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AN INITIAL EXAMINATION OF THE EPIDEMIOLOGY OF MALARIA IN THE STATE OF RORAIMA, IN THE BRAZILIAN AMAZON BASIN

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SUMMARY

This study firstly describes the epidemiology of malaria in Roraima, Amazon Basin in Brazil, in the years from 1991 to 1993: the predominance of plasmodium species, distribution of the blood slides examined, the malaria risk and seasonality; and secondly investigates whether population growth from 1962 to 1993 was associated with increasing risk of malaria. Frequency of malaria varied significantly by municipality. Marginally more malaria cases were reported during the dry season (from October to April), even after controlling for by year and municipality. *Vivax* was the predominant type in all municipalities but the ratio of plasmodium types varied between municipalities. No direct association between population growth and increasing risk of malaria from 1962 to 1993 was detected. Malaria in Roraima is of the "frontier" epidemiological type with high epidemic potential.

KEYWORDS: Amazon Basin; Aggregated data analysis; Malaria; Epidemiology.

INTRODUCTION

Some aspects of the epidemiology of malaria in the Brazilian Amazon region are known. The majority of studies have investigated malaria transmission in the western Amazon basin, mainly on Rondonia. However, the Amazon is not environmentally uniform. Given the vast differences in topography, drainage patterns and economic and social development, findings in one area can not be generalized to the rest of the region. The state of Roraima has the second highest malaria transmission in the region (Pan American Health Organization [PAHO], 1996) and yet very little is known about the epidemiology of malaria there. This report describes some aspects of the epidemiology of malaria in Roraima: seasonality, parasite types, frequency, distribution and whether the increasing population changed the pattern of malaria transmission since 1962 to 1993.

Background

Efforts toward malaria eradication in Brazil started in the 1940s, resulting in such a decrease that in the 1970s malaria was practically limited to the Amazon region[4]. Since then, malaria has increased considerably in this region as a result of development projects, agriculture colonization expansion, and migrations of prospectors and gold-miners[11].

SAWYER[14] describes malaria in the Brazilian Amazon basin as occurring throughout the whole year with marked peaks in the dry season. He also relates increasing malaria to migration of non-immune into the area, new rural settlements or disorganized exploitation of natural resources. *P. vivax* has been described as the predominant parasite type and epidemic outbreaks associated to population mobility[2].

Two classifications of malaria are relevant for this study. BRUCE-CHWATT suggests classifying malaria into "stable" or "unstable"[8]. In "stable" malaria the amount of transmission is high without marked fluctuation over the years (though seasonality exists) and *P. falciparum* is the predominant species. "Unstable" malaria exists in areas of new colonization, mainly forested environments. In areas where malaria is "unstable", there is marked variation of incidence, and a gradual decline of immunity post-outbreaks which eventually creates a large number of susceptibles. SAWYER coined the term "frontier" malaria[13] (basically expanding on the concept of "unstable" malaria) where he further postulated a variable immunity level in the population depending on group characteristics. In "frontier" malaria the amount of transmission varies from year to year, from place to place and from month to month. There is an occasionally cyclical pattern and *P. vivax* is predominant but *P. falciparum* outbreaks occur and can be severe. In addition, some studies suggest that in "unstable" situations, the exploitation of forest resources and chaotic development projects increase the risk of outbreaks of *falciparum* malaria[2,12].

The setting for this study is Roraima state in the Northwest of Brazil, and part of the Amazon basin. It has an area of 239,104 sq. km and tropical climate with two seasons (a wet season from May to September and a dry season from October to April). It is divided into 8 administrative

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units (municipalities). Each has a large diversity of natural resources, population characteristics, geographic and infrastructure. There are 9 different indigenous ethnic groups (30,000) with different level of contact with the surrounding society. The epidemiological data of malaria is compiled by the local agency for the control of infectious diseases, the Fundação Nacional de Saúde (FNS) which is located in the capital city (Boa Vista).

The variation of annual parasite index (API) per 1,000 population in Roraima over 1962 to 1993 is shown in Figure 1. There was a marked variation over time, with an increase during the period 1973 to 1976; staying high, with fluctuations during late seventies and early eighties, declining during the eighties with a small increase from 1989 to 1991, and a fall from 1991 to 1993. Several factors may be associated with these variations. From 1973 to 1976 the first main road crossing the Amazon Region was built. In 1975, sources of gold, diamonds and other minerals were identified in the Amazon Basin. As a result, many prospectors and miners went to that region. In Roraima, the first illegal expeditions for mineral searching started in the late 1970s. In 1987, the Federal Government claimed lack of security for health professionals in the indigenous area and up to 1990 there was no health assistance in that area. It is likely that during that period malaria cases reported were underestimated. In 1991, the FNS was created and it was responsible for the malaria control programme in Roraima and for delivering special health care to the indigenous communities. Miners were removed from the forested area by the Ministry of Justice but in 1992 new clandestine mining shifted to the Savannah-like regions in the State.

MATERIALS AND METHODS

Dataset used and laboratory test

This paper is based on an analysis of routine data generated by passive case finding and by active searches for cases (mainly among indigenous communities in the state) by the malaria control programme in Roraima. Data on gender and age are not collected. Malaria cases are reported by place of diagnosis rather than by place of occurrence and the date on record is often the date of the report not of the diagnosis. Thick films are prepared from finger prick blood and stained with Giemsa. Diagnosis is based on the examination of 100 thick film fields read at 1000x magnification in the field. Ten percent (10%) of the slides identified as positive are re-examined at the central FNS level.

Two aggregated dataset were used. Data from 1991 to 1993 was tabulated for each municipality monthly as total population, total number of blood slides examined, and total number of positive slides by parasite species. Data from 1962 to 1993 was collated on an annual basis for the total population in Roraima as a whole consisting of number of positive slides and, from 1983, type of plasmodium.

Data entry

Data used in the study was abstracted from the FNS database and analyzed using Stata 5.

Analysis

Analysis of variance was used to compare the mean rates of slides examined, *vivax*/*falciparum* ratio and types of malaria infection by municipality, year and season during 1991 to 1993 and assess how much of the overall variation in the data was attributable to differences in between and within groups. The significance was tested using F-test.

Rates of slides examined and of positive slides per 1,000 person-years and percentage of positive slides per total slides examined were calculated for each municipality. The Annual Parasite Index (API), which in this work is the annual risk of diagnosed and reported malaria, was calculated for each municipality of Roraima by multiplying the total positive slides by 1,000 and dividing it by the total population at risk. APIs were compared within municipality group and in the 3 years of study and tested for significance using Chi-squared test. To investigate the effects of seasonality, municipality and year, rate ratios of positive slides over 3 years among the population were compared using Poisson regression.

Population growth was calculated by dividing the population in a year by the population in the year before. Linear regression and correlation were utilized to investigate whether population growth was

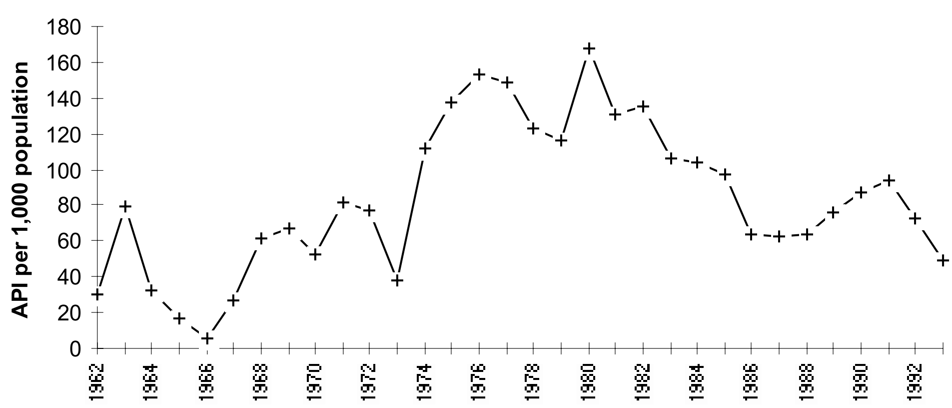

Fig. 1 - Annual Parasite Index in Roraima/1962-1993.

associated with API and increase in API. Annual population growth was considered the 'independent' variable (horizontal axis). API and increase in API were considered the response (or 'dependent') variable and plotted in the vertical axis. Both analysis included data from 1962 to 1993 for Roraima as a whole. The closeness of the association was described by the correlation coefficient, while linear regression gave the equation of the straight line that best predicts one variable from the other.

RESULTS

Slides examined

Table 1 shows the number and rate of slides examined, percentage of positive slides and API by municipality. There was a statistically significant variation in rates between municipalities (p=0.0001). The highest rates were found in the municipalities of Mucajai, Alto Alegre and Caracarai (in decreasing order). Boa Vista and Normandia presented the lowest frequency of blood examination for malaria.

Table 1
Rates of slides examined, percentage of positive slides and average API by municipality (1991 - 1993)

Municipalities	Slides Examined n^0.	Rates*	% Positive Slides	API** (per 1,000 population)
Boa Vista	90522	11.6	33	46.0
Caracarai	21768	48.0	15	116.3
Normandia	5925	14.1	26	41.5
Bonfim	21109	34.0	25	117.5
Alto Alegre	36341	78.0	28	213.0
Mucajai	51125	79.1	20	218.0
S.Luiz	14400	26.9	19	51.0
S.J.Baliza	10192	22.5	17	43.0

*Rates per 1,000 person-years.
**Mean API per 1,000 population over 3 years period (1991 to 1993).

Figure 2 illustrates the rates of slides examined monthly among the total population at risk and the percentage of positive slides among total slides examined during 1991 to 1993. The variation in percentage of positive slides seemed to be independent of the variation in slides examined.

One-way analysis of variance was used to investigate whether the variation of the means of the monthly rates of slides examined was due by chance or whether it was influenced by seasons. Two groupings were used to examine seasonal variation. The first divided months into a wet season (from May to September) and a dry season (October to April). The second included four categories: January to March (assumed as the middle of the dry season), April to June (transition to wet season), July to September (wet season) and October to December (dry season just after the rainy period). There was no statistically significant variation in rate of slides examined by season during the study period, even after controlling for municipality and year.

Risk and seasonality of malaria

The monthly parasite index (MPI per 1,000 population) by municipality over 3 years is presented in Figure 3. Each municipality plotted graphically did not show seasonal cycle for malaria transmission. However, there was a notable difference in the MPI distribution by municipality.

Figure 4 illustrates malaria API from 1991 to 1993 by municipality and overall in Roraima. API per 1,000 population in Roraima in each of the studied years was significantly different (p=0.0001). API per 1,000 population was also statistically significantly different for each municipality by year (1991: p=0.0001; 1992: p=0.0001; and 1993: p=0.0001). There was a statistically significant variation in API when different years for each municipality were compared. The Annual Parasite Index decreased from 1991 to 1993 in the majority of the areas, with two exceptions, Bonfim and Normandia, where API increased in the same period.

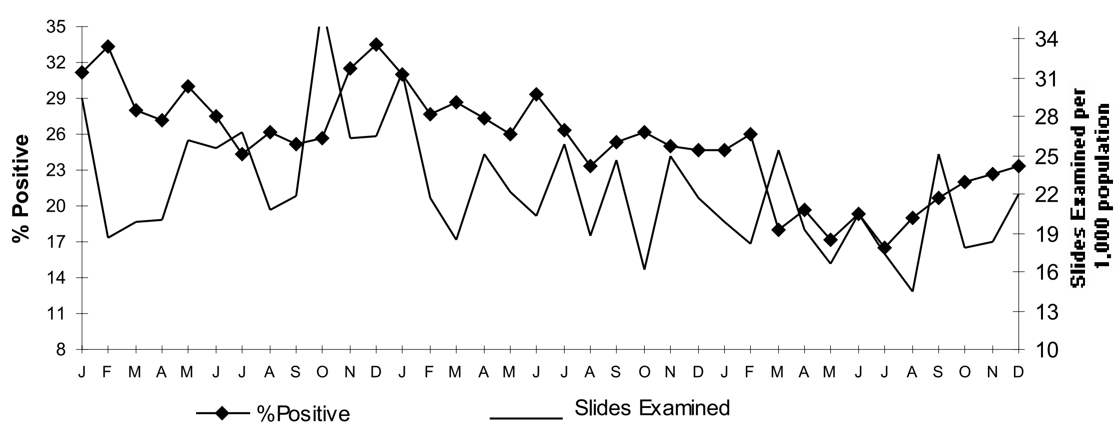

Fig. 2 - Rates of slides examined for malaria by month in Roraima and percentage of positive slides (1991-1993).

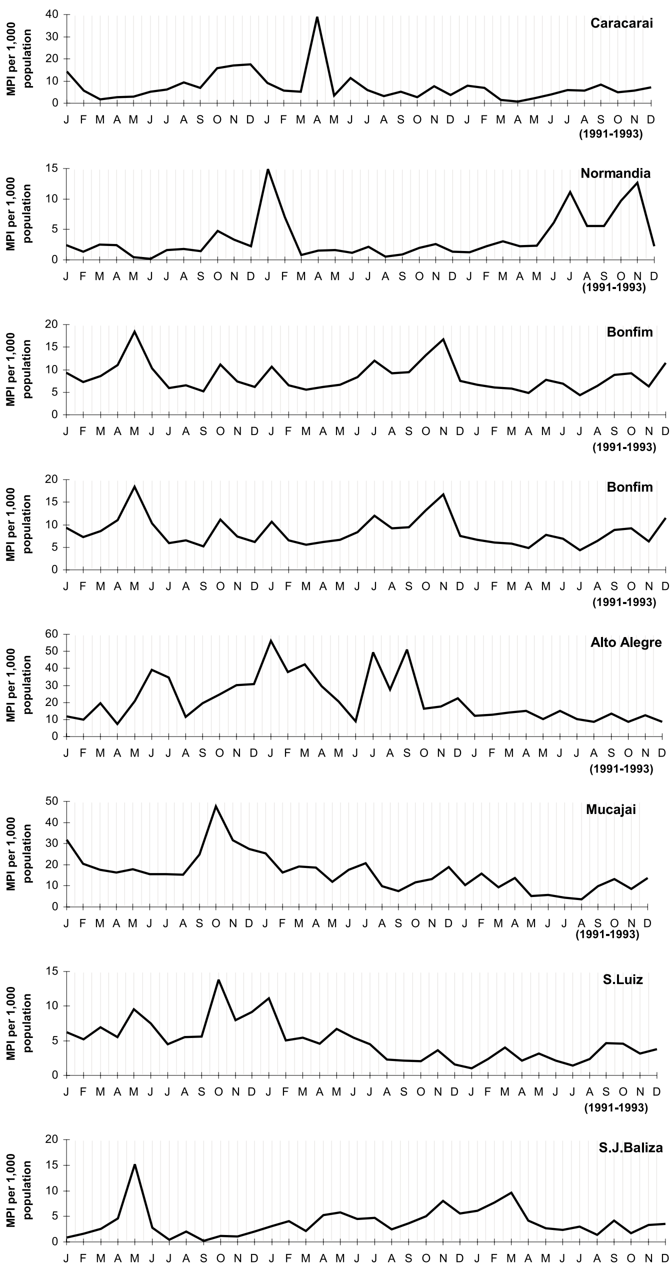

Fig. 3 - Monthly Parasite Index (MPI) by municipality, Roraima from 1991 to 1993.

The rate ratio was controlled for the effect of year, using Boa Vista as the baseline reference group. Alto Alegre was 5.6 times more likely to report malaria cases than Boa Vista and Mucajai was 4 times more likely. Bonfim and Caracarai had approximately 2 times more malaria cases reported than Boa Vista. There was no statistically significant difference between Boa Vista and S.J. Baliza (p=0.516). Normandia had lower rate ratio than Boa Vista (p=0.0001).

Table 2 shows the seasonal variation in rate ratio of malaria cases, adjusting for municipality and year. The rate ratio of malaria cases reported during the dry season was higher than in the wet season (p=0.0001). The rate ratio was statistically significantly different among four seasonal categories. Malaria cases were reduced during the wet season (from July to September). The variation in monthly rate ratio was also statistically significant. January was the month with higher rate of malaria cases reported. However, differences among seasonal categories were small and, depending on the grouping used, ranged from 15% to 23%.

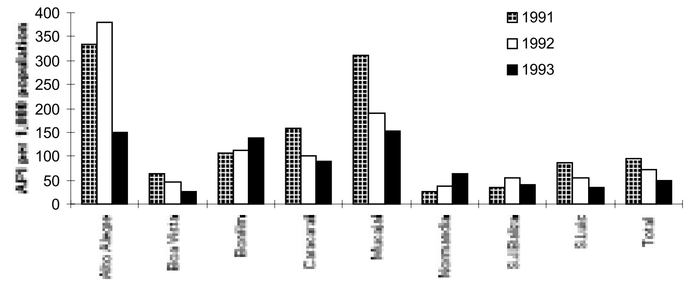

Fig. 4 - Annual Parasite Index per Municipality in the State of Roraima, 1991-1993.

Table 2

The effect of seasonality on rate ratios of malaria cases reported in Roraima (1991-1993)

	Rate Ratio**	95 % CI	p-value*
Wet Season (May - Sep)	1	-	-
Dry Season (Oct. - Apr.)	1.151	1.13 to 1.17	0.0001
Wet Season (Jul. - Sep)	1	-	-
Early Wet Season (Apr. - Jun.)	1.074	1.05 to 1.10	0.0001
Middle of Dry Season (Jan - Mar)	1.23	1.20 to 1.25	0.0001
Early after Wet Season (Oct. - Dec.)	1.20	1.17 to 1.23	0.0001
January	1	-	-
February	0.715	0.690 to 0.741	0.0001
March	0.654	0.631 to 0.679	0.0001
April	0.672	0.649 to 0.697	0.0001
May	0.688	0.664 to 0.713	0.0001
June	0.712	0.687 to 0.737	0.0001
July	0.682	0.658 to 0.707	0.0001
August	0.529	0.509 to 0.549	0.0001
September	0.718	0.693 to 0.744	0.0001
October	0.730	0.705 to 0.756	0.0001
November	0.782	0.755 to 0.809	0.0001
December	0.811	0.784 to 0.839	0.0001

* Wald test, derived via Poisson regression.

** Adjusted for municipality and year.

Malaria Species

Figure 5 illustrates the trends in *P. falciparum* and *P. vivax* API from 1983 to 1993 in Roraima. There is a gradual decline in *Plasmodium falciparum*, with constant predominance of *P. vivax* from 1985. API for mixed infection did not change over time.

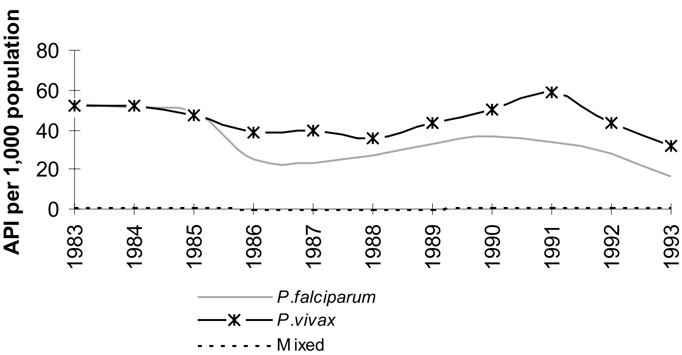

Fig. 5 - Annual Parasite Index for specific types of Plasmodium in Roraima (1983-1993).

Table 3 shows percentage of parasite species in total positive slides for each municipality during 1991 to 1993. *P. vivax* predominated in all municipalities, varying from 59% to 84% of the total positive slides. *P. falciparum* varied from 15% to 39% and mixed infection followed the distribution of *P. falciparum.*

Table 3
Percentage* of slides with *P. vivax, P. falciparum* and mixed infection by municipality (1991-1993)

	Average Percentage (Standard Deviation)		
Municipality	**Mixed Infection**	***P. falciparum***	***P. vivax***
Boa Vista	1 (0.59)	39 (5.93)	59 (6.00)
Caracarai	1 (3.81)	23 (15.95)	75 (15.96)
Normandia	1 (2.30)	30 (13.94)	68 (14.20)
Bonfim	0.19 (0.44)	28 (8.95)	72 (9.05)
Alto Alegre	2 (1.24)	38 (10.31)	59 (10.59)
Mucajai	1 (1.54)	35 (9.19)	63 (9.60)
S. Luiz	0.06 (0.26)	18 (12.14)	81 (12.10)
S. J. Baliza	0.03 (0.17)	15 (11.92)	84 (11.92)

One-way analysis of variance.
P-value from F-test : mixed infection (p=0.0001);
P. falciparum (p=0.0001); *P. vivax* (p=0.0001).
*Percentage presented is the monthly mean during 1991 to 1993.

There was no statistically significant difference in the distribution of the *vivax/falciparum* ratio according to dry or wet season (p=0.1506) nor in the four seasonal categories (p=0.09). Further analysis by year showed no relationship between the *v/f* ratio and season.

Relationship between increase in population and API, or changes in API

Figure 6 shows the regression line and the regression coefficient which best describe the correlation between population growth and increasing malaria cases. There was no evidence of an association between population growth and API per 1,000 population in this period.

Figure 7 shows the correlation and linear regression with predict Y estimation between population growth and increasing API. There was no association described in the model and the regression coefficient was close to zero suggesting that the variables were not related.

DISCUSSION

There was no association between malaria frequency and rates of slides examined in Roraima, during 1991 to 1993. Malaria occurred throughout the year but the frequency in which it occurred varied considerably by municipality and year and marginally by season, with 15% more cases of malaria in the dry season. Compared to the baseline July to September (wet season), the number of malaria cases was 23% higher from January to March and 20% higher from October to December. *Plasmodium vivax* was the predominant species (ranging from 59% to 84% of positive slides). The *falciparum/vivax* ratio varied significantly between municipalities but not by season. During 1962 to 1993, there was no direct association between population growth and malaria risk or increase in malaria risk.

Variation in malaria frequency between municipalities may reflect to certain degree the balance between passive and active case-finding. This variation is unlikely to be fully explained by the testing frequency since the number of slides examined was not associated with the percentage of positive slides, suggesting that the variation in rates of slides examined reflects demand and thus that variation in the rate of positive slides diagnosed reflects a true variation in frequency of malaria. A further potential problem is misclassification as cases were registered according to the place of diagnosis rather than the place of infection and some might have been diagnosed and counted as a case in the neighboring municipality.

Other studies[5,9] in the Amazon basin have also described malaria as present throughout the year and a predominance during the dry season but with more marked variation than the 15% found in this. Studies done in Rondonia (western Amazon region) reported 40% to 60% more cases in the dry season than in the wet season[3,14]. The seasonal effect in our study may have been diluted by delays as data coming from remote areas were often entered as collected at the time of receipt at the FNS. Variation in climatic conditions, such as temperature and humidity have a profound effect on the life cycle of a mosquito and on the development of malaria parasites producing seasonal variation in the transmission of the disease[6,10]. If the mild variation in seasonal malaria incidence found in Roraima is true, an understanding of the reasons behind it would require information on other factors such as average rainfall and temperature during each season, vector density, migration and immunity in the population, deforestation and gold mining activities.

There is a possibility of a misclassification in diagnosis of malaria species. It is unlikely that this would have been frequent enough to affect the observed findings. Recent malaria studies in the Amazon basin have shown a similar proportion of plasmodium species as reported in Roraima, with predominance of *vivax* species, ranging from 65 to 85% of the total positive slides[2,3]. This is consistent with the area being a "frontier",

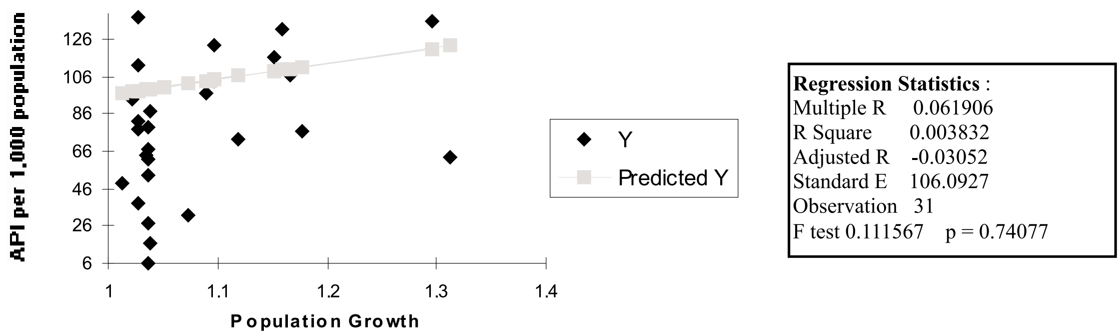

Fig. 6 - Linear regression between API per 1,000 population and population growth, Roraima (1962 to 1993).

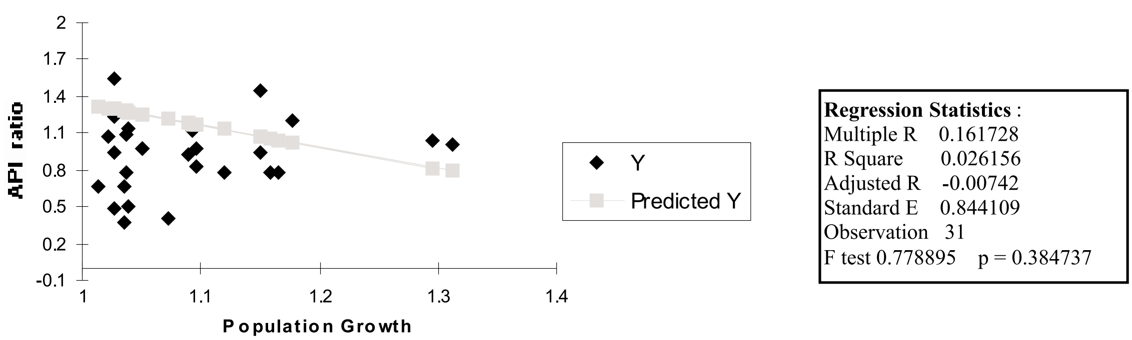

Fig. 7 - Linear regression between API ratio and population growth, Roraima (1962 to 1993).

"unstable" malaria epidemiological type. On the other hand, in Roraima even a municipality includes a very diverse environment and population (forest, Savannah, mountains, urban areas, indigenous population etc.). So, though the results showed a predominance of *vivax* over *falciparum*, stratification by areas smaller than a municipality may have found areas with predominance of *falciparum*.

The literature has consistently suggested that human mobility affects malaria transmission[7,15,16]. MARQUES[11] describes that the Amazon region received nearly 1 million immigrants from 1970 to 1980 and that frequency of malaria increased steadily over the same period. Studies done in some new colonization projects and new settlements in Rondonia also attributed the increasing malaria risk to population mobility[12,14]. In this data there was no direct association between changes in population in Roraima as a whole and frequency of malaria or even increases in frequency of malaria. Available routine demographic data might have underestimated the number of clandestine migrants. Data on overall population size does not differentiate between recent migrants to the area and long-term residents, and thus is not a good estimate of the number of susceptibles. Further stratification by municipality, ethnic group, urban/rural area and whether migrant or not might reveal an association between growth in specific subpopulations and malaria incidence. Information on age and sex of cases, changes in data collection, diagnostic procedures and malaria control programme over time and on number of slides examined before 1991 would also contribute to a better understanding of the complexity of the malaria epidemiology in Roraima and variations in malaria frequency from 1962 to 1993.

Alto Alegre and Mucajai, with the two highest reported API in the State, include forested areas where the indigenous group Yanomami live and also where a large concentration of clandestine minings exist. These factors may affect malaria transmission by changing the local environment, movement of individuals and contact between indigenous communities and migrants from other regions of the country. Another area with high API is Caracarai which has a large shipping port which deals with most of the imports to the State since the roads are in very poor condition. This results in Caracarai being an area of constant population movement and presumably generates contact between the local communities and immune or non-immune people coming from other regions of the country. Bonfim and Normandia, where API increased from 1991 to 1993, are areas with Savannah-like type of vegetation and inhabited by the indigenous people Makuxi, Wapixana, Taurepang and Ingarico. In early 1992 there was marked movement of miners toward their lands.

CONCLUSION

Roraima shares with other Amazonian states socio demographic characteristics of a colonization frontier with mining settlements, uncontrolled human migrations and environmental and geographical diversity. Based on the results of this analysis, malaria in Roraima can also be classified as a "frontier" epidemiological type where the frequency of malaria varies between areas, from year to year and from season to season, and *P. vivax* predominates. This, and the population mobility, suggests that this area is at risk of malaria outbreaks.

Malaria in Roraima however differs from that described in other Brazilian Amazon states by not showing a marked seasonal variation nor a clear relationship between frequency of disease and increasing population size in the last decades. The diversity of the Amazonian region should be borne in mind when undertaking research or providing services in the area.

RESUMO

Exame epidemiológico preliminar da malária no Estado de Roraima, na Bacia Amazônica, Brasil

Este estudo primeiramente descreve a epidemiologia da malária em Roraima, Bacia Amazônica, Brasil, entre 1991 a 1993: a predominância de especies de plasmódios, a distribuição de lâminas de sangue examinadas, o risco de malária e sua sazonalidade; e também investiga se o crescimento populacional de 1962 a 1993 estava associado com o aumento no risco de malária. A freqüência de malária variou significativamente entre os diversos municípios. Significativamente, mais casos de malária foram notificados durante a estação de seca (Outubro a Abril), mesmo depois de controlar por ano e município. *Vivax* foi o tipo predominante em todos os municípios, mas a razão entre tipos de plasmódios variou entre municípios. Nenhuma associação direta entre crescimento populacional e aumento no risco de malária entre 1962 e 1993 foi detectado. Malária em Roraima é do tipo epidemiológico dito "de fronteira", com alto potencial para epidemias.

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