



Malarial Epidemiology among Patients in Al-Medina Al-Munawara, KSA

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Abstract: Worldwide, malaria is the most important disease caused by parasites and responsible for a yearly estimation of 225 million clinical cases. The risk of the disease covers almost half of the world's population and the annual death has been estimated as 800,000. Children under five years of age are mainly affected. Pregnant women and adults with immunosuppression become victims of cerebral manifestations or anaemia and frequently die. Almost 40% of the world's population is at risk to acquire the infection. Human malaria is caused by four *Plasmodium* species among which the most prevalent is *Plasmodium falciparum*. Because of the higher global prevalence, morbidity and mortality rate of *P. falciparum*, most research efforts on malaria pathogenesis have been focused on this species. Recent studies have reported the clinical outcomes that originate from regions where *P. falciparum* and *P. vivax* are equally prevalent. This in turn could make the clinical tools inappropriate for use in managing vivax mono infections. Thus, the present study was aimed to identify the epidemiology and clinical features of the malarial cases of the Referral laboratory, Al Madinah, Saudi Arabia. A retrospective case series study was conducted among the patients reported from January 2016 to December 2016 using a specially designed data collection form. Out of the 182 confirmed cases, 143 were non-saudi and 39 were Saudi cases. Most of the cases reported in the month of September due to seasonal change. Gender distribution showed a higher dominance of male patients compared to females. No cases were reported to be caused due to *P. malariae*. The predominant species was found to be *P. Vivax* (87%) while *P. falciparum* with only 13% incidence. Further investigations in large sample sizes are recommended to explore the other aspects in reducing the malaria burden.

Keywords: Malaria, *P. Falciparum*, *P. Vivax*, *P. Malariae*, Cerebral Manifestations, Vivax Mono Infection

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1. INTRODUCTION

Malaria is caused by protozoan parasites from genus *Plasmodium* is a serious and sometimes fatal disease. *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium ovale* and *Plasmodium vivax* are the four main different species of malarial parasites that cause infection in humans. The disease is transmitted by the female *anopheles* mosquitoes which carry these parasites while feeding human blood. Malaria has become a global health challenge and many countries consider it as a public health concern.¹ Worldwide, it is the most important parasitic disease with around 225 million clinical cases and the annual mortality has been estimated as 781,000 which confirms the severity.² The disease risk covers almost half of the world's population, mainly in children under five years of age with 800,000 annual deaths.³ Malarial endemic spreads over more than 100 countries of the world.⁴ Around 219 million malaria cases were reported worldwide in 2017, out of which the largest burden was laid upon the African countries with 200 million cases (92%), seconded by the countries of South-East Asia (5%) and lastly placed were the eastern Mediterranean countries (2%).⁵ Many travelers from the pre-Islamic era have mentioned the prevalence of malaria in the Arabian Peninsula.⁶ Arabian Gulf and its surrounding countries has a record of several infectious and contagious diseases like malaria.⁷ Out of the four *Plasmodium* species that are responsible for causing malaria in humans, the most prevalent is that of *Plasmodium falciparum*. This higher global prevalence of *P. falciparum* shows increased morbidity and mortality rates and thus, much focus has been laid on this species to study the pathogenesis of malaria.⁸ The early perception of *P. vivax* to be a non-fatal infection has changed gradually in current situation and it has been identified to cause severe malarial infection. Estimates show that 25-40% of the cases reported are due to this highly prevalent species.⁹ *P. vivax* was falsely believed to cause a benign disease. But, however recent evidences prove the increased prevalence of *P. vivax* cases with severe and complicated side effects including severe anaemia.¹⁰ The species distribution of malaria cases shows that *P. vivax* causes around 74% of infections, 25% by *P. falciparum* and < 0.01% by *Plasmodium malariae*. The overall estimated mortality caused by malarial infections of all species is less than 0.1%.¹¹ Pregnant women and children below five years of age are the most susceptible populations for this severe and complicated disease, specifically in malaria-endemic regions. There is a progressive reduction of the frequency and severity of the disease in older children and adults who suffer malaria infections repeatedly. All groups of people in the low endemicity areas or who live in areas of seasonal exposure get affected by this infection as they do not develop proper immunity.¹² Pregnant women are more susceptible to the disease which affects both the mother, the foetus, and subsequently the newborn. A wide range of factors are responsible for the clinical manifestations of malaria like the factors related to the parasite, parasite-host interactions, host factors and other socio-economic conditions. Immunity is one among the host factors which are studied in-depth and includes the production of pro and anti-inflammatory cytokines, genetic traits, α or β -thalassemia, Fy phenotype, sickle cell traits and age related factors. Endemicity, species, multiplication rates of parasites, drug resistance and antigenic polymorphism are the factors

related to parasites and exhibit great relevance for the development of anaemia. The clinical outcomes and recent reports on the predictors from regions where *P. falciparum* and *P. vivax* are equally prevalent, could convert the clinical tools inappropriate to be used in managing mono infections of the *P. vivax*.¹³ Thus, the present study was planned to identify the severity of the different species and to estimate the associated risk factors in malarial cases. The study also highlights the demographic, clinical and hematological features of the disease that helps in providing suitable recommendations to the concerned.

2. MATERIALS & METHODS

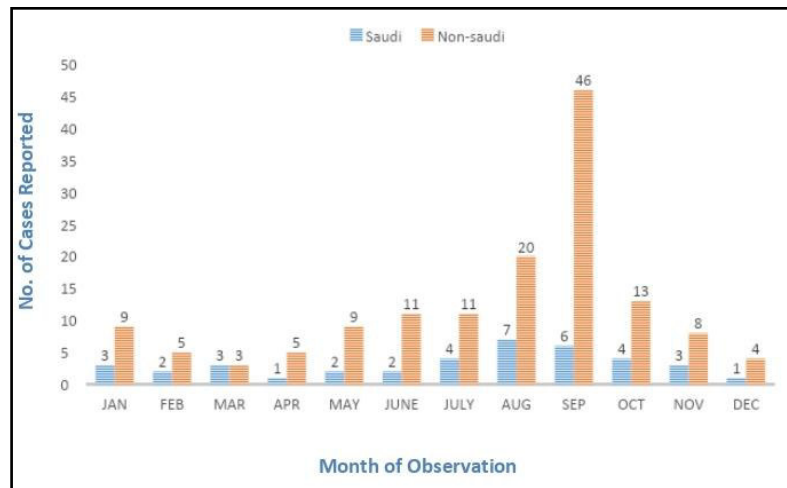
A retrospective clinical case series study was conducted among 182 patients reported to the Malaria centre – Referral laboratory, Madinah, KSA from January 2016 to December 2016. The study protocol was performed according to the Helsinki declaration and institutional ethics committee approval was obtained from the College of Medicine, University of Hail, Saudi Arabia. (reference no. 10/Apr/015). The study population included patients who reported ill with fever, headache, vomiting and other clinical signs. The study included patients of age 20–60 years, both genders with a positive result for malaria parasite on hematological examination and who accepted the informed written permission. Patients who reported a negative result in the blood test were excluded from the study.

2.1 Hematology Test

The patients suspected for malaria infection were subjected to hematological investigations. A drop of blood well formed at the tip of the finger was squeezed in a microscopic slide to form a smear of around 1cm² and subjected to microbiological analysis. The blood spread into the slide as a thick film was allowed to dry in the air. The air dried slide was dipped into field's stain A for 3mins, washed with water, then dipped in field's stain B for 3mins and again washed with water. Finally, the well stained slide was allowed to stand vertically and air dried. The dry slide was subjected to microscopic examination at the edges as well as the centre of the film. The center of the film may be thick or cracked while the edges show a better film. The malarial parasites appear with a deep red chromatin and a pale blue cytoplasm in a well stained film. A thick film at the center may show white blood cells and platelets along with the malarial pigmentation. The nuclei of the leukocytes would be stained in purple colour with pale blue cytoplasm. Lysis of red blood cells with stroma at the background alone remains, which is not the case with the occasional red cell. Schizonts and gametocytes if present may also be identified by thorough examination of the slide at least for 10mins for approximately 200 oil immersion fields.¹⁴

3. RESULTS

Totally, 182 patients who showed positive results for malarial infection were subjected for the analysis. The nationality of the patients was identified, which showed that a higher number of cases were of non-saudi origin (143) when compared to the Saudi patients (39) as indicated in figure -I.



In figure-1, the x-axis represents the incidence in the specific months and the y-axis shows the number of cases reported. It could also be identified that except in the month of March, the non-saudi cases were higher than the Saudi cases.

Fig 1: Nationality based distribution of cases

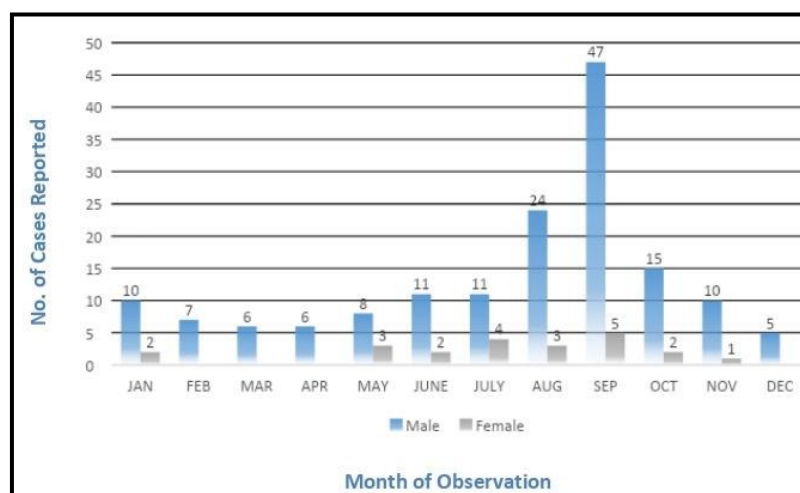


Fig 2: Distribution of cases based on gender

Figure-2 shows the number of male and female cases reported in the entire duration of the study. As it is indicated, there is a male predominance in the occurrence of the infection. In contrast to that, no female cases were

recorded in the months of February, March, April and December. Totally, 160 male and 22 female cases were registered showing the dominance in men.

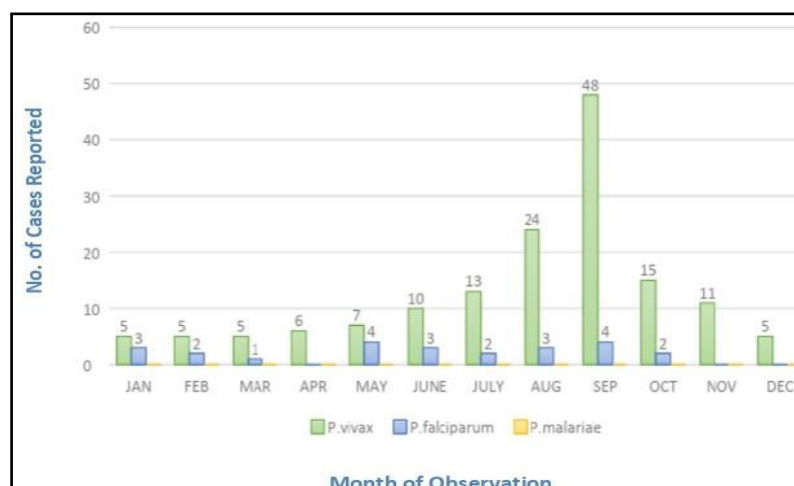


Fig 3: Case distribution based on causative species

The hematological reports showed 158 samples with *P.Vivax* and 24 with *P.Falciparum* while none of the samples seemed to possess *P.Malariae* as shown in figure-3. *P.Vivax* was

identified to be highly prevalent (87%) among the study population and *P. falciparum* showed only 13%.

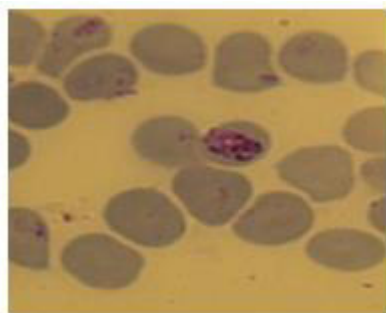


Fig 4: Microscopical observation of developmental stage of *P.vivax*

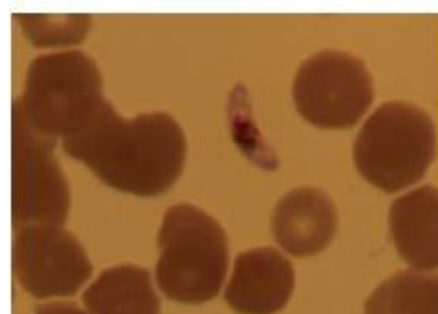
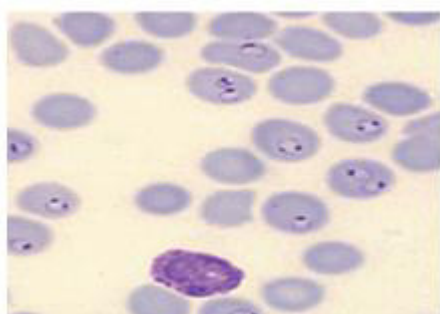


Fig 5: Microscopical observation of developmental stage of *P. falciparum*

The microscopical observations of the blood samples of the patients are shown in figure-4 & 5. Both the figures show the developmental stages of the different species in the blood. The deep red stain indicates the chromatin with the exterior

being the cytoplasm stained in blue colour. The slides also show the presence of leukocytes and platelets when examined for at least 10mins in 200 oil immersion fields.

Table I Month wise positive malaria cases reported			
Month	Male	Female	Total
Jan	10	2	12
Feb	7	0	7
Mar	6	0	5
Apr	6	0	5
May	8	3	11
June	11	2	13
July	11	4	15
Aug	24	3	27
Sep	47	5	52
Oct	15	2	17
Nov	10	1	11
Dec	5	0	5
Total	160	22	182

The cases were at higher rates in the month of September which may be attributed to seasonal changes. 47 male cases and 5 females (52 cases out of 182) were confirmed with the infection during this month. This data shows that more cases were seen in September when compared to the other months as mentioned in table-I.

4. DISCUSSION

In the tropical and subtropical countries, malaria is the most widespread infectious disease that is caused by the *Plasmodium* spp since ancient days. The female *Anopheles*

mosquito bites are the main mode of transmission and other routes include the trans placental route, infected blood transfusion and the needle stick injuries.¹⁵ More than one million patients die due to the disease every year. The study was aimed to assess the demography, clinical and hematological features of the cases reported to the Malaria centre – referral laboratory in Al-Mdinah, Saudi Arabia during the period between January 2016 and December 2016. The results of our study indicated that the male cases were dominant over the female cases which was in contrary to the previous reports showing that the infection mostly affects children and women.¹⁶ Our study results may be attributed

to the fact that male patients having more exposure than the females and also, the traditional dress code may be a protection for the females. Although, the genetic factors may also cannot be ruled out. Malaria affects the entire blood components and it has been proved to be transmitted hematologically.¹⁷ Present study reports show hematological features in concurrence to previous studies. Most of the patients reported clinical bleed in the form of epistaxis and GI bleed. The lytic effect seen in the hematological reports may be due to the immunological reactions, sequestration and oxidative stress as reported in the previous studies.¹⁸ *P.vivax* has been reported to be the cause for increased number of severe cases when compared to all the other species.¹⁹ Around 50% of cases reported in the south east asia are found to be due to *vivax* as per the 2010 WHO reports.²⁰ This is in line with the results of our study showing that the cases of *p.vivax* is high when compared to the other species. 87% of the infection was due to *p.vivax* which matches with the previous reports of Nabil et.al 2016.²¹ Most of the cases reported positive were due to *P.Vivax* as reported by the studies conducted earlier.^{22,23,24} Neurological involvement in *P.falciparum* is frequent and almost all the cases who survive cerebral malaria, promote neurological sequelae.²⁵ Our reports are in contrary to previous study results showing highest infection caused by *P. falciparum*.^{26,27,28} The infection appears to be predominant among non-saudi patients (143 cases) than among the Saudi patients (39 cases). This may be either due to their residence in endemic areas or travel through such areas. Our result is supported by the other studies showing 93% of the cases reporting a history of travel to the south western part of KSA.¹⁸ The low rainfall and the effective control protocol practiced between 2000 and 2014 have brought a significant reduction in the number of cases that are acquired locally.²⁹ Our study shows that most of the cases were identified in the month of September which is in line with the earlier studies conducted in Jazan, stating that even though the cases were reported throughout the year, an increased number of cases were identified in the peak periods like February-March and September-October. These findings suggest that the higher level of transmission might be either due to the increase in travel during these periods or the rainfall.³⁰ The determination of the pattern of transmission is highly dependent upon the climatic conditions and its impact on human-vector activities.³¹ Seasonal changes like rainfall have a greater effect in the transmission of the disease. In Saudi

Arabia, the period between October to April seems to have rainfall which provides a comfortable environment for the growth of anopheles mosquitoes. This helps in rapid transmission of the infection while the low rainfall period between may and july shows a lesser transmission. Studies conducted in Makkah and Madinah have reported a significant increase in the malaria cases during the period of August to October. This may be attributed to the visit of the pilgrims to these places during this period.³² The increase in the number of cases may also be correlated to the visit of the laborers from the malaria – endemic regions who come to Saudi for their work.^{33,34} The study reports suggest a number of factors that are responsible for the transmission of the disease thus, suggesting proper diagnosis and assessment.

5. CONCLUSION

Early and prompt diagnosis is the important measures to be followed for effective management, treatment and control of malaria in low transmission settings. Currently available diagnostic tools must be well utilized to face the challenges that are crucial in the elimination of malaria in Saudi Arabia. However, our knowledge of the hematological profile of malaria endemic population of Al-Madinah, Saudi Arabia and its relation to promising biochemical diagnostic potential and monitoring in malarial patients are limited. Thus, we investigated the hematological alterations in the persons infected with *P. falciparum* and *P. vivax* and compared with healthy subjects from Al-Madinah, Saudi Arabia community. This study will provide a credential sign in understanding malaria pathogenesis and diagnosis.

6. AUTHOR CONTRIBUTION STATEMENT

Shady alhussayni and Sami Alharbi conceived of the presented idea. Shady alhussayni performed the computations. Sami Alharbi and Omar Amer collected the data and verified the analytical methods. Omar Amer supervised the findings of this work. All authors discussed the results and contributed to the final manuscript.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

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