

Ocheke OI  
John CC  
Ogbe P  
Donli A  
Oguche S

## The febrile child: how frequent should we investigate for urinary tract infection

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Ocheke OI (✉)  
John CC, Ogbe P, Donli A, Oguche S  
Department of Paediatrics,  
Jos University Teaching Hospital  
P. M. B 2076, Jos, Nigeria.  
Email: ieocheke@yahoo.com

**Abstract:** *Background:* Febrile illness in children remains the most common cause of emergency room visit. In many tropical countries where malaria is endemic, children presenting with fever are treated for malaria presumptuously. Current evidence suggests however that malarial parasitaemia in febrile children is declining and the prevalence of other causes of fever apparently on the increase. Therefore, highlighting such causes of fever as urinary tract infection (UTI) is indispensable. This is much so as UTI not only is common in younger children and often neglected but also associated with long term complications

*Methods:* Children aged 6-59 months with fever of less than 2 weeks were consecutively recruited. Each child had both clinical evaluation and preliminary laboratory assessment such as dipstick urinalysis. Further microbiological and radiological evaluations were performed

where necessary: blood film for malarial parasite identification and count, cerebrospinal fluid (CSF) analysis and chest X-ray.

*Results:* Of the 303 children 180 (59.4%) were males and 123 were females (40.6%). The mean age was  $21.7 \pm 14.0$  months, 54.5% were less than 24 months.

ARI accounted for 44.6% (mainly tonsillitis, 61%, pneumonia, 27% and otitis media, 12%), while malaria and UTI were observed in 38.3% and 4.6% respectively.

Five (35.7%) patients with UTI were males while 9 (64.3%) were females. Their combined mean age was  $25.4 \pm 18.6$  months, 57% of these children were less than 24 months old. In 3 (21.4%), UTI co-existed with malaria.

*Conclusions:* Acute respiratory infection, malaria and UTI are the three leading causes of fever in children under 5 years.

*Keywords:* Fever, Children, Acute respiratory infection, Malaria, UTI.

### Introduction

Febrile illness represents the most common cause of hospital visits and admission in children globally.<sup>1,2</sup> The underlying causes are predominantly infectious and UTI is increasingly recognised as an important cause.<sup>3</sup> Approximately two decades ago, it was noted that 30% of outpatient and 50% of inpatient children under the age of five years living in Sub-Saharan Africa had malaria.<sup>4</sup> Without a reliable case definition, children presenting with febrile illness in most cases were treated presumptively for malaria.<sup>1,5-6</sup> Current evidence suggests however that there is declining malarial transmission in many of the malarious countries in Africa. This necessitated the World Health Organisation (WHO), point-of-care rapid diagnostic test which ensures that all children presenting with fever are tested for malaria before embarking on antimalarial treatment.<sup>7</sup> In Nigeria a recent multicentre study conducted in 2009/2010 showed that

malaria parasitaemia accounted for only 35 % of 5,217 children presenting with fever.<sup>8</sup>

The pre-treatment identification of malaria parasites in a suspected case is beneficial in many ways such as only individuals with the infection are treated. A new problem as a result of this step however is, what appropriate treatment would those who test negative for *Plasmodium falciparum* parasites receive, particularly at the first and secondary-level health facilities. Available evidence suggests that with the decrease in the use of anti-malarials, there has been a corresponding increase in the indiscriminate use of antibiotics in febrile children.<sup>9,10</sup> Many times, the choice of antibiotics and their dosages are inappropriate, inadequate and unnecessary. This practice can lead to increase in the development of several resistant microbial strains. It could also lead to poor care and missed diagnosis of bacterial infections that may result in long term complications particularly in younger children.<sup>11</sup>

It has been shown that urinary tract infection (UTI) is common in children presenting with febrile illness particularly in younger age groups, and could be associated with long-term complications.<sup>12,13,14</sup> These complications could be prevented by early diagnosis and prompt treatment.

Considering these, a systematic approach to case management of febrile children, particularly those under-five years is imperative. Such a measure would include careful clinical evaluation and laboratory assessment to identify the underlying cause of fever in each child. This study was therefore, undertaken to highlight the underlying causes of fever in children six months to 59 months with specific emphasis on UTI identification in our hospital.

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## Materials and methods

This was prospective, cross-sectional and descriptive study, carried out in the paediatric emergency and outpatient units of the Jos University Teaching Hospital, Nigeria. Study participants were children aged 6 to 59 months seen in these units from the first of April to the end of October 2012. Ethical approval was obtained from the Institution's Health Research and Ethics Committee. All children who presented with fever (axillary temperature  $37.5^{\circ}\text{C}$ ), that had lasted less than two weeks and whose parental/caregiver consent had been obtained were consecutively recruited. Children with moderate to severe malnutrition according to world health organization (WHO)<sup>15</sup> reference charts, those with sickle cell anaemia or any underlying chronic illnesses (renal, cardiac and chronic infection such as tuberculosis or human immunosuppressive virus) were excluded. Similarly, children who had used antibiotics within one week prior to hospital visit were not included. All the children seen during the study, including those who participated and those who did not were given appropriate medical care following careful evaluation.

### Clinical assessment

The history of illness was obtained from the patient's parent/caregiver. Each child had physical examination to identify possible focus of infection or any other feature that could assist in making diagnosis. Those who have clinical features suggestive of acute lower respiratory infections had chest radiography. All participating subjects had their weight taken using a Seca® standing or bassinet weighing scales (infants), while height/length was measured in recumbent or standing positions based on the age of the child respectively.

The mid upper arm circumference (MUAC), was measured in all the children using an inelastic tape and measurement recorded to the nearest 0.1cm.

### Laboratory assessment

A dipstick urinalysis was done on a portion of urine specimen (catheter urine and clean catch for children 2 years and below, while mid-stream urine for older ones), for each subject who did not have any obvious focus of infection. This was to identify the presence of nitrite and or leukocyte esterase (LE). Only the urine of children whose dipstick urinalysis was positive for both nitrite and LE or for either of the two were subjected to further microbiological analysis according to National Institute for Health and Care Excellence (NICE) guidelines.<sup>16</sup> The remaining portion of such urine sample was sent to the JUTH microbiology laboratory for microscopy, culture and sensitivity within one hour of collection according to standard protocol. The confirmation of UTI was made only in children with a single bacterial isolate of  $10^5$  colony forming units (CFU) per ml of mid-stream urine and  $10^3$  CFU/ml of catheter urine.<sup>17</sup>

Venous blood was obtained for peripheral smear and subjected to Giemsa stain for *Plasmodium falciparum* identification and counting. Similarly, all children with features suggestive of acute central nervous system infections (fever with seizures, nuchal rigidity or unconsciousness) had lumbar punctures for cerebrospinal fluid (CSF) analysis.

Data obtained were entered into EPI info version 3.4.3 software for analysis. The student's 't' test was used to compare group means and the Chi-squared test to compare proportions. Fisher exact was used when cells contained observations less than 5. P value less than 0.05 was considered significant.

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## Results

A total of 303 children were recruited for the study. One hundred and eighty (59.4%) were males while 123 (40.6%) were females. Table 1 show the clinical characteristics of the subjects. The combined mean age for both males and females was  $21.67 \pm 14.02$  while the median age was 17 months. One hundred and ninety nine (65.7%) were aged less than 24 months.

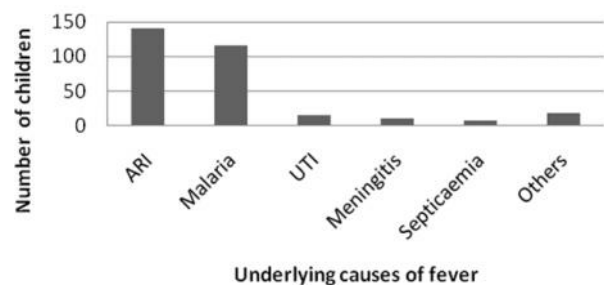
Fig 1 shows the causes of fever in the study population. Acute respiratory infection, comprising tonsillitis, pneumonia and otitis media in that order, was the leading cause of fever in the children, constituting 44.6%. Malaria was the second common cause of fever followed by urinary tract infection at 38.3% and 4.6% respectively.

Of the children with ARI, 93 (69%) were aged 24 months and below with majority, 54 (58.1%) in this group aged 12 months and less. Similarly, 86 (62.4%) of the children who had malaria were aged 24 months and below. There were 14 children with UTI, 5(35.7%) in males and 9(64.3%) in females. Their mean age was  $25.4 \pm 18.6$  months. Eight children (57%) were 24 months or less while the remaining 6 (43%) patients were older.

Three of the children with UTI also had parasitological evidence of malaria. The commonest organism

responsible for UTI was *Escherichia coli* in 8(57.1%). The other organisms included *Klebsiella* species in 3 (21.4%), *Staphylococcus aureus* 2(14.3%) and *Proteus* species in 1(7.1%). A significantly high proportion (86.4%) of the organisms isolated were sensitive to flouroquinolones, sensitivity to gentamicin was 56.8%, while to the third generation cephalosporin (ceftriaxone) was 46.2%.

**Fig 1:** Underlying diagnosis of fever in the children (Others- cellulitis, chicken pox, measles and mumps)



Variable	Total	Male	Female	P value
Study population	303	180	123	-
Age(months) (Mean±SD)	21.7 ±14.02	21.1 ±13.9	22.6 ±14.3	0.72
Axillary Temp (°C) (Mean±SD)	38.2 ±0.78	38.2 ±0.76	38.2 ±0.81	0.73
Duration of fever before presentation (days) (Mean±SD)	5.6±4.3	5.3±3.6	5.4±3.5	0.82

## Discussion

From our study, acute respiratory infection was identified as the leading infection in children presenting with fever, followed by malaria. Urinary tract infection was the third common cause of fever in these children. This general pattern is similar to findings from other studies in Africa and elsewhere in the world.<sup>18,19,20,21</sup> In a study of 418 children with fever in Gabon, Bouyou-Akotet et al<sup>18</sup> reported UTI prevalence of 4.1%, while D'Acremont et al<sup>19</sup>, in his review of the causes of fever in 1005 Tanzanian (Zanzibar) children 2 months to 10 years reported a prevalence of 5.9%. These studies also showed that acute respiratory infection was the commonest cause of fever in the children as our study demonstrated. We found that malaria was the second most common cause of fever similar to the report from Gabon,<sup>18</sup> but this contrasts with the observation from Zanzibar<sup>19</sup> where malaria was the fourth common cause of fever.

This variation may be related to capacities for further laboratory investigations, environmental and weather conditions. For instance, in mainland Tanzania, the commonest cause of fever among 870 paediatric and adult patients was bacterial zoonoses while malaria was responsible in only 1.6%.<sup>20</sup> Similarly, among 1180 hospitalized Cambodian children under 8 years with 1225 febrile episodes, Chheng et al<sup>21</sup> reported that acute respiratory infection was the foremost cause of fever followed by different kinds of viral infections. The geo-

graphical location may also have contributed as the finding from Tanzania showed; the pattern of infection in febrile children was different between the mainland and Zanzibar Island.

The prevalence of UTI in our study of 4.6% is much lower than two previous and similar studies from other parts of Nigeria.<sup>22,23</sup> Ibeneme et al<sup>22</sup> reported a UTI prevalence of 11% in febrile children aged 1 to 59 months in South East Nigeria. Their study included children of much younger age than ours. It is known that the prevalence of UTI is higher in younger infants, particularly in the first few months of life.<sup>12,14</sup> Furthermore, urine culture for microbiological confirmation of UTI was done for all their study population without initial screening for nitrite and LE, while we relied on positive urine nitrite and/or LE for further urine culture. Conversion of nitrate to nitrite does not occur with all bacteria and it takes about 4 hours or more for conversion of urine nitrate to nitrite in the bladder.<sup>24</sup> Therefore, if a child had not retained urine for such period, it was possible the screening will be falsely negative even where UTI was present. In their study from north western Nigeria, Wammanda et al<sup>23</sup> reported a UTI prevalence of 24.3% in 185 febrile children who had symptoms referable to the urogenital system. This figure is equally much higher than our finding. The higher rate they reported is likely attributable to the fact that only those children who had urinary signs and symptoms were recruited. In that study, they also compared the ability of positive urine nitrite to detect UTI with urine culture and noted that nitrite was less sensitive but had an excellent specificity.<sup>23</sup> In other words, there is likelihood for this test not to detect UTI even where infection is present.

Our study evaluated children for UTI only if they had no focus of infection and where preliminary screening for nitrite and LE was positive. It has been shown that neither absence nor presence of a focus of infection necessarily affects the existence of UTI in children.<sup>14</sup> This may have contributed to the lower prevalence rate observed in this study.

The prevalence of UTI in febrile children in our study may have come in a distant third position, but it emphasise a significant point that this condition is to be looked for in children presenting with fever when there is no focus of infection. This is more so that managing the long term complications associated with renal scarring from pyelonephritis is much more challenging and difficult in our environment.

Our study has some limitations: urine culture was carried out only in children whose dipstick urinalysis was positive for nitrite and/or LE. There may have been some of these children whose dipstick urinalysis was negative for nitrite and LE but who may actually have UTI. However, this study has shown that, for children presenting with fever in our environment, acute respiratory infection is the commonest condition, followed by malaria and then UTI, stressing the need to evaluate such children with this order in mind.

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