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Frequency of Malaria in Patients Presenting with Anemia in Pregnancy at a Tertiary-Care Hospital in Pakistan

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Abstract

Malaria in pregnant women presenting with anemia is frequently observed as compared to the non-pregnant women due to lower immunity, chances of recurrence, or other complications of gestation. The aim of the current research was to determine the accurate frequency of malaria in patients presenting with anemia during pregnancy.It was a cross-sectional cohort study conducted in thedepartment of Obstetrics and Gynecology, Civil Hospital Karachi, Pakistan, from October 12, 2018, to April 11, 2019. For this purpose,a total of 161 pregnant women (18 to 35 years) with singleton pregnancies diagnosed with anemia were included. Other known causes of anemia like thalassemia trait, vitamin B12 and folate deficiency, worm infestation, thalassemia, aplastic anemia, sickle cell anemia, chronic renal and heart disease were excluded. In all patients, the blood sample was collected from the antecubital vein under aseptic precaution for determining malarial parasite (MP) by ICT (intracytoplasmic trophozoite). The outcome variable i.e. MP-ICT was noted. The majority of patients (95; 59.01%) were between 26 to 35 years of age, while the mean gestational age was 32.70±3.23 weeks with the mean parity of 4.67 ± 1.43. The frequency of malaria in patients presenting with anemia in pregnancy was observedina totalof 58 (36.02%) women. So,the study concluded that the patientspresenting with anemia in pregnancy are at higher risk to develop malaria than non-anemic pregnant women.

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Introduction

Anemia is a condition characterized by deficient red blood cells to carry enough oxygen to the body tissues. It occurs frequently in pregnancy and about 40-60% of the outcome of maternal death is caused by this condition in developing countries. Overall, 35-75% of pregnant women in underdeveloped countries and 18% of pregnant women in developed countries are affected each year[1]. Due to a number of adverse health outcomes, timely diagnosis, and management of anemia have become a great concern. Generally saying, the hemoglobin concentration and anemic outcomes have a 'U-shaped' link; either very low or very high than normal maternal hemoglobin concentrations directly cause anemia. Mostly, the lower hemoglobin concentration is associated with perinatal and maternal mortality, premature delivery, and lower birth weght[2, 3].

Malaria is the most important medical condition caused by protozoan of genus *Plasmodium*in erythrocytes, which is transmitted to humans by the bite of an infected female mosquito*Anopheles*. During pregnancy, malarial infection is a major healthcare problem with a considerable risk of mortality for both mother and neonate. It's a disease that is worldwide distributed mostly in tropical areas, where 3.3 billion people are at high risk for malaria[4] of which pregnant women are being the second most at risk of illness, approximately 125 million worldwide[5]. It is estimated that over 50 million women reside in malarial endemic areas, 20% of which become pregnant annually and almost half of them progress malarial infections[6]. Thesoutheast Asian and Pacific countriesare at higher risk of malarial transmission demonstratingone-third of the world population[1]. In Pakistan probable figure of the yearly malarial episode is 1.5 million[1] and WHO reported confirmed cases 202,013[7]. Malarial infection in pregnancy differs in complication from the non-pregnant state disease in a way of lower immunity, have a recurrence,severe complicationssuch assevere maternalanemia, acute pulmonary edema, DIC,intrauterine growth restriction,premature delivery, maternal death, miscarriage, stillbirth, lower birth weight, fetal and neonatal death[5]. Due to atypical and mostly asymptomatic presentation of malaria in pregnancy, it requires a high index of notion to identify malaria in pregnancy[8]. Anemia is the most prominent manifestation of malaria in pregnancy[5]. Anemia is more likely tooccur between 16-30 weeks due to hemolysis of parasitized cells

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and increased demand of pregnancy iron/folate deficiency. In Africa and sub-Saharan vicinity, about 23 million pregnant women are diagnosed with malarial infection annually and approximately 0.4 millionwomen develop moderate to severe anemia in pregnancy[9], which results in 10,000 cases of malaria-related mortality in pregnancy, primarily due to maternal anemia[10,11]. Various studies in India have proved malaria-associated anemia and its ultimate complications in pregnant women[12, 13].According to a study in Ghana, pregnant girls with malarial infections were 3.5 times more likely to be anemic than non-pregnant women[14]. Likewise, many western studies reveala positive association between Malaria and anemia in pregnant women[15].

Locally, few studies conducted as in Sobhodero and in Faisalabad concluded that pregnant women with malarial infections are mostly anemic[16, 17]. However,sufficient data is not available up till now and also the international data is not applicable in our population due to demographic and genetic changes.Additionally, the prevalence of malaria is very high in Pakistan, so, the present study has been undertaken to bridge the gap and provide the basis to actively prevent, diagnose and treat malaria in pregnancy (MIP) with antimalarial drugs to improve maternal, fetal, and child health.

Materials and methods

Operational conditions

MIP was confirmedasinfection detected as HRP-2 from pregnant women diagnosed as malarial parasite (MP) by intracytoplasmic trophozoite (ICT). Anemia in pregnancy was confirmed referring toWHO specifications as hemoglobin (Hb) less than 11g/l in venous blood[18], mild anemia as Hb 10.0-10.9 g/l, moderate anemia as Hb 7.0-9.9g/l, severe anemia as Hb < 7.0g/l, and very severe (decompensated) as Hb <4.0g/l. The presence of any one of these levels was labeled as positive.

Study design and sample size

It was a cross-sectional cohort study, conducted in thedepartment of Obstetrics and Gynecology, Civil Hospital Karachi fromOctober 12, 2018, to April 11, 2019.Non-probability, consecutive sampling was done with total 161[5]samples and calculated by using Openepi software, formula for estimating a proportion with specified absolute precision. The assumptions were set asconfidence interval to be 95% and anticipated population proportion of malaria in anemic pregnant women to be 5.4%[2] with the

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absolute precision as3.5%

Inclusion and exclusion criteria

Inclusion criteria were diagnosed case of anemia, pregnant women with singleton pregnancy, age 18-35, gestational age >12 weeks of pregnancy as calculated by LMP/early dating scan, whereas, exclusion criteria wereother known causes of anemia like thalassemia trait, B12 and folate deficiency, worm infestation, thalassemia, aplastic anemia, and sickle cell anemia diagnosed by lab test, multiple pregnancies confirmed by ultrasound, women with chronic renal failure (serum creatinine >1.1 mg/dl), andwomen with heart disease diagnosed on history and echocardiography.

Data collection protocol

After permission from the ethical review committee, patients admitted via OPD/ER fulfilling the inclusion criteria were selected. After taking informed written consent detailed history was taken, antenatal record was reviewed. Gestational age was determined by the last menstrual period (LMP) and confirmed by 1^{st}-trimester scan. From all patients, blood sample was collected from antecubital vein under aseptic precaution that was sent to the Central Laboratory, Civil Hospital Karachi for the detection of malarial parasite (MP) by ICT, andthe outcome variable i.e. MP-ICT was noted. The data was logged on specialized predesigned proforma.

Statistical analysis

Statistical analysis was accomplished by using SPSS software version 21, and resultsfor quantitative variables were presented as mean and standard deviation i.e. age, parity, gestational age (GA). Frequency and percentage were calculated for the place of living (Rural/ Urban),the severity of anemia, MP (seen/ not seen). These effect modifiers were measuredthrough stratification and post-stratification Chi-square test to determine their effects on the outcome. P-value < 0.05 was considered as significant.

Results

The age range of patientsunder study was from 18 to 35 years with a mean age of 26.48 ± 4.36 years, whereas, the majority of the patients (95; 59.01%) was between 26 to 35 years of age, mean gestational age was 32.70 ± 3.23 weeks and mean parity was 4.67 ± 1.43 (Table 1). The distribution of patients according to the place of living and severity of anemia is shown in Figures 1 and 2 respectively, whereas, the frequency of malaria in

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patients presenting with anemia in pregnancy was observed in 58 (36.02%) women as shown in Figure 3. When stratification of malaria was done on age groups, it was found that there was no significant difference between different age group, while, the stratification of malaria with respect to gestational age also showed no significant difference between different gestational ages, stratification of malaria with respect to parity, place of living and the severity of anemia is presented in Table 2.

Table 1: Distribution of pregnant women(n=161) according to effect modifier.

Effect modifier	Subdivision	No. of Patients	%age
Age (in years)	18-25	66	40.99
	26-35	95	59.01
	Total	161	100.0
Mean ± SD: 26.48 ± 4.36 years			
GA (weeks)	≤30	29	18.01
	>30	132	81.99
	Total	161	100.0
Mean ± SD: 32.70 ± 3.23 weeks			
Parity	≤3	61	37.89
	>3	100	62.11
	Total	161	100.0
Mean ± SD: 4.67 ± 1.43			

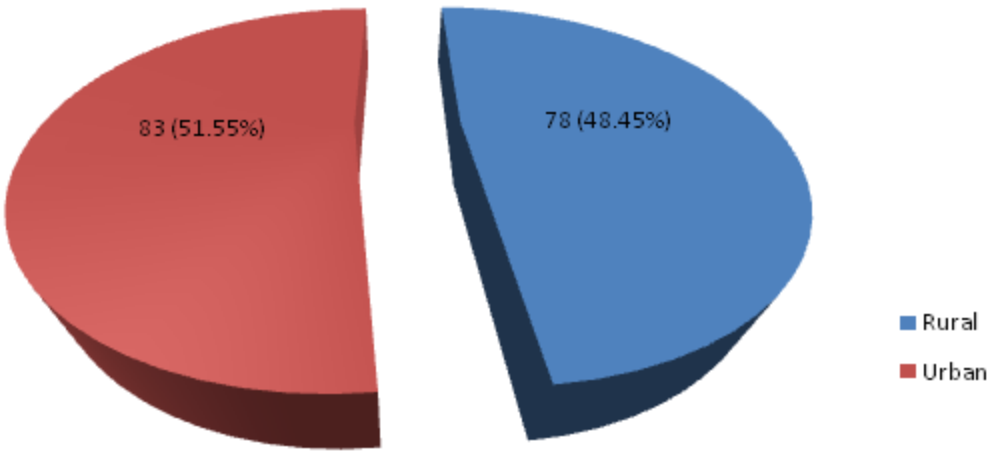

Figure 1: Distribution of patients according to the place of living (n=161), including rural and urban areas. The majority of the patients were from urban areas.

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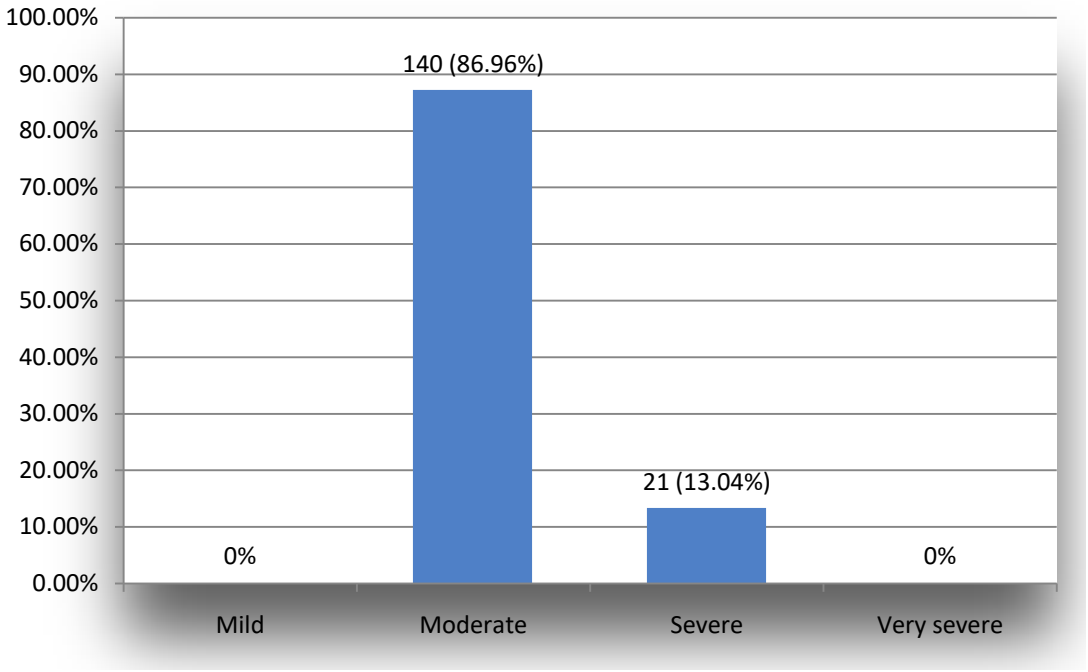

Figure 2: Distribution of patients according to the severity of anemia (n=161). The severity of anemia was categorized as mild, moderate, severe, and very severe. The majority of the cases were presenting a moderate form of anemia.

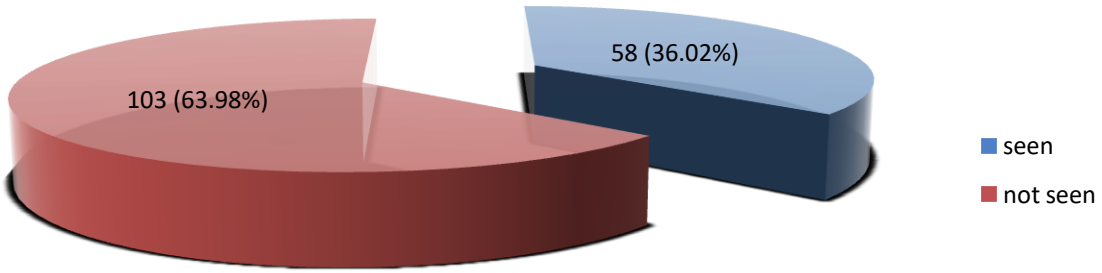

Figure 3: Frequency of malaria in patients presenting with anemia in pregnancy (n=161). In most cases, malaria was not diagnosed, still many cases were presenting malaria in addition to anemia in pregnancy.

Table 2: Stratification of malaria in pregnant women(n=161) with respect to effect modifiers.

Effect modifier	Subdivision	Malaria	p-value

Annals of R.S.C.B., ISSN:1583-6258, Vol. 26, Issue 1, 2022, Pages. 207 - 218
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		Observed	Not observed	
Age (years)	18-25	23	43	0.796
	26-35	35	60	
GA (weeks)	≤30	08	21	0.296
	>30	50	82	
Parity	≤3	17	44	0.092
	>3	41	59	
Place of living	Rural	31	47	0.341
	Urban	27	56	
Severity of anemia	Mild	00	00	-
	Moderate	51	89	
	Severe	07	14	
	Very severe	00	00	

Discussion

Malaria during pregnancy is the common complication of pregnancy[19, 20], characterized by hypoglycemia, spontaneous abortion, pulmonary edema, anemia andstillbirths[21]. Anemia in pregnancy is of great concern[22], particularly in developing countries where nutritional deficiency, worm infestation, and malaria are common[23]. Thus, accurate and early diagnosis of malarial illness is necessaryfor the effective management of the disease[24]. The current research wasaccompanied to evaluate the frequency of malaria in patients presenting with anemia in pregnancy.

The age range in the present study was from 18 to 35 years with a mean age of 26.48 ± 4.36 years,the majority of them were between 26 to 35 years of age. The frequency of malaria in patients presenting with anemia in pregnancy was observed in 58 (36.02%) women. According to a study in Ghana, pregnant girls with malarial infections were 3.5 times more probable to be anemic as compared to non-pregnant women[14]. According to a study in Burkino Faso, the occurrence of*Falciparum* asymptomatic infection among pregnant women was 30% and 61% of them were anemic[15]. Likewise, many western studies reveala positive association between anemia and malaria in pregnant women[16]. A review of studies showed the prevalence of malaria in pregnancy was 29.5% in East and South Africa while 36.1% in West of central Africa[21].

Malaria infection in pregnancy is connected with a broad range of clinical indicesthat range from acute asymptomatic to severe cases and death of both mothers and neonates[25-27]. In *P. vivax* infected pregnant patients, severe anemia has been reported.Moreover, *P. vivax*is associated withsevere malaria,moderate-to-severe anemia, and low birth weights

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in Latin America[28]. Inmany studies,Glover-Amengor et al[29] and Uddenfeldt et al[30] reported 35% and 41% in their study participants. Ofori et al[31] reported 18.8% malaria infection casesof pregnant women in his study, while, Tay et al[32] reported 12.6% total cases. The disparity in the occurrencemight be explained with aproclamation by Ofori et al[31]that there was a significantdifference in the frequency of malarial infection throughout the year. Morecasestypicallyarise after the rains thus the incidence might be affected at the time data was collected. Malaria might not be the only cause of anemia in pregnancy, as it may also be a result of other threateningconditionslikewisenutritional deficiency (folate and iron), placenta previa near the internalos of the cervical canal of the fetus, and worm infestation, especially in the developing nations. This form of anemia is probablycombinedwith malaria-induced anemia during pregnancy because in most cases,both malaria and iron deficiency causes anemia in pregnancy, which ultimatelyincreases the risk of premature delivery and adverse birth outcomes. A pregnant woman with sustained anemia further carries the risk of stillbirth,maternal death,fetal impairment, andlow birth weight[33].

Generally, the mother's immune system not only accepts the fetusbut also provides protection from infections, especially in malaria. In this way,T lymphocytesmaintain this fetal tolerance by migrating from the circulation towards the placenta and secreting immune-suppressive mediators like interleukin-10[34]. But in the case of some life-threatening infections like HIV, exposure to malarial antigens stimulates the innate immunity with impaired toll-like receptor-induced cytokines and dendritic cells which ultimately increases the susceptibility of neonatestowards other infections[35]. Other studies have reported a sudden decline in cell-mediated immune responses to malaria parasite antigens in pregnancy with anemia. It greatly depends on the living conditions, parity, patients' age, and dietary habits[36-42]. As, in the present study,the majority of the patients were belonged to urban areas and alreadypresented a moderate form of anemia.Even in some cases, malaria was not diagnosed, still,other cases were presenting malaria in addition to anemia in pregnancy. Overall, pregnant women already presenting with anemia urgently need special care and timely diagnosis and treatmentin case of some comorbidities like malarial infections to improve maternal and neonatal health.

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Conclusion and recommendation

It was concluded that thefrequency of malaria in patients presenting with anemia in pregnancy is quite higher than non-anemic pregnant women depending upon age group, parity, and, living standards. Pregnant women with older age, urbanized poor living conditions have a higher risk of developing malaria.So, we recommend theprevention, early diagnosis, and treatment of malaria in pregnancy with rational antimalarial drugs to progress maternal and fetal healthand to avoid morbidity and mortality due to malaria.

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