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Preliminary Study: The challenge of providing tertiary care for renal disease in children admitted to the University Teaching Hospital, Lusaka Zambia

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Abstract

Renal disease in children commonly presents as nephrotic syndrome of the minimal change type, glomerulonephritis, and or a combined nephritic-nephrotic clinical picture. When not responsive to steroid, underlying focal segmental sclerosis is usually attributed to diseases like malaria, schistosomiasis and a host of viral diseases with high mortality outcomes. In order to understand the profile of renal disease and the outcome obtained in a resource constrained University Teaching Hospital, without access to renal biopsy, a study of 34 children referred to the renal clinic, for tertiary care in 2003, was done.

Objective: To determine the type and clinical outcome of renal diseases in children referred to the University Teaching Hospital, Department of Paediatrics and Child Health.

Methods: All 34 case records available in the Paediatric Renal Diseases clinic, in the Department of Paediatrics and Child Health, University Teaching Hospital, were reviewed retrospectively and data analysed manually and with EPI-info, 2002 Version.

Results: The commonest reasons for referral were glomerulonephritis and nephrotic syndrome, accounting for 27 out of 34 cases. Others were haemolytic uraemic syndrome, schistosomiasis and HIV nephropathy. At the last review in the clinic, 16 had made full recovery, 7 were still symptomatic with either and or raised blood pressure, proteinuria or oedema, 7 died, while 4 were lost to follow up.

This preliminary study demonstrates improved clinical diagnosis in the post referral period. Good history, physical examination, accurate blood pressure monitoring, basic urine chemistry and microscopy of the urine, together with a clear understanding of steroid responsiveness, and judicious use of antibiotic, anti-hypertensive and supportive care, does achieve improved clinical diagnosis and subsequent improved clinical care.

Conclusion: A good history, physical examination and basic investigation provide sufficient diagnostic criteria for the most common renal conditions like nephrotic syndrome and nephritis, in a resource-constrained setting like Zambia. There is need to routinely test all children categorized as partially or non-responsive to steroids, for HIV, and other infections such as malaria. Medical treatment of nephritis and nephrotic syndome should result in improvement in more than half of the patients. Though the numbers seem few, the health system needs to cater more comprehensively for paediatric renal pathology.

Background

The University Teaching Hospital, Department of Paediatrics handles 30,000 to 35,000 children annually. Of these 10,000–14,000 cases are re-attendances. Common disease conditions include malaria, malnutrition, respiratory tract infections, tuberculosis, diarrhoeal diseases, anaemia and HIV and AIDS. Renal disease constitutes less than one percent, (0.14) percent of the total caseload. Each renal case referred, however signifies the requirement for expensive tertiary intervention, which is not available at UTH.

The **main objective** of this preliminary study was to determine and document the outcome in children with renal disease, admitted to the University Teaching Hospital in 2003, in order to improve the routine clinical care of renal cases. The **specific objectives** were:

1. To describe the type of renal disease and outcomes among paediatric patients referred to UTH.
2. To determine the course of the disease during care and follow up at the University Teaching Hospital.
3. To describe the clinical care given to paediatric renal patients and identify areas for additional support for these cases.

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Materials and methods

The study was a retrospective, descriptive medical records review of all known renal patients. Permission was sought to review patients and records from the consultant in charge of the Nephrology clinic in the Department of Paediatrics and Child Health.

Manual method and EPI-INFO were used to analyse the data. Selection bias was inevitable because the sample size of 34 was pre-determined by the number of cases followed up in the one-year period under study (2003), namely, this was the total clinic case load.

Names or physical addresses were not used on the data spread sheet and were not linked to the real patients once the spreadsheet was in use for the study. Those children who had an HIV test as part of the routine workup of their renal disease could not be linked to the HIV test results on the data spreadsheet used for data analysis.

Results

Type of renal disease: Age, sex and pre and post referral diagnosis and care by clinicians.

The clinical practice of referring and tertiary level clinicians provided data from which we were able to deduce the type of renal illness presenting to a tertiary referral facility, such as UTH. Ten of the 34 (29.4 %) children were from out of Lusaka, and representing each of the other 8 provinces of Zambia and 21 were Lusaka based. There were 64.7 per cent male to 35.3 percent female. The age range was from 2 years to 13 years, with a mean age of 7.9 years and median age 8.5 years.

The pre-referral diagnoses vary from a definite diagnosis of nephrotic syndrome in 10 children and glomerulonephritis in 1 child. The rest, 23 described a variety of clinical features such as facial swelling, nephritic syndrome, renal failure, anemia, cardiac, cough with dyspnoea, generalized body swelling, haematuria, oliguria, pulmonary tuberculosis, recurrent nephritis, rheumatic heart disease, scabies, severe malnutrition and pneumonia. Three children had no diagnoses or description.

The prereferral treatment was as diverse as the diagnoses.10 out of 34 children were not on any treatment at presentation, and 24 of the 34, on combinations of prednisolone, frusemide and penicillin. Duration of illness before referral ranges from 2 days (in one patient), to 12 weeks of illness with an *average of two weeks*. Thirty-six point four per cent of the children had suffered with illness for two weeks, before referral to UTH, followed by 33 per cent with 10 days of illness. Average length of illness before referral ranges from 10 days to two weeks, before referral to UTH for 69 % of referred children.

Table 1 Pre-referral and post referral Diagnosis

Diagnosis	Pre-referral		Post-referral	
Gloumenulo Nephritis	1	2.9%	15	44.1% p-value <0.001
Nephrotic syndrome	10	2.9%	12	35.3% p-value = 0.278
Nephritic Nephrotic	None	–	3	8.8%
Haemolytic Uraemic	None	–	2	5.8%
Schistosomiasis	None	–	2 schistosomiasis earlier identified as	5.8%
HIV nephropathy	None	–	1	2.9%
Other (descriptive)	18	52%	Nil	–
No diagnosis	3	8.8%	–	–
Renal Failure	2	5.9%		–
Total		**100%**	**34**	**100%**

Glomerulonephritis (44.1 %) occurred more frequently than nephrotic syndrome (35.3 %) in the 2003 renal clinic. Referring health practitioners, outside of the specialist setting of the University Teaching Hospital, do not seem to be able to recognize glomerulonephritis despite it being among the two most common renal conditions in children. Nephrotic syndrome appears to be the easier diagnosis for them to make. Data shows a significant difference in diagnosis between referring health practitioners (1 case of Glomerulonephritis) and specialists (15 cases of Glomerulonephritis), with a p-value of 0.01, which was significant.

Post-referral cases have a more definitive diagnosis than in the pre-referral period. Given that no major

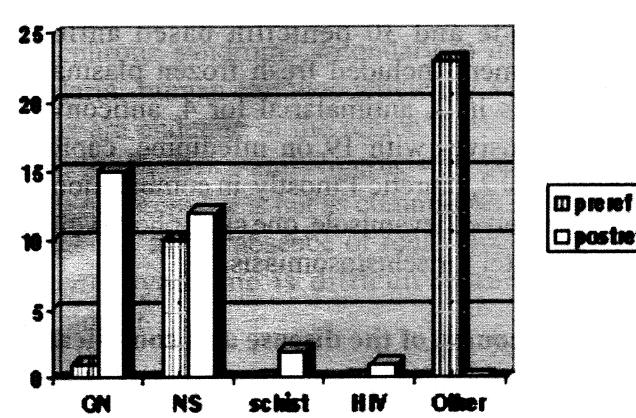

Figure 2: Demonstrates the value of clinical diagnosis offered in a

intervention, apart from clinical diagnosis and laboratory backup for chemistry, the value of clinical observation is demonstrated here. (GN =Glomerulonephritis, NS = Nephrotic Syndrome, Schist = Schistosomiasis).

Clinical care provided in the post-referral period: investigations, treatment, complications and follow up

Investigations

The study was unable to compare pre-referral investigations with post referral investigations given that these were not recorded in detail in the referral notes. A number of children had the following investigations done in the post- referral period:

25 of the 34 children had urine chemistry and microscopy and culture, of which 7 of the 25 were normal. Eighteen had abnormal findings, such as pus cells, casts, bacteriuria. Bacteria or parasites found included *Escherichia coli, klebsiella, pseudomonas* and *schistosomiasis* in 2 children.

Other Infective agents identified on serology included HIV in one of two tests. No hepatitis B was found in the 5 samples taken for Hepatitis B serology. Of the 2 malaria blood slides done, both were positive. The study design, being retrospective is limited in not being able demonstrate causal links. Malaria, HIV, schistosomiasis and bacteria were found and are known associations of glomerulonephritis. *Ultrasound of the abdomen* was done for 7 children. No special findings were described in these children. No renal biopsy was done in all the children at the University Teaching Hospital in 2003.

Treatment

Twenty of the 34 children received prednisolone, 21 frusemide and 30 penicilin based antibiotics. Other treatment included fresh frozen plasma for 3, Packed cells in 2, antimalarial for 4, anticonvulsant, antihypertensive- with 19 on nifedipine, captopril 5, proporanalol 2, diuretic 1 mostly in combination. Three children received levamisole, one cyclophosphamide and 2 praziquantel for schistosomiasis.

Outcome, course of the disease and complications

In the initial two to three weeks of treatment, 18 of the 34 children showed good response to medical treatment, with 16 being asymptomatic when last seen. Follow up in this study is for one episode of illness, and ranges from 4 days (lost to follow up) to 38 days. More than half, 52.9 per cent of all children, were asymptomatic at last follow up date. Most of those who improved, did so in the second week of hospitalization. Children were sent back to the referring practitioner, with recommendation for further actions. Seven children died, while 4 were lost to follow up. Complications were recorded as 20 out of 34 with hypertension, 4 out of 34 congestive cardiac failure and 3 out of 34 encephalopathy and acute renal failure. Tables 3a and 3b summarise these facts.

Response	Number of Children
Good	18
Poor	9
Fair	6
Unknown	1
Total	34

Table 3: a. Initial clinical response to therapy

Response	Number of Children
Asymtopmatic	16
Symtopmatic	7
Died	7
Lost to follow up	4
Total	**34**

Table 3: b. Status of the patient when last seen:

Discussion

The University Teaching Hospital (UTH), as a tertiary level hospital, is expected to deal with difficult renal cases in children. Cases were referred from all 8 provinces of Zambia. UTH however, is not adequately equipped to provide tertiary renal care. A number of reports, from Ghana, Nigeria and South Africa base their reports on the basis of biopsy results to guide diagnosis

and therapy.

Inspite of this constraint, this study provides the opportunity to document the effect of clinical interventions, in a setting without biopsy and without raising ethical issues on withholding of renal biopsy. [8] During the post referral period, clinical diagnosis was more definitive,indicative of the level of expertise available at the University Teaching Hospital in comparison to the referring institutions. The average length of illness before referral was from 10 days to two weeks. This gave the specialists sufficient time to try steroid therapy. The 2003 paediatric renal clinic was unable to do renal biopsy to confirm the clinical diagnosis.

Recognition and diagnosis of renal conditions

Patient diagnosis in a resource-constrained setting will depend on the competence of the referring practitioner. Most children referred for specialist care, 21 of the 34 (61.8 %), did not have a definite diagnosis. They had descriptions ranging from 'facial swelling, anaemia and even protein energy malnutrition'.

Glomerulonephritis and nephrotic syndrome were found to be the most common renal conditions among our children. Fifteen out of 34 (44.1%), had glomerulonephritis and 12 of 34 (35.3 %) had nephrotic syndrome. There was no significant difference between referring practioner and specialists in diagnosing nephrotic syndrome.

Parasitic infections can cause the whole range of glomerular lesions known, but most of them are proliferative. Glomerular lesions with little or no proliferation, such as in membranous glomerulopathy, focal segmental glomerulosclerosis, and minimal-change disease, are also seen [11,12,13,14,15,16].

Health practitioners should be able to make these diagnosis, based on a good history and basic investigations, fairly easily. The gap between pre-referral and post-referral diagnosis, needs to be closed by improving the clinical proficiency of referring practitioners. Facilities to investigate urine, urea and electrolytes are lacking and few personnel are trained in the care of children. Routine examination of urine such as "multistix", urea and electrolytes, serum proteins, would easily distinguish the two most common reasons for referral. The average length of referral was two weeks, which is short. This is fortunate as it provides the opportunity for the patient to begin timely investigation, steroid and antibiotic therapy at the tertiary level.

The management of glomerulonephritis in children

Glomerulonephrits occurred with the greatest frequency among the children seen at UTH in 2003. The 15 nephritis patients presented with the usual urinary findings of haematuria, hypertension and acute renal failure. Seven of them (11.8 %) progressed rapidly to severe renal failure, hypertensive encephalopathy and death. It is presumed that some of them might have had HIV infection (one tested positive of two tests done). Post infectious nephritis in Zambia is presumed due to beta haemolytic streptococcus and other pathogens. Malaria, HIV, schistosomiasis and other bacterial causes were found in some of our children. These agents are known associations with glomerulonephritis.[8,9, 10]

All the patients who received antibiotics,were on penicillin based antibiotic, considered safe in renal disease. [5,7] Medical and supportive management is therefore crucial and must include the use of antibiotics as indicated, water and salt restriction, use of diuretics and antihypertensive drugs. The choice of antihypertensive drugs was determined by availability. Most children received nifedipine, and diuretic. There was inconsistent supply of anti-hypertensives which meant patients had to buy from outside pharmacies.

The management of nephrotic syndrome in children

Literature suggests that the pattern of Nephrotic Syndrome may vary between different African countries.[8,9,10-16] Children in Ghana thought to have nephrotic syndome, were found to most frequently present with minimal change disease and focal segmental glomerulosclerosis (FSGS).[8] In the absence of adequate investigation, we assume that steroid responsive nephrotic syndrome or focal segmental glomerulosclerosis are the most likely pathologies in our children. We should however note that nephrotic syndrome secondary to infections such as malaria, human immunodeficiency virus, Hepatits B virus are endemic in the region[12,13,14,15,16]. Studies in Africa, South Africa and Nigeria, suggest that minimal change nephropathy is not as common as in the western hemisphere. In the absence of renal biopsy, idiopathic nephrotic syndrome is difficult to rule out in our environment.

For therapy of nephrotic syndome, we emphasize that despite the limited therapeutic facilities, half of these

patients may benefit from corticosteroids; however, steroid resistance and FSGS resulted in a high mortality.[8,9] In our study, more than half of the children were steroid responsive, suggesting minimal change nephropathy in Zambian children.

Studies have shown the association of [3, 8, 9, 16] HIV with focal segmental glomerulosclerosis. Most of those referred to the specialist clinic were likely to have focal segmental glomerulosclerosis or more complex underlying pathology, such as HIV or malaria.[12,13,14,15,16] Our study showed a mortality of 7 out of 34 children, or 23.5 % mortality. Mortality was high in this group possibly due to the fact that patients referred to UTH are usually very ill and we may not have identified disease like HIV in them.

Literature cited indicates that ethnic differences occur with black patients more likely to be steroid unresponsive. [3, 12,13,14,15,16] The histological pattern for nephrotic syndrome appears to be changing with more focal segmental glomerulosclerosis occuring.[8,11]

Given the fact that focal segmental glomerulosclerosis is a frequent finding in children with HIV disease, we would postulate that some of our steroid resistant cases are the result of focal segmental glomerulosclerosis due to HIV disease. [8,9,10,11] We therefore recommend routine screening of all steroid unresponsive cases of nephrotic syndrome for HIV disease, with appropriate counseling and support.

Steroid responsiveness therefore remains the most important tool for diagnostic and prognostic decision making, in our environment, until biopsy is consistently available.

All the nephrotic syndrome patients were put on the basic recommended doses of prednisolone with at least the induction phase and some going onto maintenance phases of the cycle of treatment. [1,2,3]

The more difficult steroid non-responsive cases, in addition to prednisolone, were tried on levamisole and or alkylating agent depending on availability.[3]

Conclusion

Although this study has yielded useful preliminary results, more studies to understand the pattern of renal disease in children in Zambia are required. Children with nephropathy require good basic routine care and investigations as well as more invasive and sophisticated renal investigations such as renal biopsy, and therapies including, alkylating agents, levamisole and other immune modulators, antihypertensive drugs and dialysis . The University Teaching Hospital has a challenge to fulfill the role of tertiary care giver and trainer for Zambian health professionals and patients.

Based on these findings, it is clear that children with renal disease are receiving sub-optimal care, at all levels of the healthcare system. Though the numbers of cases seem small, appropriate interventions need to be made available for children with renal disease, in order to improve outcome. Good care will attract more referrals. Health institutions through out Zambia, need to build capacity among health workers in the identification, recognition, investigation and initial treatment of renal disease, before referral for second opinion and tertiary care.

Routine testing for HIV, particularly in steroid non-responsive cases, is an important added dimension to the management of renal pathology in Zambia. The authors recommend testing for HIV, in all non-steroid responsive nephropathies, in addition to renal biopsy, for children in Zambia.

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