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Original Research Paper

Pathology

A RETROSPECTIVE STUDY ABOUT PERSISTENT PROTEINURIA IN CHILDREN.

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ABSTRACT

INTRODUCTION Proteinuria influences the rate of progression of CKD. Persistent proteinuria is a the signal indication of glomerular lesion.It also may play a central role in the progression of glomerular lesions to later stages of CKD.The prevalence of proteinuria on a single test of urine is estimated to be 5-15%.

MATERIAL AND METHOD Data was collected on urine protein examination fromMay 2018 to June 2021 of all the patients less then 16 years in a tertiary medical centre. During this 3 year period , 15320 children received urinalysis and their medical records for age of presentation, clinical diagnosis,duration of symptoms and renal function were noted.

RESULTS During this 3 year period , 15320 children received urinalysis,which included 8618 boys (43.4%) and 11202 girls (56.6%), all aged less 16 years. Of these 15320 children, 3604 (18.1%) had HYPERLINK "https:// www. science direct. com/ topics/ medicine-and-dentistry/proteinuria"proteinuria on at least one occasion. 742 children had persistant proteinuria .Among 742 cases, 322 cases presented with mild proteinuria,328 with moderate persistant proteinuria while 92 presented with serve persistant proteinuria. Among moderate proteinuria , sepsis was the most commom cause comprising 115 cases of the total 341, followed by steroid dependent nephritic syndrome cases (31 cases). For severe proteinuria cases, sepsis,SD nephrotic syndrome ,RPGN,SLE were recorded as the most important cases.

CONCLUSION This study concluded that assessing those children with persistent proteinuria is crucial as substantial of them develop HYPERLINK "https://www.sciencedirect.com/topics/medicine-and-dentistry/chronic-kidney-disease"chronic kidney disease and many clinical diseases other than primary renal disease also had renal involvement and manifest as proteinuria initially.

KEYWORDS : Proteinuria,urinalysis.

INTRODUCTION

Proteinuria in children is common and its etiology differs from that in adults. It can be a transient condition during a fever, dehydration, exercise, or stress, however it can also be persistent. Chandar et al. reported that after excluding transient proteinuria in children with isolated proteinuria, 72% had orthostatic proteinuria.(1) Furthermore, persistent proteinuria not explained by orthostatic proteinuria can increase the risk of underlying renal diseases.(2,3)

In a study conducted by Lin et al. in Taiwan, a mass urinary screening program among students aged 6–15 years showed that 7% had abnormal results in second urinalysis from samples collected in the morning.(4) In follow-up, 35% of these children with persistent proteinuria had a urine protein level greater than 100 mg/dl (equivalent to 2 + in a dipstick test) with or without concomitant hematuria, and they also had many different underlying renal diseases.(5) Pediatric urinary tract infections (UTI) account for 0.7% of physician office visits and 5–14% of emergency department visits by children annually.(6) Accurate diagnosis of UTI has important clinical implications; most febrile infants with UTI show evidence of renal parenchymal involvement (pyelonephritis).(7)

Proteinuria influences the rate of progression of CKD. Persistent proteinuria is a the signal indication of glomerular lesion.It also may play a central role in the progression of glomerular lesions to later stages of CKD. (8,9) The prevalence of proteinuria on a single test of urine is estimated to be 5-15%.The national kidney foundation consenus panel on Proteinuria,Albumenuria,Risk,Assessment,Detection & Eliminaion (PARADE) reported that even after 4 tests,10.7% of children haveproteinuria in 1 of 4 specimens.(10) However, only 0.1% had positive protein results in all 4 specimens, emphasizing that it is the persistence of proteinuria that is significant, than a positive result for the presence of protein if only a single specimen is tested. The current consensus is that lessening the degree of proteinuria is an imperative of renoprotective therapy.

AIM

The aim of the study is to review urinalysis results of children under 18 years of age over a period of 3 years and identify the etiology in those with significant persistent proteinuria.

MATERIAL AND METHOD

Data was collected on urine protein examination fromMay 2018 to June 2021 of all the patients less then 16 years in a tertiary medical centre.During this 3 year period , 15320 children received urinalysis and 3604 were found to have persistent proteinuria.We received their medical records for age of presentation, clinical diagnosis,duration of symptoms and renal function.According to level of proteinuria,children were divided into 3 gp (mild, moderate, severe).The urine analysis was done on urilyser DS 100 .The children presenting with proteinuria 1+ ,urine examination was repeated after 1 weak. Urine protein to creatinine ration, serum creatinine were also performed in some cases.

Exclusion Criteria

High risk subgroups e.g. malnourished,premature were excluded.

Inclusion Criteria

Children below 16 yrs of age.

The ethical clearance for the study was obtained from the institutional ethics committee under no IEC/GMC/Cat C/2022/745 with registration no C-242.

RESULTS

In total 19820 children underwent urine analysis ,at our hospital in the 3 years study period,which included 8618 boys (43.4%) and 11202 girls (56.6%), all aged less 16 years. Of these 15320 children, 3604 (18.1%) had proteinuria on at least one occasion.

Proteinuria was first time noted in OPD (34.2%),emergency (30.3%) and during hospitalization of children (29.3%). In a

total of 3604 cases,1872 showed proteinuria only on one occasion.990 children proteinuria on more than one occasion but not persistent proteinuria while 742 children had persistant proteinuria .Among 742 cases, 322 cases presented with mild proteinuria,328 with moderate persistant proteinuria while 92 presented with serve persistant proteinuria as shown in Figure 1

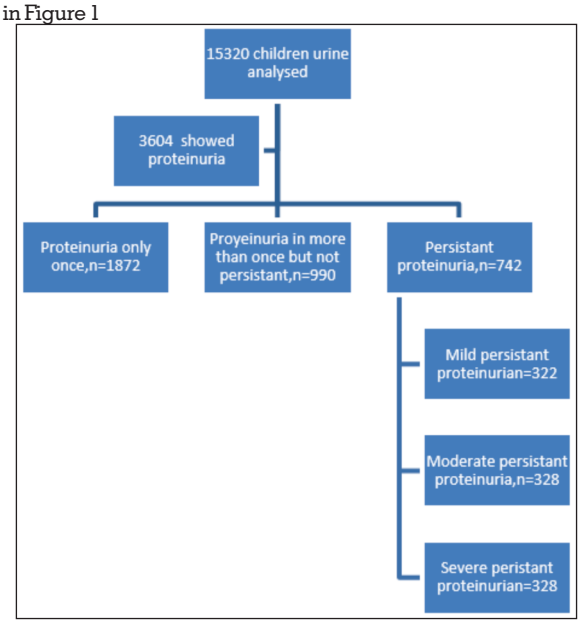

FIG 1: Urinylasis of children

Table 1: Sex wise Distribution of cases

SEX	NO. OF CASES
MALES	8618(43.4%)
FEMALES	11202(56.6%)
TOTAL	19820

The median age at presentation was 11.6 years.The prevalence was higher in girls then in boys and included 8618 boys(43.4%) and 11,202 girls (56.6%) with female to male ratio 1.2:1.

Table 2 : Sex Wise Distribution Among Persistant Proteinuria Cases

SEX	MILD P P	MODERATE P P	SEVERE P P	TOTAL
MALES	164	126	26	316(42.5%)
FEMALES	145	215	66	426(57.4%)
TOTAL	309	341	92	742

Among persistent proteinuria cases(742 cases), the boys(316 cases ,42.5%) usually presented with mild to moderate proteinuria while 26 cases were of severe persistant proteinuria,out of total 92 cases.The females in comparsion comprised 57.4% of total cases varing for mild to severe persistant proteinuria as shown in table 2.

Table 3: Causes Of Moderate & Severe Proteinuria

CAUSES	Moderate proteinuria	Severe proteinuria
SEPSIS	115(33.7%)	17(18.4%)
RECURRENT UTI	30(8.7%)	5(5.4%)
IgA Nephropathy	11(3.2%)	6(6.5%)
VASCULITS	17(4.9%)	4(4.3%)
S D NEPHROTIC SYNDROME	31(9%)	11(11.9%)
UROTHIASIS	15(4.3%)	4(4.3%)
HEMORRHAGIC CYSTITIS	3(0.8%)	1(1%)
SLE	17(4.9%)	8(8.6%)
HUS	3(0.8%)	2(2.1%)
RENAL VEIN THROMBOSIS	3(0.8%)	3(3.2%)
ATN	7(2%)	3(3.2%)
ALPORT SYNDROME	1(0.2%)	1(1%)
KAWASAKI DISEASE	2(0.5%)	1(1%)
APGN	19(5.5%)	6(6.5%)
RPGN	11(3.2%)	10
Congential anomalies of kidney	24(7%)	6(6.5%)
DKA	9(2.6%)	4(4.3%)
MALIGNANCY	15(4.3%)	5(5.4%)
Post major operation	7(2%)	2

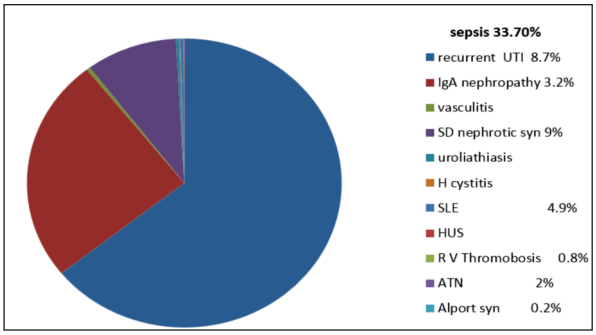

Fig2: Distribution Of Moderate Proteinuria

Among moderate proteinuria , sepsis was the most commom cause comprising 115 cases of the total 341, followed by steroid dependent nephritic syndrome cases (31 cases).Third in frequency was 30 cases of recurrent UTI. Other important causes included congential anomalies of kidney(24 cases of whom 10 had ureteropelvic junction obstruction (UPJO), 4 had vesicoureteral reflux, 2 only had diagnosis of hydronephrosis, 2 had renal dysplasia,3 had a posterior ureteral valve, 3 had autosomal recessive polycystic kidney disease (ARPKD), acute progressive glomerulonephritis cases(19 cases), vasculities (17 cases) and SL E(17 cases).Uncommon cases included alport syndrome,Kawasaki disease,HUS ,renal vein thrombosis as depicted in table 3

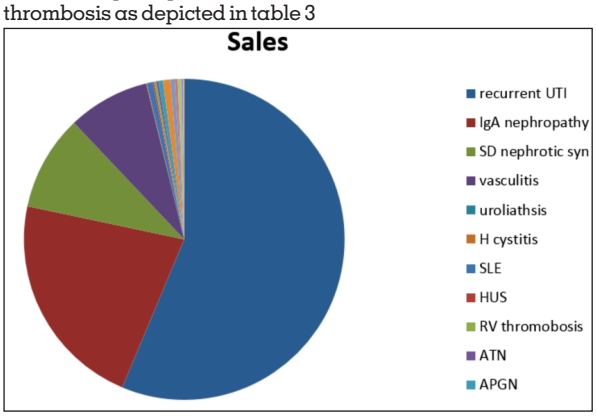

Fig2: Distribution Of Severe Proteinuria

For severe proteinuria cases, sepsis,SD nephrotic syndrome ,RPGN,SLE were recorded as the most important cases.1 case each of Kawasaki disease,alport syndrome and hemorrhagic cystitis were seen.

DISCUSSION

The reported prevalence of persistent proteinuria in general population in previous studies ranges from 0.03% to more than 15% depending on the characteristics of the patients. (10,11,12) In the present study, the prevalence of at least one positive urine protein result was 18.1 %, with the children being predominantly female. We also found that 3.7% of the children had persistent proteinuria, which is consistent with a previous cohort study including 8954 children between 8 and

15 years of age, in which 2.5% of the children had proteinuria at least twice out of four samples.(13) Another study on urinalysis results of hospitalized children in the US reported a prevalence rate of proteinuria of around 2–4%.(14) Almost all previous studies have reported that the prevalence was higher in females than in males with proteinuria, which is consistent with our findings. Proteinuria is common during renal injury, and suggests kidney damage in addition to an elevated serum creatinine level. It is well known that AKI is associated with the outcome of critically ill pediatric patients, and even in neonates (15,16) In a retrospective study with 1900 adult critical patients, the odds ratio of mortality increased along with the severity of proteinuria as assessed using dipstick tests, and the authors suggested that proteinuria with AKI was associated with an increased risk of mortality.(17) .In our study we also correlated the severity of diseases with degree of proteinuria. A recent review showed that proteinuria may not only represent an early marker of renal injury, but that it is also an important marker of chronic kidney disease.(18)

Infection-related nephropathy other than with UTIs has also been reported.(19,20) The 132 children(30.4%) with significant persistent proteinuria in this study were found to have proteinuria during septic work-up. Half of these children had bacteremia, and proteinuria resolved in all of these patients near to or at the end of the infectious course.

It has been reported that during UTI, dipstick results positive for urine protein may occur as a consequence of the reaction of the protein test pad with leukocytes and bacterial proteins rather than renal leakage of protein.(21) However, in cases with true pyelonephritis, glomeruli inflammation causing morphologic changes may actually result in glomerular dysfunction.(22) We noted significant persistent proteinuria in the patients with refractory or recurrent UTIs(8% cases), suggesting parenchymal damage after prolonged pyelonephritis rather than post-renal proteinuria.

Other exceptional causes such as diabetic ketoacidosis (14 cases), Kawasaki disease (KD) (3 cases), were also associated with persistent proteinuria. Orban et al. reported that the incidence of DKA-related renal injury and related proteinuria was high among the children they studied.(23) The renal involvement in KD may the consequence of an immune complex-mediated mechanism or cytotoxic T cells leading to kidney image and subsequently proteinuria. (24)

Few case reports have reported malignancy-related proteinuria in children, which accounts for up to 4.6% in our study. Vankalakunti et al. reported 12 cases with non-Hodgkin lymphoma, chronic lymphocytic leukemia, acute lymphoblastic leukemia, Burkitt's lymphoma, intravascular lymphoma, Hodgkin lymphoma and chronic myeloid leukemia with renal involvement. Among these patients, 66% had proteinuria with a nephrotic range or non-nephrotic range, and the renal biopsy results revealed lymphomatous interstitial infiltration in 75% of the cases.(25)

CONCLUSION

It can be easily concluded that assessing those children with persistent proteinuria is crucial as substantial of them develop chronic kidney disease. Many clinical diseases other than primary renal disease also had renal involvement and manifest as proteinuria initially. This retrospective review of children with persistent proteinuria will help in evaluation of persistent proteinuric children.

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