

Stillborn in Brazil: could neonatal mortality be just the tip of the iceberg?

Natimortos no Brasil: a mortalidade neonatal pode ser apenas a ponta do iceberg?

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ABSTRACT

INTRODUCTION: Stillbirth has an estimation of more than 2.5 million cases across the world. A great percentage of the cause of stillbirths is reported as unknown or unexplained. The aim of this study was the identification of the causes, incidence and profile of the fetal and also the mothers in a maternity hospital in the State of Sergipe. **METHODS:** This was an observational and cross-sectional study in which all stillbirths of the maternal hospital in the State of Sergipe from June 2020 to May 2021 were included. Fetal death investigation forms were analyzed and some women were interviewed through telephone calls. The interview was based on the **SAMPLE VA** questionnaire 1 from the WHO Verbal autopsy instrument and an additional list to assess the maternal, pregnancy and labor history, and also history of signs and symptoms of COVID-19 infection. **RESULTS:** A total of 10375 births were delivered at the hospital and the months with highest births were May and March of 2021. We found 64 cases of stillbirth. Forty-two cases of neonatal deaths were also registered. Only 11 women with cases of stillbirth were interviewed in our study. The major participants were married or living with a partner (60%) and finished secondary education (63.63%). There were 5 cases of women with gestational age at 37 weeks or greater. Antenatal care was completed by 90.9% (n=10) of women. The majority (54.5%) had *Unknown* or *unexplained* causes of death. The remaining categories also showed relevant results. **CONCLUSION:** Fetal deaths were responsible for approximately 60% of perinatal deaths, in which the most reported cause in our interview were unexplained or unknown. The total number of deaths when neonatal deaths were added almost duplicated the percentage of the mortality rate at the maternity hospital. All women went into labor with less

than 42 weeks of gestational age and greater or equal to 22 and most were healthy and had no diagnosed diseases.

Keywords: cause of death, neonatal death, stillbirth .

RESUMO

INTRODUÇÃO: O número de casos de natimortos tem uma estimativa de mais de 2,5 milhões em todo o mundo. Uma grande porcentagem da causa de natimortos é relatada como desconhecida ou inexplicada. O objetivo deste estudo foi a identificação das causas, incidência e perfil do feto e também das mães em uma maternidade do Estado de Sergipe. **MÉTODOS:** Trata-se de um estudo observacional e transversal no qual foram incluídos todos os natimortos de uma Maternidade do Estado de Sergipe no período de junho de 2020 a maio de 2021. Foram analisadas fichas de investigação de óbito fetal e entrevistadas por telefone com algumas mulheres. A entrevista foi baseada no questionário SAMPLE VA 1 do instrumento de autópsia verbal da OMS e uma lista adicional para avaliar a história materna, gestacional e do parto e, também, história de sinais e sintomas de infecção por COVID-19. **RESULTADOS:** Um total de 10.375 partos foram realizados na maternidade e os meses com números mais altos de nascimentos foram em maio e março de 2021. Encontramos 64 casos de natimortos no período. Também foram registrados 42 casos de óbitos neonatais. Apenas onze mulheres com casos de natimortos foram entrevistadas em nosso estudo. A maioria das participantes eram casadas ou viviam com o companheiro (60%) e tinham ensino médio completo (63,63%). Houve cinco casos de mulheres com idade gestacional maior ou igual a 37 semanas. O pré-natal foi concluído por 90,9%(n=10) das mulheres. A maioria (54,5%) teve causas de morte desconhecidas ou inexplicadas. As demais categorias também apresentaram resultados relevantes. **CONCLUSÃO:** Os óbitos fetais foram responsáveis por aproximadamente 60% dos óbitos perinatais, e as causas mais relatadas em nossa entrevista foram inexplicadas ou desconhecidas. O total de óbitos quando somados aos óbitos neonatais quase duplicou o percentual da taxa de mortalidade da maternidade. Todas as mulheres entraram em trabalho de parto com idade gestacional menor que 42 semanas e maior ou igual a 22 e a maioria era saudável e sem doenças diagnosticadas.

Palavras-chave: causa da morte, morte neonatal, natimorto.

1 INTRODUCTION

Fetal death presents differently across countries and continents in the world [10]. The number of deaths found in developing and underdeveloped countries was higher than in developed countries [10]. The definition of fetal death by the International Classification of Diseases 10 (ICD-10) can be divided into early and late death [27]. Early fetal death is based on the fetus having completed 22 weeks of gestational age or weighing 500 grams or 25 cm in length. Late death is classified as the fetus completing 28 weeks or weighing greater than or equal to 1000 grams or 35 cm in length [27]. More than 2.5 million fetal deaths were estimated in 2015 considering fetuses over 28 weeks of gestational age [3], which is the gestational age that is recommended by the WHO [28].

An important indicator for the assessment of socioeconomic development conditions, access to quality health resources and estimation of the risk of death for live births in their first year of birth is the infant mortality rate, which is calculated by the number of deaths children under 1 year of age multiplied by 1000, divided by the number of live births [5]. The infant mortality rate can demonstrate which directions the health planning should take; however, it needs additional information to be carried out properly [5]. The fetal mortality rate estimates the fetus being born with no sign of life, understanding the quality of care provided by the health service, from antenatal care to delivery [5].

Deaths may be associated with variable risk factors that include the fetus, socioeconomic, maternal and situational factors. Non-booking for antenatal care, previous stillbirths or obstetric complications and also the mode of delivery are some of the risk factors described in the literature [16].

Worldwide, one of the most common causes of fetal deaths is described as an unknown or unexplained cause [2,20] but causes such as fetal distress, birth defects, maternal hypertension, infections and others have also been prevalent [2,22]. Fetal death can be classified as antepartum in which the death occurs before labor and also in intrapartum, which occurs during labor but before birth [10]. Intrapartum death is considered to be the most prevalent one, especially in underdeveloped countries [10].

Brazil is considered a heterogeneous country with great diversity and, therefore, regions often present different socioeconomic and cultural characteristics [6]. In 1998, 40.321 fetal deaths were documented in the Brazilian regions and in 2019, it reached 29.105 cases, reducing approximately 27.8% when compared to the last decade [4]. In a study including the prevalence of stillbirths in Brazil, 14.82 per 1000 births were identified, with the North and Northeast regions having the highest rate [6]. However, according to the official morbimortality data available by DATASUS, which is an information technology department of the Public Health Care system of Brazil (SUS), the Northeast and southeast region had the highest rate of fetal deaths in the last past decades [23].

Despite the declining number of fetal deaths described in the literature, there are still many cases, including the ones considered to be preventable, which makes it necessary to understand the reasons behind the slow decline of deaths [10]. It is important that we identify the main causes of deaths, in order to plan strategies to reduce the number of cases. Therefore, the present study focus on the investigation of fetal deaths in a maternity hospital in the State of Sergipe with the aim of evaluating their incidence, socioeconomic profile, identification of causes and possibly associated risk factors.

2 METHODS

The present observational and cross-sectional study included women who experienced stillbirths at a usual risk maternity hospital in the State of Sergipe from June 2020 to May 2021. In this study, stillbirths were considered only if the death occurred before the onset of labor or during labor, but before the fetus was born and over 500g and/or 22 weeks of gestational age. The number of births, live births, vaginal cesarean section delivery along with fetal deaths and neonatal deaths were also described along with data from previous years from the maternity hospital. Fetal death investigation forms were previously analyzed. The forms included the mother's name, date of occurrence of fetal death, contact number, address, gestational age, fetal birth weight and VDRL test result. After the analysis of the fetal death investigation forms, an interview period was carried out with the mothers through telephone calls using the contact information informed by them at the time of admission to the Maternity hospital.

The interview questions were based on the World Health Organization (WHO) Verbal autopsy instrument from 2016 plus the new updates from 2020 regarding the SARS-CoV-2 virus, using questions from the SAMPLE VA questionnaire 1: death of a child aged under four weeks, which is used to determine various causes including fetal death, in addition to including a list of questions that assess signs and symptoms the mother went through during the final time of pregnancy, also pregnancy history and other factors related to the history of labor. The questions were divided into identification, cause of death, previous gestational history, history of labor, characteristics of the fetus, history of signs and symptoms of COVID-19 virus. In order to only include fetal deaths, the data obtained were carefully evaluated so that early neonatal deaths or abortions were not included. It was also estimated the distance between the maternity hospital and the residence using *Google Maps* tools according to the answer given during the interview. The following situations were also excluded from this paper: refusal to start or continue the interview, withdrawn consent or unable to send consent and impossibility of contacting the mother.

The epidemiological factors included maternal age, marital status, maternal education level, gestational age and also sex of the baby. Maternal factors included antenatal care, previous abortions, use of alcohol or drugs, doses of Tetanus vaccine, diagnosis of gestational Hypertension or gestational Diabetes and results of VDRL and HIV test. The causes of fetal deaths were divided after using the verbal autopsy instrument, which were separated according to maternal reports and diagnoses informed by the physicians.

The mothers were only invited to participate with at least 40 days after the time from the occurrence of the fetal death, since WHO recommended the VA to be conducted as soon as

possible but after a period of mourning. Also, WHO suggests caution in interpreting recalls of more than 1 year [28]. One study agreed to the recommendations by WHO that VA collected within more than one year to be analyzed carefully since the accuracy was reported to decline each month during the period [21]. Ethical approval for this study was obtained from the Research Ethics Committee of Tiradentes University, identified under the following approval number 4.374.909.

3 RESULTS

A total of 10375 births were registered during these 12 months, out of which 7365 were from vaginal delivery and 2992 were from cesarean section delivery that are also presented in table 1. The mean of live birth was 864.6 per month during the period evaluated. The months with highest numbers of births were May and March of 2021, with the total of 1059 and 942 births, respectively. On the opposite, December of 2020 and February of 2021 were the months with the least number of births, registering 772 births each month.

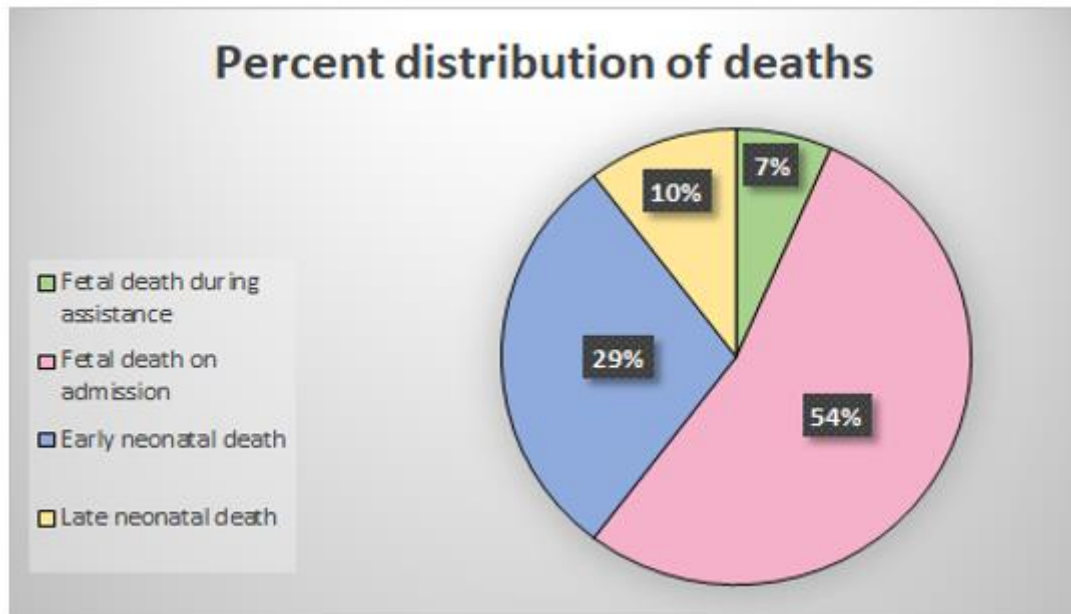
Table 1. Variables according to admission of a Maternal Hospital of Sergipe during June 2020 to May 2021.

Variable	jun/20	July/20	Aug/20	Sep/20	Oct/20	Nov/20	Dec/20	Jan/21	Feb/21	Mar/21	Apr/21	May/21	Total	Mean
Number of births	864	932	838	813	819	829	772	817	772	942	918	1059	10375	864,6
Live births	858	928	836	810	811	821	767	814	769	932	911	1054	10311	859,3
%	99,31	99,57	99,76	99,63	99,02	99,03	99,35	99,63	99,61	98,94	99,24	99,53	****	99,4
Vaginal delivery	630	696	608	553	601	578	546	570	545	623	637	778	7365	613,8
%	72,92	74,68	72,55	68,02	73,38	69,72	70,73	69,77	70,60	66,14	69,39	73,47	****	70,9
Cesarean section delivery	228	236	230	260	218	246	226	247	227	319	274	281	2992	249,3
%	26,39	25,32	27,45	31,98	26,62	29,67	29,27	30,23	29,40	33,86	29,85	26,53	****	28,9
Fetal death during assistance	0	0	0	0	1	0	2	0	0	2	1	1	7	0,583
%	0	0	0	0	0,12	0	0,26	0	0	0,21	0,11	0,09	****	0
Fetal death on admission	6	4	2	3	7	8	3	3	3	8	6	4	57	4,75
%	0,69	0,43	0,24	0,37	0,85	0,97	0,39	0,37	0,39	0,85	0,65	0,38	****	0,5
Early neonatal death	5	2	3	4	6	1	1	4	2	2	1	0	31	2,6
%	0,58	0,22	0,36	0,49	0,74	0,12	0,13	0,49	0,26	0,21	0,11	0,00	****	0,3
Late neonatal death	2	0	2	1	0	0	1	2	0	1	1	1	11	0,9
%	0,23	0,00	0,24	0,12	0,00	0,00	0,13	0,25	0,00	0,11	0,11	0,09	****	0,9

We found the numbers of deaths were distributed into fetal death, early neonatal death and late neonatal death. Fetal deaths represented 0.6% (n=64) of the total births in this study and were divided into fetal death on admission or during the assistance in which there was no fetal heartbeat. Fetal death on admission is described as the highest percent of deaths, reaching

54% of total when compared to the other variables given in figure 1. Early neonatal death has also demonstrated to be significant in the distribution of deaths, behind only of fetal death on admission.

Figure 1. Percent distribution of deaths of a Maternal Hospital during June 2020 to May 2021.



There were 41.383 live births registered from 2017 to 2020. During the year of 2019, 11.353 live births were delivered at the Hospital. Throughout the years, the number of fetal deaths during admission has increased ranging from 38,57% in 2017 of the deaths reported to 51,8% in 2020. The number of early neonatal death has maintained considerably stable as shown in table 2.

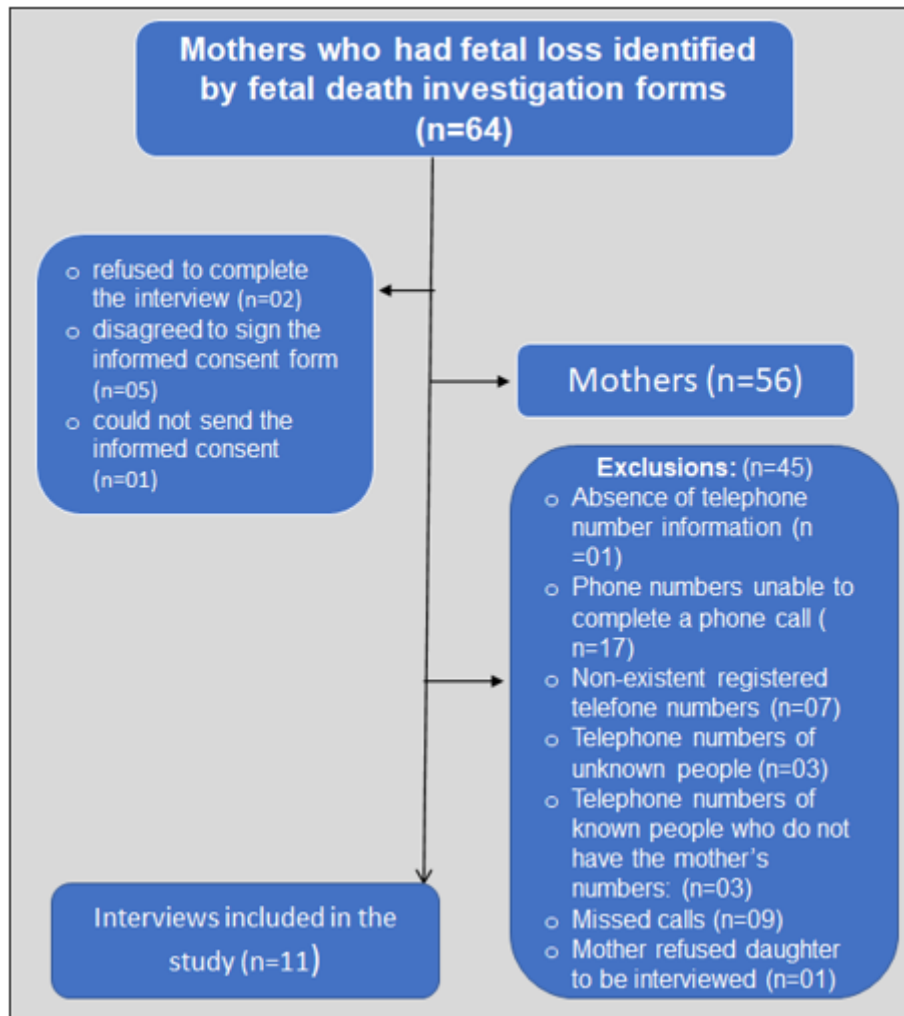
Table 2. Live births, stillbirths and neonatal deaths from 2017 to 2020 in the Maternity Hospital.

Year	Live births	Fetal death during admission	Fetal death during assistance	Early neonatal death	Late neonatal death
2017	8.733	23	4	30	13
2018	10.871	51	0	37	20
2019	11.353	43	0	32	25
2020	10.432	52	5	36	17

We initially found 65 fetal death cases through the fetal death investigation forms, in which 31 were between more than 37 weeks and less than 42 weeks of gestational age, 15 ranged from 33.1 to 36.6 weeks of gestational age and nineteen ranged from 22 to 32.6 weeks of gestational age. It is important to highlight that seven women had a VDRL test positive according to the forms.

A total of 12 women were interviewed but one was excluded because the cause of death was classified as early neonatal death, 05 disagreed to sign the informed consent form, 01 could not send the informed consent form due to technological issues, 02 refused to complete the interview and 44 were excluded as described in figure 2.

Figure 2. Flowchart summarizing the inclusion of interviews related to fetal death investigation from a local Maternity Hospital, 2020 -2021.



The epidemiological profile collected during interviews is given in Table 3. The maternal age ranged from 18 to 38 years old and women in the group of 34–38 years had 18.18%, reaching the lowest percentage. More than 60% were married or lived with a partner and there was no description of divorces or other marital status. Only two women completed a higher education and 63.63% finished secondary education. Female babies had a greater rate than male ones. Babies born at the gestational age of 37 weeks to less than 42 weeks were rated at 45.45%.

Table 3. Characteristics of Stillbirth in the public maternity of Sergipe.

Characteristics:	Stillbirths:
Number of sample	11
Maternal age (Years old)	
○ 18-23	3
○ 24-28	3
○ 29-33	3
○ 34-38	2
Marital status	
○ Single	4
○ Married or living with a partner	7
○ Widow	0
○ Divorced	0
Maternal education level	
○ No formal education	0
○ Primary	2
○ Secondary	7
○ Higher	2
Gestational age	
○ 22-24.6	1
○ 25.1-28.6	2
○ 29.1-32.6	1
○ 33.1-36.6	2
○ > 37 - < 42	5
Sex of the baby	
○ Male	5
○ Female	6
Maternal factors	
Antenatal care	10
Tetanus vaccine doses	10
Gestational Hypertension	1
Gestational Diabetes	0
Illicit drug use	0
Alcohol use	0
VDRL test	10
HIV test	11
Previous abortions	2
Causes	
○ Renal Insufficiency	1
○ Infection	1
○ Acute fetal distress	1
○ Placental abruption	2
○ Unknown or unexplained	6

Antenatal care was completed for most women in the study, as well as the tetanus vaccine prophylaxis. It was not reported abuse of alcohol or use of illicit drugs. Only one case

of gestational hypertension was documented. Women were tested for VDRL and HIV however the majority tested negative. Two cases of previous abortions were also reported and it is presented in table 3 along with the maternal factors described above.

Half of the causes of death were attributed to unknown or unexplained causes. Placental abruption was also identified in two cases. The remaining fetal deaths were caused by renal insufficiency, infection and acute fetal distress and it is presented in table 3.

Only one woman reported symptoms of COVID-19 and also had a positive RT-PCR test diagnosed by a physician. Three women said they experienced symptoms of urinary tract infection at least 3 months before delivery and were all prescribed medications by a medical professional.

We estimated the distance between the maternity hospital and the residence according to the address informed by the mothers during the interview. There were six different cities, which are nominated from I to VI on the table below (table 04). The VI city had a total of five different districts which it was assessed the mean distance.

Table 04. Approximate distance between Maternity hospital and residence of the mothers.

City	(n=11)	Distance (km)
I	2	53.4
II	1	33.0
III	1	28.7
IV	1	23.5
V	1	13.9
VI	5	11.54*

*Mean distance of five different districts.

Every mother admitted at the maternity hospital were evaluated at the time of the arrival by a health professional in which were investigated the history of present illness, along with the physical exam, especially the fetal heartbeat sign and also complementary investigation when necessary. In our study, 90.9% (n=10) of the women interviewed reported that the health professional informed them that the fetal showed no sign of heartbeat. The high rate of pregnant women who arrived at the maternity hospital with no presence of fetal heart beats could demonstrate that are some missing points in the maternal support system during the antenatal period.

4 DISCUSSION

In our study, we had some difficulties in reaching the mothers for the interview because many registered phone numbers were invalid or unable to complete the phone call. Christiansen-Lindquist, Lauren et al. 2016, reported 26 cases out of 149 eligible women without an existing phone number and emails on the fetal death certificate. The situation demonstrates the need to change the strategies in order to ensure the registration of an existing telephone contact number on the forms. It is important to highlight that due the pandemic situation of COVID-19 of the coronavirus (SARS-CoV-2) we could not plan a home visit in order to interview the mothers.

In a review approaching the challenges in classifications assignment of causes of stillbirths, they found that the evaluation of the fetal heart rate as soon as the mothers arrives at the maternal hospital can help at determining whether the fetus was alive or not at the time of admission, since it is important to comprehend if the stillbirth happened antepartum or intrapartum [18]. The majority of the women who went through the interview and were admitted in the maternity hospital had no heartbeat sign.

The distance from the residence to the maternity hospital, can lead to delay in diagnosis and/or bring adverse prenatal outcomes [9] and, in some cases, it could be fatal, increasing the perinatal mortality [11]. In the literature, it was described that the lower the economic status of the mother, it was more likely that the mother would not go into hospital in order to deliver [24]. A study in Netherlands evaluated the impact of travel time at the start or during labour on the way to hospital from home and found that it was associated to a higher mortality rate, along with neonatal mortality within 24 hours of birth and adverse outcomes the longer was the time of travel. [19]. In our study, five mothers had to travel at least 23.5 km from the house to the maternity hospital, with two of them travelling approximately 53.4 km. The others one traveled less than 14 km to reach the maternity hospital.

Almost all women we interviewed had prenatal care checkups during the COVID -19 pandemic situation. Di Wu et al. reviewed the management of pregnancy during the COVID-19 pandemic and found that the routine pregnancy examinations could be postponed or canceled, depending on the individual and also the gestational age, except at 11-13 weeks due the nuchal translucency exam, at 15-20 weeks due the Oscar test and at 20-24 weeks due the fetus ultrasound. However, they recommended providing online consultations, remote monitoring and telemedicine to avoid the increased risk of possible infection by the virus SARS-CoV-2 [29].

The category *unexplained or unknown* is an important cause of stillbirth across the world [20]. Reinebrant, H et al. 2018, in a systematic review of stillbirths involving low-income countries and high-income countries, it was found, the occurrence of 41% and 32.1% of unexplained cases, respectively. We registered 64 stillbirths out of 10.375 births during a period of twelve months, in which 54.5% were classified as unexplained or unknown. Asphyxia contributes to a great number of stillbirths [1], McClure, Elizabeth M et al. 2020, registered 44% of all cases in their paper, but none of our interviewees reported it in our study.

Syphilis infection has been described as an important cause associated with stillbirth [10]. In low-income countries the percentage of stillbirths associated with syphilis is higher when compared to high income countries, especially in Sub-Saharan Africa and Southern Asia [10]. In the interview, only one woman had a reactive VDRL test, however, in the fetal death investigation form we found seven reactive cases. It was observed in another study, TORCH infection in nine women, as a probable or possible cause of stillbirth. Those women went through placental pathology and fetal autopsy. One of the cases was diagnosed as syphilis infection after the visualization of spirochetes on the histological examination [17]. Thus, it is necessary to understand if antenatal care is being effective and comprehend the reasons why the diagnosis is being delayed in order to prescribe an appropriate treatment.

There were three cases of symptomatic urinary tract infection in our study. Only one stillbirth caused by infection also had the diagnosis of urinary tract infection, the remainder was diagnosed with acute fetal distress and unknown. Stillbirths caused by infection are identified as an important factor, especially in low-income countries [20]. Page JM, et al., 2019 analyzed 512 stillbirths in a prospective study in the United States and reported 12.9% of the cases as caused by a probable or possible infection. The predominant organisms related were *Escherichia coli*, *group B streptococcus* (GBS) and *enterococcus species* [17]. It was also described as the placental pathology and fetal autopsy as one of the most important tests for the identification of signs of infection or inflammation [17].

The postmortem examination has some obstacles especially because the procedure needs to be initiated as soon as the occurrence of the death, also because sometimes the family do not consent or restrict the procedures, lack of specialists and a proper infrastructure is not always available [15]. Placental histological evaluation has also been widely used in order to better understand the mechanisms involved in death [7,14]. MAN, J et.al 2016, reported 575 placenta from stillbirths that were submitted to postmortem examination. One third had some abnormality registered on the histological examination; placental cause in 168 out of 575 cases, in which had infection associated, some diagnosed as placental abruption, growth restriction

and pre-eclampsia and others [12]. The best plan to determine the cause of the death is still unclear even though there are plenty of exams nowadays [26].

Uncompleted or incorrect filling out the fetal death certificate by medical professionals is also analyzed in the literature, a situation that can interfere and cause confusion with the identification of mechanisms associated with the cause of death [5].

A total of forty-two deaths of neonates during the period of our study were registered. McNamara K, O'Donoghue and R. A. Greene, 2018 found 81 intrapartum fetal deaths in which the causes of the death were related to chorioamnionitis, abnormalities in the central nervous system, congenital malformations, intrapartum asphyxia, antepartum hemorrhage from placental abruption and others. Twenty-one out of thirty-six infants died secondary to hypoxic ischemic encephalopathy (HIE) having at least one of the following obstetric factors: chorioamnionitis, ruptured vasa previa, placental disorders, unexplained or presentation of infections [14]. Thus, it is also important to understand neonatal mortality, since the risk factors prior or during birth can lead to stillbirth, and could also influence the neonates [14]. In our previous samples from the live births and deaths occurred from 2017 to 2020 at the maternity hospital, we found 41389 live births in which were registered 178 fetal deaths and 210 neonatal deaths. In the last decades, Brazil had at least 1448802 deaths, in which 52% were due to fetal deaths and 48% related to neonatal deaths [23].

5 CONCLUSION

Over half of perinatal deaths were represented by fetal deaths in our study, demonstrating the matter has been affecting locally as well as globally. Early neonatal deaths reached higher percentage when compared to late neonatal deaths. The major cause of fetal death reported in the interviews were *Unexplained* or *Unknown*, followed by *Placental abruption* and *Renal Insufficiency*, *Infection* and *Acute fetal distress*. Most women completed prenatal visits, however, there were seven mothers with a reagent VDRL on the investigation form, which could increase the risk factors of gestation and, therefore, the fetus lives. The mothers were at more or equal to 22 weeks of gestational age and less than 42 weeks and their age varied from 18 to 38 years old and mostly didn't present any comorbidities. We believe the postmortem examination is important in the investigation of stillbirths. Neonatal mortality and stillbirth have shown to have a correlation and the preventive action plans to reduce stillbirths could also increase the neonatal survival rate.

Limitations

We had difficulties trying to reach the mothers through telephone calls and we were not able to visit the mothers due the pandemic of COVID-19. Our study was limited because only eleven out of sixty-four women who had a stillbirth were interviewed, however the study was important to evaluate the situation in the Public Maternity Hospital of Sergipe in order to have a comprehensive understanding of the occurrences of fetal deaths

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