Open Access Library Journal
2024, Volume 11, e11368
ISSN Online: 2333-9721
ISSN Print: 2333-9705

Urinalysis of Children with Severe Malaria

Ajetomobi Ajayi[1], Olanrewaju Prisca Olanrewaju[1], Ojuawo Ayodele[2], Adedoyin Olanrewaju Timothy[2]

[1]Federal Teaching Hospital, Lokoja, Nigeria
[2]Faculty of Clinical sciences, University of Ilorin Teaching Hospital, Ilorin, Nigeria
Email: drajetajet@gmail.com

How to cite this paper: Ajayi, A., Olanrewaju, O.P., Ayodele, O. and Timothy, A.O. (2024) Urinalysis of Children with Severe Malaria. *Open Access Library Journal*, **11**: e11368.
https://doi.org/10.4236/oalib.1111368

Received: February 27, 2024
Accepted: June 27, 2024
Published: June 30, 2024

Abstract

Severe malaria is a major cause of mortality among children when not diagnosed and treated at an early stage. It is classified as a medical emergency. In this study, the urinalysis was done using the dipstick method on 82 (50%) children with severe malaria and another 82 (50%) without severe malaria, serving as controls. Data collated during the study were analyzed using chi-square and p-value with the aid of SPSS 23 software. The study shows that the urine pH and specific gravity were normal in all subjects after four weeks under consideration. Renal involvement in severe malaria recovers in four weeks.

Subject Areas

Pediatrics

Keywords

Malaria, Urinalysis, Proteinuria, Haematuria, Bilirubinuria

1. Introduction

Mortality in severe malaria ranged from none in well-equipped centers to as high as 45% in resource-poor facilities [1] [2] [3] [4] [5]. The main manifestations of severe malaria among semi-immune, residents of malaria-endemic countries are cerebral malaria and severe anaemia. Renal failure is not common [2] [4] [5]. Where renal failure occurs, damage to the kidneys might persist beyond the acute illness, as has been described in *P. malariae* infection and this could progress to nephrotic syndrome [6] [7] [8].

In a study of renal involvement in cerebral and uncomplicated malaria among Gambian children, Weber found Twenty-five percent of children with cerebral malaria, and 4% of children with mild malaria had an elevated serum creatinine above 62 μmol/l. Increased urinary protein excretion was frequent: 53% of

children with cerebral malaria had a glomeruli-tubular pattern of protein excretion, and 46% had a tubular pattern. Median albuminuria was 68 mg/l in children with cerebral malaria, 18 mg/l in children with mild malaria, and 9 mg/l in febrile children with other diseases ($P < 0.0001$) [2]. Shieban also indicated that acute renal failure was a recognized complication of *Plasmodium falciparum* malaria in non-immune individuals, affecting up to 30% as compared to 1% - 5% in natives in endemic areas, and representing a major contributor to mortality from malaria [3]. A similar study done by Sowunmi in Ibadan reported an incidence of 45% for acute renal dysfunction in children with acute *Plasmodium falciparum* malaria. Mild proteinuria occurred in 40% during the acute illness which was not related to creatinine clearance or peripheral parasite density [4]. Proteinuria was absent after recovery. Other features included oliguria in addition to systemic effects of malaria [3].

During the past decade, proteinuria has taken on new importance, and recent clinical and experimental data have suggested that proteinuria is an independent risk factor for the progression of renal diseases [9]-[15]. Not only is proteinuria associated with glomerular injury and loss of perm-selective properties, but experimental data have demonstrated that protein-tubular cell interactions have inflammatory and fibrogenic consequences that can contribute to interstitial damage and fibrosis [2] [4] [9]. Albuminuria was found in children with cerebral malaria, and in children with mild malaria, as well as children with febrile illnesses from other diseases [2] [3] [4] [5]. There was no significant association between the proteinuria and height of fever or the degree of parasitaemia, and there was no significant association between death and signs of renal impairment. Renal proteinuria is common in children with malaria in The Gambia, with prerenal, glomerular, and tubulo-interstitial factors contributing. It is more pronounced in children with cerebral malaria than in those with mild malaria. However, renal dysfunction is relatively mild and does not indicate a worse prognosis [2].

2. Materials and Methods

2.1. Sample Size

The minimum sample size was determined using the formula

$$n = \frac{Z^2 Pq}{d^2} \quad [16]$$

Where;

n = desired sample size

Z = the standard normal deviation usually set at 1.96% (or simply at 2.0) which corresponds to 95% confidence interval.

P = the proportion in the target population estimated to have a particular characteristic (renal impairment in severe malaria).

A reasonable estimated mean was 5.9% [2]. The quoted estimate was that of renal involvement in severe malaria as reported by several authors in the earlier

studies [17] [18] [19].

d = tolerable margin of error usually set at 0.05

$q = 1.0 - p = 1.0 - 0.05 = 0.95$

Thus, the minimum sample size:

$$n = \frac{1.96 \times 1.96 \times 0.059 \times 0.95}{0.05 \times 0.05}$$

$$n = \frac{3.8416 \times 0.0475}{0.0025}$$

$$n = 72.9 = 73$$

The minimum sample size was 73

Allowing for an attrition rate of 10%, a total of 82 children with severe malaria and 82 children with uncomplicated malaria were recruited into the study.

2.2. Subject Recruitment

Children between the ages of 6 months and 11 years presenting in the EPU with features of severe malaria were recruited consecutively as they presented. Those with features of uncomplicated malaria presenting in the General Outpatient Department (GOPD) as well as EPU between the ages of 6 months to 11 years were recruited as controls. Recruitment of subjects was carried out by the researcher, with the assistance of the resident doctors assigned to EPU, the Children's Ward and the General out Patient Department (GOPD). The children that meet the recruitment criteria were recruited serially into the study.

2.3. Ethical Considerations

Ethical clearance was obtained from the Ethics and Research Committee (ERC) of the Hospital. Informed consent was obtained from the mother, or both parents or caregivers before subject recruitment after clear explanation of the study in the language they best understood.

2.4. Study Population

A total of 164 children that meet the recruitment criteria were recruited serially into the study, out of which 82 (50%) had severe malaria and another 82, without severe malaria, served as controls. The male-to-female ratio was 1:1 in the subjects and 1.4:1 in the controls. The median age was 36.0 months in the subjects and 36.0 months in the controls, both groups were comparable ($p > 0.05$). Children between the ages 1 to 5 years constituted 62.2% of the entire population studied.

2.5. Urinalysis

About 15 - 20 mls of freshly voided urine was collected from each child into a sterile universal bottle. Urinalysis was performed immediately by the investigator using dipstick method. Ten milliliters of urine were tested, using Multistix 10SG (Bayer Diagnostics, with sensitivity of 98.5%) [17]. The reading of the strip is carried out by placing it at the side of the strip container against each of the

parameters being tested and observing the colour change. The reading is done 30 to 40 seconds as directed by the manufacturer (*i.e.* Multistix(R) 10SG Bayer Diagnostics, UK.) [16] [17] [18] [19].

2.6. Physical Characterization of Urine

Urine collected in the Universal bottle was subjected to direct observation for colour and clarity.

2.7. Dipstick Reagent Strip

Procedure:

Part (10 mls) of the collected uncentrifuged urine was properly mixed before testing.

All reagent pads of the strip were immersed in the urine specimen and the strip was removed immediately.

The edge of the strip was run against the rim of the container to remove excess urine.

The test strip was held horizontally and the colour changes on the test areas were compared closely with colour chart on the container.

The colour changes were read at the times specified by the manufacturer.

All instructions as regarding the storage and handling of the reagent strip were observed as stipulated by the maker (*i.e.* Multistix(R) 10SG Bayer Diagnostics, UK.).

2.8. Blood Sample and Laboratory Procedure

After proper cleansing with cotton wool swab soaked in 70% ethanol, 5 mls of blood was drawn from the most visible peripheral vein on the dorsum of the hand or the forearm of each child. Sampling was done using a sterile 23G needle attached to a 5 mls syringe. The researcher collected the specimen with assistance from the registrars working in EPU. Of this, random blood sugar was determined by glucometer using a drop of whole blood; the test strips used were the ACCU-CHEK (manufactured by Roche Sensitivity is 97.5%) [17] following standard operational procedure as prescribed by the manufacturer, two milliliters was dispensed into a specimen bottle containing dipotassium salt of ethylene diamine tetra-acetic acid (EDTA) for complete blood count and malaria parasite identification and quantification [18]. The World Health Organisation (WHO) procedure was adopted for the detection and identification of malaria parasites. Thin and thick blood smears were made. The thin film was fixed in methanol. The thick film was stained in 2% Giemsa stain for 30 minutes while thin film was stained in Leishman stain. The slides were rinsed in phosphate buffer (PH 7.2) for three seconds, dried and examined with ×100 objective for malaria parasites. Parasite count was done via a count of parasites in a field containing 200 white blood cell (WBC) in the thick film, and the number of asexual forms per microlitre calculated from the WBC count using the formula [17] [18] [19] [20] [21].

$$\frac{PC \times TLC}{200}$$

where

PC = Parasite count

TLC = Total leucocytes count

An observation of a parasitaemia rate of 5% and above for the red blood cells (RBC) was regarded as severe. The counting was done under supervision of the Chief Laboratory Technologist in the Haematology Laboratory of UITH.

The packed cell volume (PCV) was expressed as the volume of erythrocytes per litre of whole blood so that it indicated the relative proportions of plasma and red cells. A heparinized capillary tube was used to take blood from the EDTA specimen bottle and centrifuged using the micro-haematocrit centrifuge at 1000 revolutions per second for five minutes. The capillary tube was transferred to the haematocrit reader and the column of the Red Blood Cells (RBCs) was measured and this corresponded to the PCV [3].

3. Results

The results obtained are summarized in Table 1.

4. Discussion

4.1. Urinalysis in the Study Population at Admission

Proteinuria occurred in 62 (75.6%) of subjects and in 26 (31.7%) controls ($p = 0.01$). However, no massive proteinuria was observed in the study population. Twenty-two (26.8%) and 13 (15.9%) subjects had haematuria and bilirubinuria respectively ($p < 0.05$). The urine pH was normal in 90.3% of the subjects and 100% of the controls. Eight (9.8%) of the subjects had alkaline pH. The specific gravity was also normal in 86.6% of the subjects, while eleven (13.4%) of the subjects had high specific gravity. Specific gravity was normal in 95.1%, high in 3.7% and low in 1.2% of the control group ($p < 0.05$) (Table 1). A similar study by Webber among Gambian children with malaria, the findings are considerably similar. Renal involvement is common in children with malaria in The Gambia, with prerenal, glomerular, and tubulo-interstitial factors contributing. It is more pronounced in children with cerebral malaria than in those with mild malaria. However, renal dysfunction is relatively mild and does not indicate a worse prognosis as was the case in this study where the proteinuria resolved four weeks into recovery.

4.2. Urinalysis in the Study Population at Admission and at Fourth Week

There were significant differences in the urinalysis findings at fourth week and those obtained at admission. Sixty-nine (87.3%) of the subjects four weeks later had no protein in their urine ($p = 0.0001$). The urine pH and specific gravity were normal in all subjects at four weeks (Table 2). The findings in this study is

Table 1. Urinalysis in the study population at admission.

Urinalysis	Subject n = 82 (%)	Controls n = 82 (%)	χ^2	P
Proteinuria				
nil	20 (24.4)	56 (68.3)	34.11	0.001
1+	50 (61.0)	26 (31.7)	15.16	0.001
2+	12 (14.6)	0 (0)	24.00	0.001
Urinary pH				
Normal pH 4.5-7.5	74 (90.3)	82 (100)	0.82	0.365
Acidic pH < 4.5	0 (0.0)	0 (0)		
Alkaline pH > 7.5	8 (9.8)	0 (0)	16.00	0.001
Specific gravity (SG)				
Normal (1015~1030)	71 (86.6)	78 (95.1)	0.66	0.417
High (>1030)	11 (13.4)	3 (3.7)	9.14	0.003
Low (<1010)	0 (0.0)	1 (1.2)		
Haematuria	13 (15.9)	2 (2.4)	16.13	0.001
Bilirubinuria	22 (26.8%)	0 (0.0)		

Table 2. Urinalysis in the study population at admission and four weeks into recovery.

Urinalysis	Subject at admission n =82 (%)	Subject at fourth week n =79 (%)	χ^2	P
Proteinuria				
nil	20 (24.4)	69 (87.3)	53.96	0.001
1+	50 (61.0)	9 (11.4)	56.98	0.001
2+	12 (14.6)	1 (1.3)	18.62	0.001
Urinary Ph				
Normal pH	74 (90.3)	79 (100.0)	0.33	0.567
Acidic pH	0 (0.0)	0 (0.0)		
Alkaline pH	8 (9.8)	0 (0.0)		
Specific gravity (SG)				
Normal (1015~1030)	71 (86.6)	79 (100.0)		
High (>1030)	11 (13.4)	0 (0.0)		
Low (<1010)	0 (0.0)	0 (0.0)		
Haematuria	13 (15.9)	0 (0.0)		
Bilirubinuria	22 (26.8)	0 (0.0)		

similar to the findings of Webber among Gambian children and Sowunmi in Ibadan Nigeria. Finding of proteinuria at presentation indicates acute renal involvement in malaria, which demonstrated significant resolution four weeks into

recovery. Urinalysis, which is simple, easy procedure to carry out and less expensive compared to Glomerular Filtration Rate (GFR) estimation is therefore advice in children with severe malaria in Nigeria and other resource-limited tropical countries. This will serve as a major tool in preventing acute and sometimes progressive kidney damage from severe malaria.

5. Conclusion

The study of 164 children with malaria, 82 children have severe malaria serves as subjects, while another 82 with uncomplicated malaria as control shows that the urine pH and specific gravity have returned to normal in all subjects after four weeks of recovery, Sixty-nine (87.3%) of the subjects four weeks later had no protein in their urine ($p = 0.0001$). The urine pH and specific gravity were normal in all subjects at four weeks although 12.7% of the subject still having proteinuria. However, a similar study reveals that malaria has no significant effect on the chemical composition of urine with bilirubin positively correlated with the parasite density. Dipstick urinalysis can be used together with light microscopy in resource-limited malaria-endemic areas to accurately diagnose falciparum malaria infections. Another study demonstrated that malaria accounts for a significant morbidity and mortality rates around the world, especially in communities with limited access to healthcare. Some clinical signs in urine, like haematuria, coluria and proteinuria, help for early diagnosis of severe malaria cases.

6. Recommendations

1) More studies would need to be carried out particularly in other geopolitical zones of the country to determine the prevalence of ARF secondary to malaria.

2) Routine urinalysis would be of relevance as it helps in early identification of children with severe malaria.

Severe malaria predisposes to Acute Renal Failure (ARF) and measures to reduce its incidence would be an invaluable tool in preventive nephrology in Nigeria and perhaps other parts of the Tropics.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] The African Heads of State and Government (2000) Abuja Declaration on Roll Back Malaria (RBM) in Africa. African Summit on Roll Back Malaria.

[2] Weber, M.W., Zimmermann, U., Hensbroek, M.B., Frenkel, J., Palmer, A., Ehrich, J.H.H., *et al.* (1999) Renal Involvement in Gambian Children with Cerebral or Mild Malaria. *Tropical Medicine & International Health*, **4**, 390-394. https://doi.org/10.1046/j.1365-3156.1999.00409.x

[3] Sheiban, A.K. (1999) Prognosis of Malaria Associated Severe Acute Renal Failure in Children. *Renal Failure*, **21**, 63-66. https://doi.org/10.3109/08860229909066970

[4] Sowunmi, A. (1996) Renal Function in Acute Falciparum Malaria. *Archives of Disease in Childhood*, **74**, 293-298. https://doi.org/10.1136/adc.74.4.293

[5] Trang, T.T.M., Phu, N.H., Vinh, H., Hien, T.T., Cuong, B.M., Chau, T.T.H., *et al.* (1992) Acute Renal Failure in Patients with Severe Falciparum Malaria. *Clinical Infectious Diseases*, **15**, 874-880. https://doi.org/10.1093/clind/15.5.874

[6] Hendrickse, R.G. and Adeniyi, A. (1979) Quartan Malarial Nephrotic Syndrome in Children. *Kidney International*, **16**, 64-74. https://doi.org/10.1038/ki.1979.103

[7] Hendrickse, R.G., Adeniyi, A., Edington, G.M., Glasgow, E.F., White, R.H.R. and Houba, V. (1972) Quartan Malarial Nephrotic Syndrome. *The Lancet*, **299**, 1143-1149. https://doi.org/10.1016/s0140-6736(72)91373-6

[8] Kibukamusoke, J.W., Hutt, M.S.R. and Wilks, N.E. (1967) The Nephrotic Syndrome in Uganda and Its Association with Quartan Malaria. *The Quarterly Journal of Medicine*, **36**, 393-395.

[9] Afolayan, F.M., Adedoyin, O.T., Abdulkadir, M.B., Ibrahim, O.R., Biliaminu, S.A., Mokuolu, O.A., *et al.* (2020) Acute Kidney Injuries in Children with Severe Malaria. *Sultan Qaboos University Medical Journal*, **20**, e312-e317. https://doi.org/10.18295/squmj.2020.20.04.006

[10] Nakhjavan-Shahraki, B., Yousefifard, M., Ataei, N., Baikpour, M., Ataei, F., Bazargani, B., *et al.* (2017) Accuracy of Cystatin C in Prediction of Acute Kidney Injury in Children; Serum or Urine Levels: Which One Works Better? A Systematic Review and Meta-Analysis. *BMC Nephrology*, **18**, Article No. 120. https://doi.org/10.1186/s12882-017-0539-0

[11] Lagos-Arevalo, P., Palijan, A., Vertullo, L., Devarajan, P., Bennett, M.R., Sabbisetti, V., *et al.* (2014) Cystatin C in Acute Kidney Injury Diagnosis: Early Biomarker or Alternative to Serum Creatinine? *Pediatric Nephrology*, **30**, 665-676. https://doi.org/10.1007/s00467-014-2987-0

[12] Oshomah-Bello, E.O., Esezobor, C.I., Solarin, A.U. and Njokanma, F.O. (2020) Acute Kidney Injury in Children with Severe Malaria Is Common and Associated with Adverse Hospital Outcomes. *Journal of Tropical Pediatrics*, **66**, 218-225. https://doi.org/10.1093/tropej/fmz057

[13] Kwambele, L., Ndeezi, G., Ortiz, Y.A., Twesigemuka, S., Nduwimana, M., Egesa, I.W., Kumbakulu, K.P. and Yves Bafwa, Y.T. (2023) Factors Associated with Acute Kidney Injury among Children with Severe Malaria at Kiryandongo General Hospital, Uganda. *International Journal of Pediatrics*, **2023**, Article ID 2139016. https://doi.org/10.1155/2023/213901

[14] Muhamedhussein, M.S., Ghosh, S., Khanbhai, K., Maganga, E., Nagri, Z. and Manji, M. (2019) Prevalence and Factors Associated with Acute Kidney Injury among Malaria Patients in Dar es Salaam: A Cross-Sectional Study. *Malaria Research and Treatment*, **2019**, Article 4396108. https://doi.org/10.1155/2019/4396108

[15] Conroy, A.L., Hawkes, M., Elphinstone, R.E., Morgan, C., Hermann, L., Barker, K.R., *et al.* (2016) Acute Kidney Injury Is Common in Pediatric Severe Malaria and Is Associated with Increased Mortality. *Open Forum Infectious Diseases*, **3**, ofw046. https://doi.org/10.1093/ofid/ofw046

[16] Araoye, M.O. (2003) Subject Selection and Sample Size Determination. In: Araoye, M.O., Ed., *Research Methodology with Statistics for Health and Social Sciences*, Nathadex Publishers, 115-120.

[17] Narayanan, S. and Appleton, H.D. (1980) Creatinine: A Review. *Clinical Chemistry*, **26**, 1119-1126. https://doi.org/10.1093/clinchem/26.8.1119

[18] Cheesebrough, M. (2002) Examination of Urine. In: Cheesbrough, M., Ed., *District*

Laboratory Practice in Tropical Countries, Cambridge University Press, 711-712.

[19] Bradley, G.M. and Benson, E.S. (1969) Urine Examination. In: Israel, D. and Bernard, J.H., Eds., *Todd-Stanford Clinical Diagnosis by Laboratory Methods*, W.B. Saunders Philadelphia, 30-106.

[20] Bayer Reagent Strips (2003) Pamphlet on Summary and Explanation 2003.

[21] Mabry, C.C. (1987) Reference Ranges for Laboratory Tests. In: Behrman, R.E. and Klegman, R.M., Eds., *Nelson Text Book of Paediatric*, W.B. Sander Company, 1535-1558.