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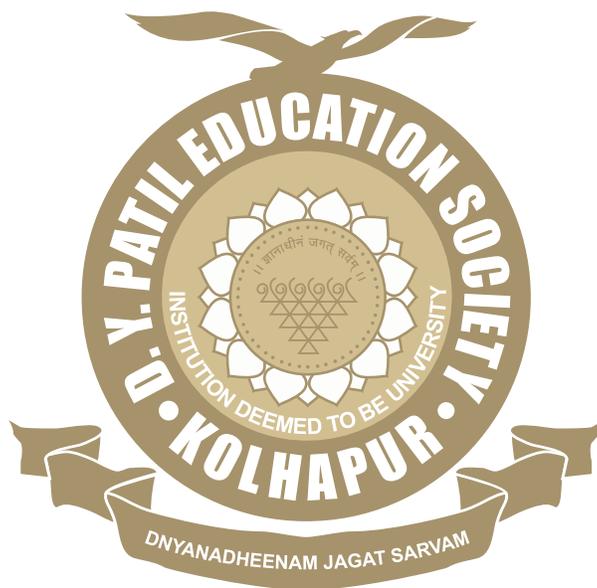
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IL-18, e GFR, AND ARTERIAL STIFFNESS IN CHRONIC KIDNEY DISEASE

Chinmay Daklia*, R. J. Khyalappa**

ABSTRACT

Background - Chronic kidney disease, also called chronic kidney failure, is a gradual loss of kidney function. Advanced chronic kidney disease can cause dangerous levels of fluid, electrolytes and wastes to build up in the body. IL-18 is a pro-inflammatory cytokine and a biomarker for kidney tubule injury and repair. Increased IL-18 levels are linked to kidney damage and inflammation, which speeds up the course of chronic kidney disease (CKD). **Methodology** - The study was conducted at tertiary care centre on total of 95 patients fulfilling the inclusion and exclusion criteria. The Cockcroft and Gault formula was utilized to estimate eGFR, while the parameters of the diabetes risk profiler were employed to evaluate AS and recorded on a case record form (CRF). IL-18 was quantified utilizing an ELISA test kit. **Result** - Males constituted a higher proportion (58.95%) of the study population compared to females (41.05%). CKD staging revealed that 9.47% of participants were in Stage 3 (eGFR 30-59 mL/min/1.73 m²), 21.05% were in Stage 4 (eGFR 15-29 mL/min/1.73 m²), and the majority, 69.47%, were in Stage 5 (eGFR <15 mL/min/1.73 m²), indicating ESRD. Lower hemoglobin levels were observed in Stage 5 CKD without RRT (8.48±0.84) compared to Stages 3 and 4 (10.32±1.79) (P<0.05). **Conclusion** - The findings revealed a significant prevalence of severe AS among CKD patients, particularly in those at Stage 5. Elevated IL-18 levels were prominently associated with severe AS, indicating its potential role as a biomarker for increased cardiovascular risk in CKD patients.

Keywords : Chronic kidney disease, IL-18, eGFR, stiffness

INTRODUCTION

“Chronic kidney disease (CKD)” is a health condition marked by persistent kidney grievance or an “estimated glomerular filtration rate (eGFR)” below 60 ml/min/1.73 mt², irrespective of the underlying cause.^[1] Signs of kidney damage include high urinary albumin excretion rates, irregularities in urine sediment, and pathological abnormalities in imaging studies or renal biopsies. The 2012 KDIGO CKD classification system offers a framework for identifying the reason for CKD and categorizing it into 6 groups. founded on glomerular filtration rate (GFR) (G1 to G5, with

G3 further subdivided into 3a and 3b). Additionally, albuminuria-based staging is used, in which every step of CKD is fragmented down into sub-stages centered on the urinary albumin-creatinine ratio obtained from an early-morning “spot” urine sample and reported in either mg/gm or mg/mmol.^[2,3]

As a result of pathogen-associated molecular patterns (PAMPs) and danger-associated molecular patterns (DAMPs), the inflammasome, a complex of several proteins, forms inside cells. Procaspase-1 is converted

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to active caspase-1, and this conversion outcomes in the construction of interleukin 1beta (IL-1) and IL-18.¹⁴¹IL-18 plays a serious role in the generation of interferon-gamma (IFN- γ -) and the activation of a powerful Th1 response. Its significance arises from the fact that IL-18 is actively intricate in inflammation, which is the underlying reason for several acute and chronic renal diseases. IL-18 is a pro-inflammatory marker and a biomarker of kidney tubule injury and repair.¹⁵¹ The key factor increasing the harshness of CKD is the high pervasiveness of “cardiovascular (CV) disease”. CV is a more common reason for expiry in CKD patients than the improvement of “end-stage renal disease (ESRD)”, which necessitates dialysis or replacement.¹⁶¹ ESRD patients have a 10–30 times superior frequency of CV mortality than the age-matched general population and 30–60% of ESRD-ill people pass away from CV illnesses.¹⁷¹The danger of newborn baby or nonfatal CV actions increased inversely when expected GFR (eGFR) drops lower the onset of 75 ml/min/1.75 m² and/or when the “albumin-to-creatinine ratio” rises overhead the onset of 5 mg/g.^{18,91} The discovery that even a little amount of leftoverRF is concomitant with a decreased impermanence threat in hemodialysis patients brings attention to the impression of KF on CV projection.¹⁰⁰

The kidneys filter a large volume of blood while maintaining low vascular resistance. This makes them susceptible to barotrauma from excessive pulsatile flow caused by aortic stiffness. Studies have shown a correlation between aortic stiffness and CKD, including conditions like albuminuria and low eGFR.¹¹¹ These comorbidities can independently contribute to both arterial stiffness (AS) and a decline in kidney function over time. Additionally, AS in these studies was often assessed using “pulse wave velocity (PWV)”, a metric

predisposed by blood pressure levels at the time of measurement.¹¹²¹

Stiffness parameter β , another measure of AS, may be less affected by blood pressure levels during measurement. This parameter has been utilized to develop the cardio-ankle vascular index (CAVI), a clinically available measure of AS. CAVI has been linked to a higher risk of future cardiovascular events, independent of traditional cardiovascular risk factors.¹³¹

Aortic stiffening leads to renal damage and dysfunction through hemodynamic mechanisms involving pressure and flow. Specifically, aortic stiffening increases pulsatile pressure in the aorta, which is transmitted into the vulnerable microvasculature of high-flow organs such as the kidneys and brain. This increased pulsatile tensile stress can result in microvascular damage, endothelial dysfunction, oxidative stress, and chronic inflammation. These changes align with microscopic findings in renal tissue, often showing inflammatory changes around the microvasculature, glomeruli, or tubules. Such findings are observed not only in severe hypertension (malignant nephrosclerosis) but also in milder hypertension (benign nephrosclerosis) and diabetic nephropathy. Clinically, increased aortic PWV and widened pulse pressure are independent predictors of albuminuria, which is associated with elevated C-reactive protein levels.¹⁴¹

IL-18 is a pro-inflammatory cytokine and a biomarker for kidney tubule injury and repair. Elevated levels of IL-18 are related to inflammation and damage within the kidneys, contributing to the progression of CKD. eGFR is a crucial measure of kidney function, with lower eGFR indicating reduced kidney function and advancing CKD. AS, often evaluated by PWV, is linked

to CKD progression. Increased AS can exacerbate kidney damage by transmitting higher pulsatile pressures into the renal microvasculature, leading to further decline in eGFR and worsening CKD. Studies show that AS and elevated IL-18 levels are significant predictors of antagonistic renal outcomes in CKD subjects.^[15]

The above study was conducted to examine the relationship between IL-18, eGFR, and AS in CKD.

MATERIALS AND METHODOLOGY

The study was conducted in OPD & IPD of the Dr. D.Y. Patil Medical College, Hospital & Research Institute, Kolhapur after institutional ethical committee approval. The sample size take for the study was 95 patients.

Inclusion criteria

Patient belonging to both the genders, aged above 18 years with CKD of stages 3, 4, and 5.

Exclusion criteria

Patients with ischemic heart disease, acute kidney injury on CKD, malignancy, known cases of Peripheral vascular disease- Berger's disease, Raynaud's disease, sepsis, any Allergic inflammation, patients on drugs that can increase blood pressure (Amphetamines, MAO inhibitors, SNRI, TCA, Sympathomimetics, OCPs, Systemic Corticosteroids) and of extreme old age (age >85 years)

Written informed consent was taken before the initiation of the study. The participants were provided with a concise overview of the study's methodology. The Cockcroft and Gault formula was utilized to estimate eGFR, while the parameters of the diabetes risk profiler

were employed to evaluate AS and recorded on a case record form (CRF). Furthermore, additional parameters for examining AS, including the "Ankle Brachial index (ABI), Augmentation Index (AIX), and PWV", were measured. IL-18 was quantified utilizing an ELISA test kit. After measuring all parameters master chart was prepared in MS Excel and data collection and analysis was done using SPSS 28 software.

ABI Measurement

$$\text{ABI} = \frac{\text{Highest SBP Posterior tibial artery or dorsalis pedis artery}}{\text{Highest Brachial SBP}}$$

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

RESULT

The mean age of the study subjects was 50.85±15.59 years. The age of the study subjects ranged from 19 to >80 years. The majority (31.58%) were between 50-59 years, indicating that middle-aged adults constituted the largest age group.

Table 2 : Distribution of CKD stages

Stages of CKD	Frequency (n)	Percentage (%)
3	9	9.47
4	20	21.05
5	66	69.47
Total	95	100

Stage 3 CKD, characterized by a moderate decrease

in GFR between 30 and 59 mL/min/1.73 m², and was observed in 9 participants, representing 9.47% of the total study population. Stage 4 CKD, indicating a severe reduction in GFR between 15 and 29 mL/min/1.73 m², was noted in 20 participants, accounting for 21.05% of the population. The majority of the participants, 66 individuals (69.47%), were in Stage 5 CKD, defined by a GFR of less than 15 mL/min/1.73 m², signifying ESRD.

Table 3 : Comparison of duration of CKD according to stages of CKD

Stages of CKD	Duration of CKD (years)		P-value
	Mean	SD	
3 and 4	1.88	1.71	<0.05 ^a
5 without RRT	2.81	1.75	<0.05 ^b
5 with RRT	3.10	2.52	>0.05 ^c

a: stage 3 & 4 vs stage 5 without RRT, b: stage 3 & 4 vs stage 5 with RRT, c: stage 5 without RRT vs stage 5 with RRT.

Stage 5 with RRT patients (3.10 years) had a significantly higher duration of CKD compared to stage 3 and 4 CKD patients (1.88 years). Stage 5 without RRT had a significantly longer duration of CKD (2.81 years) compared to stages 3 and 4 (1.88 years) (P<0.05).

Table 3.1: Comparison of duration of renal replacement therapy according to stages of CKD

Stages of CKD	Duration of RRT (Months)		P-value
	Mean	SD	
3 and 4	0	0	>0.05 ^a
5 without RRT	0	0	<0.05 ^b
5 with RRT	13.97	21.35	<0.05 ^c

a: stage3&4 vs stage5withoutRRT, b: stage3&4 vs stage5withRRT, c: stage5withoutRRT vs stage5withRRT.

Only stage 5 with RRT had subjects undergoing renal replacement therapy, with a mean duration of 13.97 months.

Table 4 : Comparison of hematological variables according to stages of CKD

Hematological variables	Stages of CKD			P-value
	3 and 4	5 without RRT	5 with RRT	
Hemoglobin	10.32±1.79	8.48±0.84	9.65±2.71	<0.05 ^a
TLC	11370±24434.2	9795.2±24690.5	15092.09±24173.9	>0.05 ^{abc}
Platelets	262666±105824	246700±105960	246515.15±111374	>0.05 ^{abc}

a: stage 3 & 4 vs stage 5 without RRT, b: stage 3 & 4 vs stage 5 with RRT, c: stage 5 without RRT vs stage 5 with RRT.

There was a substantial difference in hemoglobin levels, with stage 5 without RRT having the lowest levels (8.48±0.84) compared to stage 3 and 4 subjects (10.32±1.79) (P<0.05). No significant variances were observed in TLC and platelet counts among the stages CKD (P>0.05).

Table 5 : Comparison of serum urea according to stages of CKD

Stages of CKD	Serum urea		P-value
	Mean	SD	
3 and 4	68.82	34.91	<0.05 ^a
5 without RRT	106.52	35.16	>0.05 ^b
5 with RRT	77.69	34.59	<0.05 ^c

a: stage 3 & 4 vs stage 5 without RRT, b: stage 3 & 4 vs stage 5 withRRT, c: stage 5 without RRT vs stage 5 with RRT.

For Stage 3 and 4 CKD, the mean serum urea level was 68.82 mg/dL, with a standard deviation (SD) of 34.91

mg/dL. This group showed a statistically significant difference when compared to Stage 5 CKD without RRT ($P < 0.05$). Participants in Stage 5 CKD without RRT had a higher mean serum urea level of 106.52 mg/dL, with an SD of 35.16 mg/dL, but this was not significantly different from the levels observed in Stage 5 CKD with RRT ($P > 0.05$). Meanwhile, those in Stage 5 CKD with RRT had a mean serum urea level of 77.69 mg/dL, with an SD of 34.59 mg/dL, and this difference was statistically significant compared to Stage 3 and 4 CKD ($P < 0.05$).

Table 6 : Comparison of serum creatinine according to stages of CKD

Stages of CKD	Serum creatinine		P-value
	Mean	SD	
3 and 4	2.83	1.32	$<0.05^a$
5 without RRT	4.89	1.34	$<0.05^b$
5 with RRT	6.47	2.65	$>0.05^c$

a: stage 3 & 4 vs stage 5 without RRT, b: stage 3 & 4 vs stage 5 with RRT, c: stage 5 without RRT vs stage 5 with RRT.

Stage 5 with (6.47) and without (4.89) RRT had significantly increased serum creatinine levels compared to patients with stage 3 and 4 CKD (2.83) ($P < 0.05$).

Table 7 : Comparison of e GFR according to stages of CKD

Stages of CKD	E GFR		P-value
	Mean	SD	
3 and 4	28.27	13.80	$<0.05^a$
5 without RRT	11.87	1.52	$<0.05^b$
5 with RRT	13.30	7.45	$>0.05^c$

a: stage 3 & 4 vs stage 5 without RRT, b: stage 3 & 4 vs stage 5 with RRT, c: stage 5 without RRT vs stage 5 with RRT.

Stage 5 with (13.30) and without (11.87) RRT had significantly decreased GFR levels compared to patients with stage 3 and 4 CKD (2.83) ($P < 0.05$).

Table 8 : Comparison of Ankle-brachial index according to stages of CKD

Stages of CKD	Ankle-brachial index	
	Right	Left
3 and 4	1.04±0.13	0.96±0.15
5 without RRT	1.11±0.15	1.01±0.13
5 with RRT	1.05±0.13	1.04±0.12
P-value	$>0.05^{abc}$	$>0.05^{abc}$

a: stage 3 & 4 vs stage 5 without RRT, b: stage 3 & 4 vs stage 5 with RRT, c: stage 5 without RRT vs stage 5 with RRT

There was no significant difference in the ABI when compared between stages of CKD ($P > 0.05$)

Table 9: Comparison of aortic augmentation index (AIX) according to stages of CKD

Stages of CKD	AIX		P-value
	Mean	SD	
3 and 4	35.14	11.38	$>0.05^a$
5 without RRT	35.31	6.31	$>0.05^b$
5 with RRT	33.06	13.08	$>0.05^c$

a: stage 3 & 4 vs stage 5 without RRT, b: stage 3 & 4 vs stage 5 with RRT, c: stage 5 without RRT vs stage 5 with RRT.

There was no significant difference in the AIX when compared between stages of CKD ($P>0.05$).

Table 10 : Comparison of eGFR according to severity of AS

Severity of AS	eGFR		P-value
	Mean	SD	
No	22.76	11.08	>0.05 ^{abcdef}
Mild	25.39	11.02	
Moderate	14.93	11.23	
Severe	16.48	11.68	

a: no vs mild, b: no vs moderate, c: no vs severe, d: mild vs moderate, e: mild vs severe, f: moderate vs severe.

In patients with moderate and severe AS, the mean eGFR was decreased compared to patients with no and mild AS however, the difference was statistically in significant ($P>0.05$).

Table 11: Comparison of IL-18 according to severity of AS

Severity of AS	IL-18		P-value
	Mean	SD	
No	1150.83	3522.01	>0.05 ^{ab}
Mild	1722.36	3814.05	>0.05 ^d
Moderate	2467.72	3254.54	-
Severe	4778.97	3209.25	<0.05 ^{cef}

a: no vs mild, b: no vs moderate, c: no vs severe, d: mild vs moderate, e: mild vs severe, f: moderate vs severe.

In patients with severe AS, IL-18 was found to be significantly increased compared to patients with no, mild, and moderate AS ($P<0.05$).

DISCUSSION

The mean age of the study subjects was 50.85 years, with a wide age range spanning from 19 to over 80 years. The majority of the subjects were middle-aged adults (50-59 years), constituting 31.58% of the population. This age distribution is consistent with the known epidemiology of CKD, which often affects middle-aged and older adults due to the cumulative impact of risk factors such as hypertension and diabetes over time.^[16-17]

The majority of the participants (69.47%) were in Stage 5 CKD, among these patients n=50 required RRT. A smaller proportion of participants were in Stage 3 (9.47%) and Stage 4 (21.05%) CKD. This distribution reflects the severe nature of CKD among the study population and the high demand for RRT among these patients. Similarly, in the study of Yong K. et al 45.45% of patients had stage 3 and 4 CKD whereas 54.55% of patients had stage 5 CKD. ^[18]

Hemoglobin levels were significantly lower in Stage 5 CKD without RRT (8.48 g/dL) compared to Stage 3 and 4 CKD (10.32 g/dL), reflecting the severity of anemia in advanced CKD stages. There was no substantial variation in total leukocyte count (TLC) and platelet counts among the different stages of CKD. Serum urea and creatinine levels were significantly higher in Stage 5 CKD (with and without RRT) compared to Stage 3 and 4 CKD, indicating worsening renal function with disease progression. Similarly, eGFR levels were significantly lower in Stage 5 CKD, emphasizing the severe decline in kidney function.

It is well-documented that patients with ESRD undergoing maintenance dialysis exhibit elevated

levels of IL-12 and/or IL-18 compared to the general population. Nonetheless, it remains uncertain whether these cytokines are similarly elevated in the early stages of CKD. Studies involving 18 pediatric patients with stage 3–4 CKD and 27 adult patients with stage 4 CKD have demonstrated increased intracellular monocyte IL-12 expression and higher serum IL-18 levels, respectively, indicating that these pro-atherogenic cytokines may be elevated in the early stages of CKD.^[19]

In ESRD patients on maintenance dialysis, serum IL-12 and IL-18 levels are at least 1.5 times higher than those in the general population, although the ratio remains similar. This increase is likely due to reduced renal clearance, but uraemic toxins and oxidized LDL (also elevated in CKD) may lead to abnormal dendritic cell stimulation, resulting in excessive IL-12 and IL-18 production.^[19, 20, 21, 22] Similarly, in above study it was found elevated IL-18 levels in CKD stage 3 and 4 patients compared to those in stage 5 with and without renal replacement therapy, although the difference was not statistically significant. These findings are consistent with the results reported by Yong K. et al.^[18]

AS was assessed among the participants, with a significant proportion (60%) experiencing severe AS. This high prevalence underscores the relationship between CKD and cardiovascular complications, as Arterial Stiffness is a known predictor of cardiovascular morbidity and mortality in CKD patients. The progression of CKD is often accompanied by worsening AS due to factors such as uremia, oxidative stress, and inflammation.

There is significant interest in the role of pro-inflammatory biomarkers and cytokines in the pathogenesis of cardiovascular disease (CVD) in CKD.

C-reactive protein (CRP) is elevated in 30–50% of ESRD patients and serves as a strong predictor of CVD and all-cause mortality. IL-6 is a pro-inflammatory cytokine produced by T-cells, monocytes, adipocytes, and endothelial cells, and is associated with atherosclerosis, CVD, and all-cause mortality in ESRD patients. In a prospective CKD cohort (stages 2–5), IL-6 was linked to a 1.7-fold increased risk of all-cause mortality.^[19]

In the general population, IL-12 and IL-18 are linked to acute coronary events, while IL-18 is an independent predictor of CVD events and mortality in individuals with or without a history of CVD.^[21, 24] In our study, patients with severe AS, IL-18 levels were significantly higher compared to those with no, mild, or moderate AS ($P < 0.05$). Similar findings have been reported by Yong K. et al.^[18]

In a study involving 102 ESRD patients on maintenance dialysis, Porazko et al. demonstrated a significant association between IL-18 and aortic PWV (B-coefficient = 0.04; $p < 0.05$) as well as CRP ($r = 0.24$; $p < 0.05$). [94] However, IL-12 and augmentation index (Aix) were not measured in this study. Conversely, Yong K. et al. did not find any association between IL-12 or IL-18 and CRP, aortic PWV, or Aix, which is comparable with the present study findings.^[18]

CONCLUSION

The findings revealed a significant prevalence of severe AS among CKD patients, particularly in those at Stage 5. Elevated IL-18 levels were prominently associated with severe AS, indicating its potential role as a biomarker for increased cardiovascular risk in CKD patients. However, IL-18 levels did not significantly differ across

CKD stages, suggesting that its association with AS is independent of CKD progression. Hematological and biochemical analyses underscored the severe impact

of CKD on hemoglobin and serum creatinine levels, with significant reductions in hemoglobin and marked increases in serum creatinine in advanced CKD stages.

REFERENCES

1. Floege J, Barbour SJ, Cattran DC, Hogan JJ, Nachman PH, Tang SC, Wetzels JF, Cheung M, Wheeler DC, Winkelmayer WC, Rovin BH. Management and treatment of glomerular diseases (part 1): conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney international*. 2019 Feb 1;95(2):268-80.
2. Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, Tamura MK, Feldman HI. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. *American Journal of Kidney Diseases*. 2014 May 1;63(5):713-35.
3. Isakova T, Nickolas TL, Denburg M, Yarlagadda S, Weiner DE, Gutiérrez OM, Bansal V, Rosas SE, Nigwekar S, Yee J, Kramer H. KDOQI US commentary on the 2017 KDIGO clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease—mineral and bone disorder (CKD-MBD). *American Journal of Kidney Diseases*. 2017 Dec 1;70(6):737-51.
4. Martinon F, Burns K, Tschopp J. The Inflammasome: A molecular platform triggering activation of inflammatory caspases and processing of proIL-13. *Molec Cell*. 2002;10:417-26.
5. Akira S. The role of IL-18 in innate immunity. *Current opinion in immunology*. 2000 Feb 1;12(1):59-63.
6. Keith DS, Nichols GA, Gullion CM, Brown JB, Smith DH. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. *Archives of internal medicine*. 2004 Mar 22;164(6):659-63.
7. Vlagopoulos PT, Samak MJ. Traditional and nontraditional cardiovascular risk factors in chronic kidney disease. *Medical Clinics*. 2005 May 1;89(3):587-611.
8. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *New England Journal of Medicine*. 2004 Sep 23;351(13):1296-305.
9. Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *The Lancet*. 2010 Jun 12;375(9731):2073-81.
10. Shemin D, Bostom AG, Laliberty P, Dworkin LD. Residual renal function and mortality risk in hemodialysis patients. *American journal of kidney diseases*. 2001 Jul 1;38(1):85-90.
11. Sedaghat S, Mattace-Raso FU, Hoorn EJ, Uitterlinden AG, Hofman A, Ikram MA, Franco OH, Dehghan A. Arterial stiffness and decline in kidney function. *Clin J Am Soc Nephrol* 2015; 10:2190–2197.
12. Briet M, Bozec E, Laurent S, Fassot C, London GM, Jacquot C, Froissart M, Houillier P, Boutouyrie P. Arterial stiffness and enlargement in mild-to-moderate chronic kidney disease. *Kidney international*. 2006 Jan 2;69(2):350-7.
13. Shirai K, Utino J, Otsuka K, Takata M. A novel blood pressure-independent arterial wall stiffness parameter; cardio-ankle vascular index (CAVI). *Journal of atherosclerosis and thrombosis*. 2006;13(2):101-7.

14. O'rouke MF, Hashimoto J. Mechanical factors in arterial aging: a clinical perspective. *Journal of the American College of Cardiology*. 2007 Jul 3;50(1):1-3.
15. Shi C, He A, Wu X, Wang L, Zhu X, Jiang L, Yang J, Zhou Y. Urinary IL-18 is associated with arterial stiffness in patients with type 2 diabetes. *Frontiers in Endocrinology*. 2022 Oct 3;13:956186.
16. Rai PK, Rai P, Bhat RG, Bedi S. Chronic kidney disease among middle-aged and elderly population: a cross-sectional screening in a hospital camp in Varanasi, India. *Saudi Journal of Kidney Diseases and Transplantation*. 2019 Jul 1;30(4):795-802.
17. Ravender R, Roumelioti ME, Schmidt DW, Unruh ML, Argyropoulos C. Chronic Kidney Disease in the Older Adult Patient with Diabetes. *Journal of Clinical Medicine*. 2024 Jan 8;13(2):348.
18. Yong K, Ooi EM, Dogra G, Mannion M, Boudville N, Chan D, Lim EM, Lim WH. Elevated interleukin-12 and interleukin-18 in chronic kidney disease are not associated with arterial stiffness. *Cytokine*. 2013 Oct 1;64(1):39-42.
19. Carrero JJ, Yilmaz MI, Lindholm B, Stenvinkel P. Cytokine dysregulation in chronic kidney disease: how can we treat it? *Blood Purif* 2008;26:291-9.
20. Lim WH, Kireta S, Leedham E, Russ GR, Coates PT. Uremia impairs monocyte and monocyte-derived dendritic cell function in hemodialysis patients. *KidneyInt* 2007;72:1138-48.
21. Hansson GK, Hermansson A. The immune system in atherosclerosis. *Nat Immunol* 2011;12:204-12.
22. Dogra G, Irish A, Chan D, Watts G. Insulin resistance, inflammation, and blood pressure determine vascular dysfunction in CKD. *Am J Kidney Dis* 2006;48:926-34.
23. Rabkin SW. The role of interleukin 18 in the pathogenesis of hypertension-induced vascular disease. *Nat Clin Practice Cardiovascular Med* 2009;6:192-9.

“A Comparative Study To Evaluate The Effectiveness Of Kaleidoscope Vs Cartoon Video On Pain During Venipuncture Procedure Among Hospitalized Children At Selected Hospitals Of Kolhapur.”

Priya Shinde, Janaki Shinde***

ABSTRACT

Background : During hospitalization, children may undergo a wide range of interventions, many of which can be traumatic, stressful and painful. The procedure made by a syringe in children are the most common source of pain and Venipuncture has been evaluated as one of the most painful interventions commonly applied to children. Distraction helps the child to focus attention on something other than the pain. Distraction techniques are effective because, they provoke curiosity in children. **Methods :** A quasi experimental, randomized block design was used for this study. Total 60 participants were selected based on from the inclusion & exclusion criteria and they were divided into four groups, 2 groups comprising of 3-6 years, one group receiving kaleidoscope and the other group receiving cartoon video. Similar procedure was applied to the other 2 groups of 6-12 years. The level of pain was assessed by using Wong baker faces pain rating scale during procedure. **Results:** The result showed that, in A1 & A2 groups (3-6 years), the unpaired “t” calculated value ($t_{cal} = 4.053^*$) is greater than tabulated value ($t_{tab} = 2.05$). Hence H_1 is accepted. In B1 & B2 groups (6-12 years), the unpaired “t” calculated value ($t_{cal} = 2.460^*$) is greater than tabulated value ($t_{tab} = 2.05$). Hence H_2 is accepted. This indicates that kaleidoscope and cartoon video is statistically significant at $p < 0.05$ level. **Conclusion :** This study finding revealed that there was reduction in the pain during venipuncture among the experimental groups. Hence, it was inferred that cartoon video is more effective on reduction of pain during venipuncture procedure than the kaleidoscope across all ages.

Keywords : Evaluate; Effectiveness; Kaleidoscope; Cartoon Video; Pain; Venipuncture Procedure; Children; Selected Hospitals

INTRODUCTION

Pain management in hospitalized children remains a critical concern, as procedures like venipuncture are among the most distressing and painful interventions. Despite advancements in pharmacological and non-pharmacological methods, many children experience significant pain during such procedures, with long-

term effects on pain perception and behavior.¹ The International Association for the Study of Pain defines pain as a subjective experience influenced by sensory, emotional, and developmental factors, underscoring the importance of addressing pain comprehensively.²

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Non-pharmacological techniques such as distraction have shown promise in alleviating procedural pain by diverting attention.³ Tools like kaleidoscopes and cartoon videos engage visual and auditory senses, promoting emotional distraction and reducing pain perception. Kaleidoscopes create captivating symmetrical patterns through reflection, stimulating curiosity and engagement.⁴ Cartoon videos leverage humour, sound effects, and visual appeal to elicit positive emotions, offering an effective distraction during painful procedures.⁵

This study aims to compare the effectiveness of kaleidoscope-based distraction and cartoon video distraction in reducing pain among children undergoing venipuncture, providing evidence to support their use in pediatric pain management.

MATERIALS AND METHODS

In the present study, focusing on the nature of the research problem and to fulfil the objective, a quantitative, evaluative survey research approach was considered to carry out the study.

As this study involves evaluating the effectiveness of two different distraction strategies on pain level of hospitalized children, quasi experimental, randomized block design was chosen for this study.

Symbolic representation of Quasi experimental, randomized block design

→ Age in yrs	3 – 6yrs	6 – 12yrs
↓ Intervention	(A)	(B)
Kaleidoscope (1)	A1	B1
Cartoon video (2)	A2	B2

This study was conducted at selected Tertiary Care Centre, Kolhapur. The settings were chosen on the basis of feasibility and in terms of availability of children admitted in paediatric ward at these hospitals. In the present study, population comprised of children of age group 3-12 years admitted in hospitals. In this study the sample/ participants comprised of children of age group of 3-12years, fulfilling the inclusion and exclusion criteria and admitted in paediatric ward of selected hospitals at Kolhapur. **Sample size** Sample size was calculated with the guidance of statistician and guide. Sample size is calculated for confidence interval 95%, 80% power and effect size 0.6167 by using software G*Power version 3.1.9.4. Total Sample size calculated was 60. For the present study, 60 children were chosen, from age group 3 – 12 years in 4 groups namely, Experimental group A1 (15)& A2 (15) (3-6 years) and Experimental group B1(15)& B2 (15)(6-12 years) .Using Non-probability, purposive sampling, samples were first chosen followed by which, samples were randomly assigned to different treatment groups using lottery method. **Children admitted in paediatric ward who are**, between 3 – 12 years of age, undergoing venipuncture procedure for the first time whose parents are willing to give consent for participation were included. **Children who are**, chronic ill, consuming pain reducing drugs, mentally challenged, with sensory problems (visually & audio problems) with venipuncture for blood sampling were excluded.

RESULTS

The data was collected using the Wong Bakers FACES Pain Rating Scale to assess the pain level during venipuncture among 60 hospitalized children at selected paediatrics hospitals, Kolhapur. The collected data were coded, organized, analyzed and interpreted

by using descriptive and inferential statistics. Tables, graphs and figures were used to explain the results.

Table 1: Frequency and percentage distribution of participants of pain scores during venipuncture procedure in experimental group A1 and experimental group A2 (3-6 years)

Wong Bakers FACES Pain Rating Scale (pain scores during venipuncture procedure)	3-6 years			
	Experimental group A1 (kaleidoscope)		Experimental group A2 (cartoon video)	
	Frequency (f)	Percentage (%)	Frequency (f)	Percentage (%)
No pain. (Pain scores – 00)	01	3.33	03	10
Pain little Bit (Pain scores – 02)	02	6.67	08	26.67
Pain little more (Pain scores – 04)	03	10	01	3.33
Pain even more (Pain scores – 06)	01	3.33	01	3.33
Pain whole lot (Pain scores – 08)	03	10	01	3.33
Pain worst (Pain scores – 10)	05	16.67	01	3.33

Table 1 indicates that, among 30 participants,

In experimental group A1 (kaleidoscope) maximum 05 (16.67%) participants had worst pain (pain scores – 10) and minimum 1(10%) had no pain (pain scores – 00), where as in experimental group A2 (cartoon video) maximum 08 (26.67%) participants had little pain(pain scores – 02)

It was found that pain scores during venipuncture among participants in experimental group A2 who received cartoon video is lesser than the pain scores of participants in experimental group A1 who received kaleidoscope, which indicates that the cartoon video intervention is more effective that Kaleidoscope in toddler age group.

Table 2: Frequency and percentage distribution of participants of pain scores during venipuncture procedure in experimental group B1 and experimental group B2 (6-12 years)

Wong Bakers FACES Pain Rating Scale (pain scores during venipuncture procedure)	6-12 years			
	Experimental group B1 (kaleidoscope)		Experimental group B2 (cartoon video)	
	Frequency (f)	Percentage (%)	Frequency (f)	Percentage (%)
No pain. (Pain scores – 00)	02	6.66	04	13.33
Pain little Bit (Pain scores – 02)	03	10	06	20
Pain little more (Pain scores – 04)	03	10	02	6.67
Pain even more (Pain scores – 06)	01	3.33	01	3.33
Pain whole lot (Pain scores – 08)	05	16.67	01	3.33
Pain worst (Pain scores – 10)	01	3.33	01	3.33

Table 2 : indicates that, among 30 participants,

In experimental group B1 (kaleidoscope) maximum 05 (16.67%) participants had pain whole lot (Pain scores – 08) where as in experimental group B2 (cartoon video) maximum 06 (30%) participants had pain little Bit (pain scores – 02)

It was found that pain scores during venipuncture among participants in experimental group B2 who received cartoon video is lesser than the pain scores of participants in experimental group B1 who received kaleidoscope.

TESTING OF HYPOTHESIS

H₀₁: There is no significant difference between pain scores during venipuncture procedure among hospitalized children in experimental groups A1 and A2. (3-6 years of age)

H₁: There is a significant difference between pain scores during venipuncture procedure among hospitalized children in experimental groups A1 and A2. (3-6 years of age)

Table no 3 : Mean difference, Standard Error Difference, Unpaired “t” Test of participants of pain scores during venipuncture procedure in experimental group A1 (kaleidoscope) and experimental group A2 (cartoon video) (3-6 years)

n=30

Mean difference	Standard Error Difference (SED)	Unpaired “t” Test Calculated value	Table value	Degree of freedom (df)
3.47	0.856	4.053*	2.05	28

NOTE: * Indicates significance.

Table 5 indicates that. In A1 & A2 groups (3-6 yrs). The unpaired “t” calculated value ($t_{cal} = 4.053^*$) is greater than tabulated value ($t_{tab} = 2.05$). Hence H_1 is accepted & H_{01} is rejected. This indicates that kaleidoscope and cartoon video is statistically significant at $p < 0.05$ level. Therefore, it can be inferred that cartoon video is more effective on reduction of pain during venipuncture procedure. That indicates $H_1 = \mu \neq \mu_0$

H₀₂: There is no significant difference between pain scores during venipuncture procedure among hospitalized children in experimental groups B1 and B2. (6-12 years of age)

H₂: There is a significant difference between pain scores during venipuncture procedure among hospitalized children in experimental groups B1 and B2. (6-12 years of age)

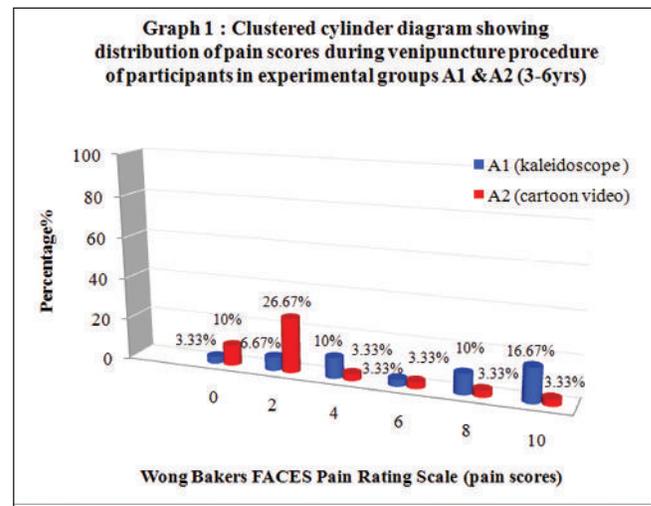
Table no 4 : Mean difference, Standard Error Difference, Unpaired “t” Test of participants of pain scores during venipuncture procedure in experimental group B1 (kaleidoscope) and experimental group B2 (cartoon video) (6-12years)

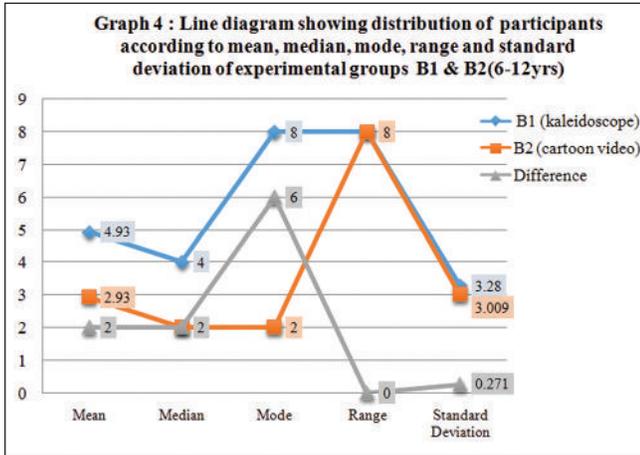
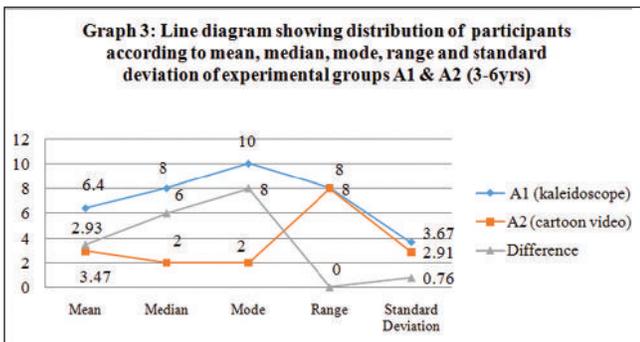
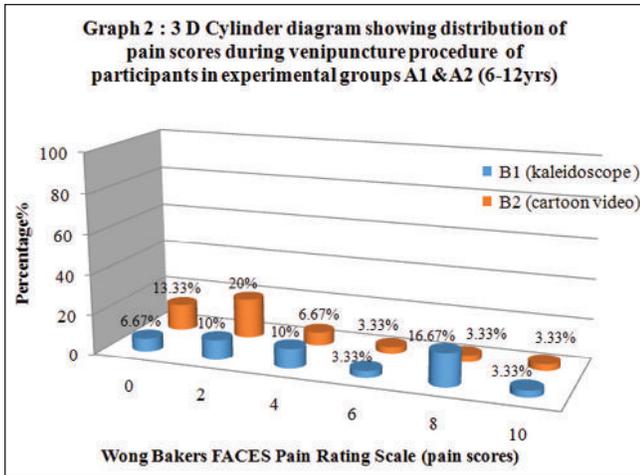
n=30

Mean difference	Standard Error Difference (SED)	Unpaired “t” Test Calculated value	Table value	Degree of freedom (df)
2	0.813	2.460*	2.05	28

NOTE: * Indicates significance.

Table 6 indicates that, In B1 & B2 groups (6-12 yrs). The unpaired “t” calculated value ($t_{cal} = 2.460^*$) is greater than tabulated value ($t_{tab} = 2.05$). Hence H_2 is accepted & H_{02} is rejected. This indicates that kaleidoscope and cartoon video is statistically significant at $p < 0.05$ level. Therefore, it can be inferred that cartoon video is more effective on reduction of pain during venipuncture procedure. That indicates $H_2 = \mu \neq \mu_0$





DISCUSSION

This study aimed to evaluate the effectiveness of kaleidoscope and cartoon video distractions on pain levels during venipuncture among hospitalized children. The findings revealed that the cartoon video distraction technique was more effective in reducing pain compared to the kaleidoscope distraction,

regardless of the children’s age group.

In the toddler group (experimental group A), a significant number of participants in the cartoon video group (A2) experienced minimal pain. The maximum number of participants (26.67%) reported little pain (pain score 2), while only 10% of participants reported no pain (pain score 0) in the kaleidoscope group (A1). Furthermore, 16.67% of participants in group A1 reported worst pain (pain score 10). These findings indicate that cartoon video distraction is superior in minimizing pain perception in toddlers.

Similarly, in the school-age group (experimental group B), cartoon video distraction also demonstrated greater effectiveness. In group B2, 30% of participants reported little pain (pain score 2), while in the kaleidoscope group (B1), 16.67% of participants experienced severe pain (pain score 8). This highlights the consistent advantage of cartoon videos in managing procedural pain, even among older children.

The observed efficacy of cartoon videos can be attributed to their ability to engage multiple sensory modalities—visual, auditory, and emotional. Research has shown that audiovisual distractions are highly effective in diverting attention from pain by stimulating the brain’s reward and pleasure centers, thereby reducing the perception of pain.⁶⁻⁸ In contrast, kaleidoscopes rely primarily on visual stimulation, which may not be as immersive or engaging as cartoon videos.

Our findings align with previous studies emphasizing the effectiveness of audiovisual distraction techniques in pediatric pain management. Birnie et al. found that audiovisual distractions, such as cartoon videos, significantly reduced needle-related pain and distress

in children.⁹ Similarly, Gupta et al. demonstrated that cartoon videos elicited positive emotions, reducing both pain and anxiety during invasive procedures.¹⁰

The effectiveness of cartoon videos may also be linked to developmental factors. Younger children, especially toddlers, have a limited ability to comprehend and manage pain, making them more susceptible to engaging distractions.¹¹ Additionally, the humorous and entertaining nature of cartoons may evoke laughter and positive emotions, further counteracting the emotional distress associated with painful procedures.

Despite the demonstrated benefits of distraction techniques, it is important to consider individual

differences in pain perception and response to interventions. Factors such as temperament, previous experiences, and cultural context may influence the efficacy of these methods. Future research should explore the role of these factors in optimizing distraction-based pain management strategies for different pediatric populations.

In conclusion, this study provides evidence supporting the use of cartoon videos as an effective non-pharmacological intervention to alleviate procedural pain during venipuncture in hospitalized children. By leveraging audiovisual stimulation, cartoon videos can serve as a simple, cost-effective, and engaging tool for improving pediatric pain management practices.

REFERENCES

1. International Association for the Study of Pain. IASP Pain Terminology. 2020.
2. Fitzgerald M, Walker SM. Infant pain management: a developmental neurobiological approach. *Nat Clin Pract Neurol*. 2009;5(1):35-50.
3. Birnie KA, Noel M, Parker JA, et al. Systematic review and meta-analysis of distraction and hypnosis for needle-related pain and distress in children and adolescents. *J Pediatr Psychol*. 2014;39(8):783-808.
4. Brewster D. *The Kaleidoscope: Its History, Theory, and Construction*. London: John Murray; 1819.
5. Gupta HV, Gupta VV. Efficacy of cartoon distraction on pain perception and distress in children during medical procedures. *Int J Pediatr*. 2020;7(2):215-22.
6. Gupta HV, Gupta VV. Efficacy of cartoon distraction on pain perception and distress in children during medical procedures. *Int J Pediatr*. 2020;7(2):215-22.
7. Wang Y, Sun H, Huang J, et al. Effects of audiovisual distraction on pain and anxiety during venipuncture in children: a systematic review and meta-analysis. *J Clin Nurs*. 2018;27(1-2):e12-23.
8. Ramesh B, Byrareddy P, Suman L, et al. Comparison of various distraction techniques in reducing pain during venipuncture in children. *Indian J Pediatr*. 2021;88(3):238-43.
9. Birnie KA, Noel M, Parker JA, et al. Systematic review and meta-analysis of distraction and hypnosis for needle-related pain and distress in children and adolescents. *J Pediatr Psychol*. 2014;39(8):783-808.
10. Klassen JA, Liang Y, Tjosvold L, et al. Music for pain and anxiety in children undergoing medical procedures: a systematic review of randomized controlled trials. *Ambul Pediatr*. 2008;8(2):117-28.
11. McGrath PJ, Stevens BJ, Walker SM, Zempsky WT. *Oxford Textbook of Paediatric Pain*. Oxford University Press; 2014.

Study Of Cognitive Function And Eeg Patterns In Patients Of Kidney Disease Newly Starting Haemodialysis Over A Period Of 6 Months

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ABSTRACT

Background : Studies assessing cognitive functions in patients undergoing dialysis for chronic kidney disease (CKD) are predominantly cross-sectional. A longitudinal study could provide novel insights into the progression of cognitive functions following the initiation of dialysis. **Methodology** : 50 patients diagnosed with CKD, on maintenance hemodialysis, were assessed with THINC-IT app & EEG for baseline evaluations at day 0. Repeat assessments were done at the end of 3 & 6 months. **Results** : The EEG showed normal alpha dominant activity for 88% at baseline, 92% at 3 months, and 80% at 6 months; with 14% showing diffuse slowing by the end of 6 months. Analysis of THINC-it® results using paired t tests showed statistically significant improvement in CRT and TMT at 0 - 3 months ($p < 0.05$). **Conclusion** : Improvement in CRT, TMT suggests that certain functions (reaction time, attention, task shifting) may benefit from hemodialysis. Initial improvements followed by a subsequent decline in EEG normalization suggest, while hemodialysis is beneficial in reducing neurotoxicity, it may also introduce new neurological challenges over time.

Keywords - EEG patterns, kidney, haemodialysis, CKD, cognitive function.

INTRODUCTION

Chronic kidney disease (CKD) represents a significant global public health challenge due to its widespread occurrence and high prevalence rates.¹ Cognitive impairment is frequently observed in individuals with chronic kidney disease (CKD), especially those undergoing dialysis treatment.^{2,3} Chronic kidney disease (CKD) is defined by enduring structural or functional abnormalities in the kidneys that extend for a period exceeding three months, and these abnormalities have significant health implications. The diagnosis hinges on specific criteria, which include a reduced glomerular filtration rate (GFR) of less than

60 mL/min/1.73 m² or evidence of kidney damage such as albuminuria, tubular disorders, abnormal urine sediment, histological or imaging findings, or a history of kidney transplantation.⁴

The disease is categorized into five stages based on GFR, and risk levels are further refined based on albuminuria levels. These CKD stages are linked to various adverse outcomes, including all-cause mortality, cardiovascular-related deaths, anemia, and bone and mineral metabolism disorders, among other complications.⁵ The prevalence of both CKD and

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cognitive impairment (CI) rises with advancing age. Cognitive alterations manifest in the early stages of CKD, often occurring when the glomerular filtration rate (GFR) falls below 60 mL/min/1.73 m².^{6,7}

Conflicting findings have been reported regarding the EEG alterations that occur during haemodialysis in individuals with CKD. EEG changes induced during haemodialysis are significant, as they can provide insights into the underlying mechanisms and identify potential risk factors for neurological complications that may arise during or shortly after haemodialysis, a condition referred to as dialysis disequilibrium syndrome (DDS).^{8,9} Uremic encephalopathy significantly elevates the morbidity and mortality risk among individuals with CKD.¹⁰ In cases of acute kidney injury, the associated symptoms are reversible upon initiating dialysis and effectively removing toxic substances. Similarly, for individuals with end-stage renal disease (ESRD), the worsening of the condition can be decelerated through dialysis or kidney transplantation. Severe complications, such as seizures and coma, can unfortunately result in fatalities. Recognizing neurological symptoms early in the presence of impaired kidney function is crucial to prevent morbidity or mortality. Prompt initiation of dialytic therapy can contribute to reducing mortality rates.¹¹

The most recent version of the Diagnostic and Statistical Manual of Mental Disorders defines neurocognitive disorder (NCD) as primarily cognitive conditions that are acquired and progressive.¹² This deterioration can impact one of six cognitive domains: complex attention, executive function, learning and memory, language, perceptual-motor skills, and social cognition. In cases of mild NCD, which corresponds to what is

typically referred to as ‘mild cognitive impairment’ (MCI), individuals maintain functional independence. However, in major NCD, which encompasses what is known as ‘dementia,’ cognitive impairment is severe enough to compromise social and/or occupational functioning.¹³ Among cognitively impaired CKD patients, there is often evidence of executive dysfunction, similar to what is typically observed in vascular neurocognitive disorder. Additionally, CKD patients face a higher risk of developing Alzheimer’s disease and experiencing increased mortality when compared to the general population.¹⁴ Studies have identified a positive correlation between the severity of CKD and the prevalence of cognitive impairment. As CKD progresses through its stages, there is an increased likelihood of cognitive decline. This suggests that individuals with advanced CKD are more susceptible to cognitive impairment, highlighting the need for early detection and intervention.

Electroencephalography (EEG) is a valuable tool for assessing brain activity by recording electrical signals generated by the brain’s neurons. In the context of chronic kidney disease (CKD) and the initiation of haemodialysis, studying EEG patterns provides insights into the impact of renal dysfunction on brain function. Here, we delve into the significance of EEG patterns in CKD patients newly starting haemodialysis.¹⁵ Electroencephalography (EEG) serves as a valuable tool for assessing patients with uremic encephalopathy and monitoring their clinical progress. EEG findings exhibit correlations with clinical symptoms, thereby offering diagnostic insights. Additionally, EEG can aid in excluding other potential causes of confusion, such as infections or structural abnormalities.¹⁶ In cases of uremic encephalopathy, EEG recordings

typically demonstrate abnormalities characterized by generalized slowing of brainwave activity, which tends to intensify as the condition advances. In CKD, EEG patterns usually exhibit irregular low voltage with a slowdown of the posterior dominant alpha rhythm, occasionally interspersed with bursts of theta waves. Notably, distinctive patterns emerge, such as prolonged bursts of bilateral, synchronous slow and sharp waves or spike and wave complexes, which are characteristic of the condition. These EEG abnormalities tend to stabilize with the initiation of dialysis treatment. EEG irregularities associated with uremic encephalopathy are manifested through the presence of theta waves, the disappearance of normal basic rhythms, diminished EEG responsiveness to sensory input, and an increased prominence of generalized delta activity. These changes are typically more evident in the frontal leads of the EEG recording.¹⁷

As CKD progresses to end-stage renal disease (ESRD), patients often require haemodialysis as a life-sustaining therapy. Beyond its well-established impact on kidney function, CKD can also affect cognitive function. Cognitive impairment in CKD patients can lead to diminished quality of life, increased morbidity, and higher healthcare costs. This study aims to investigate the alterations in cognitive function and EEG patterns in patients with kidney disease who are newly commencing haemodialysis over 6 months.

MATERIALS AND METHODS

The study was performed at Tertiary care hospital, Kolhapur for 2 years after institutional ethical committee approval in December 2022. A total of 50 patients were included based on specific inclusion and exclusion criteria. Before conducting the study, written

consent/assent was obtained from the patient's guardian or parents. Furthermore, a clear explanation of the procedure was provided to ensure their understanding and cooperation. The detailed medical history of the patient was collected, and appropriate precautionary measures were taken during the diagnosis to ensure the safety of the patient. The patient's guardian or parents were informed about the need for a follow-up.

Inclusion Criteria:

Patients with an established diagnosis of kidney disease.

Patients on maintenance haemodialysis therapy.

Literate patients/received formal education at least up to the third standard.

Exclusion Criteria:

Patients with epilepsy or on anti-epileptic drugs for any indications

Patients with known neurological disorders or procedures result in changes in cognitive ability and EEG changes.

Patients who had any life-threatening medical emergency in the last twelve months.

Patients with any other psychiatric disorders and patients on psychiatric medication.

Patients with an established diagnosis of Encephalopathy.

1. THINC-it® app:

THINC-it® is a screening tool for the assessment of

cognitive functioning. Free app, 39 MB size with 5 thousand+ downloads Available on both Google Playstore and Apple Store It is comprised of the PDQ–5D (a short questionnaire for the patient to complete), and four neuropsychological tests - Spotter, Symbol check, Code Breaker, and Trails test.

- a. Code breaker evaluates executive function, processing speed, and attention/concentration
- b. Spotter primarily evaluates attentional skills, but also elements of executive function
- c. Symbol Check evaluates working memory, executive function, and attention/concentration
- d. Trails evaluate executive function.
- e. PDQ-5D is a 5-item self-report scale that broadly evaluates subjective awareness of deficits.

2. The Mini-Mental State Examination (MMSE)

Scale: The Mini-Mental State Examination (MMSE) is a tool that can be used to systematically and thoroughly for assessment of mental status. It is an 11-question measure that tests five areas of cognitive function: orientation, registration, attention and calculation, recall, and language. The maximum score is 30. A score of 23 or lower is indicative of cognitive impairment. The MMSE takes only 5-10 minutes to administer and is therefore practical to use repeatedly and routinely.

3. **EEG Machine:** 21 lead portable digital EEG Machine Photic Stimulator present.

Frequency band: up to 150 Hz Suitable for OPD, IPD, and ICU patients.

Data were collected and entered in a Microsoft Excel sheet. Findings were analyzed using the paired t test.

When required, statistical analysis was performed using SPSS (Version 23.0). A significance level of ($P < 0.05$) was employed to determine statistical significance.

RESULTS

Age Group	No of Patients	Percentage
31 to 40	6	12.00%
41 to 50	13	26.00%
51 to 60	16	32.00%
61 to 70	15	30.00%
Total	50	100.00%

Out of 50 patients studied, 16 (32%) of patients fell under the age bracket of 51-60 years, and 15 patients (30%) were under the age bracket of 61-70 years. 13 (26%) of the patients were between 41 to 50 years and 6 (12%) of patients were between 31 to 40 years of age.

MMSE	0 months		3 months		6 months		P-value
	No of Patients	Percentage	No of Patients	Percentage	No of Patients	Percentage	
Cognitive impairment (mild)	24	48.00%	23	46.00%	22	44.00%	0.92
Normal Score	26	52.00%	27	54.00%	28	56.00%	
Total	50	100.00%	50	100.00%	50	100.00%	

24 patients (48%) of the patients scored between 18-23 on Mini Mental Status Examination indicating mild impairment of cognition, whereas 26 (52%) scored between 24-30. At 3 months, 23 (46%) had mild impairment of cognition, while 27 (54%) of patients scored between 24-30. At 6 months, 22 (44%) had mild

impairment of cognition, while 28 (56%) of patients scored between 24-30.

EEG Findings at 0 Months	No of Patients	Percentage
Abnormal theta and delta waves	2	4.00%
Diffuse slowing of background rhythm	2	4.00%
Slowing in the occipital region	1	2.00%
Spike and slow wave complexes	1	2.00%
Normal Background activity alpha dominant	44	88.00%
Total	50	100.00%

At baseline assessment, 44 (88%) showed normal alpha dominant background activity, whereas 2 (4%) of the patients showed diffuse slowing in background rhythm and 2 (4%) showed presence of abnormal theta and delta waves. 1 (2%) had spike and wave complexes in EEG and 1 (2%) had slowing in occipital region.

EEG Findings at 3 Months	No of Patients	Percentage
Abnormal theta and delta waves	1	2.00%
Diffuse slowing of background rhythm	2	4.00%
Slowing in the occipital region	1	2.00%
Normal	46	92.00%
Total	50	100.00%

At 3 months follow up, 46 (92%) showed normal alpha dominant background activity, whereas 2 (4%) of the patients showed diffuse slowing in background rhythm and 1 (2%) showed presence of abnormal theta and delta waves, 1 (2%) had slowing in occipital region.

EEG Findings at 6 Months	No of Patients	Percentage
Abnormal theta and delta waves	1	2.00%
Diffuse slowing of background rhythm	7	14.00%
Spike and slow wave complexes	2	4.00%
Normal	40	80.00%
Total	50	100.00%

At 3 months follow up, 40 (80%) showed normal alpha dominant background activity, whereas 7 (14%) of the patients showed diffuse slowing in background rhythm and 1 (2%) showed presence of abnormal theta and delta waves, 2 (4%) had spike and wave complexes in EEG.

Comparison of THINC-it® tests over follow ups in patients undergoing twice weekly haemodialysis. (Paired t-test used)

Cognitive Tests	Months	Mean	S.D.	p-value
CRT	0 Month	859.44	182.86	
	3 Months	821.19	196.03	0.0006*
	6 Months	806.19	189.06	0.0005*
Nback	0 Month	11.00	3.78	
	3 Months	11.00	3.90	0.5
	6 Months	11.06	3.64	0.454
DSST	0 Month	23.31	7.68	
	3 Months	24.06	8.43	0.189
	6 Months	23.75	9.43	0.365
TMT	0 Month	32.88	12.04	
	3 Months	31.13	11.14	0.037*
	6 Months	29.19	11.87	0.031*

(*indicated p-value (<0.05) is significant.)

THINC-it® assessment of patients undergoing twice weekly dialysis, it was found that:

- a) Choice Reaction Time (CRT), measured as latency of response in milliseconds, was (859.44 ± 182.86) msec at baseline. At three months, mean reaction time reduced to (821.19 ± 196.03) msec and at six months, mean reaction time showed further reduction to (806.19 ± 189.06). Using paired t test, p value was significant for 0-3months ($p=0.0006$) and significant for 0-6 months ($p=0.0005$).
- b) Nback test, measured in terms of number of correct responses, was (11.00 ± 3.78) at baseline, at three months it was (11.00 ± 3.90) and at six months it was (11.06 ± 3.64). Using paired t test, p value was not significant for 0-3 months ($p=0.5$) and not significant for 0-6 months ($p=0.45$).
- c) Digit Symbol Substitution Test (DSST), measured in terms of number of correct responses, was (23.31 ± 7.68) at baseline; at 3 months it was (24.06 ± 8.43) and at 6 months it was (23.75 ± 9.43). Using paired t test, p value was not significant for 0-3 months ($p=0.189$) and not significant for 0-6 months ($p=0.365$).
- d) Trails Test (TMT), measured as time taken to complete the trail in seconds, was (32.88 ± 12.04) sec at baseline. At three months, completion time reduced to (31.13 ± 11.14) sec and at six months, completion time showed further reduction to (29.19 ± 11.87). Using paired t test, p value was significant for 0-3 months ($p=0.037$) and significant for 0-6 months ($p=0.031$).

Comparison of THINC-it® tests over follow ups in patients undergoing 3 times weekly haemodialysis. (Paired t-test used)

Cognitive Tests	Months	Mean	S.D.	p-value
CRT	0 Month	863.81	236.92	
	3 Months	825.12	232.88	0.0001*
	6 Months	802.81	246.74	0.0001*
Nback	0 Month	9.96	3.79	
	3 Months	9.96	3.76	0.5
	6 Months	10.04	4.05	0.421
DSST	0 Month	24.50	8.84	
	3 Months	24.35	8.93	0.398
	6 Months	24.73	9.64	0.387
TMT	0 Month	33.81	15.16	
	3 Months	31.04	13.79	0.001*
	6 Months	30.81	14.31	0.005*

(*indicated p-value (<0.05) is significant.)

THINC-it® assessment of patients undergoing thrice weekly dialysis, it was found that:

- a) Choice Reaction Time (CRT), measured as latency of response in milliseconds, was (863.81 ± 236.92) msec at baseline. At three months, mean reaction time reduced to (825.12 ± 232.88) msec and at six months, mean reaction time showed further reduction to (802.81 ± 246.74). Using paired t test, p value was significant for 0-3months ($p=0.0001$) and significant for 0-6 months ($p=0.0001$).
- b) Nback test, measured in terms of number of correct responses, was (9.96 ± 3.79) at baseline, at three months it was (9.96 ± 3.76) and at six months it was (10.04 ± 4.05). Using paired t test, p value was not significant for 0-3 months ($p=0.5$) and not significant for 0-6 months ($p=0.421$).

- c) Digit Symbol Substitution Test (DSST), measured in terms of number of correct responses, was (24.50 ± 8.84) at baseline; at 3 months it was (24.35 ± 8.93) and at 6 months it was (24.73 ± 9.64). Using paired t test, p value was not significant for 0-3 months ($p=0.398$) and not significant for 0-6 months ($p=0.387$).
- d) Trails Test (TMT), measured as time taken to complete the trail in seconds, was (33.81 ± 15.16) sec at baseline. At three months, completion time reduced to (31.04 ± 13.79) sec and at six months, completion time showed further reduction to (30.81 ± 14.31). Using paired t test, p value was significant for 0-3 months ($p=0.0001$) and significant for 0-6 months ($p=0.0005$).

Comparison of THINC-it® tests over follow ups in patients undergoing 4 times weekly haemodialysis. (Paired t-test used)

Cognitive Tests	Months	Mean	S.D.	p-value
CRT	0 Month	936.13	227.81	
	3 Months	878.00	218.04	0.0196*
	6 Months	878.25	237.66	0.0271*
Nback	0 Month	7.50	2.88	
	3 Months	8.13	2.59	0.1526
	6 Months	8.63	3.29	0.1095
DSST	0 Month	25.88	8.87	
	3 Months	27.75	9.53	0.1213
	6 Months	26.38	11.04	0.3753
TMT	0 Month	39.25	12.90	
	3 Months	31.63	14.16	0.0015*
	6 Months	32.75	14.30	0.0083*

(*indicated p-value (<0.05) is significant.)

THINC-it® assessment of patients undergoing thrice weekly dialysis, it was found that:

- a) Choice Reaction Time (CRT), measured as latency of response in milliseconds, was (936.13 ± 227.81) msec at baseline. At three months, mean reaction time reduced to (878.00 ± 218.04) msec and at six months, mean reaction time showed further reduction to (878.25 ± 237.66). Using paired t test, p value was significant for 0-3 months ($p=0.0196$) and significant for 0-6 months ($p=0.0271$).
- b) Nback test, measured in terms of number of correct responses, was (7.50 ± 2.88) at baseline, at three months it was (8.13 ± 2.59) and at six months it was (8.63 ± 3.29). Using paired t test, p value was not significant for 0-3 months ($p=0.1526$) and not significant for 0-6 months ($p=0.1095$).
- c) Digit Symbol Substitution Test (DSST), measured in terms of number of correct responses, was (25.88 ± 8.87) at baseline; at 3 months it was (27.75 ± 9.53) and at 6 months it was (26.38 ± 11.04). Using paired t test, p value was not significant for 0-3 months ($p=0.121$) and not significant for 0-6 months ($p=0.375$).
- d) Trails Test (TMT), measured as time taken to complete the trail in seconds, was (39.25 ± 12.90) sec at baseline. At three months, completion time reduced to (31.63 ± 14.16) sec and at six months, completion time showed further reduction to (32.75 ± 14.30). Using paired t test, p value was significant for 0-3 months ($p=0.0015$) and significant for 0-6 months ($p=0.0083$).

Comparison of THINC-it® tests over follow ups in patients. (Paired t-test used)

Cognitive Tests	Months	Mean	S.D.	p-value
CRT	0 Month	873.98	216.89	
	3 Months	832.32	215.95	2.554E-08*
	6 Months	815.96	225.45	1.5707E-08*
Nback	0 Month	9.90	3.77	
	3 Months	10.00	3.70	0.320
	6 Months	10.14	3.83	0.209
DSST	0 Month	24.34	8.36	
	3 Months	24.80	8.78	0.165
	6 Months	24.68	9.64	0.290
TMT	0 Month	34.38	13.79	
	3 Months	31.10	12.71	2.232E-06*
	6 Months	30.60	13.35	3.4226E-05*

(*indicated p-value (<0.05) is significant.)

Eliminating the frequency of dialysis as a parameter, on overall analysis of THINC-it® results revealed:

- a) Choice Reaction Time (CRT), measured as latency of response in milliseconds, was (873.98±216.89) msec at baseline. At three months, mean reaction time reduced to (832.32±215.95) msec and at six months, mean reaction time showed further reduction to (815.96± 225.45). Using paired t test, p value was significant for 0-3months (p=2.554E-08*) and significant for 0-6 months (p=1.5707E-08*).
- b) Nback test, measured in terms of number of correct responses, was (9.90± 3.77) at baseline, at three months it was (10.00 ± 3.70) and at six months it was (10.14 ± 3.83). Using paired t test, p value was not significant for 0-3 months (p=0.320) and not significant for 0-6 months (p=0.209).
- c) Digit Symbol Substitution Test (DSST), measured in terms of number of correct responses, was (24.34±8.36) at baseline; at 3 months it was (24.80± 8.78) and at 6 months it was (24.68±9.64). Using paired t test, p value was not significant for 0-3 months (p=0.165) and not significant for 0-6 months (p=0.290).
- d) Trails Test (TMT), measured as time taken to complete the trail in seconds, was (34.38 ±13.79) sec at baseline. At three months, completion time reduced to (31.10 ± 12.71) sec and at six months, completion time showed further reduction to (30.60 ± 13.35). Using paired t test, p value was significant for 0-3 months (p=2.232E-06) and significant for 0-6 months (p=3.4226E-05).

DISCUSSION

Patients recruited in this study were initially assessed on the basis of MMSE score, to exclude patients of moderate to severe cognitive impairments that might have been a result of neuro-psychiatric or general medical condition, which may act as a hindrance in a) associating cognitive progression with the intervention of dialysis and b) lead the patient incapable of instruction and comply with demands of the testing. Analysis of MMSE score, done at day of recruitment (0 months) as a screening tool showed 48% of all

patients scored between 18-23 on MMSE, depicting mild cognitive defects; whereas 52% of patients scored 24 and above. While almost half of the patients showed baseline cognitive deficits in this study, Murray found 13.9% of patients having mild cognitive defects, and about 66% patients had moderate to severe defects, when assessments were done for the domains of memory, executive function and language, in patients of haemodialysis.¹⁸

A recent study by Levassort, that implicated domains of MMSE to predict patterns of changes in cognition, found that eGFR decline was linked with deterioration in orientation, attention and calculation, language and praxis domain scores, but not with the memory domain.¹⁹

MMSE scoring was performed twice in this study, as a part of follow ups, for the rationale of eliminating patients that might have been incapacitated to meet the requirements of the study, owing to high risk of cerebrovascular accidents²⁰, and kidney disease independently posing as a high-risk factor of cardiovascular and all-cause morbidity and mortality.²¹

MMSE conducted on three months revealed 46% of the patients had a score between 18-23, falling under the category of mild cognitive impairment and 54% of patients had scores more than 24, befalling under the domain of normal scores. MMSE conducted on six months classified 44% as mild impairment, 56% were placed under normal. While this projects an increase in number of patients with normal scoring, it was not statistically significant. ($p>0.05$)

It is worthwhile to mention here that although MMSE is standardized and widely used tool, it may be

influenced by comparison of patients across age groups and therefore may require age specific norms²², which was beyond the scope of this study. A number of other parameters such as differences in cognitive reserve in form of differences in formal educational levels²³, differences in lifetime occupation as a measure of social class²⁴, etc. ought to be matched for obtaining further precision in results.

In above study, at the initiation of haemodialysis (zero months), the majority of patients (88%) exhibited normal EEG activity with alpha-dominant background rhythms. However, a minority of patients showed abnormalities, including abnormal theta and delta waves (4%), diffuse slowing of the background rhythm (4%), slowing in the occipital region (2%), and spike and slow wave complexes (2%). These findings are consistent with previous research indicating that patients with renal failure can exhibit EEG abnormalities even before the commencement of dialysis, likely due to the accumulation of uremic toxins affecting brain function -Khatri et al., 2015²⁵

At the three-month mark, there was a noticeable improvement in the EEG patterns. The incidence of abnormal theta and delta waves decreased to 2%, while the proportion of patients with normal EEG activity increased to 92%. The persistence of diffuse slowing of the background rhythm (4%) and slowing in the occipital region (2%) indicates that while some patients showed marked improvement, others continued to exhibit mild EEG abnormalities. This improvement could be attributed to the removal of uremic toxins through haemodialysis, leading to better overall brain function (de Lima et al., 2019).²⁶

At six months, a slight decline in EEG normalization

was observed. The proportion of patients with normal EEG activity decreased to 80%. The percentage of patients with abnormal theta and delta waves remained at 2%, while diffuse slowing of the background rhythm increased significantly to 14%. Additionally, there was an emergence of spike and slow wave complexes in 4% of patients. These findings suggest a complex relationship between prolonged haemodialysis and EEG changes. While initial improvements are evident, some patients may develop new neurological issues over time, potentially due to ongoing metabolic imbalances or dialysis-related factors (Brouns & De Deyn, 2004).²⁷

The initial improvement in EEG patterns at three months suggests that haemodialysis effectively reduces the neurotoxic burden in patients with kidney disease, leading to enhanced cerebral function. However, the subsequent decline in EEG normalization at six months raises concerns about the long-term neurophysiological impact of haemodialysis. The increase in diffuse slowing of the background rhythm and the appearance of spike and slow wave complexes might reflect chronic cerebrovascular changes, fluctuations in blood pressure during dialysis sessions, or other dialysis-related complications as suggested by Meyer et al., 2015.²⁸

These findings underscore the importance of continuous neurological monitoring in patients undergoing haemodialysis. Regular EEG assessments can help identify emerging neurological issues early, allowing for timely interventions. Additionally, optimizing dialysis protocols to minimize cerebrovascular stress and addressing other metabolic factors may help mitigate the long-term neurological impacts on these patients.

For the study of cognitive capacity and to be able to quantify changes that occurred during the process of haemodialysis, THINC-it® application provided the following tests: a) The Spotter game, which is inspired from the Choice Reaction Time (CRT) test, which has been attributed to abilities of attention and executive function; b) Symbol Check game representing the Nback task, allowing the evaluation of working memory, attention, concentration and diverse sub-domains of executive function; c) Code-Breaker game, representation of Digit Symbol Substitution Test (DSST), apt for quantifying deficits of executive function, processing speed along with domains of attention and concentration d) Trails game derived by Trail Making test, capable of evaluating executive function.

CONCLUSION

The observed improvements in CRT and TMT suggest that certain cognitive functions, particularly those related to reaction time, attention & concentration, and task shifting abilities, may benefit from regular haemodialysis treatment. These findings align with the understanding that managing the physiological effects of CKD through haemodialysis can have positive effects on certain cognitive domains.

However, the lack of significant changes in Nback (validated test of working memory) and DSST (executive function, processing speed, complex attention, etc) highlights the complexity of cognitive impairments in CKD patients and suggests that not all cognitive domains may respond similarly to haemodialysis. This could point to the need for additional supportive measures or interventions, such as cognitive training or rehabilitation, to address specific cognitive deficits.

The persistent improvement in CRT and TMT in patients irrespective of frequency of dialysis sessions, as well as slight to none improvement in DSST and Nback suggesting that some cognitive domains might be resilient to dialysis, suggests that increased frequency of dialysis might not directly suggest increased improvements of cognition domains.

Future research should explore the underlying mechanisms driving these cognitive changes and assess whether similar patterns are observed in larger and more diverse patient populations. Longitudinal studies with more extended follow-up periods and additional

cognitive tests could provide deeper insights into the cognitive trajectories of haemodialysis patients. Moreover, investigating the potential impact of adjunct therapies, such as exercise or pharmacological interventions, on cognitive outcomes could offer valuable information for optimizing patient care.

In conclusion, while haemodialysis appears to support improvements in certain cognitive domains, a comprehensive approach addressing all aspects of cognitive health is essential for enhancing the quality of life in patients with chronic kidney disease.

REFERENCE

1. Levey AS, Coresh J. Chronic kidney disease. *The lancet*. 2012 Jan 14;379(9811):165-80.
2. Kalirao P, Pederson S, Foley RN, Kolste A, Tupper D, Zaun D, Buot V, Murray AM. Cognitive impairment in peritoneal dialysis patients. *American Journal of Kidney Diseases*. 2011 Apr 1;57(4):612-20.
3. Weiner DE, Scott TM, Giang LM, Agganis BT, Sorensen EP, Tighiouart H, Sarnak MJ. Cardiovascular disease and cognitive function in maintenance haemodialysis patients. *American Journal of Kidney Diseases*. 2011 Nov 1;58(5):773-81.
4. Perez-Gomez MV, Bartsch LA, Castillo-Rodriguez E, Fernandez-Prado R, Fernandez-Fernandez B, Martin-Cleary C, Gracia-Iguacel C, Ortiz A. Clarifying the concept of chronic kidney disease for non-nephrologists. *Clinical kidney journal*. 2019 Apr;12(2):258-61.
5. Quinn MP, Cardwell CR, Kee F, Maxwell AP, Savage G, McCarron P, Fogarty DG. The finding of reduced estimated glomerular filtration rate is associated with increased mortality in a large UK population. *Nephrology Dialysis Transplantation*. 2011 Mar 1;26(3):875-80.
6. Murray AM. Cognitive impairment in the aging dialysis and chronic kidney disease populations: an occult burden. *Advances in chronic kidney disease*. 2008 Apr 1;15(2):123-32.
7. Berger I, Wu S, Masson P, Kelly PJ, Duthie FA, Whiteley W, Parker D, Gillespie D, Webster AC. Cognition in chronic kidney disease: a systematic review and meta-analysis. *BMC medicine*. 2016 Dec;14:1-0.
8. Kennedy AC, Linton AL, Luke RG, Renfrew S. Electroencephalographic changes during haemodialysis. *The Lancet*. 1963 Feb 23;281(7278):408-11.
9. Arieff AI. Dialysis disequilibrium syndrome: current concepts on pathogenesis and prevention. *Kidney international*. 1994;45(3):629-35.
10. Tw M, Hostetter TH: uremia. *N Engl J Med*. 2007;357(13):1316-25.

11. Rehman IU, Idrees MK. Outcome of end-stage renal disease patients with advanced uremia and acidemia. *Journal of the College of Physicians and Surgeons Pakistan*. 2016 Jan 1;26(1):31-6.
12. Levey AS, Becker C, Inker LA. Glomerular filtration rate and albuminuria for detection and staging of acute and chronic kidney disease in adults: a systematic review. *Jama*. 2015 Feb 24;313(8):837-46.
13. Sachdev PS, Mohan A, Taylor L, Jeste DV. DSM-5 and mental disorders in older individuals: an overview. *Harvard review of psychiatry*. 2015 Sep;23(5):320.
14. Hugo J, Ganguli M. Dementia and cognitive impairment: epidemiology, diagnosis, and treatment. *Clinics in geriatric medicine*. 2014 Aug 1;30(3):421-42.
15. Giang LM, Weiner DE, Agganis BT, Scott T, Sorensen EP, Tighiouart H, Sarnak MJ. Cognitive function and dialysis adequacy: no clear relationship. *American journal of nephrology*. 2011 Oct 21;33(1):33-8. Gadewar P, Acharya S, Khairkar P, Shukla S, Mahajan SN. Dynamics of electroencephalogram (EEG) in different stages of chronic kidney disease. *Journal of Clinical and Diagnostic Research: JCDR*. 2015 Mar;9(3):OC25.
16. Gadewar P, Acharya S, Khairkar P, Shukla S, Mahajan SN. Dynamics of electroencephalogram (EEG) in different stages of chronic kidney disease. *Journal of Clinical and Diagnostic Research: JCDR*. 2015 Mar;9(3):OC25.
17. Rabie MM, Abdelkader AA, Alsayed AH, El-Zamarany EH. Prevalence of Polyneuropathy and Encephalopathy in Children under Regular Haemodialysis. *GEGET*. 2022 Dec 1;17(2):50-9.
18. Murray AM, Tupper DE, Knopman DS, Gilbertson DT, Pederson SL, Li S, Smith GE, Hochhalter AK, Collins AJ, Kane RL. Cognitive impairment in haemodialysis patients is common. *Neurology*. 2006 Jul 25;67(2):216-23.
19. Levassort H, Boucquemont J, Alencar de Pinho N, Lambert O, Helmer C, Metzger M, Teillet L, Frimat L, Combe C, Fouque D, Laville M. A new approach for cognitive impairment pattern in chronic kidney disease. *Nephrology Dialysis Transplantation*. 2024 May;39(5):848-59.
20. Wyld M, Webster AC. Chronic kidney disease is a risk factor for stroke. *Journal of Stroke and Cerebrovascular Diseases*. 2021 Sep 1;30(9):105730.
21. Tonelli M, Wiebe N, Culeton B, House A, Rabbat C, Fok M, McAlister F, Garg AX. Chronic kidney disease and mortality risk: a systematic review. *Journal of the American Society of Nephrology*. 2006 Jul 1;17(7):2034-47.
22. Bleecker ML, Bolla-Wilson K, Kawas C, Agnew J. Age-specific norms for the mini-mental state exam. *Neurology*. 1988 Oct;38(10):1565-.
23. Wu Y, Zhang Y, Yuan X, Guo J, Gao X. Influence of education level on MMSE and MoCA scores of elderly inpatients. *Applied Neuropsychology: Adult*. 2023 Jul 4;30(4):414-8.
24. Frisoni GB, Rozzini R, Bianchetti A, Trabucchi M. Principal lifetime occupation and MMSE score in elderly persons. *Journal of Gerontology*. 1993 Nov 1;48(6):S310-4.
25. Khatri, M., Himmelfarb, J., & Choi, M. J. (2015). Uremic encephalopathy: A reversible condition. *American Journal of Kidney Diseases*, 65(5), 812-818
26. de Lima JJG, Leite ALA, Filho JRN, Guerra JR. EEG patterns in patients with chronic kidney disease and the effects of haemodialysis: a longitudinal study. *J Clin Neurophysiol*. 2019;36(5):382-387.
27. Brouns R, De Deyn PP. Neurological complications in renal failure: A review. *Clin Neurol Neurosurg*. 2004;107(1):1-16.
28. Meyer KB, Levey AS, Nissenson AR. Chronic kidney disease and the aging population. *Am J Kidney Dis*. 2015;66(3):450-457.

A Study Of Comparison Austrian Prehospital Stroke Scale And Cincinnati Prehospital Stroke Scale With National Institute Of Health Stroke Scale In Acute Cerebrovascular Accident

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ABSTRACT

Introduction- Stroke is associated with high levels of disability and mortality on a global scale. Despite efforts in stroke inhibition, both primary and secondary, the burden remains substantial. Stroke epidemiologic statistics indicate it as the second foremost reason of death globally, following ischemic heart disease. **Methodology-** This Comparative Observational study was started after approval of Institutional Research Committee and Institutional Ethics Committee. Subjects fulfilling the inclusion and exclusion criteria were taken for study. valid, informed, written consent for being a part of the study was taken from the participants before enrolling them. Every patient underwent MRI and MR angiography as per standard protocol Final diagnosis and results of MRI, MR Angiography along with lipid profile were recorded. Application of stroke severity scales to each patient by examining each parameter of the study was done and noted for assessment of severity and involvement of large vessels. **Results-** In the present study on CVA, out of 101 patients, the majority, 45 (44.6%) belong to the age group 61 to 80 years followed by 41 (40.6%) from “age group 41 to 60 years and 13 (12.9%) belong to age group 21 to 30 years. There was a slight male preponderance. Most common vessel involvement was MCA in 26 (25.7%) patients, ICA in 12 (11.9%), PCA in 10 (9.9%) and CCA in 5 (5.0%) patients. As compared to CPSS (0.872), AUC of APSS score was higher (0.949) so it can better predict severity of CVA. As compared to CPSS (0.520), the AUC of APSS score was higher (0.631) so it can better predict involvement of a Large Vessel, keeping MRI Angiography as gold standard. **Conclusion-** As compared to CPSS score, APSS can better predict severity of CVA with higher sensitivity and specificity, keeping NIHSS as gold standard. Similarly, as compared to CPSS score, APSS score can better predict involvement of Large Vessel with higher sensitivity and specificity, keeping MRI Angiography as gold standard.

Keywords : Stroke, MRI, MR Angiography, CPSS score, APSS score, acute cerebrovascular accident.

INTRODUCTION

Stroke is associated with high levels of disability and mortality on a global scale. Despite efforts in stroke inhibition, both primary and secondary, the burden remains substantial. Stroke epidemiologic statistics indicate it as the second foremost reason of death

globally, following ischemic heart disease.

In about 30% of cases, these stroke scales used in prehospital settings fail to identify strokes adequately⁽¹⁾. There are specialized prehospital stroke scales

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established to recognize “large vessel occlusion (LVO) strokes” much like regular stroke recognition methods but around 20% of such strokes still go unrecognized by these scales⁽²⁾. These include the National Institutes of Health Stroke Scale (NIHSS), Modified Rankin Scale (mRS), Glasgow Coma Scale (GCS), ABC/2 score, Acute Ischemic Stroke Severity Score (AIS-SSS), THRIVE Score, and ABCD2 Score. Each scale consists of several variables for observing signs & symptoms, each categorized for scoring⁽²⁾.” The NIHSS can predict stroke outcomes. A reliable correlation exists between lower NIHSS scores (less than 4 within the first 48 hours) and good clinical outcomes. Conversely, some scales help determine eligibility criteria; for instance, patients experiencing recurring stroke with a mRS greater than 2 are not considered suitable contenders for “mechanical thrombectomy per American Heart Association/American Stroke Association (AHA/ASA) guidelines⁽³⁾” The Austrian Prehospital Stroke Scale (APSS) was established to predict large vessel occlusion and optimize prehospital transportation triage. The APSS demonstrates accuracy comparable to in-hospital NIHSS & has significantly improved prehospital workflows for patients with potential LVO. Patients scoring 4 or higher on APSS are transported directly to a comprehensive stroke center⁽²⁾. The “Cincinnati Prehospital Stroke Scale (CPSS)” simplifies the NIH Stroke Scale into a three-item measure. Scored from 0–3, the CPSS is widely used and serves as an effective prehospital screening tool for LVO recognition, especially with cut-points of 2 or higher optimizing sensitivity and specificity balance⁽³⁾. The present study was conducted to Compare APSS and CPSS with NIHSS for assessment of severity and Large Vessel Involvement in Acute Cerebrovascular accidents (CVA).

METHODOLOGY

The study was started after getting approval from the Institutional Ethical Committee. All patients and relatives of patients included in this study were explained about the study. Valid written, informed consent was taken in relative’s own language from the relative of the patient. Patients presenting with a clinical diagnosis of acute cerebrovascular accident presenting to OPD and EMD were included in the study and fulfilling the inclusion and exclusion criteria were considered for the study. The demographic data like gender, age, addictions of the patient’s duration of addiction, associated comorbid conditions, and duration were collected and compiled. A detailed history of each patient with general physical examination and neurological examination was done and recorded according to the proforma. Every patient underwent MRI and MR angiography as per standard protocol. Final diagnosis and results of MRI, MR Angiography along with lipid profile were recorded according to proforma and transferred to an excel sheet. Application of stroke severity scales to each patient by examining each parameter of the study was done and noted for assessment of severity and involvement of large vessels. This Comparative Observational study was started after approval of Institutional Research Committee and Institutional Ethics Committee at department of General Medicine, Dr. D.Y. Patil Medical College Hospital and Research Institute, Kolhapur, Maharashtra” Data collection was done from December 2022 to April 2024.

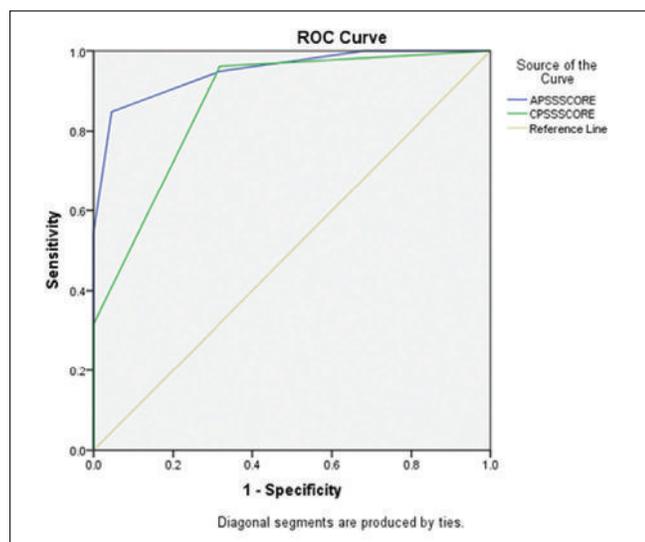
Inclusion criteria All subjects presenting with a clinical diagnosis of acute cerebrovascular accident, age group more than 18 years, all genders, **exclusion criteria**: At the time of presentation:

Patients with old CVA, patients with alcohol intoxication or Psychosis, patients under the effect of sedatives,

patients on medication affecting level of consciousness, subjects with h/o “traumatic brain injury, Patients with space-occupying lesions, Patients with meningitis, Patients with epilepsy or seizure disorder.

RESULTS

In the present study on CVA, out of 101 patients, the majority, 45 (44.6%) belong to the age group 61 to 80 years followed by 41 (40.6%) from “age group 41 to 60 years and 13 (12.9%) belong to age group 21 to 30 years. The mean age of the patients was 59.5±13.3 years, ranging from 24 to 87 years.” There was a slight male preponderance. Out of 101 patients, 58 (57/4%) were males and 43 (42.6%) were females. 1.4:1. Most common vessel involvement was MCA in 26 (25.7%) patients, ICA in 12 (11.9%), PCA in 10 (9.9%) and CCA in 5 (5.0%) patients. Hypoplastic Vertebral Artery was present on left side in Left in 21 (20.8%), Right in 14 (13.9%) and absent in 66 (65.4%) patients. Based on NIHSS score, Severity of CVA was observed in 79 (78.2%) patients.



Graph 1. Comparison of APSS and CPSS with NIHSS (score ≥5) in predicting severity of acute cerebrovascular accident (CVA)

Table no 1 : Area under the curve

Scores	Area	Std. Error	p-value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
APSS Score	0.949	0.021	<0.001	0.908	0.991
CPSS Score	0.872	0.045	<0.001	0.785	0.960

As compared to CPSS (0.872), AUC of APSS score was higher (0.949) so it can better predict severity of CVA, keeping NIHSS as gold standard (score ≥5) (p value <0.001).

Table 2 : Comparison of Sensitivity and Specificity of Scores for Predicting Severity of CVA

Scores	Cut-off Value	Sensitivity	Specificity	PPV	NPV
APSS Score	1.50	96.2%	68.2%	91.6%	83.3%
CPSS Score	0.50	94.9%	68.2%	91.5%	78.8%

So, as compared to CPSS (Sensitivity 94.9%, Specificity 68.2%), APSS (Sensitivity 96.2%, Specificity 68.2%) score can better predict severity of CVA, keeping NIHSS as gold standard (score ≥5).

Graph 2 : Comparison of APSS and CPSS with NIHSS (score ≥10) in predicting severity of acute CVA :

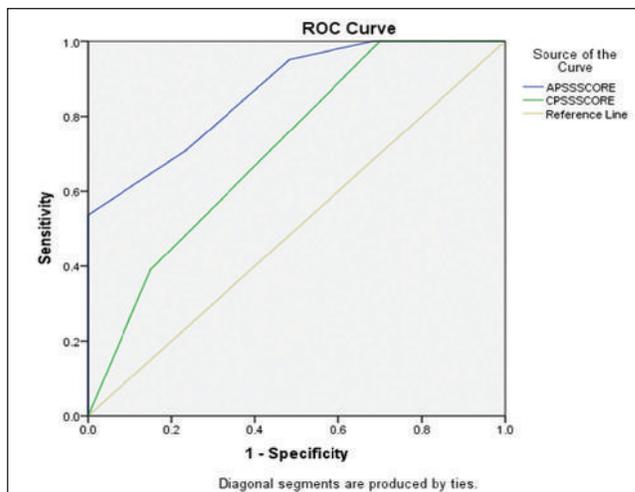


Table no 3 : Area under the curve

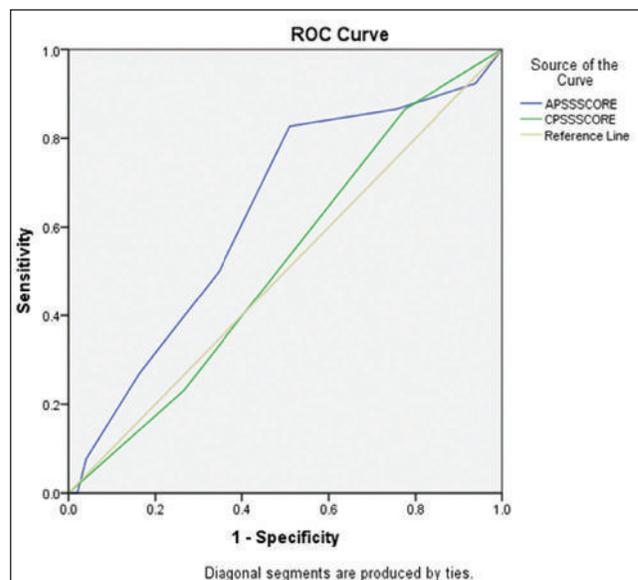
Scores	Area	Std. Error	p-value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
APSS Score	0.864	0.035	<0.000	0.795	0.934
CPSS Score	0.712	0.050	<0.000	0.613	0.810

As compared to CPSS (0.712), the AUC of APSS score was higher (0.864) so it can better predict the severity of CVA, keeping NIHSS as gold standard (score ≥ 10) (p value <0.001).

Table no 4 : Comparison of Sensitivity and Specificity of Score for Predicting Severity of CVA.

Scores	Cut off Value	Sensitivity	Specificity	PPV	NPV
APSS Score	3.50	70.7%	76.7%	91.6%	42.2%
CPSS Score	1.50	39.0%	85.0%	90.3%	27.9%

So, as compared to CPSS (Sensitivity 70.7%, Specificity 76.7%), APSS (Sensitivity 39.0%, Specificity 85.0%) score can better predict severity of CVA, keeping NIHSS as gold standard (score ≥ 10). Large Vessel Involvement was present in 52 (51.5%) patients.

**Graph 3. Comparison of APSS and MR angiography in predicting involvement of Large Vessel in patients of CVA:****Table no 5 : Area under the curve**

Scores	Area	Std. Error	p-value	95% Confidence Interval	
				Lower Bound	Upper Bound
APSS Score	0.631	0.056	0.023	0.521	0.742
CPSS Score	0.520	0.058	0.734	0.406	0.633

As compared to CPSS (0.520), the AUC of APSS score was higher (0.631) so it can better predict involvement of a Large Vessel, keeping MRI Angiography as gold standard (p value 0.023).

Table 6. Comparison of Sensitivity and Specificity of Scores for predicting involvement of Large Vessel:

Scores	Cut off Value	Sensitivity	Specificity	PPV	NPV
APSS Score	0.50	86.5%	22.4%	56.9%	61.9%
CPSS Score	5.50	78.8%	36.7%	54.2%	60.9%

As compared to CPSS (Sensitivity 78.8%, Specificity

36.7%), APSS score can better predict involvement of Large Vessel (Sensitivity 86.5%, Specificity 22.4%), keeping MRI Angiography as gold standard.

Table 7. comparison of MRI findings with MR angiography findings:

MRI Findings	MR Angiography Findings						Total
	CCA	ICA	MCA	ACA	PCA	NAD	
Capsuloganglionic Region	2	2	12	0	0	12	28
Fronto Parietal	0	3	3	0	0	13	19
Parietal and temporal	1	3	3	0	0	1	8
Occipital and temporal	0	1	0	0	4	2	7
Parietal Occipital	1	0	1	0	0	2	4
Basal Ganglia, Temporal Lobe, Thalamus	1	2	5	0	0	7	15
Cerebellum	0	1	1	0	5	6	13
Brain Stem	0	0	1	1	1	4	7
Total	5	12	26	1	10	47	101

APSS score ≥ 4 can predict involvement of ICA (66.7%).

DISCUSSION

The World Health Organization defined stroke as ‘rapidly developed clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin’⁽⁶⁾. “Treatable LVO was defined as occlusion of the CCA, ICA, carotid T, middle cerebral artery (segment M1 or M2), proximal anterior artery (segment A1), basilar artery, or proximal posterior artery (segment P1).” “The presence of an LVO in patients with AS is linked to significantly worse outcomes compared to those without proximal artery occlusion. Due to the suboptimal recanalization rates following the administration of tissue plasminogen activator (tPA) in patients with LVO, endovascular

treatment has been developed as a tool for treating LVO⁽⁶⁾. Previously published scores show various levels of sensitivity, specificity and prehospital practicability.” In the present study on Cerebro-vascular Accident, out of 101 patients, the majority, 45 (44.6%) belong to the age group 61 to 80 years followed by 41 (40.6%) from the “age group 41 to 60 years and 13 (12.9%) belong to age group 21 to 30 years. The mean age of the patients was 59.5 ± 13.3 years, ranging from 24 to 87 years.”

Gender distribution of the patients: “In the present study, there was slight male preponderance. Out of 101 patients 58 (57.4%) were males and 43 (42.6%) were females. 1.4:1.

Characteristics of the Cerebro Vascular Episode (based on MRI findings): Infarct was seen in 97 (96.1%) and Haemorrhage in 4 in (3.9%). Large Vessel Involvement was present in 52 (51.5%) patients. Left side was affected in 27 (26.7%), Right in 23 (22.7%) and Both in 5 (5.0%) patients. Most common vessel involvement was MCA in 26 (25.7%) patients, ICA in 12 (11.9%), PCA in 10 (9.9%) and CCA in 5 (5.0%) patients .

Comparison of APSS and Comparison of CPSS with NIHSS in predicting severity of acute CVA: So, as compared to CPSS (AUC 0.872, Sensitivity 94.9%, Specificity 68.2%), APSS (AUC 0.949, Sensitivity 96.2%, Specificity 68.2%) score can better predict severity of CVA, keeping NIHSS as gold standard.

Large Vessel Involvement (Based on MRI Findings): Large Vessel Involvement was present in 52 (51.5%) patients.

Comparison of APSS, CPSS and NIHSS in predicting

involvement of Large Vessel in patients of CVA: As compared to CPSS (AUC 0.520, Sensitivity 78.8%, Specificity 36.7%), APSS score can better predict the involvement of a Large Vessel (AUC 0.631, Sensitivity 86.5%, Specificity 22.4%), keeping MRI Angiography as the gold standard (p-value 0.023)

Association between findings on CNS Examination and large vessel involvement: Involvement of large vessels was maximum in Facial Palsy (61.8%) followed by Lower Limb Hemiparesis (60.4%), Speech Aphasia (60%) and Arms Hemiparesis (59.9%). Association between Facial Palsy and large vessels involvement was significantly associated.

Association between scores of APSS (≥ 4), CPSS (≥ 2) and NIHSS (≥ 5) with Vessel involvement: APSS score ≥ 4 was associated with involvement of ICA (66.7%). CPSS score ≥ 2 was associated with involvement of ACA (100%) involvement. NIHSS ≥ 5 was associated with involvement of AC.

APSS showed accuracy comparable to in-hospital NIHSS and significantly optimized prehospital workflows for patients with potential LVO. While simpler stroke scales may provide a faster initial assessment, they typically require the use of additional scales to determine stroke severity or predict LVO. However, using multiple scales can be error-prone and complicate communication with receiving hospitals. Despite the growing focus on developing better prehospital stroke recognition tools, accurately distinguishing true strokes from mimics often requires substantial experience and training.”

CONCLUSION

As compared to CPSS score, APSS can better predict severity of CVA with higher sensitivity and specificity, keeping NIHSS as gold standard. Similarly, as compared to CPSS score, APSS score can better predict involvement of Large Vessel with higher sensitivity and specificity, keeping MRI Angiography as gold standard. APSS can better predicts involvement of ICA. “APSS demonstrated accuracy comparable to NIHSS in significantly identifying patients with severe stroke and large vessel involvement and helps quicker initial assessment. The history and neurological examination are vital for identifying and treating patients with suspected cerebrovascular disease, particularly soon after symptom onset and before neuroimaging is available. This study has various limitations. While clinical scales can suggest the severity and LVO, their reliability is poor when based solely on history and physical examination. Neuroimaging is essential to rule out hemorrhage, and to identify the ischemic stroke subtype, exact location of the Lesion, and target of therapeutic site. This information is essential to make therapeutic decisions for the patient, which is not possible with uncertain diagnosis. Other limitations of the study include small sample size which limits the generalizability of the results, indicating the need for a multicentric study with a larger sample size. Further research is necessary to determine whether these assessments significantly enhance detection and impact patient routing and management in a prehospital setting.”

REFERENCES

1. Kelly-Hayes M, Beiser A, Kase CS, Scaramucci A, D'Agostino RB, Wolf PAJJoS, et al. The influence of gender and age on disability following ischemic stroke: the Framingham study. 2003;12(3):119-26.
2. Krishnamurthi RV, Moran AE, Feigin VL, Barker-Collo S, Norrving B, Mensah GA, et al. Stroke prevalence, mortality and disability-adjusted life years in adults aged 20-64 years in 1990-2013: data from the global burden of disease 2013 study. 2015;45(3):190-202.
3. Danaei G, Finucane MM, Lin JK, Singh GM, Paciorek CJ, Cowan MJ, et al. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5· 4 million participants. 2011;377(9765):568-77.
4. Crowe RP, Myers JB, Fernandez AR, Bourn S, McMullan JT. The cincinnati prehospital stroke scale compared to stroke severity tools for large vessel occlusion stroke prediction. *Prehospital Emergency Care*. 2021 Jan 2;25(1):67-75.
5. Krebs S, Sykora M, Krammel M, Girska M, Auer A, Roth D, et al. Prehospital triage optimization of patients with large vessel occlusion by APSS. *Acta Neurologica Scandinavica*. 2022 May 20.
6. Lakomkin N, Dhamoon M, Carroll K, Singh IP, Tuhim S, Lee J, Fifi JT, Mocco J. Prevalence of large vessel occlusion in patients presenting with acute ischemic stroke: a 10-year systematic review of the literature. *Journal of neuro-interventional surgery*. 2019 Mar 1;11(3):241-5.
7. Cummock J S, Wong K K, Volpi J J, et al. Reliability of the National Institutes of Health (NIH) Stroke Scale Between Emergency Room and Neurology Physicians for Initial Stroke Severity Scoring. *Cureus* 15(4): e37595.

Stromal Tumor Of Uncertain Malignant Potential Of Prostate

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ABSTRACT

Mesenchymal tumors of the prostate are rare and have a wide variety of diseases ranging from benign to malignant. Patients usually present with obstructive symptoms and prostatomegaly on ultrasound. It is an often a challenge for pathologists to diagnose on histopathology. Open prostatectomy with radiotherapy is used in the management.

This case report illustrates the case of middle-aged man who presented with urinary complaints, with ultrasound suggestive of prostatomegaly which on immunohistochemistry was diagnosed with prostatic stromal sarcoma.

Keywords : Prostatomegaly, sarcoma, mesenchymal tumors, STUMP, Prostatic stromal sarcomas

INTRODUCTION

There is a wide spectrum of benign and malignant mesenchymal neoplasms of the prostate, which is less than 1% of all prostatic tumors.¹ These include distinctive tumors that arise from the specialized prostatic stroma and site-agnostic neoplasms such as smooth muscle tumors, fibrous or myofibroblastic neoplasms, neurogenic tumors, vascular tumors, and a plethora of sarcoma.²

The current WHO classification includes two diagnostic categories of Prostate stromal proliferation: stromal tumor of uncertain malignant potential (STUMP) and stromal sarcoma. STUMP occurs between the ages of 27 and 83 years with a peak incidence between 6th and 7th decades. They can be in the white, tan, solid or solid-cystic pattern and up to 15 cm in size.⁷

STUMPs have been classified into four histologic patterns.⁵ firstly, hypercellular stroma showing

Classification of Mesenchymal Tumors of Prostate and Seminal Vesicles

Stromal tumors

Stromal tumor of uncertain malignant potential (STUMP)

Stromal sarcoma

Benign or potentially malignant nonstromal tumors.

Leiomyoma

Schwannoma

Solitary fibrous tumor (SFT)

Inflammatory myofibroblastic tumor (IMT)

Perivascular epithelioid cell tumor (PEComa)

Paraganglioma

Gastrointestinal stromal tumor (GIST)

Malignant nonstromal tumors

Lciomyosarcoma

Rhabdomyosarcoma

Synovial sarcoma

Angiosarcoma

Post-radiation therapy sarcoma

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degenerative atypia with benign glands, secondly, bland, fusiform stromal cells with eosinophilic cytoplasm with benign glands, third, benign phyllodes tumor-like hypercellular stroma with cytologically atypical/nonatypical benign glands, fourth, bland stromal cells in myxoid stroma without prostate glands

Recently, Sadimin and Epstein described a novel round cell pattern.⁶

IHC of STUMP's shows CD34 (+), vimentin (+), progesterone (+), S100 (-) and C-kit (-) staining patterns.

Absence of atypical mitosis and presence of degenerative appearance of atypical nuclei with benign prostate glands help distinguish it from malignant tumors. ¹ PSSs are divided into two subgroups as low- and high-grade. High-grade tumors involve moderate-evident cytologic atypia, hypercellularity, increased mitotic activity and necrosis. Low-grade PSSs are local invasive and high-grade, most common metastasize to the lung and bone.³

PRESENTATION OF CASE

60year old male presented with complaints of increase frequency of micturation, nocturia (4-5 times) since 1year but symptoms got aggravated since 1month. There were no comorbidities(ASA grade II). He has operative history of cystoscopy and urethral dialation on 10 march 2022. He was a chronic alcoholic and tobacco user.

His *serum PSA* 2.0ng/dl. *USG* shows prostate enlarged in size with median lobe indenting the base of bladder (vol. 135cc), foci of calcification with pre-

void (212cc) and significant post void residue(137cc). *Retrograde urethrogram* shows extrinsic mass effect at bladder base due to grossly enlarged prostate. *MRI scan* shows a well-defined mass lesion is seen replacing the entire prostate gland. It is measuring about 5.3(craniocaudal) X 5.0 (AP) X 4.0 (transverse). It appears heterogeneously hypertense on T2 and hypo intense on T1 weighted images. Areas of restricted diffusion are seen within the lesion on DWI. On post contrast images it shows heterogeneous enhancement. Antero-superiorly the lesion infiltrating into inferior wall of urinary bladder. Inferiorly it reaches up to the root of the penis and infiltrating the prostatic urethra. Posteriorly the fat planes with anterior wall of rectum are maintained. Laterally it is abutting the levatorani muscles bilaterally with no obvious infiltration. Patient had undergone open prostatectomy and evidence of prostatomegaly with enlargement of median anof median and lateral lobe.

HPR shows sheets of spindled cells exhibiting pleomorphic, hyperchromatic nuclei to vascular nuclei and few with prominent nucleoli and moderate cytoplasm. Few multinucleate gaint cells are noted. Proliferating blood vessels with necrotic areas. S/O **MALIGNANT MESENCHYMAL TUMOR**. IHC reveals *Vimentin, Desmin- positive, CD-34positive* in blood vessel and negative in tumor cells, *CK,PR, PSA,SMA- negative*. It suggestive of **PROSTATIC STROMAL SARCOMA**, low grade with necrosis.

CT Scan of chest shows a sclerotic focus in body of D8 vertebra and body of D12 vertebra. Patient was treated with external beam radiotherapy using SRT technique to a dose 36.25Gy in 05 fraction.

DISCUSSION

Although the fact that mesenchymal tumors of the prostate constitute less than 1% of all tumors, their differential diagnosis is difficult and includes a broad spectrum of conditions. ⁴So, it is important that clinical and radiological findings are reported to pathologists and

adequate biopsy specimens are obtained. In our patient, due to the size of prostate causing pressure symptoms, an open prostatectomy was performed and diagnosed as mesenchymal tumor on HPR and as prostatic stromal sarcoma (low grade) on Immunohistochemistry.

REFERENCES

1. Mesenchymal neoplasm of prostate; radiographic and pathologic correlation RSNA journal vol 42, no.2
2. Cheville J, Algaba F, Epstein JI, Lopez-Beltran A. In: Moch H. WHO classification of tumours of the urinary system and male genital organs. 4th ed. Lyon: The International Agency for Research on Cancer press, 2016, pp 175-177
3. Öznur M. Mesenchymal Tumors of the Prostate. J UrolSurg 2018;5:59-62.
4. Gaudin PB, Rosai J, Epstein JI. Sarcomas and related proliferative lesions of specialized prostatic stroma: a clinicopathologic study of 22 cases. Am J SurgPathol 1998;22:148-162
5. 9. Tavora F, Kryvenko ON, Epstein JI. Mesenchymal tumours of the bladder and prostate: an update. Pathology 2013;45:104-115.
6. Sadimin ET, Epstein JI. Round cell pattern of prostatic stromal tumor of uncertain malignant potential: a subtle newly recognized variant. Hum Pathol 2016;52:68-73.
7. Herawi M, Epstein JI. Specialized stromal tumors of the prostate: a clinicopathologic study of 50 cases. Am J SurgPathol 2006;30:694-704.

Echocardiography Evaluation Of pulmonary Artery Hypertension In Different stages Of Ckd

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ABSTRACT

Introduction : Chronic kidney disease (CKD) is a prevalent health concern on a global scale. Pulmonary Arterial Hypertension (PAH) may be highly prevalent in individuals with CKD. PAH in CKD patients can be asymptomatic, leading to underdiagnosis until signs of right ventricular (RV) dysfunction. PAH is defined as having a mean “pulmonary artery pressure (PAP)” equal to or exceeding 25 mmHg at rest, or 30 mmHg during activity. **Methodology :** Observational cross-sectional study was conducted at tertiary care centre. Total of 95 patients fulfilling inclusion and exclusion criteria were involved in the study. Written informed consent was taken. 2D ECHO was performed on all the patients of CKD. **Results :** The correlation analysis between the stages of CKD and the presence of PAH yielded a correlation coefficient of -0.059 with a p-value of 0.5647. This indicates a very weak and statistically non-significant negative correlation between CKD stages and PAH. The association between diabetes and PAH showed that 45.45% of patients with PAH had diabetes, compared to 30.95% of those without PAH. **Conclusion :** The weak correlation between CKD stages and PAH suggests that PAH screening should not be limited to late-stage CKD patients alone. Age, sex, and hypertension did not show significant associations with PAH, highlighting the multifactorial nature of PAH development in CKD.

Keyword - Chronic kidney disease (CKD), pulmonary Arterial Hypertension (PAH), ventricular dysfunction.

INTRODUCTION

Chronic kidney disease (CKD) is a prevalent health concern on a global scale, with a significant portion of the adult population estimated to be affected.¹ In 2017, the worldwide prevalence of CKD Stages 1–2 was approximately 5%, Stage 3 accounted for 3.9%, Stage 4 for 0.16%, Stage 5 for 0.07%, and dialysis and kidney transplantation made up smaller percentages of the population.² Among CKD patients, cardiovascular disease stands out as the primary cause of morbidity and mortality, encompassing conditions such as heart

failure (HF), coronary heart disease (CHD), and cardiac arrhythmias.³

It is now acknowledged that “pulmonary arterial hypertension (PAH)” may be highly prevalent in individuals with CKD. PAH in CKD patients can be asymptomatic, leading to underdiagnosis until signs of right ventricular (RV) dysfunction, such as increased fatigue, dyspnea, and syncope, become apparent.⁴ Recent research indicates an elevated prevalence

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of PAH in CKD patients when compared to their healthier counterparts.⁵ PAH is defined as having a mean “pulmonary artery pressure (PAP)” equal to or exceeding 25 mmHg at rest, or 30 mmHg during activity. In CKD, the underlying mechanisms of PAH remain unclear.⁶ It arises from a combination of various alterations in cardiovascular physiology. Myocardial dysfunction is the primary contributor to PAH in CKD, resulting in increased “left ventricular (LV) filling pressure” and subsequent pulmonary venous hypertension.⁷

The prevalence of PAH among individuals with end-stage renal disease varies between 27% and 58%.⁸ In contrast, those with earlier stages of CKD exhibit a lower prevalence, ranging from 8% to 39%.⁸

Even though right heart catheterization (RHC) remains the gold standard for PAH diagnosis, its invasive nature restricts its applicability for broad-scale screening. Echocardiography, as a noninvasive method, is extensively employed for PAH screening, disease progression monitoring, and assessing treatment responses. Echocardiography is used to screen individuals considered for kidney transplantation, evaluating potential cardiovascular complications, including PAH, that could impact outcomes during the peri- and post-transplantation phases. A nonspecific test may lead to unwarranted invasive procedures or even disqualification from transplantation. Despite echocardiography’s widespread use in screening for CKD-associated PAH, its diagnostic performance in the CKD population has not yet been validated.⁹

¹¹ Transthoracic echocardiography (TTE) offers both direct and indirect indicators of increased PAP and can provide valuable insights into the etiology and prognosis of PAH. Consequently, it is now

recognized as an excellent noninvasive screening tool for individuals exhibiting symptoms or risk factors associated with PAH. Doppler echocardiography allows for a reliable estimation of PAP, as the maximum “tricuspid regurgitation velocity (TRV)” jet speed and RV outflow tract acceleration time, measured by RHC, demonstrate linear positive and negative correlations with pulmonary artery systolic pressure (PASP) and mean PAP, respectively.¹² Therefore, the present study was undertaken to assess PAH in different stages of CKD patients with the help of non-invasive technique of 2D echo.

METHODOLOGY

The present prospective Observational cross-sectional study was conducted at OPD & IPD of the Tertiary care centre Kolhapur for 2 years after institutional ethical committee approval. A total of 95 patients satisfying below inclusion and exclusion criteria were involved in the study.

Inclusion criteria : Age above 18 years, CKD patients with creatinine levels of more than 2.0 mg%, Symptomatic or asymptomatic CKD, eGFR<60 or <45 of CKD patients, CKD of any etiology, Drug-induced hypertension, **Exclusion Criteria:** Known CV diseases except hypertension, Known/diagnosed c/o COPD, Known/diagnosed c/o congenital heart diseases.

Known/diagnosed c/o Connective tissue disorders like scleroderma and SLE, Pregnant or lactating mothers, known case of Peripheral vascular disease- Berger’s disease, Raynaud’s disease, or Drug-induced hypertension Acute on chronic kidney failure, all patients who don’t give consent for the study.

Written informed consent was taken from all the subjects before the initiation of the study. For evidence of early or asymptomatic cardiovascular changes, 2D ECHO was performed on all the patients of CKD included in the study. 2DECHO was done as 2DECHO is a reasonably good non-expensive and non-invasive method. The mean PAP formula is used to measure PAH.

RESULTS

Age

The mean age of the study subjects was 55.02 ± 15.73 years. Among the 95 participants, the largest group was aged 51-60 years, comprising 29.47% of the total. This was followed by the 41-50 year age group, which constituted 16.84%, and the 61-70 year age group, accounting for 17.89%. The age groups of 31-40 years and 71-80 years both represented 11.58% of the participants each. The ≤ 30 year age group included 7.37% of the participants, while those aged >80 years made up the smallest proportion at 5.26% (Figure 1).

Sex

Out of the 95 participants, 60 were male, representing 63.16% of the total sample. The remaining 35 participants were female, accounting for 36.84%.

Stages of CKD

Among the 95 participants, 2 (2.11%) were classified in Stage 3 CKD, 48 (50.53%) were in Stage 4 CKD, and 45 (47.37%) were in Stage 5 CKD. This distribution reflects a predominance of advanced stages of CKD within the study population, with the majority of participants being in Stages 4 and 5 (Table 1)

Table 1. Distribution of stages of CKD

Stages of CKD	Frequency (n)	Percentage (%)
3	2	2.11
4	48	50.53
5	45	47.37
Total	95	100

PAH

It shows that the majority, 84 individuals (88.42%), did not have PAH. Mild hypertension was observed in 1 participant (1.05%), moderate hypertension in 3 participants (3.16%), and severe hypertension in 7 participants (7.37%). This distribution indicates that while the majority of participants did not exhibit significant PAH, a notable proportion had varying degrees of the PAH (Figure 1).

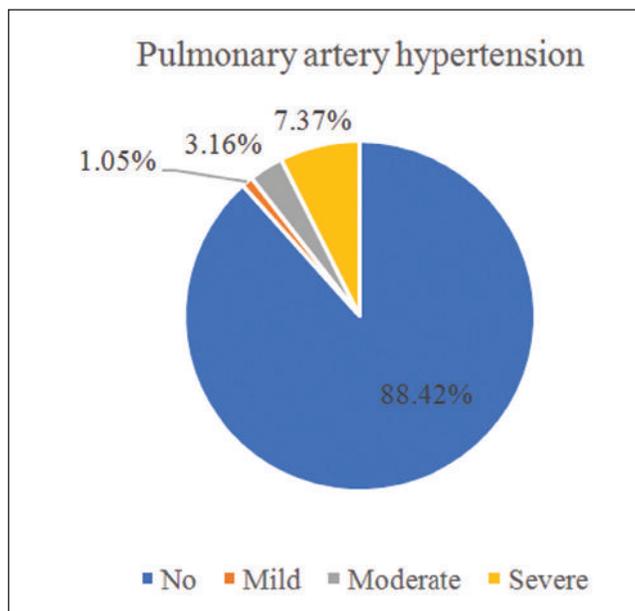


Figure 1. Distribution of PAH

Distribution of subjects according to stages of CKD and PAH

In Stage 3 CKD, no patients were reported to have PAH, with only 2.38% of individuals in this stage being free of PAH. In Stage 4 CKD, 63.64% of those with PAH were classified in this stage, contrasting with 48.81% of patients without PAH. For Stage 5 CKD, 36.36% of patients with PAH were found, whereas 48.81% of patients without PAH also belonged to this stage (Figure 2).

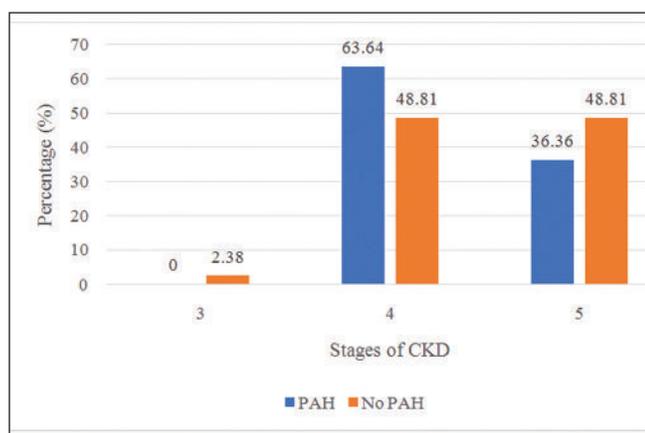


Figure 2. Distribution of subjects according to stages of CKD and PAH

Correlation between stages of CKD and PAH

The correlation analysis between the stages of CKD and the presence of PAH yielded a correlation coefficient of -0.059 with a p-value of 0.5647. This indicates a very weak and statistically non-significant negative correlation between CKD stages and PAH (Table 2).

Table 2. Correlation between stages of CKD and PAH

Correlation variables	Correlation coefficient (r)	P-value
Stages of CKD and PAH	-0.059	0.5647

Comparison of age according to PAH

The mean age of patients with PAH was 46.09 years with a standard deviation of 15.83, while the mean age of those without PAH was 56.19 years with a standard deviation of 15.48. The p-value of 0.6929 indicates that the difference in age between the two groups is not statistically significant (Table 3).

Table 3. Comparison of age according to PAH

PAH	Age (years)		P-value
	Mean	SD	
Yes	46.09	15.83	0.6929
No	56.19	15.48	

Distribution of sex according to PAH

The distribution of sex among patients with PAH showed that 36.36% of females and 63.64% of males had PAH. In contrast, among those without PAH, 36.90% were female and 63.09% were male. The total number of females and males in the study were 35 and 60, respectively. The p-value of 0.9723 indicates that there is no significant difference in the prevalence of PAH between males and females in this sample (Figure 3).

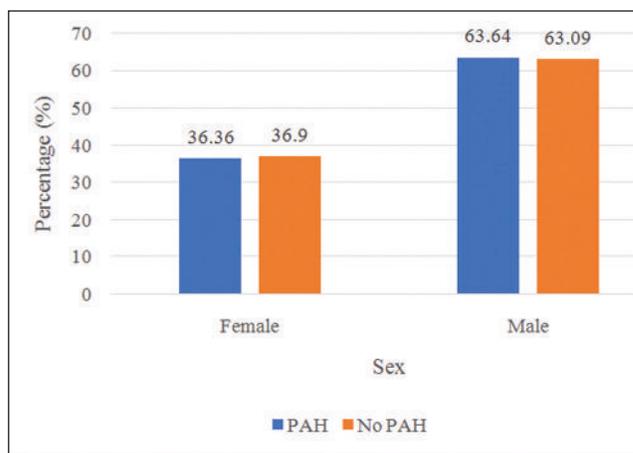


Figure 3. Distribution of sex according to PAH

Distribution of diabetes according to PAH

The association between diabetes and PAH showed that 45.45% of patients with PAH had diabetes, compared to 30.95% of those without PAH. Among the total number of patients with diabetes, 32.63% had PAH. Conversely, 54.55% of patients with PAH did not have diabetes, while 69.04% of those without PAH were also without diabetes. The p-value of 0.4015 indicates that the presence of diabetes does not significantly affect the likelihood of having PAH in this sample (Figure 4).

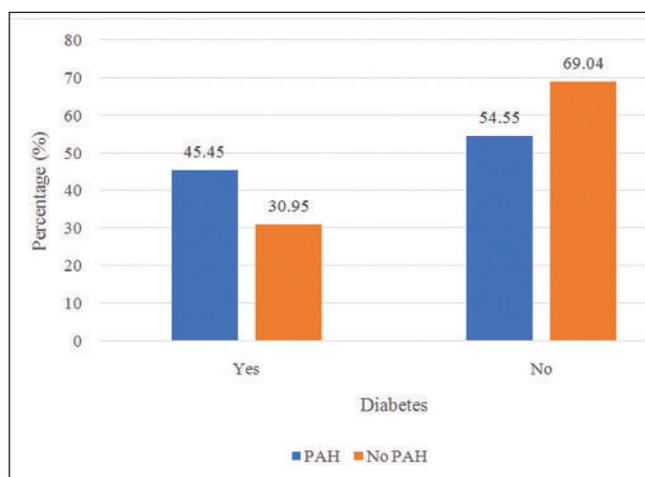


Figure 4. Distribution of diabetes according to PAH

Distribution of hypertension according to PAH

The analysis of the association between hypertension and PAH revealed that 45.45% of subjects with PAH had hypertension, compared to 50% of subjects without PAH. Among the total number of patients with hypertension, 49.47% had PAH, while 50% of those without PAH also had hypertension. The p-value of 0.7777 indicates that there is no substantial relationship between hypertension and PAH in this sample (Figure 5).

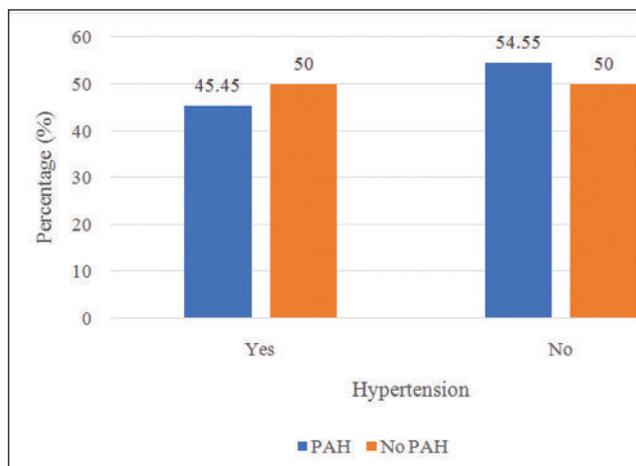


Figure 5. Distribution of hypertension according to PAH

DISCUSSION

PH is a condition marked by increased pressure in the pulmonary arteries, which progressively worsens and complicates various heart, lung, or systemic diseases, leading to increased morbidity and mortality regardless of its underlying cause.²² Recent findings have identified PH as a significant independent predictor of both morbidity and mortality in patients undergoing HD.¹³⁻²³ In an observational study involving 58 HD patients with an average follow-up period of 30 months, those with PH exhibited a mortality rate of 30.4%, compared to 8.5% in those without PH ($p < 0.03$).²⁴ Similarly, Yigla et al. reported in their cohort of CKD patients that those with PH had markedly lower survival rates compared to those without PH, with one-year, three-year, and five-year survival rates of 78.6% versus 96.5%, 42.9% versus 78.8%, and 25.2% versus 66.4%, respectively ($p = 0.0001$).²² There is a lack of extensive research on the incidence of PH in CKD patients within the Indian context. The present study aimed to evaluate PAH across diverse stages of CKD using echocardiography. The findings reveal several critical insights into the relationship between CKD progression and the prevalence of PAH,

providing valuable data for clinical management and further research in nephrology and cardiology.

The study's age distribution revealed that the largest group of participants was aged between 51-60 years (29.47%), followed by those aged 61-70 years (17.89%), and 41-50 years (16.84%). This pattern is consistent with the general demographic of CKD patients, who are typically older adults. The incidence of CKD increases with age due to the cumulative effects of hypertension, diabetes, and other comorbidities over time. The mean age of 55.02 ± 15.73 years in this study underscores the importance of focusing on middle-aged and elderly populations for CKD and its complications, such as PAH. The sex distribution in this study showed a male predominance, with 63.16% of participants being male and 36.84% female. This aligns with other studies suggesting a greater occurrence of CKD in males than females.²²⁻²³ The reasons behind this gender disparity might include differences in health behaviors, genetic predispositions, and the prevalence of risk features such as "hypertension and diabetes", which are more common in men.

In this study, the majority of the study subjects were in advanced stages of CKD, with 50.53% in Stage 4 and 47.37% in Stage 5. Only 2.11% of participants were in Stage 3 CKD. This distribution reflects the high morbidity and referral bias, as subjects with more severe diseases are more likely to be referred for echocardiography evaluations. The predominance of late-stage CKD in this sample highlights the crucial necessity for primary recognition and management to slow CKD progression and manage complications effectively.

In this study, a substantial majority of participants

(88.42%) did not exhibit PAH, with only a small proportion showing mild (1.05%), moderate (3.16%), or severe PAH (7.37%). The overall prevalence of PAH was 11.57%, indicating that while most CKD patients did not present with PAH, a notable minority did. The presence of PAH in CKD patients, even at relatively low prevalence, remains clinically significant. PAH can exacerbate the overall disease burden, negatively impact patients' quality of life, and influence their prognosis, making it an important factor in managing CKD.

Comparatively, studies on the prevalence of PAH in CKD patients show considerable variability. Mehta KS et al. stated a substantially greater prevalence of 60.5%,⁸⁷ whereas Tarras F et al. found a much lower rate of 26.74%.²⁵ Moniruzzaman M et al. detected a high incidence of 68.6%.²⁶ Additionally, a study by Patel et al. in India found occurrence of 41% among patients undergoing various forms of dialysis, with the highest prevalence observed in those on HD (33%).²⁷

These discrepancies highlight the variability in PAH prevalence across different studies and settings, possibly due to differences in study populations, diagnostic criteria, or regional factors. The results underscore the necessity for continuous monitoring and evaluation of PAH in CKD patients, as its presence can significantly impact patient management and outcomes.

In this study, the association between CKD stages and PAH was explored. Among patients with stage 3 CKD, none had PAH. In Stage 4 CKD, a higher proportion of patients with PAH (63.64%) was observed compared to those without PAH (48.81%). Conversely, in Stage 5 CKD, the incidence of PAH among subjects was 36.36%, similar to the 48.81% of patients without PAH in this stage. The correlation analysis showed a very

weak, statistically non-significant negative correlation between CKD stages and PAH (correlation coefficient of -0.059, p-value of 0.5647). This recommends that the progression of CKD does not straightforwardly correlate with the development of PAH. The deficiency of a substantial correlation might be because of the multifactorial nature of PAH, which involves various pathophysiological mechanisms not solely dependent on CKD stage.

This contrasts with findings from other studies. For instance, Mehta KS et al. reported a statistically substantial association between advanced CKD stages and increased prevalence of PH ($p < 0.001$), indicating that as CKD progresses, the likelihood of PAH increases.⁸⁷ This disparity could be attributed to variances in study design or patient populaces. Our study's cohort, consisting predominantly of patients in advanced CKD stages (III, IV, and V), may have influenced the findings. Additionally, Yang QM et al. observed a prevalence of PAH in earlier CKD stages (23.76% in Stage II and 48.15% in patients with GFR < 60 mL/min/1.73 m²), highlighting that PAH can be present before significant declines in GFR.⁹² Li Z et al. further supported the notion that severe PAH and cardiovascular morbidity are more common as CKD advances, particularly in Stage V and end-stage renal disease.²⁹

Overall, while the study's findings suggest that PAH may not be directly proportional to CKD stage progression, other research indicates that advanced CKD stages are often associated with higher PAH prevalence. This underscores the importance of early screening and management of PAH in CKD patients, even in earlier stages of the disease.

The mean age of patients with PAH was 46.09 years, whereas those without PAH had a mean age of 56.19 years. The difference was not statistically significant (p-value of 0.6929). This indicates that age alone may not be a determining factor for the development of PAH in CKD patients. However, it highlights the necessity of monitoring younger CKD patients for early signs of PAH. These findings are similar with the studies conducted by Mehta KS et al.²³ Tarrass F et al.²⁵ Patel P et al.,²⁷ and Mazdeh MM et al.³⁰

In our study, the sex distribution among patients with PAH revealed no significant difference (p-value of 0.9723), with both males and females being equally affected. This observation aligns with the findings of Tarrass F et al., who reported similar sex distribution among PAH patients.²⁵ This contrasts with the broader CKD population, where a higher prevalence of males is often observed.²³⁻²⁶ This discrepancy suggests that the risk of PAH in CKD patients may not be influenced by sex, indicating that other factors beyond gender might play a more significant role in the development of PAH within this group.

In this study, no substantial correlation was observed between hypertension and diabetes with PAH, with p-values of 0.4015 and 0.7777, respectively. This lack of significant correlation stands in contrast to other research findings. For example, Mehta KS et al. observed a statistically substantial association between both diabetes and hypertension with PH, with a p-value of less than 0.001.²³ Similarly, Agarwal R reported a significant statistical association with diabetes ($p = 0.04$), although systemic hypertension was not significantly associated ($p = 0.2$).⁵ Fabbian F et al. found strong statistical associations between both diabetes ($p = 0.021$) and hypertension ($p = 0.0074$) with

PH.31 These discrepancies suggest that while diabetes and hypertension are often linked to PAH in other studies, this association may not be as pronounced in the population studied here. The absence of a significant association in our study might be due to the specific characteristics of our cohort or variations in disease progression and management.

The study underscores the need for comprehensive cardiovascular evaluation in CKD patients, particularly those in advanced stages. Despite the weak correlation between CKD stages and PAH, the presence of PAH in a subset of patients calls for vigilant screening and management strategies. Early identification and treatment of PAH can potentially improve the quality of life and outcomes for CKD patients.

REFERENCE

1. Webster AC, Nagler EV, Morton RL, Masson P. Chronic kidney disease. *The Lancet*. 2017 Mar 25;389(10075):1238-52.
2. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, Adebayo OM, Afarideh M, Agarwal SK, Agudelo-Botero M, Ahmadian E. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *The lancet*. 2020 Feb 29;395(10225):709-33.
3. Virzi GM, Goh CY, Cruz DN, Vescovo G, Ronco C. Cardiorenal Syndrome Type 4: A Review. *CardioRenal Medicine*. 2013 Apr 1;3(1).
4. Hoepfer MM, Bogaard HJ, Condliffe R, Frantz R, Khanna D, Kurzyna M, Langleben D, Manes A, Satoh T, Torres F, Wilkins MR. Definitions and diagnosis of pulmonary hypertension. *Turk Kardiyoloji Dernegiarsivi: Turk KardiyolojiDernegininyayinorganidir*. 2014 Oct 1;42:55-66.
5. Agarwal R. Prevalence, determinants and prognosis of pulmonary hypertension among hemodialysis patients. *Nephrology Dialysis Transplantation*. 2012 Oct 1;27(10):3908-14.
6. Bolignano D, Rastelli S, Agarwal R, Fliser D, Massy Z, Ortiz A, Wiecek A, Martinez-Castelao A, Covic A, Goldsmith D, Suleymanlar G. Pulmonary hypertension in CKD. *American journal of kidney diseases*. 2013 Apr 1;61(4):612-22.
7. Naik M, Naik R, Bangi V, Khan SK, Jaiswal S, Patel S. A Cross Sectional Study of Pulmonary Hypertension in Chronic Kidney Disease Patients by Echocardiography at MGM Medical College, Aurangabad, Maharashtra. *Ann Med Health Sci Res*. 2022;12:S1:121-124.
8. Bossone E, Citro R, Blasi F, Allegra L. Echocardiography in pulmonary arterial hypertension: An essential tool. *Chest*. 2007 Feb 1;131(2):339-41.

CONCLUSION

This study offers valuable understandings into the prevalence and characteristics of PAH in CKD patients. Despite a high prevalence of advanced CKD stages among participants, PAH was relatively uncommon but still present in a notable minority. The weak correlation between CKD stages and PAH suggests that PAH screening should not be limited to late-stage CKD patients alone. Age, sex, and hypertension did not show significant associations with PAH, highlighting the multifactorial nature of PAH development in CKD. Studies with larger sample sizes and longitudinal designs are needed to further elucidate the relationship between CKD and PAH and to develop targeted interventions for this high-risk population.

9. Galie N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, Simonneau G, Peacock A, VonkNoordegraaf A, Beghetti M, Ghofrani A. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the joint task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *European heart journal*. 2016 Jan 1;37(1):67-119.
10. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, Williams PG, Souza R. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *European respiratory journal*. 2019 Jan 1;53(1).
11. Lentine KL, Villines TC, Axelrod D, Kaviratne S, Weir MR, Costa SP. Evaluation and management of pulmonary hypertension in kidney transplant candidates and recipients: concepts and controversies. *Transplantation*. 2017 Jan 1;101(1):166-81.
12. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography: endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *Journal of the American society of echocardiography*. 2010 Jul 1;23(7):685-713.
13. Sise ME, Courtwright AM, Channick RN. Pulmonary hypertension in patients with chronic and end-stage kidney disease. *Kidney international*. 2013 Oct 1;84(4):682-92.
14. Dupuis J, Hoepfer MM. Endothelin receptor antagonists in pulmonary arterial hypertension. *European Respiratory Journal*. 2008 Feb 1;31(2):407-15.
15. Liu C, Chen J, Gao Y, Deng B, Liu K. Endothelin receptor antagonists for pulmonary arterial hypertension. *Cochrane Database of Systematic Reviews*. 2021(3).
16. Lau EM, Giannoulatou E, Celermajer DS, Humbert M. Epidemiology and treatment of pulmonary arterial hypertension. *Nature Reviews Cardiology*. 2017 Oct;14(10):603-14.
17. Barnes H, Yeoh HL, Fothergill T, Burns A, Humbert M, Williams T. Prostacyclin for pulmonary arterial hypertension. *Cochrane Database of Systematic Reviews*. 2019(5).
18. Wardle AJ, Seager MJ, Wardle R, Tulloh RM, Gibbs JS. Guanylate cyclase stimulators for pulmonary hypertension. *Cochrane Database of Systematic Reviews*. 2016(8).
19. Barnes H, Brown Z, Burns A, Williams T. Phosphodiesterase 5 inhibitors for pulmonary hypertension. *Cochrane Database of Systematic Reviews*. 2019(1).
20. Edmonston DL, Rajagopal S, Wolf M. Echocardiography to screen for pulmonary hypertension in CKD. *Kidney International Reports*. 2020 Dec 1;5(12):2275-83.
21. Martin KB, Klinger JR, Rounds SIS. Pulmonary arterial hypertension: new insights and new hope. *Respirology*. 2006;11:6-17.
22. Yigla M, Fruchter O, Aharonson D, Yanay N, Reisner SA, Lewin M, et al. Pulmonary hypertension is an independent predictor of mortality in hemodialysis patients. *Kidney Int*. 2009;75:969-75.
23. Mehta KS, Shirkande AK, Bhurke SP, Pajai AE, Swami RS, Jadhav SN. Pulmonary hypertension in various stages of chronic kidney disease in Indian patients. *Indian Journal of Nephrology*. 2019 Mar 1;29(2):95-101.
24. Stallworthy EJ, Pilmore HL, Webster MW, Sidhu KK, Curry EM, Brown P, et al. Do echocardiographic parameters predict mortality in patients with end-stage renal disease? *Transplantation*. 2013;95:1225-32.

25. Tarrass F, Benjelloun M, Hachim K, Benghanem MG, Ramdani B. Pulmonary hypertension in patients with end-stage renal disease. *Indian J Nephrol.* 2005;15:223–6.
26. Moniruzzaman M, Islam MN, Alam MB, Alam M, Khan MMH, Ali Z, et al. Pulmonary Hypertension in Hemodialysis Patients. *Cardiovasc J.* 2012;4:148–52.
27. Patel P, Abraham G, Pratap P, Ramalakshmi R, Mathew M, Jeevan JM, et al. Clinical and Biochemical parameters in Chronic Kidney Disease with Pulmonary Hypertension. *Indian J of Nephrol.* 2007;17:4–6.
28. Yang QM, Bao XR. Pulmonary hypertension in patients with stage 1-3 chronic kidney disease. *Genet Mol Res.* 2014;13:5695–703.
29. Li Z, Liang X, Liu S, Ye Z, Chen Y, Wang W, et al. Pulmonary Hypertension: Epidemiology in Different CKD Stages and Its Association with Cardiovascular Morbidity. *PLoS One.* 2014;9:e114392.
30. Mazdeh MM, Mousavi SA, Yahyazadeh H, Azadi M, Yoosefnejad H, Ataiipoor Y. Pulmonary hypertension in hemodialysis patients. *Saudi J Kidney Dis Transpl.* 2008;19:189–93.
31. Fabbian F, Cantelli S, Molino C, Pala M, Longhini C, Portaluppi F. Pulmonary hypertension in dialysis patients: A cross-sectional Italian study. *Int J Nephrol.* 2010;11:463–75.

Efficacy of static stretching Versus Proprioceptive Neuromuscular Facilitation (PNF) stretching on hip adductor flexibility in recreational football players.

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ABSTRACT

Adductor strain is most commonly seen in football players, to help ease groin pain and improve the flexibility of muscles stretching techniques like ballistic stretching, static stretching, etc. can be used. Static hip adductor stretching is effective whereas a new technique to increase muscle flexibility is Proprioceptive Neuromuscular Facilitation stretching. This study examines the effects of two stretching techniques on tight hip adductors: static stretching and proprioceptive neuromuscular facilitation stretching. Method: Fifty people were chosen based on the inclusion criteria. There were two groups of subjects. Proprioceptive neuromuscular facilitation and static adductor stretching were administered to Group A. Group B received adductor stretching, and these methods were used for three different days. Using a goniometer, Abduction-Range of Motion was measured prior to the start of the first session and at the conclusion of the last one. Flexibility was measured before the start of first session and at the end of last treatment session by groin flexibility test. The inter Group analysis for ROM between Group A versus Group B showed statistically significant difference by using unpaired ‘t’ test. **Results :** Group A’s post-intervention flexibility values were 17.23, whereas group B’s were 13.5. There was a statistically significant difference between Group A and Group B in the intergroup analysis of flexibility. The unpaired “t” test was used for this. **Conclusion :** It is concluded that Proprioceptive Neuromuscular Facilitation stretching exercises had a statistically significant effect on the abduction range of motion and groin flexibility scores.

Key Words : Adductor tightness, Flexibility, Groin pain, Hip abduction, Proprioceptive Neuromuscular stretch.

INTRODUCTION

The primary purpose of Recreational sports participation, along with the goals of improving physical fitness, fun, and social involvement. Recent studies have established recreational football, carried out as small-sided games can be characterized as having a high aerobic component with mean heart rates of 80-85% of maximum heart rate, which is similar to values observed for elite football players has been shown

by recent studies. Stretching procedures are used to improve the flexibility and avoid tightness. Stretching promotes the growth of muscle.¹⁻² When stretching, force is applied without regard to the tissue’s voluntary motion.³ Football players frequently have groin pain from adductor strain, which progresses to degenerative arthropathy of the pubic symphysis in its severe stages. In sports like football, groin strains are frequently seen

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in players with a history of hip adductor injuries, reduced range of motion, an imbalance in the strength of the hip adductor compared to the abductor, or diminished performance.⁴ Static, ballistic, and proprioceptive neuromuscular facilitation (PNF) stretching are the three most common stretching methods.⁵⁻⁷ The Procedure of Static stretching involves stretching a muscle (or a muscle group) to the furthest point. This position is maintained for a definite period of time.⁸ Static stretching which is the commonest method⁹ composes gradual lengthening a joint to an elongated position before the start of pain. A static stretch is usually held for 30 second duration. The perform the static stretching the protocol which should be followed is that the stretch should be in a slow, gradual manner and held at end-range just before the point of discomfort.¹⁰ This static stretching is energy efficient over any other stretching method as it requires less energy to perform along with low injury risk. Proprioceptive neuromuscular facilitation [PNF] is a new form of stretching technique which takes the help of proprioceptive stimulation and aids neuromuscular responses. To increase the joint range of motion, different combinations of alternating contraction and relaxation of the agonist and antagonist muscle groups are used.¹⁰⁻¹¹ The agonist, or prime mover is passively moved in which the muscle needs to be elongated, and is taken up to end-range and contracted isometrically. This is then followed by a contraction which is eccentric to the antagonist muscle.¹² Football as a sport requires skills like rapid change of directions and speed several times in order to dodge the opponent and gain better control over the ball. This action implies a lot of stress on the adductor muscles as the player has to apply force rapidly on the ground.¹³ This force which is required during a sudden lateral change of directions, which helps enable a player to position himself in a better manner during

the gameplay is absorbed by the adductor muscle.¹⁴ Strengthening adductor muscles improves the player's performance along with reducing eccentric stress. The chances of sustaining a groin injury are also reduced as these injuries often result in prolonged standing pain and tenderness in the groin and thigh region, affecting the play time and also it leads to a long time absence from the game.¹⁵

MATERIALS AND METHODOLOGY

For this study, the source of population was College students, 60 healthy male recreational football players, who were willing to participate after signing an informed consent form were eligible for this study. Age between 15-25 years and subjects not undergoing any hip adductor stretching program was the inclusion criteria. Subjects who had a history of previous muscle injury over a period of 6 weeks, any recent surgery or lower limb fractures, or had problems related to bones, joints or muscle which could limit stretching were excluded. All 60 players fulfilled the pre-requisites, and inclusion criteria and completed the study. The subjects were divided into two equal groups by simple randomization. Throughout the trial, there were no observed dropouts from any of the groups. Krishna Institute of Medical Sciences is the main data source. considered to be Karad University (KIMSDU), This kind of research is an experimental study. Study design: comparative prospective observational study, Sample size: sixty, determined by applying Cochran's formula ($n = z^2pq/d^2$). Method of sampling: random sampling Four weeks were spent studying. Flexibility was measured with a groin flexibility test. In this test, participants had to sit on the floor and tried to pull their feet as close as they can to the body, Range of motion was measured by a standard goniometer.

PROCEDURE : The KIMSDU Institutional Ethical Committee granted approval for the project. The consent form was required of the subjects on the first visit. Two sets of subjects were randomly selected based on the inclusion criteria. **Group A** was given Static Adductor stretch and Proprioceptive neuromuscular facilitation Adductor stretching was given to **group B**, Techniques were performed on individuals for three days alternatively. Before first session, and at the end of last session. Abduction range was measured with the help of a goniometer. Flexibility was measured before the start of first session and at the end of last treatment session by groin flexibility test. **Group A:** On the treatment table, static stretching was administered while the patient's second leg was propped up at a 90-degree angle outside the table. One hand was put on the knee's medial side, and the other on the medial portion of the foot. The leg was then abducted to its greatest range of motion and maintained there for 30 seconds. Four sets of this were performed, with a 30-second break in between each set.¹⁵ **Group B:** Group B received Proprioceptive neuromuscular facilitation technique. In supine lying, on the treatment table, subject was positioned. While other leg rested outside the table with knee positioned at 90 degrees. The affected leg was stretched for 10 seconds passively, then against resistance an active muscle contraction for 10 secs against was imposed by the evaluator at the inner thigh region. At the finally stage hip muscles were extended for another 10 seconds. With separation by 30-second interval, 4 sets were performed. The Abd-ROM was measured both before and after the operation using a conventional 360-degree goniometer.¹⁶⁻¹⁷ The subject was placed in a supine posture and had her pelvis stabilized with the use of a mobilization belt. Using a goniometer, the imaginary line connecting the anterior

superior iliac spine (ASIS) and the stationary arm was aligned. The moveable arm was positioned across the femur's midline, with unilateral ASIS serving as the fulcrum's center of mass. The contralateral leg was maintained on the couch's edge during the hip abduction.¹⁶ The values for the dominant and the non-dominant leg were evaluated. Prior to the beginning of the study on Day 1 the Pre-intervention values of all the outcome measures were noted in the subjects. This intervention was carried for 4 weeks. After 4 weeks the post-intervention measures were taken and both the values were compared at the last treatment day.

All of the parameters' pre- and post-treatment values were noted and compared for both intra- and intergroup analysis. The sample size was determined based on the requirement for a minimal clinical change, and a level of significance of less than 10% was assumed. The power standard deviation and standard error were computed in order to compile the data and do analysis. Less than that threshold was regarded as significant, and the p level was maintained at 0.05. The analysis was conducted using the Instant program.

MS Excel was used for drawing various graphs with given frequencies and for master chart.

Table 1 : Statistics For The Subjects' Characteristics.

Characteristics	Group	Mean	SD
Age (Years)	1	21	2.754
	2	21.23	2.775
Height (m)	1	1.7203	2.553
	2	1.7136	2.526
Weight (Kgs)	1	69.26	4.299
	2	70	4.034
BMI	1	23.38	0.8918
	2	23.80	0.7697

Table 2 : Abduction Of The Subjects On Two Occasions In Both Static And Pnf Groups: Descriptive Statistics. (N=30) Range of Motion values

	Group A			Group B		
	Mean Sd	't'	P value	Mean SD	't'	P value
Pre Test RIGHT	38.2±1.518	137.86	>0.10	38.23±1.547	135.40	0.0219
LEFT	37.8±1.627	127.22	0.0350	38.36±1.497	140.40	0.0003
Post Test RIGHT	41.2±2.041	110.57	<0.0001	44.5±0.6297	387.05	<0.0001
LEFT	41.5±1.697	133.96	<0.0001	44.8±0.4068	603.14	<0.0001

The pre-interventional values of ROM of right and left side were 38.2 and 37.8 respectively of Group A and of Group B right and left side were 38.23 and 38.36 respectively, whereas the post-intervention values of ROM of right and left side were 41.2 and 41.5 respectively of Group A and of Group B right and left side were 44.5 and 44.8 respectively. The inter Group analysis for ROM between Group A versus Group B showed statistically significant difference. This was done by using unpaired 't' test.

Table 3 : Outcome Measure Groin Flexibility Score Values

Groin Flexibility	Group A		Group B	
	Pre	Post	Pre	Post
Mean	20.63	17.23	20.66	13.5
SD	1.790	1.775	2.057	1.137
't'	63.120	53.17	55.039	65.025
P value	0.0024	0.0074	0.0198	0.0027

The pre-intervention values of FLEXIBILITY were 20.63 in group A and 20.66 in group B respectively, whereas the post-intervention values of flexibility were 17.23 in group A and 13.5 in group B respectively.

The inter group analysis for flexibility between Group A versus Group B showed statistically significant difference. This was done using unpaired 't' test

RESULTS

From the comparison between the two stretching groups, both Static Stretching and PNF Stretching exercises showed improvement in abduction range and on hip adductor flexibility on recreational football players, however the results showed that: PNF stretching exercises had a statistically significant effect on the abduction range of motion and groin flexibility scores. It can be concluded that PNF stretch training considerably increased range because the average range of motion after PNF stretching (44.6) was compared to the mean range of motion before PNF stretching (38.2).

DISCUSSION

Performing structured exercise has been included not only by athletes, but also by recreational participants, both young and old. This is partly because of participant interest and availability of recreational resources.¹⁸ As participating in these sports continues to increase, it requires high performance criteria, such as: hockey, soccer, skiing, basketball, football, gymnastics, dance and martial arts¹⁸⁻¹⁹ A large amount of hip mobility is required for this activities as the participants require high mobility skills like sudden changes in direction that could increase the risk of hip adductor strains²⁰⁻
²¹The comparative study of both the interventions has not been done before on hip adductor for recreational football players. There is evidence according to the available literature that shows the effect of stretching for hip adductor tightness. When given for subacute duration the result can be compared with conventional

stretching protocols. The values of pre-treatment and post-treatment were analysed. Statistically significant technique was PNF stretching technique and when compared with the other group, from both the techniques PNF technique is more significant. According to Bradley PS et al. where they found the effect of static, light ballistic, PNF stretching on strength performance.²²The other form of stretching does enhance the strength performance as does the PNF stretch, because muscle inhibition is initiated while doing PNF stretch.²²According to Sady et al. where they compared the static and PNF stretching technique for flexibility of hamstring. To measure Range of motion, A Leighton flexometer was used. The PNF group had an increase in flexibility as compared

to the control group.²³Ligaments that are the external supporting structures of the hip, restrict flexibility²⁴. ROM is limited into hip abduction in individuals who have a shorter ligament.

CONCLUSION

PNF stretching exercises had a substantial impact on the abduction range of motion, according to research on the benefits of static stretching and PNF stretching exercises for hip adductor flexibility in recreational football players.

CONFLICT OF INTEREST : “The authors declare no potential conflicts of interest with respect to research, authorship, and/or publication of this article”.

REFERENCES

1. Weerapong P, Hume PA, Kolt GS. Stretching: mechanisms and benefits for sport performance and injury prevention. *Phys Ther Rev* 2004;9(4):189-206.
2. He L, Yan X, Li J, Guan B, Ma L, Chen Y, et al. Comparison of 2 dosages of stretching treatment in infants with congenital muscular torticollis: a randomized trial. *Am J Phys Med Rehabil* 2017;96(5):333–40.
3. Madding SW, Wong JG, Hallum A, Medeiros J. Effect of duration of passive stretch on hip abduction range of motion. *J Orthop Sports Phys Ther* 1987;8(8):409
4. Ibrahim A, Murrell GAC, Knapman P. Adductor strain and hip range of movement in male professional soccer players. *Journal of Orthopaedic Surgery*. 2007;15(1):46–49.
5. Feland JB, Myrer JW, Schulthies SS, Fellingham GW, Measom GW 2001. The effect of duration of stretching of the hamstring muscle group for increasing range of motion in people aged 65 years or older. *Physical Therapy*, 81(5): 1110-1117.
6. Magnusson SP, Simonsen EB, Aagaard P, Dyhre-Poulsen P, McHugh MP, Kjaer M. Mechanical and physical responses to stretching with and without preisometric contraction in human skeletal muscle. *Arch Phys Med Rehabil* 77: 373–378, 1996
7. Miyahara Y, Naito H, Ogura Y, Katamoto S, Aoki J. Effects of proprioceptive neuromuscular facilitation stretching and static stretching on maximal voluntary contraction. *J Strength Cond Res* 27: 195–201, 2013
8. Sharman MJ, Cresswell AG, Riek S, Proprioceptive neuromuscular facilitation stretching *Sports Med* 36: 929–939, 2006
9. Weerapong P, Hume PA, Kolt GS 2004. Stretching: Mechanisms and benefits for sport performance and injury prevention. *Physical Therapy Reviews*, 9: 189–206.
10. Feland JB, Myrer JW, Merrill RM. Acute changes in hamstring flexibility: PNF versus static stretch in senior athletes. *Phys Ther Sport* 2: 186–193, 2001

11. Moore MA, Hutton RS. Electromyographic investigation of muscle stretching techniques. *Med Sci Sports Exerc* .1980; 12:322–329. Google ScholarCrossrefPubMed
12. Sozbir K 2006. The Effects of Two Different Stretching Exercises Together with Plyometric Training on EMG Values and Some Physiological Parameters. Master Thesis. Institute of Health Science. Bolu: Abant IzzetBaysal University.
13. Andreas. Serner, Andrea Britt Mosler, Johannes L Tol & Roald Bahr. Mechanism of acute adductor longus injury in male football players: A systematic visual video analysis. *British journal of sports medicine*. 2018;53(3): 099246.
14. Harris NK, Cronin JB, Hopkins WG, Hansen KT. Squat jump training at maximal power load vs heavy loads: Effect on sprint ability. *Journal of Strength Conditioning Research*. 2008;22(6): 1742-1749.
15. Rubini EC, Souza AC, Mello ML, Bacurau RF, Cabral LF, Farinatti PT. Immediate effect of static and proprioceptive neuromuscular facilitation stretching on hip adductor flexibility in female ballet dancers. *J Dance Med Sci* 2011;15(4):177-81.
16. Nussbaumer S, Leunig M, Glatthorn JF, Stauffacher S, Gerber H, Maffiuletti NA. Validity and test-retest reliability of manual goniometers for measuring passive hip range of motion in femoroacetabular impingement patients. *BMC Musculoskelet disord* 2010; 11:194.
17. Verrall GM, Hamilton IA, Slavotinek JP, Oakeshott RD, Spriggins AJ, Barnes PG, et al. Hip joint range of motion reduction in sports-related chronic groin injury diagnosed as pubic bone stress injury. *J Sci Med Sport* 2005;8(1):77- 84
18. Roux A, Evenson K, McGinn A, Brown D, Moore L, Brines S, Jacobs D., Jr Availability of recreational resources and physical activity in adults. *Am J Public Health*. 2007;93(3):493–499.
19. Renstrom P, Peterson L. Groin injuries in athletes. *Br J Sports Med*. 1980;14(1):30–36.
20. Nicholas S, Tyler T. Adductor Muscle Strains in Sport. *Sports Med*. 2002;32(5):339–344
21. Young WB. The use of static stretching in warm-up for training and competition. *Int J Sports Physiol Perform*. 2007; 2:212–216
22. Bradley PS, Olsen PD, Portas MD. The effect of static, ballistic, and proprioceptive neuromuscular facilitation stretching on vertical jump performance. *The Journal of Strength & Conditioning Research*. 2007 Feb 1;21(1):223-6.)
23. Sady, S. M. Flexibility training: ballistic, static or PNF *Arch. Phys. Med Rehabilitation.*,1882;63(6)
24. Clippinger K. *Dance Anatomy and Kinesiology*. 2nd ed. Champaign, IL: Human Kinetics; 2007

Plagiarism in Scholarly Publishing : Detection, Prevention and Ethical Implications

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INTRODUCTION

Plagiarism, the act of using someone else's work or ideas without proper attribution, is a continuing challenge in academic and scientific publishing. Publications are the end-products of the scientific work, and their quantity and citability are keys to the promotion of scientists. Once published, a scholarly paper becomes a source for references, post-publication review and critique. To contribute to the bulk of knowledge of evidence-based medicine (EBM), the paper should be credible¹. It should be based on optimal research design and reporting^{2,3}. Researchers and authors of scholarly papers have to follow ethical codes of Good Scientific Practice (GSP)⁴⁻⁷.

As the pressure to publish increases, authors may resort to unethical practices, such as plagiarism, to meet deadlines for their publication record. Plagiarism dates back to the foundation of science communication as a discipline. According to the World Association of Medical Editors (WAME) strict definition, plagiarism is when six consecutive words are copied^{6,8}. 7 to 11 words are overlapping set of 30 letters⁹. In the context of manuscript preparation, plagiarism can significantly damage the academic and professional reputation of authors and undermine the integrity of the entire research process. This article delves into the various types of plagiarism, its causes, consequences, methods of detection, and strategies for prevention.

Types of Plagiarism in Manuscripts

Direct Plagiarism: This is the most obvious form of plagiarism, where an author copies text, figures, or ideas directly from a source without attribution. This is easily detectable and is considered a serious ethical breach.

Self-Plagiarism: Self-plagiarism occurs when an author reuses their own previously published work without proper acknowledgment. While the content may be original to the author, its reuse without clear citation misleads the reader into thinking the material is new, which compromises the novelty of the manuscript

and also the relevance of the published data.

Mosaic Plagiarism: Also known as "patchwriting," mosaic plagiarism involves copying portions of text from various sources and blending them with the author's own work. The intention may not always be malicious, but it can result in significant overlaps between the original and newly written content. It also affects the readability of the text.

Paraphrasing Plagiarism: In this form, an author rewrites someone else's ideas or text in their own

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words but fails to credit the original source. While paraphrasing can be an acceptable practice in academic writing, it becomes unethical when proper attribution is omitted.

Accidental Plagiarism: This occurs when an author unintentionally fails to cite sources or paraphrases inadequately due to a lack of knowledge about citation practices or because of poor note-taking during research.

Causes of Plagiarism in Manuscripts

Many emerging researchers or students do not fully grasp what constitutes plagiarism, especially when it comes to paraphrasing or self-plagiarism. A lack of awareness about proper citation practices is a common cause. Deadlines and the pressure to produce manuscripts quickly can lead to corners being cut, with some authors turning to plagiarism to meet their publishing goals. The proliferation of digital resources and databases has made it easier to access vast amounts of information. However, this easy access can also lead to unintentional plagiarism when authors fail to track or cite all their sources properly.

Paraphrasing is a complex skill that requires reworking an idea or text into one's own words while retaining the original meaning. Inadequate paraphrasing often leads to plagiarism, even when it is unintentional.

Impact of Plagiarism on Manuscripts

Plagiarism can severely damage an author's reputation, leading to loss of academic credibility. Researchers involved in plagiarism scandals often face difficulties in securing future research funding, publishing

opportunities, and even positions in academic institutions. Journals and publishers are increasingly vigilant in detecting plagiarism. Manuscripts found to contain plagiarized content are often rejected outright, and authors may be banned from submitting to the journal in the future. In severe cases, plagiarism can lead to legal action. The original authors or copyright holders can file lawsuits against the plagiarist for intellectual property infringement, with serious financial and legal repercussions. Plagiarism undermines the integrity of research findings and can mislead the scientific community. When plagiarized content is published, it contributes to the spread of misinformation, which can have broader consequences, especially in fields like medicine, law, and public policy.

Detection and Prevention of Plagiarism

There are no universal regulations on plagiarism prevention suitable for all scientific and academic institutions¹. The International Committee of Medical Journal Editors (ICMJE) gave a detailed explanation of what is not a duplicate publication⁸. COPE attempted to tackle the problem of plagiarism by recommending cooperation with research institutions and retraction of untrustworthy material¹⁰. Tools like Turnitin, iThenticate, and Copyscape are commonly used by academic institutions and publishers to detect plagiarism. These programs compare the manuscript against vast databases of published content, including academic papers, websites, and in addition to software tools, the peer review process plays a critical role in identifying potential plagiarism. Reviewers often spot instances of plagiarized content through their familiarity with the literature, although this process is not foolproof. books, to identify similarities.

To prevent plagiarism, institutions and researchers must prioritize education on proper citation practices, paraphrasing, and intellectual property rights. Workshops, seminars, and online courses can help researchers understand how to avoid plagiarism and recognize its implications. Encouraging originality in research is one of the most effective ways to prevent plagiarism. Researchers should focus on conducting unique studies and presenting their findings in a way that highlights their contribution to the academic community.

Ethical Considerations and Addressing Plagiarism

Properly crediting all contributors to a manuscript, including those who provided data, insights, or suggestions, is essential for maintaining ethical research practices. Co-authors should also be aware of each other's contributions to avoid misunderstandings related to authorship. Authors must ensure full transparency in their work by disclosing funding sources, conflicts of interest, and acknowledging previous works that influenced their research. This level of transparency reduces the likelihood of plagiarizing or accidentally misrepresenting the work of others.

Academic institutions, publishers, and funding agencies have a responsibility to promote ethical research practices. They should establish clear guidelines and provide support for researchers to avoid plagiarism.

University Grants Commission

The University Grants Commission (UGC) of India has established comprehensive regulations to promote academic integrity and prevent plagiarism in higher educational institutions. These guidelines, detailed in the 2018 document titled "Promotion of Academic

Integrity and Prevention of Plagiarism in Higher Educational Institutions," define plagiarism as the practice of taking someone else's work or idea and passing it off as one's own.

Levels of Plagiarism:

The UGC categorizes plagiarism into four levels based on the percentage of similarity:

- **Level 0** : Similarity up to 10% – Minor similarities; no penalty.
- **Level 1** : Similarity above 10% to 40%.
- **Level 2** : Similarity above 40% to 60%.
- **Level 3** : Similarity above 60%.

Penalties for Students:

- **Level 1** : The student is required to submit a revised script within a stipulated time not exceeding six months.
- **Level 2** : The student is debarred from submitting a revised script for one year.
- **Level 3** : The student's registration for the program is canceled.

Penalties for Faculty, Researchers, and Staff:

- **Level 1** : Required to withdraw the manuscript.
- **Level 2** : Required to withdraw the manuscript; denied one annual increment; barred from supervising new Master's, M.Phil., or Ph.D. students for two years.
- **Level 3** : Required to withdraw the manuscript; denied two successive annual increments; barred from supervising new students for three years.

These measures aim to uphold the quality and credibility of academic work within Indian higher educational institutions.

CONCLUSION

Plagiarism in manuscripts is a serious concern that can have wide-reaching implications for authors, journals, and the academic community as a whole. Its causes are multifaceted, ranging from a lack of understanding to pressure for quick publication. However, with the

advancement of plagiarism detection technology, greater emphasis on education, and the implementation of robust ethical guidelines, plagiarism can be minimized. Authors, institutions, and publishers must work collaboratively to uphold academic integrity and ensure that research is conducted and presented ethically. Ultimately, promoting a culture of originality and proper attribution will contribute to the advancement of knowledge and the credibility of scholarly work.

REFERENCES

1. Masic I. Ethical aspects and Dilemmas of Preparing, Writing and Publishing of the Scientific Papers in the Biomedical Journals. *Acta Inform Med.* 2012;20(3):141–148. doi: 10.5455/aim.2012.20.141-148. doi:105455/aim.2012.20.141-148. [DOI] [PMC free article] [PubMed] [Google Scholar]
2. Masic I. How to Search, Write, Prepare and Publish the Scientific Papers in Bimedical Journals. *Acta Inform Med.* 2011;19(2):68–79. doi: 10.5455/aim.2011.19.68-79. doi:10.4555/aim.2011.19.68-79. [DOI] [PMC free article] [PubMed] [Google Scholar]
3. Wager E, Kleinert S. Cooperation Between Research Institutions and Journals on Research Integrity Cases: Guidance from the Committee on Publication Ethics (COPE) *Acta Inform Med.* 2012 Sep;20(3):136–140. doi: 10.5455/aim.2012.20.136-140. doi: 10.5455/aim.2012.20.136-140. [DOI] [PMC free article] [PubMed] [Google Scholar]
4. International Committee of Medical Journals Editors. Uniform Requirements for Manuscript Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication. (Updated October 2008). Available: <http://www.icmje.org/>
5. Council of Science Editors. CSE's White Paper on Promoting Integrity in Scientific Journal Publications. Editorial policy committee (2005-2006) Available: [http://www. Council Science Editors.org](http://www.CouncilScienceEditors.org) .
6. World Association of Medical Editors. WAME recommendations on Publication Ethics and Policies for Medical Journals.
7. Committee On Publication Ethics. COPE. Code of Conduct and Best Practice Guidelines for Journal Editors.
8. Committee On Publication Ethics. COPE. Code of Conduct and Best Practice Guidelines for Journal Editors. Available: <http://publicationethics.org/resources/guidelines>
9. Amstrong JD. Plagiarism what is it, whom does it offend, and how does one deal whit it? *Am J Roentgenol.* 1993;161:479–484.
10. Available: <http://www.ori.dhhs.gov>

Urban vs Rural : A Comparative Analysis of High –Risk Populations and Diabetes Prevalence in Kolhapur

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ABSTRACT

BACKGROUND : In recent decades, non-communicable diseases (NCDs), particularly diabetes mellitus (DM), have become the leading cause of global mortality. India, identified as the “diabetes capital of the world,” faces a stark contrast in diabetes prevalence between urban (10.9%) and rural areas (6.5%) In Maharashtra, urbanization with its associated lifestyle changes and socio-economic disparities, exacerbates the risk of diabetes. The IDRS, developed specifically for the Indian population, was used for predicting undiagnosed diabetes. **METHODOLOGY :** A cross-sectional study was conducted at D.Y. Patil medical college OPD & IPD, Maharashtra. A total of 330 participants aged 18 years and above were screened for risk factors, including age, waist circumference, family history of diabetes and physical activity. Random testing of the blood glucose level of participants with a high risk score was carried out using a glucometer. Statistical data analysis was performed by using the chi-square test. **RESULT :** Area wise percentage of participants under high risk in rural area was found to be 60 (58%) while in urban area it was found to be 162 (71%). The prevalence of high risk and newly diagnosed diabetic patients in rural area was 1.52% while in urban area it was 6.06% , which was considerably higher. Malkapur had the highest number of participants 30 (14%) who were at the risk of developing diabetes while Kurundwad had the lowest 2 (1%). **CONCLUSION :** Urban areas exhibit both a higher proportion of individuals at high risk for diabetes and a higher prevalence of newly diagnosed diabetes

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INTRODUCTION

In recent decades, “non-communicable diseases (NCDs)” have become the foremost cause of death worldwide, exceeding all other causes combined. Among these diseases, diabetes stands out as particularly called the disease of urbanization.^[1] “Diabetes mellitus (DM) is a metabolic disease, involving inappropriately elevated blood glucose levels.^[2] The prevalence of diabetes is rapidly rising all

over the globe at an alarming rate. India leads the world with the largest number of diabetic subjects earning the dubious distinction of being termed the “diabetes capital of the world”.^[3] It is stated that the incidence of DM differs from 16% in urban India to 3% in rural India.^[4] In 2001, 28% of India’s population lived in urban areas, a figure predictable to rise to about 50% (605–618 million) by 2021–25. “Demographic trends

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indicate that while the urban growth rate stabilized at 3% over the past decade (1991–2001), the growth rate in slums doubled. Projections suggest that while the urban population will double in the next decade, the urban poor will double in just five years. The urban poor face the worst of both worlds—they adopt a more urbanized lifestyle, increasing their risk for NCDs, and have poor access to healthcare due to limited financial resources.^[1]

DM is more common among migrant Asian Indians compared to other ethnic groups. Research on native Indian populations also indicates a high prevalence of DM in urban areas. Dietary habits and lifestyle choices play a significant role in the increased incidence and prevalence of obesity and DM in these urban populations. The rising prevalence of DM in India, especially in urban regions, has become a significant concern recently.^[11] Rural populations in India, typically at low risk for diabetes, face increased risks when they migrate to metropolitan cities. “In cities, they often settle in urban slums and take on daily wage jobs, leading to several lifestyle changes: shifting from traditional, modest eating habits, exposure to severe stress, decreased physical activity, and increased smoking, tobacco chewing, and alcohol intake. The ageing population, rapid urbanization, and transition from agrarian life to wage-earning modern city life are reported as major contributors to the increased unhealthy lifestyle pattern in urban areas.^[5]

The rapid rise in T2DM and associated conditions like obesity and hypertension over the past 50 years is largely due to lifestyle variations from modernization, including higher fat diets and decreased physical activity. This “epidemiological transition” has improved longevity but also increased the prevalence

of new-age diseases.

Early identification of risk factors and preventive interventions are crucial to curbing DM and its difficulties.^[3] Evidence suggests that primary recognition of DM through appropriate screening approaches, particularly in individuals with increased risk, can aid delay microvascular and macrovascular problems, thereby decreasing the clinical, social, and economic burden of the disease. The most effective way to lessen the socioeconomic burden of diabetes is early diagnosis using brief questionnaires to assess diabetes risk. Various risk factors for T2DM, such as increased age, central obesity, positive family history, physical inactivity, stress, and dietary habits, are well established. The Indian Diabetes Risk Score (IDRS), developed by the Madras Diabetes Research Foundation (MDRF) and Ramachandran A et al., has been validated to assess risk. The IDRS, is a cost-effective, straightforward screening tool designed to predict Undiagnosed diabetes cases.^[9] This score, also known as MDRF-IDRS, originates from data collected during the CURES, derived from known risk factors for diabetes.^[10, 11] The IDRS may also predict metabolic syndrome and cardiovascular disease, as three of its factors (age, physical activity, and waist circumference) are common risk factors for these conditions.

Therefore, this study was undertaken to do a comparative analysis of the prevalence of diabetes and the association of its risk factors on urban and rural areas of Kolhapur using IDRS on the undiagnosed diabetic population.

METHODOLOGY

A prospective, cross-sectional study was conducted at

Dr. D.Y. Patil Medical Collage Hospital and Research Institute, Kolhapur, Maharashtra, and various camps organized by the institute. Data collection was done from December 2022 to April 2024. The sample size taken for the study was 330.

Inclusion criteria

All men and women above the age of 18 years.

Population not aware of their diabetic status.

Exclusion criteria

Any participant already diagnosed with T2DM/T1DM and/or taking any medication for it. Participants on pre-existing corticosteroid therapy.

Female participants with PCOS and taking oral hypoglycemic as a part of their treatment regime.

Pregnant and/or lactating women.

Participants who have undergone complex surgeries in the past like Whipple's surgery, pancreatic pseudo cyst resection, and carcinoma pancreas.

Participants unable to interpret the questionnaire.

Participants taking medications of unknown formula.

Indian Diabetes Risk Score Components :

Particulars	Score
1. Age in years	
<35	0
35 – 49	20
≥50	30
2. Abdominal obesity	
Waist <80cm (F); <90cm (M).	0
Waist 80-89cm (F); 90-99cm (M).	10
Waist >90cm (F); >100cm (M).	20
3. Physical activity	
Vigorous exercise [regular] or strenuous [manual] work at home / work	0
Moderate exercise [regular] or moderate physical activity At home / work	10
Mild exercise [regular] or mild physical activity at home / Work	20
No exercise and sedentary work home/work	30
4. Family history	
No family history	0
Either parents	10
Both parents	20

Assessment of risk of type 2 diabetes according to IDRS

History was gathered using a predesigned, pretested proforma from the study participants; this included information on sociodemographic characteristics, family history of diabetes and physical activity, etc., to assess risk factors, after taking written informed consent. This included personal and medication histories, as well as measurements of weight, height, waist circumference, and other anthropometric parameters. "Waist circumference was measured using a non-stretchable tape to the nearest 0.1 cm at the midpoint between the tip of the iliac crest and the last costal margin at the back, and at the umbilicus at the front, with the subject standing erect and exhaling normally. Abdominal or central obesity was defined as a waist circumference ≥ 80 cm in women and ≥ 90 cm in men. BMI was calculated using the formula weight in kilograms divided by the square of height in meters. Blood glucose levels were assessed using random

capillary blood samples obtained with a standardized digital glucometer (Accu-Check, Roche Diagnostics, Germany). Physical activity levels were categorized according to WHO STEPS definitions, ranging from sedentary to vigorously active. Undiagnosed diabetes was identified through random blood sugar tests conducted with the same glucometer. Risk scores were then correlated with random blood sugar levels to classify participants as diabetic (RBS \geq 200 mg/dL) or non-diabetic (RBS $<$ 200 mg/dL), following ICMR guidelines to determine their diabetic status.” The collected data was entered into a Microsoft Excel using MS Excel 2016. $P < 0.05$ was considered as level of significance using the Chi-square test.

RESULTS

Table no. 1 Area wise Percentage of Participants under High risk

Area	No. of Participants at high risk & newly Diagnosed Diabetes	Prevalence	P value
Rural	60	58%	0.01*
Urban	162	71%	

In table no 1, area wise percentage of participants under high risk in rural area was found to be 60 (58%) while in urban area it was found to be 162 (71%). The P-value was 0.01 which is found to be significant.

Table no. 2 Area wise Percentage of Participants under High risk and newly diagnosed

Area	No. of Participants at high risk & newly Diagnosed Diabetes	Prevalence	P value
Rural	5	1.52%	0.001*
Urban	20	0.06%	

In table no.2, the prevalence of high risk and newly diagnosed diabetic patients in rural area was 1.52% while in urban area it was 6.06% , which was considerably higher. The P-value was 0.001 which is significant.

Table no.3 Area wise risk in females

Female					
Risk	No. of female Participants in Rural Area	Percentage	No. of female Participants in Rural Area	Percentage	P value
High	31	60%	69	63%	0.35
Moderate	20	38%	40	36%	0.4
Low risk	1	2%	1	1%	0.3
Total	52	100%	110	100%	

In table no.3, the percentage of the female patients in rural areas with high risk of diabetes was found to be 31(60%), moderate risk 20 (38%) and those with low risk was 1(2%) whereas in the urban area, 69 female patients (63%) were categorized as high risk followed by moderate female patients to be 40 (36%) and low risk 1(1%). No significant difference was observed among the females at high risk from the urban and the rural area.

Table no.4 Area wise risk in males

Male					
Risk	No. of female Participants in Rural Area	Percentage	No. of female Participants in Rural Area	Percentage	P value
High	29	57%	93	79%	0.001*
Moderate	22	43%	22	19%	0.0005*
Low risk	0	0%	2	2%	0.15
Total	51	100%	117	100%	

*indicates significance (P value $<$ 0.05)

In table no.4, the percentage of the male patients with

high risk of diabetes in rural areas was found to be 29 (57%), moderate risk 22 (43%) and those with low risk was 0(0%) whereas in the urban area, 93 male patients (79%) were categorized as high risk followed by moderate male patients to be 22 (19%) and low risk 2(2%).

In high risk group, percentage of males in the urban area (79%) is significantly higher than the rural area (57%) (P-value=0.001).

Also, the percentage of males at moderate risk in the rural area (43%) is significantly higher than the percentage of males at moderate risk in the urban area (19%) (P-value=0.0005)

The percentage of males at low risk in the rural area was lower 0 (0%) as compared to the percentage of males in urban areas which is 2%(2)

Table no.5 Area wise family history of diabetes

Area	Family History in Urban	High	Moderate	Low risk	P value
Urban	Both parents	35	4	0	0.0004*
	Either parent	33	3	0	
	No diabetes in parents	94	55	3	
Area	Family History in Rural	High	Moderate	Low risk	P value
Rural	Both parents	16	4	0	0.036*
	Either parent	10	2	0	
	No diabetes in parents	34	36	1	

Table no.5 represents the family history of Diabetes amongst the parents of the participants in both the areas.

Accordingly, in the urban area, **both parents** having family history of diabetes belonging to high prevalence group was found to be 35, while 4 were moderate and 0

in the low risk group.

In the rural area, **both parents** having family history of diabetes belonging to high prevalence group was found to be 16, while 4 were moderate and 0 in the low risk group.

In urban area, among the **either parent** group with family history of diabetes, 33 were found under the high prevalence group while 3 under moderate with 0 in the low risk group.

In rural area, from the **either parent** group, 10 belonged to the high prevalence group while 2 belonged to the moderate group with 0 in the low risk group.

In urban area, 94 parents had **no family history** of diabetes with 55 in the moderate group and 3 in the low risk group while in the **rural area** 34 belonged to the high prevalence group with 36 among the moderate and 1 to the low risk group. The P-value in the urban area was 0.0004.

Table no.6 Area wise Physical activity

Area	Physical Activity	High	Moderate	Low risk	P value
Urban	Exercise regular + strenuous	0	0	1	<0.000001*
	Exercise regular or strenuous	18	19	0	
	No exercise and sedentary work	144	43	0	
Area	Physical Activity	High	Moderate	Low risk	P value
Rural	Exercise regular or strenuous	17	22	1	0.02*
	No exercise and sedentary work	43	20	0	

*indicates significance (P value < 0.05)

Table no.6 represents area wise the number of participant's performing physical activities like regular exercise, strenuous workout or having a sedentary work with no exercise.

In urban areas, participants performing regular exercise+ strenuous, 1 participant had low risk of diabetes with 0 participants in the high and moderate group.

Those performing regular exercise or strenuous in **urban areas**, 18 belonged to the high risk group with 19 belonging to the moderate risk group and 0 in the low risk group.

In **rural areas** 17 participants performing regular exercise or strenuous belonged to the high risk group with 22 under the moderate and 1 under the low risk group.

144 participants from the **urban area** had high risk of diabetes who did no exercise and had sedentary work. 43 belonged to the moderate and 0 to the low risk group.

The P-value for the urban area participants performing physical activity was 0.000001 which is significantly greater than the rural area (P-value=0.02)

In **rural area**, where participants do not perform any exercise and have sedentary work, 43 had the high risk of diabetes while 20 participants had the moderate risk with 0 in the low risk group.

Table no.7 Area wise percentage of participants at high risk of developing diabetes

Address	No. of Participants at High Risk	Percentage
Malkapur	30	14%
Kolhapur city	26	12%
Kagal	25	11%
Ichalkaranji	22	10%
Panhala	19	9%
Hatkanagale	16	7%
Shirol	13	6%
Gargoti	12	5%
Kale	11	5%
Murgud	10	5%
Gadhinglaj	9	4%
Pethvadgaon	7	3%
Ajra	6	3%
Shahuwadi	6	3%
Jaysingpur	5	2%
Chikhali Kasba	3	1%
Kurundwad	2	1%

Malkapur had the highest number of participants 30 (14%) who were at the risk of developing diabetes followed by Kolhapur 26 (12%), Kagal 25 (11%) and Ichalkaranji 22 (10%).Panhala had moderate number of participants 19 (9%) with high chances of developing diabetes followed by Hatkanagale 16 (7%), Shirol 13 (6%), Gargoti 12 (5%) Kale 11 (5%) and Murgud 10 (5%).

Kurundwad had the lowest number of participants 2 (1%) who were at the risk of developing diabetes followed by Chikhali Kasba 3 (1%), Jaysingpur 5 (2%), Shahuwadi 6 (3%), Ajra 6 (3%), Pethvadgaon 7 (3%) and Gadhinglaj 9 (4%).

DISCUSSION

This study undertook an analysis of the IDRS to identify the population at high risk of developing diabetes and prevalence of diabetes in urban and rural areas of Kolhapur district. By examining various demographic and health parameters, the study aimed to provide insights into the incidence of DM in urban and rural population and the role of the IDRS in predicting the disease.

In this study, a total of n=330 adult subjects were recruited. Percentage of participants under high risk in rural area was found to be 60 (58%) while in urban area it was found to be 162 (71%). The P-value was 0.01 which is found to be significant. Individuals found to be at high risk and who were newly diagnosed as diabetic in rural areas were 5 the prevalence of which was 1.52% while in urban area 20 people were newly diagnosed with 6.06% prevalence, which was considerably higher with p-value 0.001 and is significant.

In the above study, “the overall prevalence of diabetes among the study participants was found to be 7.57%,” the prevalence of high risk and newly diagnosed diabetic patients in rural area was 1.52% while in urban area it was 6.06%, which was considerably higher, with all cases concentrated over 50 years of age. The P-value of which is significant 0 .001.

Comparing these results with other studies provides further context. Arun A et al. reported a higher overall diabetes prevalence of 13.78%, which might indicate regional or sample size variations. ^[15] An even higher prevalence of 21.3% was found among women in an industrial urban area in Hyderabad, pointing to possible environmental or occupational factors influencing

diabetes risk.^[7] Similarly, a study in the urban population of Jhalwar described a diabetes incidence of 14.44%, suggesting that urbanization and lifestyle factors could contribute to increased diabetes rates.^[11] The data indicates that diabetes prevalence varies significantly across different populations and regions, influenced by age, urbanization, lifestyle, and possibly occupational factors. The comparison with other studies suggests that urban and industrial settings might present higher risks, necessitating targeted public health strategies in these areas.

In our study, the percentage of the female participants in rural areas with high risk of diabetes was found to be 60% & whereas in the urban area was 63%. Percentage of the male patients with high risk of diabetes in rural areas was found to be 57% , in urban area 79% which is significantly higher than the rural area (57%) (P-value=0.001). These findings are on similar lines with a study conducted at Bolor locality in Mangalore male participants were found to have much higher risk for developing type 2 DM compared to females. ^[18] In contrast to the above conducted study, Arora et al. noted that more high-risk cases were women than men in urban Haryana, and there was a statistically significant association.^[16] However, a study done by Misra et al.^[17] in an urban slum of Delhi showed no statistically significant association by sex.

In our study, both in rural and urban areas a large no. of populace belonging to high risk category had no family history of diabetes, although family history is a proven factor for the risk of diabetes, in distinction to this in a study conducted in Pune, participants with first-degree relatives, or parental history of diabetes, developing had high incidence of diabetes more than 50% of the participants.^[19]

The above study shows a significant association of risk for developing diabetes with participants with no exercise and sedentary work compared to participants performing regular + strenuous exercise in both urban and rural populations which is similar to study conducted in Pune ^[19], but in contrast to study by Kaushalet al. conducted at Himachal Pradesh ^[20] where the odds of diabetes increased with the strenuous work or regular exercise.

Furthermore, the analysis of diabetes risk across different areas of Kolhapur revealed significant geographic variability among urban and rural population, Malkapur, Kolhapur city, Kagal, Ichalkaranji showing the highest risk levels according to idrs, this geographic variability indicates that targeted community-specific interventions in urban areas are in dire need of early preventive measures and intervention for managing diabetes risk and reduce overall prevalence more than rural areas.

CONCLUSION

The IDRS is a cost effective, easy to use, tool used in a community-based study to detect individuals at high risk for diabetes. In my study urban population was found to be at higher risk of developing diabetes,

prevalence being 6.06% compared to rural population with 1.52% prevalence, burden accredited to sedentary lifestyle and dietary habits non-modifiable.

Risk factors like advanced age and existent family history of diabetes, and modifiable risk factors like lack of adequate physical activity and sedentary lifestyle and central obesity were key factors found in participants who were at high risk for diabetes. Routine screening and awareness about modifiable risk factors in general population is advisable for identification of participants at high risk for development of diabetes. Implementation of primary and secondary preventive approaches, including lifestyle and dietary modifications, is recommended for these high-risk participants.

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REFERENCES

1. Anand K, Shah B, Yadav K, Singh R, Mathur P, Paul E, Kapoor SK. Are the urban poor vulnerable to non-communicable diseases? A survey of risk factors for non-communicable diseases in urban slums of Faridabad. *National Medical Journal of India*. 2007 Jun;20(3):115.
2. Sapra A, Bhandari P. *Diabetes mellitus*. StatPearls; Stat Pearls Publishing: Treasure Island, FL, USA. 2021:1-5.
3. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. *Indian journal of medical research*. 2007 Mar 1;125(3):217-30.
4. Panda PS, Jain K, Soni GP, Gupta SA, Chandrakar A, Pradhan SK. Screening for risk of diabetes among adult population of Raipur city using Indian diabetic risk score. *Int J Med Sci Public Health*. 2017 Jun 1;6: 1038-41.
5. Misra A, Pandey RM, Rama Devi J, Sharma R, Vikram NK, Khanna N. High prevalence of diabetes, obesity and dyslipidaemia in urban slum population in northern India. *International journal of obesity*. 2001 Nov;25(11):1722-9.
6. Neel JV, Weder AB, Julius S. Type II diabetes, essential hypertension, and obesity as "syndromes of impaired genetic homeostasis": the "thrifty genotype" hypothesis enters the 21st century. *Perspectives in biology and medicine*. 1998;42(1):44-74.
7. Bala S, Pandve H, Kamala K, Dhanalakshmi A, Sarikonda H. Performance of Indian diabetic risk score as a screening tool of diabetes among women of industrial urban area. *Journal of Family Medicine and Primary Care*. 2019 Nov 1;8(11):3569-73.
8. Menon VU, Kumar KV, Gilchrist A, Sugathan TN, Sundaram KR, Nair V, Kumar H. Prevalence of known and undetected diabetes and associated risk factors in central Kerala—ADEPS. *Diabetes research and clinical practice*. 2006 Dec 1;74(3):289-94.
9. Mohan V, Deepa R, Deepa M, Somannavar S, Datta M. A simplified Indian Diabetes Risk Score for screening for undiagnosed diabetic subjects. *The Journal of the Association of Physicians of India*. 2005 Sep 1; 53:759-63.
10. Joshi SR. Indian diabetes risk score. *JAPI*. 2005 Sep; 53:755-7.
11. Jain M, Kumar V, Jain M, Garg K, Shekhawat R, Gupta PK. Indian Diabetes Risk Score (IDRS) as a strong predictor of diabetes mellitus: A cross sectional study among urban population of Jhalawar
12. Schwarz PE, Li J, Lindstrom J, Tuomilehto J. Tools for predicting the risk of type 2 diabetes in daily practice. *Hormone and metabolic research*. 2009 Feb;41(02):86-97.
13. Bernabe-Ortiz A, Perel P, Miranda JJ, Smeeth L. Diagnostic accuracy of the Finnish Diabetes Risk Score (FINDRISC) for undiagnosed T2DM in Peruvian population. *Primary care diabetes*. 2018 Dec 1;12(6):517-25.
14. Akter N, Qureshi NK. Comparison of IDRS, ADA and FINDRISC Diabetes Risk Assessment Tools: A Cross-Sectional Analysis in a Tertiary Care Hospital. *Sri Lanka Journal of Diabetes Endocrinology and Metabolism*. 2020 Aug 25;10(2):10-20.
15. Arun A, Srivastava JP, Gupta P, Sachan B, Prakash D, Zaidi ZH. Indian diabetes risk score (IDRS), a strong predictor of diabetes mellitus: A cross sectional study among urban and rural population of Lucknow. *Int J Appl Res*. 2015;1(7):135-8.
16. Ramachandran A, Snehalatha C, Vijay V, King H. Impact of poverty on the prevalence of diabetes and its complications in urban southern India. *Diabetic Medicine*. 2002 Feb;19(2):130-5.

17. Misra A, Pandey RM, Rama Devi J, Sharma R, Vikram NK, Khanna N. High prevalence of diabetes, obesity and dyslipidaemia in urban slum population in northern India. *International journal of obesity*. 2001 Nov;25(11):1722-9.
18. SauravBasu, VanshMaheshwari, Debolina Roy, MahiraSaiyed, RutulGokalani, Risk assessment of diabetes using the Indian Diabetes Risk Score among older adults: Secondary analysis from the Longitudinal Ageing Study in India, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, Volume 18, Issue 5, 2024,
19. Pune - Patil RS, Gothankar JS. Assessment of risk of type 2 diabetes using the Indian Diabetes Risk Score in an urban slum of Pune, Maharashtra, India: a cross-sectional study. *WHO South-East Asia J Public Health* 2016; 5(1): 53–61.
20. Himachal- Kaushal K, Mahajan A, Parashar A, Dhadwal DS, Jaswal V, Jaret P, et al. Validity of madras diabetes research foundation: Indian diabetes risk score for screening of diabetes mellitus among adult population of urban field practice area, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India. *Indian J EndocrMetab* 2017; 21:876-81.

A Study of Biochemical Markers in Alcoholic Liver Cirrhosis

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ABSTRACT:

Liver Cirrhosis is an irreversible result of various disorders that damage liver cells over time. When damage becomes extensive, there is distortion of the normal structure of the live leading to impairment of the liver function. Progressive fibrosis and cirrhosis, clinically presenting as end-stage liver disease are common outcomes in alcoholic Liver disease (ALD) patients. A variety of laboratory tests are available to assist in the progression and diagnosis of cirrhosis to end stage liver disease. The aim of this study is to identify biomarkers for progression of cirrhosis to end-stage liver cirrhosis. A total of 50 subjects were participated in this study. Were diagnosed as alcoholic liver cirrhosis and 50 were normal health subjects. The biomarkers evaluated in this study included liver function indicators including Total proteins, albumins, Globulins, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), Alkaline phosphatase, urea and creatinine, Na, K.

KEY WORDS : Alcohol, Biochemical marker, Total proteins, albumins, Globulins, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), Alkaline phosphatase, urea and creatinine, Na, K,.

INTRODUCTION

Chronic alcohol consumption is a major risk factor for chronic liver disease worldwide. Cardinal features of alcoholic liver disease include simple fatty liver, alcoholic hepatitis, fibrosis or, more seriously, cirrhosis and hepatocellular carcinoma. Over the years Alcohol has been blamed as a true hepatotoxin agent causing liver damage. Cirrhosis is a chronic liver disease that is the result of damage to liver tissue with scarring of the liver causing progressive decrease in liver function, excessive fluid in the abdomen, bleeding disorders, increased pressure in the blood vessels, and brain function disorders. Excessive alcohol use is the leading

cause of cirrhosis. Health risk of alcoholism includes variety of abnormalities including liver disease, heart disease, pancreatitis, central nervous system disorders and certain forms of cancer¹. Alcohol can be manifested in liver damage from fibrosis to end stage of cirrhosis and may eventually lead to carcinoma of liver. The liver is particularly vulnerable to disease related to heavy drinking, most commonly termed as alcoholic hepatitis or cirrhosis. The progression of alcoholic liver disease is characterized by inflammation, necrosis and cirrhosis. When severe liver Cirrhosis ultimately leads to death². Chronic consumption of alcoholic beverages

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is a primary cause of liver injury. Chronic and excessive consumption of alcoholic beverages provokes membrane lipidperoxidation³. The current study can serve as potential diagnostic tools for more specific biomarkers of ethanol-induced diseases. Hence, in our study evaluation of the effect of chronic alcohol consumption on blood, renal and hepatic biomarkers is attempted.

MATERIAL & METHODS:

The present study was carried out in the Department of Biochemistry, Tertiary Care Centre, Sangli. In this study a total number of 100 subjects between age 30 yrs to 60 yrs matched with age and sex are included. The diagnosis of the patients with Liver Cirrhosis was done by the physicians from this hospital on the basis of detailed clinical history, clinical examination & other relevant biochemical investigations.

Inclusion criteria-Age group- 30-60 yrs

Parameters	Group A (Controls) n= 50	Group B (Patients) N=50	'p' value	't' value
AST	29.1 ± 9.9	94.5 ± 88.0	0.0007	3.482
ALT	29.3 ± 9.1	95.1 ± 65.5	0.0084	2.690
ALP	80.3 ± 35.7	110.1 ± 81.64	0.0199	2.366
Total Bilirubin	1.88 ± 1.20	8.73 ± 6.78	<0.0001	4.417
Direct Bilirubin	0.79 ± 0.45	5.53 ± 3.95	0.0001	4.033
Indirect Bilirubin	0.43 ± 0.24	3.95 ± 2.83	<0.0001	4.306
Total Protein	5.66 ± 1.36	5.95 ± 0.72	0.1989	1.293
Albumin	3.07 ± 0.58	3.87 ± 0.96	<0.0001	5.120
Globulin	2.62 ± 0.69	2.87 ± 0.60	0.0548	1.944

Selection- Both males and females

Exclusion criteria- Patients above 60 years and below 30 years of age were excluded from our studies.

Sample size- Total number of samples 100.

OBSERVATIONS AND RESULTS:

Table No.1

Sr. No	Clinical category	No. of patients studied	Study group
1	Control subjects	50	A
2	Liver Cirrhosis	50	B

Table No 2 – Liver Function Tests

Parameters	Group A (Controls) n= 50	Group B (Patients) N=50	'P' value	't' value
AST	29.1 ± 9.9	94.5 ± 88.0	0.0007	3.482
ALT	29.3 ± 9.1	95.1 ± 65.5	0.0084	2.690
ALP	80.3 ± 35.7	110.1 ± 81.64	0.0199	2.366
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AST – Aspartateaminotransferase ALT- Alanine aminotransferase

Table No 3 – Renal Function Tests

Parameters	Group A (Controls) n= 50	Group B (Patients) n=50	'P' value	't' value
Blood Urea	22.42 ± 7.17	56.44 ± 39.33	<0.0001	6.017
Serum Creatinine	0.80 ± 0.30	1.86 ± 1.36	<0.0001	5.408
Na	136.7 ± 4.29	135.06 ± 6.45	0.1377	1.497
K	3.58 ± 0.33	3.79 ± 0.56	0.0280	2.231

DISCUSSION

Excessive chronic consumption of alcohol results in profound alterations in the blood chemistries which may be associated with alterations in metabolic activities of cell resulting in several clinical and/or biochemical changes.

Effect of Chronic Alcohol Consumption on Liver

Chemistries The aspartate aminotransferase, bilirubin and albumin are considered to be well known markers of cirrhosis. We have measured liver function tests, Total protein, renal function test, Glucose. Hyperbilirubinemia were also observed to be common features with alcoholics in our study. The serum transaminases viz, aspartate aminotransferase (AST) and alanine amino-transferase (ALT) are significantly elevated in decompensated cirrhosis as compared to controls and compensated cirrhosis. Following heavy alcohol consumption there has been evidence of mitochondrial damage. In Mitochondrial damage, the elevation in ratio of mitochondrial AST to total AST has also been reported in heavy alcohol consuming individuals. This rise is proportionately higher in alcoholic individuals than healthy individuals which contribute only 10% of mitochondrial AST activity in serum⁴. The pattern of aberration in AST and ALT observed in our study has been correlated well with the reports in the past Ozenirler et. al.⁵ reported rise in values of ALT in decompensated cirrhosis than that of compensated cirrhosis. The values of total bilirubin as reported by Agnieszka-Szuster-Ciesieka et. al. in compensated cirrhosis showed upward trend with progression of cirrhosis⁶. Alkaline phosphatase is a well-known biomarker of liver disease. The article attempts to locate the determinants of alkaline phosphatase of some liver and non-liver patients.

Background Many previous research reports consider alkaline phosphatase as a continuous, homogeneous and normally distributed response variable. In practice, alkaline phosphatase is positive, heterogeneous and non-Normally distributed response variable. There is a little study considering the real fact that the alkaline phosphatase as a non-Normal, heterogeneous and positive response variable

Most data indicate that the elevation of serum ALP occurs because of the accelerated de novo synthesis of the enzyme and subsequent regurgitation into the serum⁷. A number of diseases are related to the elevation of serum ALP. The study of the etiologies of high serum ALP can be useful data in diagnosis. Sepsis-associated cholestasis is a well-known condition, and increased ALP is a common laboratory finding in the patients with intra- or extra-hepatic cholestasis⁸. According to the study of Lee et al, elevated ALP was common in patients who had liver abscess with superimposed Klebsiellabacteraemia⁹

Effect of chronic Consumption on Renal

Chemistries- Our present findings of kidney profile comprising slightly elevated blood urea and serum creatinine in alcoholic cirrhosis when compared to controls and compensated cirrhosis are quite similar to earlier reports of Das et al⁴. The values of bilirubin are associated with urea and creatinine as observed by us may be used as markers in combination for diagnosis for ALD. It has been reported that liver disease has been associated with renal disorders¹⁰. Serum creatinine, another marker of renal function, is a component of the Model for End-stage Liver Disease score, which is used for prognostication and liver transplant

prioritization in patients with various liver conditions¹¹. Accordingly, high urea level also correlates with poor liver outcomes. Recently, several experimental studies revealed that urea synthesis is impaired even in early CLD and this correlates with hepatic fibrosis¹². Additionally, urea cycle dysregulation contributes to carcinogenesis. Therefore, CLD patients with low urea level may have more advanced disease and be at risk of disease progression¹³.

Elevation in serum creatinine is a common laboratory finding for patients with cirrhosis and can indicate the presence of either an acute kidney injury (AKI) or chronic kidney disease (CKD). However, creatinine may underestimate the actual extent of renal impairment, and both serum creatinine and creatinine-based equations for glomerular filtration rate estimation have been proven to be inaccurate for cirrhotic patients¹⁴. Therefore, clinicians should have a low threshold for diagnosis and treatment of kidney injury among patients with cirrhosis. Providers should be cognizant that cirrhotic patients often have lower baseline creatinine levels because of the presence of protein-calorie malnutrition, reduced muscle mass, impaired creatinine production from the liver, and increased renal tubular creatinine excretion¹⁴. Thus the clinical relevance of a single creatinine value requires a comparison with prior laboratory values and interpretation within clinical context. For purposes of this focused review, we will concentrate on the diagnosis and management of AKI, which is the most common

cause of elevated creatinine in cirrhotic patients, occurring in nearly 20% of all cirrhotic hospitalizations. Hyponatremia is an electrolyte imbalance that commonly occurs in hospitalized patients. Most cases are dilutional hyponatremia caused by the impairment of solute-free water clearance. Hyponatremia resulting from the impairment of solute-free water excretion is commonly accompanied by portal hypertension. In recent years, hyponatremia has attracted interest as a possible prognostic factor for liver cirrhosis. To date, no Korean studies have been conducted to examine its prevalence or the concurrent presence of its complications^{15,16}.

CONCLUSION

Alcohol has been blamed as a true hepato toxic agent causing liver damage. Cirrhosis is a chronic liver disease that is the result of damage to liver tissue with scarring of the liver causing progressive decrease in liver function, excessive fluid in the abdomen, bleeding disorders, increased pressure in the blood vessels, and brain function disorders. The present study has found significant association between severity of liver dysfunction and some parameters of renal dysfunction. Further studies are warranted to find out correlation between the concentration & period of alcohol exposure, degree of liver damage and alterations in liver chemistries. This will help the physicians to treat and early remedial measures for alcoholic liver cirrhosis.

REFERENCES

1. Alcoholics – A case control study, B. Usharani, R. Vennila and N. Nalini. *Biochemical changes in Alcoholics – A case control study*. 2012, 3 (1): 201-205.
2. Felver ME, Merzey E and Herlong HF. Plasma tumor necrosis factor, a predicts decreased long term survival in severe alcoholic hepatitis. *Alcohol Clin. Exp Res*. 1990; 31: 117-134.
3. Uma DJ. Serial review: Alcohol, oxidative stress and cell injury free. *Radi. Biol. Med*. 2002; 32: 303-308.
4. SK Das, P Nayak and D.M.Vasudevan, Biochemical markers for alcohol consumption, *Indian Journal of clinical biochemistry*. (2003), 18 (2) 111-118.
5. AgnieszkaSzuster-ciesielska, Jadwiga Danlluk, MartyaKandferSzerszen. Oxidative stress in the blood of patients with alcoholrelated liver. *Med Sci Monit*, (2002); 8 (6): CR 419-424.
6. SerenOzenirler, BanuSancak and Ugur Coskun. Serum and ascitic fluid superoxide dismutase and malondialdehyde levels in patients with cirrhosis. *Biomarker Insights*, (2008); 3: 141-145.
7. Reichling JJ, Kaplan MM: Clinical use of serum enzymes in liverdiseases. *Dig Dis Sci*1988, 33:1601-1614
8. Jansen PL, Muller M: Early events in sepsis-associated cholestasis. *Gastroenterology* 1999, 116:486-8.
9. Lee KH, et al: Klebsiellabacteraemia: a report of 101 cases from National University Hospital, Singapore. *J Hosp Infect*1994, 27:299-305
10. Larson K.Determination of serum creatinine *clin.chem. acta*(1972);41.209Francoz C, Prie D,
11. Yip TC, Chan HL, Tse YK, Lam KL, Lui GC, Wong VW, et al. On-treatmentimprovement of MELD score reduces death and hepatic eventsin patients with hepatitis B-related cirrhosis. *Am J Gastroenterol*2018;113:1629-1638
12. Thomsen KL, Grønbaek H, Glavind E, Hebbard L, Jessen N, CloustonA, et al. Experimental nonalcoholic steatohepatitis compromisesureagenesis, an essential hepatic metabolic function. *Am J PhysiolGastrointest Liver Physiol* 2014;307:G295-G301.
13. Lee JS, Adler L, Karathia H, Carmel N, Rabinovich S, AuslanderN,et al. Urea cycle dysregulation generates clinically relevant genomicand biochemical signatures. *Cell* 2018;174:1559-1570.e22.
14. Abdelrazek W, Moreau R, Mandot A, Belghiti J, et al. Inaccuracies of creatinine and creatinine-based equations in candidates for liver transplantation with low creatinine: impact on the model for end-stage liver disease score. *Liver Transpl* 2010;16:1169-1177.
15. Adrogué HJ, Madias NE. Hyponatremia. *N Engl J Med* 2000; 342:1581-1589.
16. Gines P, Berl T, Bernardi M, et al. Hyponatremia in cirrhosis: from pathogenesis to treatment. *Hepatology* 1998;28:851-864.