Effect of Inter-pregnancy Interval on Risk of Spontaneous Preterm Labor

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Abstract

Background: Spontaneous preterm labor, is the onset of labor that occurs before the 37th week of gestation and poses significant health risks for mothers and newborns. Both short (under 18 months) and long (over 59 months) inter-pregnancy intervals can increase risks, highlighting the need for tailored prevention and management strategies.

Aims of the study: To assess the influence of interpregnancy intervals on the occurrence of spontaneous preterm labor, providing insights into factors affecting gestational outcomes.

Methods: A case-control study was conducted to assess the impact of interpregnancy interval on spontaneous preterm labor risk among women delivering at two Basrah hospitals from the 1st of November 2023 to the 1st of September 2024. It included 140 cases who experienced spontaneous preterm labor and 140 controls, who had full-term deliveries, matched for age, BMI, and parity, with data collected via a structured questionnaire and routine examinations.

Results: The study included 280 women. Significant findings included irregular antenatal care in 49.3% of cases versus 28.6% of controls ($p = 0.001$). Previous complications like preeclampsia ($p = 0.035$), stillbirth ($p = 0.047$), and preterm labor ($p = 0.001$) were higher in cases. The mean inter-pregnancy interval was significantly shorter in cases (10.8 ±2.3) months compared to controls (21.3 ±5.4) months ($p < 0.001$).

Conclusion: Short inter-pregnancy intervals significantly increase the risk of spontaneous preterm labor, while regular antenatal care reduces it; however, sociodemographic factors, gestational diabetes mellitus and parity do not predict preterm labor risk in this population.

Keywords: Inter-pregnancy Interval, Risk, Spontaneous Preterm Labor, Basrah.

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Introduction

Spontaneous preterm labor is defined by the World Health Organization as the onset of labor that occurs before the 37th week of gestation, disrupting the conventional full-term pregnancy duration of 37 to 42 weeks (1). Preterm birth stands as the predominant cause of neonatal morbidity and mortality on a global scale, subjecting the child to an array of long-term health challenges (2). Preterm labor exhibits significant variability based on geographical and demographic factors. The occurrence of spontaneous preterm labor, affecting a notable proportion of pregnancies globally, demonstrates incidence rates spanning from 5% to 18% across different regions (3). Recent years have witnessed subtle shifts in the dynamics of preterm birth rates, influenced by factors such as maternal age, the prevalence of assisted reproductive

technologies, and enhanced survival rates for preterm infants due to advancements in neonatal care (4).

Identifying the numerous factors that increase the risk of spontaneous preterm labor is critical for developing effective prevention and management strategies. Notably, women with a history of cardiovascular disease or pregnancy-related infections face an elevated risk (5). Environmental exposures, such as air pollution and occupational hazards, further amplify this risk (6). Moreover, lifestyle choices, including smoking and inadequate prenatal nutrition, contribute significantly to the likelihood of preterm labor, highlighting the importance of promoting healthier behaviors during pregnancy (7). Furthermore, psychological stress emerges as a significant risk factor, with research indicating that elevated levels of stress and anxiety can detrimentally impact pregnancy outcomes (8).

Additionally, a spectrum of other risk factors includes a history of preterm delivery, premature rupture of the membrane, anemia, low socioeconomic status, multiple gestations, and a short inter-pregnancy interval. This multifaceted approach to risk identification is essential for tailoring interventions and improving overall maternal and neonatal health (9).

The relationship between inter-pregnancy interval and adverse outcomes of preterm delivery has been a subject of study, yet there lack of consistency in defining an appropriate inter-pregnancy interval across different research (10). The inter-pregnancy interval (IPI), defined as the time between the end of one pregnancy and the start of the next, has been shown to influence various pregnancy outcomes, including preterm labor. Research indicates that both short and long inter-pregnancy intervals can affect the risk of preterm birth, with varying mechanisms (11).

Short inter-pregnancy intervals are often defined as durations of fewer than 18 months. Research has repeatedly shown that shorter intervals correlate with a heightened risk of premature labor (12).

Infants delivered to moms with short interpregnancy intervals have an increased risk of being underweight at birth, potentially resulting in additional health issues.(١٢) Developmental Delays: Short intervals may lead to an increased prevalence of developmental delays or cognitive impairments in children .(١٣) The combination of low birth weight and preterm delivery may exacerbate the risk of infant mortality. (١٢,13) Elevated Rates of Neonatal Intensive Care Unit (NICU) Admissions: Infants delivered from closely spaced pregnancies may have further care immediately post-delivery, resulting in prolonged NICU hospitalisation. (14) Chronic Health Complications: Both mothers and children may have enduring health issues, including chronic disorders associated with dietary deficiencies or stress. (14) Socioeconomic Strain: Families may have financial challenges resulting from the rapid succession of offspring, impairing their capacity to provide sufficient care and resources (14).

Aims of the study

This study aims to assess the influence of interpregnancy intervals on the occurrence of spontaneous preterm labor, providing insights into factors affecting gestational outcomes

Patients and Methods

This study is a case-control study conducted to assess the effect of inter-pregnancy interval on the risk of spontaneous preterm labor. The research was conducted for the period from 1st of November 2023 to 1st September 2024 at the Obstetrics Department in Basrah Maternity and Child Hospital and AlBasrah Teaching Hospital.

The population for this study consists of women who have given birth at the two hospitals where the study was conducted, Basrah Maternity and Child Hospital and Albasrah Teaching Hospital during the study period .

- The case group includes 140 women who experienced spontaneous preterm labor, which is defined as labor that begins before 37 completed weeks of gestation without medical induction. (15)

- The control group consists of 140 women who had full-term deliveries, defined as labor that begins after 37 completed weeks of gestation. (15)

- Both groups were matched for age, BMI and parity.

Inclusion criteria for the study consisted of women who had singleton. The exclusion criteria included women with multiple pregnancies, primigravida, women who had post-term delivery and pregnancies resulting from assisted reproductive technologies. Additionally, pregnant women with medical conditions such as diabetes mellitus and hypertension, as well as pregnancies complicated by congenital anomalies or chromosomal abnormalities.

Direct interviews conducted using a carefully constructed questionnaire were used to collect the data. The following elements are included in the questionnaire: the mother's age, residence, degree of education, and social status. The duration of the inter-pregnancy interval—which was determined as the time between the birth of the last previous kid and the delivery of the present child, minus the gestational age of the current pregnancy. In addition to the obstetric history, parity, gravidity, and other factors. There are three categories for the interpregnancy interval: < 12 months, 13-24 months, and >24 months. Additionally prior surgical and medical experience Then each woman underwent a general and obstetric examination, and the vital signs were also assessed (blood pressure, Heart rate, and temperature) .Routine investigations (CBC, RBS, and GUE) were done .

Anthropometric measures were done including Height and weight. The BMI was calculated (calculated as weight in kilograms divided by height in meters squared). Mothers BMI was then classified according to the WHO classification into underweight (<18.5), normal weight (18.5–24.9), overweight (25–29.9) and obese (>30). (16)

Ethical approval for this study was obtained from the University of Basrah, College of Medicine, ensuring adherence to ethical standards in conducting research involving human participants. The data were collected and analyzed from all patients as verbal consent was taken for this study.

Statistical analysis was performed using IBM SPSS Statistics Version 25.0. Categorical variables were analyzed using the Chi-square test, with Fisher's exact test applied when expected cell counts were less than 5. A p-value of <0.05 was considered statistically significant.

Results

The study includes 280 patients divided into 140 cases and 140 control healthy women. More than half of women were between 20-29 years and there is no significant difference between the two groups p-value=0.403.

Regarding the address, most women live in urban areas and there are no significant differences p-value=0.537.

Most of the women were housewives, the highest percentage of them had secondary education and were of medium socioeconomic level. No statistical difference between the two groups regarding the above variables since the p-value >0.05. all these data in Table 1.

Table 1 sociodemographic data distribution among women in both groups

Variables		Cases (No. 140)	Controls (No. 140)	P-value
Age	**< 20 years**	18 (12.9)	14 (10.0)	0.403
	20-29 years	74 (52.9)	76 (54.3)	
	30-39 years	42 (30.0)	48 (34.3)	
	≥ 40 years	6 (4.2)	2 (1.4)	
Address	**Urban**	85 (60.7)	90 (64.3)	0.537
	Rural	55 (39.3)	50 (35.7)	
Occupation	**Housewife**	86 (61.4)	80 (57.1)	0.465
	Employee	54 (38.6)	60 (42.9)	
Educational level	**Illiterate**	26 (18.6)	22 (15.7)	0.745
	Primary education	44(31.4)	40 (28.6)	
	Secondary education	46 (32.9)	48 (34.3)	
	Higher education	24 (17.1)	30 (21.4)	
Socioeconomic level	**Low**	50 (35.7)	47 (33.6)	0.834
	Medium	65 (46.4)	70 (50.0)	
	High	25 (17.9)	23 (16.4)	

Table 2 shows the obstetric characteristics among women, highest percentage of women had more than 4 children and around one-quarter of them had 1 child. Still, there are no significant statistical differences between them p-value= 0.785. The antenatal care for women in the case group was irregular among 49.3% of them while 64.3 of women in the control group had regular ANC. P-value=0.001 which indicates a highly significant statistical difference between the groups.

The previous obstetrical complications were also assessed, high percentages of preeclampsia, preterm labor and stillbirth were noticed among the case group and these differences are of significant statistical differences p-value < 0.05.

Table 2: the obstetric characteristics among women in both groups

Variables		Cases (No. 140)	Controls (No. 140)	P-value
Parity	**1**	36 (25.7)	41(29.3)	0.785
	2-3	48 (34.3)	47 (33.6)	
	>4	56 (40.0)	52 (37.1)	
Antenatal care	**Regular**	56 (40.0)	90 (64.3)	0.001
	Irregular	69 (49.3)	40 (28.6)	
	Nill	15(10.7)	10 (7.1)	
Previous obstetrical complications	**Gestational diabetes mellitus**	32 (22.9)	35 (25.0)	0.674
	Preeclampsia	41 (29.3)	26 (18.6)	0.035
	History of stillbirth	33 (23.6)	20 (14.6)	0.047
	Preterm labor	50 (35.7)	23 (16.4)	0.001
	Abnormal placental	51 (36.4)	42 (30.0)	0.253
Gestational age	**Mean ±SD**	35.2± 2.9	38.6 ±3.01	0.001

The BMI distribution of the women is presented in Table 3. Nearly half of the women in the two groups were overweight and there is no significant statistical difference p-value=0.790.

Table 3: the BMI distribution of the women under study

Variables	Cases (No. 140)	Controls (No. 140)	P-value
Mean ±SD	28.5± 3.8	29.1 ± 4.8	0.790
Normal (18.5-24.9)	48 (34.3)	50 (35.7)	
Overweight (25.0-29.9)	70 (50.0)	72 (51.4)	
Obese ≥ 30	22 (15.7)	18 (12.9)	

The interpregnancy intervals for women are presented in Table 4. the mean for women in the case group was 10.8 months VS 21.3 months among women in the control group. This difference was highly significant statistically with p-value <0.001.

Table 4: The inter-pregnancy intervals among women in both groups

Variables		Cases (No. 140)	Controls (No. 140)	P-value
Inter pregnancy intervals	**Mean± SD**	10.8 ±2.3	21.3 ±5.4	0.001
	≤12 months	58 (41.4)	13 (9.3)	
	13-24 months	69 (49.3)	31 (22.1)	
	>24 months	13 (9.3)	96 (68.6)	

Discussion

The inter-pregnancy interval has been increasingly recognized as a significant factor influencing maternal and neonatal outcomes, including the risk of spontaneous preterm labor (17). This study aimed to investigate the effect of the inter-pregnancy interval on the risk of spontaneous preterm labor in a population of women giving birth at Basrah Maternity and Child Hospital and Al-Basrah Teaching Hospital.

In this study, sociodemographic variables such as age, urban versus rural residence, and occupation did not show a significant difference between cases and controls. This is due to the matched nature of the case-control design, which balanced several confounders as it is well known that younger maternal age as reported by Esposito, et al. (2022) and lower socioeconomic status as evidenced by McHale et al. (2022) may increase the risk of preterm birth therefore these factors are matched in this study to eliminate the confounding effect (18, 19).

The present study found a significant association between short inter-pregnancy intervals (≤12 months) and the risk of spontaneous preterm labor, with 41.4% of the cases falling into this category compared to only 9.3% of the controls (p=0.001). Additionally, the mean inter-pregnancy interval in the case group (10.8 ± 2.3 months) was significantly shorter than that of the control group (21.3 ± 5.4 months). These results are consistent with prior studies that have reported an increased risk of preterm birth associated with inter-pregnancy interval such as Tanigawa et al. (2023) and Ahrens et al. (2019) who found that interpregnancy intervals <6 months increase the risk of preterm labor (20, 21). The biological reasoning behind this association may include incomplete maternal recovery from the previous pregnancy, leading to a suboptimal uterine environment, or micronutrient depletion, particularly folate deficiency, which has been implicated in preterm labor (22). Folate, in particular, is crucial for DNA synthesis, repair, and methylation, and its deficiency has been associated with a higher risk of preterm birth. During a short inter-pregnancy interval, the mother may not have sufficient time to replenish these nutrients, especially folate, which plays a critical role in fetal development and placental function. Folate deficiency has been linked to impaired placental formation, increased oxidative stress, and inflammatory processes, which can trigger premature labor (23) Moreover, a short interval between pregnancies may result in residual hormonal imbalances that could affect the subsequent pregnancy. For example, insufficient progesterone support may lead to an incompetent cervix, increasing the risk of preterm labor. Hormonal recovery is essential for maintaining

uterine quiescence during pregnancy, and disruptions to this balance can lead to premature uterine contractions (24). This study found that women with irregular or no antenatal care had a higher likelihood of experiencing preterm labor compared to those who had regular antenatal care (p=0.001). Specifically, 49.3% of the cases had irregular care compared to 28.6% of the controls. These findings align with research that highlights the protective role of antenatal care in reducing adverse pregnancy outcomes, including preterm birth. A study by Agarwal et al. (2024) emphasize that inadequate antenatal care limits the early detection and management of risk factors for preterm labor, such as infections or pregnancy-induced hypertension (25).

A history of preterm labor, preeclampsia, and stillbirth was more common in the case group, highlighting the role of obstetrical history in predicting preterm birth. For example, 35.7% of cases had a history of preterm labor compared to 16.4% of controls (p=0.001). This is consistent with findings from other studies, such as the research by Yang et al. (2016), which demonstrated that women with prior preterm deliveries are at significantly higher risk of recurrence (26). The pathophysiology may involve uterine or cervical abnormalities persisting across pregnancies, or unresolved underlying conditions such as inflammation or infection (27).

In this study, a significant association was found between a history of preeclampsia and spontaneous preterm labor (29.3% in cases vs. 18.6% in controls; p=0.035). This relationship is consistent with the work of An et al. (2021), which shows that prior hypertensive disorders of pregnancy significantly elevate the risk of spontaneous and indicated preterm birth (28).

The study also found a significant association between a history of stillbirth and spontaneous preterm labor (23.6% in cases vs. 14.6% in controls; p=0.047). This is in line with previous research that has shown that women with a history of stillbirth are at increased risk for several adverse outcomes in subsequent pregnancies, including preterm birth (29).

The findings of this study did not show a significant association between BMI and the risk of spontaneous preterm labor (p=0.790), with the majority of women in both groups falling into the overweight category. This is in contrast to some studies such as the one by Shaw et al. (2014) that suggest both underweight and obese women are at increased risk of preterm birth (30). However, the lack of significant findings in this study due to the homogeneity of the BMI distribution within the population studied, where both groups had similar mean BMI values as we ensured matching the two groups to limit the confounding effect.

Conclusion

Short inter-pregnancy intervals significantly increase the risk of spontaneous preterm labor, while regular antenatal care reduces it; however, sociodemographic factors, gestational diabetes mellitus and parity do not predict preterm labor risk in this population.

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تأثير الفاصل الزمني بين الحمل على خطر الولادة المبكرة

الخلفية:الولادة المبكرة ، وهي بدء المخاض قبل الأسبوع السابع والثلاثين من الحمل، تمثل مخاطر صحية كبيرة على الأمهات والمواليد. يمكن أن يؤدي كل من الفاصل الزمني القصير (أقل من ١٨ شهرًا) والطويل (أكثر من ٥٩ شهرًا) بين الحملين إلى زيادة المخاطر، مما يبرز الحاجة إلى استراتيجيات وقائية وإدارية مخصصة.

أهداف الدراسة:تقييم تأثير الفاصل الزمني بين الحملين على حدوث الولادة المبكرة وتقديم رؤى حول العوامل المؤثرة على نتائج الحمل.

الطرق:أُجريت دراسة حالة-شاهد لتقييم تأثير الفاصل الزمني بين الحملين على خطر الولادة المبكرة بين النساء اللاتي ولدن في مستشفيين في البصرة خلال الفترة من ١ نوفمبر ٢٠٢٣ إلى ١ سبتمبر ٢٠٢٤. تضمنت الدراسة ١٤٠ حالة عانت من ولادة مبكرة عفوية و١٤٠ شاهدًا، لديهن ولادات مكتملة، تم مطابقتها حسب العمر، مؤشر كتلة الجسم، والولادات السابقة. تم جمع البيانات باستخدام استبيان منظم وفحوصات روتينية.

النتائج:شملت الدراسة ٢٨٠ امرأة. ومن النتائج المهمة أن الرعاية السابقة للولادة غير المنتظمة كانت أعلى بين الحالات (٤٩,٣٪) مقارنة بالشواهد (٢٨,٦٪) ($p = 0.001$). كما كانت مضاعفات سابقة مثل تسمم الحمل ($p = 0.035$)، والإملاص ($p = 0.047$)، والولادة المبكرة ($p = 0.001$) أكثر شيوعًا بين الحالات. وكان متوسط الفاصل الزمني بين الحملين أقصر بشكل ملحوظ بين الحالات (١٠,٨ ±٢,٣ شهرًا) مقارنة بالشواهد (٢١,٣ ±٥,٤ شهرًا) ($p < 0.001$).

الاستنتاج:تزيد الفترات الزمنية القصيرة بين الحملين بشكل كبير من خطر الولادة المبكرة ، بينما تقلل الرعاية المنتظمة السابقة للولادة من هذا الخطر. ومع ذلك، فإن العوامل الاجتماعية والديموغرافية، وسكري الحمل، وعدد الولادات السابقة لا تتنبأ بخطر الولادة المبكرة في هذه المجموعة السكانية.

الكلمات المفتاحية: الفاصل الزمني بين الحمل، الخطر، الولادة المبكرة ، البصرة.