Assessment Of The Relationship Between Malaria and Musculoskeletal Pain: A Cross-Sectional Study In Owerri, Imo State.

Comment [CdM1]: could be replaced by muscle pain, since the musculature associated with the skeleton is skeletal striated

ABSTRACT

Malaria presenting with musculoskeletal pain has been a public health concern. This study was carried out to assess the relationship between malaria and musculoskeletal pain (MSP) on patients attending a private hospital in Owerri, Imo State between January and October 2017. The medical history and malaria parasitemia of 235 participants within 10years and above were assessed using standard procedures. The data generated were analysed with descriptive chi-square statistics. Results revealed malaria prevalence and musculoskeletal pain prevalence of 62.55% and 63.83% respectively. Of the 235 participants, 97(41.26%) had malaria with musculoskeletal pain representing 64.67% of 150 patients with musculoskeletal pain; while 11(7.33%) had malaria and musculoskeletal pain with co-existing diseases. There was a positive relationship between malaria and musculoskeletal pain ($R=0.6599$ and $p<0.05$). The three most frequently reported sites of malaria-associated musculoskeletal pain were lower back (37.11%), knee (26.80%) and shoulder (21.65%). Females had a significantly higher malaria prevalence of 72.72% than males (51.75%) ($p<0.05$). Likewise, there was a significant sex-related prevalence of malaria with MSP with females (73.17%) recording higher infection than males (54.41%) ($p>0.05$). Age-related prevalence of malaria was significant with a frequency rate exceeding 50% except for the age group 40-49 years with a prevalence of 45.61%. Age was not significantly associated with malaria-associated MSP ($P>0.05$) with a range of 50.00% in 20-29 years to 72.73% on ≥60 years respondents. The relationship between MSP and malaria portrays a possible incorporation of MSP in the algorithm currently used in the diagnosis of malaria infection.

Keywords: Malaria, Musculoskeletal pain, Relationship, clinical algorithm.

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INTRODUCTION

Malaria has threatened human life for thousands of years and persists in many parts of the world despite intensive efforts over the last century to understand and control the disease. Malaria is an acute febrile illness caused by *Plasmodium* parasites that are transmitted to people through the bites of infected female Anopheline mosquitoes. The disease is a huge source of concern around the world, not only because it kills millions of people each year, but also because of the enormous economic cost it incurs (Acemoglu and Johnson, 2007). According to the World Health Organization, malaria affects approximately 500 million people each year in a variety of nations, killing over 400,000 people (WHO, 2016). Malaria commonly expresses itself as intermittent fevers with spells of exhaustion in between, although the patient looks to be in fair health overall. Symptoms associated with febrile paroxysms include high fever, rigours, sweats, and headache, as well as myalgia, back pain, abdominal pain,

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nausea, vomiting, diarrhoea, pallor, and jaundice (Krause, 2007). However, approximately 50-70 per cent of cases have a classical appearance, with the rest having atypical manifestations (Shital et al., 2018). Due to the development of immunity, rising resistance to antimalarial medications, and the indiscriminate use of antimalarial treatments in endemic areas, malaria might present with atypical symptoms (Singh *et al*.,1994). Atypical musculoskeletal manifestations reported with malaria include rhabdomyolysis, myositis, and periodic paralysis (Mishra *et al*.,2010, Shital *et al*., 2018).

The majority of malaria research, on the other hand, concentrates on the disease's mosquito-borne parasite, ignoring the disease's effects on skeletal muscles and the heart. Malaria disease affects skeletal muscles and the heart at moderate to high levels, and even people with mild cases of malaria complained of muscle pain and exhaustion (Brotto *et al*., 2005). In reality, many of the above-mentioned malaria symptoms can be ascribed to musculoskeletal system dysfunction.

The impact of musculoskeletal pain on the individual and society and its relationship to malaria was the motivation for pursuing this study. Studies on malaria in Nigeria have been centred on prevalence with considerable attention on fever as a symptom. There are no records in the literature available to the researcher on the prevalence and pattern of malaria-associated musculoskeletal pain.
Accurate malaria diagnosis remains a cornerstone of global control efforts. However, several authors have noted that malaria misdiagnosis in endemic areas is common, resulting in harm to vulnerable populations[5]. It is estimated that practical and accurate diagnostic tests for malaria diagnosis have the potential to avert 400 million unnecessary treatments and save 100,000 lives annually[6].

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The World Health Organization recommended in 2010, that all suspected malaria patients be tested for the disease before being treated. In rural Africa, light microscopy is relatively uncommon. The majority of persons were given antimalarial medications on the assumption that they had malaria. The Integrated Management of Childhood Illnesses (IMCI) recommendations, which are being followed, aim to ensure that children under the age of five receive appropriate treatment for both general and malaria-specific morbidity and death. Various clinical algorithms have been used in a number of studies across Africa to improve the specificity of malaria case diagnosis. Few research, however, have looked into the effect of algorithms in improving clinical malaria diagnosis in older children and adults in malaria-endemic areas of Africa. Incorporating an additional common symptom in the algorithms currently in use could fill the gap and offer better symptom-based diagnosis of malaria in resource deprived and high endemic communities in Nigeria.

METHODOLOGY

Study Area

This study was conducted from January-August 2019 in a Private Hospital in Amakohia, Owerri, Imo State. Amakohia is a town in Owerri North Local Government Area in Owerri Senatorial Zone of Imo State. Owerri, the capital city of Imo state is one of the three zones in the state. It is located on latitude 5.485°N and longitude 7.035°E, South Eastern Nigeria (NPC,2006). It is bordered by the Otamiri River

to the east and the Nworie River to the south (NPC, 2006). It has an estimated population of about 401,873 (NPC, 2006).

The study was selected based on convenience and on the level of health care, the hospital provides within the state, the eastern heartland of Nigeria. It is a 20-bed capacity private hospital with wards and departments providing 24 hours emergency, surgical, medical and maternal/child health services.

Study Sample Size/ Population

The population of this cross-sectional survey research comprised males and females, aged 10 years and above, attending a private hospital in Owerri, Imo state. The proportion of individuals within this age group attending the health facility within the 8 month study period was estimated to be 82% (0.82) of the total attendance. Therefore, the sample size formula for qualitative cross-sectional surveys used by Igwesi-Chidobe (2012) was adopted:

$$n = z^2pq/d^2$$

where: n = the desired sample size

z = the standard normal deviate, set at 1.96 corresponding to 95% confidence level

p = the proportion of persons 10 years and above attending the health facility for medical services within study period q = 1.0 - p

d =precision/ absolute error tolerated, set at 0.05

$$n = \frac{1.96^2 \times 0.82\ (1-0.82)}{0.05^2} = 226 \text{ participants.}$$

Consequently, a total of 235 participants made up of 114 males and 121 females were then drawn from day-to-day clinical care of patients (direct observation/consultation-oriented).

Ethical Clearance

Ethical approval for this study was obtained from the Research and Ethics Committee of the Department of Animal and Environmental Biology, Imo state University, Owerri. The consent of the hospital authorities in the study area was also obtained following a detailed explanation of the study objectives to enhance participation. A full verbal explanation of the study was given to selected individuals and verbal informed consent was obtained before inclusion as participants. Participants were given the right to refuse to take part in the study as well as to withdraw at any time during the interview/consultation. Privacy and confidentiality were maintained throughout the study.

Data Collection

Data was collected with the help of assistants comprising doctors and laboratory scientists. Data was collected via detailed history taking, accompanied by laboratory evaluation for malaria. For malaria testing, capillary blood samples were collected from finger-pricked blood. using Rapid Diagnostic Test kit (ICT COMBO, Core Diagnostic, U.K) for detection of *Plasmodium falciparum* and pan malaria antigen Pf/Pan for non-*falciparum* species. In the end, the data obtained was analysed and reported.

Statistical Analysis

Data obtained from the empirical study were analysed and interpreted using descriptive statistics. The Chi-Square test was used to test the association between variables. Five (5%) level of probability was considered significant ($p < 0.05$). The Statistical Package for Social Sciences (SPSS) Version 20.0 was used in statistical analyses of part of the data obtained from the study.

RESULT

Table 1 reveals the sex-related prevalence of malaria and its association with musculoskeletal pain. A total of 147 participants had malaria over the 8-month study period with an overall prevalence of 62.55%.

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Table 1: Sex-related prevalence of malaria and association with musculoskeletal pain

Sex	Number examined(%)	MSP with only malaria(%)	MSP + malaria with other diseases (%)	Malaria without MSP (%)	Total number with malaria (%)
Male	114	37 (32.57)	6 (5.26)	16(14.03)	59(51.75)
Female	121	60 (49.59)	5 (4.13)	23 (19.01)	88 (72.72)
Total	235	97(41.28)	11(4.68)	39 (16.60)	147(62.55)

MSP- Musculoskeletal pain
Other diseases- Sickle cell disease, Arthritis, Trauma, Sepsis

Females had significantly higher malaria prevalence of 72.72% than males (51.75%) ($\chi 2=11.0224$; def=1 p (0.0009) <0.05). The result revealed 41.28% occurrence rate of respondents having musculoskeletal pain and only malaria consisting of 37(32.57%) males and 60(49.59%) females. Furthermore, 4.68% (11) of the respondents had MSP with malaria and other diseases. Overall, 39 participants had malaria without MSP representing prevalence of 16.00% (14.03% males vs 19.01% females). Statistical analysis revealed no significant difference in the prevalence of malaria + MSP and Malaria + No MSP ($\chi 2=0.0175$; df=1; p(0.8948)>0.05). Likewise, the sex related prevalence showed no significant difference ($\chi 2=0.0175$;df=1; p(0.8948)>0.05).

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Table 2 reveals the age-related prevalence of malaria and the association with MSP.

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Table 2: Age-related prevalence of malaria

Age (years)	Number examined (%)	MSP + only malaria (%)	MSP + malaria +other diseases (%)	Malaria without MSP (%)	Total number with malaria (%)
10-19	51	18 (35.30)	1 (1.82)	11 (21.57)	30 (58.82)
20-29	28	10 (35.71)	1 (3.57)	6 (21.43)	17 (60.71)
30-39	41	22 (53.66)	1 (2.44)	6 (14.63)	29 (70.73)
40-49	37	16 (28.70)	3 (5.26)	7 (12.28)	26 (45.61)
50-59	29	12 (41.38)	2 (6.90)	5 (17.24)	19 (65.51)
≥60	49	19 (38.78)	3 (15.79)	4 (21.05)	26 (53.06)
Total	235	97	11	39	147

MSP- Musculoskeletal pain; Other diseases- Sickle cell disease, Arthritis, Trauma, Sepsis

Age-related prevalence of malaria within the study period showed that malaria prevalence across the age groups exceeded 50%, except for the age group 40-49 years with a prevalence of 45.61%. The age group 30-39 years had the highest malaria prevalence of 70.73%. However, the age-related prevalence of malaria was not significantly different ($\chi 2=4.448$; def=5; p (0.4869) >0.05).

The 10-19 years age group had the highest prevalence of participants with malaria without MSP (21.57%) and the least percentage with MSP and malaria co-existing with other diseases (1.82%). Respondents that are 60 years and above recorded the highest prevalence of malaria co-existing with other diseases, while 40-49 years people had the least occurrence rate (12.28%) of malaria without MSP. The highest infection rate of only malaria and MSP patients were recorded in the 30-39 years age group (53.66%), while the least was found in 40-49years respondents (28.70%).

The Sex-related prevalence of malaria-associated musculoskeletal pain is illustrated in table 3. Of the 235 participants examined 150(63.83%) made up of 68 (59.65%) males and 82 (67.77%) females had MSP which is inclusive of 97(64.67%) that had only malaria infection.

Fig 1 illustrates the distribution of malaria-associated MSP by anatomical sites

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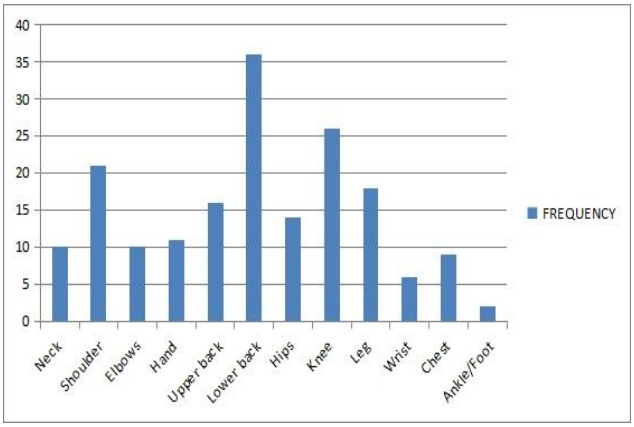

Fig 1: Distribution of malaria-associated MSP by anatomical sites

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The result revealed significant variation in frequency rate of sites of malaria-associated musculoskeletal pain ($\chi 2$ =50.425; df=11; P(0.000)<0.05). The most frequently reported site of malaria-associated MSP was the lower back, and this was reported by 36(37.11%) participants. Other common sites reported by participants are knee (26.80%), shoulder (21.65%) and upper back (16.49%). Only 6.19% of participants reported experience of wrist pain during the 8 months study. The ankle/foot (2.06%) was the least frequently reported site of MSP.

Comment [CdM14]: (Figure 1)

Lower back (21) and shoulder (12) pain were more common in males while the highest female predominance was found for the knee(15) and lower back(15) pain. Most (54.64%) of the participants who reported MSP with malaria indicated pain in two body parts while 36(37.11%) reported only one pain site. Only 8(8.24%) of participants with malaria-associated MSP reported more than 2 pain sites.

Comment [CdM15]: (Tabela 3)

Table 3: Sex-related prevalence of malaria-associated musculoskeletal pain

Sex	Number examined	Number with MSP (%)	Number with MSP and only malaria (%)
Male	114	68 (59.65)	37 (54.41)
Female	121	82 (67.77)	60 (73.17)
Total	235	150 (63.83)	97 (64.67)

The result revealed a significant sex-related prevalence of malaria with MSP with females (73.17%) recording higher infection than males (54.41%)($\chi 2$=5.7251; def=2; p (0.016724) >0.05).

The illustration of the age-related prevalence of malaria-associated musculoskeletal pain is shown in table 4.

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Table 4: Age-related prevalence of malaria-associated musculoskeletal pain

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Age (years)	Number	Number with	Number with MSP

	examined	MSP(%)	and only malaria (%)
10-19	51	33 (64.71)	18 (54.55)
20-29	28	13 (46.43)	10 (76.92)
30-39	41	31 (75.60)	22 (70.97)
40-49	37	27 (47.37)	16 (59.26)
50-59	29	19 (65.52)	12 (63.16)
≥60	49	27 (55.10)	19 (70.37)
Total	235	150 (63.83)	97 (64.67)

The result revealed significant variation in the occurrence of MSP in the age groups with 30-39 years age group having the highest prevalence of 75.60%, while the least (47.37%) was found in 40-49 age group ($\chi 2=33.20$;df=5; p(0.00)<0.05).

Comment [CdM18]: (Table 4)

The prevalence of malaria-associated MSP was over 50% in all age groups (Table 4). The age group with the highest prevalence was 20-29 years (76.92%), while 10-19 years age group had the least (54.55%). Age was not significantly associated with the prevalence of malaria and MSP ($\chi 2$ =6.237 ; df=5; P(0.284)>0.05).

Table 5 depicts a measure of the association between malaria and musculoskeletal pain in the study population. Table 5: Relationship between MSP and malaria

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	Number with musculoskeletal pain	Number without musculoskeletal pain
Number with only malaria	97 (a)	39 (b)
Number without malaria	42 (c)	46 (d)

Odd ratio (OR) = (a/c) (b/d) = (97/42) (39/46) = 2.72

The odd ratio evaluation of the relationship between malaria and musculoskeletal pain shows that there is a 2.72 chance of having musculoskeletal pain with exposure to malaria infection.

Table 6 shows the percentage of the participants with malaria and MSP co-existing with other diseases

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Table 6: Percentage of the participants with malaria and MSP co-existing with other diseases

S/N	Disease condition	Frequency	Percentage (%)
1	Sickle cell disease	2	18.18
2	Arthritis	6	54.55
3	Trauma	1	9.09
4	Sepsis	2	18.18
Total		11	100

The profile of other diseases associated with MSP other than malaria showed that Arthritis was the commonest with a prevalence of 54.55%. Sickle cell disease (SCD) and sepsis occur with the same frequency (2) revealing an occurrence rate of 18.18%), while trauma with a percentage of 9.09% was the least disease condition co-existing with malaria and MSP in the study population.

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DISCUSSION

Malaria is a serious public health concern in Nigeria. The need for a speedy diagnosis invaluable in treatment has encouraged scientific studies to identify symptoms that can serve as a diagnostic index. The results of this study revealed a higher prevalence of malaria (62.55%). It is lower than the prevalence of 76% reported by Ukpai and Ajoku, (2001) in Owerri municipal amongst out-patients attending clinics, but higher than 25.5% recorded by Ajero *et al*., 2015. The prevalence reveals active transmission of *plasmodium* encouraged by the enabling environment. The study area is a tropical area with a record in the literature on the preponderance of enabling environment for malaria infection like adequate breeding sites, poverty, exposure to infected mosquitoes to mention but a few. However, the 62.55% prevalence could be an overestimation of the status in nature as only hospitalized patients were assessed. Ajero *et al*., 2015 has noted that studies among hospital patients are sometimes biased because they are focused on sick individuals who seek medical attention in the clinics thus explaining the very high prevalence.

Females significantly had more cases of malaria infection than males. There are conflictory reports on sex-related infections of malaria. Ukpai and Ajoku (2001) reported more infections in males (78.0%) in Okigwe and Owerri, Imo State while Kalu *et al*., 2012 reported more infections in females. The higher infection in females observed in this study may be due to differences in exposure. However, the female samples also consisted of pregnant women who naturally have compromised immunity, which may have accounted for the higher prevalence in females.

The age-related prevalence was not significantly different. This contrasts reports by Ajero *et al*, 2015 which found a significant age-related infection in their study. The age groups may have been equally exposed.

The result of the empirical study revealed a 63.83% prevalence of MSP. This implies that the burden of MSP among the study participants is high. This is consistent with the reports of several authors. Picavet

and Shouten, 2003 in a 12-month study reported MSP prevalence of 74.5% in a Dutch population, while Akinpelu *et al*., 2010 reported a prevalence of 80% in a 12 months study.

The most frequently reported site of malaria MSP has been low back, and this was reported by 36 (37.11%) participants. Other common sites of MSP reported by participants are knee (26.80%) and the shoulder (21.65%). It is difficult to compare the percentage frequency of MSP by anatomical sites obtained in this study with those reported in previous studies from Nigeria. This is because previous studies (Omokhodion *et al*., 2000; Omokhodion *et al*., 2003; Gureje *et al*., 2007 Adegoke *et al*., 2008) focused on specific types of MSP, such as spinal pain, neck pain and low back pain, whereas the present study reports MSP in any body part in the presence of malaria. However, the finding that low back pain is the most frequently reported MSP agrees with the findings of Adedoyin *et al*., 2004, Udoye & Aguwa, 2007 and Adegoke *et al*., 2008 There is however no concrete explanation for the higher presence of lower back MSP in observed in this present study.

The study also showed that the prevalence of MSP is age-dependent. This is in agreement with records by the Musculoskeletal Health in Europe Report (2015) that the musculoskeletal health of an individual is determined by personal factors (include age, gender, genetics, diet, body mass index, alcohol, smoking, exercise, co-morbidities, education, housing, work type and psychological assets), by the occurrence of diseases and other health conditions, by lifestyle factors, and by the interaction of these. Many authors in the literature have also ascertained that age attracts several physical disabilities that strongly affect musculoskeletal health.

The prevalence of malaria-associated MSP was found not to be age-dependent as opposed to the prevalence of MSP alone. This age-dependent deviation in the presence of malaria is expected and may be explained by the fact that malaria affects all ages with little or no difference in the degree of propensity and may co-exist with other health conditions that may or may not be age-dependent. This is further strengthened by statistics from this study, which deduced that having a malaria infection with MSP or without MSP is neither dependent on sex nor age.

The fact that 64.67 per cent of the subjects have MSP due to simply malaria backs up Miller et al., 1989; Brotto et al., 2005; and Mishra and Newton, 2009, who claim that malaria agents have negative effects on human skeletal muscles. Microvascular sequestration of parasitized red blood cells, which results in decreased oxygen supply, blocked blood flow, and tissue hypoxia, is the fundamental pathogenic mechanism of musculoskeletal involvement in malaria (Yeo et al., 2013). Other important mechanisms include increased muscle protein breakdown from *Plasmodium* parasitization and deposition of inflammatory products as well as toxic factors (such as glycosylphosphatidylinositol (GPI)) in the joints and muscles (Miller *et al*.,1989). This study, therefore shows there is a significant association between MSP and malaria ($R=0.6599$, $\chi 2=12.633$).

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Several diseases have also been identified to cause MSP. Some of these diseases were found to coexist with malaria and MSP from our study. Arthritis is mainly an age-dependent disability rate highest with 54.55%, followed closely by Sickle cell disease (18.18%) and sepsis (18.18%). The challenge,

therefore, is how to ascertain if the MSP in these participants is caused by malaria, the co-existing disease conditions or interplay with other factors. However, the statistical analysis of this result presented an odds ratio, which means that having malaria raises the odds of having MSP by 2.72. Hence, MSP can be used as a diagnostic index in malaria diagnosis to complement the use of fever.

CONCLUSION

This study has revealed a high malaria prevalence of 62.55% in conjunction with a malaria-associated MSP prevalence of 64.67%. There is a significant positive association of malaria with MSP implying that MSP could be used as a diagnostic index in malaria. This will also go a long way in complementing fever as an index - symptom for early detection of disease in resource-efficient regions and the development of specific interventions for the protection of the musculoskeletal system from malaria infection.

Comment [CdM23]: this correlation is sufficient for this conclusion??????

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