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THE EVALUATION OF THE PATHOGENIC THRESHOLD IN REGIONS WITH HIGH PERMANENT TRANSMISSION OF MALARIA, AS WELL AS THE MEASUREMENT OF MALARIA-RELATED PNEUMONIA

Praveenkumar Periyasamy[1*], Pragathi Munnangi[2], Aliu Olalekan Olatunji[3], Bilal Fattani[4], Mohit Lakkimsetti[5], Abubakar Ali[6]

[1*]Lecturer, Department Anatomy, Levy Mwanawasa Medical University, Lusaka, Zambia
Email: praveenkumar.periyasamy@lmmu.ac.zm
[2]Graduate, Department of Internal Medicine, N.R.I Medical College, Guntur, India
Email: pragathimunnangi1@gmail.com
[3]Doctor, Department of Medical Microbiology and Immunology, University of Toledo Ohio State, USA, Email: aliu_my2004@yahoo.com
[4]House Officer, Department of Surgery, Jinnah Medical College Hospital, Pakistan
Email: fattanib98@gmail.com
[5]MBBS, Mamata Medical College, Khammam, India, Email: mlakkimsetti@gmail.com
[6]University Institute of Medical Lab Technology, Faculty of Allied Health Sciences, The University of Lahore, Pakistan, Email: 70106835@student.uol.edu.pk

***Corresponding Author:-**Praveenkumar Periyasamy
[*]Lecturer, Department Anatomy, Levy Mwanawasa Medical University, Lusaka, Zambia
Email: praveenkumar.periyasamy@lmmu.ac.zm

ABSTRACT:
Background: Epidemiological surveys in malaria-endemic regions with permanent transmission require a simple, rapid, and cost-effective method to evaluate parasitemia.
Objective: To develop and validate a method for measuring parasite density using micro-hematocrit red blood cell counts on smears.
Methods: Procedure: The parasite density was measured by counting the number of red blood cells in micro-hematocrit smears.
Microscopy: Parasitemia was assessed by reading 75 to 100 microscopic fields at 100x magnification.
Statistical Analysis: The formula for determining parasitemia was statistically justified and explained.
Results: Participants: 1,163 healthy individuals and 534 consultants were included.
Age Groups: Analysis was conducted across different age groups.
Thresholds for Harmful Parasitemia:
Children: Harmful parasitemia threshold ranged between 3,000 and 6,000 trophozoites per milliliter of blood.
Adults: Threshold was lower than 1,000 trophozoites per milliliter of blood.

Conclusion: The method developed for evaluating parasitemia is effective for epidemiological surveys in malaria-endemic regions. Maintaining the diagnosis of malaria at the established parasitemia thresholds is crucial to prevent morbidity.

KEYWORDS: Epidemiological surveys, Malaria endemic regions, Parasitemia evaluation, Micro-hematocrit smears, Parasite density measurement, Microscopy, Statistical analysis, Malaria diagnosis, Morbidity prevention.

INTRODUCTION:

When working on the epidemiology or morbidity of malaria, one of the most significant methodological challenges involves the assessment of the disease's prevalence (Moxon et al., 2020). Generally speaking, three categories of criteria are maintained: - The clinic is the primary basis of judgment, and it is left up to the discretion of the attending physician (Amimo, 2024). The primary argument is that the central temperature and the threshold for this criterion vary depending on the studies. - The parasitological criterion is sometimes quantitative. When parasitemia is evaluated using smear and thick drop specimens, it is possible to consider discriminating limitations (Amimo, 2024). In most cases, the evaluation is qualitative, which may be deemed insufficient in areas where malaria is endemic (Benasseni et al., 1987; Baudon & aZ., 1988) (Cirera et al., 2023). Last but not least, the evolution of the disease while it is being treated is an additional point that can occasionally be decisive (Gwarinda, 2021). This variety can be attributed to the fact that diagnosis is difficult due to the absence of investigational methods, that there are several potential sources of mistake, that specific criteria are subjective, that there are logistical issues, and so on (Kho et al., 2021). A discussion can be had about even the components that appear to be objective, such as temperature; in fact, temperature can be observed during defervescence (Brito & Tchonhi, 2019). When working on the epidemiology or morbidity of malaria, one of the most significant methodological challenges involves the assessment of the disease's prevalence. Generally speaking, three categories of criteria are maintained: - The clinic is the primary basis of judgment, and it is left up to the discretion of the attending physician. The primary argument is that the central temperature and the threshold for this criterion vary depending on the studies. - The parasitological criterion is sometimes quantitative (Organization, 2022). When parasitemia is evaluated using smear and thick drop specimens, it is possible to consider discriminating limitations. In most cases, the evaluation is qualitative, which may be deemed insufficient in areas where malaria is endemic (Benasseni et al., 1987; Baudon & aZ., 1988). Last but not least, the evolution of the disease while it is being treated is an additional point that can occasionally be decisive (Kullaya, 2019).

Criteria	Description	References
Clinical	Judgment is based on the discretion of the attending physician. Varies depending on central temperature and study.	Moxon et al., 2020; Amimo, 2024
Parasitological (Quantitative)	Evaluated using smear and thick drop specimens. Includes discriminating limitations.	Amimo, 2024
Parasitological (Qualitative)	Often deemed insufficient in endemic areas.	Benasseni et al., 1987; Baudon & aZ., 1988; Cirera et al., 2023
Disease Evolution During Treatment	Can be a decisive point for assessment.	Gwarinda, 2021

Factors Affecting Diagnosis	Description	References
Absence of Investigational Methods	Leads to diagnostic difficulties.	Kho et al., 2021
Potential Sources of Mistake	Various sources can cause errors in diagnosis.	Kho et al., 2021
Subjective Criteria	Specific criteria can be subjective.	Kho et al., 2021
Logistical Issues	Practical challenges in conducting diagnostic procedures.	Kho et al., 2021
Temperature Variations	Temperature can vary, particularly during defervescence.	Brito & Tchonhi, 2019

Additional Criteria	Description	References
Clinical Criteria	Judgment left to physician discretion; variation in temperature thresholds.	Amimo, 2024
Parasitological Criteria (Quantitative)	Evaluated via smear and thick drop specimens with limitations.	Organization, 2022
Parasitological Criteria (Qualitative)	Often considered insufficient in endemic areas.	Benasseni et al., 1987; Baudon & aZ., 1988
Evolution During Treatment	The evolution of disease during treatment can be decisive.	Kullaya, 2019
Temperature Observation	Discussion about objective components like temperature, especially during defervescence.	Fançony et al., 2019

This variety can be attributed to the fact that diagnosis is difficult due to the absence of investigational methods, that there are several potential sources of mistake, that specific criteria are subjective, that there are logistical issues, and so on. A discussion can be had about even the components that appear to be objective, such as temperature; in fact, temperature can be observed during defervescence (Fançony et al., 2019).

MATERIAL AND METHOD:

2.1. Selection of topical areas: During the study, epidemiological surveys were conducted longitudinally in two different neighborhoods of Cotonou. The samples that were obtained in Agblangandan included 177 children ranging in age from six months to twelve years old (Trasia, 2023). These children were collected between October 1985 and July 1987, resulting in a total of 668 samples having been collected. A survey of the same sort was conducted in Ladji, and it included two visits: one during the dry season (March 1987) and the other during the rainy season (August 1987). A total of 285 samples were collected from the children who participated in the survey. All of the samples that were included were taken from youngsters who were in good health. In the province of Zou, which is located in the wooded Liberian-Nigerian savannah zone, two villages, Lissa and Sozoumé, were subjected to cross-sectional surveys during the dry season and at the beginning of the rainy season. The surveys were done for both children and adults. We collected 210 samples in total (Trasia, 2023). Between May 1986 and December 1987, a morbidity study was conducted in the Agblangandan dispensary, which is located in the lagoon area fringes of Cotonou.

Five hundred and thirty-four patients of varying ages were examined through the use of two or three consultations per week on a variety of days (Adediran, 2022). 2.2: The measurement of parasitemia: The fingertip was used to collect all of the samples, and a vaccine-style technique was used. Fixing and coloring the smears with RAL* (Rhône Poulenc) is something that is done. It is necessary to collect a capillary heparinized microhematocrit blood sample.

ASSESSING THE QUANTITY OF RED CELLS IN THE BODY:

Following the centrifugation of the capillary, the hematocrit allowed us to generate a chart that provided an approximation of the total amount of red blood cells. Following the findings of the participants with whom we connected hematocrit and red blood cell count, this previous conclusion was reached (Galactionova, 2019). The method of counting red blood cells that were utilized (a manual or an automatic counter) also had a role in our comparison of these characteristics in healthy patients and sick individuals. An abacus is formed by the linear regression line that was obtained (Nyiro et al., 2022). In addition, we used the hematocrit to determine the average number of red blood cells that were present in each microscopic area. Using fifty separate slides that were randomly selected from the various groups of individuals, we counted the number of red blood cells that were visible on ten fields (ocular x ten big fields, x one hundred immersion objective).

DETERMINE THE TOTAL NUMBER OF FIELDS THAT NEED TO BE READ DOWN:

After reading 10, 25, 50, 75, 100, 150, and 200 smear fields, we analyzed a total of 139 slides and compared the results to one another. When we were determining the plasmodial index, individual parasitemia, and average parasitemia for each group, we took into consideration the fact that the figures obtained after reading 200 fields served as the reference. There were statistical tests carried out 5% is the significance limit for all of the comparisons of frequencies, means, and correlations (Ssewanyana, 2021).

ASSESSING THE THRESHOLD FOR THE PRESENCE OF PATHOGENS:

All of the criteria that were used were deductive (Fink et al., 2021). By utilizing the geometric growth of reason 2, we were able to determine the number of individuals who belonged to each category of parasitemia in the healthy population (Morais et al., 2024). The fact that this particular distribution of parasitemia was typical in a healthy population was acknowledged by us. By following the same procedure, we were able to determine the prevalence of parasitemia among respondents (Durán et al., 2019). We acknowledged that the patients who sought consultations might have a parasitemia whose distribution was comparable to that seen in the healthy population. This was one of the latter groups. To determine the distribution of parasitemia in healthy subjects, we decided to calculate the number of theoretical consultants for each category of parasitemia. It is always the case that the number of consultants is lower than the theoretical numbers that are calculated based on the distributions that are observed among the healthy subjects when the parasitemia is low (Abdalal, 2021). In contrast, it seems that the number of consultants in the classes with high parasitemia is higher than the number that was anticipated in the theoretical framework. Given that these individuals are not only sick but also carrying an "abnormal" parasitemia, there is a strong likelihood that they will be attacked by malaria (Organization, 2019).

RESULT:

Table 1: distribution of the numbers by age. The number of smears taken in total is indicated in parentheses. Age distribution of the sample population. The total number of thin smears that were evaluated is indicated in brackets.

Age	Count of subjects in good health	Amount of outpatients	Total

From six months to two years	129	147	276
Three to four years of age	100	63	163
Between the ages of 5 and 12	186	202	388
The adults	144	105	249
Total	559	517	1076

1697 samples were taken from a total of 1076 participants who participated in the study. 3.1: The assessment of parasitemia: Assessing the quantity of red blood cells in the body There is a substantial association between hematocrit and the state of health as well as the method that is used to count red blood cells. The correlation coefficient is 0.83 for ddl = 103 when the measurements are performed automatically, and it is 0.74 for df = 129 when you perform the measurements manually. There are discrete variations that occur around the value Y = 0.08 X + 1, where Y is the number of red blood cells expressed in millions and hematocrit is expressed as a percentage. The equation of the line that is obtained for each set of measurements has distinct effects on these variations. For our abacus, we have kept the equation of the linear regression line, which is Y = 0.085 X + 0.913. This equation takes into consideration all of the measurements. To determine the degree of independence between the various hematocrit levels, we compared the average amount of red blood cells that were present in each microscopic field. The value of F was determined to be 1.12 after analyzing the variance of the averages of the amount of red blood cells per field. Our calculations were based on the average value of 280, which we acquired by obtaining an average of 281.6 red blood cells per field (Cl = 19 and n = 500). The amount of fields that can be selected Within the context of the amount of fields that are read, the plasmodial index exhibits a linear growth. Although it is notably different from the results obtained for reading 200 fields, it is still significantly different up to 75 fields. For the most part, however, the average level of parasitemia is very consistent. Under no circumstances is there a substantial difference in the average between reading 200 fields and witnessing any number of fields. As the number of pairings increases from 75 to 200, the correlation coefficient between the parasitemias that were recorded for each blade (r = 0.94 for df = 137) becomes extremely significant. For the 100/200 and 150/200 pairs, it is also a neighboring pair. To determine the level of parasitemia: Individual parasitemia, denoted by the letter P, is represented by the equation. H (0,85 X + 0,913) x 106 280XnHere, H stands for the number of red blood cells that have been parasitized, X stands for the hematocrit, and N is the number of fields that have been read. "parasitemia" refers to the number of red blood cells parasitized per cubic millimeter (GRP/mms).

3.2.1 Evaluation of the threshold

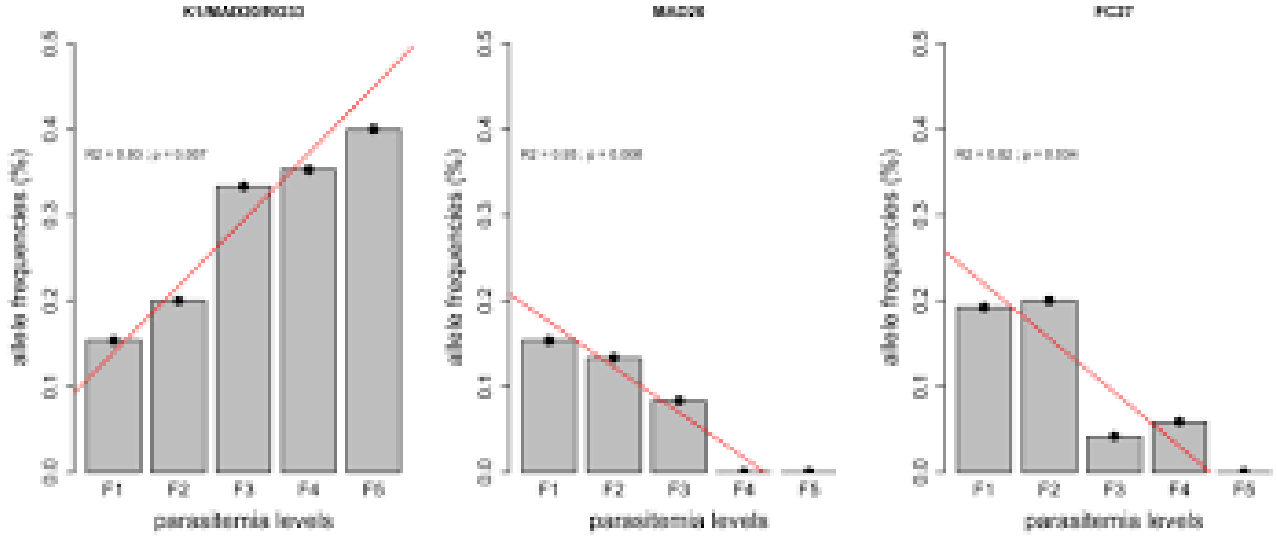

Figure 1: Depiction 1 There was a correlation between the cumulative frequencies of 6-mile parasites observed in healthy people and their ages. A cumulative frequency of Plasmodium falciparum density among humans, with age being a dependent variable.

Figure 1 illustrates the amount of variance in parasitemia that occurs in healthy persons based on their age. More than ninety-five percent of adults have plasmodial burdens that are significantly lower than 500 trophozoites per cubic millimeter. In around thirty percent of instances, youngsters have higher loads, more significant than one thousand trophozoites per millimeter of skin. They have parasitemias that are more than 10,000 parasites per cubic millimeter, which is a threshold that is widely believed to be adequate to cause an attack of malaria. These children make up between 1.5% and 2% of the total number of healthy samples taken from children. A representation of the frequencies of "abnormal 99" parasitemias in consultants is shown in Figure 2. These frequencies vary according to age. The prevalence of these parasitemias is higher than the prevalence of parasitemias seen in a population that appears to be in complete and whole health. Through the process of deducing the frequencies of parasitemias observed in patients and the frequencies of parasitemias reported in healthy persons, the curves were obtained. We have reason to believe that these individuals, who were previously referred to as "surplus 99," are suffering from an outbreak of malaria. According to him, the essential threshold is somewhere around 3,000 parasites per mm3 in youngsters and somewhere around 1,000 parasites per mm3 in people who are protecting themselves from the disease.

DISCUSSION:

Regarding morbidity research conducted in a hospital environment and at a dispensary on the periphery, we will not discuss the clinical or evolutionary criteria that will be discussed in other places. Following our consideration, we concluded that the subject's attendance at a medical consultation indicated a request that enabled us to categorize them as sick. Two issues arise when considering the parasitological argument: counting parasites and interpreting clinical or biological data that can be provided. For example, according to Trape (1985), the count of parasites on a thick drop has a very high sensitivity, which enables the detection of two parasites per mm3 of blood after scanning 200 fields. When using a smear, it would be necessary to read around 7,500 fields to meet such a threshold. Because the importance of the parasitemia level has not been demonstrated, the interest in detecting such a level of parasitemia is not essential. This method, on the other hand, was advantageous for the smear because of its speed and its ease of use. When the assessment of parasitemia is based on the calculation of the number of red blood cells, rather than on an average number of leukocytes, the accuracy of the measurement is significantly improved. In addition to the

fact that the latter is highly variable (by a factor of 1 to 36) in a population that is exposed to a large number of diseases, it is quite likely that the distribution of white blood cells on a thick film is not random. By measuring hematocrit on a capillary tube with adequate precision (variations of 15%), it is possible to identify the number of red blood cells in a mass campaign with greater ease. This is because the number of variations is 15%. The required level of sensitivity should be taken into consideration when selecting the number of fields to read. Because the plasmodial index depends on the amount of fields read, there is probably no solution that can be regarded as satisfactory in this scenario. We can say with absolute certainty that the identification of novel Plasmodium carriers would have been possible if a bigger number of fields had been scanned. On the other hand, the parasite density is a criterion that is not much impacted by the number of fields that are observed, provided that the latter is adequate. Based on the comparison of the various findings, it seems that reading 75 fields is a compromise that may be considered satisfactory. The presence of considerable parasitemia has a hundred percent possibility of being discovered, according to its probability. When weighed against the drawbacks, the advantages of reading on more than one hundred different fields are relatively insignificant in terms of performance. Two distinct groups may be distinguished from one another thanks to the distribution of parasitemia that was identified in healthy patients (graph 1). There is a possibility that children under the age of 12 could have significant parasitemia without exhibiting any clinical symptoms. Those who are adults appear to have a better ability to control their parasitemia. Children are frequently found to have significant parasite loads (Baudon et al., 1984; Picq, 1982; Trape, 1985; Trape et al., 1985). This discovery has been recorded on numerous occasions. There is some debate about the true meaning of this term. The equilibrium between the host and the parasite is probably unstable within this population during the process of obtaining its protection. Within a few hours of identifying a particularly high parasite rate, they would be required to perform a clinical examination on these youngsters and evaluate their parasitemia levels. As a component of the logic behind what has just been discussed, the high malaria pathogenic threshold in youngsters (figure 2) is an important consideration. Before the age of twelve, it seems that there is a certain tolerance for quite high parasitemia. This holds regardless of the age. The threshold is substantially lower in adults than it is in children. The idea of a pathogenic threshold needs to be taken into consideration with extreme caution. Given the epidemiological characteristics, it is quite probable that it varies greatly from one instance to another. In the strategy that we utilized, there was no correlation between a specific clinical criterion and the parasite density levels. We take a more empirical approach, which emphasizes the evidence of an aberrant frequency of parasitemia in people who appear with a condition that is more or less well-defined. This critical threshold, which may be characterized as a presumptive limit of malaria attack, cannot be adequately characterized by the word pathogenic threshold because it is the most specific phrase available. The pyrogenic thresholds that were established in Congo by Richard and a!. (1988) are the same for adults and adolescents, but they are much greater for small children. This difference can surely be explained by the specific clinical criterion that these writers have maintained, which is the temperature; nevertheless, this theory is based on the assumption that temperature is a consistent and unchanging indicator of access malaria in all of its stages.

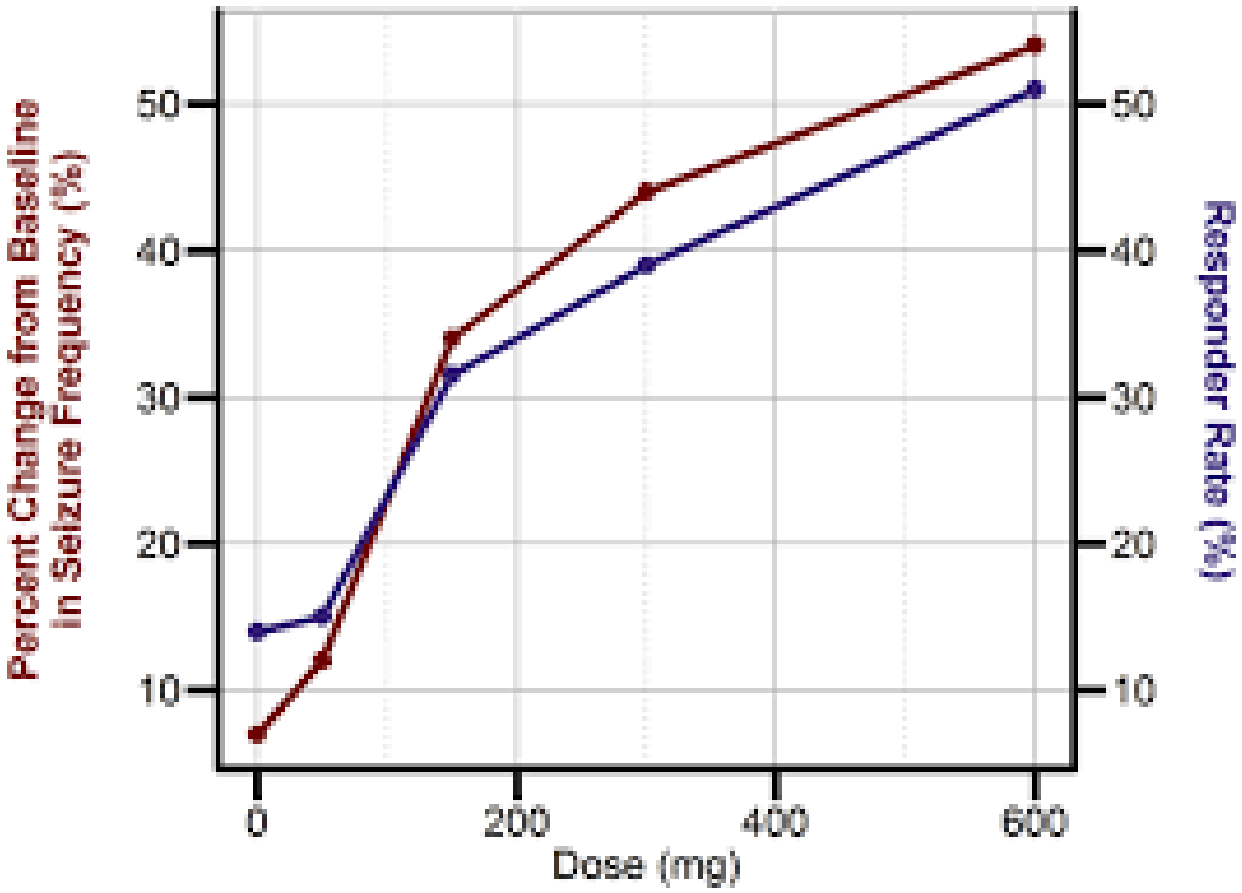

Figure 2 Frequencies of parasitemia observed in sick subjects after deduction

CONCLUSION:

In conclusion, the evaluation of the pathogenic threshold in locations with high permanent transmission of malaria, in conjunction with the measurement of pneumonia due to malaria, highlights the complex relationship that exists between infectious diseases and the effects that they have on public health. By doing exhaustive research and conducting surveillance, we can get priceless insights into the dynamics of these diseases, which in turn allows us to guide targeted interventions and preventative approaches. Furthermore, having an understanding of the thresholds of pathogenicity not only helps to advise clinical management but also contributes to the construction of resilient healthcare systems that can reduce the burden of malaria and the consequences that are associated with it. Even though we continue to probe deeper into this complexity, collaboration between researchers, healthcare providers, and policymakers continues to be important in our collaborative efforts to eradicate malaria and protect the well-being of people worldwide.

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