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Original Article

Gestational toxoplasmosis serological transition in territories marked by environmental vulnerability*

Transição sorológica da toxoplasmose gestacional em territórios de vulnerabilidade ambiental

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Filipe Augusto de Freitas Soares[1,3]
Rômulo Oliveira Barros[2]
Kerla Joeline Lima Monteiro[1]
Maria Regina Reis Amendoeira[3]

ABSTRACT

Objective: to describe the temporal trend and spatial distribution of gestational toxoplasmosis in territories marked by socioenvironmental vulnerability. **Methods:** an observational study with a time-spatial approach based on laboratory records of pregnant women subjected to serological tests to detect infection by *Toxoplasma gondii*. The analyses included relative frequencies, trend assessments and spatial clustering to identify territorial susceptibility patterns. **Results:** predominance of acquired immunity and a high proportion of susceptible pregnant women were verified. A discrete inversion in the serological profile was observed from 2020 onwards, suggesting a reduction in environmental exposure to the parasite. Susceptibility proved to be higher among adolescents and young women. The spatial analysis evidenced three territorial patterns: High, Intermediate and Low susceptibility, with better immunity in the North area and more vulnerability in the Midsouth part of the state. **Conclusion:** the findings indicate a gestational toxoplasmosis serological transition, with a relative increase in the number of susceptible pregnant women in specific areas of the territory, reinforcing the importance of early screening, of retesting susceptible subjects and of regionalizing surveillance actions. **Contributions to practice:** the study supports improving the surveillance for gestational toxoplasmosis, guiding territorialized interventions during the pre-natal period, prioritizing vulnerable areas and strengthening public policies. **Descriptors**: Toxoplasmosis, Congenital; Seroepidemiologic Studies; Disease Susceptibility; Prenatal Care; Public Health Surveillance.

RESUMO

Objetivo: descrever a tendência temporal e a distribuição espacial da toxoplasmose gestacional em territórios de vulnerabilidade socioambiental. **Métodos:** estudo descritivo e observacional, com abordagem temporal e espacial a partir de registros laboratoriais de gestantes submetidas a exames sorológicos para detecção de infecção por *Toxoplasma gondii*. As análises incluíram frequências relativas, avaliação de tendência e agrupamento espacial para identificação de padrões territoriais de suscetibilidade. **Resultados:** verificou-se predominância de imunidade adquirida e proporção elevada de gestantes suscetíveis. A partir de 2020, observou-se discreta inversão do perfil sorológico, sugerindo redução da exposição ambiental ao parasito. A suscetibilidade mostrou-se mais elevada entre adolescentes e mulheres jovens. A análise espacial evidenciou três padrões territoriais: alta, intermediária e baixa suscetibilidade com maior imunidade na região norte e maior vulnerabilidade no centro-sul do estado. **Conclusão:** os achados indicam transição sorológica da toxoplasmose gestacional, com aumento relativo de gestantes suscetíveis em áreas específicas do território, reforçando a importância da triagem precoce, do reteste das suscetíveis e da regionalização das ações de vigilância. **Contribuições para a prática:** o estudo subsidia o aprimoramento da vigilância da toxoplasmose gestacional, orientando intervenções territorializadas no pré-natal, priorização de áreas vulneráveis e fortalecimento das políticas públicas. **Descritores**: Toxoplasmose Congênita; Estudos Soroepidemiológicos; Suscetibilidade a Doenças; Cuidado Pré-Natal; Vigilância em Saúde Pública.

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[1]Escritório Técnico Regional Fiocruz Piauí. Teresina, PI, Brazil.
[2]Instituto Federal do Piauí. Teresina, PI, Brazil.
[3]Instituto Oswaldo Cruz. Rio de Janeiro, RJ, Brazil.

Corresponding author:
Filipe Augusto de Freitas Soares
Rua Magalhães Filho, 519, Centro (Norte).
CEP: 64000-128. Teresina, PI, Brazil.
E-mail: filipesoaresthe@gmail.com

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Introduction

A disease caused by the *Toxoplasma gondii* infection, toxoplasmosis is one of the most relevant parasitoses for global Public Health. Its importance is even greater among pregnant women, due to the risk of vertical transmission and the development of the congenital form, associated with serious outcomes for the fetus and newborn. In humans, the infection is predominantly acquired through the intake of oocysts eliminated by cats that contaminate waters and soils or of tissue cysts found in raw or insufficiently cooked meat[1-2]. Although many infections remain asymptomatic, primary ones during pregnancy can evolve to miscarriages, stillbirths, ocular alterations and severe neurological lesions, exerting an important impact on maternal-child morbidity and mortality[3-4].

In Brazil, the prevalence of the infection by this parasite presents important variations across regions, influenced by behavioral and socioenvironmental factors and by those related to accessing health services. In particular, the Northeast region presents high exposure levels frequently associated with its hot and humid weather, with presence of domestic cats, with social vulnerability and with lesser access to basic sanitation and treated water[5-6]. On the other hand, recent improvements in urban living conditions and infrastructure have contributed to reducing environmental exposure to *T. gondii*, increasing the number of women with no previous serological evidence of the infection, characterized by absence of anti-*T. Gondii* IgG and suggesting a possible change in the infection serological profile. This serological transition scenario combines persistence of favorable conditions for transmission with formation of susceptibility foci among pregnant women, which demands differentiated responses from health surveillance services[7-8].

In this context, gestational toxoplasmosis in the northeastern states (mainly Piauí) represents a challenge for health professionals, managers and researchers. This is due to the coexistence of multiple classical risk factors for the infection and to a still insufficient serological screening coverage in pregnant women, even in a context characterized by high coverage levels in terms of Primary Health Care services. Similar studies can be used as a comparative parameter for other territories with the same environmental vulnerability profile[9-10].

The scarcity of population-based regional studies integrating time and spatial analyses from large laboratory databases limits understanding the disease dynamics in the Piauí territory, as well as identifying priority areas for intervention and surveillance. In this context, the objective of the current study was to describe the time trend and spatial distribution corresponding to gestational toxoplasmosis in territories marked by socioenvironmental vulnerability.

Methods

Research design type

This is a descriptive and observational study with time and space approach, based on secondary laboratory records from the Laboratory Management System (GAL) from the Piauí Public Health Central Laboratory (*Laboratório Central de Saúde Pública do Piauí*, LACEN-PI). The serological tests included were those used to detect antibodies against *T. gondii* in pregnant women, constituting a laboratory census encompassing the period from January 2018 to October 2024. This time clipping was adopted because it corresponds to the systematic standardization and availability of the GAL laboratory records in the state scope from 2018 onwards, allowing for a continuous time series analysis. The data were collected in November 2024.

Study population, selection criteria and sample calculation

The population under study was comprised by all the laboratory records corresponding to pregnant women living in municipalities from the state of Piauí

that underwent toxoplasmosis serological tests. The tests included were those classified as reactive, non-reactive or undetermined for the IgG and IgM antibodies. Duplicate records, without any identification of the municipality of residence or belonging to non-pregnant women were excluded. For being a census, all 110,593 valid records were analyzed and sample calculation was waived, which confers high precision to the estimates obtained.

Data collection and measuring instruments

The data were obtained directly from the GAL/LACEN-PI system and encompassed the last seven years, following audit and verification routines for information integrity. The variables extracted and analyzed were as follows: pregnant women's municipality of residence, maternal age, gestational age (when available), year when the test was performed and IgG and IgM serological results for *T. gondii*. The laboratory tests were performed according to protocols established by the state laboratory surveillance service, ensuring validity and reliability of the serological measurements used in classifying the immunological profiles.

Data analysis

The statistical treatment and analysis were performed in the R software (version 4.5.1), complemented by consistency routines in Microsoft Excel 365. The serological results were coded according to the laboratory record standard adopted in the GAL/LACEN-PI system (1 = Non-reactive, 2 = Reactive, 3 = Undetermined) and combined to define the following serological profiles: Susceptible to the infection (IgG−/IgM−); Infection in the past/Acquired immunity (IgG+/IgM−); Possible recent infection (IgG+/IgM+); and Undetermined (inconclusive IgG and or IgM).

Descriptive analyses with calculation of absolute and relative frequencies were performed, as well as an assessment of the time trend corresponding to the proportions of susceptible and immune women. In addition, the data were stratified by age group and gestational trimester; all records lacking gestational age were excluded from the analyses referring to this variable.

The spatial analysis consisted in aggregating the proportions of susceptible women across municipalities, only including those with at least 25 tests during the period, thus ensuring statistical stability. The data were linked to the official geographical grid of the state of Piauí and used to prepare choropleth maps, graphical representations in different shades of colors that show the spatial variation of the susceptibility proportions across municipalities. In order to identify territorial patterns, the unsupervised K-means clustering method was applied, defining three as the ideal number of clusters, according to the elbow criterion and to the silhouette index. Thus, the municipalities were classified into High susceptibility, Intermediate susceptibility and Low susceptibility/High immunity patterns, sorted according to the median of the susceptibility/immunity proportions observed in each group. A 5% significance level ($p<0.05$) was adopted for all the applicable statistical tests.

Ethical considerations

This study was approved by the Research Ethics Committee of the Oswaldo Cruz Institute, according to Certificate of Submission for Ethical Appraisal No. 69426223.1.0000.5248 and Opinion No. 6,120,671/2023. All the stages followed the ethical principles recommended in National Health Council Resolution No. 466/2012 and in the General Data Protection Law, ensuring information confidentiality and anonymity.

Results

Table 1 presents the combined distribution of the IgG and IgM results. Most of them (50.1%) presented reactive IgG and non-reactive IgM, indicating previous immunity; 45.2% were susceptible, but with no detectable antibodies; and reactive IgM was detected

in <0.1% (n=62) of the women. The undetermined cases corresponded to nearly 4.7%. "Negative" indicates absence of detectable antibodies; in turn, "Positive" represents presence of specific antibodies for *T. gondii*.

Table 1 – Absolute and relative frequencies corresponding to the combined serological results for *Toxoplasma gondii* in pregnant women. Teresina, PI, Brazil, 2018-2024

IgG ↓ / IgM →	Negative (%)	Positive (%)	Undetermined (%)	Total (%)
Negative	49,961 (45.2)	13 (0.0)	62 (0.0)	50,036 (45.2)
Positive	55,397 (50.1)	46 (0.0)	695 (0.6)	56,138 (50.8)
Undetermined	4,404 (4.0)	3 (0.00)	12 (0.0)	4,419 (4.0)
Total	109,762 (99.3)	62 (0.1)	769 (0.7)	110,593 (100.0)

IgG: Immunoglobulin G; IgM: Immunoglobulin M

Figure 1 presents the combined profiles, evidencing an inversion in the pattern after 2020, with predominance of susceptible pregnant women (IgG−/IgM−); immunized subjects (IgG+/IgM−); possible recent infection (IgG+/IgM+); isolated reactive IgM; and undetermined results (inconclusive IgG and/or IgM).

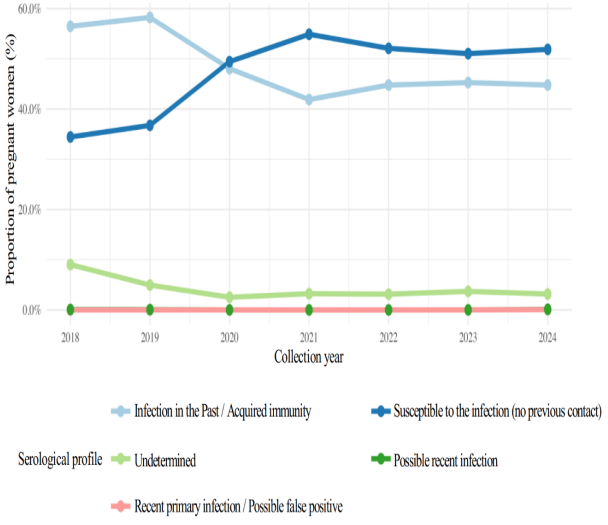

Figure 1 – Annual evolution of the serological profiles corresponding to *Toxoplasma gondii* in pregnant women. Teresina, PI, Brazil, 2018-2024

Figure 2 reveals higher susceptibility in the Midsouth and Southeast areas, and better immunity in northern and northeastern Piauí. The thematic map shows the proportion of susceptible women (IgG−/IgM−) by municipality (2018-2024). Purple represents areas with low proportions of susceptible subjects (high immunity), whereas yellow indicates areas with high proportion of susceptible women.

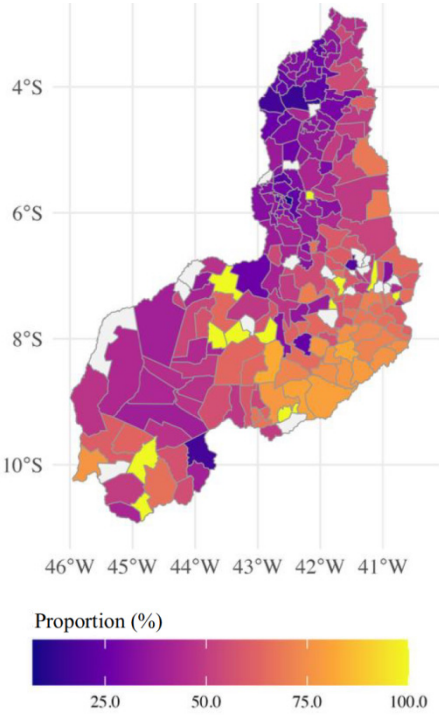

Figure 2 – Proportions of pregnant women susceptible to the infection (without previous contact), by municipality of residence. Teresina, PI, Brazil, 2018-2024

The spatial clustering analysis included 140 municipalities that met the sample stability criterion (≥25 tests). Three different territorial patterns for toxoplasmosis susceptibility were identified when applying the *K-means* method.

Cluster 2 grouped 48 municipalities (34.3%) characterized by high susceptibility, with a median of 71.07% of seronegative pregnant women for anti-*T. Gondii* IgG, reaching up to 84.62% in some places. These territories also presented low previous immunity levels (median of 28.93%), configuring areas marked by higher vulnerability to the primary infection during pregnancy.

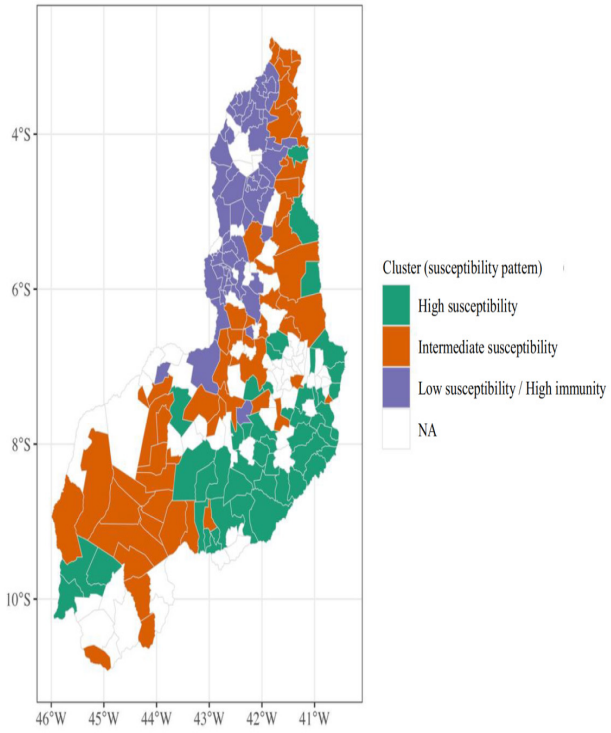

Figure 3 – Spatial distribution of the patterns corresponding to toxoplasmosis susceptibility in pregnant women, by municipality. Teresina, PI, Brazil, 2018-2024

Classified as with intermediate susceptibility, Cluster 1 was the most frequent one and encompassed 54 municipalities (38.6%) with a median close to 50%, indicating a balanced serological profile between susceptible and immune pregnant women.

Cluster 3 grouped 38 municipalities (27.1%) with low susceptibility and high immunity (median of 66.78%), suggesting higher historical environmental exposure to the parasite. The spatial distribution of these patterns evidenced high susceptibility concentration in the Midsouth region of the state; in turn, the municipalities with the highest immunity levels were predominantly from the North (Figure 3).

Table 2 shows a decreasing trend in susceptibility to the *T. gondii* infection as maternal age increased, indicating a higher proportion of acquired immunity among women from older age groups. The adolescent and young pregnant women (10-24 years old) presented higher susceptibility proportions; in turn, immunity prevailed among those aged over 30. The possible recent infection cases and the undetermined results presented low frequency values in all the age groups analyzed.

Table 2 – Proportional distribution of the serological profiles corresponding to *Toxoplasma gondii* according to the age group of the pregnant women tested. Teresina, PI, Brazil, 2018-2024

Age group (years old)	Susceptible to the infection (without previous contact)	Infection in the past / Acquired immunity	Undetermined	Possible recent infection	Recent primary infection / Possible false positive	Total tests
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
10-19	11,047 (51.4)	9,347 (43.5)	1,090 (5.1)	13 (0.1)	4 (0.0)	21,501 (19.4)
20-24	14,925 (48.5)	14,321 (46.6)	1,484 (4.8)	14 (0.0)	2 (0.0)	30,746 (27.8)
25-29	11,743 (44,8)	13,281 (50.6)	1,196 (4,6)	5 (0,0)	3 (0.0)	26,228 (23.7)
30-34	7,309 (39.3)	10,477 (56.4)	786 (4.2)	7 (0.0)	2 (0.0)	18,581 (16.8)
35-39	3,805 (37.1)	5,966 (58.2)	477 (4.6)	2 (0.0)	1 (0.0)	10,251 (9.3)
40-44	969 (34.2)	1,748 (61.7)	112 (4.0)	3 (0.1)	0 (0.0)	2,832 (2.6)
45-49	57 (26.3)	144 (66.4)	14 (6.5)	1 (0.5)	1 (0.5)	217 (0.2)
>50	14 (23.7)	40 (67.8)	4 (6.8)	1 (1.7)	0 (0.0)	59 (0.1)
Not reported	92 (51.7)	73 (41.0)	13 (7.3)	0 (0.0)	0 (0.0)	178 (0.2)
Total	49,961 (45.2)	55,397 (50.1)	5,176 (4.7)	46 (0.0)	13 (0.0)	110,593 (100.0)

Discussion

The findings of this study evidence that the state of Piauí presents a scenario marked by moderate endemicity and in a serological transition process regarding *T. gondii* infections, characterized by concomitance of pregnant women with acquired immunity and a significant proportion of women susceptible to the infection. Such configuration suggests progressive changes in the pattern of exposure to this parasite, possibly associated with fluctuations in the socioenvironmental, sanitary and behavioral conditions of the female population of reproductive age, a phenomenon also described in other Brazilian regions[11-13].

The distribution corresponding to susceptibility to *T. gondii* infections is heterogeneous in the territory. The influence exerted by environmental factors, eating and hygiene habits, access to treated water, cat population density and coverage of Primary Health Care services can be associated with this epidemiological scenario[12-13]. Some municipalities from the North and Northeast regions of the state (Parnaíba, Luís Correia and Piripiri) presented higher immunity proportions, suggesting previous cumulative exposure to the parasite. On the other hand, municipalities from the Midwest and Southeast (Picos, Floriano and São Raimundo Nonato) indicated a possible reduction in environmental exposure to the parasite and an increase in the number of women at a higher risk of primary infection during pregnancy.

Recent studies reinforce that susceptibility to the *T. gondii* infection is directly related not only to individual characteristics but also to territorial ones. In Currais Novos (Rio Grande do Norte), the highest seropositivity for the infection by this parasite was associated with inadequate sanitation conditions, more exposure to contaminated environmental sources and lesser scope of health prevention actions, representing a risk spatial pattern[14]. In addition, space-time analyses of childhood mortality associated with congenital toxoplasmosis performed in Brazil between 2000 and 2020 identified clusters mainly in the North and Northeast, regions with areas marked by deeper social vulnerability and lower care coverage, reinforcing the understanding that the infection organizes itself into specific territorial patterns that are sensitive to structural inequality and to frailty of the care network[15-16].

The clustering into three susceptibility patterns (High, Intermediate and Low) added programmatic value to the surveillance policies, as it allowed for a territorial focalization of educational, screening and follow-up pre-natal actions. Diverse evidence in Brazil associate higher susceptibility with social vulnerability and with lower Primary Health Care coverage, in addition to rural and peri-urban contexts[17-18]. Thus, regionalized strategies integrating laboratory surveillance, dietary education and pre-natal care prove to be in line with the national guidelines for the prevention and control of gestational toxoplasmosis[19-21].

The inversion in the serological profile noticed from 2020 onwards, with more susceptible than immunized women (even if slightly) suggests a transition in the seroprevalence of toxoplasmosis. This finding indicates a progressive reduction in environmental exposure to *T. gondii* and, consequently, an increase in the number of pregnant women at a higher risk of primary infections during pregnancy. Corroborating what has been described and combined with improved sanitary and Public Health conditions, the urbanization process may have contributed to this scenario[13,22-23]. In parallel, the COVID-19 pandemic exerted significant impacts on access to public health services during the same period, resulting in fewer appointments, pre-natal screening tests and case follow-ups[20]. Altogether, these phenomena support the hypothesis that recent socioenvironmental and situational changes have shaped the new epidemiological profile of gestational toxoplasmosis in Piauí.

In relation to the extremely low positivity for IgM antibodies, the analysis and interpretation should be cautious, as it may not only reflect low exposure to the parasite but also limitations inherent to the sero-

logical tests, such as the short life of IgM, variations in diagnostic sensitivity and the collection moment in relation to the infection. The progressive decline in the number of undetermined results suggests improvements in the technical processes and better standardization of the laboratory criteria throughout the period analyzed[24-26].

In relation to age groups, the higher susceptibility detected among adolescent and young women (aged between 10 and 24 years old) coincides with the peak fertility period. This finding points to prioritizing educational strategies and repeating the tests during the pre-natal period for susceptible women as essential actions for congenital toxoplasmosis prevention programs in the state of Piauí, as per the Ministry of Health recommendations[19-21].

As for the moment when the tests were performed by gestational trimesters, a progressive advance was noticed in recruiting pregnant women already in the first trimester, which indicates an improvement in adherence to the official early screening recommendations. However, incomplete filling-in of the "gestational age" record limits more in-depth analyses about the time dynamics of the infection, underscoring the need to qualify information systems to strengthen epidemiological surveillance[19,21,23].

Study limitations

The study presented limitations inherent to using secondary data, such as filling-in variability and inconsistencies in mandatory fields. The partially significant lack of information on gestational age in the records hindered performing more robust stratified analyses. The fact that the capital city (Teresina) was under-represented due to municipal laboratory processing reasons also restricted generalization of the findings for this municipality. Despite the limitations, the large sample size, the extended time series and having used spatial techniques with stability criteria (n≥25) conferred robustness to the analysis.

Contributions to practice

The results pointed to the need to strengthen early screening, to repeat serological tests in susceptible pregnant women and to regionalize actions according to territorial vulnerability patterns. Having identified spatial clusters allowed recognizing priority areas, supporting intersectoral planning in terms of surveillance, sanitation, primary care and health education, contributing to preventing congenital toxoplasmosis and to qualifying maternal-child care.

Conclusion

It was evidenced that congenital toxoplasmosis in the state of Piauí presents a serological transition scenario, with a relative increase in terms of susceptibility among pregnant women and heterogeneous distribution of immunity in the territory. Higher vulnerability was observed among adolescents and young women; in addition, it was noticed that three different susceptibility territorial patterns were formed. Regionalizing surveillance actions, early screening and retesting susceptible pregnant women emerged as essential measures to strengthen congenital toxoplasmosis prevention and to qualify pre-natal care in vulnerable areas.

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Authors' contributions

Idea and project or data analysis and interpretation; writing or critical review of the intellectual content; final approval of the version to be published; and full

responsibility for the accuracy and integrity of the manuscript: **Soares FAF**. Analysis and interpretation of the results, critical review of the intellectual content and final approval of the version to be published: **Barros RO**. Critical review of the intellectual content and final approval of the version to be published: **Monteiro KJL**. Study idea, critical review of the intellectual content and final approval of the version to be published: **Amendoeira MRR**.

Data availability

The data come from confidential laboratory records provided by the Piauí Public Health Central Laboratory and are subject to ethical and institutional restrictions related to the patients' confidentiality and to data protection. It is for this reason that the full dataset cannot be made publicly available. Nevertheless, the aggregated and anonymized data sustaining the results and conclusions of this study are presented in the full text of the article.

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