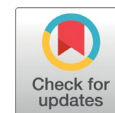




ORIGINAL ARTICLE



## Frequency of reagent samples for syphilis in pregnant women treated at Distrital Leste Laboratory, Manaus, Amazonas, Brazil

*Frequência de amostras reagentes para sífilis em gestantes atendidas no Laboratório Distrital Leste, Manaus, Amazonas, Brasil*

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### KEYWORDS

Congenital syphilis  
Diagnosis  
Disease prevention  
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### ABSTRACT

**Objective:** Checking the frequency of reagent samples for syphilis in pregnant women treated at the Distrital Leste Laboratory in the city of Manaus from January 2016 to December 2018, comparing the positive VDRL (Venereal Disease Research Laboratory) cases with the confirmatory FTA-Abs (Fluorescent Treponemal Antibody Absorption Test).

**Methods:** The study was cross-sectional and assessed the results of two syphilis diagnostic tests, VDRL and FTA-Abs. Data were obtained using the database of the electronic program SoftLab® and the Laboratory Environment Manager (GAL) and were quantitatively analyzed.

**Results:** In 2016, 9,028 VDRL tests were performed on pregnant women, 8,562 tests in 2017 and 5,064 in 2018. From this total, 1020 tested positive for syphilis; 392 in 2016, 320 in 2017 and 308 in 2018, increasing from 4 to 6%. Comparison with the FTA-Abs was only made possible in 2016 when the diagnosis was confirmed in 82% of the tests.

**Conclusion:** It was possible to check the frequency of pregnant women with positive and confirmatory results from 2016 to 2018, showing that although this pathology is easily preventable, it remains a challenging public health issue in pregnant women.

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**PALAVRAS-CHAVE**

Controle de infecções  
Diagnóstico  
Mulheres grávidas  
Prevenção de doenças  
Sífilis congênita

**RESUMO**

**Objetivo:** Verificar a frequência de amostras reagentes para sífilis em gestantes atendidas no Laboratório Distrital Leste da cidade de Manaus no período de janeiro de 2016 a dezembro de 2018, comparando os casos positivos de VDRL (*Venereal Disease Research Laboratory*) com o FTA-Abs (*Fluorescent Treponemal Antibody Absorption Test*) confirmatório.

**Métodos:** O estudo foi de caráter transversal avaliando resultados de dois testes para diagnóstico da sífilis, o VDRL e o FTA-Abs. Os dados foram obtidos por meio do banco de dados do programa eletrônico SoftLab® e Gerenciador de Ambiente Laboratorial (GAL) e analisados quantitativamente.

**Resultados:** Foram realizados 9.028 testes VDRL em gestantes em 2016, 8.562 em 2017 e 5.064 em 2018. Destes, 1.020 foram considerados positivos para a sífilis, sendo 392 em 2016, 320 em 2017 e 308 em 2018, resultando em um aumento de 4 para 6%. A relação com o FTA-Abs só foi possível em 2016 onde foi confirmado o diagnóstico em 82% dos testes.

**Conclusão:** Foi possível verificar a frequência de mulheres gestantes com resultados positivos e confirmatórios de 2016 a 2018 mostrando que, embora essa doença seja facilmente evitável, continua sendo um problema desafiador de saúde pública em mulheres grávidas.

**INTRODUCTION**

Still described as a serious global health issue today, syphilis is a chronic, infectious and contagious disease, exclusive to humans and asymptomatic in many cases, caused by the microorganism *Treponema pallidum*. It comprises two main forms of transmission, sexual and vertical, presenting itself in acquired and congenital forms; the latter occurs when the pregnant woman is not treated, or treatment is improperly performed. It remains asymptomatic in 70% of cases or can evolve to more severe cases<sup>1-3</sup>.

For congenital syphilis, the most pronounced risk factors are the absence of prenatal care, inadequate anamnesis, in addition to the lack of serology in the first trimesters of pregnancy, failure to acknowledge signs of maternal syphilis, and lack of treatment by the sexual partner, which increases the progression of the disease<sup>4-5</sup>.

Today, syphilis still affects many pregnant women worldwide; America has the second-highest incidence of congenital syphilis and the third-largest number of general cases<sup>6-7</sup>. It is estimated that nearly two million pregnant women are infected with active syphilis every year. However, only 10% are diagnosed and receive proper treatment, of which 90% occur in developing countries, although there are cases of reappearance in developed countries<sup>8</sup>.

In Brazil, approximately 50 thousand pregnant women are diagnosed with syphilis. Its prevalence is 1.1 to 11.5%, resulting in up to 12 thousand live births diagnosed with congenital syphilis<sup>9</sup>. Amazonas, specifically Manaus, lacks studies that focus on the positive diagnosis of syphilis in pregnant women. The Eastern District Laboratory, located in Manaus's eastern zone, treats 7,500 pregnant patients on average every year and requires research that can guide preventive measures to be adopted at an early stage for this group.

To date, there is no vaccine against syphilis and no protective immunity after contact with etiological agent *T. pallidum*, which allows the disease to be acquired whenever one is exposed to the bacteria<sup>5</sup>. However, recommendations for control include prevention and timely diagnosis, with particular attention to the most exposed populations<sup>10</sup>. Therefore, this research assessed

the frequency of pregnant women who tested positive for syphilis in the Distrital Leste Laboratory in the city of Manaus, from January 2016 to December 2018, comparing positive VDRL cases with the confirmatory FTA-Abs.

**METHODS**

This cross-sectional study assessed the frequency of a given disease in a given group and collected retrospective data<sup>11</sup>. The studied sample was pregnant women who underwent VDRL testing, from January 2016 to December 2018, at the Distrital Leste Laboratory (LDL), of the Municipal Health Department of Manaus (SEMSA), Amazonas, Brazil, located in the East Zone of the city.

In order to characterize the frequency of the disease, data were collected from two immunological tests: VDRL (Venereal Disease Research Laboratory) and FTA-Abs (Fluorescent Treponemal Antibody Absorption Test) - the latter is to confirm the VDRL reagent tests (cut-off value of 1:2) - both obtained through a local electronic bank (SoftLab™) and the GAL (Laboratory Environment Manager).

Data was quantitatively analyzed, as such analysis utilizes data collection to test hypotheses, based on numerical measurements and statistical analysis that allows the establishment of standards and the proving of theories<sup>12</sup>.

This research was conducted according to the principles expressed in the Declaration of Helsinki and was approved by the State University of Amazonas's Research Ethics Committee under number 3.140.866.

**RESULTS**

The Distrital Leste Laboratory (LDL) performed 22,654 VDRL tests on pregnant women; 9,028 in 2016, 8,562 in 2017 and 5,064 in 2018. From this total, 1,020 tested positives for syphilis; 392 in 2016, 320 in 2017, and 308 in 2018. This result shows a decrease in the number of positive samples compared to 2016 and nearly a 50% decrease in the demand for testing in 2018.

However, the comparison between reactive and non-reactive tests each year showed that the percentage of reactive samples was 4% in 2016 and 2017, while it increased to 6% in 2018. Therefore, the total number of positive tests for syphilis represented 5% of the tests performed from 2016 to 2018.

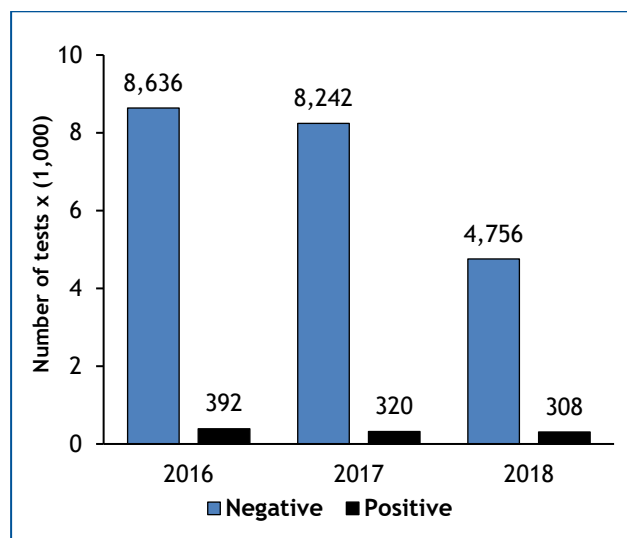
It is worth noting that these amounts include follow-up tests; that is, pregnant women diagnosed with syphilis were periodically re-tested to check the progress or return of the disease. Therefore, of the 1,020 positive samples, 192 were follow-up tests, of which 102, 83, and 7 comprised follow-ups in 2016, 2017, and 2018, respectively. Thus, the 828 new VDRL-positive test cases were distributed as follows: 290 in 2016, 213 in 2017, and 301 in 2018 (Figure 1) showing an increase in the incidence. In contrast, there was a decrease in the demand for follow-up tests.

Comparing the monthly distribution of positive cases for syphilis in pregnant women from 2016 to 2018 shows a decrease in almost all months of 2018, especially in July, compared to the months of 2016 (Figure 2). However, this may be due to less demand for the test or technical problems, such as the absence of reagents or system failures, which rendered it impossible for tests to be performed.

Regarding the age of the 828 pregnant women, it is possible to note that the VDRL test had more positive results in pregnant women aged 18 to 22 (Figure 3), totaling 129 tests in 2016, 104 in 2017, and 127 in 2018. It is also possible to observe a high rate of pregnant women aged 23 to 27, followed by those aged 13 to 17, demonstrating that the disease's highest incidence occurs in women aged 20 to 30.

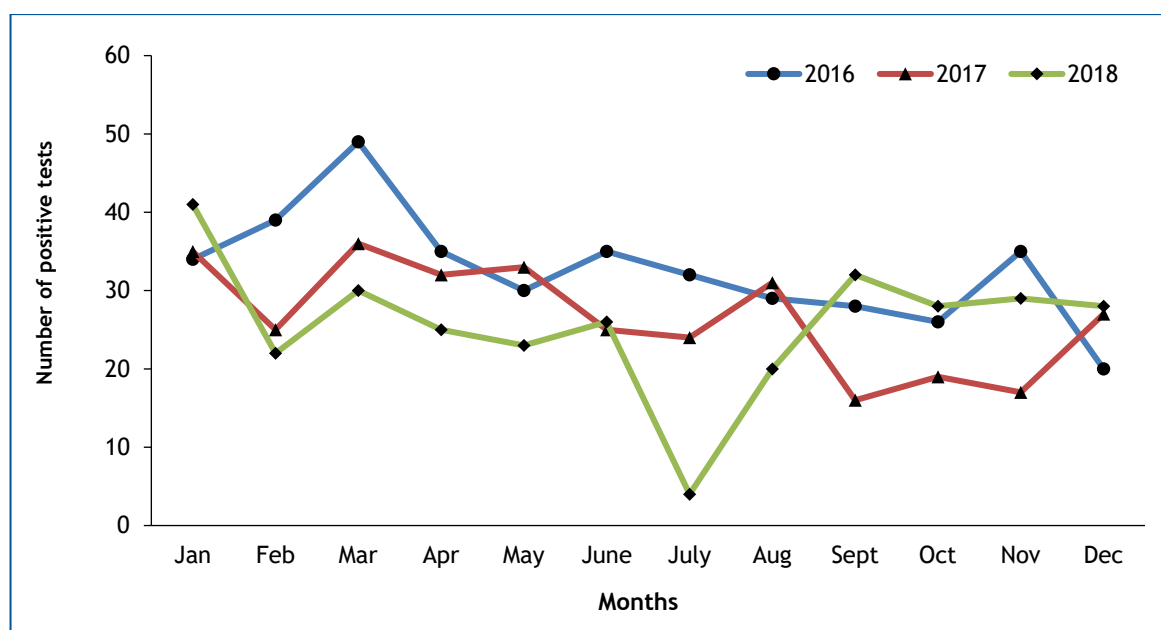
As for the gestation period, the number of pregnant women in the first trimester of pregnancy who had a positive result in the VDRL reached 52 in 2016, 56 in 2017 and 70 in 2018 (Figure 4). It is essential to highlight that these figures may be higher, considering that 135

pregnant women did not say their gestation period. However, the highest incidence of pregnant women who obtained a positive result in the VDRL test was found in the second ( $n = 318$ ) and third ( $n = 197$ ) trimester.



**Figure 1** - Distribution of syphilis tests (VDRL or FT-Abs) performed in pregnant women from 2016 to 2018. Manaus, AM, Brazil ( $N = 22,654$ ).

Regarding titration (Figure 5), 51% of the pregnant women presented a positive VDRL sample with low titration, i.e., 1:2 ( $n = 174$ ), 1:4 ( $n = 131$ ), and 1:8 ( $n = 118$ ). Among the high titers, the main registered were 1:16 ( $n = 110$ ), 1:32 ( $n = 113$ ), and 1:64 ( $n = 97$ ). However, 85 pregnant women still had extremely high titers, reaching 1:4096. Low titers were recorded for all years assessed, being 2018 the year with the lowest titers.



**Figure 2** - Monthly distribution of syphilis-positive tests (VDRL or FT-Abs) in pregnant women from 2016 to 2018. Manaus, AM, Brazil ( $n = 1,020$ ).

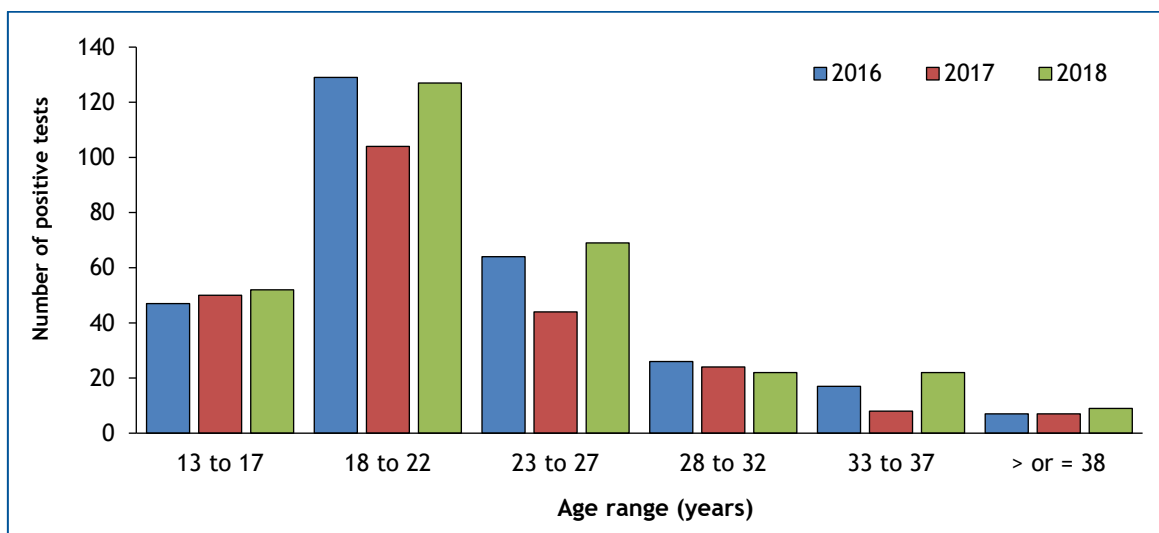


Figure 3 - Distribution of syphilis-positive tests (VDRL or FT-Abs) in pregnant women by age group, from 2016 to 2018. Manaus, AM, Brazil (n = 1,020).

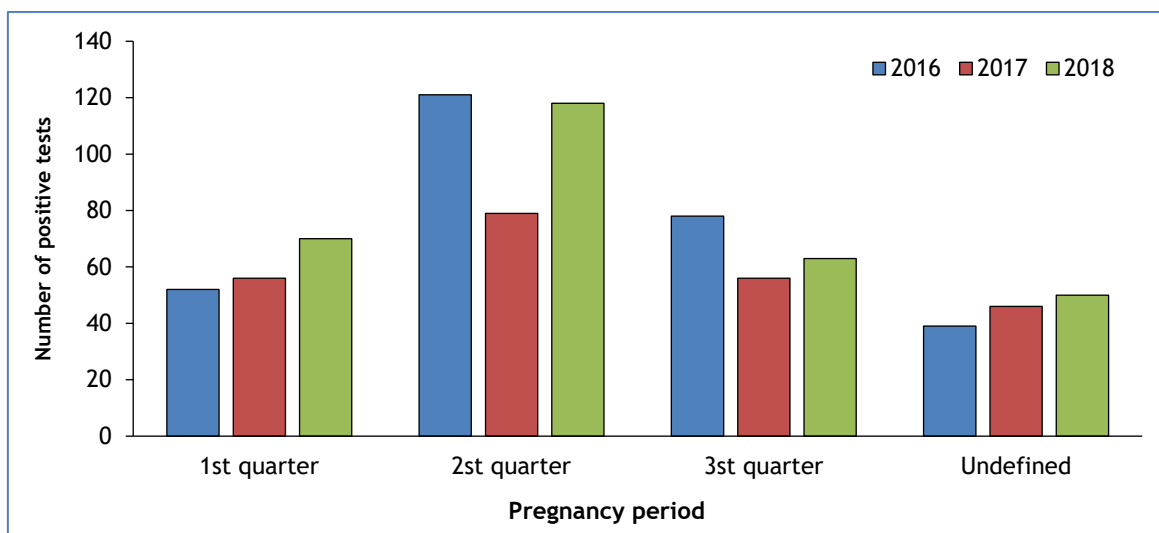


Figure 4 - Number of positive tests in pregnant women according to the gestation period in the years 2016 to 2018. Manaus, AM, Brazil (n = 1,020).

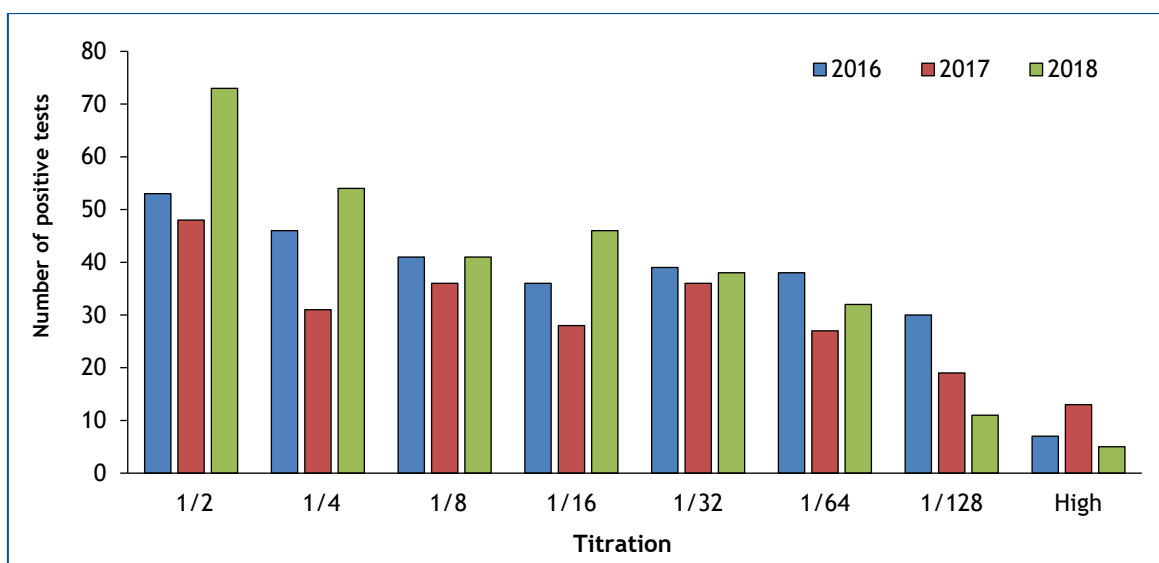


Figure 5 - Main titrations of the VDRL tests registered in pregnant women from 2016 to 2018. Manaus, Brazil (n = 1,020).

Regarding the FTA-Abs, a confirmatory test for syphilis, only data from 2016 were obtained, as the Central Laboratory of Public Health of Amazonas (LACEN/AM) could only perform a few tests in 2017 and 2018 due to the lack of resources, a significant setback. Therefore, only the 2016 data were analyzed. From the 290 pregnant women who obtained a positive VDRL result in 2016, syphilis was confirmed in 82% (n = 238) FTA-Abs tests, 8% tested negative (n = 23) and 10% (n = 29) were not tested.

## DISCUSSION

The Brazilian Ministry of Health recommends prenatal serological screening for syphilis and the realization of the VDRL test essentially during the first medical appointment. It should be repeated at the beginning of the third trimester if the woman obtains a negative result on the first test. For pregnant women who test positive in the first test, treatment must be monitored through periodic tests every month until the baby is born<sup>5</sup>.

For decades, the increase in syphilis cases has been reported worldwide, and congenital syphilis has been the main issue. To the extent that, in 2011, the incidence was 3.3 cases per 1,000 live births in Brazil; the northeast and southeast regions obtained the highest percentages. Such a rising number of new cases resulted in the intensification of campaigns to eradicate the disease by the end of 2015, according to the World Health Organization's goals<sup>13</sup>. However, the incidence in Brazil reached 6.8 cases per 1,000 live births in 2016. In Manaus, the rate was 10/1,000 live births for the same period<sup>14</sup>. Therefore, it was observed that this rate would increase to 50/1,000 live births if no early detection occurred in 5% of pregnant women who had a positive VDRL result.

In this context, initial detection becomes essential for reducing congenital syphilis. However, in Manaus, the obtained results demonstrate that this challenge is still far from being overcome. Nevertheless, one can see that the strong tendency in the incidence rate of syphilis in pregnant women is due to a considerable increase in the number of notifications rather than an actual increase in the number of cases. Therefore, these data should not be misinterpreted, as the observed behavior may not reflect the actual situation of the disease in the country. Lower incidence rates of congenital syphilis could demonstrate a possible deficiency in early diagnosis and timely notification of syphilis cases in pregnant women<sup>14</sup>.

According to the Technical Manual for the Diagnosis of Syphilis<sup>15</sup> of the National Quality Control Program, it is estimated that false-positive results occur in 0.2 to 0.8% of the tests and, in general, are associated with titers of less than 1:4. However, it is essential to note that this cannot define suspected false-positive cases. According to the World Health Organization<sup>16</sup>, samples with false-positive results may also have high titers, for example, in people who use injectable drugs and HIV and leprosy carriers.

It is noteworthy to understand that the non-treponemal test (VDRL) alone does not determine

syphilis diagnosis. The diagnosis must be confirmed through a treponemal test such as the FTA-Abs. These tests are also useful in diagnosing late syphilis since in approximately 85% of cases treponemal tests remain positive throughout the life of syphilis carriers, due to their high sensitivity<sup>5</sup>.

Recently, Brazil has shown a considerable increase in the number of syphilis cases. This increase is considered three times higher than that of 2010 and 2016, when there were approximately 6.8 and 12.4 cases/1,000 live births, respectively<sup>14</sup>. The considerable increase in the amount of congenital syphilis and syphilis cases in pregnant women can be mainly attributed to a reduction in the use of condoms, an increase in testing coverage, low supply of antibiotics, among others. In contrast, an improved surveillance system can affect the number of reported cases<sup>14,17</sup>.

However, in this research, we observed a notable increase in the cases of syphilitic pregnant women in the eastern zone of Manaus, supporting the pre-established hypothesis, since, in 2018, the number of positive cases increased, and that of tests performed decreased. This is due to failure to perform confirmatory FTA-Abs tests for comparison with the positive VDRL tests, caused by the lack of test kits in the Central Laboratory, which performs the confirmatory tests of all district units of the city. Thus, comparing 100% of the VDRL-FTA-Abs tests performed in pregnant women, as initially defined in the research, was not possible.

Despite being easily preventable, this disease remains a challenging public health issue. It is observed that, despite the importance of conducting screening and confirmatory tests in pregnant women and the population in general, these people are still neglected within municipal, state, or federal programs and public policies. There are still discontinuities in diagnoses and treatments in certain state localities, which should not occur when faced with a threat that can lead pregnant women and unborn children to irreparable damage. The results allowed us to visualize an increase in the frequency of pregnant patients with a positive VDRL test result for this period. Based on these data, proposals can be made for raising public awareness of this disease and its consequences, stimulating the search for earlier diagnosis and treatment, in order to decrease the amount of cases at the local level.

## CONCLUSION

This ongoing work shows that although there are an effective diagnosis and treatment of congenital and gestational syphilis, it persists as a serious public health problem. The results showed an increase in the frequency of pregnant women with a positive VDRL test for the years 2016 and 2017. However, the number of tests performed in 2018 may influence these data. The highest rates of positive cases were between 18 and 22 years old in all study years. Based on these data, proposals can be made to make the population aware of the disease and its consequences, stimulating the search for an earlier diagnosis and treatment so that the number of cases decreases locally.

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### Indications about the contributions of each author:

Conception and design of the study: RGSF, CPA  
 Analysis and interpretation of data: JCC, APO, CPA, RGSF  
 Data collection: RGSF, JCC, APO  
 Writing of the manuscript: CPA, JCC, APO  
 Critical revision of the article: RGSF, CPA  
 Final approval of the manuscript\*: RGSF, CPA, JCC, APO, ACCS, ESS, JTS  
 Statistical analysis: CPA  
 Overall responsibility: RGSF

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