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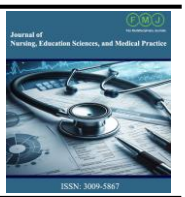

Research article

Descriptive analysis of risk factors for preterm infants with birth weight

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Abstract

Introduction: Prematurity is defined as a birth occurring before the 37th week of amenorrhea, calculated from the 1st day of the last menstrual period and/or an ultrasound scan performed during the first trimester of pregnancy. Premature birth continues to be the world's leading cause of infant and child mortality, sensorimotor disability, and neurodevelopmental difficulties. Objective: Our work aims to describe the incidence and risk factors of prematurity and compare our results with those of other studies.

Materials and methods: This is a cross-sectional, retrospective, descriptive study conducted over two years, from June 1, 2021, to June 30, 2023, at the neonatology and neonatal intensive care unit of CHU HASSAN II in Fez. Statistical analyses were performed using the JAMOVI software. Qualitative variables were expressed as frequencies and percentages, while quantitative variables were presented as means with standard deviations (SD) or medians with interquartile ranges (IQR).

Results: The neonatology and neonatal resuscitation department welcomed 241 premature newborns with a birth weight ≤ 1500g, representing 8.80% of all hospitalizations in the department. 127 (53%) were female, and 114 (47%) male. The mean gestational age was 30.6 ± 2.4 weeks of amenorrhea. 71% of newborns (170) were born spontaneously preterm, and 29% (71) induced preterm. Factors associated with prematurity were mainly the threat of preterm delivery (36%), lack of medical follow-up of pregnancy (21%), gravidic hypertension in 18.67%, and gestational diabetes in 5.80% of cases.

Conclusion: This study determined the frequency of premature delivery and identified certain risk factors, some of which are already targeted by the national perinatal program. The results of our study are intended to sound the alarm about the need to implement a management plan to improve the monitoring and management of premature pregnancies and births at all levels of care.

Keywords: Prematurity, very low birth weight, risk factors, neonatal morbidity, neonatal mortality.

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1. Introduction

Each newborn is characterized by its "gestational age" or "term," which corresponds to the duration of the pregnancy (Alexandre et al., 2009). Gestational age, expressed in weeks of amenorrhea, is defined chronologically from the first day of the last menstrual period to birth and/or estimated by ultrasound in the first trimester of pregnancy (Compan, 2015; Beillat, 2012). The World Health Organization (WHO) defines prematurity as birth before 37 completed weeks of amenorrhea (or 259 days after the first day of the last menstrual period). A distinction is usually made between late prematurity (birth between 34 and 36 completed weeks of amenorrhea), moderate prematurity (32 to 33 completed weeks of amenorrhea), extreme prematurity (28 to 31 completed weeks of amenorrhea), and very extreme prematurity (< 28 completed weeks of amenorrhea) (Compan, 2015). It's during the last trimester of pregnancy that most organs acquire the functionality they need to adapt to life outside the womb. Any premature birth, therefore, carries the risk that a series of functions controlling homeostasis and the necessary adaptations to the new aerial environment will not be effective (Dehan et al., 1997). The risk incurred is all the greater when the gestational age is low. The prognosis is correlated with conditions of care in antenatal, perinatal, and postnatal care, as well as with the

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quality of reception. The global incidence of premature births is approximately 15 million per year or one in 10 (Purisch et al., 2017). It is estimated that complications related to these births are responsible for 35% of the 1 to 3 million annual neonatal deaths worldwide (Blencowe et al., 2012). More than 60% of premature births occur in Africa and South Asia, but the problem is truly global. In the poorest countries, an average of 12% of babies are born prematurely, compared with 9% in higher-income countries. According to the WHO, the rate of premature births each year in Morocco is estimated at 13.41% of births, or around 91,400 (Moroccan ministry of health, 2019).

Low birth weight (LBW) is an indicator of prematurity, defined by the WHO as any live birth weighing less than 2,500 g. It is subdivided into the following categories: Low birth weight: birth weight < 2500g. Very low birth weight: birth weight < 1500g. Extremely low birth weight: birth weight < 1000g (World Health Organization, 2023).

Low birth weight (LBW) is a major factor in neonatal morbidity and mortality and a genuine public health problem in developing countries. It is an important predictor of child survival and subsequent development (Liu et al, 2019).

Despite considerable efforts to improve neonatal care, data specific to very low birth weight premature babies in Morocco remain limited. Identifying the risk factors associated with prematurity in specific hospital settings, such as level 3 academic centers, is essential to guide prevention and intervention strategies.

Our objectives are to determine the hospital frequency of premature newborns with a birth weight less than or equal to 1500 g in the Neonatology and Neonatal Intensive Care Unit (NNRN) of the Hassan II University Hospital in Fez and to describe the socio-demographic characteristics of the mothers of premature newborns and the risk factors associated with prematurity.

2. Methods

The study took place in the Neonatology and Neonatal Intensive Care Unit of the Hassan II University Hospital in Fez, a tertiary-level center located on the third floor of the Mother and Child Hospital. The department welcomes newborns referred primarily by the maternity unit of the CHU Hassan II de Fès, as well as provincial hospitals and clinics in the city of Fez and neighboring regions. The department comprises a day hospital and two hospitalization units: a neonatal intensive care unit and a premature babies unit.

This is a cross-sectional, retrospective, and descriptive study conducted over two and a half years, from June 1, 2021, to June 30, 2023. A total of 241 records of premature newborns with a birth weight (DBW) ≤ 1500 g were included in this study.

The inclusion criteria were as follows: neonates with a gestational age of less than 37 weeks of amenorrhea and a birth weight of less than or equal to 1500 g, regardless of the reason for hospitalization. We isolated a total of 241 cases. Excluded were all term and post-term neonates with a birth weight less than or equal to 1500 g, premature babies with a birth weight greater than 1500 g, those whose gestational age and/or weight were not specified in the record, and incomplete records.

To carry out this work, we collected information in two stages: Firstly, the files were identified by consulting the hospitalization registers for the years 2021, 2022, and 2023. This first step allowed us to extract information on the number, sex, gestational age, and reason for hospitalization, as well as some evolutionary data such as the death or survival of premature babies. It also enabled us to count all hospitalizations in the department. In the second phase, data from patient records and the computer archive were collected in ascending chronological order from June 2021 to June 2023, using a pre-established evaluation sheet to analyze the following aspects:

Anamnestic data: gender, date of birth, gestational age, time to delivery, reason for hospitalization, maternal characteristics.

Clinical and paraclinical data: weight, adaptation to extrauterine life, malformations detected, etc.

Statistical analyses were performed using JAMOVI software for Windows 2016. Qualitative variables were presented as frequencies and percentages, while quantitative variables were presented as mean ± standard deviation (SD) or median (interquartile range, IQR).

3. Results

During the study period (from June 1, 2021, to June 30, 2023), the Neonatology and Neonatal Resuscitation Department at CHU Hassan II in Fès admitted 2,736 newborns. Among these, 1,127 were hospitalized in the premature unit, representing a hospitalization rate of 41.19%. Premature infants with a birth weight ≤ 1500 g numbered 241, accounting for 21.38% of the premature infants and 8.80% of all hospitalizations in the department. Our study revealed a slight female predominance, with 127 girls (53%) compared to 114 boys (47%), resulting in a sex ratio (M/F) of 0.9.

In our cohort, 71% of the newborns (170 cases) were born following spontaneous preterm labor, while 29% (71 cases) were due to medically induced preterm labor. The average gestational age was 30.6 ± 2.4 weeks of gestation (WG), with the most common method of determination being the date of the last menstrual period (77.17%).

The average age of the mothers was 29.19 ± 6.85 years, ranging from 17 to 45 years. The most common age group was 18 to 35 years, representing 67.63% of cases. Among the admitted cases, 220 were born to married mothers (91.28%) and 4 to single mothers (1.65%). Marital status was not specified in 17 cases (7.05%).

Mothers from urban areas accounted for 109 cases (45.22%), while those from rural areas represented 72 cases (29.87%). The place of residence was not specified in 24.89% of cases, and consanguinity (of any degree) was noted in 12.44% of the cases.

Table 1: Sociodemographic Characteristics of Mothers

Characteristic	Categories	Number (n = 241)	Percentage (%)
Maternal Age (years)	< 18	11	4.56
	18 to 35	163	67.63
	> 35 years	62	25.72
	NS	5	2.07
Occupation	Paid Work	15	6.22
	Housewife	154	63.90
	NS	72	29.87
Marital Status	Married	220	91.28
	Single	4	1.65
	Not Specified	17	7.05
Consanguinity	Yes	30	12.44
	No	172	71.36
	NS	39	16.18
Place of Residence	Urban	109	45.22
	Rural	72	29.87
	NS	60	24.89

NS: Not Specified

Pauciparous women constituted the majority, representing 39.41% of the mothers in our series. They were followed by primiparous women (35.68%) and multiparous women (20.33%). Grand multiparous women accounted for only 4.56%.

Medical and Surgical: History: 87.96% of mothers had no significant medical or surgical history. Hypertension was found in 0.82% of cases (2 cases). Diabetes was present in 3.31% of cases (8 cases). Other notable medical histories included: 7 cases (2.90%) of anemia, 2 cases (0.82%) of thyroid dysfunction, 2 cases (0.82%) of epilepsy, 2 cases (0.82%) of chronic kidney disease (with one hemodialysis session per day during pregnancy), and 2 cases (0.82%) of deep-vein thrombosis.

Gynecological and Obstetric History: The vast majority of mothers had no notable gynecological or obstetric history. At least one history of prematurity or abortion was found in 7.46% and 17.42% of cases, respectively, which corresponds to 18 and 42 cases. Other notable abnormalities included 2 cases (0.82%) of pre-eclampsia, 1 case (0.41%) of ectopic pregnancy, 2 cases (0.82%) of uterine hypoplasia, 1 case (0.41%) of cervical cancer, 1 case (0.41%) of breast cancer, 1 case (0.41%) of intracavitary uterine fibroid, and 2 cases (0.82%) of secondary infertility. In total, there were 10 cases (2.41%) of other gynecological and obstetric abnormalities.

No cases of smoking or alcohol use among the mothers were recorded.

Risk factors for prematurity: Pregnancy was monitored in **76%** of cases (184 cases) and not monitored in **21%** (51 cases). Twin pregnancies accounted for **25%** of cases, while triplet pregnancies represented **3%**. The threat of Preterm Labor marked 36.09% (87) of pregnancies. Only 17.24% (15) of patients benefited from tocolysis. Premature Rupture of Membranes occurred in 80 parturients (33.19%). The duration of membrane rupture ranged from 5 hours to over 96 hours. Amniotic fluid was clear in 77.17% of cases (186 cases) and tinted in 8.7% (21 cases).

More than two-thirds of the mothers (65.56%) experienced at least one pathology during pregnancy. The pregnancy was complicated by a threat of preterm labor in 36.09% of cases and by third-trimester bleeding in 4.97% of cases. Gestational hypertension and gestational diabetes were present in 18.67% and 5.80% of cases, respectively. The infectious history was positive in 41.9% (101) of the parturients. Suspected infections included cervical-vaginal infections in 29.41% of cases (30 cases), urinary infections in 25.49% of cases (26 cases), and isolated fever reported in 6.86% of cases (7 cases). Finally, newborns from singleton pregnancies represented the majority of cases, accounting for 72%.

4. Discussion

Incidence of prematurity

In most industrialized countries, prematurity has increased over the past three decades, representing a significant public health issue. Preterm births contribute substantially to neonatal morbidity and mortality in these regions (Lacroz, 2015). Several factors explain this rise, one of the main ones being the increase in multiple pregnancies, which is linked to the use of fertility treatments and advanced maternal age at delivery (Liu et al., 2019).

Estimates conducted in partnership with the World Health Organization reported a global preterm birth rate of 9.6% in 2005 and 11.1% in 2010, corresponding to approximately 13 million and 15 million preterm births, respectively (Zeitlin et al., 2015). Over 60% of these preterm births occurred in South Asia and Sub-Saharan Africa, which account for 52% of global live births. In other regions, Europe and North America recorded around 0.5 million preterm births, while Latin America and the Caribbean accounted for nearly double that number, with approximately 0.9 million preterm births (Blencowe et al., 1990).

In developed countries, Preterm birth complicates approximately **11%** of pregnancies in the United States, reflecting a relative increase of over **25% since 1980** (Torchin et al., 2015). In Europe, the highest rate of preterm births is recorded in **Cyprus** at **10.4%**, while the lowest is in Iceland, with a rate of **5.3%** (Liu et al, 2024). In **Germany**, the incidence has remained stable since 2008 at just over **8%**,

placing it among the lower rates in Europe (Ramsey et al., 2012). In **France**, the preterm birth rate has risen from **5.9% in 1995** to **7.2% in 2003** and **7.4% in 2010** (Zeitlin et al., 2015).

In the poorest countries, an average of 12% of babies are born preterm, compared to 9% in higher-income countries. Within these countries, the poorest families face an increased risk (Berger et al., 2012). In Africa, there is limited research on this issue despite its high prevalence, with reported rates varying between 11% and 22% (Bocoum and Youssouf, 2021). Additionally, in these regions, the impact of prematurity is exacerbated by other challenges, such as wars, famine, underdevelopment, and poverty (Bocoum, 2015). In Latin America, particularly in Brazil, the situation is concerning as the prevalence of prematurity has significantly increased, rising from 6% in 1982 to 16% in 2004. This contrasts with the relatively low rate observed in Chile, which was 7% in 2000 (Ouattara et al., 2015). The burden of preterm births is notably heavy in Asia (Hoh, 2019) with the Indian subcontinent leading the statistics. A recent systematic review published in *The Lancet* estimates that India has a preterm birth rate of 13.6% (Padonou, 2014). According to the World Health Organization, the annual preterm birth rate in Morocco is estimated at 13.41% of all births, which corresponds to approximately 91,400 cases (Moroccan ministry of health, 2019).

Low birth weight is a major public health problem in both developing and developed countries. (Liu et al., 2024)

Between 1997 and 2001, WHO and UNICEF (UNICEF 2004) carried out a census of all births worldwide based on national data and registers. According to the report, of the 130 million children born worldwide each year, 20 million are born with low birth weight, representing an overall prevalence of 15.5%. Indeed, of these 20 million children born with low birth weight, 95.6% occur in developing countries, resulting in a great disparitý in prevalence between developed (7%) and developing countries (16.5%) (UNICEF 2004). The continents most affected are Asia and Africa, with 72% and 22%, respectively, of all children born with LBW. (Padonou, 2014)

Morocco is ranked 126th in the UNICEF development report with a very high rate of LBW (12%) and neonatal mortality (36‰) despite national programs developed for maternal and child health. (Isaf, 2017)

A study was conducted at the National Reference Center for Neonatology and Nutrition at the Children's Hospital of Rabat from January to December 2015. One hundred twenty premature newborns with very low birth weight were included, representing 25% of the premature infants admitted to the center during this period (Evily, 2017).

Another study was conducted on premature newborns in the Neonatology Department of the Mohammed VI University Hospital in Marrakech over two years, from January 1, 2006, to December 31, 2007. A total of 459 premature newborns (of all birth weights) were included. The very low birth weight preterm infants numbered 162, representing 35% of all premature infants (Ouatarra, 2019)

Our current study places the Neonatology and Neonatal Resuscitation Center of CHU Hassan II in Fez at the bottom of the list, with a hospitalization rate of 21% of all premature infants.

Risk factors for prematurity

Maternal sociodemographic factors

Several authors have reported that maternal age influences the duration of gestation, with extreme ages (< 20 and > 35 years) being predisposing factors for preterm birth. Indeed, the impact of maternal age on pregnancy outcomes becomes noticeable at 35 years and is significant at 40 years. Advanced maternal age is associated with induced prematurity due to an increased risk of maternal complications such as gestational or chronic hypertension and diabetes. The risk of placenta previa is reported to be nine times higher in women aged 40 and older compared to those in their twenties (Lardeux, 2014). Furthermore, several recent studies based on cohorts or registries of singleton pregnancies have shown an increased overall risk of prematurity among younger women, particularly those under 18 years of age. Younger maternal age is more frequently linked to spontaneous preterm birth (Torchin et al., 2015). In our study, 4.56% of the parturients were under 18 years old, while 25.72% were over 35 years of age.

The meta-analysis by Prakesh S. Shah et al. (Shah et al, 2011), conducted in 2011, found an association between marital status and the overall risk of prematurity, which was higher for women living alone compared to married women. Our sample includes four newborns from single mothers, accounting for 1.65% of all newborns.

The socioeconomic situation is a complex, multifactorial concept that encompasses various dimensions, including education level, income, and employment status (Torchin et al., 2015). Pregnant women in precarious social circumstances, regardless of the often-complex causes, face significant barriers to accessing rights and healthcare. This leads to a higher incidence of perinatal complications, particularly prematurity (Lejeune, 2008).

In our study, the socioeconomic status of the mothers was considered "precarious" based on the World Health Organization's poverty indicators, specifically their place of residence (rural area), employment status (unemployed), education level, and housing conditions. These indicators were present in 63.90% of the mothers, with 29.87% residing in rural areas. Such high rates warrant attention as they are likely key determinants in the occurrence of prematurity.

Gynecological and obstetric factors:

The literature presents discordant findings regarding the association between parity and prematurity. A retrospective study by Koulali et al. (Koullali et al., 2020), conducted in

the Netherlands between 2010 and 2014, demonstrated an independent association between nulliparity and spontaneous preterm birth before 37, 32, and 28 weeks of gestation. It also showed an increased risk of spontaneous preterm birth among women in their fifth pregnancy. Conversely, a meta-analysis by Prakesh S. Shah et al., published in 2010 and based on data from developed countries, did not find an association between parity and the overall risk of prematurity, whether in nulliparous or grand multiparous women, with women of parity 2 to 4 serving as the reference group. In our study, the rates of primiparity, multiparity, and grand multiparity were 35.68%, 20.33%, and 4.56%, respectively.

The risk of prematurity is significantly higher in twins compared to singletons. In the United States, the twin birth rate reached a record high in 2013, with 33.7 twins born per 1,000 total births. National vital statistics revealed that the preterm birth rate was 56.6% among twins, compared to 9.7% among singletons, indicating a risk more than 12 times greater. The rate of prematurity before 32 weeks was 11.3% for twins and 1.5% for singletons (Fuchs et al., 2016). In our sample, 28% of the preterm infants were from multiple pregnancies (twins and triplets). This rate is consistent with findings from the Neonatology Unit of Ibn El Jazzar Regional Hospital in Kairouan, Tunisia, which reported a rate of 30.9% (Amri et al., 2008).

Intrauterine infection may account for 25% to 40% of preterm births; however, this figure is likely underestimated due to challenges in detecting bacteria in the choriodecidual space and the limitations of conventional culture techniques (Petit et al., 2012).

Premature rupture of membranes (PROM) refers to any confirmed spontaneous rupture of membranes that occurs before the onset of labor (Beillat, 2012). When this occurs prior to term, it increases the risk of intrauterine infection, which can lead to heightened maternal morbidity as well as neonatal morbidity and mortality (Beucher et al., 2018). Infection may result from ascending bacterial contamination and is often a consequence of the rupture itself (Beillat, 2012). In our series, the history of infection was positive in 41.9% of the mothers, and PROM complicated 33.19% of the cases. Our findings align with those of the study by LB Ouattara and A. Aboussad (Ouattarra, 2009), conducted at CHU Mohamed VI in Marrakech, which reports an association between prematurity and PROM in 31.5% of cases.

In multiparous women, a history of preterm birth or late miscarriage increases the risk of subsequent preterm birth by 2 to 5 times. The risk of recurrence rises as the number of previous incidents increases (McManemy et al., 2007). The French study by C. Prunet et al. (Prunet et al., 2017), conducted in 2010, revealed that having at least one previous preterm birth was associated with a high risk of recurrence, whether the preterm birth was spontaneous or induced. In our study, at least one history of preterm birth or miscarriage was found in 7.46% and 17.42% of the cases, respectively.

Early pregnancy monitoring, particularly with the first prenatal visit occurring in the first trimester, may serve as a protective factor against prematurity. Prenatal care plays a significant role in pregnancy outcomes. The RIGI study conducted in French Guiana from 2013 to 2014 revealed that among women who had one to three prenatal visits during their pregnancy, 59% of the observed cases of prematurity could be attributed to inadequate obstetric follow-up. Additionally, birth preparation and prenatal counseling have been identified as protective factors, with prematurity rates decreasing by approximately 60% and 50%, respectively (Dorilas, 2019). In our study, pregnancy was presumed to be monitored in 76% of the cases, while 21% were not monitored.

Threatened preterm labor (TPL) is characterized by cervical changes along with regular and painful uterine contractions occurring between 22 and 36 completed weeks of gestation. In the absence of treatment, TPL can progress to actual delivery (Compan,2015). Tocolysis is an integral part of managing threatened preterm labor, with the primary objective of improving neonatal outcomes and long-term health for the child. Secondary goals include prolonging the pregnancy to facilitate in-utero transfer and the administration of antenatal corticosteroids and magnesium sulfate, if necessary (Doret et al., 2016). In our series, TPL complicated the pregnancies of 36.09% of the parturients, with only 17.24% receiving tocolytic treatment.

Regarding maternal comorbidities, the prevalence of gestational diabetes was 5.80%, while the prevalence of gestational hypertension was 18.67% among the mothers. This latter rate is consistent with that found by Ouattara and Aboussad (Ouattarra, 2009), which was 19.4%. In terms of gestational diabetes, a study conducted at CHU Mustapha Bacha in Algiers by S. Mimouni Zerguini et al. (Mimouni-Zerguini et al, 2009) showed that the rate of prematurity was significantly higher in the gestational diabetes cohort compared to the controls.

Uterine malformations are associated with an increased risk of prematurity. A meta-analysis by Christos A. Venetis et al. (Venetis et al., 2014) found an overall increased risk of prematurity in cases of septate uterus (complete or partial septum) and Müllerian duct anomalies (didelphys, bicornuate, and unicornuate uterus). In our population, we identified 2 cases of preterm births from mothers with uterine hypoplasia.

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Advanced maternal age is associated with induced prematurity due to an increased risk of maternal complications such as gestational or chronic hypertension and diabetes. The risk of placenta previa is reported to be nine times higher in women aged 40 and older compared to those in their twenties (Lardeux, 2014). Furthermore, several recent studies based on cohorts or registries of singleton pregnancies have shown an increased overall risk of prematurity among younger women, particularly those under 18 years of age. Younger maternal age is more frequently linked to spontaneous preterm birth (Torchin et al., 2015). In our study, 4.56% of the parturients were under 18 years old, while 25.72% were over 35 years of age.

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Regarding maternal comorbidities, the prevalence of gestational diabetes was 5.80%, while the prevalence of gestational hypertension was 18.67% among the mothers. This latter rate is consistent with that found by Ouattara and Aboussad (20), which was 19.4%. In terms of gestational diabetes, a study conducted at CHU Mustapha Bacha in Algiers by S. Mimouni Zerguini et al. (Mimouni-Zerguini et al., 2009) showed that the rate of prematurity was significantly higher in the gestational diabetes cohort compared to the controls.

Uterine malformations are associated with an increased risk of prematurity. A meta-analysis by Christos A. Venetis et al. (Venetis et al., 2014) found an overall increased risk of prematurity in cases of septate uterus (complete or partial septum) and Müllerian duct anomalies (didelphys, bicornuate, and unicornuate uterus). In our population, we identified 2 cases of preterm births from mothers with uterine hypoplasia.

The use of psychoactive substances (alcohol, tobacco, and drugs) during pregnancy poses a significant public health challenge due to the risks they present to the unborn child. Tobacco's effect on prematurity has been the subject of several studies, and it is recognized as a risk factor for preterm birth (Dumas et al., 2014). In our study, no cases of maternal smoking or alcohol consumption were reported.

5. Conclusion

This study provided valuable data on the risk factors associated with morbidity and mortality in very low birth weight preterm infants in our setting. Based on our results, we can conclude that the incidence of prematurity remains high despite remarkable progress in the fields of obstetrics and neonatology. The pregnancy-related conditions influencing premature births include premature rupture of membranes, preeclampsia, and maternal infection.

To effectively address these challenges and plan preventive actions, it is crucial to implement concrete measures, emphasizing the importance of:

Identifying pregnant women at risk of preterm delivery who are eligible for preventive treatment (outside of emergencies).

Coordinating and collaborating among perinatal network professionals: obstetricians, neonatologists, midwives, etc.

Strengthening staff capacities to improve the quality of prenatal consultations.

Actively involving pregnant women in monitoring their pregnancies.

Equipping neonatal services to align needs with available resources.

Statement of Ethics

Not applicable.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data availability statement

Data will be available upon request from the corresponding author.

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