplasty	1	5.26	12	8.51	
Lap Appendicectomy	6	31.58	78	55.32	
Lap Cholecystectomy	5	26.32	7	4.96	
Open Cholecystectomy	0	0	4	2.84	
Other Organ resection	1	5.26	0	0	
Total extra peritoneal repair	0	0	3	2.13	

The average age with the patients with SSI was 57.97 years and without SSI was 37.67 years and this difference was statistically significant. The average hospital stay was 12.78 days among the patients with SSI and 7.41 days without SSI in the present study. ($p<0.05$)

DISCUSSION

The current study aims to examine the umbilicus's microbiota in connection to the emergence of SSI after laparotomy.[1] The umbilicus was selected because it stands in for the area that is most polluted and challenging to clean during antiseptic skin preparation. It has been proposed that stomach hair serves as a collection point for clothing fibres, which then gather alongside skin scales, fat, and proteins in the umbilicus where they are compressed.[7]

Prevalence of SSI and different factors affecting SSI

Present study: The prevalence of SSI was 24 out of 160 cases in the present study. i.e. 15%. The average age with the patients with SSI was 57.97 years and without SSI was 37.79 years and this difference was statistically significant. The average hospital stay was 13.08 days among the patients with SSI and 7.17 days without SSI in the present study. ($p<0.05$) Rest all factors did not yield any statistical significance in the present study. With a focus on the umbilical region, Kleeff J et al[7] prospectively evaluated the efficacy of antiseptic skin preparation in a cohort of 93 patients having laparotomy. Age, gender, BMI, ASA score, diabetes mellitus, cortisol, or anticoagulant therapy had no effect on the frequency of SSI. But among patients who received antibiotics prior to surgery, the likelihood of SSI increased substantially. Patients who experienced SSI had significantly longer postoperative hospital stays (median 21 versus 13 d; p = 0.01) and

longer preoperative stays (median three versus two d; p = 0.13).

According to Yaegeshi M. et al, complications in 15 (3.3%) patients included superficial SSI, of which 7 (1.5%) patients had organ/space SSI.[10] No cases of profound SSIs were reported. 13 individuals experienced superficial SSI at the umbilical incision, and the drain port site was infected in 2 patients with rectum cancer. Anastomosis (ileocolic resection/right hemicolectomy; enter colostomy) [7 (46.7%) vs. 97 (22.1%); p =0.026] and preoperative albumin (Alb) value were discovered to be significant risk variables for superficial SSI in colorectal surgery. Age (79 vs. 67; p = 0.033), blood loss (61 vs. 11; p = 0.045), stoma (7 (100%) vs. 61 (13.7%); p 0.001], tumour site (rectum) (p = 0.003), and Hartmann/abdominal perineal resection (APR) (p = 0.001) were also significant risk variables for organ/space SSI. To assess for relationships with SSI, multivariate analysis was performed on the characteristics that univariate analysis had determined to be significant. The most significant predictor linked to a propensity for superficial SSI was determined to be the preoperative Alb value (p = 0.037; OR = 3.11; 95% CI 1.06-9.27).

In a study by Sutter ST et al, the rate of SSI over the study period was 4.04% (41/1014). Organ-space infections made up the bulk of SSIs (23, 56.1%), followed by deep incisional infections (13, 31.7%), and superficial infections (5, 12.2%). Male sex, diabetes, a T-time that was too long, and repeated procedures were all major risk factors for the emergence of SSI.[8] The likelihood of developing an SSI was also substantially correlated with increasing wound contamination class and ASA score. Most patients (34, 94.4%) with substantial growth following incisional site cleaning did not experience an SSI. Diabetes, ASA score, and reoperation were identified by multivariate analyses as significant risk factors for SSI.

Antisepsis preparation pre and post microbiological profile:

Present study:

Staphylococcus hominis, Corynebacterium spp-not specified, Coagulase-negative staphylococci not specified and Staphylococcus epidermidis were the most common organisms before the antiseptic skin preparation was done in the umbilical area. Enterococcus faecalis, apathogenic streptococci and Klebsiella pneumonia were the most common transient organisms before antiseptic skin preparation. The transient and resident micro flora significantly reduced after anti-sepsis preparation in the present study.

With a focus on the umbilical region, Kleeff J et al[7] prospectively evaluated the efficacy of antiseptic skin preparation in a cohort of 93 patients having laparotomy. After antiseptic skin preparation, the study of the resident germ spectrum revealed that staphylococcus hominis and epidermidis were the dominating species. In 93 pre-operative swabs, 136 coagulase-negative staphylococci were found. This bacterial burden was reduced by 83% by antiseptic skin preparation. The second most prevalent category of microbes was corynebacteria, and antiseptic skin treatment significantly decreased the bacterial burden by 97%.

Yaegeshi M et al.[10] obtained bacterial samples from 329 of the 453 individuals who were a part of this investigation for cultivation both before and after antiseptic skin preparation. Coagulase-negative The most frequent bacteria from umbilical swabs were Staphylococci and Corynebacterium sp. Skin

preparation reduced these bacterial burdens by nearly 90%. Twenty-one (6.4%) individuals reported negative bacterial cultures prior to antiseptic skin preparation. Antiseptic skin treatment reduced the bacterial burden by 52% in the positive bacterial cultures. Prior to wound closure, lavage drastically reduced the bacterial load by 85%. SSI and incisional umbilical swabs were used to identify numerous bacterial strains in addition to the indigenous microflora.

According to Roth JA et al., there was no discernible difference between the reduction of mean square root-transformed microbial skin counts with three versus two paints among the 239 recruited patients (P = 0.2).[9] However, in a predetermined analysis, colony forming unit (CFU) distributions reduced from paint 2 to 3 (P = 0.002). Strong data pointed to a higher percentage of patients having no CFU after paint 3 compared to paint 2 (P = 0.003). The discovery of more than five CFUs and/or one pathogen, which is considered to be an inadequate reduction of microbial skin counts after two paints, was not associated with any risk factors.

Microbiological profile of surgical site infection:

A total of 19 cases of surgical site infections were studied in detail. Of them, 2 cases had infections due to Staph Epidermidis which was present pre antisepsis and post anti-sepsis also. Rest all were caused by the different organism than when compared to micro profile before anti-sepsis preparation.

A study conducted by Kleeff J et al[7] reported that a variety of micro-organisms could be isolated from umbilical swabs in addition to the local microbiota. Escherichia coli was isolated three times, streptococcus species six times, and enterococcus species nine times. When the information from the resident and transitory umbilical microbiota is combined, 70 patients (75%) had negative swabs following antiseptic skin preparation. Additionally, bacterial swabs were obtained from the seven patients who experienced SSI. It's interesting that only one instance of the same bacterium being isolated at the SSI before, after, and after skin preparation. The pathogen discovered in the SSI was absent from the pre-operative swabs in the other instances. However, after antiseptic skin preparation, only two of the seven patients who experienced SSI had negative bacterial cultures.

According to Hamzaoglu I et al, Serratia marcescens was the most prevalent microbe (50%), followed by MR coagulase-negative Staphylococcus spp (25%), Acinetobacter baumanii, and Corynebacterium spp (25%).[11]

CONCLUSIONS

Among 160 cases studied, 29.38% had Diabetes, 24.98% had hypertension, 5% had IHD and 6.88% had previous history of laparotomy. Lapartomy was the most common type of surgery done (52.50%). The prevalence of surgical site infection was 11.87% in the present study. Age and Hospital stay were two significant factors which were predicted the surgical site infection. The average hospital stay was 8.06 days. Staphylococcus hominis, Corynebacterium spp- not specified, Coagulase-negative staphylococci not specified and Staphylococcus epidermidis were the most common organisms before the antiseptic skin preparation was done in the umbilical area. Enterococcus faecalis, apathogenic streptococci and Klebsiella pneumonia were the most common transient organisms before antiseptic skin preparation. A total of 24 cases of surgical site infections were studied in detail. Of them, 2 cases had infections due to Staph Epidermidis which was present pre antisepsis and post anti-sepsis also. Rest all were caused by the different

organism than when compared to micro profile before anti-sepsis preparation. In conclusion, antiseptic skin preparation fails to completely eradicate the microflora of the umbilical region in small set of the patients. However, at least in abdominal surgery, the vast majority of SSI are most likely caused by intra-abdominal contamination rather than the skin/umbilical microflora.

I would like to thank all my professor, guide and head of the department for giving their valuable guidance during my research. I would also like to thank my friends and family for their constant encouragement and support during the research period.

Conflict of Interest- The author declares no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975 as revised in 2000.

Authors Contribution- All authors certify that they have participated satisfactorily in the work to make proper concepts, designs, and definition of intellectual content, they helped in literature search, also clinical studies, experimental studies, data acquisition, bio-statistician also contributed for data analysis, statistical analysis, also medical copywriter's contributed for the manuscript preparation and manuscript editing, and manuscript review. Public responsibility for the content, including involvement in the concept, design analysis, writing, or revision of the manuscript. Dr. Jineshwar Nyamgoud takes responsibility for the integrity of the work as a whole from inception to the published article.

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ORIGINAL ARTICLE

EXAMINING THE ROLE OF KANGAROO MOTHER CARE IN LOW BIRTH WEIGHT BABIES IN HOSPITAL AND AT HOME

Vinayana Duvvuru, Suhas Kulkarni**, **Anil Kurane******

ABSTRACT

Introduction : Low birth weight refers to babies born weighing less than 2.5kg. Although some of them are healthy even with a low weight, most of the times, LBW can cause some serious health problems like difficulty in eating, weight gaining and also with the immunity to fight infections. In such cases, Kangaroo Mother Care can prove to be very beneficial for the baby. Preterm new-borns are cared for by kangaroo mothers, who carry them in skin-to-skin contact. It is a potent, simple strategy for promoting the well-being of both full-term and preterm infants. **Methodology :** The present study was performed at tertiary care hospital. A total of 60 neonates were recruited in the study. All the required materials were made available before starting the study. All the mothers of the neonates were demonstrated regarding positioning, duration of KMC, frequency, and holding of the neonate for breastfeeding. **Results :** Among study subjects, 60% of the babies were exclusively breastfed whereas, 40% of the babies were not exclusively breastfed. 20% of the mothers faced difficulty in administration of KMC. **Conclusion :** The KMC has a beneficial role in terms is exclusive breastfeeding. KMC is effective in weight gain in neonates with LBW. There were some difficulties in administration of KMC at home for some section of people with low socio-economic status and nuclear families.

Keywords : KMC, LBW, babies, preterm, new-born

INTRODUCTION

Low birth weight refers to babies born with weight less than 2.5kg. Although some of them are healthy even with a low weight, most of the times, LBW can cause some serious health problems like difficulty in eating, weight gaining and also with the immunity to fight infections. Babies may encounter complications in the neurologic development as a result of their NICU experiences and clinical issues from preterm.[1] To encourage the better neurodevelopment of preterm infants, several methods have been introduced.[2] Skin-to-skin contact between the mother and the infant is one of these methods because it promotes multisensory stimulation and lessens the infant's perception of stress and discomfort.[3-4] Skin-to-skin contact encourages improved motor and physiological system organization, which leads to greater weight growth, fewer illnesses and deaths, better temperature stabilization and behavioural advantages such as decreased crying time and reduced stress and pain symptoms.[5-6] These findings have led to the recommendation of kangaroo mother care as a method that can aid in improving preterm infant's development. [7] KMC is now regarded

*Junior Resident **Associate Professor, ***Professor & Head of Department, Department of Paediatrics, D.Y. Patil Medical College, Kolhapur.
Corresponding Email - drkuraneanil@yahoo.com

as the gold standard of care for LBW new-borns across all settings after being initially developed as an alternative to traditional technology-based care. Only preterm new-borns without medical issues or stabilized new-borns have evidence of the efficacy and safety of KMC. It is a potent, simple strategy for promoting the well-being of both full-term and preterm infants. Its key features include ideally exclusive breastfeeding, prolonged skin-to-skin contact between the mother and the baby. It is an efficient approach that prevents the usual agitation preterm infants encounter in a busy ward. It begins at a hospital and could go on at home. Instances when neonatal critical care or referral are unavailable and where skilled healthcare professionals are present are being evaluated via ongoing research and observational studies to see how well this strategy works. KMC before stabilization could offer the highest chance of good survival in those conditions. [8-9]

In order to better understand the role of kangaroo mother care in the hospital and at home for infants weighing less than 2 kg, this research was conducted. One of the goals of this study procedure is to determine the function of kangaroo mother care in terms of exclusive breastfeeding.

MATERIALS AND METHODS

The present cohort study was conducted at tertiary care hospital after getting the institutional ethics approval from the Institutional Ethical Committee. Written informed consent was obtained from the parents of the babies before the initiation of the study Sample size taken for the study was 60 neonates. Neonates with birthweight <2kg, delivered by any mode of delivery, and parents ready to give informed written consent along with willingness for follow up were included for the study. Sick and very small neonates of weight less than 1200 grams which required special care like radiant warmer, sick babies with severe cardiac anomalies, critically sick babies requiring emergency surgeries, and babies whose parents are not willing to give informed written consent were excluded from the study. All the required materials such as KMC gowns or clothes and chairs were made available before starting the study. All the mothers of the neonates were demonstrated regarding positioning, duration of KMC, frequency, and holding of the neonate for breastfeeding. All the queries were answered and anxieties were allayed with patience. Mothers starting KMC were encouraged to interact with mothers already practicing KMC. The outcomes such as weight gain and exclusive breastfeeding were assessed. On discharge, the mother and relatives were advised to continue KMC at home and advised follow-up after 7 days and 28 days of discharge.

STATISTICAL ANALYSIS

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. One-Way ANOVA was used to find the difference between variables. $P<0.05$ was considered statistically significant.

RESULTS

Gestational Age

The neonates were 33.69 weeks gestational age on average. The majority of the new-borns (51.67%, n=31) were under 34 weeks gestational age, while 48.33% (n=29) were over 34 weeks. (Fig.1)

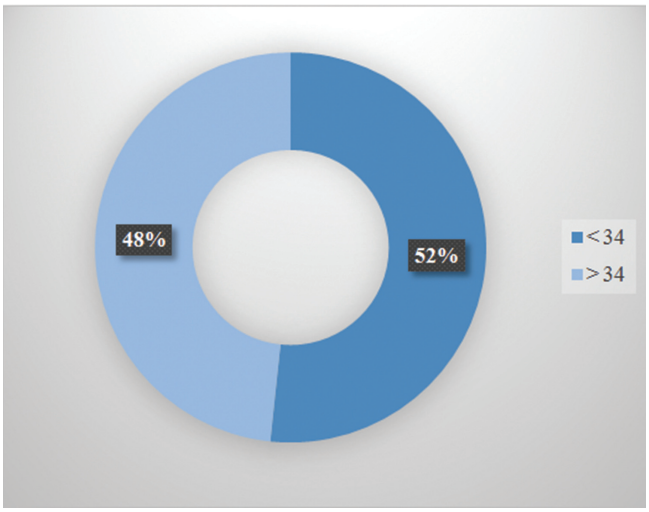

Fig. 1 : Distribution of subjects according to gestational age

Sex

Among included neonates, 50% were male and female respectively. The detailed distribution of subjects according to sex is demonstrated in Table 1.

Table 1 : Distribution of subjects according to sex

Sex	Frequency (n)	Percentage (%)
Male	30	50
Female	30	50
Total	60	100

Birth weight

The mean neonatal weight immediately after birth was 1.54±0.16 kg. The majority of neonates (75%, n=45) had 1.3-1.5 kg weight at birth followed by 16.67% (n=10) and 8.33% (n=5) of neonates had 1.6-1.8 kg and >1.8 kg of weight at birth respectively. The detailed distribution of babies according to weight at birth categories is shown in Fig. 2.1.

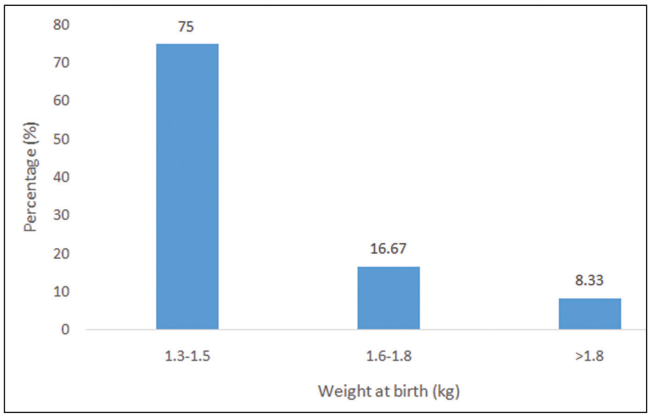

Fig. 2 : Distribution of babies according to weight at birth categories

The mean neonatal weight on the 7th day was 1.39±0.15 kg. On the 7th day, 80% (n=48) of the neonates had 1.2-1.4 kg weight whereas, 20% (n=12) babies had 1.5-1.7 kg weight. The detailed distribution of neonatal weight on the 7th day is illustrated in Figure 2.2.

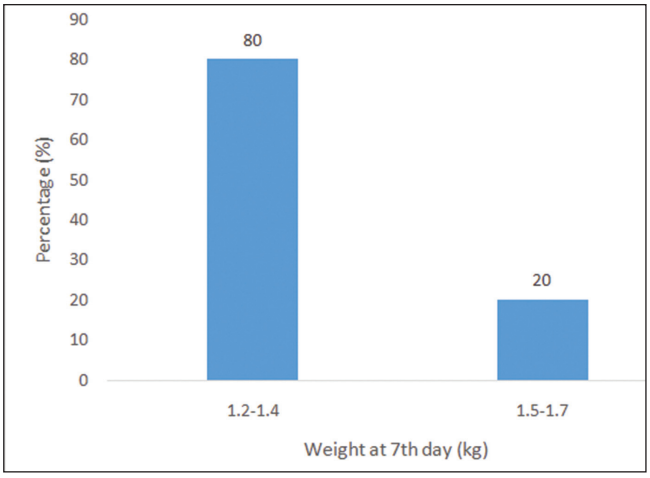

Fig. 3 : Distribution of neonatal weight on the 7th day

The mean neonatal weight on the 28th day was 2.02±0.18 kg. In 56.67% (n=34), 35% (n=21), and 8.33% (n=5) of the neonates the weight at 28th was 1.7-19 kg, 2.0-2.2kg, and ≥2.3 kg respectively. The detailed distribution of neonatal weight on the 28th day is illustrated in Fig. 2.3.

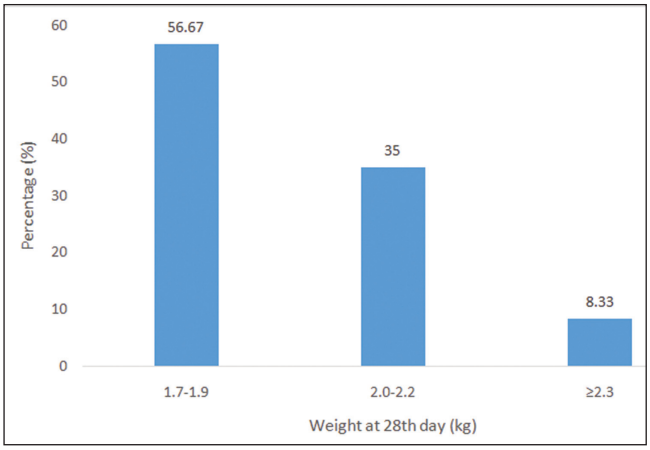

Fig. 4 : Distribution of neonatal weight on the 28th day

Comparison of birth weight at different assessment points

The mean neonatal weight on the 28th day was significantly increased (2.02±0.18 kg) compared to the mean neonatal weight at birth (1.54±0.16kg) and on the 7th day (1.39±0.15 kg) (P<0.0001). The detailed comparison of mean neonatal weight at different assessment points is depicted in Table 2.

Table 2 : Comparison of mean neonatal weight at different assessment points

Assessment points	Weight, kg (mean±SD)	Difference	P value
At birth	1.54±0.16	0.48	<0.0001
7th day	1.39±0.15	0.63	
28th day	2.02±0.18	-	

Exclusive breastfeeding

40% of the study participants' infants were not exclusively breastfed, compared to 60% of the infants who were. The detailed distribution of subjects according to exclusive breastfeeding is shown in and Fig. 3.

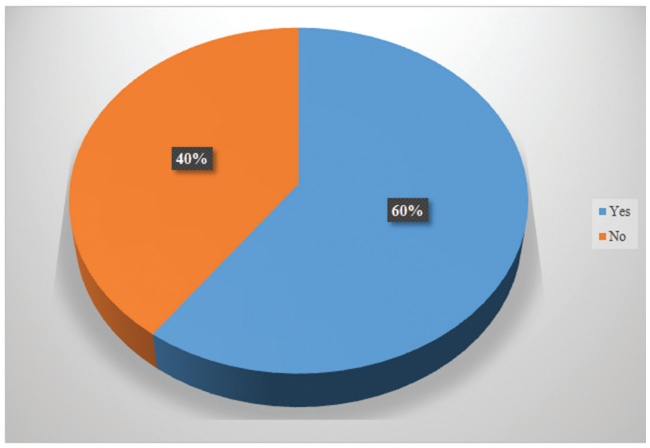

Fig. 5 : Distribution of subjects according to exclusive breastfeeding

Acceptability for giving KMC

Majority of mothers (90%, n=54) accepted giving KMC to babies whereas, it was not accepted by 10% (n=6) of mothers (Fig. 4)

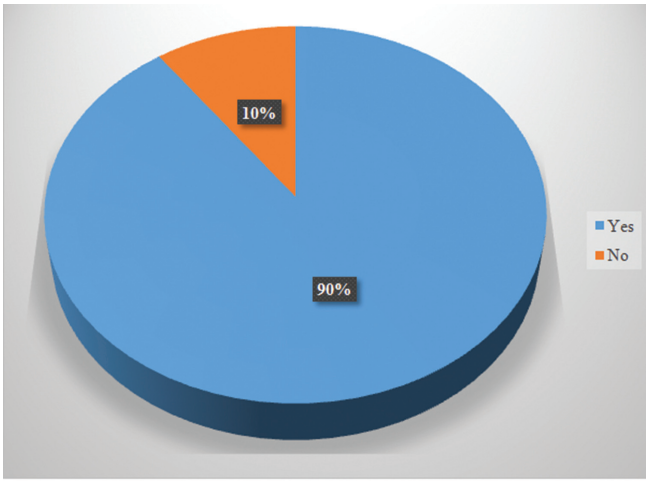

Fig. 6 : Distribution of subjects according to acceptability for giving KMC

Difficulty in KMC administration

In most of the mothers (80%, n=48), there was no difficulty in KMC administration whereas n=12 (20%) mother felt difficulty in KMC administration (Fig. 5)

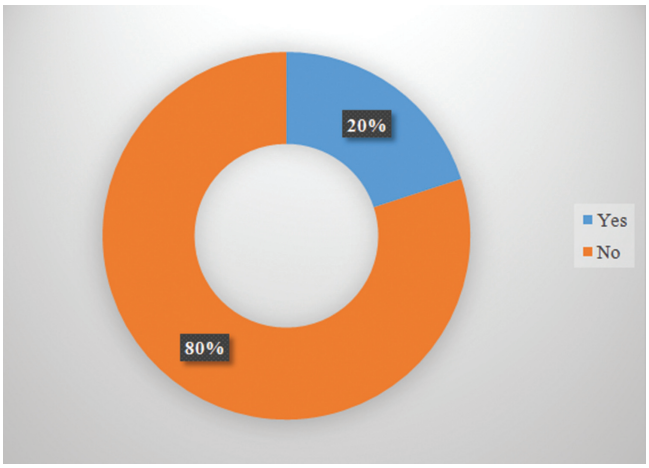

Fig. 7 : Distribution of subjects according to difficulty in KMC administration

Distribution of difficulty of KMC administration

Among the mothers, difficulty of KMC administration was found in 20% mothers(n=12). Difficulty to administer KMC due to space availability (n=4, 33,3%), household work (n=3, 25%), sleep deprivation (n=4, 33.3%) and having more children (n=3, 25%). The detailed distribution of difficulties in KMC administration is depicted in the Fig.6

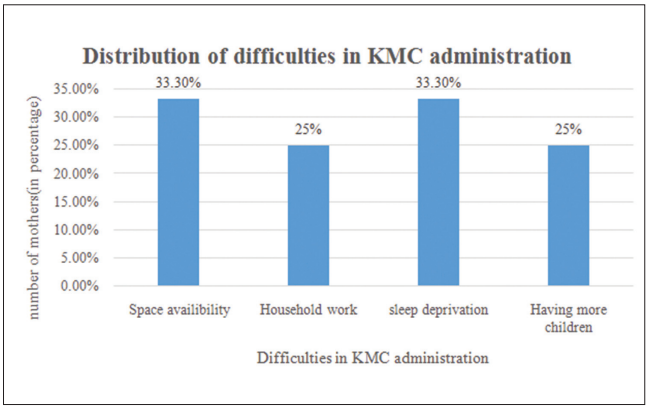

Fig. 8 : Distribution of difficulties in KMC administration

DISCUSSION

In the above study, the significant findings of the study were the mean neonatal weight was significantly increased on the 28th day compared to weight at birth and weight on the 7th day (P<0.0001). Most of the babies (60%) were exclusively breastfed. These findings suggested that the KMC had a beneficial impact on neonatal weight gain and exclusive breastfeeding.

Gestational age- In low birthweight babies, the organ functions are inadequate including sucking and swallowing reflexes are still weak and depend on the GA. [10] In this study, the mean gestational age of the neonates was 33.69±1.24 weeks. Here, GA in 51.67% of neonates was <34 weeks whereas 48.33% of neonates had GA >34 weeks. Similarly, the mean gestational age in the study of Samra NM. et al. was 31.1±2.5 weeks. [11] Phirke DS et al. reported GA of 32-34 weeks in 50% of neonates .[12] Whereas, in the study of Jagadish AS. et al. the mean GA was 32.7±1.79 weeks.[13]

Sex- In India, it is reported that female neonates are predominantly present with low birth weight. [14] However, most of the Indian regions are male predominant and there might be chances of increased prevalence of males in low birth weight data due to a male being reconcile and receiving more care. In this study, to overcome this bias we included 50% of males and 50% of females in the study. The study from Bangladesh conducted to assess the effect of KMC on LBW babies showed male predominance in study subjects (60%). [15] Similarly, the male-female ratio in the study of Suman Rao PN. et al. was 55:48.[16] In the study of Dawar R. et al., the prevalence of males was reported to be 65%. [17]

Weight- The weight gain in LBW babies is inhibited till the first 7 days. Babies were kept ventral surface to ventral surface on the mother's chest making skin-to-skin contact and kept upright. This way the mother becomes the niche and habitat for the baby just as is

done by the kangaroos.[18] In this study, the mean weight of babies at birth was 1.54±0.16 kg. The majority of neonates (75%, n=45) had 1.3-1.5 kg weight at birth followed by 16.67% (n=10) and 8.33% (n=5) of neonates had 1.6-1.8 kg and >1.8 kg of weight at birth. In the study of Samra NM. et al. the mean weight of the neonates at birth was 1.38±3.91 kg. [11] In the study of Phirke DS et al., the mean birth weight of the neonates was 1.62 kg. In their study, 66.25% of the babies weighed the range of 1-1.5kg whereas, 18.75% and 15% of babies belong to the 1.5-2.5 kg and <1kg weight categories. [12] These findings are comparable with the present study findings. Post initiation of KMC we assessed neonatal weight on the 7th day and 28th day. During the first 7 days of life neonatal weight was found to be decreased compared to birth weight (1.54±0.16 kg vs 1.39±0.15 kg) which is also similar to the findings of Samra NM. et al. and Phirke DS et al .[11-12] The reason for this may be inadequate organ functions including the sucking and swallowing ability of the neonate.

On the 28th day, the average weight of the neonates was 2.02±0.18 kg. This suggested a significant weight gain in neonates compared to weight at birth and on the 7th day (P<0.0001). Similarly, Samra NM. et al. administered KMC on the 8th day of birth they found that KMC-treated patients had weight gain two times more compared to control group neonates. Moreover, they reported a 22.1gm rate of weight gain.[11] Similarly, Suman Rao PN et al. reported an average weight gain per day in KMC babies of 23.99g which was 15.58 gm in the conventional method of care.[16] Various other studies have reported weight gain in babies using different inclusion criteria, administration of KMC at different postpartum ages, and implementation of either intermittent or continuous KMC .[10, 12, 13, 17, 19-20] The weight gain may be due to skin contact with the mother and causes sensory stimulation in neonates including emotional, tactile, proprioceptive, vestibular, olfactory, auditory, visual, and thermal stimulation. It also enhances sleep quality, stable thermal regulation, heart rate, respiration rate, and oxygen saturation. Moreover, KMC decreases the energy expenditure required for metabolism and thermal regulation and is utilized for growth. [4,21-22]These findings suggest that KMC is effective in weight gain in LBW neonates.

Exclusive breastfeeding- In this study, the rate of exclusive breastfeeding was 60% which was 85%, 98% in the study conducted by Ramanathan KP et al. and Suman Rao PN et al.[10,16] These results suggest that intermittent KMC may help combat the low breastfeeding rates for preterm infants.

Difficulties in KMC administration- In this study 20% (n=12) of the mother faced difficulty in administration of KMC. The most common reasons for the difficulties were space availability (n=4, 33.3%), sleep deprivation (n=4, 33.3%), house hold work (n=3, 25%), and having more children (n=3, 25%). These findings are comparable with previous reports.[19-20] These difficulties may be due to lower socioeconomic status, crowded homes, etc.

The strength of the study was the adequate sample size and uniform application of the protocol. Patients were followed up successfully during the study period and no patient left the follow-up. The study findings suggest that KMC has a beneficial effect on weight gain in LBW babies and it also improves the rate of exclusive breastfeeding. The limitation of the study was single centred and the investigator was not blind which could have led to some bias. The other important

limitations including the control group were not studied, and parameters such as body temperature, rate of weight gain, and hemodynamic variables were not assessed. Further, a single-blind multicentre study with an adequate sample size including all the variables is the further recommendation of the study.

CONCLUSION

The study aimed to examine the role of kangaroo mother care in babies with LBW in hospitals and homes. The above study brings us to the conclusion that, KMC has a beneficial role in terms is exclusive breastfeeding. KMC is also effective in weight gain in neonates with LBW. There were some difficulties in administration of KMC at home for some section of people with low socio-economic status and nuclear families.

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ORIGINAL ARTICLE

POSTERIOR NUTCRACKER SYNDROME AKA RETROAORTIC LEFT RENAL VEIN : A RARE ANOMALY

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

ABSTRACT

Left renal vein that travels behind the abdominal aorta is referred to as the "Retroaortic Left Renal Vein," and this anomaly is rather uncommon. Haematuria and flank or abdominal pain have both been linked to retroaortic left renal vein as symptoms. Increased pressure in the left renal vein is most likely the cause of urological symptoms in posterior nutcracker syndrome. The 35-year old woman who was admitted via the emergency department after experiencing left flank pain for several days is the subject of a highly unusual case that we will discuss here. Using contrast-enhanced computed tomography, a thorough examination revealed that the left renal vein was severely compressed and mildly dilated at its proximal end due to compression between the abdominal aorta and the anterior margin of the L1 lumbar vertebral body. Many venous collaterals were seen, the majority of which drain into the hemiazygos vein and the remaining into the inferior vena cava. The left gonadal vein appeared dilatated. These characteristics pointed to posterior nutcracker syndrome.

Keywords : Renal vein variation; retroaortic left renal vein

INTRODUCTION

Gillot and Bergman et al. have described the anatomical variations and congenital malformations of the renal vein. One of the many forms of the left renal vein that is considerably less well-known is the retroaortic route. Left renal veins that pass behind the abdominal aorta are referred to as "retroaortic left renal veins," and this abnormality is relatively uncommon. This condition typically appears in the third or fourth decades of life and affects women more than men. There are four different main types for retroaortic left renal veins, with type 1 being the most prevalent.[2-3] When considering left renal surgery, the retroaortic left renal veins are important surgically. Kidney damage and serious bleeding could occur if these anomalies are not recognized. Acknowledging it is essential to preventing complications during retroperitoneal surgery or interventional procedures. Urological issues like haematuria, varicocele, and obstruction of the ureteropelvic junction are introduced because of the compression of the retroaortic left renal vein between the aorta and the vertebra.[1-3] Over time, this increased drainage pressure in the afferent venous system can cause left-sided varicocele in men and pelvic congestion syndrome in women. The detection of left renal vein stenosis, potential renal failure, and varicocele due to venous congestion in the left renal vein is facilitated by first-line imaging with Doppler ultrasound. A CE-CT scan makes it possible to precisely identify vascular

*Post-graduate resident, **Professor, Department of Radiodiagnosis, D. Y. Patil Medical College *DNB Radio diagnosis, Krystal Scan, Kolhapur. **Corresponding E-mail** : dr.patildyp55@gmail.com

structures, determine how they associate to the organs around them, and rule out other compression-related causes.

CASE PRESENTATION

A 35- year old woman with past history of infrequent haematuria and periodic left sided abdominal flank pain with no history of trauma, any menstrual complaints or fever. Initial abdominal-pelvic ultrasound revealed a mildly enlarged left kidney. The other organs were normal, and there were no calculi in the kidneys or ureters. After undergoing contrast CT, it was discovered that the patient had a mildly bulky left kidney and that the left renal vein had proximal dilatation and was severely compressed between the anterior margin of the L1 lumbar vertebral body and the abdominal aorta. At the level of the left renal hilum, numerous venous collaterals were visible, the majority of which were seen draining into the hemiazygos vein and the remainder into the inferior vena cava. Left gonadal vein appeared dilated. These characteristics raised the possibility of posterior nutcracker syndrome. (Fig. A, B,C,D)

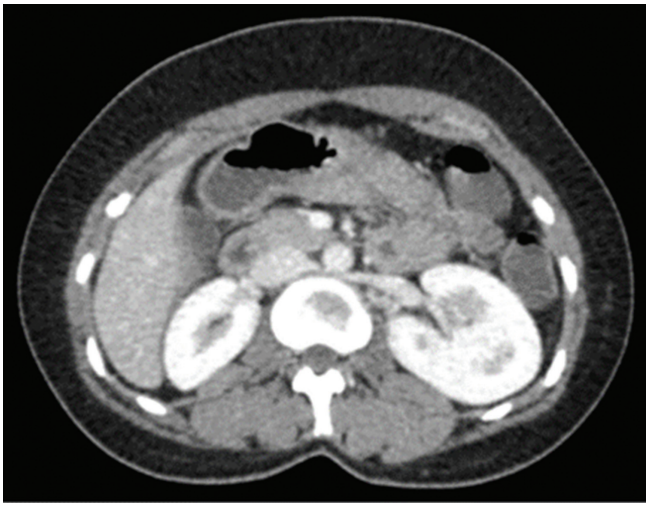

Fig. 1 : CE CT (venous phase) - Showing left renal vein compressed between aorta and anterior margin of L1 vertebral body with mild proximal dilatation

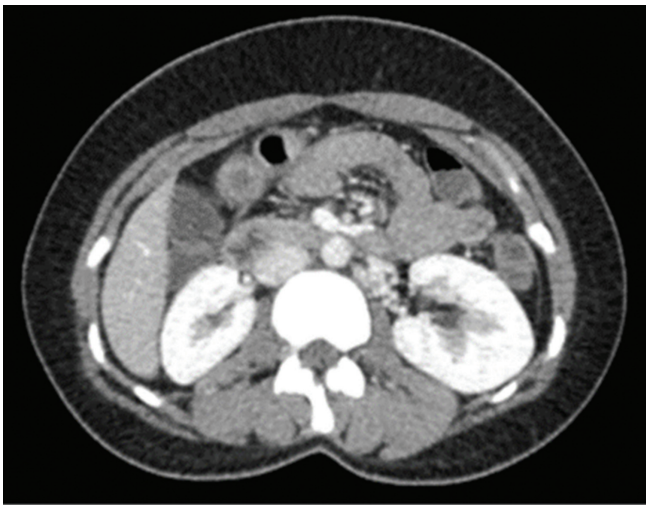

Fig. 2 : CE CT (venous phase) - Multiple venous collaterals were seen at the level of the left renal hilum, majority of which were seen draining into the hemiazygos vein and the rest in inferior vena cava

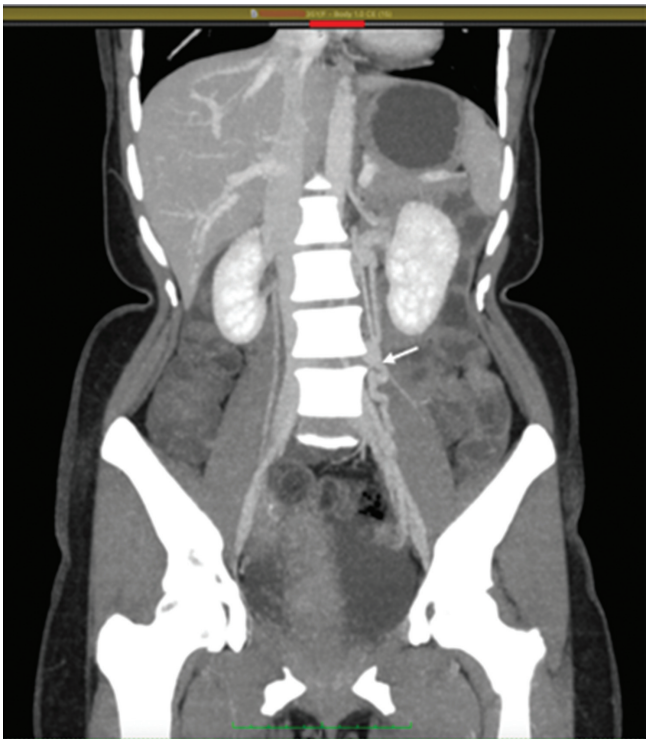

Fig. 3 : CE CT reconstructed coronal image - Showing dilated left gonadal vein

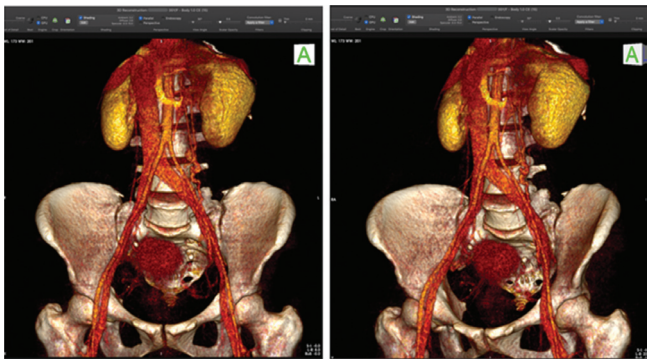

Fig. 4 : CE CT 3D reconstructed image - Showing dilated left gonada vein along its course

Additionally, the patient underwent renal doppler ultrasound, which revealed that the left renal vein had variable course between the aorta and vertebral body and that it was compressed. There was aliasing on the right of aorta with increased PSV of the left renal vein around 60 cm/s - suggestive of post stenotic venturi effect. No history of renal thrombosis. There was mild dilatation of proximal gonadal vein. (Fig. 1,2,3)

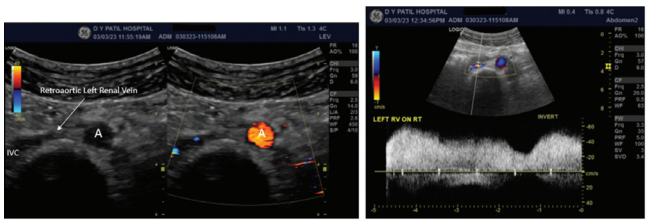

Fig. 5 : Left renal vein with variable course between the aorta and vertebral body with increased PSV of stenosed renal vein around 60 cm/s

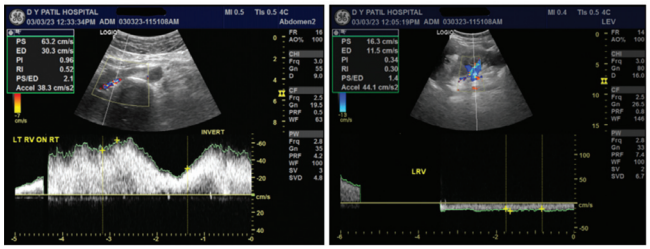

Fig. 6 : Stenosed Left renal vein PSV under Venturi effect - (A) Post stenotic 63.2 m/s (B) Pre stenotic near hilum - 16.3 cm/s

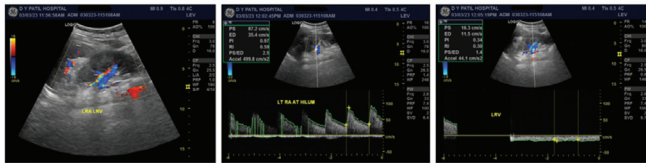

Fig. 7 : Left Renal Artery and Vein with their corresponding dopplers

The patient was managed on conservative treatment and did not have other complications such as pelvic congestion syndrome. Since any endovascular or surgical intervention is generally indicated in cases of persistent haematuria, severe flank pain, or serious dysfunction, a follow-up was advised.

DISCUSSION

The formation of the renal veins is an important step in the complex process of the inferior vena cava development. The process starts in the fourth week of conception and lasts until around the eighth week. The posterior cardinal veins, sub-cardinal veins, and supra cardinal veins, in order of appearance, are three pairs of parallel veins that together form a vast network in the communication. The hepatic sinusoids and hepatic vein make up the hepatic portion, the right sub-cardinal vein forms the Prerenal portion of the inferior vena cava, the Renal part is formed by an anastomosis between the sub-cardinal and supra cardinal veins, and the Postrenal part is formed by the right sub-cardinal vein. The four segments of the inferior vena cava are created by the regression and persistence of these veins. The renal veins are created by the continual anastomosis of the sub-cardinal and supra cardinal veins. Some of the major venous anomalies of the inferior vena cava include duplication of the inferior vena cava, transposition of the inferior vena cava (left IVC), circumaortic (left) renal vein, retroaortic (left) renal vein, and absence of the hepatic portion of the inferior vena cava. The dorsal limb of the embryonic

left renal vein and the dorsal arch of the renal collar (intersupracardinal anastomosis) persists, resulting in both circumaortic and retroaortic left renal veins. However, the ventral arch retracts in the retroaortic left renal vein, allowing a single renal vein to pass posterior to the aorta.[5]

According to where they join the IVC, the "Retroaortic left renal veins" are divided into four different categories: [2-3]

those that join the IVC orthotopically (Most Common)

those that join the IVC at the level of L4-L5.

those that form a collar around the aorta and include both anterior and retroaortic LRVs.

those that join the left common iliac vein.

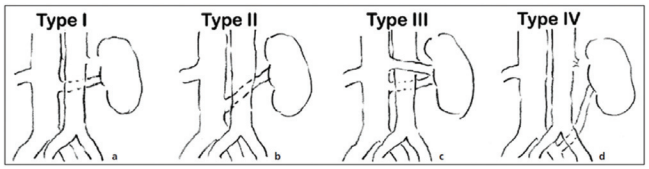

Fig. 8 : Classification scheme of the RLRV : (A) Type I that joins the IVC orthotopically; (b) Type II that joins the IVC at lower level of L4-L5; (c) Type III circumaortic renal vein collar - Composed of both preaortic and orthotopic retroartic renal veins; (d) Type IV that joins the left common iliac vein

Theoretically, compression of the left renal vein increases pressure in the left renal vein, which leads to haematuria and congestion of the left kidney and venous communications.[1-3] It is known that the gonadal, ascending lumbar, adrenal, ureteral, and capsular veins are potential collateral venous pathways in cases of renal vein compression or obstruction. These anomalous communication channels are responsible for haematuria. Over time, this increased drainage pressure in the afferent venous system can lead to pelvic congestion syndrome in women and left-sided varicocele in men.

The diagnosis of renal vein anomalies is crucial information for retroperitoneal surgery. Due to the possibility of bleeding, nephrectomy, and even death if this situation is not recognized during retroperitoneal surgery. The left renal vein is preferred in renal transplants due to its length. Hence The course of the left renal vein must be understood. Renal vein anomalies must also be taken into consideration for a proper diagnosis of retroperitoneal lymph node pathologies in patients with renal or testicular tumours.

For treatment, endovascular or surgical intervention may be indicated, after 2 years of follow-up, in cases of persistent haematuria, severe flank pain, or serious dysfunction. The aortic wall could erode as a result of placing a stent between the vertebral column and the aorta, and an arterovenous fistula could form as a result. Open surgery with left renal vein transposition has been suggested to treat Posterior Nutcracker Syndrome in order to relieve compression.[4]

CONCLUSION

In conclusion, the retroaortic left renal vein rarely causes symptoms. It can occasionally cause haematuria, flank pain, varicocele in men, pelvic congestion syndrome in women, and abdominal pain. It is essential to confirm the presence of the Retroaortic left renal vein before performing any recommended retroperitoneal surgery, interventional procedures, or any other surgical procedure in this area. The abnormality could be quickly and simply identified by using CT, MRI, or more conveniently ultrasound. The most effective method for identifying this anomaly is colour Doppler ultrasound due to its various advantages, with convenience playing the most important role.

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CASE STUDY

ANAESTHETIC MANAGEMENT IN SUSPECTED ECLAMPSIA WITH INTRACRANIAL PATHOLOGY

Srashti Singh, **Sandeep Kadam****

ABSTRACT

Introduction : Hypertensive disorders of pregnancy have wide range of intracranial complications like subdural, extradural, intraparenchymal hematoma. It is difficult to differentiate with other intracranial pathology which can cause poor maternal and fetal outcome. **Case Presentation :** My patient primi with 8 months of amenorrhea came with complaint of giddiness and 2 episodes of vomiting she was disoriented, after evaluating the fetal distress. Her blood pressure was 150/100 mmHg, emergency LSCS was done under general anaesthesia after assessing airway, blood profile and with rapid sequence intubation technique. Primary diagnosis was complication of hypertensive disorder. Later MRI was done later showed large temporal lobe and capsuloganglionic intracerebral hematoma (85*42mm) and immediately decided to post for craniotomy for right sided decompressive craniotomy under general anaesthesia. Conclusion: Intracranial haemorrhage remains a serious condition for which aggressive care is warranted.

Keywords : Intracranial haemorrhage, hypertensive, MRI, pre-eclampsia, pregnancy

INTRODUCTION

Intracranial bleed is rare yet devastating event in pregnancy. There are risk of maternal mortality/ morbidity and poor fetal outcome. Intracranial hemorrhage can be subdural, extradural, subarachnoid, intraparenchymal. Causes of bleeding include trauma, jaundice, pre-eclampsia, eclampsia, venous thrombosis, urgent neurosurgical, obstetrician and anesthetic intervention needs to be taken for better maternal and fetal outcome.

CASE PRESENTATION

We report a case of 22 yrs. old primi gravida patient with 34 week of gestation came to hospital with complaint of giddiness and 2 episodes of vomiting since morning. Patient's GCS was 10/15 and was diagnosed with Impending Eclampsia with fetal distress and provisional diagnosis of ICH. Prichard regimen (mgso4) was given. Emergency lower segment cesarean section was done in view of fetal distress and Right sided decompressive emergency craniotomy was done later. On examination, patient was irritable temperature was afebrile, heart rate was110 bpm, blood pressure recorded was 140/90 mmHg, CVS: S1S2 heard, RS: AEEBS, no pallor, no icterus, no cyanosis, no oedema was observed.

Investigations:

CBC: Hb 12.8 gm/dl
Platelet count- 1,47,000/mcl
TLC 7,800.

*Junior Resident **Professor and HOD, Department of Anaesthesia D. Y. Patil Medical College, Kolhapur
Corresponding E-mail : kadamsandeep@gmail.com

RFT : Urea 18.7 , Creatinine 0.8

LFT : WNL

PT/INR : 14/14/1.10

ECG : WNL

Fig. 1 :

MANAGEMENT

Difficult airway cart and emergency drugs were kept ready , informed valid written consent , high risk consent were taken. Premedication with Inj. Glycopyrrolate 0.2mg, Inj. Ondansetron 4mg, Inj. fentanyl 50 mcg, Inj. Lox card 60 mg i/v was given. General anesthesia was given using rapid sequence intubation using video laryngoscope. Induction was done. Inj. Propofol 100mg and Inj. Succinylcholine100mg, Intubation was done using cuffed endotracheal tube no. 7.00 cm, Patient was maintained on O2 + Air+ Sevoflurane and vecuronium. After delivering of baby, inj. Loxicard 60 mg iv and inj. Fentanyl 50 mcg iv was given. After completion of surgery patient was extubated shifted to SICU. Later on next morning patient became drowsy again. emergency neurologist opinion was taken and MRI was done which showed ICH. Patient was immediately shifted to operation theater and right sided decompressive surgery was done, after completion of surgery patient was shifted to sicu and electively ventilated for 3 days on SIMV and later extubated. Patient neurologically improved and comes for follow up. Both mother and baby are healthy.

On MRI: Large temporal lobe capsuloganglionic intracerebral hematoma (80*42mm), effacement of ipsilateral right lateral ventricle, midline shift of approx. 1.2 cm towards left suggestive of falcine herniation.

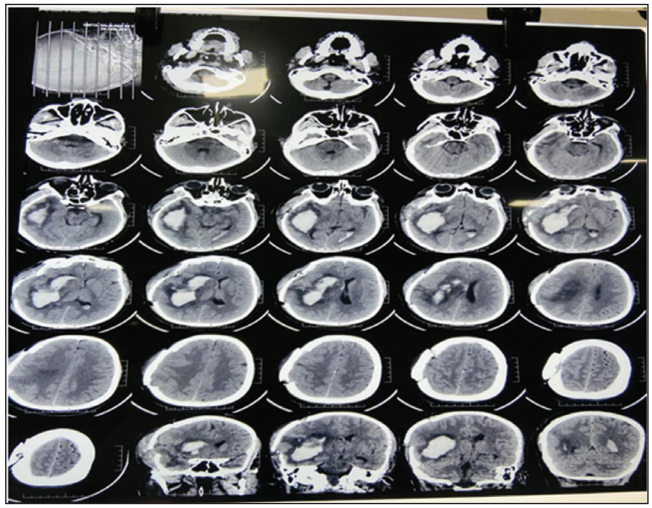

Fig. 2 :

On CT BRAIN PLAIN: Intraparenchymal hemorrhage in right fronto-parieto-temporal region with mild to moderate perilesional oedema causing significant mass effect and midline shift of 7 mm to the left as described above. There is intraventricular extension of bleed into the occipital horn of left lateral ventricle. There were changes of cerebral edema.

DISCUSSION

A thorough preoperative evaluation is crucial to plan for definitive intraoperative and postoperative management and we should keep backup plan ready in case of any untoward complication such as Difficult intubation, aspiration, hypertension/Hypotension, intrapartum or postpartum hemorrhage. In case of parturient patient with giddiness first thing comes to our mind is Hypertensive diseases of pregnancy and its complications. As we saw disorientation, we immediately thought of that but as other parameters

like normal LFT and no proteinuria, we thought of doing MRI to evaluate any intracranial pathology and 2 hours surprise it came out as Intracranial Hemorrhage.

CONCLUSION

Even in cases of pregnant patient apart from PIH and Pre-eclampsia , we have to keep our mind to open in view of Intracranial pathology like intracranial hematoma.

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