"PREVALENCE OF MASKED HYPERTENSION IN CHILDREN WITH CHRONIC KIDNEY DISEASE AND EVALUATION OF LEFT VENTRICULAR FUNCTION- A CROSS SECTIONAL STUDY"

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LIST OF ABBREVIATIONS USED

CKD	CHRONIC KIDNEY DISEASE
HTN	HYPERTENSION
FSGS	FOCAL SEGMENTAL GLOMERULOSCLEROSIS
SSNS	STEROID SENSITIVE NEPHROTIC SYNDROME
SRNS	STEROID RESISTANT NEPHROTIC SYNDROME
ABPM	AMBULATORY BLOOD BRESSURE MONITORING
CBP	CASUAL BLOOD PRESSURE
RBC	RED BLOOD CELL
ESRD	END STAGE RENAL DISEASE
KDIGO	KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES
CAKUT	CONGENITAL ANOMALIES OF KIDNEY AND URINARY TRACT
AKI	ACUTE KIDNEY INJURY
LVH	LEFT VENTRICULAR HYPERTROPHY
CKD-ND	CHRONIC KIDNEY DISEASE NOT ON DIALYSIS
ROD	RENAL OSTEODYSTROPHY
SHPT	SECONDARY HYPERPARATHYROIDISM
ECHO	ECHOCARDIOGRAPHY
ANA	ANTI NUCLEAR ANTIBODY
MH	MASKED HYPERTENSION
SLE	SYSTEMIC LUPUS ERYTHEMATOUSUS

ABSTRACT

"PREVALENCE OF MASKED HYPERTENSION IN CHILDREN WITH CHRONIC KIDNEY DISEASE AND EVALUATION OF LEFT VENTRICULAR FUNCTION- A CROSS SECTIONAL STUDY"

Background:

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for at least 3 months, with implications for health. Common causes include congenital anomalies of kidney and urinary tract (CAKUT), focal segmental glomerulosclerosis (FSGS) and lupus in older children. Hypertension and left ventricular hypertrophy are commonly associated co morbidities. Hypertension may be missed clinically but detected by ambulatory bp measurement. This is called masked hypertension. It is associated with accelerated disease progression. Due to limited studies in India, our study aims to fill this lacuna that is important for early risk stratification and management

Objectives:

- Primary Objective: To identify the prevalence of masked hypertension in children with chronic kidney disease
- Secondary objective: to evaluate left ventricular hypertrophy in children with chronic kidney disease using echocardiography

- **Settings and Design:** It is a cross-sectional study carried out in 30 patients who had chronic kidney disease presented to Pediatric department of Dr Prabhakar Kore Hospital & MRC Belagavi, Karnataka, India. clinical data were collected from patients. Measurements of casual blood pressure and ambulatory blood pressure 24 hour was taken. 2d echocardiography was done.

Results: The data contains measurement on 30 subjects whose age ranges from 4 to 17 years with mean age 11.57 ± 3.83 years. Out of 30 subjects, 21 (70%) were males and 9 (30%) were females. Among 30 subjects, 12 (40%) were found to have masked hypertension, whereas 18 (60%) were not found to have masked hypertension. Out of 30 subjects, 7 (23.33%) had stage 4 CKD while 10 (33.33%) had stage 5 CKD. LVH on ECHO showed Mitral regurgitation in 1 (3.33%) subject.

Conclusion:

Ambulatory blood pressure monitoring should be considered as gold standard to detect masked hypertension since it gives an important clue for early identification of hypertension as well as cardiovascular risk stratification in children with chronic kidney disease. As hypertension is a co morbidity known to be associated with accelerated disease progression, early screening and management can help in better treatment and prognosis.

Keywords: chronic kidney disease, ambulatory blood pressure monitoring, masked hypertension, left ventricular hypertrophy

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INTRODUCTION

Chronic Kidney Disease (CKD) involves a gradual loss of kidney function and kidneys lose their ability to filter waste and fluid out of blood. [1]

According to global association for evidence-based knowledge on kidney problems, Kidney Disease Improving Global Outcomes (KDIGO), "CKD is defined as abnormalities of kidney structure or function, present for at least 3 months, with implications for health." [2]

Chronic kidney disease does not have many symptoms and has a silent progression as it is associated with compensation by the other working nephrons.

Hypertension (HTN) can appear at disease onset itself in contrast to other complications that present only in late stages. [3]

It is seen in children affected with CKD commonly and is also involved in acceleration of the disease process. Studies done in the western world have observed that around one fourth of total patients of CKD have elevated casual blood pressure (CBP) that is measured by sphygmomanometer. Such cases of hypertension are common but most of them are not on any treatment for the same. [4,5] This further stresses that the diagnosis of hypertension may not be brought to light early in patients.

Blood pressure (BP) monitoring done by Oscillo metric device over 24 hours is called ambulatory bp monitoring (ABPM). This is more beneficial in detecting HTN in CKD than office bp recording. This is known as masked hypertension that is missed clinically. It helps in early identification of hypertension. [6]

Due to its silent progression, it is extremely important to know about the course of disease and the co morbidities associated with it. The most common co morbidities associated with ckd include hypertension, diabetes and hyperlipidaemia and left ventricular failure. [7] In a study done by mitsefenes et al [8], it was found that a 17% of patients had LVH. Elevated casual bp was seen in18% . there is lack of information on ckd in children, hence it is difficult to comment in the burden of ckd in the country. [9] In the largest multicentric prospective study done on children with ckd, the effects of elevated blood pressure and cardiac ailments in CKD were noted on the disease process as well as on the implications on future health. [7] It was noteworthy that masked hypertension was seen in more than twice the patients with clinically confirmed hypertension. The children who had hypertension were at higher risk of developing LVH than their normotensive counterparts. [8]

ABPM helps in detection of masked hypertension. More patients with masked hypertension were seen to have LVH and hence it is shown to be of greater importance than office bp recording in CKD patients.

The prevalence of LVH in CKD ranges from one fourth to half of the total diseased population and thus raises concerns. [9] the pathogenesis of hypertrophy might start early on and if the acceleration is not watched for, it may lead to complications. It may progress to irreversible damage to the cardiovascular system. [10] The role of hypertension in the development of LVH has been discussed widely in the adult population but less so in children. [8] In adults with CKD, LVH is a common cause of morbidity and mortality.

Multiple obstacles and limitations have caused delayed diagnosis of disease, mostly in the late stages. More than half of the patients are diagnosed when they have developed 5th stage. [11] Hence it is of paramount importance to have robust screening programs for this disease with silent progression. Identifying and staging childhood kidney disease (CKD) requires a strict methodology suitable for children who have a higher chance of developing the disease.

This needs to be emphasized to not only by specialists of various fields but by all health care workers. [12] CKD in children carries a significant impact. The mortality that is associated with ESRD in children who receive dialysis is estimated to be at least 30 times higher than that in the general pediatric population. [13]

Our goal is identification of masked hypertension and noting its role in LVH. [14] Existing literature shows that the high prevalence of masked hypertension and its association with LVH supports early echocardiography and ambulatory BP monitoring to evaluate cardiovascular risk in children with CKD. [8] Further vision of this study include-

- Timely identification of hypertension in such children and initiation of management of the same, have improved clinical outcome, quality of life and shorter duration of hospital stay.

- Planning the course of treatment for a child with chronic kidney disease (CKD) is aided by the early identification of factors that may accelerate the progression of renal disease.

The disease management is focussed on arresting further acceleration and preventing complications. Timely diagnosis and management have a favorable effect on the outcome and the quality of life. Providing access to interventions that can have a positive impact if given in time is paramount. [15] In patients who are diagnosed early, proper medical management and emphasis on holistic development of the child such as in education, growth, social standing and vocational training can help in improving the future aspects of the child.

AIM & OBJECTIVES

OBJECTIVES:

- Primary Objective: To identify the prevalence of masked hypertension in children with chronic kidney disease

- Secondary objective: to evaluate left ventricular hypertrophy in children with chronic kidney disease using echocardiography

REVIEW OF LITERATURE

Background

CKD is a slowly progressing disease and leads to serious health implications including death in paediatric population. It cannot be only referred to as failure as previously called since it is a spectrum and not limited to the end stage only.

Clinical suspicion, appropriate laboratory test and imaging plays a role in diagnosis. CKD is classified into various numerical stages on the basis of estimated glomerular filtration rate (eGFR). Since nearly two thirds of renal function has already been compromised by the time absolute s. creatinine rises, it is a late sign of kidney injury. [16]

In children, the most frequently used creatinine-based eGFR equation is the revised bedside Schwartz: [(0.413 × Height (cm)) / Scr (mg/dL)]. [17] This is the formula used for children between 2-18 years of age.

Stage	Description	eGFR(ml/min/1.73m2)
I	Kidney damage with normal or increased GFR	>90
II	Kidney damage with mild decrease GFR	60-89
III	Moderate decrease GFR	30-59
IV	Severe decrease GFR	16-29
V	Kidney failure	<15

Table 1- stages of chronic kidney disease according to KDIGO

Incidence

Worldwide, It is variable between 3-12 per million in pediatric population [18] The reported prevalence of CKD in different regions also varied widely. [19,20] Lack of uniformity in choosing the cut off for the disease in earlier studies and lack of reporting from low resource countries are two important lacunae in data around the disease.

Fortunately, newer cases are not emerging at the same rate that they were 2 to 3 decades back. [21] However due to marked advancement in treatment and timely diagnosis, the prevalence has been on an increasing trend.

Pathophysiology

Barry Brenner of the Brigham and women's hospital, author of the well-known book, "The Kidney" postulated in 1988 that low birth weight and preterm babies have a lower number of working nephrons and this is a risk factor developing CKD. [22] Intrauterine growth retardation (IUGR) and low birth weight are strongly associated epidemiologically with hypertension. This is explained by the fact that the remaining nephrons' compensatory hyperfiltration causes sodium and fluid retention, which raises the risk of hypertension and glomerular injury and accelerates the process of renal decline. [23]

The genetic background of the disease is complex. Not only the disease-causing genes, that are known for disease determination but also many other genes are now recognized as involved in the disease process. APOL1 is one such gene implicated and heightens adverse possibilities.

Normally, the APOL1 genes make a helpful immune system protein. one or both APOL1 genes can be mutated. It can cause damage to the glomerulus and can cause cell death which leads to damage and scarring in the kidneys and can lead to kidney failure. if one inherits a mutation in both copies of the APOL1 gene, you have a 10 times higher chance of FSGS than people without the gene mutation. [(24)]

Growth hormone and insulin like growth factor 1 levels get altered in the disease. Decreased vitamin D levels, increased parathyroid hormone levels and acidosis also affect growth. [(25)] phosphate accumulation and reduced calcium assimilation from GIT and kidneys leads to impaired metabolism. There is secondary rise in parathormone thus leading to renal osteodystrophy (ROD). [(26)] This leads to fibrosis that hinders growth of bones.

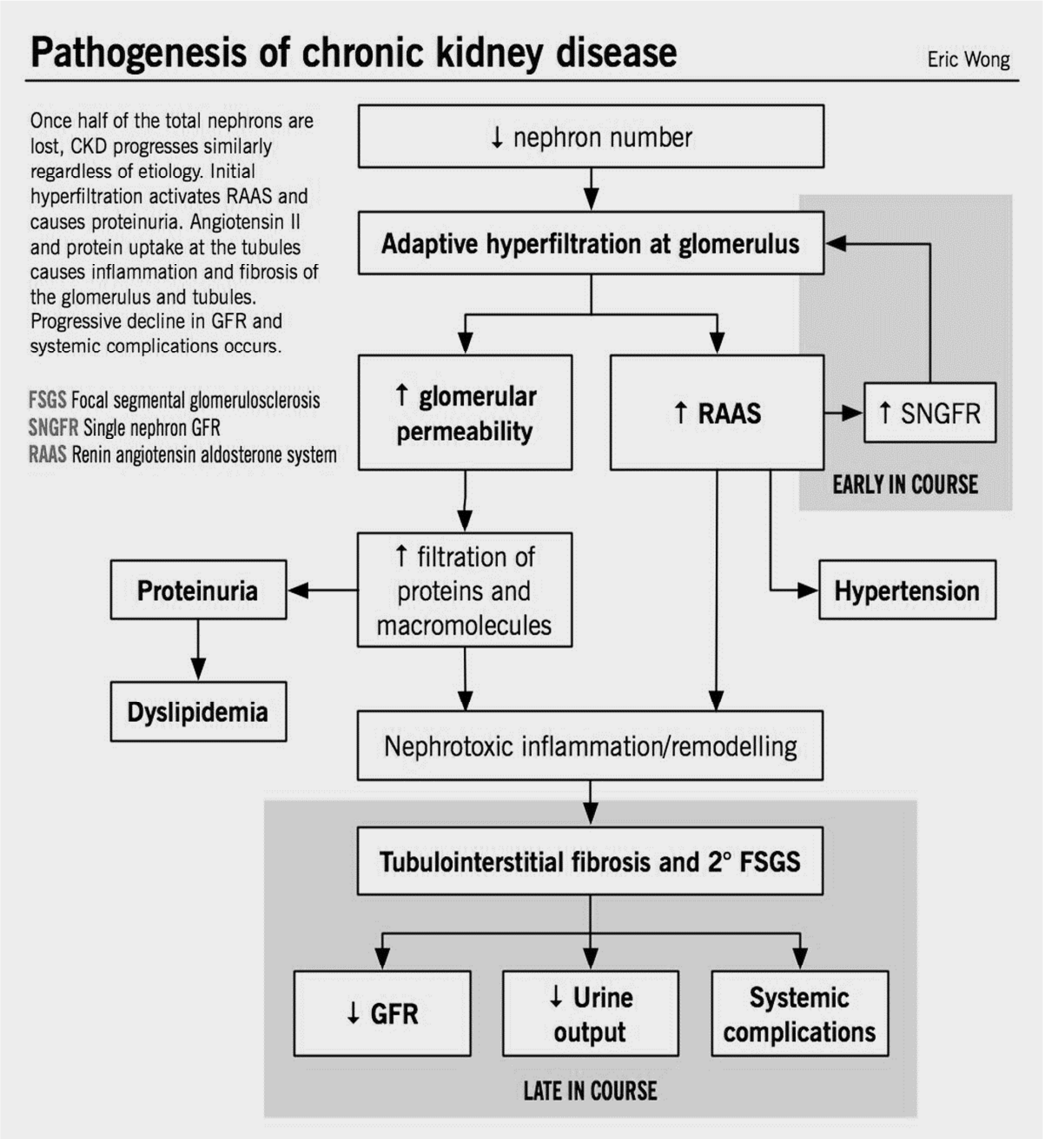

Figure 1 pathogenesis of chronic kidney disease [(27)]

Etiology

The causes of CKD vary according to age. In newborns, causes include congenital anomalies of kidney and urinary tract (CAKUT) that encompasses posterior urethral valve (PUV) especially those with concomitant vesicoureteric reflux, renal dysplasia, polycystic kidney disease (PCKD) among others.

A study by Xinmiao Shi et al [28] in China threw light on the inpatient load of pediatric ckd patients in the country. Nephrosis due to other disease was shown to be the most common cause followed by CAKUT then glomerular problems and multicystic disease. IgA nephropathy was the most common finding in biopsy of the children.

In infancy, causes include congenital nephrotic syndrome, hydronephrosis, hemolytic uremic syndrome of complement mediated type.

In younger children, focal segmental glomerulosclerosis (FSGS) and diffuse mesangial sclerosis (DMS) are histological types commonly associated with progression to CKD. Glomerular diseases are seen after 2 years of age. They include IgA glomerulopathy, Henoch Schoenlein purpura, membranoproliferative glomerulonephritis, Alport's syndrome.

Autoimmune causes like lupus is seen in older children. [28]

CKD Etiology	Percentage (range)	ESRD Etiology	Percentage (range)
CAKUT*	48%–59%	CAKUT	34%–43%
GN†	5%–14%	GN	15%–29%
HN‡	10%–19%	HN	12%–22%
HUS¶	2%–6%	HUS	2%–6%
Cystic	5%–9%	Cystic	6%–12%
Ischemic	2%–4%	Ischemic	2%

Rare causes include congenital NS, metabolic diseases, cystinosis. Miscellaneous causes depend on how such entities are classified.
*CAKUT: Congenital anomalies of the kidney and urinary tract
†GN: Glomerulonephritis, ‡HN: Hereditary nephropathy, ¶HUS: Hemolytic uremic syndrome
From Harambat, *et al*. CKD data are from NAPRTCS, the Italian Registry and the Belgian Registry.
ESRD data are from ANZDATA, ESPN/ERA-EDTA, UK Renal Registry and the Japanese Registry.

Figure 2 causes of ckd data from various international studies [29]

Clinical presentation

Clinical features of CKD also vary according to age.

Newborns and Infancy

Persistent vomiting, failure to thrive and persistent anemia are seen. In patients with PUJ obstruction, presentation may be with recurrent episodes of fever with poor stream of urine and burning micturition indicative of urinary tract infection.

Early Childhood

Failure to gain weight and height is noted along with features of rickets, earliest sign being bowing of legs after the child starts walking. Growth impairment is a commonly seen complication. Anemia is a common complication in children with CKD causing many adverse clinical consequences, including poor quality of life, depressed neurocognitive ability, reduced exercise capacity and progression of cardiovascular risk factors, such as left ventricular hypertrophy (LVH). An important marker to differentiate between nutritional rickets and vitamin D resistant rickets secondary to chronic kidney disease is the association of failure to thrive in the latter.

Hypertension in CKD

Multiple factors like impaired vascular regulation with fluid overload, peripheral vascular resistance, increased cardiac output can lead to HTN. [30] Due to reduced blood flow to the kidneys that causes kidney damage, there is secretion of rennin. This causes angiotensin 2 to be released and leads to constriction of vessels. There is also sodium accumulation which could be volume dependent or independent. Increased arterial pressure and decreased nephrons stressing to increase their filtration rate are other factors that contribute to HTN. [31]

A child is diagnosed with hypertension when their average blood pressure is at or above the 95th percentile for their age, sex and height when measured multiple times over at least three visits. [32] A very stark contrast exists between prevalence of hypertension in children being only up to 9% while HTN being prevalent in almost half the children with CKD. [33]

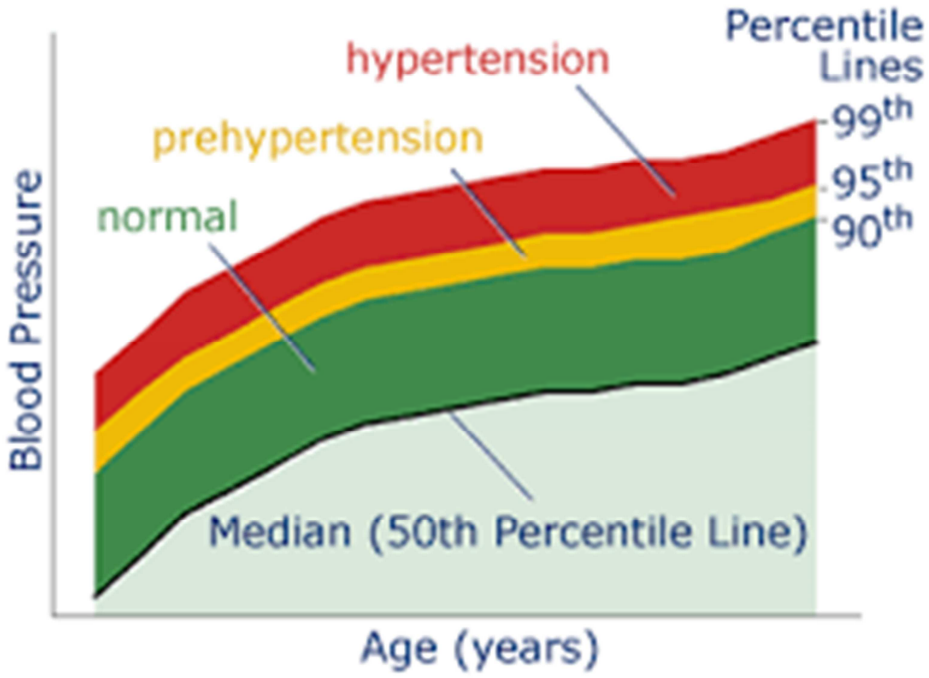

Figure 3 Blood pressure reference

TABLE II–*Blood Pressure (BP) Levels for Girls by Age and Height Percentile*

Age (yr)	BP percentile	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile							Height percentile						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79

Figure 4 normative data on blood pressure values, based on age and height percentiles, derived from a large multiethnic cohort of children in USA

One of the largest multicentric studies done on children with CKD noted that nearly half of the children with CKD had HTN by ABPM [(7)] This finding was then reinstated by a registry which also showed that almost half the pediatric population with CKD was affected with HTN. [(34)] Bp can be measured by manual sphygmomanometer which is known as office bp. A disadvantage is that it can lead to erroneous reading due to anxiety in the patient at the time of measurement in hospital setting. This is known as white coat hypertension. [(35)] Ambulatory BP monitoring is considered the gold standard technique for BP assessment; studies have shown that it helps in stratifying cardiovascular risk better. [(36)]

In a recent study by Goulas et al [37] an overall pooled masked HTN prevalence of 27% was estimated in 1110 participants of chronic kidney disease. Ambulatory bp monitoring can help in detecting hypertension early.

A recent update from American heart association states that It was noted that the major advantages of ABPM are to mitigate spuriously elevated BP from measurement anxiety (i.e. white coat hypertension [WCH]), and to assess circadian BP patterns. Masked hypertension is diagnosed when the casual BP is normal but ambulatory blood pressure is above normal limits. it can be identified as isolated elevated wake BP, isolated elevated sleep BP (nocturnal hypertension), or the combination. A recent update in the system takes into account single cut off point for elevated ambulatory BP and negates the use of BP load. [38] Although there are multiple studies done across Europe and America, there is still paucity of literature in the Indian pediatric population. [39]

category	Clinical SBP OR DBP		Mean ambulatory SBP or DBP	
	<13 years	>13 years	<13 years	>13 years
Normal BP	<95th centile	<13o/8o	<95th centile	<125/75 24 hr or <130/80 wake period and <110/65 sleep
White coat hypertension	≥95th centile	≥13o/8o		
Masked hypertension	<95th centile	<13o/8o	≥95th centile	≥125/75 24 hr or ≥130/80 wake period and ≥110/65 sleep
Ambulatory hypertension	≥95th centile	≥13o/8o		

Table 2- updated key for ABPM studies in children

A study done by Gupta et al [(6)] on ambulatory bp monitoring in children with chronic kidney disease showed that ambulatory bp monitoring was better in detecting hypertension in children with ckd. This masked hypertension was also found to be associated with left ventricular hypertrophy. Although it is one of the few such studies done in Indian pediatric population, shortcomings of this study were that children on antihypertensives were also included in the study. This made diagnosing masked hypertension difficult and erroneous. The duration of CKD since diagnosis was taken as 2 months. This would exclude a few newly diagnosed patients that could be part of the study.

LVH in CKD

Conditions like coronary artery disease, congestive heart failure, arrhythmias, and sudden cardiac death are the primary contributors to illness and death among individuals with CKD and is said to be a part of cardiorenal syndrome. [41]

[42] although well known in older population, it is not as well understood in children. [8]

In a study done by Mitsefenes et al,[8] LVH, with a prevalence ranging from one fourth to almost half the patients with CKD is the most common cardiac irregularity seen. This reiterates the fact that it develops early into the disease process and it increase the chances of cardiac disease. To decrease the risk of future morbidity and mortality it is imperative to understand the determinants that cause this LVH.

Aetipathogenesis of LVH in CKD can be attributed to a host of factors.

Firstly, HTN as discussed earlier involved RAAS activation that leads to increased arterial pressure and this is seconded by eventual decreased vessel wall compliance. This causes concentric remodeling and thickening of the LV. Sodium and water retention causes intravascular fluid expansion. The presence of anemia in patients with CKD further contributes to increase in preload. This causes eccentric LV remodeling.

Both factors related to afterload and preload work together causing a synergistic result. [42] Consequently, this myocardium thickening causes release of apoptotic enzymes and increased extracellular matrix production, both of which cause fibrosis. This progressively impairs contractility, stiffens the myocardial wall, and causes dysfunction, eventually resulting in failure. It also causes re-entry arrhythmia due to disturbance in passage of electrical signals. Activation of the RAAS leads to

increased aldosterone levels, which causes activation of growth factors that promote fibrosis.

Other factors that promote LVH include reduced erythropoietin or fall in vitamin D and iron levels. AV fistulas cause increased blood flow causing heightened work for the heart.

A study done in India [(43)] focused on comorbidities in children with CKD. Commonly seen co morbidities included HTN, decreased vitamin D levels, stunting, increased triglyceride levels, LVH, hyperparathyroidism. HTN, LVH were present even during disease onset unlike other co morbidities that manifest in later stages.

A study in Spain [(44)] In this study it was noted that masked hypertension is a predecessor of sustained hypertension and left ventricular hypertrophy in older children.

In a cohort study conducted on Left ventricular mass and cardiac function in a population of children with chronic kidney disease, in Italy in 2014, [(45)] The study cohort comprised 34 pediatric patients with CKD and 34 healthy children (mean ± standard deviation: age 9 ± 4.6 and 8.2 ± 4.3 years, respectively). LVH was defined as a left ventricular mass index (LVMI) of >95th percentile (38 $g/h^{2.7}$). Left ventricular hypertrophy was present in 13 patients (38 %) .

In a study by Matteucci et al [(46)] Concomitant echocardiograms and 24-h ambulatory BP monitoring (ABPM) profiles were obtained from seven European countries. This study also showed that remodelling occurred in the heart early on in the disease. In the study it was noted that LVH was more common in boys and those who had anaemia and no correlation with BP was seen. The study was done 15 years

back and many technological advancements in ABPM device and readings have been made so as to make it more accurate. Hence the absence of correlation of bp and left ventricular hypertrophy does not hold meaning in the current scenario.

In a study done by Anke Doyon et al [47] which conducted tissue doppler studies on CKD patients showed reduced LV function. The study also described how RAAS blockers benefitted patients in preserving LV function. Therefore the stage of kidney disease as well as antihypertensive contributed to diastolic function. Subtle changes in systole can be detected by doppler even in presence of normal echo findings.

This study done with advanced technology like doppler further reiterates how left ventricular dysfunction is an important and significant comorbidity associated with chronic kidney disease. The limitation of the study is that it only includes participants from advanced kidney disease where chances of all morbidities are higher.

A study by Katherine R. Tuttle et al.[48] The Center for Kidney Disease Research, Education, and Hope (CURE-CKD) registry has comprehensive patient-level electronic health record from more than 2.6 million adults and children with CKD and at risk of CKD during 12 inclusive years i.e. from 2006 to 2017 in USA.

The study focused mainly on co morbidities predisposing to ckd in adults and the adverse effects of use of nephrotoxic drugs like Non-steroidal anti-inflammatory drugs (NSAIDs) and the role of Reno protective agents like ACE inhibitors.

A study done by Kula AJ et al [49] shows the plight of pediatric patients of CKD in the United States where some regions do not have a certified nephrologist. These children receive renal replacement therapy as either dialysis treatment or transplant late as they are detected late into the disease. The length of stay of advanced stage disease, often in presence of LVH was also noted to be longer than normal hospitalisation, putting emphasis on the socioeconomic burden of the disease.

Treatment

The 2009 KDOQI Clinical Practice Guideline for Nutrition in Children with CKD [50] and A set of recommendations by an international taskforce [51] suggested that the children should eat protein that is the maximal limit of recommended dietary allowance at disease onset itself so as to improve growth and then can be modulated on the basis of urea levels. Fat intake and simple carbohydrate intake should be limited and patients should be encouraged to take more complex carbohydrates and fibre rich diet.

Good nutrition with judicious calcium supplementation that is required for growth is important. Vitamins can be supplemented in deficient patients.

Antihypertensives in CKD

In the ESCAPE trial [52], calcium-channel blockers were used as first choice anti-hypertensive co-medication (in 38% of patients), followed by diuretics (in 36%) and beta-blockers (in 26%), without differences between the randomization groups. Other guidelines suggest diuretics or calcium-channel blockers as the most suitable second-line agents.

Kidney international [53] recommends that in children with non-dialysis dependent CKD (CKD ND), BP lowering treatment is started when BP is consistently above the 90th percentile for age, sex, and height.

Additional recommendations suggest that in children with CKD ND, especially those with proteinuria, blood pressure should be lowered consistently to attain systolic and diastolic readings equal to or below the 50th percentile for the said induvial. It has also been shown that ACE inhibitors or ARB have a reno protective role are of benefit even in patients losing protein in their urine in high amounts.

New Therapeutic Perspectives For Paediatric CKD

Table 1: Pipeline clinical trials in pediatric CKD patients.

Clinical target	Mechanism	Drug	Trial phase	Trial identifier
Bone metabolism	Calcium-sensing receptor agonist	Cinacalcet	III	NCT02138838
Bone metabolism	Calcium-sensing receptor agonist	Cinacalcet	III	NCT01290029
Bone metabolism	Calcium-sensing receptor agonist	Cinacalcet	II	NCT01439867
Bone metabolism	Calcium-sensing receptor agonist	Cinacalcet	III	NCT02341417
Bone metabolism	Calcium-sensing receptor agonist	Etelcalcetide	III	NCT03633708
Bone metabolism	Calcium-sensing receptor agonist	Etelcalcetide	I	NCT02833857
Bone metabolism	Calcium-sensing receptor agonist	Etelcalcetide	III	NCT03969329
Anemia	HIF2 inhibitor	Vadadustat	III	NCT05082571
Anemia	HIF2 inhibitor	Vadadustat	III	NCT05082584
Anemia	HIF2 inhibitor	Roxadustat	III	NCT04925011
Hypertension	MRAs	Finerenone	III	NCT05196035
Hypertension	MRAs	Finerenone	III	NCT05457283
Bone metabolism	Phosphate binder	Lanthanum Carbonate	II	NCT01696279
Hyperkalemia	Potassium binder	Patiromer	II	NCT03087058
Inflammation	Triterpenoid	Bardoxolone	III	NCT03749447

Figure 5 clinical trials in children with CKD [54]

In coming few years calcium metabolism targeted drugs similar to cinacalcet are expected to enter into use.

Recent preliminary studies indicated that SGLT2 inhibitors are shown to be helpful in proteinuria. Although results are promising, trials have not been registered specifically to CKD patients.

Prognosis

The demand for paediatric nephrologists in a developed superpower like USA[56] only goes on to reflect the dire need for the specialists in developing, large population, low income resource limited countries like India. [55] Due to improved healthcare and better survival, children with CKD have a longer lifespan now. The emergencies in childhood like acute kidney injury is being managed timely therefore improving the lifespan and survival.

Therefore proper management and prevention of complications in childhood can result in healthier adulthood devoid of co morbidities. Hence it is important that physical, cognitive, and social resources be made accessible to all paediatric patients. special attention should be given to children with ckd because their disease aetiology, progression and effect on growth and development varies vastly from that of adults.

Chronic kidney disease is a disease with gradual progression hence without adequate monitoring it may lead to delayed treatment and patient will already be in later stages.

METHODOLOGY

Study design

Cross sectional study design was chosen to meet the objectives of the study. Cross-sectional studies are carried out either at one time point or over a short period. They're frequently used to figure out how common a particular outcome is in a given population. Individual characteristics, such as risk factor exposure, can also be collected, as well as information on the outcome. In this way cross-sectional studies provide a overview of the outcome and the characteristics associated with it, at a specific point in time. Hence, this study design was considered appropriate for the present study.

Study population

- Children with chronic kidney disease admitted in the department of Pediatrics at KLE's Dr Prabhakar Kore Hospital & MRC Belagavi, Karnataka, India.

Study Time:

Research study was conducted for 12 months from January 2023 to December 2023.

Sampling procedure

Sampling is defined as the process of selecting a number of subjects from all the subjects available in a particular group or universe. A conclusion based on sample results may be attributed only to the population sampled.

In this study we considered all eligible patients consecutively admitted in the department of Pediatrics at Dr Prabhakar Kore Hospital & MRC Belagavi with chronic kidney disease till we meet the sample size.

Inclusion criteria

- All children aged from 3 to 18 years diagnosed with chronic kidney disease.

Exclusion criteria

- Children with chronic kidney disease on antihypertensives
- Congenital heart disease
- Acquired heart disease

Sample size

Sample size was calculated assuming the proportion of chronic kidney disease as 6.3% as per the study by Varma PP **e**t al [(56)] sample size took into account 5.8% absolute precision and ninetyfive% confidence. The formula shown below was used in our study. Hospital health data was examined and it was suggested that fifty potential eligible subjects would come to the hospital during study period. Therefore for 50 population correction was done. Daniel WW et al. [(57)] was followed to make the sample size.

Where n = Sample size

N= Population Size= 50

Z= Z statistic for a level of confidence level= 1.960

P = Expected prevalence/proportion of outcome= 0.063

d = Precision= 0.057999999999999996

The sample size according to the formula used was 29. 1more sample is taken to cover for not agreeing for participation. There fore the final sample size becomes thirty.

Method of data collection

All subjects were explained regarding the study method and due informed consent was taken verbally and in writing. Cases are those patients with idiopathic nephrotic syndrome admitted in the department of Pediatrics at KLE's Dr Prabhakar Kore Hospital & MRC Belagavi.

Criteria for diagnosing chronic kidney disease was according to KDIGO guidelines.

We recorded casual bp using sphygmomanometer with age-appropriate size cuff. Bp was taken with the patient in supine position, the bp machine being placed at the level of the heart. Average of 3 readings were taken. We have then attached on Trak spacelabs monitor Oscillo metric device [58] with age-appropriate cuff and recorded 24hour ambulatory bp. Daytime readings were taken thrice in an hour at 20 minute interval and nighttime readings were every 30 minutes. SBP and DBP means were calculated for 24 hours that included sleep and awake categories. The monitor was attached at the arm and secured with a sling. The patient was instructed to carry out all daily activities and to only remove the monitor at the time of bathing. 2D echocardiography was done.

Age, sex, stage of kidney disease, etiology of the disease, symptoms, anthropometric data such as weight for age and height for age, presence of masked hypertension, nocturnal dip, albuminuria, left ventricular hypertrophy on echocardiography, anemia were our study parameters.

Measured parameters:

- Masked hypertension
- Left ventricular hypertrophy
- Anthropometric data
- The various lab parameters studied are

✓ Hemoglobin

✓ Total leucocyte count

✓ Platelet count

✓ Peripheral smear

✓ Urea

✓ Creatinine

✓ Serum albumin

✓ Urine albumin

Figure 1 spacelabs ontrak ambulatory bp monitor validated internationally [59]

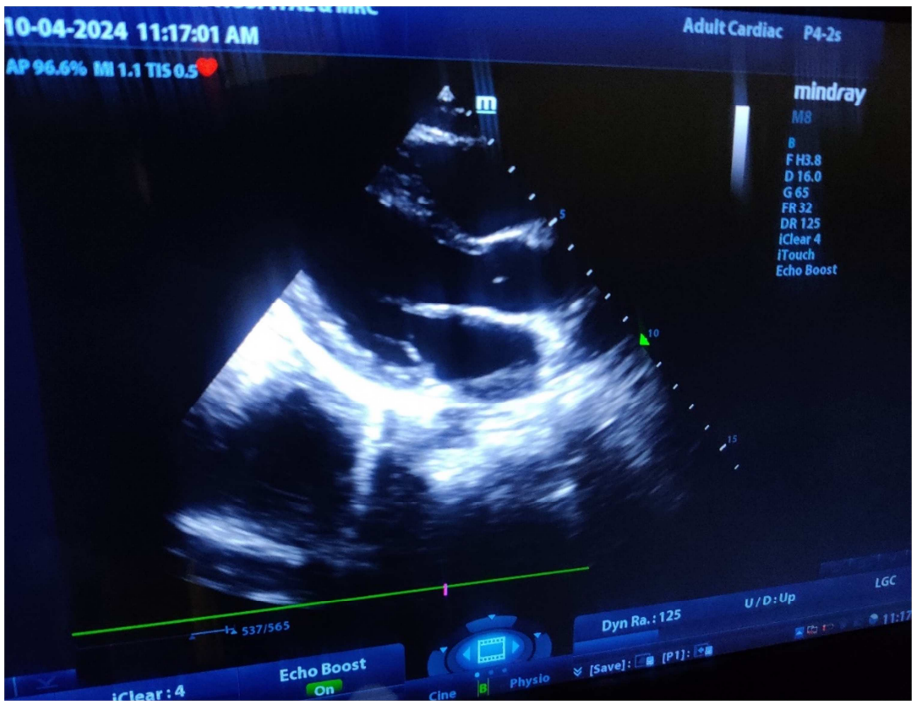

Figure 2 2D echocardiography

Ethical Consideration

Ethical clearance was taken from Ethical Committee of Dr Prabhakar Kore Hospital & MRC Belagavi before conducting the study.

Statistical Analysis

R software version 4.3.3 and MS excel were used to analyzing the data. frequency table was made for variables that could be made into categories. variables that were continuous were given in Mean taking into account standard deviation. Other values such as Median (Min, Max) form was included. Employing Chi-square test helps in dependency among variables that are categorical. Variable normality is checked by two tests that are Shapiro Wilk test and also QQ plot. Two-sample t-test is undertaken so that mean of variables over masked hypertension can be juxtaposed. Mann Whitney U test was used to compare the distributions of variables over masked hypertension. P-value ≤ 0.05 was considered statistically significant.

RESULT :

The data provided includes 30 subjects. The age group starts from 4 up to 17 years. 11.57 ± 3.83 years is the mean age. Demographic details are described in the below mentioned table.

Table 3: Distribution of subjects according to demographic details.

Variables	Sub Category	Number of subjects (%)
Age (years)	Mean ± SD	11.57 ± 3.83
	Median (Min, Max)	12 (4, 17)
Sex	Female	9 (30%)
	Male	21 (70%)

Out of 30 subjects, 21 (70%) were males and 9 (30%) were females.

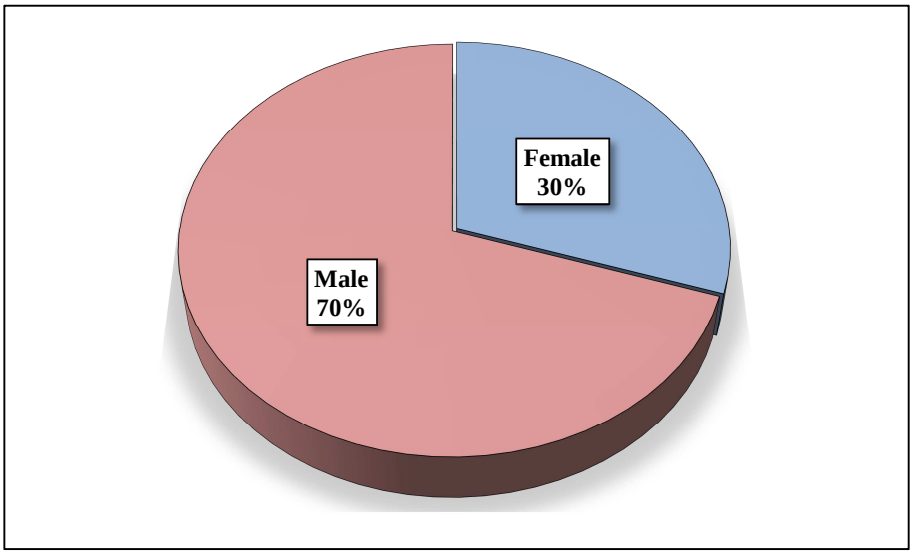

Figure 8: sex description of subjects

Masked hypertension has been delineated in the below mentioned table.

Table 4: masked hypertension in the study.

Masked Hypertension	Number of subjects (%)
No	18 (60%)
Yes	12 (40%)

Among 30 subjects, 12 (40%) were found to have masked hypertension, whereas 18 (60%) were not found to have masked hypertension.

White coat hypertension was not seen in any patient.

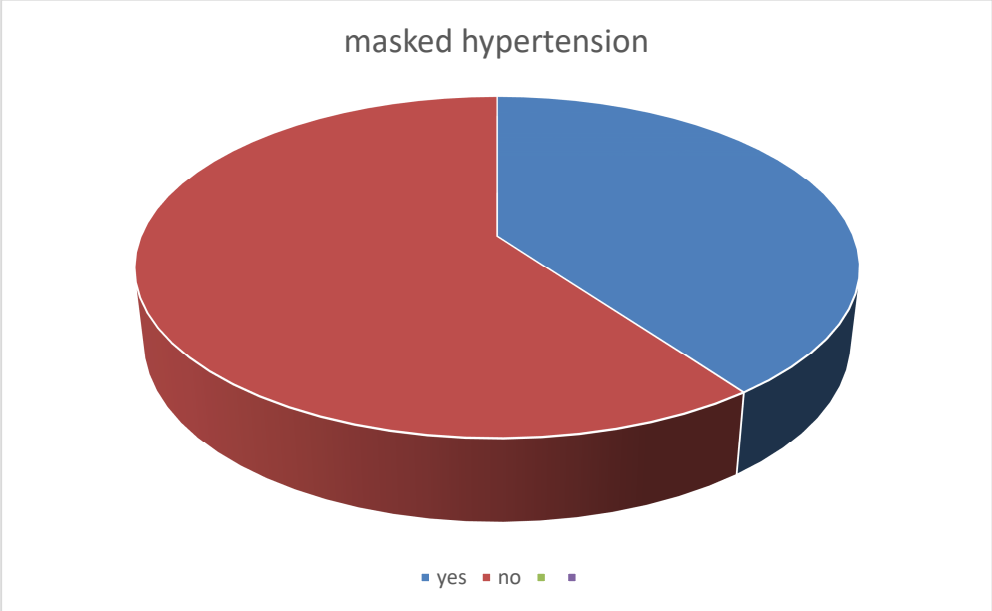

Figure 9: masked hypertension depicted in study

Different variables being depicted in the study in the below mentioned table.

Table 5: different variables depicted in the study

Variables	Sub Category	Number of subjects (%)
CKD Stage	1	2 (6.66%)
	2	5 (16.66%)
	3A	3 (10%)
	3B	3 (10 %)
	4	7 (23.33%)
	5	10 (33.33%)
Casual SBP	Mean ± SD	112.13 ± 7.65
	Median (Min, Max)	110 (98, 128)
Casual DBP	Mean ± SD	73 ± 5.60
	Median (Min, Max)	72 (60, 84)
Ambulatory SBP	Mean ± SD	116.67 ± 7.51
	Median (Min, Max)	116 (95, 130)
Ambulatory DBP	Mean ± SD	79.47 ± 7.02
	Median (Min, Max)	80 (67, 92)
Nocturnal DIP	5	4 (13.33%)
	6	3 (10%)
	8	3 (10%)
	10	5 (16.67%)
	14	2 (6.67%)
	20	2 (6.67%)
	No	11 (36.67%)
LVH on ECHO	Mitral regurgitation	1 (3.33%)
	No	29 (96.67%)
HB	Mean ± SD	9.58 ± 1.95
	Median (Min, Max)	9.75 (5.6, 13.6)

U Albumin	Absent	7 (23.33%)
	Trace	8 (26.67%)
	1	7 (23.33%)
	2	8 (26.67%)
Weight for Height (Centile)	Less than 3rd	15 (50%)
	3rd-10th	5 (16.67%)
	10th-50th	8 (26.67%)
	50th	2 (6.67%)
Height for Age (Centile)	Less than 3rd	14 (46.67%)
	Less than 10th	1 (3.33%)
	3rd-10th	4 (13.33%)
	10th-50th	11 (36.67%)
Etiology	B/L Dysplastic Kidneys	4 (13.33%)
	B/L Hydronephrosis	10 (33.3%)
	B/L Small Kidneys	3 (10%)
	Juvenile Nephrophthisis	1 (3.33%)
	Bartter syndrome	1 (3.33%)
	Recurrent UTI	1 (3.33%)
	Steroid dependent NS	2 (6.67%)
	Steroid resistant NS	4 (13.33%)
	VUR	1 (3.33%)
	unidentified	3 (10%)

Out of 30 subjects, 7 (23.33%) had stage 4 CKD while 12 (40%) had stage 5 CKD. LVH on ECHO showed Mitral regurgitation in 1 (3.33%) subject. U albumin was absent in 7 (23.33%) subjects.

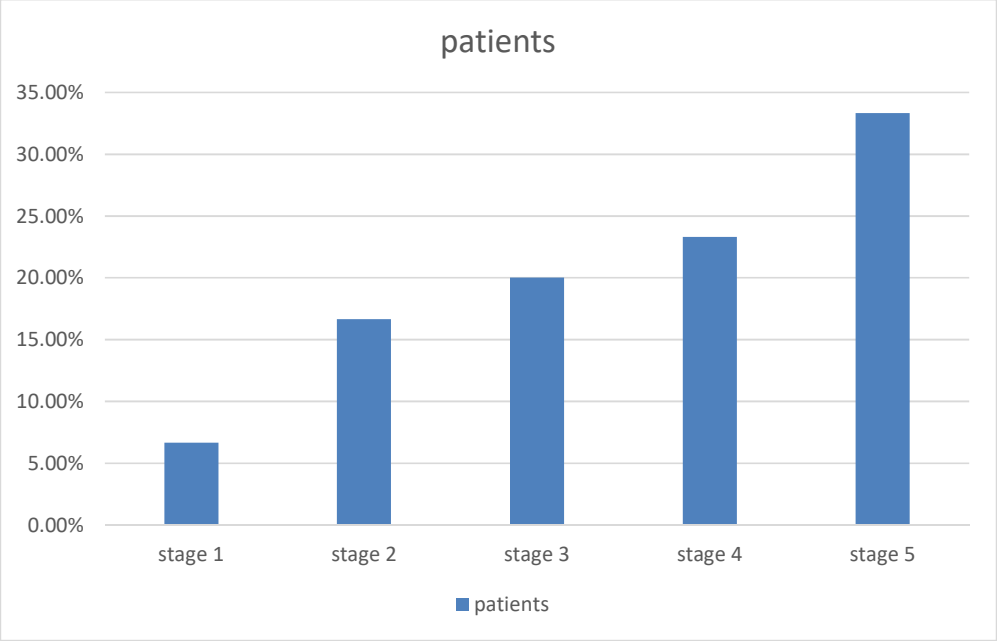

Figure 10: Distribution of subjects according to CKD stage.

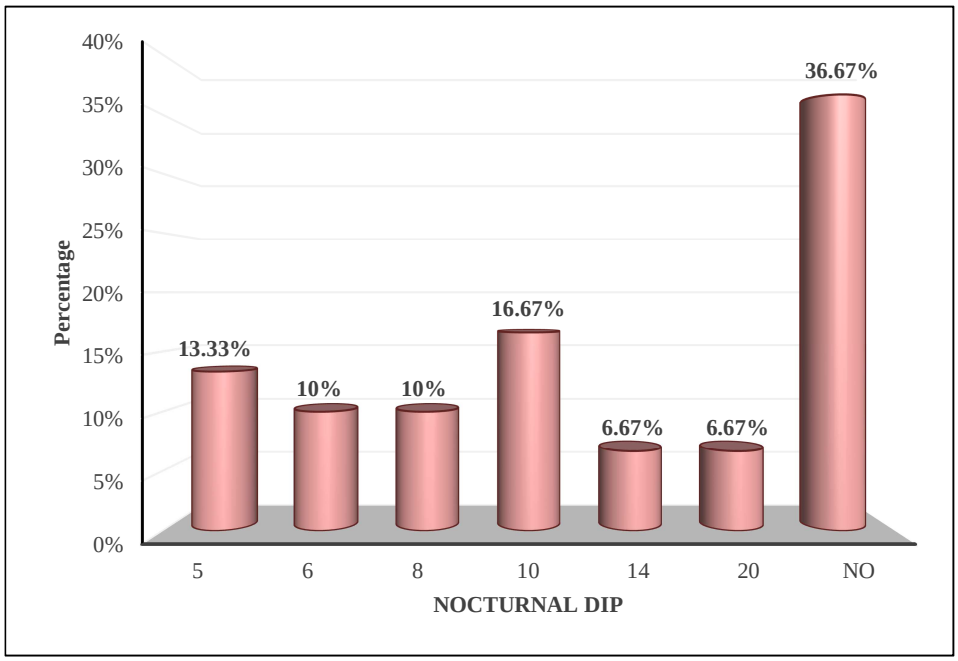

Figure 11: Description of nocturnal DIP among subjects.

CKD stages with Masked hypertension are juxtaposed in the below mentioned table

Table 6: Comparison of CKD stages with Masked hypertension.

CKD stages	Masked hypertension		p-value
	No	Yes	
1	2 (100%)	0 (0%)	**0.0209^{MC}***
2	5 (100%)	0 (0%)	
3A	3 (100%)	0 (0%)	
3B	2 (66.67%)	1(33.33%)	
4	3 (42.85%)	4 (57.20%)	
5	3 (30%)	7 (70%)	

*Abbreviation: MC – Chi square test with Monte Carlo simulation, * indicates statistical significance.*

In CKD stage 1,2 all individuals (100%) do not show masked hypertension, whereas in CKD stages 4 and 5, the majority of individuals (57.20% and 70%, respectively) exhibit masked hypertension. masked hypertension over CKD stages shows significant difference (p-value = 0.0209). this is highlighted by the chi square test.

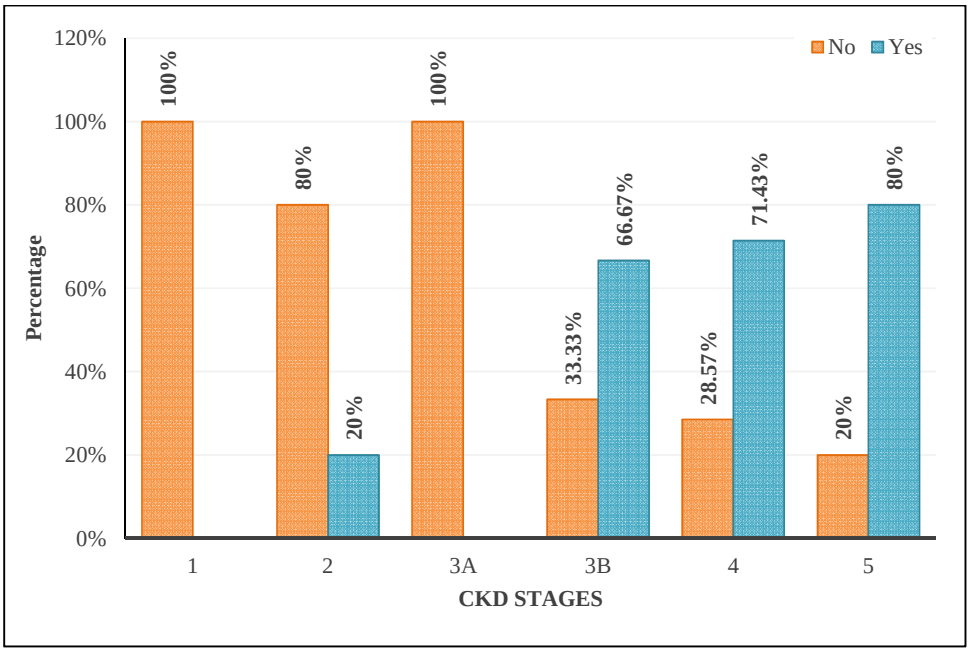

Figure 12: Distribution of masked hypertension over CKD stages.

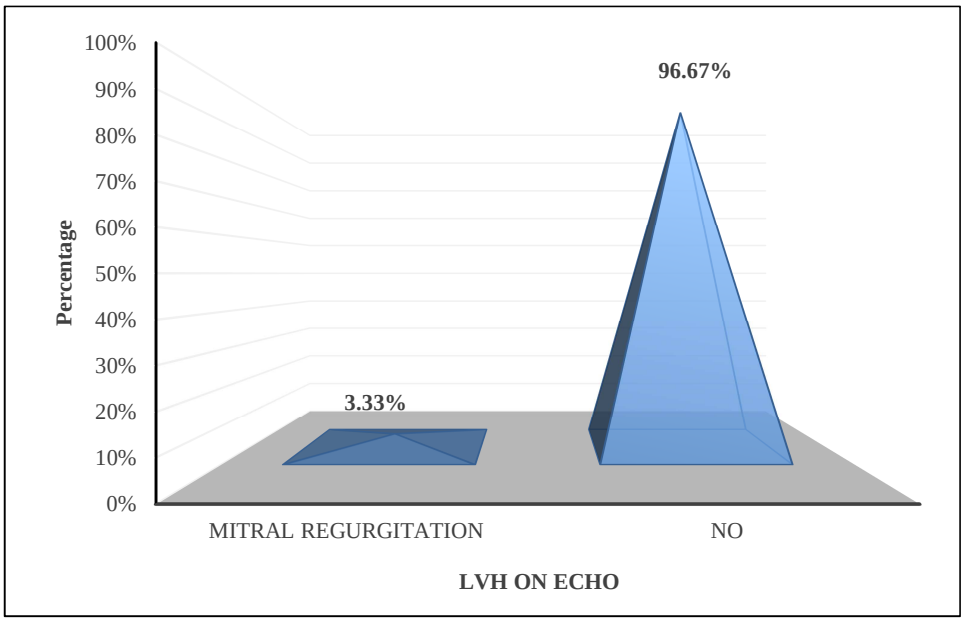

Figure 13: Distribution of subjects according to LVH on ECHO.

Other echocardiographic abnormalities that were noted were that 1 patient had tricuspid regurgitation (mild) and one patient had aortic stenosis.

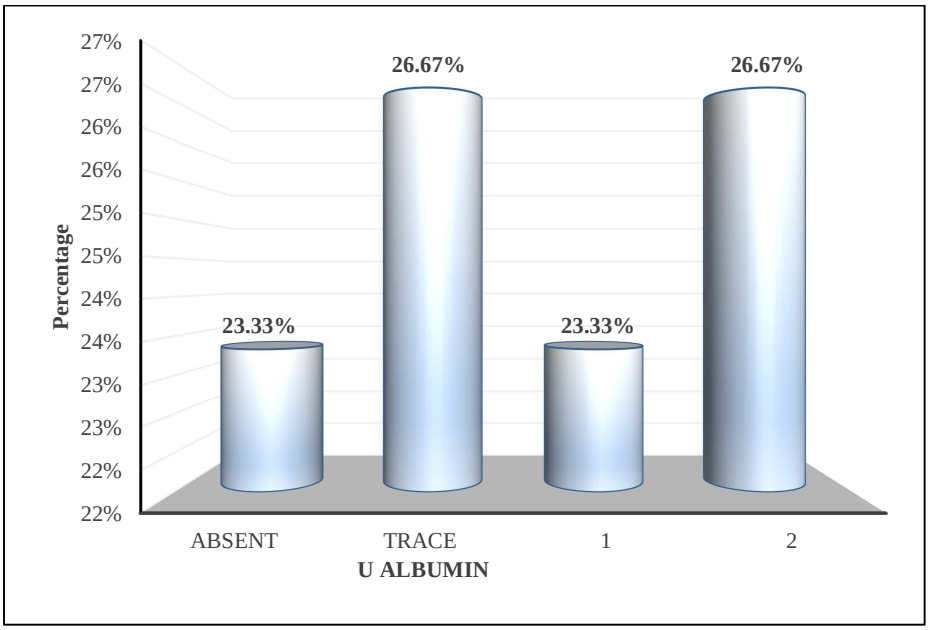

Figure 14: Distribution of subjects according to U Albumin.

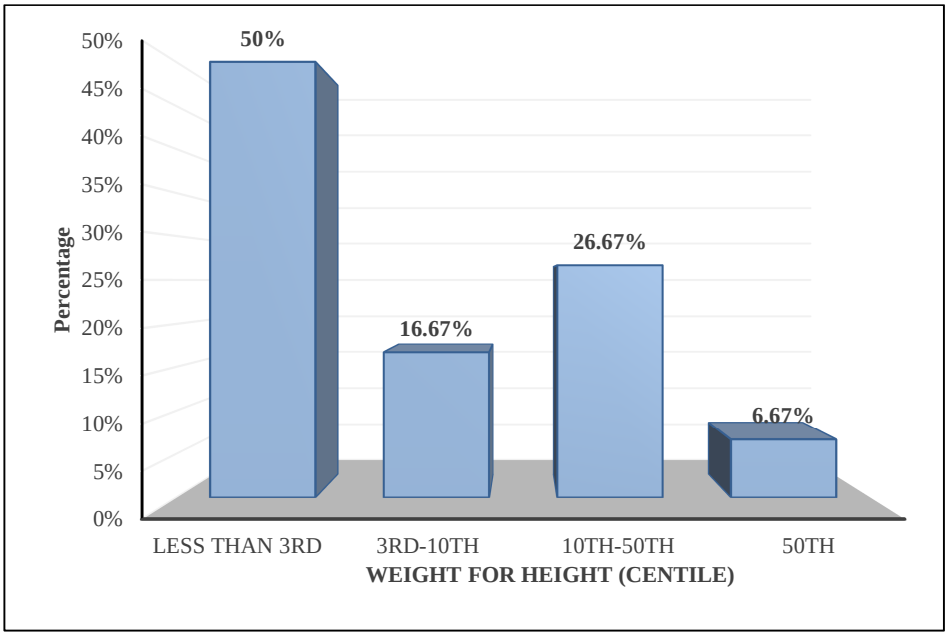

Figure 15: Distribution of subjects according to weight for height.

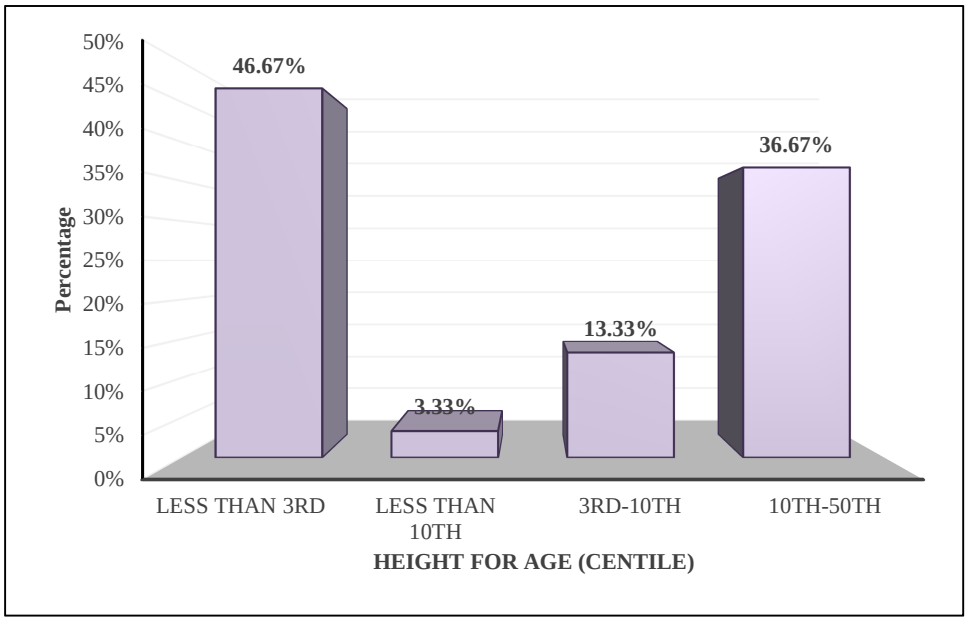

Figure 16: Depiction of height for age.

Different variables with masked hypertension are described in the below mentioned table

Table 7: Different variables with masked hypertension described.

Variable	details	Masked hypertension		p-value
		No	Yes	
Age (years)	Mean ± SD Median (Min, Max)	11.75 ± 4.05 12.5 (4, 17)	11.2 ± 3.52 11 (5, 16)	0.7177[t]
Sex	Female	4 (20%)	5 (50%)	0.2169[MC]
	Male	16 (80%)	5 (50%)	
CKD Stage	2	2 (10%)	2 (20%)	0.7951[MC]
	3	2 (10%)	1 (10%)	
	3A	2 (10%)	1 (10%)	
	3B	0 (0%)	1 (10%)	
	4	5 (25%)	2 (20%)	
	5	9 (45%)	3 (30%)	
Casual SBP	Mean ± SD Median (Min, Max)	112.2 ± 8 110 (98, 128)	112 ± 7.3 110 (102, 124)	0.9476[t]
Casual DBP	Mean ± SD Median (Min, Max)	73 ± 6 73 (60, 84)	73 ± 5.01 71 (66, 82)	> 0.9999[t]
Ambulatory SBP	Mean ± SD Median (Min, Max)	113.2 ± 6.86 112 (95, 130)	123.6 ± 1.58 124 (122, 126)	**< 0.001[MW]***
Ambulatory DBP	Mean ± SD Median (Min, Max)	76.7 ± 6.39 76 (67, 90)	85 ± 4.64 84 (80, 92)	**0.0011[t]***
Nocturnal DIP	5	3 (15%)	1 (10%)	0.9845[MC]
	6	2 (10%)	1 (10%)	
	8	2 (10%)	1 (10%)	
	10	3 (15%)	2 (20%)	
	14	1 (5%)	1 (10%)	
	20	2 (10%)	0 (0%)	
	No	7 (35%)	4 (40%)	
LVH on ECHO	Mitral regurgitation	1 (5%)	0 (0%)	> 0.9999[MC]
	No	19 (95%)	10 (100%)	

HB	Mean ± SD Median (Min, Max)	9.57 ± 1.78 9.8 (5.6, 12)	9.6 ± 2.38 9.5 (5.9, 13.6)	0.9743[t]
U Albumin	Absent	4 (20%)	3 (30%)	0.9600[MC]
	Trace	6 (30%)	2 (20%)	
	1	5 (25%)	2 (20%)	
	2	5 (25%)	3 (30%)	
Weight for Height (Centile)	Less than 3rd	11 (55%)	4 (40%)	0.9450[MC]
	3rd-10th	3 (15%)	2 (20%)	
	10th-50th	5 (25%)	3 (30%)	
	50th	1 (5%)	1 (10%)	
Height for Age (Centile)	Less than 3rd	10 (50%)	4 (40%)	0.0885[MC]
	Less than 10th	0 (0%)	1 (10%)	
	3rd-10th	1 (5%)	3 (30%)	
	10th-50th	9 (45%)	2 (20%)	

*Abbreviation: t – Two sample t test, MW – Mann Whitney U test, MC – Chi square with Monte Carlo simulation, * indicates statistical significance.*

From two sample t test, it is observed that mean ambulatory DBP is significantly higher among those who had masked hypertension compared to those who didn't have masked hypertension. There is no significant difference in the mean of Age, Casual SBP, Casual DBP and haemoglobin over masked hypertension.

Anaemia and stage of chronic kidney disease

The following table gives the comparison of hemoglobin over CKD stages.

Table 8: Comparison of hemoglobin over CKD stages.

CKD stage	Hemoglobin		p-value
	Mean ± SD	Median (Min, Max)	
1	12.25 ± 0.49	12.25 (11.9, 12.6)	**< 0.001[K]***
2	11.5 ± 1.36	11.4 (9.8, 13.6)	
3A	11.07 ± 0.64	10.8 (10.6, 11.8)	
3B	10.63 ± 0.76	10.8 (9.8, 11.3)	
4	8.8 ± 1.52	9 (5.8, 10.4)	
5	7.38 ± 0.99	7.45 (5.9, 9)	

Abbreviation: K – Kruskal Wallis test

**show difference that is significant*

From Kruskal Wallis test, hemoglobin over CKD staging (p-value < 0.001) is statistically significant. Further from Dunn's test, it is observed that, there is significant difference in the hemoglobin levels between stage 5 and stage 1 (p-value = 0.0209) as well as between stage 5 and stage 2 (p-value = 0.0052).

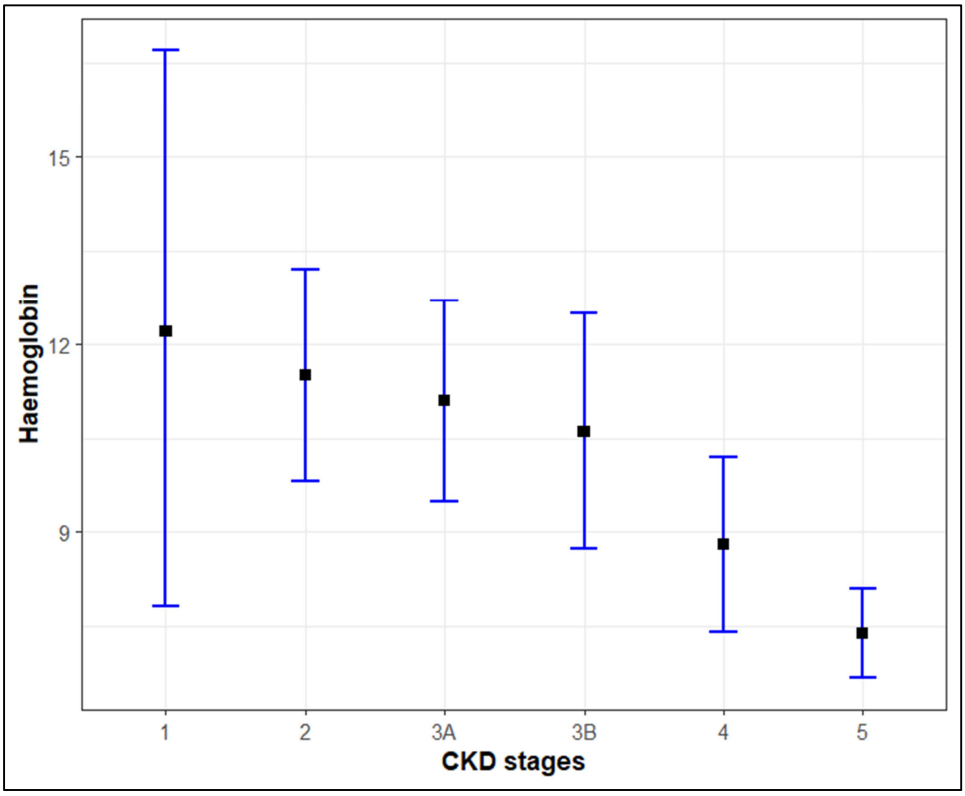

Figure 17: Mean plot of haemoglobin over CKD stages.

Mean haemoglobin levels correlate with stage of chronic kidney disease.

Anaemia is more prevalent in later stages of chronic kidney disease.

From Mann Whitney U test, it is observed that Ambulatory SBP is significantly higher among those who had masked hypertension compared to those who didn't have masked hypertension.

From Chi square test, it is observed that, Sex, CKD Stage, Nocturnal DIP, LVH on ECHO, U Albumin, Weight for Height and Height for Age are not significant statitically over masked hypertension.

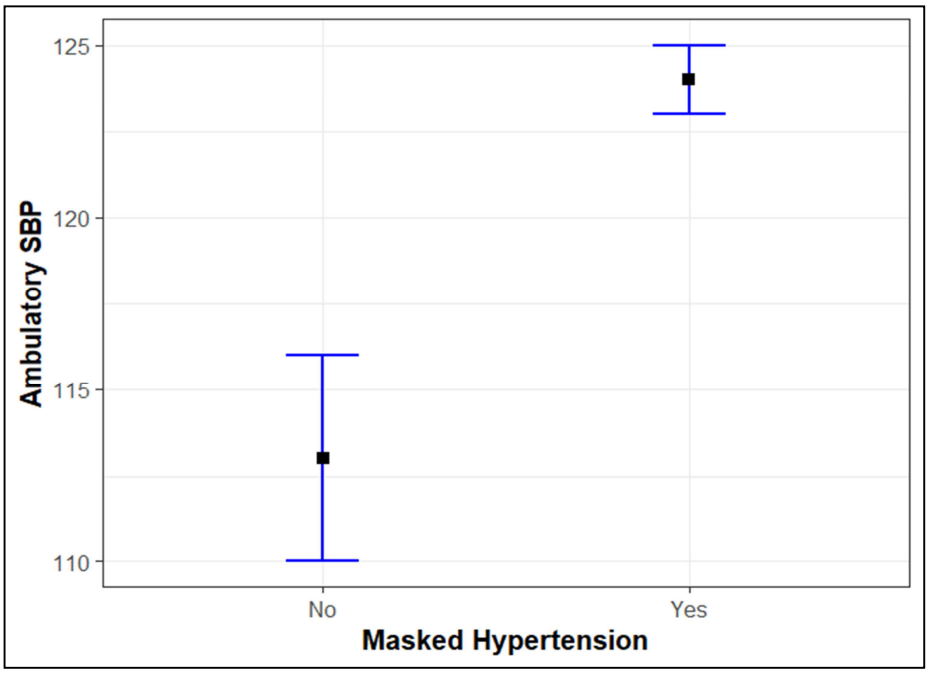

Figure 18: Mean plot of ambulatory SBP over masked hypertension.

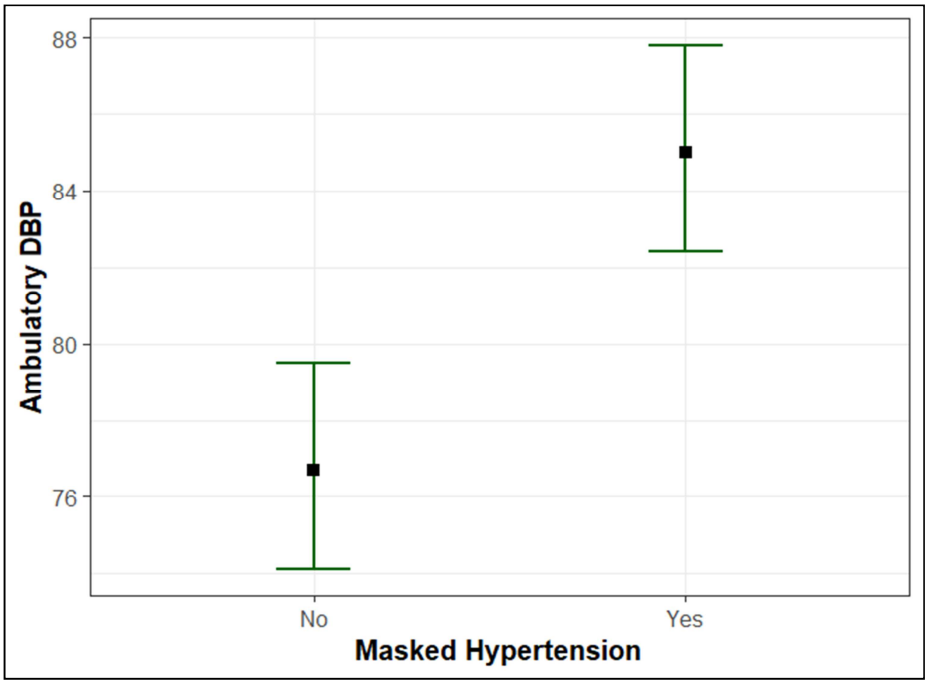

Figure1 9: Mean plot of ambulatory DBP over masked hypertension.

DISCUSSION

Chronic kidney disease is a gradually progressing disease involving increasing number of children in India. Its silent clinical picture and lack of monitoring facilities in resource limited settings contribute to its late diagnosis and establishment of complications. Early identification of co morbidities such as hypertension and left ventricular hypertrophy would help in identifying the disease seriousness early on. The goal of our study was to identify the prevalence of masked hypertension in children diagnosed with chronic kidney disease. The study shows that 33.3% patients were girls and 66.6% patients were boys with mean age 11.57 ± 3.83 years. This is in accordance with Francessa et al [(60)] who stated that the prevalence of chronic kidney disease was more in males.

Masalskienė J et al [(61)] also reported that majority were boys and 10 years was the mean age noted in their study. Similar mean age was noted in both sexes. Gianluigi Ardissino et al [(62)] reported that among 1197 children in the study, mean age at onset was lower by 3 years i.e. 7 years with females being diagnosed later than males. Harambat J et al [(19)] reported that In view of a dearth of national registries and surveys, estimating the causes of CKD in children in low and middle income countries is difficult. Kanitkar et al [(12)] from India only stated that ckd constituted 10 % of total outpatient admission without delving into age and sex details.

33.33 % of our patients were in stage 5 of ckd termed as end stage renal disease followed by stage 4 which were 23.33%. 6% of our patients were having a transplanted kidney during the course of the study. According to a study by Masalskienė J et al [(61)] stage 2 was the most prevalent stage among patients. While the

proportion of children with stage 2-4 increased over the course of 30 years, it can be attributed to advancement in screening and diagnosis.

Causes of chronic kidney disease in the study were noted to be majorly nephrotic syndrome followed by CAKUT particularly vesico ureteric reflux. In a report from Lithuania, Jūratė Masalskienė et al [(62)] reported the commonest cause to be CAKUT. In a recent NAPRTCS (north American pediatric renal trial and corroborative studies) report [(34)] congenital causes, including congenital anomalies of the kidney and urinary tract (CAKUT) (48%) and hereditary nephropathies (10%), were the most common cause followed by glomerulopathy (14%).

In our study, masked hypertension was seen in 40 % patients. Of this, Stage 5 constituted 45%, stage 4 constituted 18%, stage 3 is 18%, stage 2 also 18% . Masked hypertension was significantly more present in stage 5 compared to stage 1 and 2. Another point to note, masked hypertension was seen in stage 3 in 18% compared to 0% in stage 2. These findings further highlight that ambulatory bp monitoring is essential for early identification of hypertension and thus early risk stratification.

According to stages of ckd, in a large multicentric study, masked hypertension has been detected in 38% of 366 children with CKD stages 2–4 [(1)]

This in accordance with a study done by Seeman et al [(63)] that showed Children with CKD stage 5 on chronic hemodialysis or peritoneal dialysis have also high prevalence of MH being present in 12–37% of children.

Multiple studies done on masked hypertension in patients with chronic kidney disease have followed older classification taking only those with under 60 eGFR and thus included patients with advanced disease only. white coat hypertension has been

tried to be eliminated from our study as average of multiple readings from sphygmomanometer is taken. This would allay anxiety in the patients that is a cause of white coat hypertension.

In our study, left ventricular hypertrophy as such was not seen in patients. Mitral regurgitation was present in 1 patient. This in in accordance from united states renal data system (2015) (64) that shows that although commonly seen in adults, cardiac problems are not as common in children with advanced disease. In a small study by mitsenefes et al, 6 patients (23.3%) had left ventricular hypertrophy in cases of chronic kidney disease. In a larger study on 366 patients, the same researcher noted that 17% of total patients had LVH.

These findings are also substantiated by an Indian study by Gupta et al [(6)] Masked hypertension was detected in 19.6% and 21.7% had confirmed hypertension. Thirty-four (73.9%) children were already receiving antihypertensive medication. In these, increased CBP was seen in 23.5% and increased ABP in 47%. In children diagnosed with hypertension as defined by ambulatory blood pressure monitoring (ABPM), left ventricular hypertrophy (LVH) was found in 32.2% of cases. Other abnormalities seen in echocardiography of patients were tricuspid regurgitation and aortic stenosis. Multiple studies have shown that the prevalence of cardiac abnormalities were more in ckd stages 4 and 5.

In a prospective study done by Lurbe et al [(45)] on masked hypertension in paediatric ckd, Out of 592 children (6-18 years) 7.6% had masked hypertension. Elevated LVMI was seen in those with HTN as compared to others.

Weight for height was less than 3rd centile in 15 (50%) patients suggestive of acute malnutrition. Height for age was less than 3rd centile in 14 (46.6%) patients suggestive of chronic malnutrition. This is known as stunting.

This is in accordance with existing literature on the disease stressing on the malnutrition and poor growth in patients with the disease. In a study done by Shen et al [(65)] in 142 cases Malnutrition was diagnosed in 50% of patients in at least one visit.

In a study by Gupta et al [(6)] , conducted in India, 60% of the children had undernutrition of either moderate or severe grade.

Mean haemoglobin was 9.57 ± 1.78. Stage 1,2 had mean haemoglobin of 11.5 g/dl while stage4,5 had mean haemoglobin of only 7.45 g/dl.

According to KDIGO (2) it is recommended that in patients of chronic kidney disease at least 11 g/dl of haemoglobin should be maintained. However, the western world has done multiple studies on anemia in CKD [(66- 69)] that have shown that in adults, risk of raising haemoglobin without taking account other factors may lead to adverse outcomes such as stroke and hyper viscosity related complications.

In a commentary by motoshi hattori et al [(70)] it was noted that results from studies on CKD cannot be extrapolated to pediatric goals of haemoglobin. To create therapeutic goals that are appropriate for each child, further research focused on paediatrics is obviously required. CKD progression results in increased expenditure for management hence it is important that the disease and the associated co morbidities are identified early. [(71)]

Our study is in accordance with other studies done on the paediatric patients of chronic kidney disease worldwide. Masked hypertension is prevalent in chronic kidney disease significantly. This hypertension is also correlated with growth failure and anaemia in the patients. Left ventricular hypertrophy is not as commonly seen in paediatric patients of chronic kidney disease as in the adult population. Nevertheless, mitral regurgitation is an important early predecessor of left ventricular hypertrophy.

SUMMARY

The study was conducted over one year from 2023 to 2024 at KLEs Prabhakar Kore Hospital. All the samples collected were patients admitted in the wards in the hospital. 24 hour ambulatory bp monitoring was recorded and 2D echocardiography was done for all patients.

Results were recorded in tabular and graphical forms Mean, median, SD and ranges were accounted for quantitative data. Chi square analysis was useful in testing for major differences between proportions and frequencies. T test was useful in testing for major differences between two means. The confidence interval was set to be at ninety five % limit, with level of the significance to be at p: < 0.05.

- The study included 30 chronic kidney disease patients on whom 24 hour ambulatory bp monitoring and 2D echocardiography was done.
- Mean age (SD) was `11.57 ± 3.83 years. Majority of the ckd patients were aged more than 10 years.
- There were 21 males (70%) and 9 females (30%) with a M: F ration of 7:3.
- Most of our study subjects were of stage 5 - 12 (40%).
- The plurality of the patients had casual systolic blood pressure of 112.13 ± 7.65 mm hg and casual diastolic blood pressure was 73 ± 5.60 mm hg.

- Majority of the patients had ambulatory systolic blood pressure of 116.67 ± 7.51mm hg and ambulatory diastolic blood pressure was 79.47 ± 7.02 mm hg.

- Among 30 subjects, 12 (39.33%) were found to have masked hypertension, whereas 18 (63.67%) were not found to have masked hypertension.
- LVH on ECHO showed Mitral regurgitation in 1 (3.33%) subject.
- Other echocardiographic abnormalities included tricuspid regurgitation and aortic stenosis in 2 patients.
- There was significant high positive correlation with stage of chronic kidney disease and masked hypertension ($p<0.01$).

- Hence masked hypertension is prevalent in chronic kidney disease and may be missed by standard method of casual bp measurement that is by sphygmomanometer.

- Ambulatory bp monitoring is essential for early detection of hypertension in chronic kidney disease. .

- As its single center study, more multi-centered and larger number of studies are required to make out findings more concrete.

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ANNEXURE-I

INFORMED CONSENT FORM

KAHERs JNMC BELAGAVI

"Prevalence of masked hypertension in children with chronic kidney disease and evaluation of left ventricular function"

Name of Student/Principal Investigator: _____

Name of Guide/Co Investigators: _____

- **Objective:** To identify the prevalence of masked hypertension in children with chronic kidney disease

Introduction: You are being invited to participate in this study to find out prevalence of masked hypertension in children with chronic kidney disease and evaluation of left ventricular function. Participation of your child will help us to know the prevalence of masked hypertension in chronic kidney disease. Chronic kidney disease is associated with many co morbidities and early diagnosis of hypertension will help in early initiation of its management and overall improvement in patient outcome and shorter hospital stay. Participation in this study is completely voluntary.

Explanation of procedure: In this study, detailed history will be taken. the child will be admitted for 24 hours in pediatric wards and their Blood pressure will be measured by an ambulatory bp monitor that will be attached on their arm throughout the period of 24 hours. They will continue their daily activities. A 2D echocardiography scan will be done for the child.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: "Name of student/PI, mobile number, email ID" If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "**Prevalence of masked hypertension in children with chronic kidney disease and evaluation of left ventricular function"** My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

ANNEXURE -II

PROFORMA

Subject number-

IP NO-

NAME-

AGE-

SEX-

DATE OF DIAGNOSIS-

DISEASE ONSET-

HISTORY OF PRESENTING ILLNESS-

PAST HISTORY-

ANTHROPOMETRY-

CHILD'S PARAMETER	OBSERVED	EXPECTED	PERCENTILE	PERCENTAGE
WEIGHT				
HEIGHT				
US:LS				

BP CENTILE CHART-

	SBP (mm hg)	DBP (mm hg)
50th		
90th		
95th		
95+12th		

BLOOD PRESSURE READING BY MERCURY SPHYGMOMANOMETER- (mmHg)

1.

2.

3.

AVERAGE-

AMBULATORY BP MONITOR FINDINGS

AVERAGE SBP-

AVERAGE DBP-

BP LOAD-

NOCTURNAL DIP-

DIURNAL INDEX-

GENERAL EXAMINATION-

Pallor-

Dehydration-

Signs of rickets-

SYSTEMIC EXAMINATION-

INVESTIGATIONS-

Urine albumin	
S. Urea	
S.creatinine	
S. Albumin	
S. Cholesterol	
Hemogram	
Hemoglobin	
Packed cell volume	
RBC count	
Total leucocytes	
Platelets	
Peripeheral smear	

eGFR- ml/kg/1.73m2

STAGE OF CHRONIC KIDNEY DISEASE-

	Stage 1	Stage 2	Stage 3a	Stage 3b	Stage 4	Stage 5
eGFR	>90	60-89	45-59	30-44	15-29	<15

ECHOCARDIOGRAPHY FINDINGS-

Left ventricular systolic dysfunction-

Left ventricular diastolic dysfunction-

Left ventricular hypertrophy

FINAL DIAGNOSIS-

PRINCIPAL INVESTIGATOR

JNMC,

KAHER

GUIDE

JNMC,

KAHER

ANNEXURE -III

KEY TO MASTER CHART

CSBP	-	Casual systolic blood pressure
CDBP	-	Casual diastolic blood pressure
Amb SBP	-	Ambulatory systolic blood pressure
Amb SBP	-	Ambulatory systolic blood pressure
Amb DBP	-	Ambulatory diastolic blood pressure
MH	-	Masked hypertension
Noc Dip	-	Nocturnal dip
LVH	-	Left ventricular hypertrophy
Hb	-	Hemoglobin
u. alb	-	Urine albumin
UTI	-	Urinary tract infection
SRNS	-	Steroid resistant nephrotic syndrome
SDNS	-	Steroid dependent nephrotic syndrome
PUJO	-	Pelvi ureteric junction obstruction
VUR	-	Vesicoureteric reflux

ANNEXURE-IV MASTERCHART

S NO	NAME	AGE(YRS)	SEX	CKD STAGE	CSBP(MMHG)	CDBP(MM HG)	Amb SBP	Amb DBP	MH	noc dip	LVH	hb	U ALB	WEIGHT FOR HEIGHT(CENTILE)	HEIGHT FOR AGE (CENTILE)	ETIOLOGY	transplant
1	PRAJWAL	15	M	5	124	80	130	84	n	20	NO	6.9	1	10TH-50TH	LESS THAN 3RD	B/L SMALL KIDNEYS WITH PUJO	yes
2	ABHISHEK	11	M	3A	116	80	112	74	N	14	NO	11.8	2	10TH-50TH	LESS THAN 3RD	SRNS	no
3	DIVYA	16	F	5	120	78	116	79	N	10	NO	8.3	TRACE	10TH-50TH	10TH-50TH	b/l SMALL KIDNEYS	yes
4	BHAGYALAXMI	12	F	3A	124	80	126	90	N	8	NO	12	2	10TH-50TH	10TH-50TH	SRNS	no
5	HARISH	6	M	4	98	66	95	67	N	NO	NO	10.4	1	3RD-10TH	10TH-50TH	RECURRENT UTI	no
6	MAHEEN	5	F	4	106	64	110	76	N	NO	NO	5.6	2	3RD-10TH	LESS THAN 3RD	B/L DYSPLASTIC KIDNEYS	no
7	AKASH	15	M	5	128	84	108	70	N	20	NO	6.5	TRACE	LESS THAN 3RD	3RD-10TH	STEROID DEPENDENT NS	no
8	RESHMI	12	F	5	122	82	126	92	Y	14	NO	6.3	1	3RD-10TH	3RD-10TH	MENORRHAGIA	no
9	SUNIL	14	M	4	124	80	126	84	Y	10	NO	10	2	LESS THAN 3RD	LESS THAN 3RD	STEROID DEPENDENT NS	no
10	SHABANA	16	F	2	118	74	122	80	Y	6	NO	11.5	2	10TH-50TH	3RD-10TH	STEROID DEPENDENT NS	no
11	ATIF	5	M	5	100	70	95	67	N	5	NO	9.2	1	3RD-10TH	3RD-10TH	URAEMIC ENCEPHALOPATHY	no
12	SUHANA	16	F	4	110	72	123	87	Y	NO	NO	11.9	2	50TH	10TH-50TH	FSGS	no
13	ARUN	9	M	2	108	70	110	82	N	NO	NO	8.6	2	LESS THAN 3RD	LESS THAN 3RD	HYDRONEPHROSIS	no
14	MAHESH	13	M	5	118	80	126	92	Y	10	NO	9.3	TRACE	LESS THAN 3RD	LESS THAN 3RD	PUJ OBSTRUCTION	no
15	DEEPAK	17	M	5	114	70	112	90	N	5	NO	9.7	TRACE	LESS THAN 3RD	LESS THAN 3RD	HYDRONEPHROSIS	no

16	IRAPPA	17	M	5	108	72	113	76	N	6	NO	8.6	1	LESS THAN 3RD	LESS THAN 3RD	SMALL KIDNEYS	no
17	PREETI	10	F	3B	114	70	122	90	Y	NO	NO	9	ABSENT	LESS THAN 3RD	LESS THAN 3RD	JUVENILE NEPHROPHTHISIS	no
18	AJAY	4	M	4	106	60	110	82	N	5		10.5	ABSENT	LESS THAN 3RD	10TH-50TH	HYDRONEPHROSIS	no
19	MAKTUMSAB	12	M	2	110	76	124	88	Y	NO	NO	13.6	ABSENT	LESS THAN 3RD	LESS THAN 3RD	HYDRONEPHROSIS SECONDARY TO VUR	no
20	PRADEEP	8	M	5	102	66	122	90	Y	10	NO	5.9	ABSENT	LESS THAN 3RD	LESS THAN 3RD	MULTICYSTIC DYSPLASTIC KIDNEYS	no
21	SAMARTH	11	M	5	118	76	112	74	N	6	NO	11.6	ABSENT	LESS THAN 3RD	LESS THAN 3RD	B/L HYDRONEPHROSIS SECONDARY TO VUR	no
22	VIRAJ	10	M	3A	106	70	124	84	Y	8	no	8.8	TRACE	10TH-50TH	10TH-50TH	NEPHROTIC SYNDROME	no
23	LAKANNA	16	M	3B	118	70	116	80	N	10	mitral regurgitation	9.7	TRACE	LESS THAN 3RD	LESS THAN 3RD	FULMINANT HEPATITIS	no
24	MEGHANA	6	F	3B	106	68	110	74	N	8	no	11.3	1	10TH-50TH	10TH-50TH	NEPHROTIC SYNDROME	no
25	RAJDEEP	14	M	4	110	74	132	100	Y	5	NO	10.2	2	50TH	10TH-50TH	HYDRONEPHROSIS BILATERAL	No
26	DIVIJA	9	F	3	106	70	116	79	Y	NO	NO	9.8	TRACE	10TH-50TH	LESS THAN 10TH	HYDRONEPHROSIS SECONDARY TO VUR	no
27	SIDDIQ	5	M	4	100	62	95	67	N	NO	NO	11.2	ABSENT	10TH -50TH	LESS THAN 3RD	NEUROGENIC KIDNEY WITH PUJO	no
28	AYESHA	14	F	2	110	74	112	70	N	NO	NO	10.5	1	LESS THAN 3RD	10TH-50TH	VUR WITH PUJO	no
29	PAVAN	14	M	1	102	70	116	79	N	NO	NO	8.9	TRACE	LESS THAN 3RD	10TH-50TH	STEROID DEPENDENT NS	no
30	SAMRUDDHI	10	F	1	114	76	112	76	N	NO	NO	9.9	ABSENT	LESS THAN 3RD	10TH-50TH	STEROID DEPENDENT NS	no