

## The associations of malaria parasite and ABO blood groups with aggressive periodontitis in Nigerians - a preliminary study

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### Abstract:

**Objective:** Aggressive Periodontitis (AgP) is a rare form of periodontitis which has been associated with aetiological factors including genetic predisposition, *Aggregatibacter actinomycetemcomitans*, and blood group B. It seems to have a racial predisposition being more common among blacks, particularly people of West African origin. The role of endemic factors such as malaria is yet to be investigated in AgP. The aim of this study was to explore the associations of malaria parasites and ABO blood groups with aggressive periodontitis.

**Method:** A preliminary case-control study on localized aggressive periodontitis patients and age and gender matched controls. Microbiological and hematological tests were performed to determine the presence of malaria parasites and ABO blood groups respectively.

**Result:** Eight LAgP patients and 9 age and gender-matched controls were seen. Six patients were positive for *Plasmodium falciparum* malaria parasite, compared with 2 controls. This difference was statistically significant ( $p=0.044$ ). The prevalence of malaria infection was not significantly associated with age ( $p = 0.44$ ) or gender ( $p = 0.34$ ) of the subjects.

**Conclusion:** This preliminary study showed a high prevalence of malaria parasites among patients with aggressive periodontitis. Malaria infection may be associated with AgP. Studies with larger sample sizes may be needed to further investigate the relationship between aggressive periodontitis and malaria infection.

**Key words:** Aggressive periodontitis, Malaria parasite, ABO blood group, Controls

### Introduction

Aggressive periodontitis (AgP) encompasses rare, distinct types of periodontitis occurring in otherwise systemically healthy young adults<sup>(1,2)</sup>. Aggressive periodontitis describes the diseases formerly classified as "juvenile periodontitis", "early-onset periodontitis", "pre-pubertal periodontitis" and "rapidly progressive periodontitis"<sup>(3)</sup>. It occurs in both localized and generalized forms, with the disease starting around adolescence and progressing rapidly, leading to loss of some teeth at an early age. Some of the clinical features include rapid attachment loss, bone destruction, minimal microbial deposits inconsistent with the degree of attachment loss.

In the localized form of the disease, the first permanent molars and incisors are usually involved at or around puberty<sup>(4)</sup>. It is seen most frequently between puberty and 20 years of age. The generalized form on the other hand, affects at least three permanent teeth other than the first molars or incisors, and is generally seen in patients less than 30 years of age<sup>(4)</sup>.

The prevalence of localized aggressive periodontitis (LAgP) in geographically diverse adolescent populations suggests a generally low prevalence of less than 2%<sup>(5-7)</sup>. In spite of these, a relatively higher prevalence of 4.3% was reported in young Israeli army recruits<sup>(8)</sup>.

In a more recent review, Demmer et al<sup>(9)</sup> suggested that the prevalence of aggressive periodontitis among individuals

younger than 35 years of age could range from approximately 1% to a maximum of 15%, depending on the age of the participants and the study.

The prevalence in some African countries could be as high as 4.2%<sup>(10,11)</sup>. A study carried out in Ibadan, Nigeria however reported a lower prevalence of 1.56% in LAgP patients<sup>(12)</sup>.

A higher female predilection has been reported in some studies<sup>(7,12,13)</sup>. A male predominance was however found among high school students in Sudan<sup>(11)</sup> and among patients in a Nigerian tertiary hospital by Ayanbadejo et al<sup>(14)</sup>.

Many risk factors have been implicated in the aetiology of aggressive periodontitis. These include the presence of a specific bacteria, *Aggregatibacter actinomycetemcomitans*<sup>(15,16)</sup> which has frequently been identified as a key factor in LAgP<sup>(17-19)</sup>. A genetically determined predisposition for AgP has also been proposed<sup>(20,21)</sup>. A familial tendency has been reported<sup>(2)</sup>, and a strong genetic influence (autosomal recessive mode of inheritance<sup>(22)</sup>, autosomal dominant triad with reduced penetrance<sup>(23)</sup>.

One finding that has been consistently demonstrated in some studies is a racial predisposition of AgP, in black people especially of African origin<sup>(11,24)</sup>.

According to the World Malaria Report, malaria is prevalent in 108 countries of the tropical and semi-tropical world, 35 countries in central Africa, 30 of which are located in sub-Saharan Africa, accounting for 98.5% of deaths in Africa. Of these, four countries alone account for approximately 50%



of deaths in the continent (Nigeria, Democratic Republic of Congo, Uganda and Ethiopia)<sup>(25)</sup>. Nigeria is in Sub-Sahara, a tropical region where malaria is endemic. Malaria is the most prevalent and widespread tropical disease in the world today with morbidity and mortality that are at unacceptably high levels. It is caused mainly by Plasmodium falciparum. The disease has been reported to affect at least 50% of the population in Nigeria, accounting for over 45% of all outpatient visits<sup>(26)</sup>. In another study, a prevalence of 30.2%<sup>(27)</sup> was reported among Nigerian blood donors. The ABO blood group has been studied extensively in Nigeria<sup>(28,29)</sup>. Blood group O has been found to be the most prevalent, while blood group AB the least prevalent.

The relationship between Malaria and the blood groups was studied more recently by Akhigbe et al<sup>(30)</sup>. Blood group O was associated with a higher prevalence of malaria parasitaemia but a lower prevalence of severe malaria which suggests that O antigen may be more susceptible to malaria infection than non O antigens but less susceptible to severe malaria. This implies that the O antigen may have a protective role in impairing rosetting and vascular cytoadhesion of parasitized red blood cells. Aggressive periodontitis was associated with blood group B in earlier studies<sup>(31)</sup>. A study in Ibadan, Nigeria also found a predominance of blood group B/AB among 20 AgP patients<sup>(12)</sup>.

It might thus be interesting to explore an association if any, between malaria, ABO blood groups and aggressive

periodontitis in Nigeria.

This pilot study was aimed at exploring the associations of malaria parasites and ABO blood groups with localized aggressive periodontitis.

**Materials and method**

This was a case control study carried out at the Periodontology clinic of the Lagos University Teaching Hospital. Fifteen consecutive patients with Localized aggressive periodontitis were seen at the clinic. The patients with AgP were selected based on the following criteria: deep periodontal pockets of more than 6mm on at least one of the first permanent molars and the incisor teeth, mobile teeth, minimal plaque deposits and radiographic evidence of vertical alveolar bone loss around the first permanent molars. Exclusion criteria included a history of diabetes, leukemia, HIV, pregnancy and smoking. The controls were healthy age and gender matched subjects without LAgP attending the oral diagnosis clinic for routine dental checkup. Verbal informed consent was obtained from the subjects prior to recruitment into the study. Microbiological and haematological tests of all the subjects were performed to determine the presence of malaria parasite and the ABO blood group in the clinical laboratory of the Lagos University Teaching Hospital. Venous blood was obtained from the patients. Thick blood films were prepared by spreading a fixed volume of blood over a fixed area, and stained with Giemsa stain. Thin blood

**Table 1: Demographics and laboratory findings of the study population**

Localized Aggressive periodontitis	Gender	Age (years)	MP status	ABO Blood Group	Rhesus Blood Group
1	Female	17	Absent	O	D+
2	Female	18	Present	A	D+
3	Female	19	Present	B	D+
4	Female	20	Present	O	D+
5	Female	19	Present	A	D+
6	Female	22	Present	AB	D+
7	Female	23	Present	B	D+
8	Male	37	Absent	O	D+
7(87.5%)female 1(12.5%)male		Mean (SD) 22.5±6.35 Range=17-37 years	Malaria parasite in 75%ofAgP		
Control	Gender	Age (years)	MP status	ABO Blood Group	Rhesus Blood Group
1	Female	17	Present	B	D+
2	Female	18	Absent	O	D+
3	Female	23	Absent	B	D+
4	Female	24	Absent	O	D+
5	Female	25	Absent	O	D+
6	Female	26	Absent	O	D+
7	Female	26	Absent	O	D+
8	Male	28	Absent	O	D+
9	Male	39	Absent	O	D+
6(66.7%) Female 3(33.3%)Male		Mean (SD) 25.1±6.34 Range=17-39 years	Malaria parasite in 22.2% of controls		

T statistic = 0.845, P > 0.05 (No significant difference between mean age of both groups)

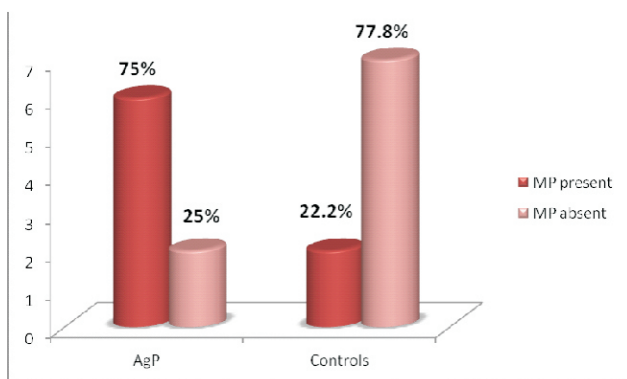
films were prepared and stained with Leishmann stain. Both films were examined under a standard light microscope at x100 magnification. Data entry and analysis were done with Epi info 2007 statistical software. Chi square test of analysis was used to determine differences. Differences were significant at  $p < 0.05$ .

## Results

A total of 8 patients with localized aggressive periodontitis (LAgP), comprising 87.7% female and 12.5% male, giving a female: male ratio of 7:1 had complete results. They were subsequently matched with 9 healthy controls. Their age ranged from 17 to 37 years (mean =  $22.5 \pm 6.3$  years). Most (87.5%) of the LAgP subjects were < 25 years, with 62.5% presenting in the juvenile state, being less than 20 years of age (**Table 1**).

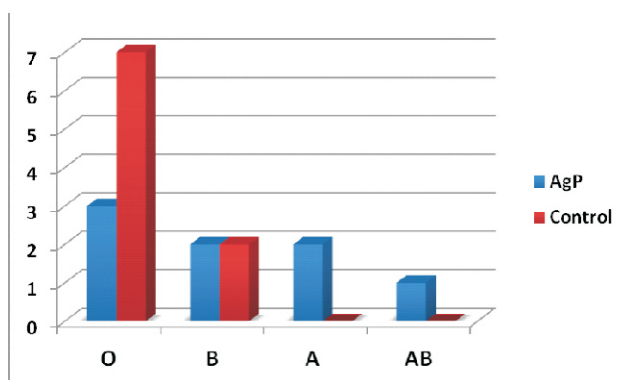
Malaria parasite was detected in the blood film of 6 of the LAgP patients and 1 of the controls respectively. Fisher's exact test showed that this difference was statistically significant ( $P=0.044$ ) (**Figure 1**). The prevalence of malaria infection was not significantly associated with age ( $p = 0.44$ ) or gender ( $p = 0.34$ ) of the subjects (**Table 1**).

The LAgP patients had a more variable ABO blood group distribution compared to the controls who were predominantly (77.8%) of O group. This difference was however, not statistically significant ( $P > 0.05$ ) (**Figure 2**).



$P = 0.044 (< 0.05)$

**Figure 1: Distribution of Malaria parasite (MP) among the study population**



**Figure 2: Distribution of ABO Blood group in the study population**

## Discussion

In this study, most of the patients with AgP (87.5%) were females and this finding is in agreement with earlier studies<sup>(6,7,12,13)</sup>. The higher female to male ratio reported in a Nigerian study<sup>(12)</sup> was significantly more associated with LAgP than generalized AgP. This finding may be due to the greater importance females place on their appearance and wellbeing than their male counterpart causing them to seek treatment earlier at dental clinics. A selection bias has also been attributed to this finding.

This finding contrasts with the study by Ayanbadejo et al in Nigeria<sup>(14)</sup> which reported a higher male proportion. This variation in the pattern of gender presentation in patients with this condition is further buttressed in the study by Savage et al<sup>(32)</sup> among Nigerian patients which showed no gender predilection.

Most of the subjects with AgP in this study were <25 years, which falls within the age criteria recently proposed for defining AgP in addition to other periodontal features<sup>(9)</sup>. Sixty-two percent (62.5%) were between 17- 20 years of age. This is similar to the finding of Arowojolu et al<sup>(12)</sup> where 17 years was the age of presentation, and not 11-13 years reported in an earlier study<sup>(5)</sup>. The slightly late presentation may be because of the late attendance at dental clinics for symptomatic treatment<sup>(33,34)</sup>.

Malaria parasite was present in 6 of the 8 subjects with aggressive periodontitis and this was significantly higher ( $P < 0.05$ ) than in the controls who had only 1 subject with the condition. The reason for this significant association is not very clear. This raises the question on whether the subjects were on malaria chemoprophylaxis prior to the time of study, though this was not indicated in the history. Research is limited in the relationship between AgP and endemic malaria, thus limiting the comparison of this particular finding with that of other studies.

The randomized study carried out by Ogunwande et al<sup>(35)</sup> may need to be revisited with regards to the study. He investigated the influence of malarial chemoprophylaxis on the rate of healing of ulcerative periodontitis lesions in Ibadan, Nigeria. He found that patients who were not on malaria chemoprophylaxis had a higher relief from their pain compared to those on chemoprophylaxis. This may suggest an association between malaria and periodontitis.

Another potential explanation is the possibility of an alteration in the immune system of host cells by the plasmodium. This was the finding of Millington et al<sup>(36)</sup> that the malaria plasmodium inhibited the induction of the adaptive immunity of host cell to heterologous antigens by modulating dendritic cells function. This was then proposed as a possible link between endemic malaria and other secondary infections.

Some other immune defects have been implicated in the pathogenesis of aggressive periodontitis<sup>(38,39)</sup>. This functional immune defect involves polymorphonuclear leukocytes and monocytes which may cause excessive production of prostaglandins leading to increased connective tissue or bone loss. These immunologic features involving both malaria parasitaemia as well as aggressive periodontitis merit further research as they are beyond the scope of this study.

Blood group O was the most frequent in both the AgP subjects (37.5%) and the controls (77.8%) respectively. This is in agreement with previous reports from other studies



among Nigerians<sup>(28,29)</sup>. Blood group AB was the least prevalent. Only two of the AgP subjects had blood group B. This differs from the earlier study<sup>(31)</sup> associating AgP with blood group B. There was no significant relationship between the blood group type and periodontitis. This is in agreement with the report of Barros et al<sup>(40)</sup>, who found no difference between subjects with or without periodontal diseases and their blood group. Interestingly, the patients with aggressive periodontitis in this study had a more variable distribution with all four blood group subtypes fairly represented.

The present study showed a significantly higher prevalence of malaria parasite in the blood film of patients with aggressive periodontitis.

This high prevalence of malaria parasite in patients with aggressive periodontitis merits further investigation requiring larger sample sizes to further explore and elucidate the association between endemic malaria infection and aggressive periodontitis.

### Conclusion

The findings of this preliminary study suggest that malaria infection may have an associated risk factor in aggressive periodontitis. The ABO blood group of the AgP patients was not associated with AgP in this study.

More studies need to be conducted with larger sample sizes to further investigate the association between malaria infection and aggressive periodontitis.

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