**Epidemiological Report** 

# **Toxoplasmosis acquired during pregnancy and Congenital Toxoplasmosis**

Historic Series 2010 – 2021

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#### INTRODUCTION

Toxoplasmosis is a zoonosis present in all countries, being one of the most widespread in the world. In Brazil, the infection has a high prevalence.

The clinical condition can range from asymptomatic infection to severe systemic manifestations. Despite this, most cases are asymptomatic, and clinical manifestations are present in the acute phase of the disease in between 10% and 20% of the infected adults. However, few of these adults have symptoms, as a healthy person's immune system usually prevents the parasite from causing illness. On the other hand, pregnant persons and individuals with compromised immune systems should be cautious, as a toxoplasma infection can cause serious health problems for them.<sup>1</sup>

In understanding the relevance of acknowledging the epidemiological scenario in the state of São Paulo (SSP), Brazil, toxoplasmosis has been considered a notifiable disease of regional interest. It used to be notified through ICD-10 B58.9 (unspecified toxoplasmosis), by the Notifiable Diseases Information System (SINAN), in the individual notification/conclusion form.

In this context, since 2015, the Health Surveillance Office of the Ministry of Health (SVS/ MS) has been working towards the construction of an integrated surveillance of toxoplasmosis in pregnancy, congenital toxoplasmosis, and toxoplasmosis acquired in outbreaks.<sup>2</sup> Thus, on February 17, 2016, Ordinance No. 205 was published, which defined a new national list of notifiable diseases and conditions, including toxoplasmosis in pregnancy (ICD-10 O98.6) and congenital toxoplasmosis (ICD-10 P37.1), which must be correctly registered in SINAN in the related notification form. Thus, acquired toxoplasmosis should only be reported when detected in outbreaks, using ICD-10 B58.

### **ETIOLOGIC AGENT**

Toxoplasmosis is a zoonosis caused by an obligate intracellular protozoan, *Toxoplasma gondii*, whose intermediate reservoirs are birds, humans, and other mammals, and whose definitive reservoirs are cats and other felines. It can persist for long periods in humans and other animals, possibly even for life.



#### **MODE OF TRANSMISSION**

- Indirect
  - o **Oral**: consumption of undercooked meat (especially pork, lamb, and venison) contaminated with tissue cysts or shellfish (oysters, mollusks, or mussels) without thorough hand washing after handling; ingestion of food and water contaminated with oocysts or from knives, utensils, cutting boards, and other foods that have encounter raw meat or infected shellfish.
  - o **Rare routes**: inhalation of contaminated aerosols, accidental inoculation, transfusion with contaminated blood, or transplantation of infected organs.
- Vertical
  - o **Congenital**: transplacental transmission of the active form of the parasite to the fetus when the mother acquires the infection during pregnancy.

#### TREATMENT

Treatment for acquired toxoplasmosis is recommended only in symptomatic cases when the individual is immunocompetent. There are, however, exceptions: acute infection during pregnancy, duration of impairment of other organs, such as chorioretinitis and myocarditis, and atypical evolution of the disease. In pregnant people, newborns, and immunosuppressed patients, the treatment must follow the current recommendations in the documents published by the Ministry of Health. In addition, it is recommended to consult an ophthalmologist to screen for any ocular manifestation of toxoplasmosis.<sup>3</sup>

It should be noted that the drugs spiramycin, sulfadiazine, and pyrimethamine used in the treatment of the disease are made available free of charge by the Brazilian Unified Health System (SUS) and they belong to the Strategic Component of Pharmaceutical Care, according to the National Essential Medicine List (Rename 2020),<sup>4</sup> acquired by the Ministry of Health. The purchase of folinic acid (calcium folinate), which is also included in Rename, is a municipal responsibility. Exceptional cases must be handled in accordance with the protocols of the Women's Health Coordination and the Child Health and Breastfeeding Coordination of the Ministry of Health.<sup>3</sup>

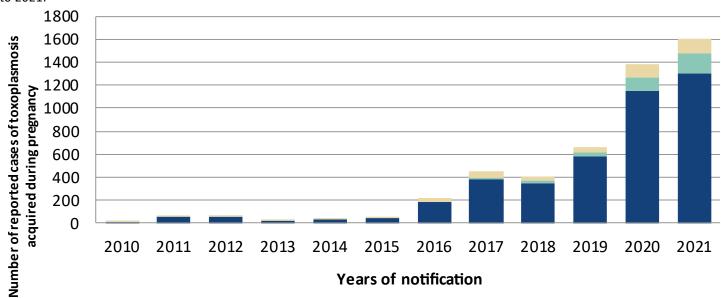
#### **EPIDEMIOLOGICAL SITUATION**

Considering the importance of understanding the epidemiological scenario of the disease, it is worth mentioning the national action of surveillance of toxoplasmosis in pregnancy and congenital toxoplasmosis, which consists of avoiding vertical transmission and detecting cases early to reduce the damage of intrauterine infection. These procedures are in line with the main objective of prenatal screening, which is the identification of pregnant people with acute toxoplasmosis for follow-up and treatment during pregnancy and the management of the child after birth.<sup>2</sup>

Thus, it should be noted that all reports using B58 (toxoplasmosis) and B58.9 (unspecified toxoplasmosis) have been carefully analyzed, which made it possible to identify cases that needed to be adjusted for the corresponding ICD-10. Thus, 2,755 records were reclassified as toxoplasmosis acquired during pregnancy and 88 as congenital toxoplasmosis, based on the observation of variables corresponding to age and gestational period. For analysis purposes, the other 639 notifications as B58 and B58.9 are not the subject of this report, since the recommendation is that the occurrence of toxoplasmosis in the general population should only be reported if linked to an outbreak with suspected food origin.

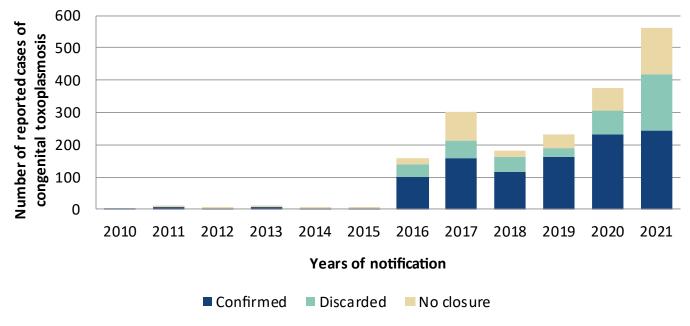
It is worth mentioning that all corrections related to the reclassification of cases according to the corresponding ICD-10 in the SINAN database were duly requested from the reporting municipalities, and the data correction process was monitored by the Division of Food and Waterborne Diseases (DFWD). It is already possible to verify the correction of 82 notifications in the period from May 2022 to July 2022.

That said, considering the cases of toxoplasmosis acquired during pregnancy and congenital toxoplasmosis, it is possible to observe that the number of records has been increasing over time (<u>Graphs 1</u> and <u>2</u>). This fact may be directly related to the regulation of the national compulsory notification, in 2016, and to the centralization in the Ministry of Health of the acquisition and financing of drugs (spiramycin, pyrimethamine, and sulfadiazine) for the treatment of the disease, in 2017.



**Graph 1**. Reported cases of toxoplasmosis acquired during pregnancy according to year of notification, SSP, Brazil, 2010 to 2021.\*

Source: DFWD/ESC/DCC/SHD-SP. \*Data extracted from SINAN and handled by DDTHA on June 2, 2022.



Graph 2. Reported cases of congenital toxoplasmosis according to year of notification, SSP, Brazil, 2010 to 2021.\*

Source: DFWD/ESC/DCC/SHD-SP. \*Data extracted from SINAN and handled by DDTHA on June 2, 2022.

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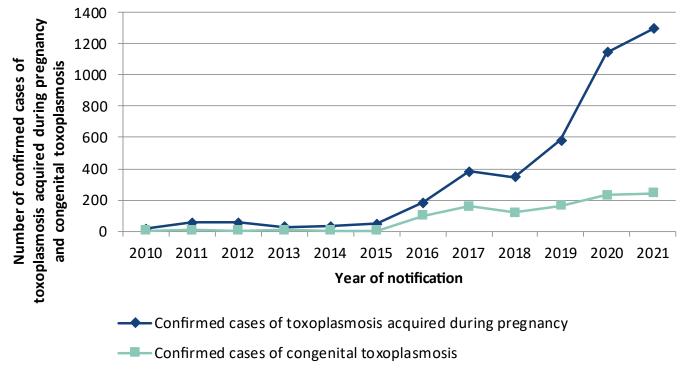
Thus, by Ordinance No. 1,897, of July 26, 2017, it was established that the drugs for the treatment of toxoplasmosis in pregnancy and congenital toxoplasmosis became part of Rename. This measure established greater rigor in the dispensing of these drugs, as it requires the nominal list of patients directly linked to the notification.

In this sense, when observing the cases registered in the system, it is possible to state that of the 5,015 notifications of toxoplasmosis acquired during pregnancy, 4,153 (82.8%) were confirmed, 381 (7.6%) were discarded, and 481 (9.6%) had not yet been closed. The year 2021 had the highest absolute number of reported cases (<u>Graph 1</u>).

The same behavior has been observed in the notifications of congenital toxoplasmosis, from the 1,847 notifications evaluated in the period, 1,035 (56%) were confirmed, 420 (22.7%) were discarded, and 392 (21.2%) had not yet been properly closed in the SINAN. This year had the highest absolute number of notifications (<u>Graph 2</u>).

By observing the confirmed cases reported, it is possible to infer that, at the time of production of this report, the context of toxoplasmosis in the SSP was still being identified, even with the increase in notifications. This is because, given the reasons presented above, it is not possible to say whether the state experiences an outbreak scenario or the occurrence of cases beyond the expected. In this sense, even considering that there is underreporting, there was not a higher number of confirmed cases of congenital toxoplasmosis than that of toxoplasmosis acquired during pregnancy. This shows a satisfactory behavior of the surveillance system regarding notification, which is an indicator that shows significant improvement from 2016 onwards (Graph 3).

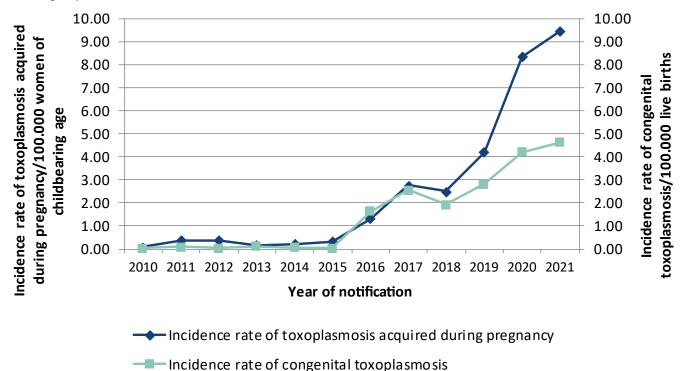




**Graph 3**. Confirmed cases of toxoplasmosis acquired during pregnancy and congenital toxoplasmosis according to year of notification, SSP, Brazil, 2010 to 2021.\*

In view of this, and considering data published by the Ministry of Health in its epidemiological report,<sup>5</sup> in which studies show the number of between 5 and 23 infected people for every 10,000 live births in Brazil, the ESP has not reached, so far, this range of detection. In 2021, there was an incidence of 4.6/10,000 live births in São Paulo (<u>Graph 4</u>).

Source: DFWD/ESC/DCC/SHD-SP. \*Data extracted from SINAN and handled by DDTHA on June 2, 2022.



**Graph 4**. Incidence rate of toxoplasmosis acquired during pregnancy and incidence rate of congenital toxoplasmosis according to year of notification, SSP, Brazil, 2010 to 2021.\*

Source: DFWD/ESC/DCC/SHD-SP. \*Data extracted from SINAN and handled by DDTHA on June 2, 2022.

Despite this, it is possible to note that from 2019 to 2020 the incidence rate of toxoplasmosis acquired during pregnancy more than doubled, going from 4.2 cases/100,000 women of childbearing age to 8.3 cases/100,000. When compared to previous years, it is possible to observe an upward trend in this rate, which reinforces the need for early detection and adequate treatment. This effort aims to reduce the incidence of congenital toxoplasmosis as much as possible, until, in an ideal scenario, there are no more cases of this nature.

For calculating the incidence rate for toxoplasmosis acquired during pregnancy, the female population of childbearing age for each year was used as denominator, that is, the total number of women aged 10 to 49 years, according to the definition of the Ministry of Health of 2008. As for the incidence rate of congenital toxoplasmosis, the denominator used was the number of live births each year, extracted from the State Data Analysis System Foundation.

When observing the distribution of notifications of confirmed cases by epidemiological surveillance group (ESG), it is noted that there is a higher incidence of toxoplasmosis acquired during pregnancy from 2016 onwards, without significant differences between the regions of the SSP. The

exception is ESG Itapeva, where it is possible to observe a higher incidence throughout the evaluated period (Table 1).

INCIDENCE	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Araçatuba	0.00	0.00	0.00	0.00	0.00	0.46	0.91	5.02	3.20	5.48	6.97	8.82
Araraquara	0.00	0.00	0.00	0.00	0.00	0.00	1.37	1.02	0.68	2.39	6.53	6.87
Assis	0.00	0.00	0.00	0.00	0.00	0.00	0.72	2.17	0.00	3.61	11.03	7.35
Barretos	0.00	0.00	0.00	0.00	0.00	0.80	0.00	1.59	1.59	0.00	11.41	7.34
Bauru	0.00	0.00	0.00	0.30	0.00	0.00	0.00	0.30	0.00	0.90	4.54	5.75
Botucatu	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.30	4.59	5.74	5.72	5.15
Campinas	0.00	0.15	0.00	0.00	0.31	0.15	0.15	0.59	1.48	2.21	3.21	5.40
Capital	0.00	0.00	0.00	0.00	0.00	0.03	1.25	3.79	2.94	4.88	5.15	7.92
Caraguatatuba	0.00	0.00	0.00	3.27	2.18	0.00	0.00	0.00	2.04	1.02	14.84	17.80
Franca	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.97	0.00	0.00	12.20	4.88
Franco da Rocha	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.55	11.64	18.51
Itapeva	9.24	5.78	8.09	0.00	3.47	10.55	16.40	22.26	31.64	35.15	40.75	27.57
Jales	0.00	0.00	0.00	0.00	0.00	0.00	4.07	9.50	4.07	4.07	7.10	12.78
Marília	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.10	7.95	7.95
Mogi das Cruzes	0.00	0.00	0.11	0.00	0.00	1.19	2.82	1.52	3.36	7.80	20.79	14.86
Osasco	0.11	0.43	0.22	0.65	0.76	0.53	2.14	2.24	0.96	1.82	8.02	9.74
Piracicaba	0.00	0.00	0.00	0.00	0.45	0.00	2.41	3.51	2.41	3.73	6.57	6.35
Presidente Prudente	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.49	0.00	1.49	13.76	8.41
Presidente Venceslau	0.00	0.00	0.00	0.00	0.00	1.19	3.57	5.95	4.76	8.33	13.59	8.65
Registro	3.56	3.56	0.00	1.19	1.19	3.60	1.20	4.79	7.19	20.37	20.76	21.98
Ribeirão Preto	0.00	0.00	0.00	0.00	0.00	0.91	0.91	3.42	3.20	1.83	14.42	11.27
Santo André	0.00	4.49	4.84	1.42	0.35	0.00	0.36	2.64	0.24	1.68	2.84	8.77
Santos	0.00	0.00	0.38	0.00	0.00	0.19	0.19	1.12	3.91	8.38	17.50	12.89
São João da Boa Vista	0.42	0.00	0.42	0.00	0.42	0.00	0.00	1.27	2.53	4.64	20.32	18.16
São José do Rio Preto	0.00	0.27	0.00	0.00	0.53	0.00	7.66	10.30	8.98	5.81	14.39	27.44
São José dos Campos	0.31	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.62	1.24	5.28
Sorocaba	0.00	0.00	0.00	0.32	0.63	0.77	0.77	4.01	3.70	6.94	8.11	10.86
Taubaté	0.00	0.00	0.00	0.00	0.31	0.93	1.87	3.11	1.24	5.29	9.44	8.18

**Table 1.** Incidence rate of toxoplasmosis acquired during pregnancy according to year of notification, by ESG of residence, SSP,Brazil, 2010 to 2021.\*

Source: DFWD/ESC/DCC/SHD-SP. \*Data extracted from SINAN and handled by DDTHA on June 2, 2022.

It is important to note that, referring to data by municipality, there is no concentration of cases in a specific city. In addition, it is possible to verify variation in the incidence rates in all the municipalities of ESG Itapeva in different years. This fact can point to two paths: there is a higher incidence of cases in this region, or the surveillance system is more sensitive to case detection.

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In addition, although more expressive rates of toxoplasmosis acquired during pregnancy are observed in ESG Itapeva, fortunately, over the period verified, this group does not concentrate the highest incidence of congenital toxoplasmosis (Table 2).

Table 2. Incidence rate of congenital toxoplasmosis according to year of notification, by ESG of residence, SSP, Brazil, 201	0
to 2021.*	

INCIDENCE	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Araçatuba	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.30	3.30	2.32	12.45	5.10
Araraquara	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.63	3.48	3.54	6.40
Assis	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.94	0.00	3.57	3.65	1.94
Barretos	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.90	1.96	2.03	4.18
Bauru	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.87	0.00	9.33	3.25
Botucatu	0.00	0.00	0.00	0.00	0.00	0.00	2.55	12.85	2.54	5.29	8.31	5.66
Campinas	0.00	0.18	0.00	0.00	0.00	0.00	0.17	0.83	1.82	1.03	1.81	2.43
Capital	0.00	0.06	0.00	0.06	0.00	0.00	1.85	3.77	2.00	3.28	2.74	5.68
Caraguatatuba	0.00	0.00	0.00	2.28	2.20	0.00	0.00	2.07	0.00	0.00	6.30	2.21
Franca	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.77	1.27
Franco da Rocha	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.11	1.13	3.53	1.19	7.25
Itapeva	0.00	0.00	0.00	0.00	0.00	0.00	2.48	4.93	2.41	7.18	2.53	0.00
Jales	0.00	0.00	0.00	0.00	0.00	0.00	3.63	6.66	0.00	0.00	3.52	0.00
Marília	0.00	0.00	0.00	0.00	0.00	0.00	1.33	0.00	1.29	7.99	12.46	4.34
Mogi das Cruzes	0.00	0.22	0.00	0.00	0.00	0.00	0.89	0.44	0.66	4.07	5.24	5.27
Osasco	0.00	0.00	0.00	0.20	0.00	0.00	4.13	5.89	6.36	3.65	4.11	3.33
Piracicaba	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.02	0.53	2.21	1.73
Presidente Prudente	0.00	0.00	0.00	0.00	0.00	0.00	1.73	3.36	0.00	1.80	7.52	5.98
Presidente Venceslau	0.00	0.00	0.00	0.00	0.00	0.00	2.85	0.00	0.00	0.00	6.49	3.42
Registro	4.95	2.41	0.00	0.00	2.42	0.00	0.00	0.00	0.00	21.22	5.53	5.66
Ribeirão Preto	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.56	0.56	1.14	7.06	11.65
Santo André	0.00	0.55	0.55	0.56	0.55	0.27	0.57	3.67	0.29	1.52	4.87	4.89
Santos	0.00	0.00	0.39	0.80	0.00	0.40	4.61	0.00	4.17	5.77	5.84	3.33
São João da Boa Vista	0.00	0.00	0.00	0.00	0.00	0.00	1.06	0.00	0.00	1.20	1.27	6.69
São José do Rio Preto	0.00	0.00	0.00	0.00	0.00	0.00	13.98	10.37	3.84	3.87	5.92	4.83
São José dos Campos	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	10.63	8.63
Sorocaba	0.00	0.00	0.00	0.00	0.00	0.33	0.34	0.66	1.00	1.39	2.84	2.56
Taubaté	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.71	2.95	3.08	4.00

Source: DFWD/ESC/DCC/SHD-SP. \*Data extracted from SINAN and handled by DDTHA on June 2, 2022.

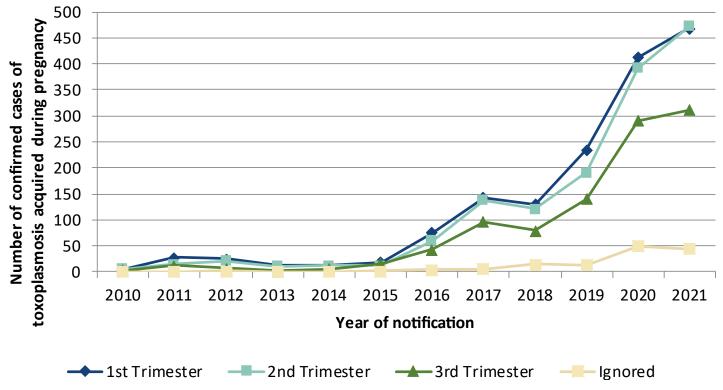
Thus, it is important to highlight the need for early detection of cases of toxoplasmosis acquired during pregnancy so that appropriate treatment can be carried out and, consequently, reduce vertical transmission.

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In 2021, the region of Ribeirão Preto had the highest incidence rate of congenital toxoplasmosis (11.65 cases/10,000 live births), followed by São José dos Campos (8.63 cases/10,000 live births). Among infected newborns, approximately 85% of the cases had no obvious clinical signs at birth. However, these children may have changes such as intrauterine growth restriction, prematurity, and visual and neurological abnormalities. Late sequelae are more frequent in untreated congenital toxoplasmosis. There are reports of previously undiagnosed sequelae of the disease appearing only in adolescence or adulthood.<sup>5</sup> Those with clinical manifestations may have signs in the neonatal period or in the first months of life. These cases usually have severe sequelae, such as visual impairment in varying degrees, intellectual disability, motor abnormalities, and deafness. The sequelae are even more frequent and more severe in newborns that already show signs at birth, such as visual impairment in varying degrees, intellectual disability, seizures, motor abnormalities, and deafness.<sup>5</sup>

From this perspective, regarding the detection of toxoplasmosis acquired during pregnancy, 38% (1,565) of confirmed cases from 2010 to 2021 were detected in the first trimester of pregnancy, 35% (1,449) in the second trimester, and 24% (1,008) in the third trimester, and in 3% this information was ignored. With the annual observation of the detection of cases, it is possible to state that the incidence is concentrated, over the years, mostly in the first and second trimesters of pregnancy.

It is worth noting that in the first infection of pregnant people, the risk of vertical transmission is 2% in the first eight weeks of pregnancy, 6% up to the 13th week, 72% up to the 36th week, and 81% when the primary infection occurs after the 36th week.<sup>5</sup> Thus, the highest concentration of toxoplasmosis acquired during pregnancy is expected to occur in the first trimester of pregnancy, a fact that was not observed in 2021, when 36.42% of the cases were detected in the second trimester (Graph 5).



**Graph 5**. Confirmed cases of toxoplasmosis acquired during pregnancy according to gestational age of detection, by year of notification, SSP, Brazil, 2010 to 2021.\*

In view of this, when the data by ESG is observed in the period evaluated, there is a need to observe the flows established in Jales, Santos, and Araraquara regarding the detection of toxoplasmosis acquired during pregnancy. This is because these ESG have the highest detection rate in the third trimester of pregnancy, being equivalent to 40%, 37.8%, and 36.4% of the cases, respectively (Graph 6).



Source: DFWD/ESC/DCC/SHD-SP. \*Data extracted from SINAN and handled by DDTHA on June 2, 2022.

Marília Araçatuba Franco da Rocha Mogi das Cruzes Caraguatatuba Bauru Registro Sorocaba Assis Taubaté Presidente Venceslau ESG of residence Ribeirão Preto São João da Boa Vista Santo André Capital Osasco Campinas São José do Rio Preto Itapeva São José dos Campos Botucatu Franca **Presidente Prudente** Piracicaba Araraquara Santos Jales 10.0% 20.0% 30.0% 40.0% 50.0% 60.0% 70.0% 80.0% 90.0% 100.0% 0.0% Detection rate of toxoplasmosis acquired during pregnancy 1st Trimster 2nd Trimester 3rd Trimester Ignored

**Graph 6**. Detection rate of toxoplasmosis acquired during pregnancy according to gestational age, by ESG of residence, SSP, Brazil, 2010 to 2021.\*

Source: DFWD/ESC/DCC/SHD-SP. \*Data extracted from SINAN and handled by DDTHA on June 2, 2022.

Source: DDTHA/CVE/COD/SESISP. # Data extracted from SINAN and Handled by DDTHAID SCHES2, 2022, ESC

Furthermore, the ESG Assis, Bauru, and Sorocaba stand out for having the highest detection rates of toxoplasmosis acquired during pregnancy in the first trimester, corresponding to 47.1%, 46.2%, and 45.5% of the cases, respectively.

#### FORMS OF PREVENTION

To prevent the emergence of new cases, the recommendations are:

- wash your hands when handling food;
- wash fruits and vegetables well before consuming them;
- do not eat raw or undercooked meats, including cold meats (salami, coppa, etc.);
- avoid contact with soil and garden soil if necessary, wear gloves and wash your hands thoroughly afterwards;
- avoid contact with cat feces in the garbage or soil;
- after handling raw meat, wash your hands well, as well as any surface that has come into contact with the food and all the utensils used;
- do not consume raw, unpasteurized milk and dairy products, whether from cow or goat;
- suggest that someone else clean the cat litter box and, if this is not possible, clean and change it daily, using gloves and a scoop;
- feed cats with cooked meat or kibble, do not allow them to ingest game; and
- wash your hands thoroughly after contact with animals.



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