Prevalencia de TORCH positivo y screening de parvovirus B19 en embarazos complicados por polihidramnios.

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Resumen en español.

OBJETIVO: El objetivo de este estudio fue evaluar la tasa de mujeres con polihidramnios que eventualmente se sometieron a un cribado positivo a enfermedad infecciosa mediante pruebas de detección de suero para TORCH y parvovirus B19.

MÉTODOS: Se trata de un estudio observacional retrospectivo en embarazos simples con diagnóstico de polihidramnios y con exámenes serológicos de TORCH y parvovirus B19. Los pacientes fueron seguidos con ultrasonidos en serie entre 2006 y 2013. Se revisaron las características maternas, la historia médica y obstétrica. Se revisaron los parámetros del ultrasonido, incluyendo el índice del líquido amniótico y las anomalías fetales, y los resultados de las pruebas serológicas.

RESULTADOS: Doscientos noventa pacientes cumplieron los criterios de inclusión. De estos, 56 (19%) presentaron una de las siguientes patologías asociadas con polihidramnios: diabetes (13% del total de casos), lesiones gastrointestinales obstructivas (5%), isoimunización con Rhesus (0,3%), anomalías cromosómicas o síndromes genéticos %). Entre los 234 pacientes restantes, sólo tres tuvieron un resultado positivo para la enfermedad infecciosa (1%, 95% Intervalo de Confianza (IC) 0-4%): dos mujeres fueron positivas para el parvovirus B19 y una para la infección por toxoplasmosis. En ninguno de ellos el feto fue afectado, como lo confirmaron las pruebas de suero después del nacimiento y por 3 años de seguimiento.

CONCLUSIONES: El sceening para de enfermedades infecciosas no parece útil en embarazos con polihidramnios aislados

ORIGINAL ARTICLE

Prevalence of a positive TORCH and parvovirus B19 screening in pregnancies complicated by polyhydramnios

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ABSTRACT

Objective The aim of this study was to evaluate the rate of women with polyhydramnios who eventually screened positive to infectious disease by serum screening testing for TORCH and parvovirus B19.

Methods This is a retrospective observational study on singleton pregnancies with a diagnosis of polyhydramnios and who had serum screening for TORCH and parvovirus B19. Patients were followed with serial ultrasounds between 2006 and 2013. Maternal characteristics, medical and obstetric history were reviewed. Ultrasound parameters, including amniotic fluid index and fetal anomalies, and the results of serologic tests were reviewed.

Results Two hundred ninety patients met the inclusion criteria. Of these, 56 (19%) presented one of the following pathological conditions associated with polyhydramnios: diabetes (13% of total cases), obstructive gastrointestinal lesions (5%), Rhesus isoimmunization (0.3%), chromosomal abnormalities or genetic syndromes (1%). Among the remaining 234 patients, only three had a positive test result for infectious disease (1%, 95% Confidence Interval (CI) 0–4%): two women were positive for parvovirus B19 and one for toxoplasmosis infection. In none of them the fetus was affected, as confirmed by serum testing after birth and by 3 years follow-up.

Conclusions Infectious disease screening does not seem beneficial in pregnancies with isolated polyhydramnios

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INTRODUCTION

Polyhydramnios complicates 1–2% of pregnancies[1,2] and is associated with an increased risk of adverse perinatal outcome. It is defined as an amniotic fluid index of more than 25 cm or a single deepest pocket of fluid of at least 8 cm.[1,3] The etiology of polyhydramnios is diverse, involving both maternal and fetal disorders. Causes include underlying congenital fetal structural abnormalities, fetal infections, multiple gestations, isoimmunization, fetal–maternal hemorrhage, placental tumors and maternal diabetes, [4–9] but up to 50% of cases are idiopathic.[5,10] Fetal infections most commonly linked to polyhydramnios are cytomegalovirus (CMV), toxoplasmosis, syphilis, rubella and parvovirus B19 infection.[4] However, indications to infectious disease screening vary in the literature. While some authors do not mention infectious disease as a cause of polyhydramnios, others suggest that after fetal anomalies or maternal causes are excluded, the workup should include screening for maternal titers for infectious causes such as rubella, CMV, toxoplasmosis and parvovirus.[4,11] The rate of toxoplasma, rubella, CMV and herpes simplex (TORCH) and parvovirus B19 infection in polyhydramnios greatly differs in retrospective studies, ranging from 0.3 to 2.9%.[12,13] It is also interesting to note that oligohydramnios, rather than polyhydramnios, is a common finding in congenital infections, mostly for CMV, Toxoplasma gondii and rubella. The incidence of oligohydramnios in cases of confirmed CMV infection is reported to be 25%, and it can be explained by the affinity of the virus for the fetal kidneys.[14] The need for TORCH screening in cases of polyhydramnios is therefore currently the object of much debate.[15–17] The aim of this study was to evaluate the rate of positive infectious disease testing among a cohort of women diagnosed with polyhydramnios in a tertiary care setting.

MATERIAL AND METHODS

This was a retrospective observational study of singleton pregnancies with antepartum diagnosis of polyhydramnios, at a gestational age ≥20 weeks, who had serum screening for TORCH infections and parvovirus B19. Patients were followed with serial ultrasounds between 2006 and 2013 at Careggi University Hospital in Florence, Italy, which is a tertiary care center. Maternal characteristics and pregnancy outcomes were reviewed using the electronic database. Ultrasound parameters, including amniotic fluid index and diagnosis of

fetal anomalies, and the results of serologic tests were reviewed. Polyhydramnios was defined as an amniotic fluid index of 25 cm or more, or as a single deepest pocket of fluid of at least 8 cm. It was categorized as mild, moderate or severe based on amniotic fluid index of 25.0–29.9 cm, 30.0–34.9 cm or 35.0 cm or more, respectively. Cases with no infectious disease testing or with unknown delivery outcome were excluded. Cases with resolution of the polyhydramnios during the course of the pregnancy were included. Rubella and syphilis screening is routinely performed in all pregnancies in the first trimester, and therefore, it was not repeated after the diagnosis of polyhydramnios, unless there was clinical suspicion of a new-onset infection.

Confirmation of major congenital anomalies was carried out in the immediate neonatal period by the pediatricians. In cases of diagnosis of maternal infection, the neonate underwent specific testing at birth and at clinical follow-ups at 12, 24 and 36 months.

The TORCH and parvovirus B19 analyses in our laboratory consist of IgM and IgG antibodies to toxoplasma, CMV, rubella (CLIA, DiaSorin), parvovirus B19 (CLIA, Siemens) and herpes simplex (ELISA, Siemens). The diagnosis of recent infection was based on positive specific IgM results with confirmatory IgG avidity test in case of Toxoplasma, rubella and CMV.

In case of a positive result for toxoplasma infection, amniocentesis was usually performed to determine the presence of the pathogen in the amniotic fluid by amplification of DNA, using polymerase chain reaction (PCR) after 18 weeks of gestation and at least 4 weeks after the acute infection. For CMV, PCR on the amniotic fluid was performed after 20 + 4 weeks of gestation and after at least 6 weeks after the acute infection. In the case of rubella infection, PCR on amniotic fluid and PCR+IgM on fetal blood were carried out not before 21 weeks and at least 6 weeks after the acute infection. For parvovirus B19, we routinely do not perform PCR on amniotic fluid based only on positive serology. A PCR on amniotic fluid for parvovirus B19 would be performed additionally only if amniocentesis is performed for other fetal indications.

RESULTS

Three-hundred and forty-two patients were diagnosed with polyhydramnios during the study period. Of these, 35 were excluded because no infectious disease screening was performed and 17 patients were excluded because of unknown postnatal outcome. The remaining 290 patients met the inclusion criteria. The mean gestational age at the diagnosis was 31 weeks. Of these patients, 56 (19%) presented one of the following pathological conditions associated with polyhydramnios: diabetes (13% of total cases), obstructive gastrointestinal lesions (5%), Rhesus isoimmunization (0.3%), chromosomal abnormalities or genetic syndromes (1%) (Figure 1). In the remaining 234 patients, none of the aforementioned causes was identified. Forty-nine (20.9%) cases had spontaneous resolution of the polyhydramnios, at a median gestational age of 36 weeks (range 30–41).

Demographic and obstetric characteristics of the 234 cases are reported in Table 1. Results of TORCH and parvovirus screening showed a positive test result only in three patients

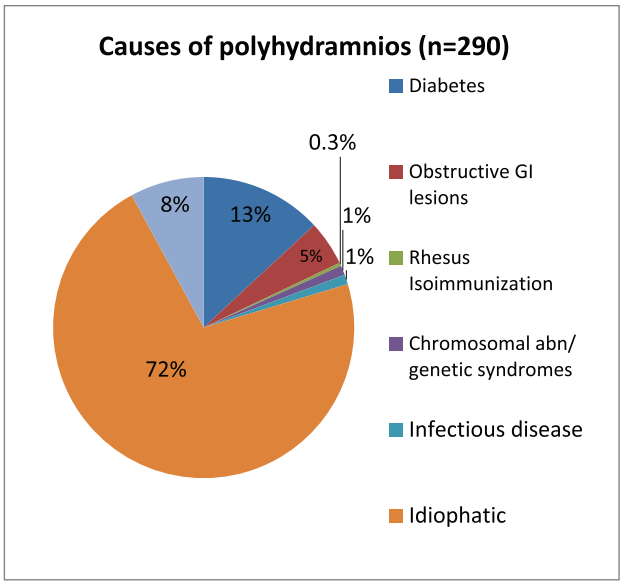

Figure 1 Causes of polyhydramnios in our cohort of patients

Table 1 Demographic and obstetric characteristics of patients with isolated polyhydramnios

	n = 234
Maternal age (y)	34.3 ± 5.2
Nulliparity	170 (73%)
GA at diagnosis (weeks)	32 (28.5, 34.5)
Polyhydramnios severity	156 (66%)
Mild (AFI 25–29.9 cm)	54 (23%)
Moderate (AFI 30–34.9 cm)	24 (10%)
Severe (AFI >35 cm)	
Positive test result for infectious disease	3 (1%)
GA at delivery	39 (38, 40)
Preterm delivery	32 (14%)
Birth weight (g)	3300 (3000, 3640)
Birth weight <10th centile	12 (5.13%)
Birth weight >90th centile	23 (9.83%)

GA, gestational age; AFI, amniotic fluid index.
Data given as *n* (%), mean ± Standard Deviation (SD) or median (25–75th percentiles).

(1% 95% CI 0–4%): two women were positive for parvovirus B19 and one for toxoplasma infection. The infection was acute based on positive IgM in all three cases, and in case of toxoplasma infection, IgG avidity test was performed. Results indicated low avidity, thus suggesting recent infection. The characteristics of the three patients with infection are reported in Table 2. In all cases, the diagnosis was made in the third trimester and the polyhydramnios persisted throughout pregnancy. In the two cases of parvovirus B19, the middle cerebral artery velocimetry was monitored during pregnancy without revealing any pathological alteration. In the case of toxoplasma infection, a PCR-DNA test of the amniotic fluid was performed, and it resulted negative. The patient was treated with oral spiramycin 9 000 000 IU per day, divided into three doses.

Table 2 Characteristics of the patients with positive infectious disease test result

Patient	Type of infection (IgM +)	Gestational age at diagnosis of polyhydramnios (weeks)	Maximum amniotic fluid index value (cm)	Fetal/ neonatal infection
1	Parvovirus	35	29	No
2	Parvovirus	28	34.5	No
3	Toxoplasma	35	26	No

The prevalence of fetal infection in idiopathic polyhydramnios was 0% (0/234, 95% CI 0–2%), as confirmed by serum testing after birth. All three cases were clinically asymptomatic at follow-up for up to 3 years.

DISCUSSION

The aim of our retrospective analysis was to determine the incidence of infectious disease in a cohort of singleton gestations with diagnosis of polyhydramnios in order to clarify the need for a maternal TORCH and parvovirus testing, after exclusion of other fetal and maternal causes of polyhydramnios. We found a very low prevalence of maternal infection (1% of cases with isolated polyhydramnios), with no case of fetal or neonatal infection, thus suggesting that a complete workup for infectious disease as a result of finding of isolated polyhydramnios is not necessary.

Recognition of polyhydramnios is important to identify pregnancies at increased risk for adverse outcome; however, it presents difficult diagnostic and therapeutic dilemmas for the obstetrician.[18] The antenatal management of polyhydramnios can be challenging as there are no formalized guidelines on the topic.[4] A comprehensive fetal evaluation, a workup to rule out maternal factors, and fetal surveillance are warranted.

The TORCH testing as a screening tool has been proposed in the seventies[19]; the use of this test for idiopathic polyhydramnios has been incorporated into clinical practice even though its real benefit is unclear.

In Italy, the rubella live attenuated vaccine has been introduced in 1972; its administration is recommended to all babies at 12–15 months. This vaccination strategy has led to a reduction of clinical rubella infection from 1800 cases in 1997 to 500 cases in 2001.[20] In the time period 2005–2008 in Italy, there have been 30 reported cases of rubella infection during pregnancy, of which only four had confirmed congenital rubella syndrome.[21]

A multicentric Italian study revealed a CMV sero-prevalence in a random sample of women of about 80%, similar to other European countries.[22] After a primary infection, reactivations can occur periodically, leading to a less severe secondary infection.[23] The incidence of primary infection during pregnancy is estimated being of 1–2%.[24–26] If the infection is transmitted to the fetus, almost 90% of infected babies are asymptomatic, and in case of maternal secondary infection, symptoms are mostly transient and less worrisome.[25–31]

The incidence of toxoplasmosis during pregnancy is very low: 3–16/10 000.[32] In an Italian study on 3426 pregnant women, a prevalence of less than 1% was reported.[33] In our cohort, we found only one maternal infection, not confirmed in the baby, in accordance with the most recent published series.[15,17]

Parvovirus B19 infection during pregnancy has not been associated with a high morbidity or mortality in infancy and childhood.[34] Guidelines recommend investigation for parvovirus B19 infection as part of the standard workup for fetal hydrops or intrauterine fetal death.[35] Other pregnancy complications such as abortion have been linked to parvovirus,[36–38] while a clear association with polyhydramnios has never been demonstrated.[38] We observed two cases of maternal parvovirus B19 infection, not followed by infant serology confirmation or clinical sequelae.

Our results are in agreement with the study by Fayyaz *et al.*,[16] which showed that the TORCH test is not beneficial in women in whom polyhydramnios is an isolated ultrasound finding, especially when it is diagnosed in the third trimester. Similarly, Abdel Fattah *et al.*,[15] after reviewing the indication and value of 462 TORCH testing requested for fetal reasons during a 10-year period, found that no cases of fetal/maternal infection were associated with polyhydramnios. In their series, there were no cases of maternal or fetal infections by any agents other than CMV. However, women were not tested for parvovirus. The same laboratory group has later reassessed the TORCH test in 158 cases of polyhydramnios.[17]

Performing useless laboratory tests increases the health-related financial costs, and we speculate that it could also raise maternal anxiety levels.

The aim of our study was to provide the clinician with information regarding the likelihood of an infectious disease in patients with an excess of amniotic fluid. We conclude that a finding of isolated polyhydramnios on routine ultrasonography may not be an indication to the infectious disease screening. Our data may help clinicians counseling patients with a diagnosis of isolated polyhydramnios.

WHAT'S ALREADY KNOWN ABOUT THIS TOPIC?

- Some studies have already criticized the utility of TORCH and parvovirus tests in case of polyhydramnios.

WHAT DOES THIS STUDY ADD?

- There is no association between congenital infections and idiopathic polyhydramnios.

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