Labor and puerperium outcomes in women with a history of urinary tract infection during pregnancy

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Bruna Thais da Rocha Paes[1], Ana Paula de Assis Sales[2], Vivian Maria Madeiro[3], Tailma Silva Lino de Souza[4], Gabrielly Segatto Brito[5], Juscilene da Silva Maciel[6], Laís Flávia de Castro Pinheiro Campos[7], Andrezza Gabrielly dos Santos Soldera[8] and Andriely Gomes dos Santos[9]

ABSTRACT

Objective: To summarize the studies that evaluate possible outcomes of labor and puerperium in women who had Urinary Tract Infection during pregnancy. Methods: Integrative literature review with a search carried out in the Virtual Health Library (VHL), National Library of Medicine National Institutes of Health (PubMed), Web of Science and CINAHL databases, with articles from 2018 to 2022 as inclusion criteria. Results: Seven articles were selected for this review, and all studies brought preterm labor as one of the main outcomes, followed by 71.4% that point to low birth weight, 42.9% emphasize neonatal death, 28.6% point to abortion and premature rupture of membranes, 14.3% associate neonatal asphyxia and preeclampsia as one of the main findings. In addition, 42.9% of the articles outlined the sociodemographic profile of these women, relating maternal age, multiparity, ethnicity, and socioeconomic conditions. Conclusion: Prematurity, low birth weight, and neonatal death were the main outcomes found in this review. It is suggested that further studies investigate whether there is a relationship between neonatal asphyxia and preeclampsia as complications of UTI in pregnancy.

Keywords: Pregnancy Complications, Pregnant Women, Urinary Infections, Nursing.

[1] Nurse graduated from the Undergraduate Nursing course at the Integrated Health Institute - Federal University of Mato Grosso do Sul.
[2] Doctor. Professor of the Nursing Course at the Integrated Institute of Health/UFMS.
[3] Undergraduate Nursing Student INISA/UFMS.
[4] Nurse. Master's student in the Master's Program in Nursing/INISA/UFMS.
[5] Nurse. Master's student in the Master's Program in Nursing/INISA/UFMS.
[6] Nurse at SESAU / Campo Grande-MS. Master's student in the Graduate Program in Health and Development in the Midwest Region of UFMS.
[7] Nurse at the Women's Unit. Maria Aparecida Pedrossian University Hospital-HUMAP/EBSERH/MEC/UFMS.
[8] Nurse. Master in Nursing from the Graduate Program in Nursing. INISA/UFMS.
[9] Obstetric Nurse. State Department of Health (SES) - Mato Grosso do Sul.

INTRODUCTION

Urinary tract infection (UTI) is a common complication during pregnancy, affecting approximately 10%-12% of pregnant women, due to the hormonal, anatomical and physiological changes that occur in the maternal body during this period[1]. Among these changes, urinary stasis caused by the reduction of ureteral peristalsis, increased urine production, glycosuria and aminoaciduria, which favor bacterial growth and promote infections, can be highlighted[2].

Organisms that cause UTI in pregnancy are the same uropathogens that commonly cause UTI in non-pregnant patients. *Escherichia coli* is the most commonly isolated organism. Other bacteria that can be observed include the species *Klebsiella pneumoniae, Staphylococcus, Streptococcus, Proteus and Enterococcus*[3].

Clinically, UTI can be classified as lower tract infection, as in cases of Asymptomatic Bacteriuria (BA) and cystitis, and urinary tract infection

Above all, BA is defined by the presence of 105 colony-forming units (CFU) per milliliter of a single pathogen, in a urine sample obtained from the midstream, and in the absence of symptoms. Its incidence is around 9% to 11% of all pregnancies. If BA is not treated, approximately 30% of the cases will progress to cystitis or pyelonephritis[1].

On the other hand, cystitis is an uncomplicated inflammation, usually treated on an outpatient basis, not requiring hospitalization. They usually present with dysuria, urinary urgency, frequency, nocturnal urination, and suprapubic pain, and are unlikely to occur with fever[4].

Pyelonephritis, in turn, is considered the most serious type of UTI and consists of infection of the renal parenchyma and its adjacent structures. The diagnosis is made by bacteriuria accompanied by systemic symptoms such as fever, tachycardia, chills, nausea, vomiting and low back pain, with a positive Giordano sign. After detection, hospitalization is mandatory due to the risk of septic syndrome, and intravenous antibiotic treatment should be initiated immediately[1].

To detect UTI cases early and prevent their complications, the Ministry of Health recommends two urine tests during pregnancy. The first should be performed in the first trimester, and the second exam in the third trimester[4].

However, if urinary tract infection is not treated correctly after its diagnosis, it can generate serious complications for both the mother and the fetus, which is the main cause of sepsis throughout pregnancy, associated with the risk of prematurity, premature rupture of amniotic membranes, abortion, low birth weight and perinatal death[5].

The recurrence of UTI can often lead women to frequent hospitalizations during pregnancy, due to the aforementioned aspects, and requires continuous surveillance from professionals who work in prenatal care as well as in hospital services, for this, control by urinalysis tests and health education have been important in the management of UTI complications in pregnant women[6].

Nursing works in primary and hospital care environments and provides care to pregnant women with UTI in different scenarios, so the study of obstetric and neonatal complications is of interest to the profession, as it broadens the scope of knowledge and improves its care practices. In view of the above, the objective of this review is to summarize the studies that evaluate possible outcomes of labor and puerperium in women who had UTI during pregnancy.

METHOD

The Integrative Literature Review (RIL) is a research method that allows the search, critical evaluation and synthesis of the available evidence on the topic investigated, with its final product being the current state of knowledge on the topic itself, the implementation of effective interventions in health care and cost reduction, as well as the identification of gaps that direct the development of future research [7]. Thus, for this RIL, the following steps were carried out: elaboration of the guiding question, literature search, evaluation of the studies, critical analysis of the included studies, discussion of the results and presentation of the integrative review [8].

The guiding question of the research (What are the outcomes of childbirth and puerperium in women who had Urinary Tract Infection during pregnancy?) was defined using the mnemonic PVO (*Population, Variables, and Outcome*), which ensured better traceability of the publications. The PVO strategy was proposed by the Latin American and Caribbean Center on Health Sciences Information (Bireme) in 2011, with the objective of facilitating the diagnosis of the various needs of research questions, optimizing the response time in document retrieval [9]. In the present study, the acronym PVO was defined as follows: P- Pregnant women; V- Urinary Tract Infection; O- Outcome in childbirth and puerperium.

The search for studies took place from March to June 2023, in the Virtual Health Library (VHL), *National Library of Medicine National Institutes of Health* (PubMed*), Web of Science,* and CINAHL databases. The Health Science Descriptors (DeCS) and MeSH Database were *Pregnant Women, Pregnancy, High-Risk, Urinary Tract Infections, Pregnancy Complications, Infant, Premature*, combined using Boolean connectors AND or OR, (Chart 1).

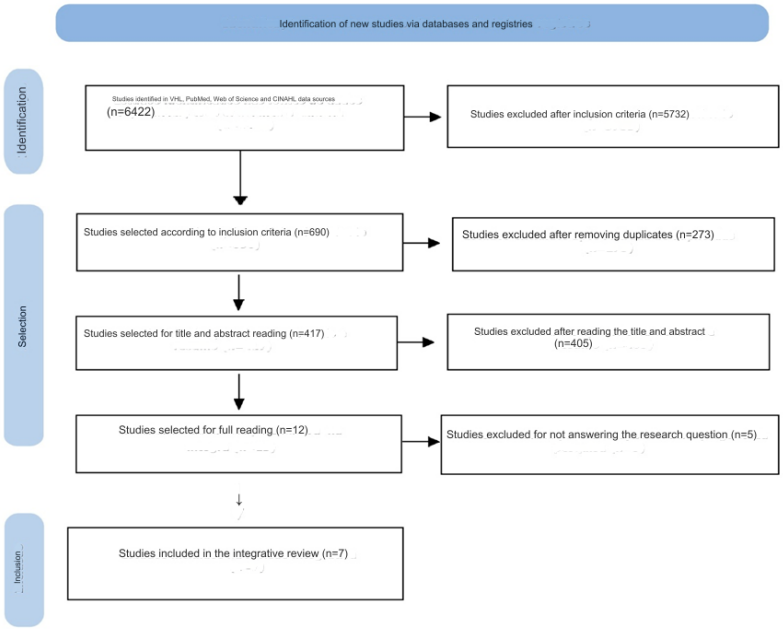
Chart 1 - Combinations of descriptors used in the search strategies. Campo Grande- MS, 2023.

DATABASE	CROSSINGS
VHL	("urinary tract infections") AND (pregnant women) AND (pregnancy complications) ("urinary tract infections") AND ("pregnancy complications") ("urinary tract infections") AND ("premature newborn") ("urinary tract infections") AND (pregnant women)
PUBMED	("Urinary Tract Infections") AND ("Pregnancy Complications") ("Urinary Tract Infections") AND ("Pregnant Women") ("Urinary Tract Infections") AND (Pregnancy) AND ("Infant, Premature")
Web of Science	(ALL=("Urinary Tract Infections")) AND ALL=(("Pregnancy Complications") (ALL=("Urinary Tract Infections")) AND ALL=("Pregnant Women") (ALL=("Urinary Tract Infections")) AND ALL=(Pregnancy)
CINAHL	(urinary tract infection or uti or tract infection or urinary infection) AND (pregnancy or pregnant) AND pregnancy complications (urinary tract infection or uti or tract infection or urinary infection) AND pregnancy complications AND infant, premature (urinary tract infection or uti or tract infection or urinary infection) AND pregnancy, high risk (urinary tract infection or uti or tract infection or urinary infection) AND (pregnancy or pregnant women)

Published primary studies, full articles available in full in English, Spanish, and Portuguese were used as inclusion criteria; between 2018 and 2022, whose theme addressed the outcomes of childbirth and puerperium in women who had UTI during pregnancy. The exclusion criteria were publications resulting from letters to the editor, reviews, editorials, expert opinions, and reviews. In addition, duplicate articles were considered only once.

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses *(PRISMA) instrument was adopted* to show the process of identification, screening, eligibility and inclusion of studies [10]. From the search carried out in the databases, 6422 studies were found, after the inclusion criteria, 690 articles were selected, in which after the removal of duplicates there were 417 studies. Thus, a detailed reading of the title and abstract was carried out and 12 articles were selected and read in full, in which 7 answered the research question, according to the flowchart (Figure 1).

Figure 1 - PRISMA flowchart: steps for article selection, Campo Grande- MS, 2023.



After these steps, the data were extracted using a structured instrument developed by the researchers, with the following items: author, year, title, country, method, sample, objective, results, and Level of Evidence.

To assess the Level of Evidence of the studies, the *Hierarchy of Evidence for Intervention Studies* was used, which proposes an analysis with seven levels of evidence: Level I, for systematic review of meta-analyses; Level II, for randomized controlled trials; Level III, for controlled trials without randomization; Level IV, for case-control or cohort study; Level V, for systematic review of qualitative and descriptive studies; Level VI, for qualitative and descriptive study, and Level VII, for expert opinion or consensus[11].

RESULTS

Seven studies were selected from the following countries: Cuba, the United States, Ethiopia, the Netherlands, Mexico, Romania and Turkey, with a total number of 146,556 pregnant women studied. Regarding the characterization of the studies, most 42.9% were developed in North American countries[12-14], all used quantitative methods and 85.8% were published in English[13-18] and 14.3% in Spanish[12]. The Levels of Evidence indicate that all studies analyzed are considered Level IV. (Chart 2).

Chart 2 - Characterization of the studies included in the integrative review. Campo Grande- MS, 2023.

Author/year	Title/Country	Method/ Sample	Objective	Results	Level of evidence
IRONING; GARCIA; PEDRO./ 2021	Pregnant women with urinary tract infection belonging to a health area of the municipality of Guanabacoa, Havana/ CUBA	Cohort/ 129 pregnant women	To characterize pregnant women with urinary tract infection, belonging to the health area of the University Polyclinic "Ángel Machaco Ameijeiras" in Guanabacoa, La Havana, Cuba, from January 2019 to January 2020.	The pregnant women included in the study were characterized, with a predominance of urinary tract infection. Low birth weight was the most represented complication.	Level IV
MICLE et al./ 2020	The prevalence of urinary tract infections in Pregnancy and implications on foetal development/ ROMANIA	Control case/ 427 pregnant women	To assess the type of bacterial etiology causing urinary tract infections, the pattern of antibiotic susceptibility in pregnant women, and whether there are correlations between asymptomatic bacteriuria and maternal and neonatal adverse effects	We found an association between UTIs and mean birth weight and prematurity.	Level IV
BECSAK et al./ 2019	Uropathogens and Gestational Outcomes of Urinary Tract Infections in Pregnancies that Need Hospitalization/ TURKEY	Cohort/ 30 pregnant women	Identify uropathogens that cause urinary tract infections (UTIs), assess hospitalization, and analyze pregnancy outcomes	Preterm labor seems to be an important complication in the pregnancies with UTIs accompanied by fever and urinary problems.	Level IV
WERTER et al./ 2021	Risk Indicators for Urinary Tract Infections in Low Risk Pregnancy and the Subsequent Risk of Preterm Birth/ HOLLAND	Cohort/ 4918 pregnant women	Identify potential risk indicators for developing a UTI in pregnancy. In addition, we explored whether the risk of preterm birth was increased in women with these risk indicators.	The risk of preterm birth was increased in women with UTI during pregnancy, however, this risk does not appear to exist in a subset of women with a history of recurrent UTI as well and with ASB in the current pregnancy.	Level IV
BAER et al./ 2019	Risk of preterm birth among women with a urinary tract infection by trimester of pregnancy./ UNITED STATES	Cohort/ 140,910 pregnant women	To assess the risk of preterm birth among women with an emergency department (ED) visit or urinary tract infection (UTI)	UTIs increase a woman's risk of having a PTB, particularly a spontaneous PTB. This risk is high	Level IV

			hospitalization per trimester of pregnancy.	regardless of the trimester of pregnancy.	
GEBREMEDHIN et al./ 2021	Maternal Complications and Adverse Pregnancy Outcomes among Pregnant Women who Acquired Asymptomatic Bacteriuria in Addis Ababa, Ethiopia/ ETHIOPIA	Cohort/ 43 pregnant women	To prospectively follow the pregnancy of women with confirmed asymptomatic bacteriuria in Addis Ababa and to explore the type and rate of occurrence of maternal complications and adverse pregnancy outcomes.	Some of the The most prevalent adverse pregnancy outcomes observed were perinatal death, miscarriage, preterm birth, low birth weight, and asphyxia.	Level IV
DAUTT-LEYVA et al./ 2018	Maternal and perinatal complications in pregnant women with urinary tract infection caused by Escherichia coli/ MEXICO	Cohort/ 99 pregnant women	OBJECTIVE: To describe maternal and perinatal complications in pregnant women with UTI caused by Escherichia coli and to know the pattern of antimicrobial susceptibility.	According to this study in a Mexican population, the number one admission diagnosis in women with UTI due to E. coli were threatened with preterm birth, fever and threatened miscarriage .	Level IV

Of the articles that make up this review, all brought premature labor as one of the main outcomes, followed by 71.4% that point to low birth weight[12,14-17], 42.9% emphasize neonatal death[14,15,17], 28.6% point to abortion[14,15] and premature rupture of membranes[12,15] and 14.3% associate neonatal asphyxia and preeclampsia as one of the main findings[15].

Regarding the profile of the women studied, 71.4% of the studies report the mean age of pregnant women with UTI, with the most common interval being 25 to 30 years[12,14-17]. In addition, 42.9% of the articles outlined the sociodemographic profile of these women, relating maternal age, multiparity, ethnicity and socioeconomic conditions[14,15,18].

DISCUSSION

In this review study, preterm birth was shown to be the worst outcome of UTI for maternal and fetal health. Defined as delivery before 37 weeks of gestation, it is the most important cause of neonatal mortality and morbidity worldwide. It is estimated that maternal infection is responsible for 50% of premature births[19]. In Mexico, preterm birth is one of the most important causes of perinatal morbidity and mortality, accounting for 75% of perinatal deaths, 50% of neurological sequelae directly attributable to prematurity, and its frequency is estimated at about 5–10% of all

pregnancies[14]. In the study conducted in Turkey, the rate of preterm birth associated with UTI was 56.3%, in Ethiopia 48.8%, in Cuba 19.23% and in the Netherlands 12.0% [12,15,17,18].

Low Birth Weight (LBW) was evidenced as one of the main neonatal complications in this study. LBW is considered when the newborn (NB) weighs < 2,500g and is associated with higher neonatal and infant mortality and morbidity, being considered the single most influential factor in survival in the first years of life[20]. Regarding the causes, infection may be an etiological factor due to endothelial damage and worsening of maternal inflammatory responses[19]. The study conducted in Cuba shows low birth weight as the main outcome of UTI during pregnancy, with its occurrence in 34.6% of the pregnant women in the sample, while in Mexico this rate corresponds to 12% and in Ethiopia 6%[14,15].

Neonatal death is also among the main outcomes of UTI in pregnancy. Understood as the death of the NB up to the 28th day of life. As for the causes, infection, premature birth and birth asphyxia are the main causes of neonatal mortality in the world[21]. There was an association of this outcome due to complications of UTI during pregnancy, and its occurrence was found in 10.0% of the cases in Turkey, 5.9% in Mexico and 4.3% in Ethiopia[17,14,15], these numbers being higher than the annual global neonatal mortality rate[22]. From this perspective, these findings are in line with the Sustainable Development Goals (SDGs), which aim to reduce neonatal mortality worldwide to at least 12 per 1,000 live births by 2030[23].

Among the obstetric outcomes observed in the components of this review, abortion stands out. According to the Ministry of Health, abortion consists of the interruption of pregnancy before 22 weeks of gestation, or of a fetus < 500g[23]. In the study carried out in Mexico, 9.9% of the risk of abortion was identified, of which 3.5% were abortions[14], while in Ethiopia this rate was 2.3%[15].

In addition, there was an association with Premature Rupture of Membranes (PPR) as an outcome found in the articles of this study. Defined as the loss of integrity of the ovular membranes before the onset of labor, regardless of gestational age, RPM usually occurs in about 8% of pregnancies[25]. This finding was found in a study carried out in Cuba, corresponding to 21.15% of the sample[12]. Thus, RPM has been shown to be a relevant factor for the worsening of fetal and neonatal health resulting from UTI.

In addition, one of the articles brought perinatal asphyxia as a neonatal complication due to UTI in pregnancy. Perinatal asphyxia develops when there is significant tissue hypoperfusion and decreased oxygen supply due to the most diverse etiologies during the peripartum period, at birth and in the first minutes of life[26]. According to the WHO, this condition is the third leading cause of neonatal death [27]. Perinatal asphyxia was found in 32.6% of Ethiopia (Ethiopia), i.e., one in three newborns were asphyxiated in their first minutes of life[15]. This finding was different from that found

in Turkey, in which the mean APGAR score, a scale that assesses the global health of the newborn, was found to be within normal parameters [17].

Furthermore, it can be seen in one of the articles that there may be a relationship between preeclampsia (PE) and UTI during pregnancy. PE is a multisystem vascular syndrome of pregnancy characterized by hypertension and proteinuria, which usually occurs after 20 weeks of pregnancy. Although its etiology remains unknown, it is believed that excessive activation of the systemic inflammatory response plays a fundamental role in its pathogenesis, and can therefore be associated with UTI[28]. In a study carried out in Ethiopia, 14% of pregnant women with BA had PE and 18.6% developed eclampsia[15].

However, it is possible to associate the influence of the Social Determinants of Health with the unfavorable outcomes of UTI during pregnancy. Thus, UTI and its complications have been shown to be more intense in low- and middle-income countries [15]. The study conducted in the Netherlands includes seven significant risk indicators for the development of UTI during pregnancy, such as: maternal age, non-European ethnicity, does not live with a partner, low education, smokers, has a history of recurrent UTI, and the presence of BA at around twenty weeks of gestation [18].

According to this, in a study conducted in Mexico, UTI is associated with ethnicity, parity, number of prenatal consultations, and socioeconomic status of women [14]. In the study carried out in Ethiopia, sexual frequency, vaginal douche, presence of anemia and history of UTI prior to pregnancy were pointed out [15]. Therefore, a study carried out in Pakistan shows the socioeconomic profile of women who have a higher risk of developing UTI during pregnancy, 74% of whom belong to the lowest economic class, multiparous, aged 26 to 30 years, with low education and a previous history of UTI [29]. These findings are similar to the articles that make up this review [14,15,18].

There is also a relationship between the number of prenatal visits and complications of UTI in pregnancy. In Mexico, 41.67% of pregnant women with UTI had inadequate prenatal control with less than four visits during pregnancy, which makes it difficult to screen for and control this disease during pregnancy [14]. In Brazil, a minimum of six consultations is recommended, and screening for BA during pregnancy occurs through urine and urine culture tests, usually requested in the first and third trimesters, depending on the protocol of each municipality [1].

Regarding Asymptomatic Bacteriuria (BA), research shows different results regarding its severity. In the Dutch study, no association was found between prematurity and BA pregnancy[18], while in Ethiopia 48.8% of premature births were identified, as well as other complications in pregnant women and newborns[15]. This difference can be explained by the disparity in relation to the economic conditions of these countries, which directly impact access to health services.

From another angle, 57.14% of the articles selected for this review provide information on the highest occurrence of UTI per trimester of pregnancy[12-14,16]. In Cuba, the study indicates that the

prevalence is higher in the first and third trimesters[12], while in Romania 68.30% of BA occurred more frequently in the third trimester[16]. On the other hand, studies conducted in the United States and Mexico indicate the severity of UTI in the second trimester, and in the USA, women in this gestational period were at greater risk of hospitalization and prematurity [13]. In Mexico, neonatal deaths and intrauterine deaths were more frequent in pregnant women exposed to the infection during the second trimester[14]. From this perspective, it can be inferred that in the second trimester of pregnancy, the occurrence and diagnosis of other morbidities that result from pregnancy, such as Pregnancy-Specific Hypertensive Syndrome (SHEG), and its pathophysiology is a factor that, associated with UTI, can aggravate the clinical condition [1].

Thus, prematurity that occurs in the second trimester of pregnancy is a major risk factor for newborns. The second trimester corresponds to between 14 and 28 weeks of gestation, and the neonate in this period is considered extremely preterm [31]. One of the major concerns of birth at this gestational age (GA) is the fact that the NB presents anatomical-physiological immaturity of the respiratory tract [32]. The maturity of this system occurs around 35 gestational weeks, when anatomical and functional adaptations allow the premature newborn to survive in the extrauterine environment. Therefore, birth before this GA is related to greater pulmonary dysfunctions[33], and the use of Invasive Mechanical Ventilation (IMV) and Noninvasive Mechanical Ventilation (NIMV) may be necessary, and prolonged ventilation time, in turn, is associated with a high morbidity and mortality rate in this neonatal period[32].

Another finding of this review concerns the relationship between single UTI and recurrent UTI. Recurrent UTI is the diagnosis of three episodes of infection over the course of 12 months, or two episodes in six months[34]. Studies conducted in the United States and the Netherlands show that the only UTI diagnosed during pregnancy has a higher chance of complications such as prematurity compared to pregnant women with recurrent UTI[13,18]. One explanation for the results found may be that the immune system has an inadequate response in women with recurrent UTI, which may result in lower prostaglandin release and, consequently, less chance of premature birth[18].

The limitations of this review include the number of publications that had been reduced in the last five years and the clinical association with other morbidities or that did not answer the question of this study.

CONCLUSION

Prematurity, low birth weight, and neonatal death were the main outcomes found in this review. It is suggested that further studies investigate whether there is a relationship between neonatal asphyxia and preeclampsia as complications of UTI in pregnancy.

It can be inferred that UTI in pregnant women is a global public health problem, especially in poorer countries, and its consequences can lead to hospitalization, as well as conditions that threaten the life of pregnant women and their fetuses. Thus, investigations that seek to understand obstetric outcomes in pregnant women with UTI should be of interest to broaden the discussion of the topic, predict negative outcomes in maternal and fetal health, and improve the practices of health teams.

It is important to emphasize that UTI is a clinically important condition for maternal, fetal/neonatal complications, prenatal care is an opportune moment of health care for pregnant women. It is essential for professionals who work in prenatal care at usual risk to appropriate soft and hard technologies in UTI monitoring.

The findings of this study highlight the importance of greater adherence to prenatal care, and that prenatal care is qualified and has professionals trained to manage UTI to screen for Asymptomatic Bacteriuria in the second trimester of pregnancy, to prevent prematurity and other unfavorable outcomes in this period.

In addition, public health policies need to be aimed at women with greater risk factors for developing UTI during pregnancy. The nurse works in prenatal care at usual risk and classifies gestational risk, which is up to this in the daily care in the maternal-infant line, seeking to improve the morbidity and mortality indicators of the mother and child binomial.

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