

Urine Findings by Dipstick Method in Patients with Plasmodium Vivax Malaria

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Abstract

Background: Plasmodium vivax is the predominant cause of clinical malaria in India. Though infection of plasmodium vivax is historically believed to be a benign form of malaria, recent reports suggest that Plasmodium vivax can also lead to several complications. The study was undertaken to document the urinary abnormalities by dipstick method in Plasmodium vivax malaria patients and to know its usefulness and correlation with level of parasitaemia. **Method:** This study was performed on patients suffering from plasmodium vivax malaria, diagnosed by peripheral smear examination. Urine samples from Plasmodium vivax infected patients and healthy controls were analysed by dipstick method and compared. Parasite grading was done semi quantitatively by examining the stained thick smears. Proteinuria in positive cases are graded semi quantitatively as trace, +, ++, +++ as per kit manufacture's guidelines. **Result:** In our study out of 100 patients 97 (97%), showed protein in urine, which is significant, compared to control group (p value < 0.05). Other urinary constituents like bilirubin and urobilinogen were also higher in these patients in comparison to control group. Also current study showed a positive correlation between proteinuria and plasmodium vivax parasitaemia and thus highlighted its usefulness as one of the diagnostic indices in identifying patients with severe plasmodium vivax malarial infestation. **Conclusion:** This study has documented proteinuria in significant number of patient with plasmodium vivax infestation. Study also showed a positive correlation between proteinuria and plasmodium vivax malaria parasitaemia. Even though urinalysis is not an alternative diagnostic tool for malaria, these urinary findings can be used as one of the diagnostic indices in identifying patients with severe plasmodium vivax malarial infestation. But further extensive researches involving large number of cases needs to be undertaken to support and justify the real benefits of these findings.

Keywords: Urine; Plasmodium Vivax; Malaria; Proteinuria; Dipstick.

Introduction

Urine analysis still remains highly valuable and most important means of diagnosis in clinical medicine [1]. The urine dipstick being a simple and fast diagnostic procedure, can determine the presence of proteins, glucose, ketones, hemoglobin, bilirubin, urobilinogen, nitrites and leukocytes in urine sample [2]. Microscopic haematuria, mild proteinuria has been found in as many as 25-50% of patients with malaria

in various studies [3].

This study is a cross sectional observational study conducted to know the various urinary changes in patients suffering from plasmodium vivax malaria. In this study, attempt was made to record the urinary findings by dipstick method in patients suffering from plasmodium vivax malaria.

Methodology

This study was performed on 100 patients suffering from plasmodium vivax malaria diagnosed by peripheral smear examination. The study is conducted in one of the tertiary health centres, at coastal

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Karnataka, over a period of one year. Initially all febrile patients presented with clinical features suggestive of malaria were thoroughly examined clinically after taking detailed history and are included in the study after confirming the clinical diagnosis by peripheral smear examination. Control population included 50 healthy individuals without history of malaria or any other medical illness of comparable age and gender who have voluntarily agreed to take part in the study. Medical history for both the groups was obtained using a standardized questionnaire, which covered age, sex and history of clinical disease, e.g. diabetes mellitus, renal disease, hypertension and urinary tract infection (UTI) symptoms. Blood was collected from both the groups in EDTA tubes for peripheral smears preparation. Thick and thin blood smears were prepared and screened for malarial parasite after staining with Leishman stain. Parasite load was estimated in those smears positive for plasmodium vivax malaria by examining the thick smears. Mid-stream urine specimen was obtained from both study and control groups and analysed within 30 minutes of collection of sample to detect the presence of Blood, protein, bilirubin and urobilinogen by dipstick method using uricol 10 urine strips. Results were interpreted as per manufacturer's instructions. Urine analysis was performed, before starting any medications, in those patients positive for plasmodium vivax malaria.

Inclusion Criteria for Study Group

- Patients with smear positive Plasmodium vivax malaria.

Exclusion Criteria for Study Group

- Patients with known renal dysfunction.
- Patients with clinical features of urinary infection
- Patients with smear positive for other species of malaria and mixed malarial infestation.
- Patients with history of malaria in recent past and treated for it.

Parasite grading was done semi quantitatively by examining the stained thick smears as follows

+	=1/100HPF
++	=2-10/100HPF
+++	=1-10/10HPF
++++	=1-5/HPF
+++++	=6-10/HPF

Proteinuria in positive cases are graded semi quantitatively as trace, +, ++, +++ as per kit manufactures guidelines.

Results

Urine findings by dipstick method were evaluated in 100 patients of Plasmodium vivax malaria visiting the hospital and compared with urine findings of 50 healthy control populations without any history of illness and drug intake.

Table 1: Age and Sex distribution of plasmodium vivax malarial subjects

Sex	Age of the patients		
	20-30 yrs	31-40yrs	41-50yrs
Male	18	15	22
Female	15	20	10

Table 2: Comparison of urine changes by dip stick method, between control and malarial subjects

Urine parameters	Number of individuals with positive urinary findings (Study group)	Number of individuals with positive urinary findings (Control group)
Bilirubin	8	0
Significant urobilinogen	9	0
Protein	97	0
Blood	7	3

Table 3: Number of patients with different grades of malaria parasitaemia

Parasite grade/load	Number of patients
+	10
++	39
+++	29
++++	20
+++++	2

Around 35% of patients were in age group 31-40 yrs, 33% of patients in age group 20-30yrs and 32% of patients belonged to the age group between 41 and 50 yrs [Table1].

Urine parameters Number of individuals with positive urinary findings (Study group) Number of individuals with positive urinary findings (Control group)

Out of 100 cases, 97 (97%) patients showed protein, 8 (8%) patients showed bilirubin, 9 (9%) showed urobilinogen and 7 (7%) showed blood in their urine. Only 3 subjects in control group showed mild

haematuria [Table 2].

Majority of the patients (39%) positive for vivax showed a parasite load of ++ (i.e 2-10 parasites/100HPF) [Table3].

The urine protein levels are statistically significant in malarial patients (p value< 0.05) compared to the control group.

Urinary abnormalities seem to increase with the severity of malaria parasitaemia as shown in the above tables. Especially, urine protein, bilirubin and urobilinogen are significantly higher at higher malaria parasitaemia [Table 4, 5, Figure 2].

Table 4: Urine parameters in relation to malaria parasitaemia

Urine parameters	Parasite load				
	+	++	+++	++++	+++++
Bilirubin	0	0	2	3	3
Significant Urobilinogen	0	0	2	5	2
Protein	7	39	29	20	2
Blood	0	0	2	3	2

Table 5: Severity/ grading of proteinuria in study group

Severity of proteinuria	Number of cases of P. Vivax with proteinuria	Number of patients (outside bracket) and Parasite load (in bracket)
Trace	42	7 (+), 35 (++)
+ proteinuria	25	21 (+++), 4(+++)
++ proteinuria	20	12 (++++), 8(++++)
+++ proteinuria	10	2 (+++++), 8(+++++)

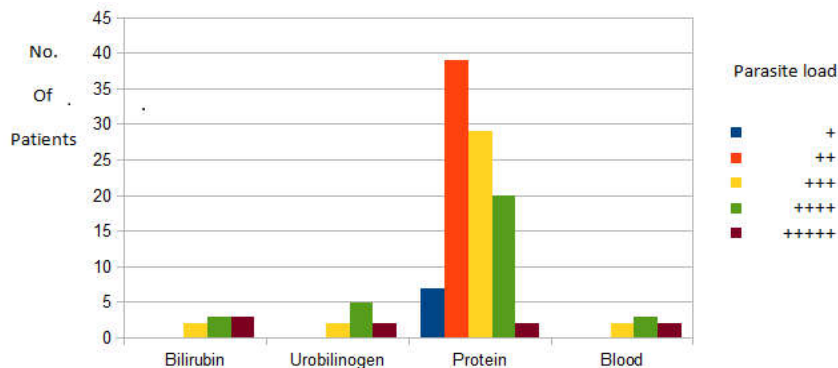
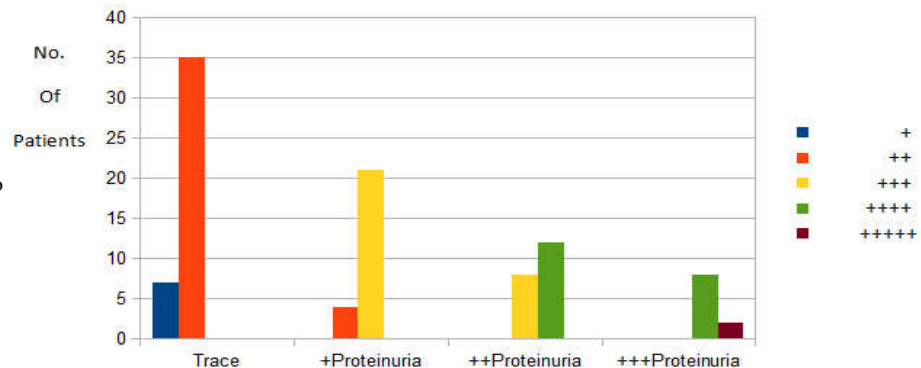


Fig. 1: Urine parameters in relation to parasite load

Fig. 2: Urine protein in relation to parasite load



Discussion

Although there is a remarkable progress in medical science in latter half of the century, yet malaria continues to be a major killer of mankind especially in developing and developed countries [4]. Every year, 200-300 million people are affected with malaria with an annual mortality rate of nearly one million [5]. *P. vivax* is the predominant cause of clinical malaria in India [6]. Though infection of *P. vivax* is historically believed to be a benign form of malaria, recent reports suggest that *P. vivax* can also lead to several complications [7,8,9]. Urinary changes were seen in 430 out of 600 patients (71.7%) in a study conducted by Karoum AO. In Kassala town of Eastern Sudan, Karoum and Mohammed reported albuminuria (71.2%), pyuria (53.8%), haematuria (45%) and granular casts (71.4%) in patients infected with malaria. Based on these observations the authors suggested that malaria may have significant effect on urine, especially producing albuminuria and to a lesser extent haematuria [3]. Kidney may be affected by malaria infections ranging from asymptomatic proteinuria to acute renal failure. A study by Nitya Nand et al showed the presence of transient proteinuria in 78% of cases in the absence of overt renal failure [10]. A study conducted by Mahrani Lubis et al observed that in children, there was weak association between proteinuria and malaria parasite counts [11] but positive correlations were found between proteinuria and malaria parasitemia, by some of the Nigerian studies [12,13]. It was concluded by a study conducted by Ugwuja EI and Ugwa NC that even though urinalysis is not an alternative diagnostic tool for malaria infection, urinary abnormalities, such as bilirubinuria, urobilinogenuria, proteinuria and haematuria may help in identifying these patients [14]. It is unlikely that a rise in temperature is the only cause of proteinuria in malarial infections. The electrophoretic analyses of proteinuria indicate that in malarial infections, reversible proteinuria may be caused by glomerular as well as tubular lesions. [15].

Our study has documented higher urinary protein, bilirubin and urobilinogen in plasmodium vivax patients in comparison to healthy controls. Significantly high incidence of urinary bilirubin and urobilinogen in malarial subjects in comparison to controls suggests either hepatic involvement or haemolysis. Similarly proteinuria may suggest renal involvement in these patients. However, we are constrained to relate these findings to the possibility of renal and hepatic impairment caused by parasitaemia in our patients, due to lack of data on renal and liver function tests.

Current study has also showed proteinuria in significant number of patients suffering from plasmodium vivax infestation and highlighted the correlation between severity of proteinuria and plasmodium vivax parasitaemia. These urinary findings may aid in clinically suspecting malaria in endemic area and to assess the severity of this disease.

Conclusion

This study has documented proteinuria in significant number of patient with plasmodium vivax infestation. Study also showed a positive correlation between proteinuria and plasmodium vivax malaria parasitaemia. Even though urinalysis is not an alternative diagnostic tool for malaria, these urinary findings can be used as one of the diagnostic indices in identifying patients with severe plasmodium vivax malarial infestation. But further extensive researches involving large number of cases needs to be undertaken to support and justify the real benefits of these findings.

References

1. Haber MH. Pisse prophesy: a brief history of urine analysis. *Clin Lab Med* 1988; 8: 415-30.
2. Ramos-Rincón JM, Cuadros-González J, Malmierca-Corral E, de Górgolas-Hernández M. El diagnóstico en medicina tropical en países con pocos recursos. *Rev Clin Esp.* 2014. <http://dx.doi.org/10.1016/j.rce.2014.05.002>
3. Karoum AO, Mohammed BA. Urine analysis in malaria in Kassala town, Eastern Sudan. *Saudi J Kidney Dis Transpl* 2000; 11: 208-9.
4. A Profile of National Institute of Malaria Research. Estimation of True Malaria Burden in India 922 of 9. Available at [http://www.mrcindia.org/MRC_profile/profile2/Estimation of true malaria burden in India.pdf](http://www.mrcindia.org/MRC_profile/profile2/Estimation_of_true_malaria_burden_in_India.pdf)
5. Wim Van Lerberghe TE, Kumanan R, Abdelhay M: World Malaria Report. World Malaria Report (Editor eds.) World Health Organization; 2008.
6. Joshi H, Prajapati KS, Verma A, Kang'a S, Carlton JM: Plasmodium vivax in India. *Trends Parasitol* 2008, 24:228-235.
7. Anvikar A, Singh D, Singh R, Dash A, Valecha N: Vivax malaria presenting with cerebral malaria and convulsions. *Acta Parasitol* 2010, 55:96-98.
8. Koibuchi T, Nakamura T, Miura T, Endo T, Nakamura H, Takashi T, Kim HS, Watawa Y, Washizaki K, Yoshikawa K: Acute disseminated encephalomyelitis

- following Plasmodium vivax malaria. *J Infect Chemo* 2003; 9:254-56.
9. Beg MA, Khan R, Baig SM, Gulzar Z, Hussain R, Smego Ra Jr: Cerebral involvement in benign tertian malaria. *Am J Trop Med Hyg* 2002; 67:230-32.
 10. Nand N, Aggarwal H, Sharma M, Singh M, systemic manifestations of malaria. *J Indian Acad Clin Med* 2001; 2:189-94.
 11. Lubis M, Rusdidjas, Ramayati R, Ramayani OR, Siregar RS, Supriatmo. Proteinuria and malaria parasite counts in children. *Paediatr Indones*, 2013; 53 (6):295-8.
 12. Ekeanyanwu RC, Ogu GI, assessment of renal function of Nigerian children infected with plasmodium falciparum. *IJMMS* 2010; 2:251-5
 13. Raphael EC, Benjamin AU. assessment of renal function of plasmodium falciparum infected children in Owerri, Eastern Nigeria *Res J Med Sci* 2010; 4:201-12.
 14. Ugwuja E.I, Ugwu N.C. Abnormal findings on dipstick urinalysis of out-patients with malaria in Abakaliki, Nigeria *J Vector Borne Dis*. 2011; 48: 205-9
 15. Origin of proteinuria in human malaria. *Tropical Medicine and Parasitology* : Official Organ of Deutsche Tropenmedizinische Gesellschaft and of Deutsche Gesellschaft fur Technische Zusammenarbeit (GTZ) 1985; 36(1):39-42.
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