Analysis of healthcare-related postpartum infections in the Campos Gerais region:

cesarean versus vaginal delivery

Avaliação das infecções pós-parto relacionadas à assistência à saúde na região dos Campos Gerais: cesárea x parto vaginal

Evaluación de las infecciones posparto relacionadas con la atención sanitaria en la región de

Campos Gerais: parto por cesárea frente a parto vaginal

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Abstract

Postpartum infections are a significant cause of prolonged hospitalization and maternal morbidity and mortality, with cesarean delivery being one of the main risk factors. This is a retrospective cross-sectional study, in which the medical records of patients affected with postpartum infection in the years 2019 to 2021 at the Hospital Universitário Regional Wallace Thadeu de Mello e Silva / Hospital Universitário Materno Infantil in Ponta Grossa were evaluated. During this period, 9097 obstetric procedures were performed, and 58 cases of obstetric infections were recorded, resulting in a rate of 0.63%, going from a rate of 1.5% (45 notifications) in 2019 to 0.27% (8) in 2020 and 0.15% (5) in 2021. The rate of healthcare-associated infections in cesarean sections was 1.78%, and showed a decrease, being 5.26% in 2019 and falling to 0.63% in 2020 and 0.27% in 2021, while the rate in vaginal delivery remained similar in the three years studied (0.11% in 2019 and 0.12% in 2020 and 2021). Among these, 79.31% were wound infections, while 12.06% were endometritis infections. It is concluded that performing cesarean sections predisposes to a higher risk of postpartum infection, especially if performed after the onset of labor. Moreover, there was a progressive increase in the cesarean rate over the years studied, reaching 40.85% in 2021, considerably higher than that recommended by the World Health Organization.

Keywords: Puerperal infection; Cesarean section; Cross infection.

Resumo

As infecções pós-parto são importantes causa de hospitalização prolongada e de morbimortalidade materna, sendo o parto cesáreo um dos principais fatores de risco. Esse é um estudo transversal retrospectivo, em que foram avaliados os prontuários das pacientes acometidas com infecção pós-parto nos anos de 2019 a 2021 no Hospital Universitário Regional Wallace Thadeu de Mello e Silva / Hospital Universitário Materno Infantil em Ponta Grossa. Nesse período, foram realizados 9097 procedimentos obstétricos e registrados 58 casos de infecções obstétricas, resultando em uma taxa de 0,63%, indo de uma taxa de 1,5% (45 notificações) em 2019 para 0,27% (8) em 2020 e de 0,15% (5) em 2021.

A taxa de infecções relacionadas à assistência à saúde em cesáreas foi de 1,78%, e apresentou queda, sendo de 5,26% em 2019 caindo para 0,63% em 2020 e 0,27% em 2021, enquanto a taxa em parto vaginal se manteve semelhante nos três anos estudados (0,11% em 2019 e de 0,12% em 2020 e em 2021). Dentre essas, 79,31% foram infecções de sítio cirúrgico, enquanto 12,06% por endometrite. Conclui-se que a realização de cesáreas predispõe maior risco de infecção pós-parto, especialmente se realizadas após o início do trabalho de parto. Além disso, houve aumento progressivo na taxa de cesáreas ao longo dos anos estudados, chegando a 40,85% em 2021, consideravelmente acima do preconizado pela Organização Mundial da Saúde.

Palavras-chave: Infecção puerperal; Cesárea; Infecção hospitalar.

Resumen

Las infecciones posparto son una causa importante de hospitalización prolongada y de morbilidad y mortalidad materna, siendo el parto por cesárea uno de los principales factores de riesgo. Se trata de un estudio transversal retrospectivo, en el que se evaluaron las historias clínicas de las pacientes afectadas con infección posparto en los años 2019 a 2021 en el Hospital Universitário Regional Wallace Thadeu de Mello e Silva / Hospital Universitario Materno Infantil en Ponta Grossa. En este periodo se han realizado 9097 procedimientos obstétricos y se han registrado 58 casos de infecciones obstétricas, lo que supone una tasa del 0,63%, pasando de una tasa del 1,5% (45 notificaciones) en 2019 al 0,27% (8) en 2020 y al 0,15% (5) en 2021. La tasa de infecciones relacionadas con la asistencia sanitaria en las cesáreas fue del 1,78%, y mostró un descenso, siendo del 5,26% en 2019 bajando al 0,63% en 2020 y al 0,27% en 2021, mientras que la tasa en el parto vaginal se mantuvo similar en los tres años estudiados (0,11% en 2019 y 0,12% en 2020 y en 2021). Entre ellas, el 79,31% fueron infecciones del sitio quirúrgico, mientras que el 12,06% se debieron a endometritis. Se concluye que la realización de cesáreas predispone a un mayor riesgo de infección posparto, especialmente si se realiza tras el inicio del parto. Además, se produjo un aumento progresivo de la tasa de cesáreas a lo largo de los años estudiados, hasta alcanzar el 40,85% en 2021, muy por encima de lo recomendado por la Organización Mundial de la Salud.

Palabras clave: Infección puerperal; Cesárea; Infección hospitalaria.

1. Introduction

Postpartum infections, defined as those that occur during the puerperium (up to 6 weeks after delivery), are an important obstetric challenge still today in the world and are one of the main causes of morbidity and mortality in this period. Despite advances in medicine and a downward trend since the beginning of the 20th century, puerperal infections are a common cause of prolonged hospitalization and readmissions, especially in developed countries (Axelsson et al., 2018; Karsnitz, 2013, Ngonzi et al., 2018; Woodd et al., 2019).

Studies show that cesarean delivery is one of the most significant risk factors for the occurrence of postpartum infection, having a higher prevalence compared to vaginal deliveries, so the incidence of postparative infection is estimated at 20 to 25% (Mohamed-Ahmed et al., 2019; Keskin et al., 2021). Cesarean section is associated with a significant rate of wound infections (WI) and endometritis, causing rates of healthcare-associated infections (HAIs) 5 to 10 times higher than in vaginal deliveries (Tita et al., 2017). Furthermore, the rate of postpartum endometritis is about ten times higher in cesarean sections performed after the onset of labor than those performed electively (Sgayer et al., 2020). The World Health Organization (WHO) recommends that the cesarean rate should be 15 to 30% to reduce obstetric complications. This rate is still very significant in Brazil, being the second country with the highest proportion of cesarean sections (about 55% of births in the country) (Keskin et al., 2021; Organização Mundial de Saúde, 2015).

Regarding vaginal deliveries, the use of forceps or extractor vacuum is associated with a higher risk of infection, as these instruments can introduce microorganisms into the genital tract increasing the risk of endometritis and more serious ascending infections. Moreover, episiotomies and lacerations can also facilitate the installation of infections (Mohamed-Ahmed et al., 2019). Furthermore, risk factors described in the literature include poor intrapartum hygiene, low socioeconomic status, primiparity, prolonged rupture of membranes, prolonged labor, performing multiple intrapartum vaginal exams, emergency cesarean sections, prematurity, obesity, and anemia (Cunha et al., 2018; Demisse et al., 2019; Ngonzi et al., 2018; Wang et al., 2020). Specifically for endometritis, which generally manifests with lower abdominal pain and purulent discharge, additional risk factors are chorioamnionitis, bacterial vaginosis, manual removal of the placenta, and nosocomial carriers of

group B streptococci (Lapinsky, 2013; Sgayer et al., 2020).

Thus, for having a great impact on public health and maternal morbidity and mortality in Brazil and worldwide, postpartum infections are a relevant issue that requires further studies, to apply preventive measures and better management of affected patients.

2. Methodology

This research consists of a cross-sectional study with a retrospective design, wherein electronic medical records of patients who developed HAIs in the postpartum period were analyzed through the files of the Núcleo de Epidemiologia e Controle de Infecção Hospitalar (NUCIH), which consists of a Hospital Infection Control Committee (In Brazil, such committees were established by law, being an advisory body to reduce as much as possible the incidence and severity of hospital infections). The study was conducted at the Wallace Thadeu de Mello e Silva Regional University Hospital (HU-UEPG) and the Materno Infantil University Hospital (HUMAI), both public hospitals belonging to the State University of Ponta Grossa. Between August and September 2020, the maternity ward was transferred to HUMAI, which became the reference hospital for habitual and intermediate-risk deliveries in the city of Ponta Grossa. IRAS notifications that occurred between January 2019 and December 2021 were included.

The study included puerperal patients (up to 42 days after delivery) with infectious conditions, who had received a clinical/laboratory diagnosis of bacterial infection. Subsequently, data regarding the delivery were collected, including the mother's age, gestational age, length of hospitalization, whether there was premature rupture of membranes, gestational risk classification in prenatal care, antibiotics used prophylactically in cesarean sections, number of prenatal visits, parity, comorbidities and underlying diseases of pregnant women, whether there was the presence of meconium amniotic fluid, and occurrence of urinary tract infection (UTI).

Concerning puerperal infection, data regarding the type of infection, time from delivery to readmission, length of hospital stay, antimicrobials used to treat the infection, culture, and antibiogram when available were selected. These data were obtained through Sistema de Gestão da Assistência de Saúde do SUS (GSUS) e Philips Tasy.

The data found were processed in Microsoft Office Excel® spreadsheets for descriptive statistical analysis, specifically mean and percentage. As for the ethical aspects, the study was submitted to the Ethics in Research Committee of the aforementioned institution and was approved, via the Brazil platform, under opinion number 4,110,874.

3. Results

In the three years that were analyzed in the study, from January 2019 to December 2021, 9097 obstetric procedures were performed in the studied hospital, of which 3000 were performed in 2019, 2910 procedures in 2020, and 3187 in 2021. Among these procedures, 5020 vaginal deliveries (1786 in 2019, 1630 in 2020, 1604 in 2021), and 2860 cesarean sections (798 in 2019, 954 in 2020, and 1108 in 2021) were conducted. With the cesarean section rate being defined as the ratio of the total number of cesarean sections to the total number of deliveries (vaginal + cesarean sections), the rate in 2019 was 30.88%, increasing to 36.92% in 2020 and to 40.85% in 2021. Considering all three years, the cesarean rate was 36.29% (Table 1).

	2019	2020	2021	Total
Obstetric procedures ^a	3000	2910	3187	9097
Total deliveries	2584	2584	2712	7880
Vaginal deliveries	1786	1630	1604	5020
Cesarean sections	798	954	1108	2860
Cesarean Rate	30,88%	36,92%	40,85%	36,29%

Table 1 - Procedures and Cesarean Rate.

^a Obstetric procedures, vaginal deliveries, and cesarean sections. Note the progressive increase in cesarean rates in the years studied. Source: Authors.

In this interval, 58 cases of obstetric HAIs were reported, resulting in a rate of 0.63%. The number of occurrences had a reduction over the years, showing a rate of 1.5% (45 notifications) in 2019, 0.27% (8) in 2020, and 0.15% (5) in 2021. The rate of HAIs in cesarean sections was 1.78%, and also showed a decrease, going from 5.26% in 2019 falling to 0.63% in 2020, and to 0.27% in 2021. The rate of HAIs in vaginal deliveries remained similar in the three years analyzed, being 0.11% in 2019, and 0.12% in 2020 and 2021 (Figure 1). In 2019, there was one case of WI due to laparotomy for an ectopic pregnancy.





HAIs: healthcare-associated infections. CS: cesarean sections. VD: vaginal deliveries. Source: Authors.

Observe the rates of obstetric infections in the years studied and the difference between the values found in infection rates in vaginal delivery and cesarean delivery, especially in 2019, which showed a considerable difference. The reasons for the drop in infections recorded in the 3 years studied are described in the Discussion.

Most of the HAIs recorded were WI, with 46 occurrences (79.31%), followed by 7 cases of endometritis (12.06%), and one of them had a concomitant WI (Figure 2). There was also one tubo-ovarian abscess, one acute abdomen with ovarian rupture, and 4 cases not specified in medical records (6.89%).



Figure 2 – Types of Postpartum Infection.

WI: wound infections. Note the percentage of wound infections, representing the majority of recorded postpartum infections, followed by endometritis. Source: Authors.

In the analysis of medical records, in part of the registers, information on some topics analyzed was missing. Thus, the total value in each point studied was different and is indicated by n in each analysis. Regarding delivery data, of the patients who had postpartum HAIs, 17.85% (n= 56) had meconium amniotic fluid and 23.21% (n = 56) had premature rupture of membranes. Gestational diabetes mellitus (GDM) was found in 7.14% (n = 56) of the patients affected by obstetric HAIs, and gestational UTI was reported in 14.03% (n = 57). From the medical records, it was not possible to determine how long between ruptured membranes and birth were.

In respect of primiparity, 37 were multiparous (64.91%), while 20 were primiparous (35.08%). Of the infections in women who underwent delivery via a high vaginal route, most occurred in those who had already gone into labor (TP). Of the 49 cesareans analyzed in this aspect, 65.30% (32 cases) were already in labor when they underwent the operation, while only 17 cases (34.69%) occurred without the onset of labor.

Concerning the gestational age of the patients who developed HAIs, 89.28% (n = 56) of the deliveries were term and 10.71% were preterm (n = 56), and none were post-term. The average age of the parturients was approximately 26 years. As for the number of prenatal visits, the average was 8.55 (n = 52). Regarding the gestational risk that these patients were assessed during prenatal care, 81.63% (n = 49) of the patients had habitual risk, 12.24% (n = 49) intermediate risk, and 6.12% (n = 49) high risk, and is worth noting that the hospital studied is a reference maternity hospital for delivery in patients with habitual and intermediate risk. These data are detailed in Table 2.

	Variável	n	%
Meconium Amniotic Fluid	Present	10	17,85
Meconium Animouc Fluid	Absent	46	82,14
Premature Rupture of Membranes		13	23,21
GDM		4	7,14
Gestational UTI		8	14,03
Parity	Primiparous	20	35,08
	Multiparous	37	64,91
Cesarean section	Após início do trabalho de parto	32	65,30
	Não entraram em TP	17	34,69
Gestational age	Term	50	89,28
	Preterm	6	10,71
Gestational risk	Habitual	40	81,63
	Intermediate	6	12,24
	High	3	6,12

Table 2 - Characterization of patients with postpartum HAIs.

GDM: Gestational diabetes mellitus, UTI: urinary tract infection. In this table, it is worth noting that almost 2/3 of postpartum infections in cesarean sections occurred in those in which the patient had already gone into labor. Also, note that in this study, most of the patients who had healthcare-related infections were multiparous. Source: Authors.

All patients studied, who underwent cesarean delivery, were submitted to antibiotic prophylaxis. The most used antibiotic was cefazolin (58.82%), followed by the administration of cephalothin in 13.72%, a combination of ampicillin and cefazolin in 3.92%, ampicillin, and cephalothin in 3.92%, clindamycin in 1.96%. In some specific cases in which the patient presented signs and symptoms of a possible infection, other antimicrobials such as ceftriaxone, metronidazole, clindamycin, and gentamicin were used in associations, which can be seen in Table 3.

	n	%
Cefazolin	30	58,82
Cephalothin	7	13,72
Ampicillin + Cefazolin	2	3,92
Ampicillin + Cephalothin	2	3,92
Ampicillin	1	1,96
Clindamycin	1	1,96
Ceftriaxone	1	1,96
Cefazolin + Cephalothin	1	1,96
Cefazolin + Ceftriaxone + Metronidazole	1	1,96
Cefazolin + Clindamycin + Gentamicin	1	1,96
Ampicillin + Cefazolin + Ceftriaxone + Metronidazole	1	1,96
Ampicillin + Cefazolin + Clindamycin + Gentamicin	1	1,96
Ceftriaxone + Azithromycin	1	1,96

Table 3 - Antibiotic prophylaxis schemes.

Observe that the majority of patients received a first-generation cephalosporin (cefazolin and cephalothin). Other antimicrobials were used in cases where the patient presented signs and symptoms of a possible infection. Source: Authors.

Three infections were caused by *Escherichia coli* (*E. coli*), one by *Enterobacter cloacae*, one by multisensitive *Staphylococcus aureus* (*S. aureus*), and one by methicillin-resistant *Staphylococcus aureus* (MRSA) were found. In addition, one patient had a lower airway infection by multidrug-resistant *Acinetobacter sp* (secondary to hospitalization for COVID).

Only one death was recorded: in March 2021, by acute respiratory distress syndrome (ARDS), caused by the SARS-CoV-2 virus. This patient underwent a cesarean section at 28 weeks and 1 day of gestation for respiratory failure due to COVID-19 and died 12 days after delivery; the newborn also died 2 days after birth. No deaths directly due to postpartum infection were recorded.

In the matter of antibiotic therapy, the most used combination was gentamicin and clindamycin, being prescribed for eleven patients. In four cases, this combination was associated, preceded, or staggered by another antimicrobial. The second most used regimen for the treatment of the infections analyzed was ceftriaxone and metronidazole, in six patients, three of whom also used other antibiotics. Another relevant use was cephalexin as monotherapy, in three patients. The description of how many times each drug was used is specified in Table 4.

Antimicrobials	n	%
Gentamicin	13	20,63%
Clindamycin	11	17,46%
Ceftriaxone	10	15,87%
Metronidazole	7	11,11%
Cephalexin	5	7,93%
Cefazolin	2	3,17%
Ampicillin	3	4,76%
Piperacillin-tazobactam	2	3,17%
Azithromycin	2	3,17%
Oxacillin	2	3,17%
Meropenem	2	3,17%
Doxycycline	2	3,17%
Vancomycin	1	1,58%
Polymyxin B	1	1,58%

Table 4 -	Antibiotic	Therapy.
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Note that the most used antibiotics were gentamicin, clindamycin, ceftriaxone, and metronidazole. Source: Authors.

4. Discussion

About the procedures performed, during the period analyzed, remained similar over time, but there was a gradual increase in the number of cesarean sections performed. Since 1985, the WHO has recommended that the cesarean rate remains between 10% and 15%. However, studies show that a rate of up to 30% does not impact maternal and newborn mortality, and above this value, currently available population data do not allow us to assess the relationship between high rates and maternal and newborn mortality (Organização Mundial de Saúde, 2015). Analyzing 2019, the percentage of cesarean sections remains close to the indication of up to 30% (30.88%) but had an increase in 2020 (36.92%) and 2021 (40.85%), staying above the recommended. One point to be taken into consideration was the transfer, in September 2020, of the maternity unit from the HU-UEPG to the HUMAI, however, this does not explain this fact

Regarding obstetric infection rates, the significant drop between the notifications in 2019 (45 cases) and 2020/2021 (8 cases in the first and 5 in the second), can be explained, at least in part, by the change in the NUCIH protocol: in 2019 a phonetic search (telephone calls) was carried out, in which through a questionnaire conducted with postpartum women, more infections were recorded. As of early 2020, due to the advent of the coronavirus pandemic, this protocol was no longer executed, and only the infections in which patients sought care in the hospitals analyzed were recorded. Thus, there was possibly underreporting in the years 2020 and 2021

Other hypotheses about this can be raised. Among them, the pandemic of COVID-19, which took hold in early 2020, may have resulted in stricter hygiene protocols and greater care by patients as well, which may have contributed to this reduction. In addition, the transfer to HUMAI, where there is reduced contact with other patients and possibly exposure to a different microbiome, may have influenced it.

Nevertheless, the obstetric HAIs rate found (0.63%) was consistent with a study conducted in Sweden between 2005 and 2012, in which 16,976 infections were recorded from a total of 795,072 deliveries performed. However, in that study

infections that occurred in the first 8 weeks after birth were considered, concluding that only 2607 infections occurred during the birth hospitalization (resulting in a rate of 0.32%), and UTI were also included (Axelsson et al., 2018).

About the rates of HAIs in cesarean sections and the decrease from 2019 to 2020/2021 (5.26% in 2019, 0.63% in 2020, and 0.27% in 2021), can also be justified by the same reason explained above (underreporting in 2020 and 2021). In a Brazilian study conducted in Fortaleza, the observed rates of postpartum infection were 1.2% and 5.0% for vaginal route and cesarean deliveries, respectively (Medeiros et al., 2019), a result similar to that found in 2019 in cesarean deliveries in the present research. Due to the bias of the difference in the number of infection cases between the three years, it was not possible to apply ODDS RATIO to compare the two types of delivery since there would be a considerable statistical error.

As to the types of postpartum HAIs, the results found (79.31% of WI and 12.06% of endometritis) were consistent with a Polish study in which the authors described that 67.2% of postpartum SAIs were due to WI and 16.8% to endometritis. However, that paper recorded 7.5% of infections being mastitis, which was not included in the present study (Kopeć-Godlewska et al., 2020).

Although primiparity is noted as a risk factor in the literature, of the patients studied, 37 were multiparous (64.91%), while 20 were primiparous (35.08%) (Ngonzi et al., 2018; Wang et al., 2020). Wang et al., 2020). This finding was divergent from a Swiss study, in which 62.4% of HAIs and 50.4% of postpartum endometritis occurred in primiparous women (Axelsson et al., 2018). Among the risk factors found in the literature (gestational DM, premature rupture of membranes, meconium amniotic fluid, and gestational UTI), only the percentages in which they occurred within the cases of postpartum HAIs were surveyed, since the medical records of only the puerperae with infection were analyzed, and it was not the objective of this study to determine the relationship between such factors and the occurrence of HAIs.

Most infections in women undergoing high vaginal delivery occurred in cesarean sections performed after the mother had already gone into labor: 32 cases - 65.30% (n = 49), while only 17 cases - 34.69% (n = 49) occurred in cesarean sections performed without the onset of labor. This finding is consistent with an American study, in which a higher risk of infection was related to emergency cesarean sections than in scheduled ones (OR 5.89; p = 0.0081), however, the sample included only cases of endometritis (Moulton et al., 2018). However, another US study found no statistically significant difference between HAIs rates in elective and non-elective cesarean sections (Sgayer et al., 2020).

Although the WHO does not officially recommend the use of antibiotic prophylaxis in all patients undergoing cesarean sections (due to the implications on global efforts to contain the emergence of resistant bacterial strains), several studies, including one published in "The Lancet" in 2019, demonstrate benefit in such a measure (Knight et al., 2019; OMS, 2015). In general, such prophylaxis is universally recommended, and, in the hospital studied, it is a protocol that all parturients who are going to perform cesarean sections receive antibiotic prophylaxis (Dalton & Castillo, 2014). In the sample analyzed, the majority of patients received a first-generation cephalosporin (cefazolin and cephalothin), so probably the variation between the specific antibiotic must have occurred by availability. Most of the patients who received ampicillin were carriers of group B streptococci.

In the matter of the data on postpartum infection, the results were limited because only part of the infections reported by the NUCIH had a record of the readmission/outpatient visit in the medical record. Few cultures and antibiograms were recorded, so most infections were treated empirically. In a 2017 study in China, in which 40 cases of puerperal infection were analyzed, 60% were caused by Gram-negative bacteria and 35% by Gram-positive bacteria, specifically, 27% by E. coli and 12.5% by S. aureus, and the current research recorded 4 cases by Gram-negative (66.67%), 50% by E. coli and 2 cases by Gram-positive (Song et al., 2020).

In respect of the average number of days from the date of delivery to readmission/outpatient consultation for postpartum infection (8.66 days), a result was found to be consistent with a study conducted in the United States that evaluated

hospital readmissions in the postpartum period, in which it was found that readmissions for infections occurred about 5 days after hospital discharge, taking into account that most women remained hospitalized for 3 days for delivery in the current study (Clapp et al., 2016).

Regarding antibiotic therapy, most patients received antimicrobials empirically since few cultures and antibiograms were performed. Although it had good results in a good part of the patients, in another portion several adjustments were necessary so that the knowledge of the specific microorganism causing the infection would optimize the use of antimicrobial agents.

There were limitations to comparing the data obtained with studies in the literature, as few studies similar to this one were found.

5. Conclusion

Postpartum infections are important complications of childbirth, contributing to higher rates of readmission, longer hospital stays, and higher costs. Therefore, the role of the Hospital Infection Control Commissions is extremely relevant, through epidemiological surveillance, prevention protocols, and asepsis.

Moreover, the fact that few cultures and antibiograms are performed in patients affected by obstetric infections restricts the microbiological knowledge that affects this population and limits antibiotic therapy to be empirically performed. The identification of bacterial agents with their susceptibility patterns is an instrument to guide therapy and a tool to develop action protocols.

Regarding the route of delivery, the present study evidenced a high rate of cesarean sections, which predispose to a higher risk of postpartum infection, especially if conducted after the onset of labor (being these performed due to some complication, therefore they were considered the best alternative for the mother-child binomial), as described in the literature. Although it was not possible to establish the odds ratio, the rates were higher in cesarean sections than in vaginal deliveries, consistent with the great majority of other studies.

Given the importance of the subject, more studies can be carried out. An analysis of a longer period of time may bring clarifications and greater depth in the understanding of such infections. Furthermore, it would be interesting to conduct a study that analyzes the risk factors for postpartum infections, establishing statistical relationships between each factor, which is lacking in the literature.

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