Original Research Article

Determination of prevalence of asymptomatic proteinuria and haematuria in 5-15 year aged school children in southern India

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ABSTRACT

Background: Chronic renal diseases remain major cause of morbidity and mortality in young children. Although idiopathic nephrotic syndrome takes on chronic course other histopathological variants can lead to rapid progression of disease. Proteinuria in children can be physiological. Hematuria in children is always should be investigated. Persistent proteinuria in children should be investigated for any significant progressive renal disease after excluding orthostatic proteinuria. Although many countries adopt high risk screening in pediatric age group many eastern countries advocate school screening for asymptomatic proteinuria and hematuria using dipstick urine screening.

Methods: A 6 month cross sectional study of asymptomatic children aged 5-15 years in metropolitan school for dipstick urine analysis for proteinuria and hematuria.

Results: The ratio of male and female children in the study is 1.2:1 (total-1999, male-1056, and female-934). Age group ranged from 5 to 15 with mean 12.13 and standard deviation (SD)-2.46. Maximum number of students in the study are above 10 years of age. Children with isolated asymptomatic proteinuria have significant differences due to their sex (p value-0.005) and hematuria (p value-0.007). Prevalence of asymptomatic proteinuria is 9.8% and hematuria is 1.05%. Prevalence of persistent proteinuria is 1.35%.

Conclusions: Prevalence of asymptomatic proteinuria and hematuria can be determined using dipstick urine analysis in school children. Mass screening is cost effective and feasible only if persistent cases of proteinuria are followed up, ruling out orthostatic proteinuria. Although study is feasible, it is cumbersome. High risk screening is the best cost effective method.

Keywords: Proteinuria, Hematuria, dipstick test, School children

INTRODUCTION

Urinary finding of an abnormal protein or blood may be an indicator of renal disease.¹ Proteinuria and or haematuria may be just an normal finding in which it may be transient or persistent or it may be an pathological abnormality in which proteinuria may be fixed proteinuria or persistent proteinuria which may on further evaluation lead to finding of an abnormal function of kidney. It is one of the alarming situation for the parents when there is macroscopic haematuria or when physician finds positive urinary dipstick for protein or blood and disclosing the

results to parents. Isolated haematuria without protein in urine is not pathological except in cases of hypercalciuria with stones, tumours and schistosomiasis.² But finding protein in urine is abnormal. It carries very important diagnostic clue in finding glomerular diseases and chronic kidney disease as well.³ Proteinuria in nephrotic range also carries prognostic importance. Persistent nephrotic range proteinuria is an independent risk factor for progressive renal injury even when the kidney function are normal. So early identification of chronic renal diseases can be possible by detecting urinary protein and blood and helps in prevention. Mass screening programmes can be useful

in identifying these urinary abnormalities although cost effectiveness of such programmes are debated.⁴ Most common feature of any glomerular disease may be excretion of plasma proteins. Proteinuria may be the cause and effect of glomerular injury and many of the systemic complications of glomerular injury. In healthy school going children urinary abnormalities can be present. Detection of urinary abnormalities may help to prevent and diagnosing renal problems early in the course of renal disease and thus reducing the progression of disease by early intervention.⁵ Prevalence of asymptomatic proteinuria varies between 6% to 10% in first screening of urine samples due to ethnic and socioeconomic reasons.⁶ On further evaluation prevalence of proteinuria it is positive only in 0.7% to 1.9%.^{6,7} Prevalence of haematuria is around 5.5% in first screening in study done in America states. Persistence of urinary abnormalities should need further follow up and evaluation to detect renal diseases early since proteinuria is an independent risk factor for progression of renal disease and cardiovascular morbidity.⁸ Only countries like Japan, Korea and Taiwan have clear consensus on screening for urine analysis and some countries have their school health programmes with examination of urine for proteinuria and haematuria as routine.⁹ There is no worldwide consensus on screening for urinary abnormalities to detect early stages of kidney diseases on large scale population and cost effectiveness of such programmes are debated.¹⁰

Furthermore epidemiological data on prevalence of early stages of chronic kidney disease (CKD) in children are scarce and limited. Some countries have epidemiological data that are not population based and have only data's on late stages of CKD. In countries like India due to lack of economic resources children are opted out of transplant and dialysis procedures due to their presentation in late stages.¹¹ There is under report of epidemiological data on CKD in children due to lack of diagnosis of early stage of kidney diseases. Moreover there is no clear definition and classification of CKD historically. Even recent classification by NKF-K/DOQI IS debated that it should include additional features like haematuria and proteinuria in stages 1 and 2 rather than classifying them as CKD. Globally children with stage 2 or lower stage constitutes about 18.5-58.3 per million children. In India prevalence of CKD with recent studies is around 0.8% to 1.9%. In Indian kidney registry that is started from 2005 up to 2010 there are 54,813 submissions out of which 1818 were paediatric cases.¹² So on the era of increasing obesity, hypertension and dyslipidemia in children in India screening of children for proteinuria and haematuria may be useful to identify CKD in early stages and thus appropriate intervention can be done at the earliest so that the course of the disease can be changed and progression of the disease can be prevented.^{13,14} Normally children excrete small amounts of protein in their urine which can be described as physiological. Protein excretion decreases from the age of newborn through childhood to adolescent period where it can reach the level of adult values of 150 mg per day. Normal rate of protein excretion in children is

constant throughout the childhood period.¹⁴ It is usually less than 150 mg/m²/day. Upper limit of normal protein excretion in children: (corrected for BSA) up to one month in full term neonate- 300 mg/m²/day, at 1 year- 250 mg/m²/day, at 10 years- 200 mg/m²/day and in late adolescent- 150 mg/m²/day. Nephrotic range proteinuria is defined as protein >40 mg/m²/hour or a first morning protein: creatinine ratio of >2-3:1. It can be expressed as >50 mg/kg body weight/24 hours. Normally children above 2 years of age will have protein creatinine ratio of less than 0.2. Any value above 2 is considered as nephrotic range proteinuria.¹⁵ Upper limit of normal urine spot PCR in children from 6 months to 2 years -0.52. In older children and adolescent children -0.2. Anything above 3 will be nephrotic range and it reflects glomerular disease. The percentage of various proteins in the urine will be albumin in the range of 15%, immunoglobulins and LMW proteins in the range of 35% and Tamm-Horsfall proteins in the range of 50%. In children who underwent dipstick urine test for proteins, approximately 10% will be positive in the initial screening. On subsequent screening with dipstick it will be negative. This phenomenon defines transient proteinuria and the cause remains elusive. Mostly urine dipstick will be <2+ in transient proteinuria. Some of the causes of proteinuria are fever, exercise etc. Orthostatic proteinuria may occur as isolated finding without hematuria in an asymptomatic individual in a random urine sample. It is the most common cause of persistent proteinuria in school going healthy asymptomatic children in 60% children. In any child having persistent asymptomatic proteinuria he or she should be evaluated for orthostatic proteinuria. In children with this condition protein excretion never exceeds 1 g/24 hours. The absence of protein in 3 consecutive early morning urine sample dipstick with protein-creatinine ratio <0.2 confirms the diagnosis of orthostatic proteinuria. Cause of orthostatic proteinuria: It may be due to altered renal hemodynamics and partial renal vein obstruction. Any children with positive dipstick for 3 consecutive early morning samples will be termed as having fixed proteinuria (dipstick 1+ or >with specific gravity. 1.015 or protein-creatinine ratio >0.2). It may indicate intrinsic renal disease or a tubular disorder. Glomerular proteinuria is defined as urinary protein excretion >100 mg/m²/24 hour or >4 mg/m²/hour. If it is present it is abnormal in children. Normally in any child with urine spot PCR >1 or proteinuria of any grade with features of renal disease should be suspected to have glomerular proteinuria. If this persistent for more than three months it is called as persistent proteinuria. Presence of blood in the urine is a frightening situation for the parents and presence of microscopic haematuria is concern for paediatrician. Prevalence of gross haematuria is around 0.13% whereas for microscopic haematuria it may be ten times as for gross haematuria. Most of the causes are identifiable in cases of gross haematuria. Repeated tests for microscopic haematuria prove that most cases are transient and its prevalence decrease to <0.5%. Microscopic haematuria indicates abnormal number of RBC'S in urine. Presence of >5 RBC'S/mm³ in uncentrifuged urine or >5 RBC'S HPF

in a centrifuged urine sample indicates significant proteinuria. Haematuria without symptoms may be either microscopic or macroscopic. It may indicate either renal, or systemic disease. It needs long term follow up to identify the cause. Dipsticks tests have 100% sensitivity and 99% specificity in detecting haematuria. Asymptomatic microscopic haematuria in the presence of significant proteinuria need special importance to look for renal diseases.¹⁷ The main objective of the study is to determine the prevalence of asymptomatic proteinuria and haematuria in 5 to 15 year old school children and the secondary objective is feasibility of the study.

METHODS

This is a descriptive study done at school children in schools around Govt. KAPV Medical College and Hospital, Trichy, Department of Paediatrics. The study protocol was approved by ethical committee for research studies of Government KAPV Medical College And Hospital after getting permission from chief educational officer of Trichy corporation. Study design was school based cross sectional study. Study period was six months-August 2019 to January 2020 study population was school children in the corporation schools of Trichy near Government KAPV Medical College are taken for study. Both the boys and girls from the age group 5 to 15 years are included in the study with a sample size of 1999. Inclusion criteria was all school children in the age group 5 to 15 years. Exclusion criteria was children with fever, children with pre-existing renal disease, children with any other chronic illness, children taking chronic drug therapy, girl children who are having their menstrual periods. Informed consent was obtained from parents. Information was given to students for the method of collecting urine in sample test tubes. Morning urine samples were collected from the students in test tubes and urine dipstick analysis was done at the same time.¹⁸ Urine analysis was made by Mission dipstick reagent strips from Acon laboratories, Inc, USA.^{19,20}

For finding blood the test is based on the peroxidase-like activity of haemoglobin which catalyses the reaction of diisopropylbenzene dihydroperoxide and 3,3',5,5'-tetramethylbenzidine. The resulting color ranges from orange to green to dark blue. Any green spots or green color development on the reagent area within 60 seconds is significant. For finding proteins the reaction is based on the phenomena of "protein error" of pH indicators. At constant pH any development of green color is due to presence of protein. Color ranges from yellow to yellow-green for negative results and green to green-blue for positive results. A color matching block greater than trace is significant. Results of dipstick for proteinuria and hematuria were compared with their colour codes and abnormal values were i.e. significant proteinuria and hematuria were taken in to account for further statistical analysis to find out the prevalence of asymptomatic proteinuria and hematuria. Children who were tested positive for proteinuria or hematuria or both are subjected

to second urinary dipstick analysis on early morning urine sample on getting up from bed at home. It's done 4 weeks later to detect any persistence of the abnormality and those children with persistent abnormalities are referred to Paediatrics Department And Nephrology Department, Govt. KAPV Medical College and Hospital for further evaluation as a part of routine follow up to rule out orthostatic proteinuria. The statistical analysis was performed using statistical package statistical package for the social sciences (SPSS) software version 21 for measuring frequencies and percentage. P value ≤ 0.05 is considered statistically significant.

RESULTS

Total number of children participated in the study is 1999. Number of male children is 1056 and number of female children is 934. The ratio of male and female children in our study is 1.2:1. So male children participation is more (Table 1).

Table 1: Sex distribution of study children.

Sex	Male	Female
Subjects	1056	943

Nearly 52.83% of male children and 47.17% of female children were participated in the study (Figure 1).

Figure 1: Sex distribution of school children.

Table 2: Age distribution of school children.

Sl. no	Age of participants	Number	Percent
1	5	56	2.8
2	6	61	3.1
3	7	58	2.9
4	8	43	2.2
5	9	59	3.0
6	10	75	3.8
7	11	176	8.8
8	12	350	17.5
9	13	450	22.5
10	14	480	24.0
11	15	190	9.5
12	16	1	0.1
Total		1,999	100.0

The age group ranges from 5 to 16 with mean 12.13 and SD 2.46. Maximum number of students participated in the study are above 10 years of age (Table 2 and Figure 2).

Figure 2: Age distribution.

Among the isolated proteinuria, isolated hematuria and persistent proteinuria only those children with persistent proteinuria have significant differences due to their age (p value=0.031) (Table 3).

There are 196 cases (9.8%) with proteinuria positive, persistent proteinuria 27 (1.35%) and haematuria 21 (1.05%). Those children with asymptomatic proteinuria

have significant differences due to their sex (p value=0.005). Children with haematuria also have significant differences due to their sex (p value=0.007). Children with persistent proteinuria have insignificant p value (p=0.509) so that their differences may not be by sex but may be on chance (Figure 3 and Table 4).

Table 3: Prevalence of proteinuria, hematuria and persistent proteinuria.

Parameter	Total positive children	Percentage of positive children	P value
Isolated proteinuria	196	9.8	0.454
Isolated hematuria	21	1.05	0.120
Persistent proteinuria	27	1.35	0.031

Figure 3: Prevalence and sex distribution.

Table 4: Prevalence and sex distribution.

Parameter	Percentage of male	Percentage of female	Percentage of total children	P value
Proteinuria	7.42	11.93	9.8	0.005
Hematuria	0.42	1.61	1.05	0.007
Persistent proteinuria	1.06	1.61	1.35	0.509

The ratio of male and female children in the study is 1.2:1 (total-1999, male-1056, and female-934). Age group ranged from 5 to 15 with mean 12.13 and S.D-2.46. Maximum number of students in the study are above 10 years of age. Children with isolated asymptomatic proteinuria have significant differences due to their sex (p value-0.005) and haematuria (p value-0.007). Prevalence of isolated asymptomatic proteinuria is 9.8%. Prevalence of asymptomatic haematuria is 1.05%. Prevalence of persistent proteinuria is 1.35%.

DISCUSSION

This study was conducted among asymptomatic school children in primary schools, middle schools and higher

secondary schools around KAPV Medical College and Hospital, Trichy. The students participated are in the age group 5-15 years. In our study ratio of male to female children is 1.2:1 which is comparable to other studies. A Iyengar et al studied school children between 5-16 years with male to female ratio of 1:1.²¹ Percentage of male children is 52.83% and percentage of female children is 47.17%. The mean age of children in the study is 12.3±SD 2.46. Prevalence of isolated asymptomatic proteinuria is 9.8% which is quiet higher than the previous studies where most of the urine dipstick shows isolated proteinuria in the range of 3.5% to 5% for example studies of Parakh et al.⁷ Some studies from the other regions of the world had values between 7% to 10% as is the case from Plata et al.²² The prevalence of asymptomatic proteinuria among various age groups is not statistically significant.

Prevalence is higher among female children about 11.93% versus male children 7.82% which is statistically significant. Prevalence of isolated haematuria in our study is 1.05% which is comparable to prevalence of haematuria in first urine sample in the study done by Shajari et al.²³ El Shafi et al in their study have found that prevalence of haematuria in initial screening was 7.3% and further dipstick analysis showed only 5.53% were positive.⁸ The values of isolated asymptomatic haematuria are not influenced by age. But female children have higher percentage of positivity than male children which is statistically significant. Age factors doesn't influence combined proteinuria and haematuria. Prevalence is high among female children when compared to male children which is not statistically significant. Its prevalence is about 0.2%. Persistent proteinuria prevalence is 1.35% which is quiet higher than previous studies like with Rao et al where study persistent proteinuria on second dipstick was 0.51%.²⁴ Persistent proteinuria varies with different age groups which is statistically significant.

The limitations of our study are the prevalence of asymptomatic proteinuria varies among various regions in the world. So the sample size may be small to identify and further evaluate to identify the children with persistent proteinuria. The study period was short compared to other studies so that the possibilities of human errors is a possibility since the study is time consuming and requires man power to execute in a well-controlled and disciplined study. The possibility of increasing prevalence of proteinuria in first screening may be due to time limitation in reading the dipstick after dipping in the urine although it is read within 1 minute duration. The age group with increased prevalence may be in higher age groups because the sample size taken for children in the age group 5-10 years was low compared to age group >10 years. Although follow up is done to evaluate the cause for persistent proteinuria which is usually persisting for 4 months and haematuria, our study doesn't include follow up data's which requires long time for further tests to confirm the causes and analyse the data.²⁵

CONCLUSION

Prevalence of asymptomatic proteinuria and haematuria can be determined using dipstick urine analysis in school children. Mass screening is cost effective and feasible only if persistent cases of proteinuria are followed up, ruling out orthostatic proteinuria and investigated properly. Although study is feasible, it is time consuming and cumbersome in doing urine analysis in school children. High risk screening is the best cost effective method and it is recommended for early diagnosis and management of renal diseases in paediatric age group.

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