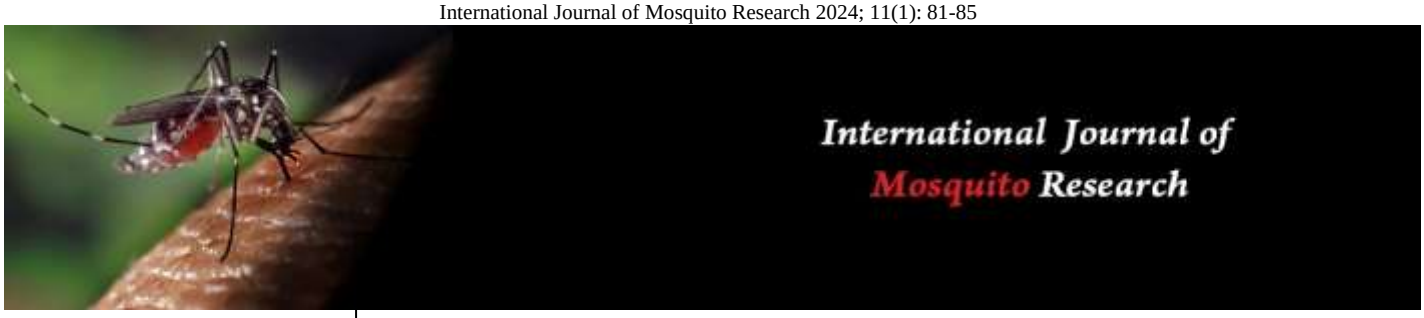

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A hospital based analytical study evaluating renal function in pregnant women with malaria

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Abstract
Aim: The aim of the present study was to assess the effect of malaria on renal function of pregnant women receiving antenatal care.
Methods: This hospital-based case-control study was carried out for the period of one year. A total of 200 patients (100 with gestational malaria as cases and 100 healthy pregnant women as controls) were recruited for this study.
Results: Gestational age, urea, and creatinine were associated with malaria infection. However, age, gravidity, parity, sodium, and potassium showed no significant association with malaria infection. There were significantly increased plasma urea and creatinine with respect to increasing degree of parasitaemia (moderate and high) com- pared to non-malaria group. There was a significant difference in levels of urea and creatinine and the degree of parasitaemia when stratified according to the gestational age. However, parity and gravidity showed no significance difference.
Conclusion: We concluded that malaria has a significant impact on renal biochemical profile (most importantly, urea and creatinine), with cases of increasing gestational age having a higher risk of the consequences of malaria. We recommend that pregnant women who report to hospitals with malaria should also be examined for kidney function.

Keywords: Renal function, pregnant women, malaria

Introduction
Malaria ranks as the second most prevalent cause of mortality associated with infectious diseases globally, behind TB. Annually, it is predicted that this condition affects a range of 350 to 500 million individuals and leads to 1 to 3 million fatalities [1, 2]. Malaria is a sudden onset of feverish sickness caused by infection with five Plasmodium species, which are protozoan parasites belonging to the phylum Apicomplexa. Plasmodium falciparum, the most common species, is known for its propensity to induce serious infections or mortality [3-6]. Anopheles spp. mosquitoes, which are prevalent in warm, tropical regions worldwide, transmit the infection by their infectious bites [3-5]. Malaria during pregnancy is a significant public health issue in tropical and subtropical areas. Pregnant women are more vulnerable to malaria compared to nonpregnant women [7]. This is because pregnant women with malaria have a diminished immune response as a result of their condition [8].
Pregnancy and malaria can exacerbate one other's symptoms. The physiological and pathological alterations resulting from malaria have a synergistic impact on the patient, hence posing challenges for the mother, child, and the attending physician [9]. Malaria during pregnancy is associated with many adverse consequences on pregnancy outcome, such as heightened neonatal mortality due to reduced birth weight and higher incidence of preterm deliveries [10].
Following a phase of development in the liver prior to the formation of red blood cells, the infection in the bloodstream, which leads to the illness, begins. The parasitic invasion of the erythrocyte results in the consumption of haemoglobin and the alteration of the red cell membrane. *P. falciparum* infected erythrocytes have the ability to cling to the inner walls of blood arteries in the brain, kidneys, and other afflicted organs. Cytoadherence and rosetting, which refer to the attachment of uninfected red blood cells, disrupt the flow of blood in small blood vessels and the metabolic processes of essential organs.

Falciparum malaria in pregnancy is characterised by the presence of parasites that are localised in the placenta. Parasites that are sequestered are able to avoid the host's defensive systems, namely the spleen's processing and filtration. Sequestration does not occur in the benign forms of malaria caused by *P. vivax*, *P. ovale*, and *P. malariae*. During pregnancy, the detrimental consequences of malaria infection arise due to:

- The systemic infection, comparable to the effects of any severe febrile illness in pregnancy: maternal and fetal mortality, miscarriage, stillbirth and premature birth.
- The parasitisation itself: fetal growth restriction and low birth weight, maternal and fetal anaemia, interaction with HIV, susceptibility of the infant to malaria.

An up-to-date investigation examining the connection between malaria and renal failure revealed a significant rise in serum creatinine levels, with 67.14% of the patients exhibiting serum creatinine levels that above the normal range [11].

Although prenatal screening for malaria is a national policy, the WHO standards recognise that certain biochemical and haematological characteristics may raise concerns about severe malaria. Therefore, periodic renal screening for malaria in pregnant women should be conducted at most [12]. Nevertheless, the proportion of negative consequences caused by malaria infection that might possibly be prevented during pregnancy is anticipated to be substantial, particularly in regards to renal biochemistry.

Consequently, we aimed to evaluate the impact of malaria on the kidney function of pregnant women who are getting prenatal treatment.

Materials and Methods

This hospital-based case-control study was carried out for the period of one year. A total of 200 patients (100 with gestational malaria as cases and 100 healthy pregnant women as controls) were recruited for this study.

Inclusion Criteria

Pregnant women with singleton pregnancies receiving antenatal care at the study center were eligible to participate in this study.

Exclusion Criteria

Exclusion criteria were participants with preexisting renal diseases, chronic kidney disease, hypertension and diabetes mellitus, human immunodeficiency virus, and acquired immune deficiency.

Ethical Considerations

Consent was sought from participants having explained to them the purpose of the research and its relevance. Participants were made to willingly opt out anytime they felt uncomfortable or had a change of mind.

Collection of Obstetric Data

With the aid of a questionnaire a resident or an intern nurse obtained sociodemographic characteristics and obstetric history (parity, gravidity) of consented participants.

Sample Collection and Processing

A volume of 5 millilitres of venous blood was collected from each patient for the purpose of conducting a blood film and a biochemistry analysis. Appropriate procedures were used to produce and stain blood smears for the investigation of malarial parasites [13]. The thick and thin films were examined to determine the parasite count per 200 white blood cells [14]. The degree of parasitaemia was categorized as follows: low (<1000 parasites/μL of blood), moderate (1000–9999 parasites/μL of blood), and severe (≥10,000 parasites/μL of blood) [15]. The BT-3000 Analyzer was used for biochemical analysis. The determination of urea and creatinine was based on the urea Berthelot reaction [16] and Jaffe's technique [17], respectively. The ion selective electrolyte (ISE) analyzer (AU600 Beckman Coulter®) was used to assess the levels of sodium, potassium, and chloride.

Statistical Analysis

Data collected were coded, entered into a computer, and cleaned. SPSS version 22 was used to analyze the data. Results were presented in tables using means and percentages. Chi-square, *P* value, and one-way ANOVA were used to assess the statistical significance. Statistical significance was decided when $p<0.05$.

Results

Table 1: Demographic and biochemical characteristics of study participants

Variable	Total N (%)	Malaria positive N (%)	Malaria negative N (%)	P value
Age (years)				
15–24	80 (40)	44 (44)	36 (36)	0.0612
25–34	80 (40)	30 (30)	50 (50)	
35–44	40 (20)	25 (25)	15 (15)	
Parity				
Nulliparous	80 (40)	35 (35)	45 (45)	0.3746
Primiparous	60 (30)	32 (32)	28 (28)	
Multiparous	60 (30)	30 (30)	30 (30)	
Gravidity				
Primigravida	50 (25)	28 (28)	22 (22)	0.8501
Secundigravida	60 (30)	32 (32)	28 (28)	
Multigravida	90 (45)	42 (42)	48 (48)	
Gestational age (Trimester)				
1st trimester	70 (35)	28 (28)	42 (42)	0.0002
2nd trimester	84 (42)	40 (40)	44 (44)	
3rd trimester	46 (23)	36 (36)	10 (10)	

Parasitaemia				
low (<1000)	23	23	0 (0.0)	N/A
medium (1000–9999)	55	55	0 (0.0)	
high (≥10,000)	22	22	0 (0.0)	
Other parameters				
Urea (mg/dL)	18.52±8.52	21.94±12.8	14.4±4.6	0.0007
Creatinine (mg/dL)	0.84±0.24	0.94±0.6	0.8±0.2	<0.0001
Sodium (mmol/L)	147.53±12.28	148±12.8	140.20±12.28	0.6410
Potassium (mmol/L)	4.12±0.68	4.2±0.8	4.2±0.7	0.8728
Chloride (mmol/L)	104.5±3.5	104.5±3.2	104.5±3.8	0.9478

Gestational age, urea, and creatinine were associated with malaria infection. However, age, gravidity, parity, sodium, and potassium showed no significant association with malaria infection.

Table 2: Biochemical parameters in relation to degree of parasitaemia and no malaria

Parameters	No malaria (0)	Low (<1000)	Moderate (1000–9999)	High (≥10,000)
Urea (mg/dL)	14.6±4.6	15.5±2.8	16.34±5.3	36.24±14.6
Creatinine (mg/dL)	0.72±0.2	0.74±0.1	0.78±0.2	1.44±0.3
Potassium (mmol/L)	4.16±0.4	4.13±0.7	4.2±0.8	3.8±1.0
Chloride (mmol/L)	104.6±3.7	104.2±3.3	104.7±3.7	104.2±2.2
Sodium (mmol/L)	147±12.0	147.3±10.2	151.2±10.8	147.3±14.4

There were significantly increased plasma urea and creatinine with respect to increasing degree of parasitaemia (moderate and high) com- pared to non-malaria group.

Table 3: Biochemical Parameters and degree of parasitaemia stratified by gestational age, parity, and gravidae

Parameter	Urea	Creatinine	Sodium	Potassium	Chloride	Parasitaemia
Gestational age						
1st trimester	17.23±4.64	0.76±0.14	147.93±11.43	4.06±0.74	104.76±3.64	2017.713±1673.17
2nd trimester	18.92±9.91	0.92±0.38	148.02±10.52	3.97±0.76	104.66±2.09	5864.16±5622.81
3rd trimester	26.79±15.91	1.05±0.37	150.78±13.99	4.31±0.86	105.02±3.79	7367.35±6068.71
P value	0.036	0.034	0.416	0.832	0.420	0.016
Parity						
Nulliparous	22.78±14.86	1.03±0.37	150.20±14.46	4.24±0.792	104.66±3.54	6472.22±5029.26
Primiparous	21.41±12.66	0.93±0.32	150.23±10.52	3.81±0.71	103.81±1.98	6268.06±5878.35
Multiparous	17.22±5.36	0.80±0.20	146.51±9.30	4.28±0.85	105.01±3.85	3013.81±4850.09
P value	0.278	0.136	0.590	0.198	0.520	0.20
Gravidae						
Primigravidae	23.47±14.78	0.98±0.34	153.01±10.32	4.28±0.78	104.50±3.33	635272±4808.03
Secundigravida	21.30±12.65	1.01±0.41	146.18±10.49	4.01±0.83	103.86±1.73	5693.63±6069.92
Multigravidae	18.95±9.25	0.82±0.20	148.48±13.94	4.11±0.81	104.99±3.84	3988.91±5098.58
P-Value	0.575	0.148	0.275	0.592	0.572	0.380

There was a significant difference in levels of urea and creatinine and the degree of parasitaemia when stratified according to the gestational age. However, parity and gravidity showed no significance difference.

Discussion

Malaria during pregnancy poses a significant public health challenge in tropical and subtropical countries. Approximately 30.3 million African women get pregnant in places where malaria is prevalent. However, only a small proportion of these women have access to effective therapies [18, 19]. Due to its significance in public health, several studies have been conducted to comprehend the clinical symptoms of malaria in pregnant women. Specifically, there is data suggesting that the way the illness appears in pregnant women is influenced by the patient's immunological state and the existence of various parasite genotypes [20-22].

Malaria infection was shown to be correlated with gestational age, urea, and creatinine levels. Nevertheless, there was no noteworthy correlation seen between malaria infection and factors such as age, gravidity, parity, sodium, and potassium. Nevertheless, research done in Sudan [23] had comparable results to those obtained in our study. The bulk of the cases occurred during the second and third trimesters, whereas most of the controls were in the first and second trimesters. The research suggests that the higher levels of parasite infection seen in pregnant individuals may be attributed to their weakened immune system and the formation of the placenta, which creates an environment conducive to parasitic growth [24].

Plasma urea and creatinine levels showed a significant rise in relation to the degree of parasitaemia (moderate and high), as compared to the non-malaria group. When categorised based on gestational age, there was a notable disparity in the amounts of urea and creatinine, as well as the extent of parasitaemia. However, there was no statistically significant difference seen in terms of parity and gravidity. The presence of high amounts of urea and creatinine in the blood of individuals with malaria indicates potential kidney damage [25]. This is reinforced by the significant association between

these parameters and the severity of malaria parasitaemia. Previously, it has been demonstrated that there is a relationship between Plasmodium falciparum infection and clinically severe renal and renal-related biochemical abnormalities [26].

Typically, during a normal pregnancy, the concentration of urea and creatinine in the blood decreases. This is caused by various factors, such as the increase in blood volume, reduced production of these substances (positive nitrogen balance), and the higher rate at which the kidneys remove them due to an increase in glomerular filtration rate caused by pregnancy [27]. However, serum urea levels do not accurately indicate the functioning of the kidneys, unlike creatinine. Urea generation is influenced by factors such as dehydration, food consumption, and tissue breakdown. Therefore, the rise in blood urea concentration together with the rise in serum creatinine concentration seen in the infected individuals, as shown in this research, indicates an impaired state of renal function. The majority of women infected with *P. falciparum* had just one genetic variant, regardless of the severity of their illness. Additionally, these women reported having lived in places where the disease is common for a longer period of time. Conversely, every infection with *P. vivax* consisted of numerous genotypes. These distinctions between P. falciparum and *P. vivax* have been documented in several regions with high malaria prevalence [28].

Conclusion

Our findings indicate that malaria has a substantial influence on the renal biochemical profile, particularly in relation to urea and creatinine levels. Additionally, we observed that the risk of malaria-related complications increases with advancing gestational age. It is advisable to do renal function tests on pregnant women who present with malaria symptoms at hospitals.

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