Characterising Childhood Blackwater Fever and Its Clinical Care at Two Tertiary Hospitals in Eastern Uganda

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Research

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Abstract

Background

In eastern Uganda, reports suggest that cases of Blackwater Fever (BWF) are on the rise. We summarise the base-line characteristics and routine care available to patients with BWF presenting at two tertiary hospitals in Eastern Uganda prior to the Phase I/II trial on use of paracetamol for acute kidney injury in children with BWF (PARIST; ISRCTN84974248).

Methods

This was a retrospective descriptive study for the period January – December 2018 for children admitted with a clinical diagnosis of BWF at Mbale and Soroti Regional Referral Hospitals in Eastern Uganda. Data on sociodemographic and clinical characteristics, routine in-patient care and outcomes were abstracted using a customised study proforma and analysed using STATA.

Results

We obtained 9578 admission records during the study period, of which 1241 (13.0%) were admitted with a diagnosis of BWF. The median age was 60 months (IQR 36–90). Male: female ratio was 1.5:1. More cases of BWF 682/1241 (55.0%) were in children > 5 years compared to 559/1241 (45.0%) ≤ 5 years [95% CI (0.41–0.59); $P = 0.0002$]. The common symptoms included fever 1109/1241 (89.4%), vomiting 599/1241 (48.3%) and abdominal pain 494/1241 (39.8%). Conversely, the common signs recorded were clinical pallor 742/1241 (59.8%), clinical jaundice 369/1241 (29.7%), fever 332/1241 (26.7%) and prostration 231/1241 (18.6%). In addition, abdominal tenderness was documented in 120/1241 (9.7%), splenomegaly in 122/1241 (9.8%) and hepatomegaly in 86/1241 (6.9%). Case records with BWF were more in the second half of the year with a peak in the months of July and September. 510/1241 (41.1%) were treated with antimalarial drugs mainly parenteral Artesunate 501/510 (98.2%). 660/1241(53.2%) of the patients were managed with antibiotics mainly parenteral ceftriaxone 616/660 (93.3%). There were 426/1241 (34.3%) patients who received blood transfusion during admission. Clinicians used steroid treatment in 388/1241 (31.3%), mainly parenteral hydrocortisone 370/388 (95.4%).

Conclusions

BWF accounted for 13% paediatric hospital admissions in the region. It was predominant in children > 5 years of age. It typically presents with passing dark urine, fever, abdominal pain, clinical jaundice and pallor. Locally there are no treatment guidelines for BWF. These data provide background data useful for future studies on BWF in the region.

Background

Blackwater fever (BWF) a clinical condition characterized by an acute intravascular haemolysis resulting in passing dark, tea or Coca-Cola coloured urine (1, 2), is almost exclusive to *P. falciparum* malaria (3). Historically, the case definition included: Caucasian who had lived or visited malaria endemic area for a long time (> 3months) without previous exposure to malaria and were taking quinine in inappropriate dose or schedule for malaria prophylaxis and/or treatment (4–6). The initial attack of malaria complicated with BWF would typically present with loin pain, abdominal discomfort, restlessness, vomiting, diarrhoea, polyuria followed by oliguria and passage of dark red or black urine. Signs included tender hepatosplenomegaly, profound anaemia and jaundice (1, 7–10). Since then, however, use of such case definitions in the African populations have been done with mixed outcomes across geographical or population strata. For instance, prevalence and mortality range from 6–59% (11–14) and 4.4–25.3% (15–17) respectively. BWF studies in African children are complex (7, 11, 18). Adult case definitions are considered inappropriate for children, where malaria related renal failure was considered a rare clinical feature (19–22). As a contrast, BWF in children is often at initial stages of illness as opposed to adults who manifest it at the end stages of malaria disease (10). Moreover, there is a low clinical index of suspicion among attending clinicians and limited capacity to investigate the differentials of dark urine in resource-limited settings. To date, there is a paucity of recent descriptions on BWF, which focus on children in Africa (7, 11, 18). Most referenced data describing the phenomenon of BWF report varying prevalence of 6–48% (11, 12) and 11–59% (13, 14) of patients with severe malaria respectively. However, most of these were observational studies in adult series involving malaria non-immune patients. Even with a recognised malaria epidemiological transition (23, 24), with reports of malaria reducing (25–29), malaria remains endemic in some regions and countries including Uganda (30). In such settings childhood severe malaria studies suggests a high prevalence of BWF. For instance, 25.3% in Kinshasa in DRC (31), 19.1% in Ibadan, Nigeria (32) and 17.2% in Togo between 2000 and 2002 (16) in contrast to a lower prevalence reported in a large randomised controlled trial of Artesunate v Quinine (AQUAMAT) in African children < 15 years of age with severe malaria (n = 5,246 at 10 sites in nine countries) that indicated BWF in 237/5,426 (4.4%) (33). Earlier studies in Eastern Uganda reported a high frequency of BWF 14.5% and 21.8% at Mbale and Soroti Regional Referral Hospitals (FEAST Trial; ISRCTN69856593) (34). As with AQUAMAT study, the FEAST study was on a highly selected group of patients, which were not representative of the facility-based disease burden. Speculation on the cause of the notable increase in frequency of BWF in this region has been linked to a possible change in the malaria treatment protocols in the last decade (34), but have not been proven. It is also possible that changes to local parasite population to a strain with a greater propensity to cause BWF are in play as hypothesised by other studies (35, 36), but this has also not been studied in the region. It is possible that BWF in the region is multifactorial and that is conceivably the reason for high number of cases. In this study, we report BWF in general admissions in Eastern Uganda.

Methods And Materials

Study Area and Sites

The study was carried out on the admission medical records at the paediatric units at Mbale and Soroti Regional Referral Hospitals (RRH) in Eastern Uganda. Both facilities are government run, not for profit and charge-free hospitals. Mbale RRH is located at the heart of Mbale City, 214KM to the east of the Capital City Kampala while Soroti RRH is located at the centre of Soroti City; 100KM north-east of Mbale City. At both facilities, four major general specialties: surgery, internal medicine, obstetrics and gynaecology, and paediatrics are offered. Mbale RRH is larger with 470 bed capacity, compared to Soroti RRH with 274 bed, but they have comparable proportions of paediatric bed capacity at 95 (20.2%) vs. 64 (23.4%) respectively. The recent annual paediatric caseload at Mbale RRH on average is 10,000 admissions from a catchment of 16 districts with a population of 4.5 million. The geographical catchment area for Mbale RRH (Elgon sub region) is hilly and situated in the range 980 to 1,800m above sea level. Conversely, Soroti RRH admits approximately 6,000 children annually from a catchment population of 2.9 million in 9 districts. Its catchment geographical area (Teso sub region) is generally flat and most districts are < 1000m above sea level.

Study design

This was a retrospective descriptive study. Records for children aged 2 months to 15 years in the paediatric units at the two hospitals with admission diagnosis of BWF for the period January 1, 2018 to December 31, 2018 were studied.

Study Procedures

The paediatrics admission registers were used to identify all the children who presented with a diagnosis of BWF. BWF was diagnosed clinically as passing dark/tea/Coca-Cola coloured urine and corresponding urine colour grade ≥ 5 on the Hillmen Urine Colour Chart (37) (Fig. 1). On admission, the axillary temperature was measured with a digital thermometer. Fever (axillary temperature ≥ 37.50C) was further categorized as mild fever (37.5-37.90C), moderate fever [(38.0-38.50C) and severe fever (> 38.50C). Prostration was defined as inability to sit upright / stand unsupported /breastfeeding age < 6 months. Comorbidity was defined as ‘any distinct additional clinical entity that has coexisted or that may occur during the clinical course of a patient who has BWF. Level of consciousness was assessed using the AVPU score (‘Alert,’ ‘Responding to Voice,’ ‘Responding to Pain only,’ or ‘Unresponsive’). Clinical jaundice was yellowing of mucous membranes noted in sufficient daylight (38). Clinical assessment of pallor of mucous membranes indicated the degree of pallor (either none, mild, moderate or severe). The admitting clinician (Clinical officer or medical officer) carried out an assessment of pallor and determined whether they felt the clinical severity of pallor would warrant transfusion.

Trained research assistants retrieved the case records and extracted data on socio-demographic characteristics including gender, age and ethnicity. They further obtained admission data on presenting symptoms, duration of illness, physical signs, co-morbidities and treatment received. Records with

missing study variables on age, gender, illegible files, those outside the study period and age range were excluded.

Use of the Hillmen Urine Colour Chart

At admission, patients with a history of passing dark urine during the course of their current illness were initially assessed by clinicians based on history, an inquiry about the child passing dark urine, defined as Coca-Cola or tea coloured urine on the day of admission was made. Furthermore, asking the parent/guardian to indicate the grade (by pointing) at the colour against the Hillmen Urine Colour Chart (HUCC) (Fig. 1) qualitatively assessed the urine colour. The HUCC had 10 colour codes ranging from mild yellow (colour code 1) to black (colour code 10). A probable and confirmed diagnosis of BWF/dark urine was made at admission. The patient/guardian was first asked to recall and match the colour of urine passed by their child on the day of admission to a colour on the HUCC. If available, urine was collected from the child using paediatric urine collection bags before it was transferred into the urine collection bottle. The study clinician then matched the urine colour to the corresponding score on the HCC scale. Children with clinician-witnessed urine or patient/guardian matched the colour of urine passed by their child on the day of admission corresponding to HCC > 5 on the chart were confirmed to have BWF/dark urine syndrome. These were the eligible patients for the study. For easy access and efficient use of the HCC, charts were displayed both in the patient admission area and in the ward.

Data management and statistical analyses

The data was entered into MS Excel, exported and analysed using STATA (version 14.0, College Station, Texas 77845 USA). All qualifying records for the period of study chosen were included. Initial descriptive and univariate analyses were carried out on the data. Means and standard deviations (SDs) were determined for normally distributed continuous variables and medians and interquartile ranges (IQRs) for non-normally distributed variables. Proportions and percentages were determined for categorical variables. Study participants were stratified by age (≤ 5years and > 5 years) and gender. Between group differences were assessed using Pearson's $\chi 2$. The difference was considered significant at $P < 0.05$.

Results

During the 12-month study period, 9578 records of children admitted to the Paediatric Acute Care Unit (PACU) at the two hospitals were retrieved. Of these 1308 (13.7%) of the records had BWF. Excluded were 67/1308 (5.1%) records because of the missing data on key variables. The remaining 1241/9578 (13.0%) were eligible records and included in the study.

Sociodemographic characteristics

The overall median age in this study population was 60-month; range 4-180 months (IQR 36–90). A male preponderance (1.5:1 male to female ratio) was observed. 559 (45.0%) ≤ 5 years vs 682 (55.0%) > 5 years [95% CI (0.41–0.59); $P = 0.0002$]. The socio-demographic characteristics are summarised in table 1.0.

Table 1
Socio-demographic characteristics of BWF cases.

Demographics	Freq.	Percent
Age		
≤ 5	559	45.04
> 5 year	682	54.96
Gender		
Female	501	40.4
Male	740	59.6
Ethnicity		
ITESOT	691	55.7
MUGISHU	205	16.5
KUMAM	133	10.7
OTHERS	212	17.1

Clinical characterization of BWF.

The clinical features of BWF participants stratified by age category are summarized in Table 1.1. Besides all patients presenting with passing dark urine /tea-coloured urine, most of the patients also commonly presented with high fever 1109 (88.7%), vomiting 599 (48.3%) and abdominal pain 494 (39.8%). The common clinical signs at presentation included clinical pallor 742 (59.8%), clinical jaundice 369 (29.7%), fever on examination 332 (26.8%) and prostration 231 (18.6%). In addition, abdominal signs of abdominal tenderness 120 (9.7%), splenomegaly 122 (9.8%) and hepatomegaly 86 (6.9%) were recorded.

Compared to ≤ 5years, the > 5years significantly presented with symptoms of abdominal pain (320 (46.9%) vs 174 (31.1%) $P < 0.001$), chest pain (72 (10.6%) vs 32 (5.7%) $P = 0.013$), vomiting (364 (53.4%) vs 235 (42.0%) $P = 0.031$) and headache (222 (32.6%) vs 87 (15.6%) $P < 0.001$). The > 5years patients were more likely to be anaemic $P = 0.002$ [moderate (135 (19.8%) vs 75 (13.4%)] and severe pallor [204 (29.9%) vs 126 (22.5%)]. They had features of impaired perfusion/ delayed capillary refill time $P = 0.023$ [2–3 sec (125 (19.8%) vs 81 (13.4%)] and > 3 sec [51 (7.5%) vs 21 (1.7%)], clinical jaundice [246 (36.1%) vs 123 (22.0%) $P = 0.000$] and abdominal tenderness [78 (11.4) vs 42 (7.5%) $P = 0.02$].

On the other hand children ≤ 5 years in comparison to the > 5 years significantly presented with symptoms of difficult breathing (45 (8.1%) vs 27 (4.0%) $P = 0.000$), fast breathing (83 (14.8%) vs 72 (10.6%) $P = 0.002$) and convulsions (49 (8.8%) vs 23 (3.4%) $P = 0.000$). The ≤ 5years patients were more likely to have severe fever (temperature > 38.5) p = 0.047 (25 (4.5%) vs 25 (3.7%)) and altered level of

consciousness AVPU score of VPU (V (21 (3.8%) vs 21 (3.1%)), P (15 (2.7%) vs 14 (2.1%)) and U (5 (0.9%) vs 0 (0%)).

Table 2
The baseline clinical characteristics of BWF cases stratified by age.

Symptoms	≤ 5	> 5 year	Total	*P-value*
N	559 (%)	682 (%)	1,241 (%)	
Fever	471 (84.3)	638 (93.5)	1109 (89.4)	0.711
Difficulty in breathing	45 (8.1)	27 (4.0)	72 (5.8)	< 0.001
Fast breathing	83 (14.8)	72 (10.6)	155 (12.5)	0.002
Hand pain	45 (8.1)	81 (11.9)	126 (18.5)	0.137
Foot pain	49 (8.8)	75 (11.0)	124 (18.2)	0.537
Abdominal pain	174 (31.1)	320 (46.9)	494 (39.8)	< 0.001
Chest pain	32 (5.7)	72 (10.6)	104 (8.4)	0.013
Vomiting	235 (42.0)	364 (53.4)	599 (48.3)	0.031
Nausea	63 (11.3)	98 (14.4)	161 (13.0)	0.465
Convulsions	49 (8.8)	23 (3.4)	72 (5.8)	< 0.001
Headache	87 (15.6)	222 (32.6)	309 (24.9)	< 0.001
Signs	≤ 5	> 5 year	Total	P value
N	559	682	1241	
Abdominal tenderness	42 (7.5)	78 (11.4)	120 (9.7)	0.02
Clinical jaundice	123 (22.0)	246 (36.1)	369 (29.7)	< 0.001
Splenomegaly	55 (9.8)	67 (9.8)	122 (9.8)	0.993
Fever on examination				0.047
Mild (37.5–37.9)	41 (7.3)	45 (6.6)	86 (6.9)	
Moderate (38.0-38.5)	74 (13.2)	122 (17.9)	196 (15.7)	
Severe (> 38.5)	25 (4.5)	25 (3.7)	50 (4.0)	
Capillary refill time (seconds)				0.023
2–3 sec	81 (14.5)	125 (18.3)	206 (16.6)	
>3 sec	21 (1.7)	51 (7.5)	72 (5.8)	
Pallor				0.002
Mild	84 (15.0)	118 (17.3)	202 (16.3)	
Moderate	75 (13.4)	135 (19.8)	210 (16.9)	

Symptoms	≤ 5	> 5 year	Total	*P-value*
Severe	126 (22.5)	204 (29.9)	330 (26.6)	
Level of Consciousness				0.023
Verbal	21 (3.8)	21 (3.1)	42 (3.8)	
Pain	15 (2.7)	14 (2.1)	29 (2.3)	
Unconscious	5 (0.9)	0 (0)	5 (0.4)	
Prostrated	88 (15.7)	143 (21.0)	231 (18.6)	0.222
Acidotic breathing	10 (1.7)	6 (0.9)	16 (1.3)	0.11

Overall, there were no significant differences in the clinical characteristics observed between the males and females.

Pattern of distribution of BWF cases in 2018

Noticeably, presentation with BWF was more in the second half of the year in 2018 with a peak in the month of July to September (Fig. 2). The patterns of distribution of BWF cases disaggregated by sex and age category revealed an overall higher number of BWF cases above 5 years compared to under 5 years for the females while the number of BWF cases under 5 was slightly higher than the above 5 for the males in the two age categories. For both the peak in the number of cases was reported in the second half of the year with the highest being the month of August. (Fig. 3).

- **Figure 2 Pattern of monthly admissions of BWF cases in 2018**
- **Figure 3. Seasonal variation of BWF cases by sex and age category in 2018.**

Routine treatment received by BWF patients

The routine treatment of patients with BWF is summarized Table 2. 510/1241 (41.1%) were treated with antimalarial drugs mainly parenteral Artesunate 501/1241 (40.4%). There were 426/1241 (34.3%) patients who received blood transfusion during this current illness of these, 281/1241(22.6%) received 1 blood transfusion and 145/1241(11.6) received ≥ 2 blood transfusion. 660/1241(53.2%) of the patients were managed with antibiotics mainly parenteral ceftriaxone 616/1241 (49.6%). Surprisingly, a considerable number of patients 388/1241 (31.3%) were treated with steroids mainly parenteral hydrocortisone 370/1241 (29.8%).

Table 3
Routine treatment received by BWF patients in this admission grouped by age category

Treatment	Overall, N (%)	Age category	
		≤ 5years (%)	> 5years (%)
Total	1241 (100)	559 (100)	682 (100)
Antimalarial			
Artesunate	501 (40.4)	220 (30.4)	281 (41.2)
Coartem	2 (0.2)	0 (0)	2 (0.3)
Fansidar	5 (0.4)	0(0)	5 (0.7)
Quinine	2 (0.2)	1 (0.2)	1 (0.1)
Blood transfusion			
1 blood transfusion	281 (22.6)	127 (22.7)	154 (22.6)
2 blood transfusions	106 (8.5)	44 (7.9)	62 (9.1)
≥ 3 blood transfusions	39 (3.1)	16 (2.9)	23 (3.4)
Antibiotics			
ceftriaxone	616 (49.6)	269 (48.1)	347 (50.9)
Ampicillin	24 (1.9)	14 (2.5)	10 (1.5)
Gentamycin	20 (1.6)	9 (1.6)	11 (1.6)
Steroids			
Hydrocortisone	370 (29.8)	132 (23.6)	238 (34.9)
Prednisolone	18 (1.5)	5 (0.9)	13 (1.9)

Discussion

Our large retrospective study provides a contribution to the descriptions of paediatric BWF in malaria high transmission settings in Eastern Uganda. The prevalence rate of BWF of 13% reported in our study was comparable to earlier descriptions of BWF in malaria endemic settings (1, 2, 31, 39–41).

The higher frequency of BWF in children aged > 5 years, 682/1241 (55.0%) compared to ≤ 5 years, 559/1241(45.0%); [95% CI (0.41–0.59); P = 0.0002], observed in this study was consistent with previous reports from Kinshasa in DRC, a similarly holo- hyperendemic malaria setting (31). This has led to questioning the link between BWF and malaria. If malaria was a direct driving factor, then children aged > 5 years who are expected to have acquired malaria immunity (1, 18, 42, 43), would be resilient to BWF. On

the other hand, if it was an innate factor then either more of the ≤ 5year old children or a similar proportion across the various age strata would have been observed with BWF. Therefore, greater understanding is still needed to elucidate the aetiopathophysiology of BWF.

We found the clinical features in childhood BWF were similar to the adult BWF case definitions (10), the cases typically presented with passing dark urine (1241/1241 (100%)), high grade fever (332/1241 (26.8%)), clinical jaundice (369/1241(29.7%)), pallor (742/1241(59.8%)) and abdominal pain (494/1241(39.8%)). Severity features reported in this study including unconsciousness (5(0.4%)), convulsions (72/1241(5.8)), prostration (231/1241(18.6%)), severe pallor/anaemia (330/1241(26.6%)) and respiratory distress/acidotic breathing (16/1241(1.2%)) seem to be similar to those reported in severe malaria series given the fact that BWF is also a form of severe malaria (38, 44–47). Of specific significance was the finding of abdominal pains (494/1241(39.8%)) and tenderness (120/1241(9.7%)) in this study population. Few data, if at all any, have described this phenomenon in relation to severe malaria or specifically BWF in African children. We think the ischaemic process following sequestration of parasitized red blood cells (48, 49) in the small blood vessels supplying mesentery may possibly lead to mesenteric infarction and thus the abdominal pain/tenderness.

A number of speculations have been made to try and explain high prevalence of BWF in these settings. For instance, the coincidence of increased cases of BWF with a roll out of Artemesinin Combination Therapies (ACTs) for control of malaria has postulated but has not been well studied (34). Elsewhere, lumefantrine, a key drug in first line ACTs has been implicated in the causation of BWF, but descriptions in African children have not been done. Similarly, the role of repeated exposure to other antimarials (18, 31, 39), and blood transfusions in the causation of BWF in children have also not been explored in these settings. High rates of index and repeat blood transfusions, in a phenomenon similar to isoimmunisation in mother-baby situation may be underlying in some of the massive haemolysis observed in these populations, but needs further research. Conversely, whereas past epidemiological studies have indicated that the interaction between host response to repeated malarial attacks, use of antimalarials, and possibly glucose-6-phosphate dehydrogenase (G6PD) deficiency are trigger factors (50), more recent descriptions in Eastern Uganda do not associate the phenomenon to G6PD deficiency(34). Alternatively, other scholars have argued that the possible cause is likely a recent change in the malaria parasite population towards a strain with a greater propensity towards causing BWF (35, 36).

The seasonal trend of BWF admissions in 2018 showed one peak in the months of July to September. Eastern Uganda receives moderate rainfall with annual rainfall averages ranging from 1100-1200mm and this is distributed between two seasons (March to July and September to November) (51). A malaria surveillance study done in all the regions of Uganda between 2015 to 2019 showed the highest peaks in monthly trends in regional malaria incidence rates were in June–July, highest in June, 2017 (Range: 13.4– 95.6 cases per 1000) and July, 2019 and the lowest troughs in February–March of each calendar year(52). Teso region home to one of the study sites (Soroti RRH) was one of the regions that persistently recorded the highest monthly incidence rates across the entire study duration (52). Possibly, the malaria incidence rate peaks of June – July of 2018 may have coincided with the peak in BWF admissions

reported in this study between July and September suggesting either similar risk factors or a cause-effect relationship between BWF and malaria in this setting.

Understanding paediatric BWF in Africa is very important for informing treatment options and plans. Currently, there are no specific treatment and prevention remedies for BWF. According to the Uganda clinical guidelines, all cases are treated as severe malaria and respective supportive treatment such as blood transfusion is given (53), which is plausible. However, with no specific management guidelines for BWF, inconsistences exist in patient care owing to the differences in clinician expertise/training, experience and acumen. This explains the variability in treatment reported in this study. The inappropriate use of antimalarial and antibiotics especially second line cephalosporin (ceftriaxone 616/1241 (49.6%)) poses a threat of antimicrobial resistance. Surprisingly, a considerable number of patients 388/1241 (31.3%) were treated with steroids mainly parenteral hydrocortisone 370/1241 (29.8%) this increases the likelihood of steroid induced side effects. Therefore, there is need to develop adjuvant treatment specific to the pathophysiology of BWF to contribute to better outcomes. In addition, the high frequency of blood transfusions among children with BWF suggests efforts and strategies should be focused on preventing severe anaemia in the post discharge period including the use of haematinics and insecticide treated mosquito nets (54, 55).

This retrospective study design had some limitations. Mainly, the diagnosis of BWF was done clinically using the Hillmen urine colour chart. No real-time laboratory investigations were done to elucidate the aetiopathophysiology of BWF in children including acute kidney injury, one of the unique features of BWF in children (56). There was no data on post discharge status and as such, repeat or late onset BWF which usually occurs after 28days was not reported, yet these data are important in understanding of the complete disease picture. Nonetheless, this study was pragmatic and done at two high volume tertiary hospitals. It made use of a large sample size, which imparts significant strength to the study findings and was based on the diagnostic capabilities of health facilities in resource-limited settings used for routine care. Therefore, this study highlights the socio-demographic characteristics, clinical features and routine care of BWF patients at two tertiary hospitals in Eastern Uganda. We describe these data in Eastern Uganda ahead of a Phase I/II trial on use of paracetamol for acute kidney injury in children with BWF (PARIST; ISRCTN84974248).

Conclusion

In conclusion, BWF remains an important cause of paediatric admissions in eastern Uganda, it accounted for 13% admissions. Its predominance in children ≥ 5 years suggests a greater role of acquired factors compared to that of inherited causes. Patients typically present with passing dark urine, fever, clinical jaundice, pallor and abdominal pain. There are no management guidelines for BWF locally and as such, patient care is supportive.

Declarations

Ethics approval and consent to participate

Ethical approval for the study was obtained from the Mbale Regional Referral Hospital Research & Ethics Committee (MRRH-REC; approval number MRRH-REC OUT 0039/2019). A waiver of informed consent was granted on grounds of this being a retrospective study. Written permission to conduct the study at each of the sites were obtained from Mbale and Soroti RRH leadership.

Consent to Publish

The Mbale Clinical Research Institute (MCRI; www.mcri.ac.ug), a research entity affiliated to the Uganda National Health Research Organization (UNHRO), approved the publication of this manuscript.

Availability of data & materials

The study data are available by request to the corresponding author.

Competing interest

The authors declare no competing interest.

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Author contribution

P-OO conceived and supervised the study. GP collected the data and wrote the first draft of the manuscript. CN designed the database and together with FO conducted the data analysis. GA data curation. CN, GA, WO, P-OO, WO, BPO, FA, JA and AK participated in development of the data collection tool, collection of data and writing the manuscript. All authors contributed to editing and approval of the final submission.

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Figures

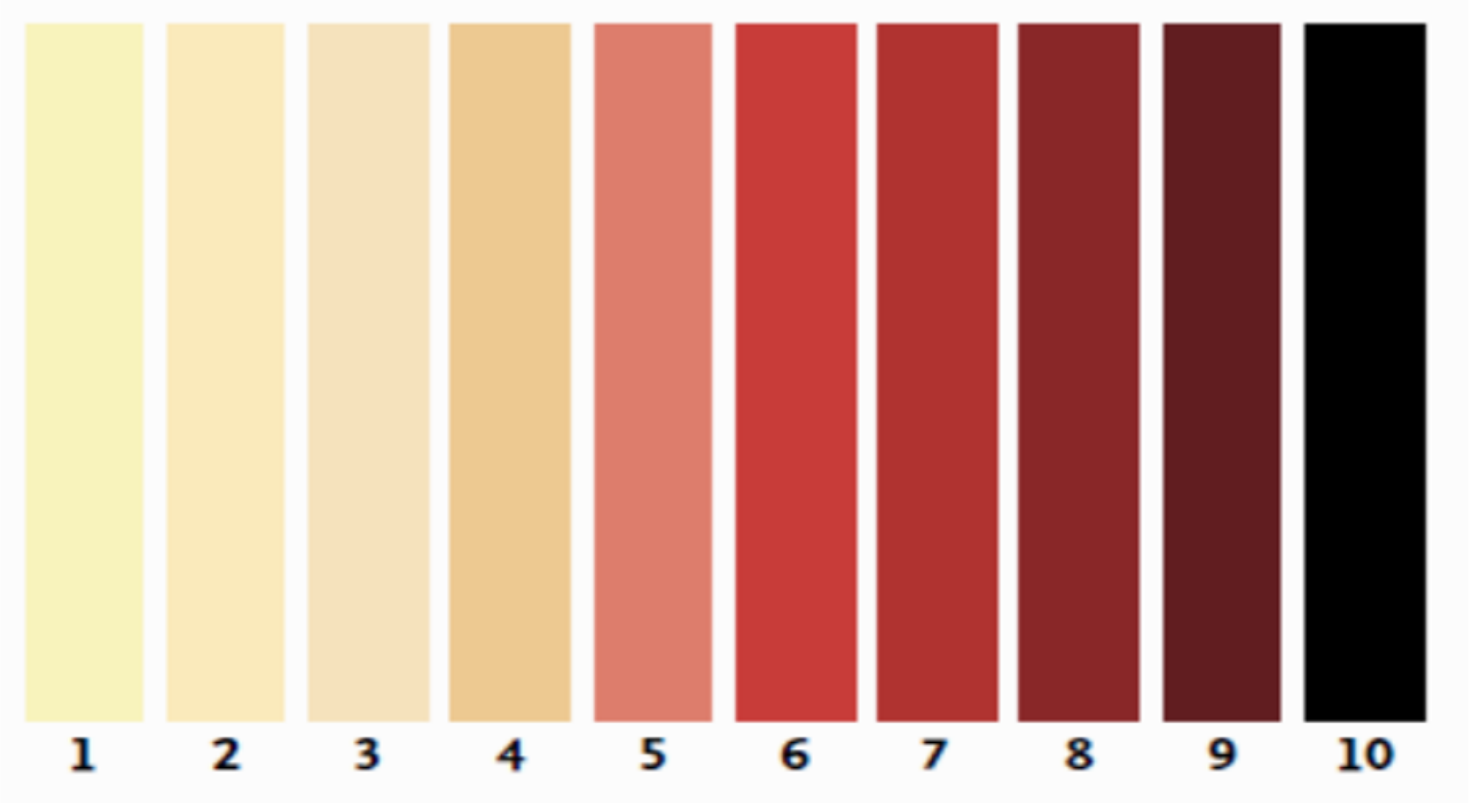

Figure 1

The Hillmen Urine Colour Chart

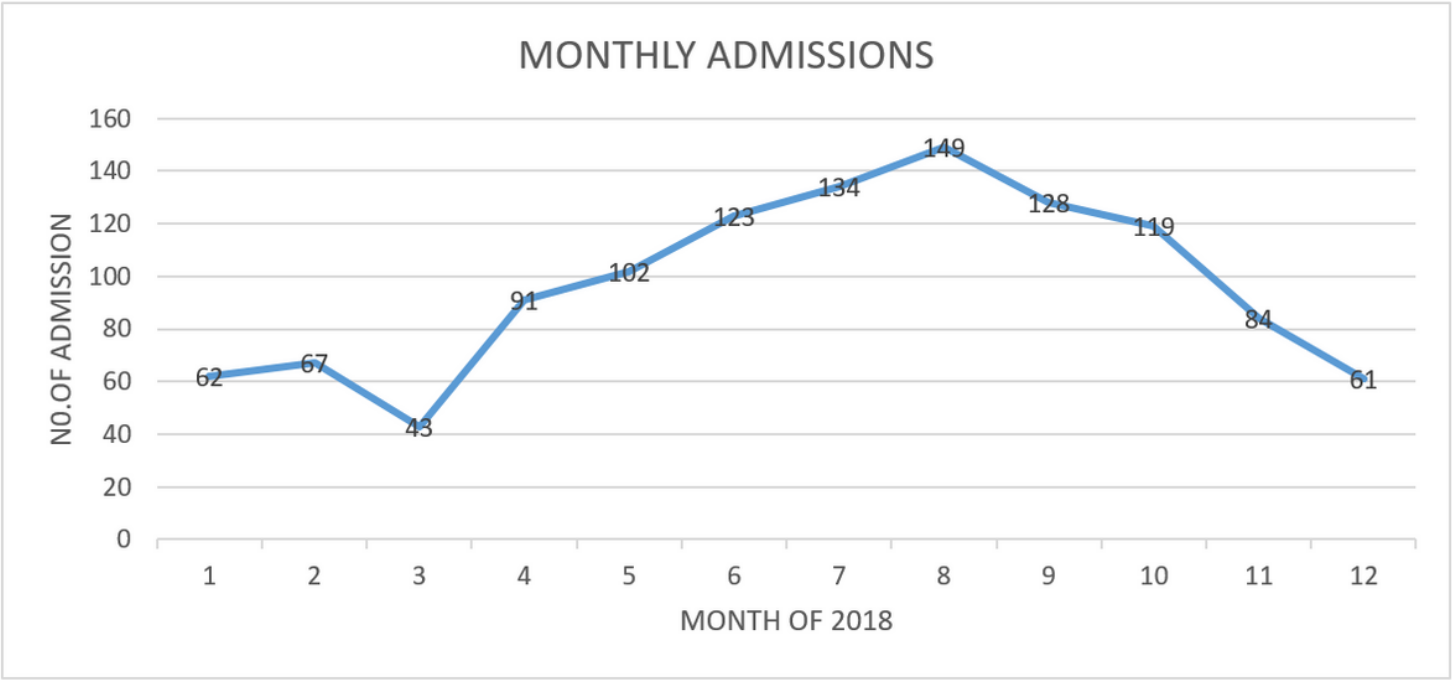

Figure 2

Pattern of monthly admissions of BWF cases in 2018

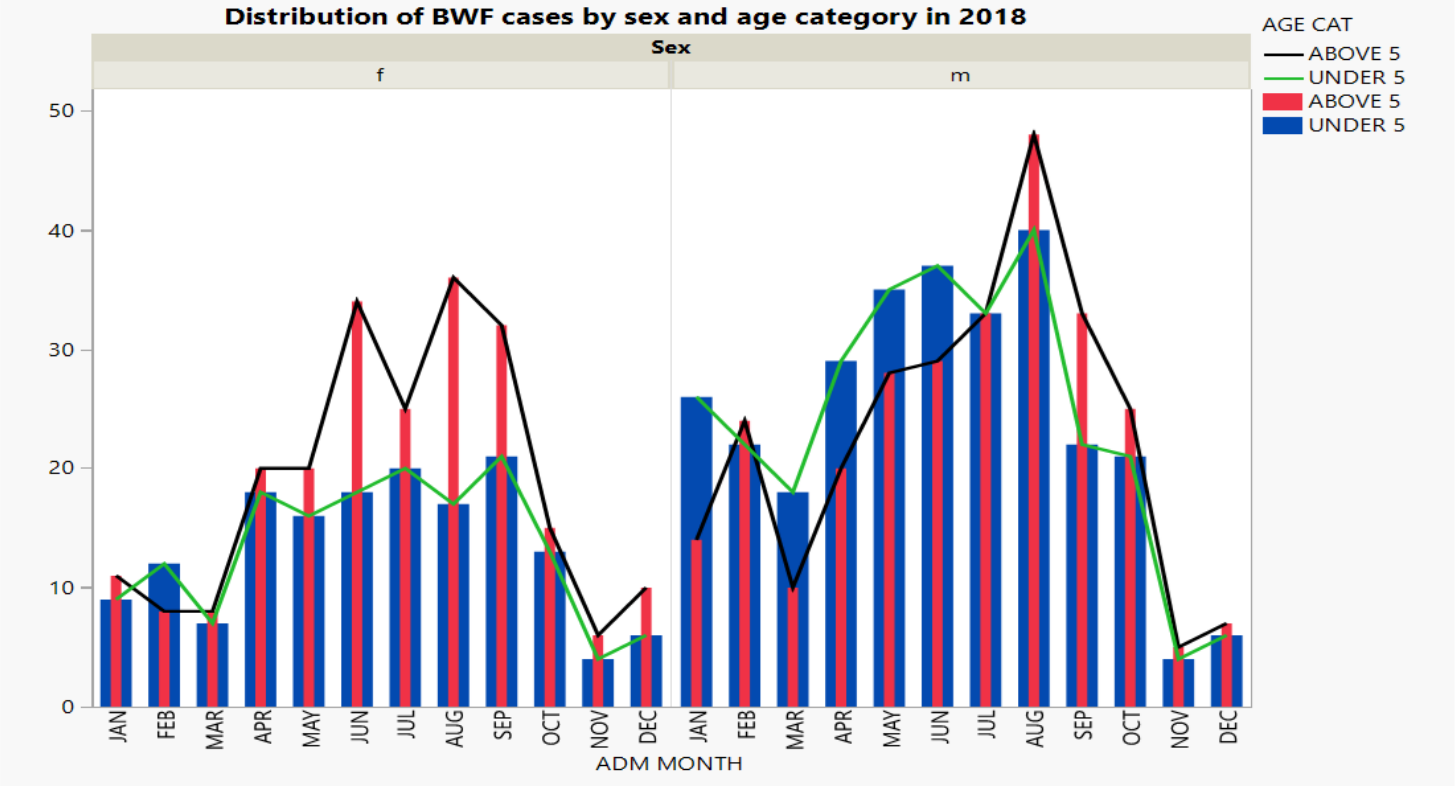

Figure 3

Seasonal variation of BWF cases by sex and age category in 2018.