

Intrauterine Toxoplasma infection – prenatal fetal ultrasound abnormalities and postnatal neonatal symptoms



Review of the literature and metaanalysis

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Objective: Examine the relationship between prenatal toxoplasma infection and postnatal complications according to scientific works of the last three decades on the topic of prenatal toxoplasma infection. **Methods:** All 1480 scientific articles available via PubMed and Embase published after 1995 and matching the search terms "toxoplasmosis", "ultrasound", "prenatal" and "infant" were screened, of which 610 abstracts and 105 full articles were reviewed. After exclusion according to the guidelines, 11 studies were analysed. The process was performed using Rayyan software.

Results: Of the 37 total cases, 4 cases of hydrops fetalis, 3 cases of ascites, 2 cases of pericardial and 2 cases of pleural effusion and 3 cases of hyperechogenic bowel were described. Brain parenchymal abnormalities were diagnosed in 15 cases, and ventriculomegaly in 19 cases. Hepatosplenomegaly was present in 3 cases. Out of the 37 investigated cases, we had data on the outcome of the pregnancy in 32 cases: there were 4 termination of pregnancy (TOP), and one case of intrauterine death. Out of 27 live births, one newborn died within 48 hours. The most common ophthalmological complication was chorioretinitis (n=16). During follow-up, 5 cases were described with severe musculoskeletal and neurological retardation, epileptic seizures and blindness.

Conclusion: Prenatal toxoplasma infection can have serious consequences for both the fetus and the newborn. In our literature review, we have tried to include case reports and comprehensive studies on this topic.

Keywords: toxoplasmosis, fetal ultrasound, postnatal symptoms, review of the literature

Introduction

Toxoplasmosis is an infection caused by *Toxoplasma gondii*, which can harm the fetus during pregnancy, along with rubella virus, cytomegalovirus, and Herpes simplex viruses (TORCH complex). In adult immunocompetent humans, the *Toxoplasma* infection is asymptomatic in half of the cases. In the remaining cases, it usually causes a mild, spontaneous illness with fever, maculopapular rash, headache, joint and limb pain and lymph node enlargement. However, in immunocompromised patients and newborn babies, it can lead to a serious and life-threatening illness.

Congenital toxoplasmosis can cause malformations or intrauterine death due to its vertical spread.

Pregnant women can contract toxoplasma parasites in two ways. Firstly (more commonly) through contact with infectious oocysts, e.g. consumption of undercooked infected meat, contact with cat litter. Less commonly, pre-existing toxoplasma infection in a dormant state may flare up in severe immunodeficiency states, for example, through over-infection with HIV.

PCR is the direct method with the highest sensitivity (97.7-100%) for the detection of toxoplasma infection [1]. Cerebrospinal fluid, peripheral blood, and amniotic fluid

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can also be used to perform the test. By definition, only the latter is suitable for the confirmation of intrauterine infection. The recommended time for PCR testing is at least four weeks from the suspected date of infection. Timely diagnosis and treatment are essential to avoid serious complications [2].

Among the indirect methods, the detection of immunoglobulin G and M from maternal blood is the most common. When interpreted in conjunction with ultrasound findings and other predisposing factors, it is a good screening method for the detection of a recent infection [3].

Treated toxoplasma infection reduces the chance of both pre- and postnatal complications. Among postnatal complications, all children with known congenital toxoplasma infection require close ophthalmologic follow-up until early adulthood because of ocular pathologies [4].

Fetal ultrasound signs that may alert to intrauterine infection are nonspecific: intracranial calcification, ventriculomegaly, hydrocephalus, hepatosplenomegaly with or without calcification involving the gastrointestinal system, and hyperechogenic bowel. In addition, ascites, pericardial effusion, hydrops, and polyhydramnios may be present. Intrauterine growth restriction/small for gestational age (IUGR/SGA) is often observed [5].

After birth, in 40% of confirmed cases of intrauterine infection, no abnormalities were found by routine neonatological investigations, but ophthalmological or neurological abnormalities were later confirmed [6]. The neonatological investigation should involve the co-specialists. In addition to serological investigations, it is worth checking the neonate's complete blood count and liver and kidney function values. MRI, if necessary lumbar puncture, ophthalmological examination are recommended. In newborns with organ damage, treatment should be started as soon as possible, and treated cases and suspected cases of infection should be kept under close pediatric supervision [5].

Ophthalmic follow-up and more frequent hearing screening are recommended. Ocular complications, early visual deterioration and hearing loss may be observed. Toxoplasmic chorioretinitis affects approximately 21,000 people worldwide each year [7].

Methods

All scientific articles available via PubMed and Embase published after 1995 and matching the search terms "toxoplasmosis", "ultrasound", "prenatal" and "infant" were screened. After a detailed analysis of the abstracts, we excluded those that were not written in English, summary studies, meta-analyses, experimental descriptions, or descriptions in

animal models, as well as articles that were not available through PubMed or Embase. In processing the abstracts, we excluded all articles that did not provide an adequate answer to our research question, i.e., which prenatal ultrasound abnormalities are associated with congenital toxoplasmosis. We excluded from processing all articles where toxoplasma and other TORCH infections were described collectively.

Results were processed using Microsoft Excel for Mac 16.86 (24060916) and statistical tests were performed using PSPP 2.0.1 for Mac.

Results

All together 1480 hits were obtained. 718 duplicates and 38 hits were excluded from processing due to foreign language. 114 animal or in vitro studies were also excluded. 610 abstracts were reviewed, of which 505 were excluded based on the guidelines detailed above. For 105 studies, the full text was analyzed. Of these, 11 studies were excluded because the full text was not available and in 83 cases the full text was not relevant to the research question. The process was carried out using Rayyan software, *Figure 1*. summarises the decision process. A summary table of the cases described in the processed studies was prepared (*Tables 1 and 2*).

The mean maternal age in the studied cases was 29.27 ± 6.03 (n = 15, 22 cases not reported). 36 cases were diagnosed with positive maternal toxoplasma IgM, one case was diagnosed postnatally. There were 30 cases with positive toxoplasma PCR (from amniocentesis), 6 cases with no data, 1 case with no amniocentesis due to postnatal diagnosis. The mean time of seroconversion ranged from 11.42 ± 9.75 to 20.21 ± 7.47 weeks (predominantly in the second trimester). The first fetal ultrasound abnormality occurred at 25.86 ± 8.54 weeks gestation (n = 22, 15 cases with no data).

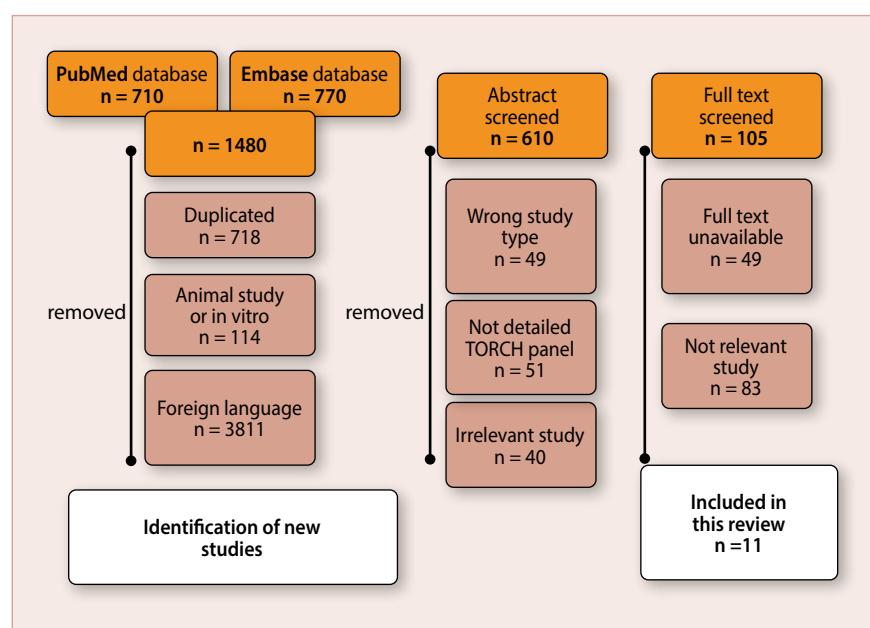


Figure 1. The algorithm we used for the systematic literature review for prenatal and postnatal analysis of toxoplasmosis.

Table 1. Summary of the cases of the processed studies. Prenatal examinations and ultrasound abnormalities during pregnancy in case of recent Toxoplasma infection

Author	Maternal age	Maternal IgM	Maternal PCR	Time of seroconversion	First US (gestational week)	First ultrasound signs										Other	Hepatosplenomegaly	Ventriculomegaly
						Hyperechogenic bowels	Brain parenchymal abnormalities	Pericardial fluid	Pleural fluid	Ascites	Hydrops fetalis	n	n	n	n			
Friedman et al 1999 [12]	26	ppp	p	N/A	27	x	x	x	x	x	x	n	10 mm	n	-			
Pedreira et al 2002 [13]	16	ppp	p	N/A	20	n	n	n	n	n	n	n	n	n	n	-		
Senat et al 1999 [14]	36	ppp	p	N/A	31	n	n	n	n	n	n	ipsilateral hyperechogenicity	16 mm unilateral	n	-			
Hernandez-Andrade et al 2002 [15]	N/A	ppp	p	N/A	22	n	n	n	n	n	n	n	n	mild	n	-		
	N/A	ppp	p	N/A	30	n	n	n	n	n	n	n	n	severe	n	-		
	N/A	ppp	p	N/A	24	n	n	n	n	n	n	n	n	severe	n	-		
	N/A	ppp	p	N/A	28	x	x	x	x	n	n	n	n	n	n	-		
	N/A	ppp	p	N/A	31	n	n	n	n	n	x	n	n	mild	n	-		
Malinger et al 2011 [16]	32	ppp	p	N/A	N/A	x	n	n	n	n	n	n	n	severe	n	-		
	33	ppp	p	N/A	N/A	n	n	n	n	n	n	n	n	severe	n	-		
	31	ppp	p	N/A	N/A	n	n	n	n	n	n	n	n	n	n	-		
	24	ppp	p	N/A	N/A	n	n	n	n	n	n	n	n	mild	n	-		
	29	ppp	p	N/A	N/A	n	n	n	n	n	n	n	n	severe	n	-		
	33	ppp	p	N/A	N/A	n	n	n	n	n	n	n	n	mild	n	-		
	34	ppp	N/A	28-30	N/A	n	n	n	n	n	n	n	n	severe	n	-		
	26	ppp	N/A	6-20	N/A	n	n	n	n	n	n	n	n	mild	n	-		
O'Connor et al 2012 [17]	36	ppp	N/A	1-8	12	n	n	n	n	n	n	n	n	n	n	n	-	
Blaakaer et al 1986 [18]	28	PN	PN	PN	33	n	x	n	n	n	x	n	n	n	n	n	-	
Estrada 2017 [19]	19	ppp	N/A	1-6	11	n	n	n	n	n	n	n	n	n	n	n	-	
Desai et al 1994 [20]	35	p	N/A	12. hét	30	n	n	n	n	n	n	n	14 mm	n	AUS			

Table 1. Summary of the cases of the processed studies. Prenatal examinations and ultrasound abnormalities during pregnancy in case of recent Toxoplasma infection (continued)

Author	First ultrasound signs											Other	
	Brain parenchymal abnormalities		Hyperechogenic bowels		Ventriculomegaly								
Maternal age	Maternal IgM	Maternal PCR	Time of seroconversion	First US (gestational week)	Hydrops fetalis	Ascites	Pleural fluid	Pericardial fluid	Hyperechogenic bowels	Brain parenchymal abnormalities	Ventriculomegaly	Other	
Dhombres et al 2016 [21]	N/A	p	p	22-27	33	n	n	n	n	5-10 parenchymal nodular foci; 1 thalamic nodular focus;	n	x	-
	N/A	p	p	22-27	34	n	n	n	n	7 parenchymal nodular foci; bilateral hyper-echo-genicity of the germinal matrix	n	x	-
	N/A	p	p	10-18	23	n	n	n	n	3 parenchymal nodular foci;	n	n	-
	N/A	p	p	11-20	29	n	n	n	n	2 parenchymal nodular foci;	n	n	-
	N/A	p	p	20-24	31	n	n	n	n	<5 parenchymal nodular foci;	n	n	-
	N/A	p	p	14-20	31	n	n	n	n	1 parenchymal focus;	n	n	-
	N/A	p	p	19	31	n	n	n	n	10 parenchymal nodular foci; extensive echogenic areas of the white matter in subcortical, periaqueductal and periventricular regions;	n	x	-
	N/A	p	p	1-22	26	n	n	n	n	10 parenchymal nodular foci;	n	n	-
	N/A	p	p	1-30	32	x	n	n	n	multiple parenchymal nodular foci;	n	n	-
DiCarlo et al 2011 [22]	N/A	p	N/A	25	N/A	n	n	n	n	calcification	n	n	-
	N/A	p	p	23	N/A	n	n	n	n	calcification	n	n	SGA
	N/A	p	p	26	N/A	n	n	n	n	calcification	n	n	-
	N/A	p	p	20	N/A	n	n	n	n	calcification	x	n	SGA
	N/A	p	p	10	N/A	n	n	n	n	n	x	n	SGA
	N/A	p	p	26	N/A	n	n	n	n	n	x	n	SGA
	N/A	p	p	22	N/A	n	n	n	n	calcification	x	n	SGA
	N/A	p	p	12	N/A	n	n	n	n	n	x	n	SGA

N/A = not available, ppp = highly positive pp = intermediate positive, p = positive, n = normal, SGA = small for gestational age, x = it is present, PN = postnatal diagnose, AUS = arteria umbilicalis singularis

The most frequent prenatal ultrasound signals suggestive of congenital toxoplasma infection based on the available literature were tabulated and the reports were summarized. Of the 37 cases summarized, 4 cases of hydrops fetalis, 3 cases of ascites, 2 cases of pericardial effusion, 2 cases of pleural effusion and 3 cases of hyperechogenic bowel were described. Brain parenchymal abnormalities were diagnosed in 15 cases, and ventriculomegaly in 19 cases. Hepatosplenomegaly was present in 3 cases. Among other abnormalities, arteria umbilicalis singularis (AUS) and SGA were present. The results are summarized in *Table 3*.

Ventriculomegaly cases were divided into mild, moderate and severe cases. Where an exact figure was not available, ventriculomegaly between 10 and 12

mm was considered mild, between 12 and 15 mm was considered moderate, and above 15 mm were considered severe [8]. The sample mean was 12.69 ± 2.62 , i.e. mostly moderate severity. The distribution is shown in *Table 4*.

In 5 of the 37 cases examined, there is no data on whether prenatal antibiotic treatment was given. In 4 of the 32 cases where data was available, the pregnant woman did not receive prenatal treatment. In 28 cases where antibiotic treatment was given, sulfadiazine was used in 1 case, sulfadiazine and pyrimethamine were used in 19 cases, and the exact combination of prenatal treatment was not indicated in 8 cases.

In 8 cases, there is data on control ultrasound. Here, the previously seen abnormality was aggravated

Table 2. Summary of the cases of the studies processed. Control ultrasound examinations and postnatal follow-up in cases of recent gestational toxoplasmosis.

Author	Therapy	Control US during pregnancy					TOP / intrauterine exitus	Ophthalmic complication	Follow-up	
		Time of the follow-up US (GW)	Follow up US	Time of the 2 nd follow-up US (GW)	2 nd follow-up US	Postnatal imaging			Follow-up	
Friedman et al 1999 [12]	P + S	29	ascites decreased	31	ascites, hydrops, pleural and pericardial fluid decreased, ventriculomegaly progressed (13,9 mm)		bilateral chorioretinitis, macula haemorrhage (bilateral)	Cranial US: normal ventricles, normal parenchyma CT: periventricular calcification in the left temporal lobe and in the right anterior horn		mild hypotonia in the upper limbs
Pedreira et al 2002 [13]	S	33	splenomegaly	–	–		microphthalmia and cataracta on the right eye, amaurosis	Abdominal US: hepatosplenomegaly Cranial CT: ventriculomegaly and intracranial calcification		mild mental and motor development delay
Senat et al 1999 [14]	not received	32	progressive hydrocephalus	–	–	33 rd week	–	–	–	–
Hernandez-Andrade et al 2002 [15]	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table 2. Summary of the cases of the studies processed. Control ultrasound examinations and postnatal follow-up in cases of recent gestational toxoplasmosis (continued)

Author	Therapy	Controll US during pregnancy					Ophthalmic complication	Follow-up		Follow-up
		Time of the follow-up US (GW)	Follow up US	Time of the 2 nd follow-up US (GW)	2 nd follow-up US	TOP / intrauterine exitus		Postnatal imaging		
Malinger et al 2011 [16]	received	–	–	–	–	in utero 35. hétten	–	–	–	–
	received	–	–	–	–	choroido-retinitis	CT: hydrocephalus, intracranial calcification	development delay, epilepsy, blindness	development delay, epilepsy, blindness	development delay, epilepsy, blindness
	received	–	–	–	–	choroido-retinitis	US: hydrocephalus, intracranial calcification	–	–	–
	received	–	–	–	–	choroido-retinitis	CT: hydrocephalus, intracranial calcification	development delay, epilepsy, blindness	development delay, epilepsy, blindness	development delay, epilepsy, blindness
	received	–	–	–	–	choroido-retinitis	CT: hydrocephalus, intracranial calcification	development delay, epilepsy, blindness	development delay, epilepsy, blindness	development delay, epilepsy, blindness
	received	–	–	–	–	choroido-retinitis	CT: intracranial calcification	–	–	–
	received	–	–	–	–	choroido-retinitis	US and MRI: hydrocephalus, intracranial calcification	development delay	development delay	development delay
	received	–	–	–	–	–	–	–	postnatal exitus in 48h	postnatal exitus in 48h
O'Connor et al 2012 [17]	not received	28	ventriculo megaly	30	progressive ventriculomegaly	–	MRI: complete destruction of the posterior, parietal and occipital lobe, decreased white matter, subcortical cysts, intracranial calcification Abdominal US: hepatosplenomegaly	–	N/A	N/A

Table 2. Summary of the cases of the studies processed. Control ultrasound examinations and postnatal follow-up in cases of recent gestational toxoplasmosis (continued)

Author	Therapy	Controll US during pregnancy					Ophthalmic complication	Follow-up		Follow-up
		Time of the follow-up US (GW)	Follow up US	Time of the 2 nd follow-up US (GW)	2 nd follow-up US	TOP / intrauterine exitus		Postnatal imaging		
Blaakaer et al 1986 [18]	not received	–	–	–	–	–	micro-phthalmy (left sided) and periferal chorioretinitis	US: mild hydrocephalus		
Estrada 2017 [19]	not received	3. trimester	unilateralis szájpad-hasadék	–	–	–	ipsilateral anophthalmy and 3 rd type craniofacial cleft palate			normal neuro-development
Desai et al 1994 [20]	P + S	33	progressive ventriculomegaly	34	ventriculomegaly and polyhydramnios		bilateralis chorioretinitis	US: lateral ventriculomegaly, intracranial calcificatio		
Dhom-bres et al 2016 [21]	P + S	–	–	–	–	–	normal	normal	normal	
	P + S	–	–	–	–	–	ventriculomegaly and polyhydramnios			normal neuro-development
	P + S	–	–	–	–	–	right sided chorioretinitis, right sided ambylopia			normal neuro-development
	P + S	–	–	–	–	–	normal			normal
	P + S	–	–	–	–	–	right sided chorioretinitis			normal neuro-development
	P + S	–	–	–	–	–	normal			normal
	P + S	31	progressive hepatosplenomegaly	–	–	33 rd week	–	–	–	hepatosplenomegaly, pulmonal laesion
	P + S	–	–	–	–	31 st week	–	–	–	no extracerebral malformation
	P + S	32	severe hydrops	–	–	34 th week	–	–	–	multi-visceral foeto-pathy

Table 2. Summary of the cases of the studies processed. Control ultrasound examinations and postnatal follow-up in cases of recent gestational toxoplasmosis (continued)

Author	Therapy	Control US during pregnancy					TOP / intrauterine exitus	Ophthalmic complication	Follow-up	
		Time of the follow-up US (GW)	Follow up US	Time of the 2 nd follow-up US (GW)	2 nd follow-up US	Postnatal imaging			Follow-up	
DiCarlo et al 2011 [22]	P + S	-	-	-	-	-		periventricular calcification		
	P + S	-	-	-	-	-		periventricular calcification		
	P + S	-	-	-	-	-		periventricular calcification		
	P + S	-	-	-	-	-		periventricular calcification	normal neuro-development	
	P + S	-	-	-	-	-	bilateral chorioretinitis	CT: intraparenchyma laesion		
	P + S	-	-	-	-	-	bilateral chorioretinitis	CT: intraparenchyma laesion		
	P + S	-	-	-	-	-	unilateral chorioretinitis			
	P + S	-	-	-	-	-	bilateral chorioretinitis	CT: intraparenchyma laesion		

P = pyrimethamine S = sulfadiazine N/A = not available TOP = termination of pregnancy GW = gestational week

Table 3. Percentage distribution of prenatal ultrasound abnormalities detected

n = 37	positive	data not available	percentage
hydrops	4	1	11,1%
ascites	3	0	8,1%
pleural fluid	2	0	5,4%
pericardial fluid	2	0	5,4%
hyperechogenic bowels	3	0	8,1%
brain parenchymal abnormalities	15	0	40,5%
ventriculomegaly	19	0	51,35%
hepatosplenomegaly	3	0	15,7%

Table 4. Severity and incidence of ventriculomegaly during prenatal ultrasound examination

	Frequency (n)	Percentage
negative	18	48,65%
mild	6	16,21%
intermediate	1	2,70%
severe	7	18,92%
no data on its size	5	13,52%
Total	37	100,0%

Table 5. Distribution of ophthalmic and neurological complications during neonatological follow-up. The percentage was calculated for the follow-up results (n = 20)

Opthalmic complications	Frequency (n)	Percentage
mild	11	55%
intermediate	6	30%
severe	1	5%
Neurological complications	Frequency (n)	Percentage
mild	2	10%
intermediate	3	15%
severe	3	15%

Table 6. Statistical analysis of the relationship between neonatal complications and prenatal ultrasound abnormalities and treatment using Spearman's coefficient on our data

	Spearman koefficiens	p
Hydrops	0.16	0.50
Ascites	0.03	0.903
Pericardial fluid	0.16	0.50
Pulmonal fluid	0.16	0.50
Hyperechogenic bowels	0.03	0.903
Brain parenchymal abnormalities	-0.69	0.001
Ventriculomegaly	0.61	0.001
Hepatosplenomegaly	-0.34	0.133
Prenatal therapy	-0.16	0.501

(although ascites decreased on control ultrasound in case 1, ventriculomegaly progressed).

There is no data regarding pregnancy outcome in 5 of the 37 cases studied. Of the 32 available cases, 4 resulted in termination of pregnancy (TOP), and in one case in utero exit at 35 weeks of gestation. There were 27 live births, of which one was reported as a perinatal exit (within 48 hours). Thus, follow-up was performed in 26 cases, of which 5 cases were missing data, and in one case only the results of imaging studies were reported by the authors (O' Connor).

The most common ocular complication was chorioretinitis (n = 16). During follow-up, 5 cases of severe musculoskeletal and neurological retardation, epileptic seizures and blindness were described. Complications were categorised according to severity. For opthalmic complications, mild severity was defined as mild chorioretinitis and unilateral chorioretinitis, moderate severity as bilateral chorioretinitis without subsequent ocular involvement, and severe complications as bilateral ocular involvement with blindness. For neurological involvement, mild was defined as mild mental and/or locomotor, moderate as moderate mental and/or locomotor, severe as severe mental and/or locomotor, and epileptic seizures. The mean of opthalmological complications (n = 18) was 1.44 ± 0.62 , and the mean of neurological

complications (n = 8) was 2.13 ± 0.83 , i.e., opthalmological abnormalities tended to be mild-to-moderate, whereas neurological abnormalities tended to be moderate-to-severe. The results are presented in *Table 5*.

We investigated whether the severity of complications was related to any prenatal factors (ultrasound findings, treatment). Our results are shown in *Table 6*. As can be seen, significant results were obtained only for ventriculomegaly and brain parenchymal abnormalities, where there is a weak positive correlation between ventriculomegaly and outcome. The test showed a weak negative correlation between brain volume abnormalities and outcome (the result is highly biased by the amount of data and the lack of follow-up, therefore it is unlikely to have clinical relevance, further analysis with larger data sets and more accurate statistical methods is recommended).

A limitation of our study is that in the early 2000s prenatal MRI was not widely used, and therefore in many cases ultrasound diagnosis was not confirmed. Moreover, the time of follow-up was variable in the reports, with only the perinatal period available in 3 case reports. As there is no extensive literature available on statistical analysis of toxoplasma and prenatal ultrasound diagnosis, we could rely mainly on case reports.

Discussion

Prenatal toxoplasma infection can have serious consequences for both the fetus and the mother. In our literature review, we included published case reports from the last 3 decades.

In 2020, Codaccioni et al. published a retrospective study from France, where 88 prenatally diagnosed cases of congenital toxoplasmosis were reviewed and followed up [9].

In our sample of cases, positive IgM serology was seen in all cases of prenatal diagnosis, with the average time of seroconversion in the second trimester. In Codaccioni's study, seroconversion occurred predominantly at the border of the first and second trimester, but it should be noted that we worked with much less data in this regard. The first positive ultrasound deviation also occurred predominantly in the second trimester.

The most common prenatal ultrasound abnormalities involved the nervous system, in the form of ventriculomegaly, and parenchymal abnormalities. A total of 34 fetuses (91.8%) had prenatal nervous system abnormalities. In the study by Codaccioni et al., this number was 80 (90%), which is proportionally similar to our study. It is therefore clear that abnormalities affecting the nervous system are present in almost all cases of congenital toxoplasmosis. In their study, Codaccioni et al. recorded a total of 15 different neurological abnormalities. In our systematic review, due to the heterogeneity of the data, only two neurological abnormalities (ventriculomegaly, and parenchymal abnormalities) were recorded, the most frequent (51.3%) being ventriculomegaly (50% in Codaccioni's work). It can be seen that ventriculomegaly, even if mild, raises the possibility of prenatal infection, and in such cases prenatal serology and PCR testing are recommended. Neurological ultrasound abnormalities as an indicator of congenital toxoplasmosis have been confirmed by several authors [2, 10].

Among ocular complications, chorioretinitis has been most frequently described, either unilateral or bilateral. The clinical significance of this is questionable, as there has been no long-term follow-up in the studies described and summarized above. Literature suggests that the long-term ocular prognosis is favourable, but this requires further research [11].

Conclusions

In conclusion, congenital toxoplasmosis is a highly heterogeneous pathology, the diagnosis and management of which still challenges clinicians today. It requires an experienced sonographer for its detection and, based on the ultrasound findings, the clinician needs to perform the appropriate serological and molecular tests to diagnose and treat congenital toxoplasmosis as soon as possible.

Prevention of toxoplasmosis is an important issue. Educating pregnant women is part of the prevention of infection. Pregnant women should avoid contact with cats, if they handle raw meat, unwashed fruits and vegetables,

thorough hand washing is recommended afterwards. Secondary prevention includes serological screening during pregnancy and close follow-up of seronegative pregnant women.

Several Hungarian publications also deal with the examination of toxoplasmosis during pregnancy. The publications discuss the rate of fresh maternal toxoplasmosis in cases of ultrasound abnormalities detected during pregnancy [23], examine the detection of Toxoplasma infection from amniotic fluid using quantitative real-time PCR [24], and examine the seroepidemiological situation of the infection in our country [25].

The literature also draws attention to the importance of ultrasound screening and the important role ultrasound examinations play in the diagnosis of the disease. We consider it important to draw attention to ultrasound signs indicating infection during the training of obstetricians and gynecologists and sonographers.

Postnatal management requires an interdisciplinary team approach, involving pediatric ophthalmologists, neurologists, pediatricians, and allied health professionals for the best outcome.

As congenital toxoplasmosis still affects thousands of people worldwide today, further research and analysis is a very important topic. In the future, a prospective study with the involvement of co-specialists and the establishment of local registries could be considered.

REFERENCES

1. Galvani AT, Christ APG, Padula JA, et al. Real-time PCR detection of Toxoplasma gondii in surface water samples in São Paulo, Brazil. *Parasitol Res* 2019; 118(2): 631–640.
2. Bollani L, Auriti C, Achille C, Garofoli F, et al. Congenital Toxoplasmosis: The State of the Art *Front Pediatr* 2022; 10: 894573.
3. Márquez-Mauricio A, Caballero-Ortega H, Gómez-Chávez F. Congenital Toxoplasmosis Diagnosis: Current Approaches and New Insights. *Acta Parasitol* 2023; 68(3): 473–480.
4. Kota AS, Shabbir N. Congenital Toxoplasmosis, in *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2023.
5. Saso A, Bamford A, Grewal K, Noori M, et al. Fifteen-minute consultation: Management of the infant born to a mother with toxoplasmosis in pregnancy. *Arch Dis Child Educ Pract Ed* 2020; 105(5): 262–269.
6. Guerina NG, Hsu HW, Meissner HC, Maguire JH, et al. Neonatal serologic screening and early treatment for congenital Toxoplasma gondii infection. The New England Regional Toxoplasma Working Group. *N Engl J Med* 1994; 330(26): 1858–63.
7. Deganich M, Boudreaux C, Benmerzouga I. Toxoplasmosis Infection during Pregnancy. *Trop Med Infect Dis* 2022; 8(1).
8. Giorgjone V, Haratz KK, Constantini S, et al. Fetal cerebral ventriculomegaly: What do we tell the prospective parents? *Prenat Diagn* 2022; 42(13): 1674–1681.
9. Codaccioni C, Picone O, Lambert V, et al. Ultrasound features of fetal toxoplasmosis: A contemporary multicenter survey in 88 fetuses. *Prenat Diagn* 2020; 40(13): 1741–1752.
10. Paquet C, Yudin MH. Toxoplasmosis in pregnancy: prevention, screening, and treatment. *J Obstet Gynaecol Can* 2013; 35(1): 78–81.
11. Wallon M, Kodjikian L, Binquet C, et al. Long-term ocular prognosis in 327 children with congenital toxoplasmosis. *Pediatrics* 2004; 113(6): 1567–72.
12. Friedman S, Ford-Jones LE, Toi A, et al. Congenital toxoplasmosis: prenatal diagnosis, treatment and postnatal outcome. *Prenat Diagn* 1999; 19(4): 330–3.
13. Pedreira DA, Diniz EM, Schultz R, et al. Fetal cataract in congenital toxoplasmosis. *Ultrasound Obstet Gynecol* 1999; 13(4): 266–7.
14. Senat MV, Bernard JP, Schwärzler P, Britten J, Ville Y. Prenatal diagnosis and follow-up of 14 cases of unilateral ventriculomegaly. *Ultrasound Obstet Gynecol* 1999; 14(5): 327–32.
15. Hernandez-Andrade E, Scheier M, Dezerega V, et al. Fetal middle cerebral artery peak systolic velocity in the investigation of non-immune hydrops. *Ultrasound Obstet Gynecol* 2004; 23(5): 442–5.

16. Malinge G, Werner H, Rodriguez Leonel JC, et al. Prenatal brain imaging in congenital toxoplasmosis. *Prenat Diagn* 2011; 31(9): 881–6.

17. O'Connor C, Stuart B, Turner MJ, Kennelly MM. A case of toxoplasmosis causing severe ventriculomegaly in association with reproductive immunotherapy. *J Obstet Gynaecol* 2012; 32(6): 595–6.

18. Blaakaer J. Ultrasonic diagnosis of fetal ascites and toxoplasmosis. *Acta Obstet Gynecol Scand* 1986; 65(6): 653–4.

19. Arce-Estrada GE, Gómez-Toscano V, Cedillo-Peláez C, et al. Report of an unusual case of anophthalmia and craniofacial cleft in a newborn with *Toxoplasma gondii* congenital infection. *BMC Infect Dis* 2017; 17(1): 459.

20. Desai MB, Kurtz AB, Martin ME, Wapner RJ. Characteristic findings of toxoplasmosis in utero: a case report. *J Ultrasound Med* 1994; 13(1): 60–2.

21. Dhombres F, Friszer S, Maurice P, Gonzales M, et al. Prognosis of Fetal Parenchymal Cerebral Lesions without Ventriculomegaly in Congenital Toxoplasmosis Infection. *Fetal Diagn Ther* 2017; 41(1): 8–14.

22. di Carlo P, Romano A, Casuccio A, Cillino S, et al. Investigation and management of *Toxoplasma gondii* infection in pregnancy and infancy: a prospective study. *Acta Pharmacol Sin* 2011; 32(8): 1063–70.

23. Beke A, Latkóczy K, Nagy GR, Dudnyikova A, Csaba Á, Szabó I, Papp C, Rigó J. Jr. Comparison of prevalence of toxoplasma and cytomegalovirus infection in cases with fetal ultrasound markers in the second trimester of pregnancy. *Prenat Diagn* 2011; 31(10): 945–8.

24. Nagy B, Lázár L, Nagy GR, Bán Z, Papp Z. *Toxoplasma gondii* kimutatása magzatvízből kvantitatív valós idejű PCR-módszerrel [Detection of *Toxoplasma gondii* in amniotic fluid using quantitative real-time PCR method]. *Orv Hetil* 2007; 148(20): 935–8.

25. Szécsényi M, Somogyvári F, Dóczsi I. A toxoplasmosis szeroepidemiológiai helyzete a várandós nők körében 2018 és 2022 között [Seroepidemiology of toxoplasmosis in pregnant women between 2018 and 2022]. *Orv Hetil* 2024; 165(5): 177–182.