DOI: 10.7860/JCDR/2017/30472.10835

Original Article

Obstetrics and Gynaecology Section

Influence of Malaria Parasitemia of Plasmodium Falciparum on the Prevalence and Severity of Premenstrual Syndrome

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ABSTRACT

Introduction: It remains unknown whether Malaria Parasitemia (MP) of *Plasmodium falciparum* might influence symptoms in Premenstrual Syndrome (PMS). Symptoms of PMS might be not only hormonal but also haematologically related. However, the link of *Plasmodium falciparum* infection and clinical manifestations of PMS has not been previously investigated.

Aim: To determine the association of MP of *Plasmodium falciparum* and Packed Cell Volume parameters (PCV) with clinical characteristics of PMS.

Materials and Methods: A cross-sectional study was carried out in 2014 among undergraduate students in the University. The study participants completed a two-part questionnaire assessing premenstrual dysphoric disorder and PMS symptoms using the Diagnostic and Statistical Manual of Mental Disorder-IV (DSM-IV) based diagnostic criteria. Peripheral blood sample for MP and PCV estimation were also collected at enrollment. Statistical analysis was performed with SPSS version 20.0 (IBM, Armonk, NY, USA). Categorical variables were summarized by absolute frequencies, percentages, and chi-square tests and continuous variables by means and standard deviation. Values were deemed statistically significant at $p<0.05$.

Results: A total of 150 randomly selected participants aged 16–30 years were enrolled. Of the 150 students, 105 (70.0%) regularly experienced symptoms suggestive of PMS. The commonest symptoms were lower abdominal pain (80.0%), joint and muscle pain (72.0%) and pimples/puffy face (65.3%) while the least frequent symptoms were cramps (33.3%) and vaginal discharge (30.0%). Thirty one (20.7%) out of 150 participants were positive for MP and 6 (4.0%) participants had low PCV (<0.33) and all of which tested positive to MP. Compared with PMS negative, the mean PCV in PMS positive participants was statistically lower (0.30±0.033 vs 0.36±0.038, $p=0.007$).

Conclusion: This is the first study to reveal a potential association of MP and PCV with clinical manifestations of PMS. PMS is a prevalent, yet undertreated, disorder among the participants with malaria parasite infestation worsening the condition leading to low PCV values, which adversely affect their quality of life and academic performance of the participants. The findings warrant further research.

Keywords: Association, Diagnostic criteria, Haematological parameter, Symptoms

INTRODUCTION

Premenstrual Syndrome (PMS) encompasses an array of emotional, physical or interactive symptoms which are often encountered by some women at the premenopausal period occurring in the secretory stage of the menstrual cycle [1,2]. The most frequent indicators include nervousness, touchiness, unhappiness, temperament, insomnia, lethargy, decreased or increased libido, pain in the breast, increased weight, headaches, increased or decreased appetite, generalized body pains and body swelling [1,2]. According to Diagnostic and Statistical Manual of Mental Disorders (DSM), Premenstrual Dysphoric Disorder (PMDD), which is a major form of PMS, occurs when an individual woman is affected by more than four distinct premenstrual symptoms which are psychological in nature [3].

The exact prevalence of PMS is not known except that it differs due to methodological tool employed in identifying and categorizing cases. In the reproductive-aged period, the frequency of PMS in women has been reported to vary from 50% to 90%. However, the frequency of severe form of PMS or the form that impede the normal day-to-day events is lower and varies from 10% to 30% [4,5].

Although the number of women whose age fall within the reproductive age bracket is soaring, malaria remains an important public health issue in Nigeria especially because malaria is endemic in Nigeria [6]. A number of general symptoms of malaria parasitemia have been described including headache, chills, myalgias, nausea, and vomiting, cough, generalized body pain and weakness of muscles, fatigue, difficulty concentrating, and confusion [7]. In cases of *Plasmodium falciparum* infection, when the diagnosis of malaria is delayed or missed, it may lead to serious consequences. For example, severe anemia or cerebral malaria could ensue and this could mimic PMS or its severe form known as PMDD [4]. Clinical manifestations of PMS include fatigue, impaired concentration, confusion, headache, and depression [1,2,4]. These clinical features are also observed in malaria.

It is possible that infection with *Plasmodium falciparum* might cause or influence some symptoms in women during the premenstrual period. Anecdotal report has revealed that severe form of *Plasmodium falciparum* infestation was associated with overwhelmed control of feelings in women suffering from PMDD (personal communication). However, it is unknown whether *Plasmodium falciparum* infection might influence symptoms in PMS. Symptoms of PMS might be not only hormonal but also haematological related. Since the link of *Plasmodium falciparum* infection and clinical manifestations of PMS has not been previously investigated, we undertook this study to determine the association of *Plasmodium falciparum* infection with clinical characteristics of PMS in women in the south east Nigeria.

The aim of this study was to describe the association of MP and PCV with the prevalence and severity of PMS in undergraduate female students in south-east Nigeria, an area with intense malaria transmission and documented high prevalence of anemia. In addition, we determined which risk factors of *Plasmodium falciparum* parasitemia were associated with anemia in this adolescent population.

MATERIALS AND METHODS

The present analysis was based on data gathered from female students of the University via questionnaires as part of the cross-sectional study carried out between February 1, 2014, and June 30, 2014. The study received ethical approval from the University Teaching Hospital, Ethics Review Board and ethics committee of Environmental Health Science under the Faculty of the Health Science and Technology of the University.

The eligibility criteria included female undergraduate student aged between 16 and 30 years and being able to provide informed consent. Participants who were currently known to have psychological or medical ailments, current intake of hormonal medications, or history of irregular menstruation were excluded from the study. The sample size was calculated using a study conducted by Antai among university students [8]. The prevalence of PMS in students aged 16-31 years was 85.5%, taking 0.05 margin of error, 95% CI. For the total population of less than 10, 000 and 10% attrition, it was adjusted and the final sample size was 150 [8].

Interviewer-based questionnaires were administered by trained research assistants at the campus premises by simple random techniques or at an alternative confidential location of the choosing participants. The questionnaire was validated by experts (content and face validity values were not reported) and consisted of two sections. The first part included socio-demographic questions as age, marital status, and residency condition. The second part included 11 self-reported symptoms assessing frequency and severity of PMS based on Diagnostic and Statistical Manual of Mental Disorder-IV (DSM-IV) which recognizes PMDD and highlights on disorders of mood [4,9-11]. The criteria-based diagnosis included the presence of at least 5 symptoms out of 11 symptoms of PMS and at least one of these symptoms should have been from the first symptoms (core symptoms). The symptoms should be present a week before menses and remit a few days after the onset of menses. These 11 symptoms include change of mood (feeling sad or crying all of a sudden), change in appetite (overeating or having little appetite), stress and anxiety, feeling of immersion or being out of control, untiring anger or personal clashes, tiredness and weariness, depressed mood, reduced interest in social relationships and work, difficulty in sleeping (oversleeping or sleeplessness), physical symptoms (back pain, nausea, abdominal bloating, abdominal pain, weight gain, chest pain, joint or muscle pain, acne, chest pain and chest sensitivity, headache) and lack of concentration [9-11]. Each symptom had a scale from 1-6, where 1= not at all, 2=minimal, 3= mild, 4= moderate, 5= severe, 6= extreme. The participants were also asked to identify symptoms they had experienced during two weeks preceding their menstruation (3 days, 4-6 days, or 7-14 days before menstruation) in the past three months [12]. The participants were required to complete the questionnaire in the two consecutive menstrual cycles. The highest score of each symptom was recorded, and the total score of PMS was calculated as the sum of the symptom's score divided by the number of symptoms. This score was finally converted to percentage and a score between 0 to less than 33% represented mild form of PMS, 33-66% was moderate form and more than 66% was defined to be a severe form of PMS [13,14].

After enrollment, participants were screened for MP and PCV by an experienced senior laboratory scientist. One blood specimens was independently collected by taking blood sample for running the test for the *Plasmodium falciparum* infection and PCV. Malaria parasite was determined by a method described by Moody in 2002 [15]. Heparinized micro-haematocrit tube was used for packed cell Volume determination.

Statistical analysis was performed with SPSS version 20.0 (IBM, Armonk, NY, USA). Categorical variables were summarized by absolute frequencies, percentages, and chi-square tests, and continuous variables by means and standard deviation. Values were deemed statistically significant at $p<0.05$.

RESULTS

A total of 150 undergraduate female students aged 16–30 years were enrolled following selection by simple randomization by alternation. Of the 150 students, 105 (70.0%) regularly experienced symptoms suggestive of PMS. The commonest symptoms were lower abdominal pain (80.0%), pimples/puffy face (65.3%), tender/painfully engorged breast (56.7%) and joint and muscle pain (72.0%). The least frequent symptoms were diarrhea (42.0%), constipation (38.7%), cramps (33.3%) and vaginal discharge (30.0%). The two symptoms that were in equilibrium were vomiting (51.3%) and confusion (50.0%). The result shows that 31(20.7%) out of 150 female student involve in the study were positive for malaria parasite in their blood and student of age 20-24 have high infection prevalence and level.

[Table/Fig-1] shows the prevalence of PMS among participants. [Table/Fig-2] shows the prevalence of malaria parasite infection (*Plasmodium falciparum*) while [Table/Fig-3] shows the comparison of PCV between premenstrual malaria positive student and premenstrual malaria negative student in Nnamdi Azikiwe University, Nnewi Campus. [Table/Fig-4] shows the mean±sd of Comparative Haematocrit of negative and positive students with malaria parasite.

	'NO' As Answer		'YES' As Answer	
	Frequency	Percentage	Frequency	Percentage
Abdominal Discomfort	30	20.0	120	80.0
Pimples	52	34.7	98	65.3
Tender Nipple	65	43.3	85	56.7
Fatigue	69	46.0	81	54.0
Diarrhea	87	58.0	63	42.0
Vomiting	73	48.7	77	51.3
Fever	54	36	96	64.0
Cramps	100	66.7	50	33.3
Confusion	75	50	75	50.0
Joint Pain	42	28	108	72.0
Constipation	92	61.3	58	38.7

[Table/Fig-1]: Prevalence of premenstrual syndrome among female students interviewed.

Age (years)	Frequency	Negative	Positive	Prevalence
(15-19)	56(37.3%)	44(29.3%)	10(6.7%)	10
(20-24)	87(58%)	70(46.7%)	20(13.3%)	20
(25-30)	7(4.7%)	5(3.3%)	1(0.67%)	1
Total	150 (100%)	119(79.3%)	31(20.7%)	31

[Table/Fig-2]: Prevalence of malaria parasite infection (*Plasmodium falciparum*) according to age of the participants.
Malaria Parasite Infection

PMS Malaria	Number	Mean±SD	T-Value	p-Value
PMS Malaria Positive	20	0.30±0.033	-2.737	0.007
PMS Malaria Negative	85	0.36±0.038		

[Table/Fig-3]: The comparison of PCV (mean±sd) between premenstrual malaria positive student and premenstrual malaria negative student interviewed.

Parameter	Groups	N	Mean±SD	T-Value	p-Value
PCV	Malaria Negative	119	0.37±0.030	4.89	<0.001
	Malaria Positive	31	0.34±0.036		

[Table/Fig-4]: The mean±sd of Comparative Haematocrit of negative and positive students with malaria parasite.

DISCUSSION

The present result shows that 31 (20.7%) of the participants involved in the study were positive for MP and 20 (13.3%) of the participants also experienced PMS and student of age 20 to 24 years have the highest infection prevalence and level. Up to 10.7% of the

participants agreed that there is worsening of the usual symptoms of PMS following MP. Up to 4.0% of the participants had low PCV and all of which tested positive of malaria parasitemia. Compared with PMS negative, the mean PCV in participants with PMS positive was statistically lower (0.30±0.033 vs 0.36±0.038, p=0.007). We found that women seropositive for *P. falciparum* had a similar mean number of signs or symptoms of PMS than seronegative women. Although, the results suggest that infection with *P. falciparum* does not influence on the number of clinical manifestations of PMS in general, however, results suggest that *P. falciparum* infection may influence qualitatively on clinical manifestations of PMS.

PMS has a variety of symptoms and signs also observed in toxoplasmosis [5]. Therefore, our hypothesis is that *P. falciparum* infections have strong influence on clinical manifestations of PMS. To the best of our knowledge, the possible association between *P. falciparum* infection and symptoms and signs of PMS has not been assessed yet [5].

This study shows that PMS is not uncommon among undergraduates in Nigerian Universities. Thus 70% of the subjects reported experiencing symptoms of PMS with varying degrees of intensity. Subjects in this study were aged between 15-30 years. Previous studies have shown that PMS symptoms may occur at any age, but onset usually begins in the early 20's [16-18]. This finding places our subjects in the high frequency group. The result is consistent with results of similar studies by Raval et al., which reported that 30-90% of menstruating women experience varying degrees of premenstrual symptoms [19]. Similar results have been reported elsewhere [20,21]. However, the present findings were general population based report, and the younger the woman the higher the severity of PMS symptoms. In a previous study by Cleckner-Smith et al., PMS was revealed to be more and more prevalent (70%) in a sample of adolescents between the age of 15 and 20 years [22].

In this study, 11 symptoms were recorded, ranging from lower abdominal pain which was most common to joint/muscle pain, increased-pimples/puffy face, tenderness/painful breasts/nipple, feverish condition, fatigue, diarrhea, constipation, and body cramps in descending order of magnitude. However, vomiting and confusion are two symptoms which were found to be in equilibrium. Similarly, a study by Antai et al., carried out on 200 Nigerian undergraduate students indicated that the prevalence of PMS in students aged 16-31 was 85.5% and the most common symptoms were muscle pain, acne, chest pain, puffy face, depression and distress [8]. Our findings are also in tandem with another study by Al-Batanony and AL-Nohair, where somatic symptoms like abdominal pain, tiredness, acne, muscle pain, abdominal bloating, headache, diarrhea, constipation, weight gain and emotional symptoms like mood changes, anger, depression, distress, and sensitivity predominated [14]. In terms of behavioural changes, change in appetite, poor concentration, and sleep disorders were also reported, akin to our findings.

Although more than 100 symptoms of PMS have been described in published literature [23], the present result shows that 20.7% of the participants involved in the study were positive for MP and student of age 20-24 have high infection prevalence and level. Up to 13.3% (20 out of 31) of the participants tested positive for malaria and 13% of the total population sampled also experienced PMS. Up to 10.7% (16 out of 20) of the study population agreed that there is worsening of the usual symptoms they usually have but no new symptom was noticed. Although changes in blood cell parameters are already a well-known feature of malarial infections, infected individuals have low PCV than non-infected individuals and this agrees with previous studies by Francis et al., Kotepui et al., and M et al., who reported that anemia is the commonest complication of malaria [24-26].

Up to 4% of the participants have low PCV and all of them also tested positive for malaria parasite in their blood. Out of the 6 students, 2 female students experience PMS and 4 female students do not experience PMS. From this findings, it could also be ascertained that PCV has no direct relationship with PMS as only 2 female students (1.3% of the population sampled) has low PCV co-existing with PMS.

Up to 30% of the total participants agreed that PMS affect their studies and attendance in class with most being absent from class at various time during the PMS period, associated with moderate to severe symptoms adversely affects students' academic performance especially when it coincides with examination period. It is an accepted fact that menstruation is a normal physiological impact in each girl life. Adolescent and younger age period of the girl is crucial phase [21]. In our culture it is believed that girls should not express their feeling toward sexual aspects. PMS is the primary reason by women to miss work, school or college. Sometimes their symptoms are so severe that they need medical care [23].

As far as we know, no previous study has emphasized on the relationship between MP and PMS, and this has become the strength of this study. Therefore, although the findings of studies in various countries are in tandem with ours, there is still debate whether the most significant changes relate to psychological changes or somatic ones.

LIMITATION

The main limitation of this study relates to the completeness of recording of PMS diagnoses and small size of the women studied. Some patients may have MP and yet may still not have symptoms. As a result, the rates of differences between the prevalence and various symptoms and signs of PMS among studies could be due to cultural differences, assessment tools, reported symptoms/or elicited signs, study type, the population selection procedures and/or that may be possible that the women interviewed may not be honest at explanation of their problems.

CONCLUSION

PMS is a prevalent, yet undertreated, disorder among female students in Nigeria Universities with malaria parasite infection worsening the condition leading to low PCV levels in these students, which adversely affected their quality of life and academic performance of these students. This finding suggested that health and educational authorities need to recognize the problem and provide appropriate, tangible and emotional support as well as giving more attention to psychological methods as counseling or cognitive behavioural therapy for female students with premenstrual disorders (especially for those with PMS and malaria). The present study for the first time points towards an association of *Plasmodium falciparum* infestation with clinical manifestations of PMS, i.e., physical symptoms. Results warrant further research and this justifies the need to support operational research that will lead to the improvement of malaria control.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **May 28, 2017**
Date of Peer Review: **Jul 21, 2017**
Date of Acceptance: **Sep 07, 2017**
Date of Publishing: **Nov 01, 2017**