



## STUDY OF ABNORMAL FINDINGS ON DIPSTICK URINE ANALYSIS IN PATIENTS WITH MALARIA IN A TERTIARY CARE HOSPITAL OF ODISHA

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### ABSTRACT

**Background:** In India Malaria is still a major health problem with many challenges. Early detection of the disease and its complication remains the key for reducing morbidity and mortality. Urine analysis is a cheap and easy but very valuable method for diagnosis of many diseases and conditions. Studies on urinalysis for abnormalities in malaria patients are limited and the extent to which abnormalities do appear in urine of the patients in this malaria-endemic area needs to be studied. In order to minimise the mortality and morbidity of malaria, accurate diagnosis and proper management are very essential. Therefore it is imperative to determine changes in urinary composition and its relationship with diagnosis and prognosis of malaria. We determined urinary abnormalities in malaria patients. The objectives of the study are (1) To document most common abnormalities in urine in patients with malaria infection and (2) To find out urinary changes which may help in predicting the diagnosis and prognosis of malaria.

**Materials and methods:** The study was carried out at Sri Ram Chandra Bhanja (SCB) Medical College and Hospital, Cuttack, Odisha from July 2016 to December 2016 during the period in which malaria transmission is usually at its peak. A total of 110 participants comprising 55 patients of confirmed malaria cases and 55 healthy individuals as controls of same age and sex were investigated. Blood was collected for routine and rapid diagnostic test (RDT) and both thick and thin smears prepared for confirmation of malaria parasites microscopically. Urine was collected and analysis was performed with Dipstick Urinalysis strips and various biochemical components were measured using automated urine analyzer and findings were analyzed. The demographic and clinical data were recorded with a set of questionnaire.

**Results:** Out of 296 fever cases of clinically suspected malaria only 55 cases were found microscopically confirmed malaria cases showing incidence of malaria is 18.6% among clinically suspected.

In the study it was observed that all the urinary parameters were elevated in malaria cases when compared with controls. Proteinuria was found in 76.4%, Urobilinogenuria in 65.5%, Bilirubinuria in 41.8% and hematuria was detected in 40% of malaria cases.

Urine protein ( $P < 0.001$ ), urobilinogen ( $P < 0.001$ ), Bilirubin ( $P < 0.001$ ) and RBCs ( $P = 0.001$ ) were significantly higher in patients with *P. falciparum* infection when compared with *p. vivax* infection.

**Conclusion:** In malaria infection there is significant changes in chemical composition of urine. The most frequent abnormalities in the urinalysis were proteinuria, increased specific gravity, urobilinuria and bilirubinuria which can be easily detected by simple Dipstick urinalysis. Even though urinalysis is not an alternative tool for malaria diagnosis this can be used together with light microscopy in resource-limited endemic areas for corroborating the diagnosis and finding signs of complications of malaria.

**KEYWORDS :** Urinalysis, Dipstick, malaria, *Plasmodium falciparum*

### INTRODUCTION

Malaria is one of the most prevalent human infections with significant morbidity and mortality in the tropical and sub-tropical regions across the globe [1,2]. It presents a diagnostic challenge to laboratories in most of the countries including India. The state of Odisha shows perennial malaria transmission but usually at its peak from July to December and contributes maximum number of malarial death in India. *Plasmodium falciparum* infection being most common Odisha is associated with high morbidity and mortality [2,3,4]. Usually the serious cases of malaria occur in *Plasmodium falciparum* infections. Early recognition of clinical symptoms and signs with detection of urinary abnormalities by urinalysis can be predictive of onset of complications and organ failures [5,6,7]. So that prompt treatment and proper care may be instituted early to prevent death and to reduce morbidity of malaria. Dipstick urine analysis remains the most easy to perform, inexpensive readily available investigation which can provide many useful information about various diseases and conditions even before symptoms do appear [8,9,10,11]. Liver dysfunction and renal impairment have been reported in severe malaria infections [12,13,14] and these observations led to suggest that malaria infections may have significant effect on urinary composition [6,14]. Studies on urinalysis for abnormalities in malaria patients are limited and the extent to which abnormalities do appear in urine and their relationship with diagnosis and prognosis of malaria in this endemic area needs to be studied.

### MATERIALS AND METHODS

The study was conducted at Sri Ram Chandra Bhanja Medical College and Hospital, Cuttack, Odisha from July 2016 to December 2016 considering the period when malaria transmission was usually at its peak. During the period total 296 cases of fever which were clinically suspected to be suffering from malaria from male and female medicine and paediatric wards of SCB Medical College and Hospital, were investigated for confirmation of malaria by microscopic examination of both thick and thin blood smears. Out of 296 fever cases admitted only 55 cases were found microscopically as confirmed malaria cases which constituted the reference group. Matching the demographic profile, age and sex of such patients we took 55 healthy individuals as controls. Thus a total of 110 participants were enrolled for the study

comprising 55 cases of malaria and 55 healthy controls.

The reference population consisted of patients of all age groups and both sex with parasitological confirmation of malaria by microscopic examination of thick and thin smears by working pathologists of the institution. Some of the patients enrolled were referred from peripheral medical centres to this tertiary care hospital during the period of study. Patients with known diseases like renal disease, liver disease and urinary tract infection and those who did not give consent were excluded from the study. Written informed consent was obtained from either from themselves or from their guardians before recruitment in to the study. All 110 participants (55 cases and 55 controls) were investigated.

Their medical record of any ailments and sociodemographic data were obtained with the help of a set of preset-structured questions.

Sample collection, preparation, staining and all associated work were performed by trained and experienced technicians working in the institution in accordance with standard operating procedure. Venous blood (2ml) was collected for routine blood tests, complete blood count, RDT for malaria and peripheral thick and thin smears were made, stained with Leishman or Giemsa for microscopic examination and species determination of malaria parasites [29,30,31].

A urine sample was obtained in a sterile container following detailed instructions to participants [28]. Urinalysis was performed using Dipstick-Reagent Strip (Bayer-Multistick 10 SG). The product manual was followed and the urine sample was examined within 1 hour of collection or was refrigerated (at 2-8 degree C) and examined within 4 hours of collection and urine samples were evaluated with Mindray urine analyser UA-66 (Shenzhen, China) for the following parameters:

- 1- Glucose: (any positive reading)
- 2- Bilirubin: (any positive reading)
- 3- Ketones: (above 5mg/dl)
- 4- Blood (whole or hemolyzed erythrocytes, including traces)
- 5- pH: (greater than 7.4 or lower than 4.8)

- 6- Protein:(>30mg/dl)
- 7- Urobilinogen:(>2mg/dl)
- 8- Nitrites(any positive reading)
- 9- Leukocytes(70/ul)
- 10- Specific gravity(>1.020)

Statistical Analysis was performed with IBM SPSS Statistics for windows,Version21.0 (IBM Corporation,Armonk,NY,USA) and statistical significance level which was adopted was 5%(P< 0.05).The doubtful result whenever encountered was ignored and was not considered as an abnormal test result.

**RESULTS**

In this study we found only 55 confirmed cases of malaria out of 296 patients who were admitted with fever with clinical suspicion of malaria during the study period .This showed the incidence of malaria in this area is 18.6% of malaria suspected fever cases(chart-1).The participants of the study included 55 malaria patients and 55 controls with matching age and sex.Out of 55 malaria cases 31(56.4) patients were of age below 14 years while 24(43.6%) patients found to be above 14 years of age(Char-2).It was observed that incidence of malaria was more in paediatric age group than that of adult population.With respect to sex of malaria patients it was noticed that out of 55 cases,male were 37(63%) and 18(32.7%)were female (Chart-3).

This observation showed malaria incidence is more common in males than females.P.falciparum infection was diagnosed in 49 (89.1%), P.vivax in 4 (7.3%) and 2 (3.6%) showed mixed infection by these species (Chart-4). Even though the malaria cases and controls were of comparable age and sex,it was observed that the malaria cases had significantly (P<0.001) lower Hb concentration than the controls.It was also observed that the concentration of all the parameters of urine were elevated in malaria cases when compared with the controls.The parameters which were found significantly increased in urine of malaria patients were protein (76.4%), urobilinogen(65.5%), bilirubin(41.8%) and blood (40%) as shown (Table-1).The other parameters found positive were leucocytes(14.5%),Ketones(7.3%),nitrites(3.6%)and glucose (1.8%).

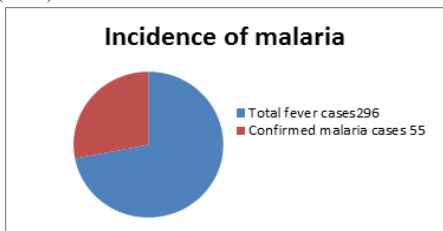


Chart-1 showing incidence of malaria:

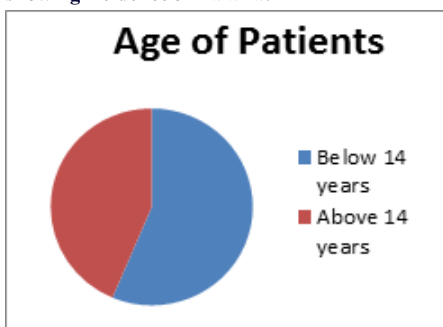


Chart-2 showing age group:

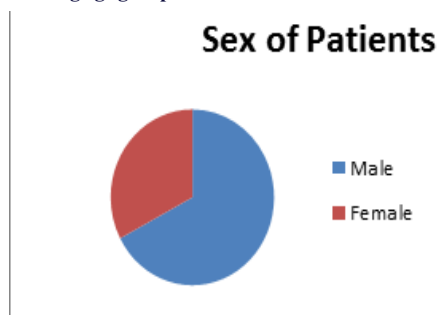


Chart-3 showing sex distribution:

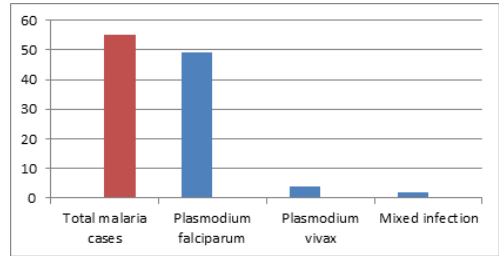
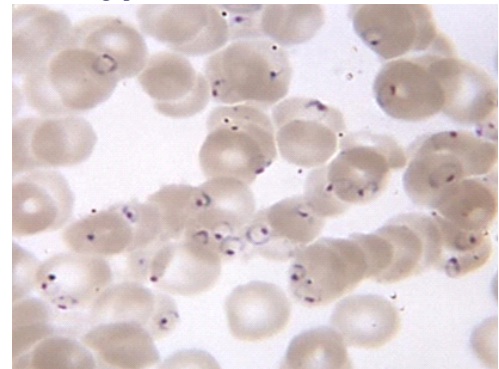


Chart-4 showing species distribution:



Picture-1 (Blood smear)

A case of cerebral malaria in the study group showing multiple P.falciparum parasites in thin smear stained with Leishman stain(10X\*100)

**urinary parameters of 55 malaria cases:**

Parameters in urine	No.of cases found elevated	Percentage(%)
PH (Normal range4.8-7.4)	50	91
Protein	42	76.4
Urobilinogen	36	65.5
Specific gravity	26	47.3
Bilirubin	23	41.8
Blood	22	40.0
Leucocytes	08	14.5
Ketones	04	7.3
Nitrites	02	3.6
Glucose	01	1.8

On analysis of urinary parameters it was found that PH of urine was within normal range in 91% cases and without any significance in this study.Where as in all malaria cases there were some abnormalities in their urine sample as compared to malaria negative control.It was found that urine urobilinogen(P<0.005), bilirubin(P<0.001), protein (P<0.001) and blood (P<0.001) were significantly increased in P.falciparum as compared to P vivax infection. Bilirubinuria, proteinuria and hematuria were positively correlated with malaria parasite density and severity of the disease.

**DISCUSSION**

Correct diagnosis of malaria remains the key for appropriate and effective management of malaria patients and in reduction of malaria-related morbidity and mortality[1,4].We studied dipstick urinalysis with the objective of using this simple test in conjunction with other diagnostic tests to accurately diagnose malaria in resource-limited malaria-endemic areas.We observed a significantly higher urine urobilinogen, bilirubin, protein and blood in individuals with malaria infection in comparison to healthy controls.Similar observation were found in other studies done in African countries[5,6]. The commonest abnormalities we observed in dipstick urine analysis of malaria patients were proteinuria (76%), urobilinuria (65.5%), increased specific gravity (47.3%), bilirubinuria (41.8%) and blood in urine (40%).

Even if the different parameters evaluated by urinalysis may be altered by various factors that reflect systemic disorders or diseases of kidney or urinary tract[11].Some studies suggest that haemoglobinuria, hematuria and bilirubinuria have not been associated with liver or kidney dysfunction as bilirubin appears in urine before other signs of liver dysfunction are apparent [11,13]. In the present study high incidence of

urinary urobilinogen and bilirubin in malaria patients in comparison to control suggests of hepatic involvement or hemolysis. Malarial involvement of liver with specific pathomorphological changes and abnormal liver function test is well documented [16,17,18]. Some other study has shown that presence of hyperbilirubinemia and bilirubinuria if there P falciparum malaria should be suspected even if blood smear be negative[15]. Jaundice in malaria infection may be caused by many factors including haemolysis of parasitized red cells, microangiopathic haemolysis of disseminated intravascular coagulation (DIC), hepatic dysfunction or drug induced haemolysis(antimalarials). Predominantly conjugated hyperbilirubinemia has been reported in P. falciparum malaria[16,17,18,19]. The demonstration of urobilinuria and bilirubinuria are common in malaria patients the fact of which may be useful for clinicians working in areas which are endemic but resource-limited like the state of Odisha[20], where dipstick urinalysis may be done to aid diagnosis. In this study the higher incidence of proteinuria and haematuria in P.falciparum infection is similar to findings of other researchers[21,22]. Some study showed the proteinuria and haematuria in malaria patients have been associated with immune complex nephritis[23]. It has been reported that renal diseases like nephritis are common in Odisha where there is high prevalence of proteinuria with or without haematuria[10,14,25], similar finding also reported by Muraguri PW from Nairobi, Kenya [24]. The renal impairment have been attributed to increased capillary permeability as a result of systemic inflammatory response to malaria infection or alteration in fluid and electrolyte balance[26,27].

## CONCLUSION

In malaria infection there is significant changes in chemical composition of urine. The most frequent abnormalities in the urinalysis were proteinuria (76.4%), urobilinuria(65.5%), increased specific gravity (47.3%), bilirubinuria(41.8%) and presence of blood in urine (40%) which can be easily detected by simple Dipstick urinalysis. Even though urinalysis is not an alternative tool for malaria diagnosis this can be used together with light microscopy in resource-limited endemic areas for corroborating the diagnosis and early detection of complications of malaria which can guide clinicians for an accurate and effective management of malaria reducing its morbidity and mortality.

## Llimitations of this study

The small sample size and short duration of the study remain the limitations of this study. Therefore it is recommended that further studies should be conducted using a large sample size with ample time duration correlating dipstick urinalysis findings with renal function and liver function markers in patients suffering from malaria which would help in assessing the diagnostic value of dipstick urinalysis in a better way.

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## Ethical approval

The study was approved by ethical committee of Sri Ram Chandra Bhanja Medical College and Hospital, Cuttack

## Consent

Written informed consent were obtained from all the participants personally or from their legal guardians in case of minors.

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Nil

## Conflicts of interest

There are no conflicts of interest.

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