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Burden of Parasitaemia, Falciparum Malaria and Serum Glucose, Urea and Creatinine among Patients in Abbs (Tehama-Hajjah), Yemen

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Abstract

Hypoglycemia and kidney failure associated with malaria is common and depends to a large extent on the local prevalence of malaria. The present study is therefore aimed at assessment of glucose, creatinine, and urea in blood serum of *Plasmodium falciparum* malaria patients in 63 subjects with malaria parasitaemia were selected as test subject based on clinical symptoms and 30 healthy subjects without malaria infection were included as control subjects. The diagnosis of malaria was carried out by thin and thick blood films. The creatinine, urea and glucose were determined with malaria parasitaemia. *P. falciparum* malaria infection resulted in significant increase in serum urea and creatinine levels of patients with group mild, moderate and high parasitaemia when compared the respective healthy subject's. The serum glucose levels were significantly reduction with all groups parasitaemia. We conclude those kidney dysfunctions and hypoglycemia are clinical features of parasitaemia malaria. This study suggesting that hypoglycemia with malaria parasitaemia may be associated with status of renal impairment.

Keywords: *Plasmodium falciparum*; hypoglycemia; urea; Creatinine; Parasitaem.

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1. Introduction

Malaria infection remains a major public health problem worldwide. The World Health Organization has estimated that malaria affects 198 million individuals, and globally 584,000 persons died from the disease in 2013 [1]. Susceptible groups are children and adults who have host or never acquired immunity [2]. Acute renal failure and hypoglycemia are serious complications of *falciparum* malaria that is common among adults in South East Asia and Africa and also carries a high mortality [3]. The contribution of malaria to the number of cases of acute renal failure and hypoglycemia in any particular setting depends to a large extent on the local prevalence of malaria [4]. Acute renal failure occurs in about 60% of all cases of complex malaria [3, 5]. *P. falciparum* malaria is recognized as an important factor in the etiology of acute renal failure in parts of India [6]. Ogbadoyi and Tembeng. Reference [7] reported that the severe proteinuria rises in blood urea. Patients with *P. falciparum* Infection are prone to develop severe malaria in 30% of cases [8], which resulted in case fatality rate of 20% [9]. Hypoglycemia is literally translated as low blood sugar. It occurs when blood sugar (glucose concentration) falls below level necessary to properly support the body's need for energy and stability throughout its cells. This can occur during severe malaria because the parasite feeds solely on glucose [10].

A few observational studies demonstrated that there was an increased risk for mortality with small increments in serum creatinine. This finding made the case for the adoption of more sensitive creatinine-based criteria for acute kidney injury (AKI) [11, 12]. Several factors, including various chemical mediators, catecholamine release, cytoadherence of parasitized erythrocytes, dehydration, intravascular haemolysis, intravascular coagulation, sepsis hyprebilirubinaemia and hyperparasitaemia have been implicated in the pathogenesis of ARF in malaria [13]. In the majority of cases *P. falciparum* is the causative agent of malarial acute renal failure (MARF), although MARF due to *P. vivax* has been occasionally reported [6]. This study was attempt and highlight investigated the kidney function and hypoglycemia in parameters among Yemeni patients with *P. falciparum* malaria and studied the relationship between kidney function and parasitaemia density.

2. Materials and Methods

2.1 Subjects

A total of 63 patients with malaria parasitaemia attending Center of Malaria in the Rural Hospital Abbs in the Abss Tehama, Hajjah-Yemen were enrolled as the test subjects. The test subjects were randomly selected between October 2014 to February of 2015, who were reported ill with fever (temperature >37.5°C), headache, vomiting, chills , diarrhea, and other clinical signs and symptoms of malaria as previously documented [14]. 60 patients included both sex and both children and adults between the ages of 8 and 38 years. Healthy subjects 30 who were symptomatic and negative for *P. falciparum* in their peripheral blood were used as control individuals. The patients who taking any anti malaria, these criteria were excluded from the study.

2.2 Malarial parasite density determination

P. falciparum parasitaemia was determined in various blood smears stained by Giemsa stain. Parasitaemia was calculated based on WHO [15]: low (+) 1-10/100 field, mild (++) 11-100/100 field, moderate (+++) 1-10/one

field and high parasitaemia (++++) >10/one field.

2.3Sample collection and preparation

Sample collection and preparation: Venous blood was collected aseptically from the subjects using 5 ml disposable syringes. The blood samples were collected and 4 ml were transferred into plain bottles for the biochemical assays whereas the remaining 1ml was transferred into EDTA bottles for malaria parasite tests. The blood samples in the plain bottles were allowed to clot and retract after which they were centrifuged at 3000 rpm for 10 min and the serum transferred into sterilized plain bottles for the biochemical analysis.

2.4 Biochemical analysis

The concentration of serum urea and creatinine was meas ured by Roche/Hitachi cobas c 311). For measurement of urea, kinetic test with urease and glutamate dehydrogenase [16] was used. Creatinine level was determined by Jaffe's reaction without deproteinization, where the samples were subjected to react with picrate in alkaline pH forming a yellow-red color with maximum absorbance at 512 nm. Glucose estimated using glucose oxidase method GOD-PAP enzymtic colometric method.

2.5 Ethical Considerations

Ethical approval was given by the Hospital Management and Center of Malaria in Abbs area.

2.6 Statistical analysis

The data were expressed as mean ± SE. The results were analyzed statistically using column statistics and one t-tests. Correlation among the investigated parameters was tested by curves and regression using linear regression to test departure from linearity with runs test. These analyses were carried out using computer statistics Prism 3.0 Package (Graph and Software, Inc, San Diego, USA). The minimum level of statistical significance was set at $P< 0.05$, 0.01, or 0.001.

3. Results

Of the 63 patients infected with *P. falciparum*, 10 (16.7%) had low intensity of infection low 1+ (1-10/100 field), 15(23.3%) had mild intensity of infection 2+ (11-100/100 field), 21(31.7%) had moderate intensity of infection 3+ (1-10/one field) and 17(28.3%) had high intensity of infection 4+ (>10/one field) (Table1).Serum urea and creatinine levels were significant difference between malarious patients with mild, moderate and high parasitaemia and malaria-free healthy. However there was no significant difference in serum urea and creatinine levels between malarious patients with low parasitaemia and malaria-free healthy. Serum urea and creatinine levels were Statistical analysis showed there was significant difference between the serum glucose levels of all malaria patients examined and the healthy individuals, also showed that there was significant difference ($p > 0.0001$) between the two groups, malaria patients and the healthy individuals (Table 2).

Table (3) reflects levels of glucose, urea and creatinine with parasitaemia level. There was significant diffeerence in serum glucose levels between malarious patients parasitaemia and malaria-free healthy. Parasitaemia was strongly associated with lower glucose in patients. Serum glucose levels were high significantly more in patients with moderate parasitaemia, then high parasitaemia infection.

Table 1: Occurrence of *P. falciparum* malaria in parasitaemia patients by intensity of infections.

Parasitaemia N=63	No. of patients with malaria %
Low (+)	10 (16.7)
Mild(++)	15 (23.3)
Moderate(+++)	21 (31.7)
High (++++)	17 (28.3)

Table 2: Effects of *P. falciparum* malaria infection on serum urea and creatinine as compared to healthy subjects.

Parameters	Patients with Malaria N=63	Healthy Subjects N=30
Glucose mg/dl	45.73±0.78***	76.27±2.56
Urea mg/dl	29.91±1.00***	22.33 ± 1.15
Craetinine mg/dl	0.69±0.02***	0.54± 0.01

**= $p<0.0001$

4. Discussion

Analysis of data obtained showed that the levels of serum urea and creatinine were higher among the test subjects than the healthy subjects. Reference [17] reported high levels of creatinine in children and adults with malaria infection. The higher values of serum urea and glucose observed in these parameters may be attributed to impairment in renal function associated with *P. falciparum* infection [18]. Increase in serum creatinine has also been reported to arise from intrinsic renal lesions, decreased perfusion of the kidney, or obstruction of lower urinary tract malaria infection [19].

Table3: Mean serum glucose, urea and creatinine levels in parasitaemia *falciparum* malaria and healthy subject's control.

Parasitaemia N=63	Glucose level (mg/dl)	Urea level (mg/dl)	Creatinine level (mg/dl)
Low (+)	52.84±1.18**	24.21±1.05	0.52±0.01
Mild(++)	49.71±0.61***	29.54±1.33**	0.61±0.02***
Moderate(+++)	39.62±0.25***	34.00±0.90***	0.83±0.03***
High (++++)	43.96±1.04***	39.29±3.24***	0.87±0.6=06***
non-parasitaemic	76.27±2.56***	23.13±0.85	0.55±0.01

**= p<0.001, ***= p<0.0001

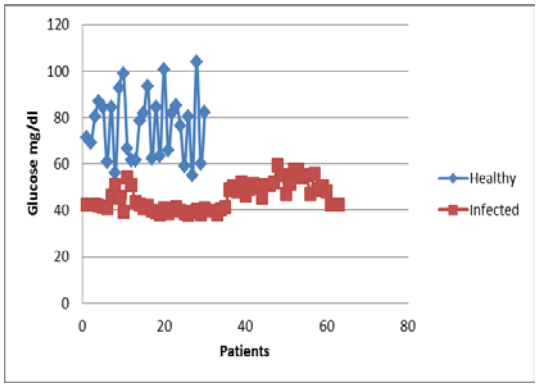

Figure 1: Effect of *P. falciparum* malaria infection on serum glucose in patients.

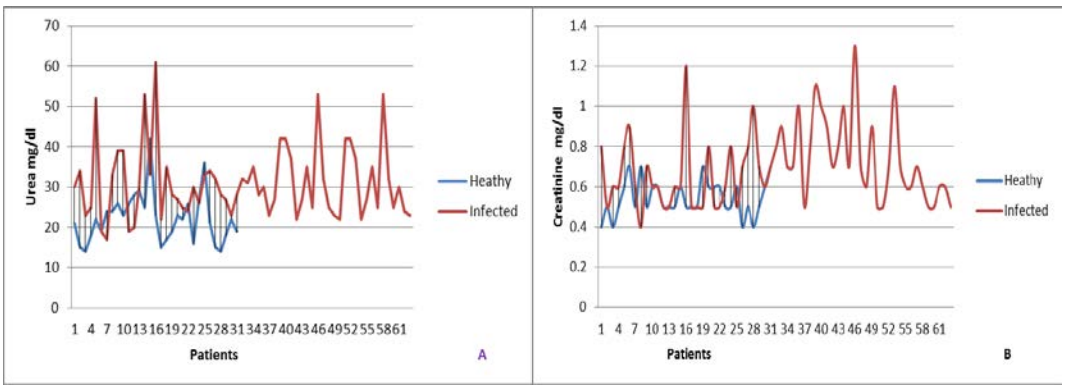

Figure 2: Effect of *P. falciparum* malaria infection on (A) serum urea and (B) serum creatinine in patients.

Elevated values of serum urea and creatinine are indicators of dysfunction in kidney [20]. Increase levels of serum urea and creatinine directly proportional to the gradually increase the intensity level parasites (Table 3). Onyeneke *and his colleagues* [21] reported that the serum creatinine levels increased in moderate and severe parasitaemia but decreased significantly in mild parasitaemia. Ekeanyanwu and Ogu in [22] obtained significant increase of serum creatinine in malarious subjects with a positive correlation to parasitaemia density.

On the other hand levels of serum glucose were lower among the test subjects than the healthy subjects. Blood sugar levels in malaria infection have reported. White and his colleagues [23] and Taylor and his colleagues [24] reported that the decreased plasma glucose in malaria patients as compared with the controls which stated that hypoglycemia were common in malaria. Studies by Onyesom and Agho [25], indicated hypoglycemia in malaria patients in Edo-Delta state. Blood glucose is the main source of energy used by the body. Blood glucose is the main source of energy used by the body. In malaria, the serum glucose concentration decreases, this is as a result of the increased consumption of glucose by the parasite [10]. *P. falciparum* induced reduction in blood glucose could be due to the invasion of the liver cells by the malarial parasite which can cause organ congestion, sinusoidal blockage and inflammation of pancreatic cells [26], leading to increased intracellular insulin, accumulation and slow receptor recycling [27]. Arem, [28] reported that hypoglycemia associated with kidney failure and is a common occurrence and is often a sign of failure for multiple devices and it's an ominous portent and falls within several mechanisms. Addition to that the detection of hypoglycemia should rely on frequent and careful glucose determinations in any patient with uremia. In healthy people, both the liver (via glucagon) and kidney (via catecholamines) equally contribute to the increase in glucose release into the circulation during counter regulation of hypoglycemia; this is largely achieved by gluconeogenesis [29, 30]. People with moderate to severe chronic kidney disease CKD have reduced renal mass, and therefore, a reduced capacity for renal glucose release. Moreover, these individuals could be malnourished and/or have muscle wasting, which decreases their hepatic glycogen stores and reduces the availability of gluconeogenic substrates [31]. It is clear that relation between decreased serum glucose and parasitaemia level (Table 3). The surprising result was significantly the low level of glucose recorded in all groups: low mild, moderate and high parasitaemia. While, glucose returned it tends toward more decline with moderate parasitaemia as compared to other parasitaemia group. The present result supports the findings of previous authors [32, 25].

5. Conclusion

Hypoglycemia and kidney dysfunctions are clinical features of parasitaemia, *falciparum* malaria in Abbs, (Tehama-Hajjah),Yemen. Clear correlations between malaria density (low, mild, moderate and high infection) and levels of blood glucose in this study.

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