Proteinuria In The Rural Primary School Setting In Nigeria - Using Combi Test Strips

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Abstract

An epidemiological survey of the prevalence of proteinuria using Combi test strips was undertaken among 894 primary school children aged 6-14 years in Imesi-Ile rural communities in Osun State of Nigeria in order to identify those with such disorders. Proteinuria was present in 69 (7.70%) and persisted in 34 (3.80%) pupils. Identified causes of persistent proteinuria were schistosomiasis in 19 (2.13%), urinary tract infection in 1 pupil, acute glomerulonephritis in 1, orthostatic pattern in 7, and in the remaining 6, the cause could not be identified. The serum proteins, electrolytes, urea and creatinine levels were within normal limits in all the pupils except in that with acute glomerulonephritis where the urea, creatinine and the 24 hour urinary protein estimates were elevated. It is concluded that since the identified causes of persistent proteinuria in this study are largely due to infections and infestations, efforts directed towards prevention and treatment of these will go a long way in preventing proteinuria and other renal complaints in this and other rural communities of the third world.

INTRODUCTION

The prevalence and pattern of renal diseases in children remain poorly defined in many developing countries. Accurate diagnosis cannot be made easily in many centres in the developing countries because of the inavailabilty of adequate investigative equipment and expertise required to identify and characterise renal disorders[1]. The presence of proteinuria, haematuria or bacteriuria either singly or in various combinations may signify renal disease. Each of these abnormalities in the urine can be identified with the use of biochemical reagent strips. These abnormalities have different causes and they arise from different pathophysiological mechanisms.

Proteinuria implies a urinary excretion of up to 150mg of protein in 24 hours.[2] Excretion of more than 6mg/m^2/hour on a timed urine collection is significant proteinuria[3] and daily urinary excretion of more than 150mg is pathologic proteinuria.[2] Plasma proteins can cross the glomerular barrier, even in health[3]. The ability of these proteins to enter the glomerular filtrate is related primarily to the size of the protein and the molecular charge.

Intermittent proteinuria indicates that protein is detectable in only some of the patient's urine samples[3]. It may be found in febrile illnesses, exercise, stress, emotional disturbance or cold[3,4]. In orthostatic proteinuria, protein appears in specimens collected in the upright posture but not during recumbency[3,4]. Although, laboratory tests with albustix may show 2^+ or 3^+ protein reactions in patients with orthostatic proteinuria, the amount of protein excreted in 24 hours rarely exceeds 1 gram. Persistent proteinuria indicates that protein is found in every urine sample tested, either in the upright or recumbent posture and it usually reflects renal or urinary tract disease[3,4]. Persistent proteinuria could result from glomerular or non-glomerular mechanisms[2,3]. Glomerular and tubular proteinuria may be distinguished by electrophoresis of the urine when the tubular proteins migrate primarily in the alpha and beta regions with little or no albumin detected.[5] In glomerular proteinuria, the major protein is albumin.

The Medi-test Combi strips[6] used in this study are for rapid determination of protein in the urine. The active ingredient consists of tetrabromophenol blue. The colour fields correspond to the following albumin concentrations:

- No colour change/yellow - Negative
- Faint green colour - 30mg%
- Faint blue-green colour - 100mg%
- Deep blue-green colour - 500mg%

The development of fast screening methods for urinary abnormalities has improved the chances of early detection and management of many renal diseases[8]. Studies have been conducted elsewhere, where protein, red blood cells and bacteria were screened for in the urine of children as markers of renal disorders[7,8]. Such a study is desirable in order to determine if there are similar or related renal disorders in the children of the target community. This was why it was decided to carry out this work in Imesi-Ile, where a rural comprehensive health centre of the Obafemi Awolowo University Teaching Hospitals Complex is located.

Imesi-Ile is a town set on a hill in Osun state, Western Nigeria with a population of about 10,000 people. It is a closed rural community with a fairly captive population, where a number of studies had already been carried out in the past, and where long-term follow-up, and patient tracing is recognised to be feasible.

SUBJECTS AND METHODS

The subjects of the study were the Primary school pupils between 6 and 14 years old, in Imesi-Ile. Excluded from the study were: (i) Pupils who did not co-operate (ii) those withdrawn from school in the course of the study (iii) the children of parents who refused to give consent. A questionnaire containing questions on such details as age, class, sex, address, symptoms and signs of renal diseases was administered on each of the 894 pupils in all the 7 primary schools in Imesi-Ile. A detailed examination was also carried out on the pupils to identify those with features of renal diseases.

TESTING WITH COMBI TEST STRIPS, MICROSCOPY AND BACTERIURIA SCREENING.

The test strip was dipped into fresh urine for approximately 1 second, then drawn across the edge of the container to remove the excess urine. After 30 seconds, the test strip was compared with the colour scale and the results were recorded immediately. Colour changes that took place after 2 minutes were regarded as of no significance. Only pupils with initial positive results for proteinuria were screened the second time. Also, only the pupils with positive results the second time were screened the third time. The interval between one screening and the other was 48 to 72 hours. Once a pupil was negative with a screening, he or she was not screened again. The investigators ensured that pupils on fruits and fruit juices were not screened until they had stopped these for 3 days. The pupils with persistent proteinuria had their urine subjected to microscopy and bacteriuria screening.

METHOD OF DETERMINING THE PRESENCE OF ORTHOSTATIC PROTEINURIA.

The bladder was emptied at bedtime, and the first morning urine specimen was collected on waking up. Another sample was collected 2 hours later when the pupil had been ambulant. If the first urine specimen was negative and the second positive for protein, an orthostatic pattern was confirmed.

STATISTICAL ANALYSIS

The proportion of events occurring between two groups was compared with the Chi-square test and the level of significance was taken to be $P<0.05$.

RESULTS

The age and sex distribution of the population under study is shown in Table I. There were 503 boys and 391 girls. Male: Female ratio was 1.2 : 1. The mean age for the entire population was 9.32 years, median age was 10 years.

Figure 1

Table 1: Age And Sex Distribution Of 894 Imesi- Ile Primary School Children Screened For Proteinuria

Age Last Birthday	No. Of Males	No. Of Females	Total	Percentage
6	49	42	91	10.18%
7	54	36	90	10.07%
8	66	54	120	13.42%
9	62	35	97	10.85%
10	103	63	166	18.57%
11	36	41	77	8.62%
12	73	69	142	15.88%
13	37	34	71	7.94%
14	23	17	40	4.47%
TOTAL	503	391	894	100.00%

Figure 2

Table 2: Result Of Screening For Proteinuria

	MALES			FEMALES			TOTAL (Males & Females)		
Screening	1ST	2ND	3RD	1ST	2ND	3RD	1ST	2ND	3RD
Negative	462	471	481	363	379	379	825	850	860
30mg%	35	26	16	25	9	9	60	35	25
100mg%	4	4	4	2	2	2	6	6	6
500mg%	2	2	2	1	1	1	3	3	3
TOTAL	503	503	503	391	391	391	894	894	894

Following screening, it was found that the number of positive samples decreased with repeated screening while the negative ones increased. Sixty nine (7.7%) pupils had

proteinuria following the first screening while 34 (3.80%) had proteinuria after the third screening (Table II).

Figure 3

Table 3: Age And Sex Distribution Of 34 Pupils With Proteinuria At The Third Screening

Age (years)*	Males	Females	TOTAL
6	2	-	2
7	1	1	2
8	1	-	1
9	2	3	5
10	5	3	8
11	3	1	4
12	5	2	7
13	3	2	5
14	-	-	-
TOTAL	22	12	34

The 34 pupils with persistent proteinuria were made of 22 males and 12 females (Male to female ratio of 1.83:1). The peak age for proteinuria was between 9 and 12 years (Table III).

Figure 4

Table 4: causes and level of persistent proteinuria identified among the 34 pupils.

	30mg%	100mg%	500mg%	TOTAL	% of 894
Schistosomiasis	13	4	2	19	2.13
Acute glomerulonephritis	-	-	1	1	0.11
Urinary tract infection	1	-	-	1	0.11
Orthostatic pattern	6	1	-	7	0.78
"Indeterminate/Idiopathic"	5	1	-	6	0.67
	25	6	3	34	3.80

Twenty five of these 34 pupils with persistent proteinuria had proteinuria of 30mg%; 6 had proteinuria of 100mg% and 3 had proteinuria of 500mg% (Table IV). The level of serum electrolytes, urea, creatinine and proteins were within normal limits in all the pupils with persistent proteinuria except the one with acute glomerulonephritis.

IDENTIFIED CAUSES OF PERSISTENT PROTEINURIA

(1) Schistosomiasis:- Nineteen (2.13%) pupils with proteinuria also had schistosomiasis (Table IV). The proteinuria was 30mg% in 13; 100mg% in 4 and ? 500mg% in 2 pupils. There were 10 pupils with symptoms of schistosomiasis less than one year and 9 pupils with the symptoms for over one year. There was a significant difference in the degree of proteinuria from schistosomiasis between children whose symptoms have been on for less than one year and those above one year. ($X^2 = 9.4$; df=2; $p<0.05$)

(2) Urinary tract Infection:- One pupil (0.1%) with urinary tract infection also had proteinuria of 30mg%. The organism identified was Proteus spp. and the pupil had shown symptoms suggestive of urinary tract infection for over 4 weeks. The urinary pH was 9 before treatment. There was no more proteinuria when re-assessed a week after completing treatment for urinary tract infection.

(3)Acute glomerulonephritis : A 6-year-old primary one pupil (0.1%) had features of acute glomerulonephritis. The diagnosis was based on the complaints of generalised body swellings, oliguria and coca-cola coloured urine. He had scabies skin lesions on presentation. The blood pressure was 110/70mmHg. There was no ascites or pleural effusion. He passed substantial amount of protein and red blood cells in the urine. He was further investigated at the Wesley Guild Hospital, Ilesa. The highest blood pressure during the Wesley Guild Hospital admission was 115/80mmHg. The highest urea level was 16.5mmol/L; creatinine 164 mmol/L. The electrolytes were within normal limits. The highest 24 hour urinary protein estimation was 2.8g per day. The dipstick estimation of proteinuria was greater than 500mg%; urine showed erythrocytes of greater than 250/microlitre. The anti streptolysin O titre could not be estimated.

He responded to fluid restriction of 400ml/m^2/24 hours + urine output of the previous day; diuretics in form of frusemide 1-2mg/kg/day. Urinary protein was 30mg% on discharge and had disappeared 4 weeks after discharge.

(4) Orthostatic proteinuria test:- This was carried out on 13 pupils whose cause of proteinuria could not be explained. In 7 (0.78%) of them, orthostatic pattern was identified. Six of these had 30mg% of proteinuria and one 100mg%.

(5) “Indeterminate/Idiopathic” proteinuria

The cause of proteinuria in 6 pupils (0.67%) could not be determined after schistosomiasis, acute glomerulonephritis, urinary tract infection and orthostasis had been excluded.

DISCUSSION

The dipstick had been used in many previous studies to screen for parameters like protein, blood and bacteria in the urine[4,7,8]. The screening method for proteinuria where only pupils with initial positive results were screened the second time, and only pupils with positive results following the

second screening were screened the third time will exclude some pupils with intermittent proteinuria. It will, however, help to identify those with persistent proteinuria- as this is the group that may have renal diseases. This screening method also reduces cost and time for screening everybody all over.

The prevalence of proteinuria (30 mg % and above) was 7.7% following the initial screening. By the time screening was repeated two more times, the prevalence had dropped to 3.80%. Both values of first and third screening were less than the value of 8.6% in Ajasin's[9] study of isolated proteinuria in Mushin, Nigeria; [10].7% in Vehaskari and Rapola's[10] study of isolated proteinuria in school age population in Finland and the prevalence rate of 77.4% in the study by Bello[7] in Ilorin, Nigeria. The prevalence rate of 7.7% at first screening is, however, higher than the value of 5.8% obtained by Akinkugbe et al [11] in their study of 2 geographical locations in Ibadan, Nigeria. In all the previous studies[7,10], screening was done only once. The higher prevalence of proteinuria in those one - time screenings could actually be due to false positive results as the prevalence of proteinuria in this study reduced with repeated screening. Though, persistence of proteinuria is very often an indication of the presence of renal pathology[4], studies by McLaine and Drummond[12], Chen and Mott[13] on different groups of patients with persistent proteinuria revealed no evidence of glomerulonephritis on renal biopsy. It would have been ideal to carry out further renal investigations like ultrasound and biopsy on the 6 pupils in whom the probable causes of proteinuria could not be determined. The parents, however, did not consent to further investigation because they believed that nothing was wrong with their children since they were not symptomatic.

Orthostatic proteinuria, which was demonstrated in 7 pupils is generally accepted as a functional variant and of no clinical importance[4]. Children with this disorder excrete normal or slightly increased amounts of protein in the supine position. In the upright position, the amount of protein in the urine may increase 10 fold or more. The cause is unknown. Haematuria is always absent in such patients and renal biopsy is often normal or may show mild non-specific alterations[4]. Follow-up studies of young adults with orthostatic proteinuria extending over 10 years have failed to demonstrate progression to overt renal disease. Most individuals ultimately lose their proteinuria, but in some, the pattern may persist[4].

Proteinuria observed in the pupil with urinary tract infection may result from irritation of the lower urinary tract, increased secretion of tissue proteins and inflammation of the accessory sex glands[3]. This is referred to as secretory proteinuria. The fact that the proteinuria disappeared following treatment in this child lends credence to one or more of the above pathophysiologic mechanisms as the cause of the proteinuria.

It has been shown in the last few decades that infective agents like Plasmodium malariae, Entamoeba histolytica, Ascaris lumbricoides, Schistosoma haematobium, Schistosoma mansonii and viral hepatitis antigen could directly cause immune complex nephritis[14]. It is also believed that endemic parasitaemia leads to persistent antibody response which results in circulating antibody - antigen complexes. In some individuals, these complexes become trapped in the glomerular basement membrane, leading to renal damage which may clinically manifest as nephrotic syndrome[14].

The environment where the study was carried out is a typical tropical rural environment where infestations or infectious agents such as Schistosoma haematobium, Plasmodium spp, filaria worms and hepatitis viruses occur. Each of these may lead to the development of nephritis. It was difficult to have correct urine samples collected for 24-hour urinary protein estimation since it was done on out-patient basis. It was discovered that un-supervised collections were tampered with as some pupils added water while some others added their sibling's urine to increase the volume of urine to be submitted. This method of screening did not take into consideration pupils with intermittent proteinuria. Such pupils could only be identified by screening all pupils the second and third times unlike in the present study in which further screening was limited only to those with initial positive results for proteinuria.

Causes identified for proteinuria in this study are largely due to infections and infestations. Efforts directed at prevention will go along way in preventing proteinuria and renal complaints in this and other rural communities of the third world.

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