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Original Article

Exploring the prognostic significance of β-HCG levels in cervicovaginal secretions and maternal risk factors for early birth

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Abstract

Preterm birth is one of the leading causes of death in the perinatal period, this study was conducted to investigate the predictive value of β-HCG levels in cervicovaginal secretions and maternal risk factors in preterm delivery. This cross-sectional study was conducted over a six-month period from January 1 to June 30, 2021, in Baghdad hospitals. The data were collected and used from the mothers who went to the hospital for delivery. Demographic information of patients and some risk factors were investigated. Vaginal secretions were sampled with a cotton swab. β-HCG level in weeks 29, 31, 33, and 35 was measured by ELISA method. Data were analyzed with SPSS Ver 25 software and a significance level of less than 0.05 was considered. The mean age of the study participants was 28.29 ± 5.68 years. There was a significant difference in the level of β-HCG between women with full-term delivery and pre-term women in weeks 29, 31, 33, and 35 of pregnancy ($P \leq 0.001$). Maternal factors such as age older than 35 years, BMI, history of thyroid disease, blood pressure, premature rupture of the amniotic sac, parity, twin and multiple births, and decreased amniotic fluid volume have been identified as factors affecting preterm delivery. The β-HCG level can also be a helpful marker for preterm birth.

Keywords: Maternal risk factors, Preterm delivery, Pregnancy, β-HCG, Neonatal, Complications.

1. Introduction

Preterm birth, defined as birth before 37 weeks of gestation, is a significant global health issue with high costs and implications for both families and healthcare systems [1, 2]. The prevalence of premature birth worldwide is around 11%, but it varies among different societies [3]. Despite advancements in prenatal care, 5-10% of pregnancies still result in preterm birth, which is responsible for a majority of infant deaths without congenital anomalies [4].

Multiple factors have been recognized as risks for premature birth, such as previous premature birth, socioeconomic factors, maternal age, multiple pregnancies, preeclampsia, infections, gestational diabetes, and maternal health conditions [5, 6]. Preterm infants face numerous adverse outcomes such as hypertension, developmental delays, respiratory issues, and neurological disorders [7, 8]. Woo et al. (2019) reported that preeclampsia was significantly associated with preterm birth [9]. In their study, Magro Malosso et al. (2018), pointed out the association between a history of miscarriage and preterm birth [10]. Other factors include ruptured amniotic sacs, membrane issues, and uterine abnormalities [11, 12].

A potential approach to predict preterm birth involves analyzing biochemical markers, including β-human chorionic gonadotropin (β-HCG), in the cervicovaginal secretions of pregnant women. β-human chorionic gonadotropin (β-HCG), a glycoprotein hormone produced by the placenta during pregnancy, has emerged as a potential biomarker for predicting preterm labor. Several studies have investigated the use of β-HCG assays as a predictive tool for preterm delivery, showing promising findings [13–15].

Preventing premature birth and improving outcomes are vital in obstetrics. Biochemical assays like β-HCG can predict preterm labor [16–18]. Although various studies have investigated the risk factors of mothers and infants in relation to prematurity, there was no study with a large sample size to provide more realistic indicators in the geography of the Middle East. Since it is important to identify maternal risk factors associated with prematurity and providing appropriate care during pregnancy can play an effective role in preventing premature birth, this study was conducted with the aim of determining the maternal risk factors of premature birth.

2. Materials and methods

This cross-sectional was performed during a period

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of six months from January 1 to June 30, 2021, on 1993 births in Baghdad hospitals. The data were collected and used from the mothers who went to the hospital for delivery. The files of all the mothers who went to the hospital for childbirth were extracted from the archive and analyzed. Gestational age was calculated based on the first day of the last menstrual period or first-trimester ultrasound. Mothers whose pregnancy was between 20 and 40 weeks were selected and included in the study using the available method. Written consent was obtained from all the participants and they were assured of the confidentiality of the information. This study complied with the Helsinki Declaration.

The inclusion criteria for the study included: mothers of premature babies requiring hospitalization in the NICU department of ABC Hospital. Exclusion criteria included: babies with congenital anomalies, congenital infection and cases of induced labor.

Demographic information of patients and some preterm risk factors based on previous similar studies such as maternal age, BMI status, history of thyroid diseases, history of high blood pressure before pregnancy, history of previous abortion (at least one abortion), history of intrauterine death (IUFD), history of diabetes, history of ectopic pregnancy, pre-labor rupture of the membranes (PROM), the occurrence of preeclampsia, parity, twin or multiple pregnancies, history of cesarean section and volume amniotic fluid; It was examined using a checklist made by the researcher.

Pre-labor rupture of the membranes (PROM) refers to the rupture of the amniotic sac before the onset of labor pain in a pregnancy less than 37 weeks [19]. Prolonged PROM means pre-labor rupture of the amniotic sac takes more than 18 hours, which is associated with a 10-fold increased risk of neonatal infection [20]. The criterion for maternal diabetes in this study was maternal blood glucose (GCT) above 140 mg/dL with symptoms such as polyuria and polydipsia [21]. Also, blood pressure criteria for preeclampsia were higher than 140/90 mmHg, proteinuria was above +1 [22]. Also, the history of previous diseases was recorded based on the information related to the patients' medical records.

Vaginal secretions were sampled with a cotton swab after inserting the speculum. The swab was placed first in the endocervix and then in the posterior fornix of the vagina for 30 seconds each, and then the swab was placed in a dry tube for transfer to the laboratory. The samples were analyzed 72 hours after being refrigerated. After adding 0.5 cc of normal saline to the tube containing the swab, the level of β-HCG was measured by the ELISA method and with a scale of milliunits per milliliter (mIU/ml). Sampling was done every two weeks until delivery.

2.1. Statistical analysis

The current data were analyzed using SPSS. Ver.23. After data collection, chi-square tests and Fisher's exact test were used to investigate maternal risk factors in premature infants. Logistic regression was also used to determine risk predictor parameters. In this study, a significance level of less than 0.05 was considered.

3. Results

In this study, the mean age of the participants was 28.29 ± 5.68 with an age range of 17 to 45 years. Also, the number of pregnancies among the subjects varied from 1 pregnancy to 10 pregnancies. The results of examining the age variable of the participants showed that 28 women (in the premature delivery group) and 210 women (in the term delivery group) were over 35 years old. However, 185 women (in the preterm group) were under 35 years old and 1570 women (in the full-term group) were under 35 years old, and there was a significant difference between the two groups of preterm and full-term women ($P \leq 0.003$). The range of BMI of the women was 13-39 kg/m2 with a mean of 24.44 ± 4.25. The study of BMI in the two groups of preterm and term delivery showed a significant correlation ($P \leq 0.035$). Analysis of the history of thyroid disease, blood pressure, rupture of the amniotic sac before delivery, parity, twin and multiple births, and decreased amniotic fluid volume showed a significant correlation between the two groups of preterm and term birth ($P \leq 0.05$). The factors influencing preterm birth were identified as follows: Age over 35 years, BMI, history of thyroid disease, blood pressure, premature rupture of membranes, parity, twin and multiple births, and decreased amniotic fluid volume. Previous miscarriages, intrauterine fetal death, history of diabetes, history of ectopic pregnancy, history of preeclampsia, and history of cesarean delivery were other maternal factors that showed no significant correlation with ectopic pregnancy. (Table 1)

The results of examining the variable β-HCG showed that, among 213 women who had premature delivery, the level of β-HCG was 91.25 mIU/ml; While in 1780 women who had term birth, the level of β-HCG was 74.52 mIU/ml. This difference in β-HCG level was significant in weeks 29, 31, 33 and 35 ($P \leq 0.001$). However, the level of β-HCG during delivery was not significant among women with term delivery and pre-term delivery. (Table 2). (Figure 1)

The results of logistic regression analysis showed that the risk of preterm delivery for pregnant women over 35 years old is OR (1.36) (P-Value ≤ 0.002 CI: 1.15 to 1.75), which increases the risk of preterm delivery by 36%. The risk of preterm delivery for women with a history of hypertension was 2.65 times higher than for women without a history of hypertension OR (2.65) (P-Value ≤ 0.001 CI: 1.52 to 3.69). The risk of preterm delivery for women who had PROM was 44% higher than for women who did not hve this history OR (1.44) (P-Value ≤ 0.001 CI: 1.22 to 1.54). More parity showed that it increases the risk of preterm delivery by 2.23 times OR (2.23) (P-Value ≤ 0.001 CI: 1.54 to 3.87). The results showed that women with a history of twins and multiple births had a higher

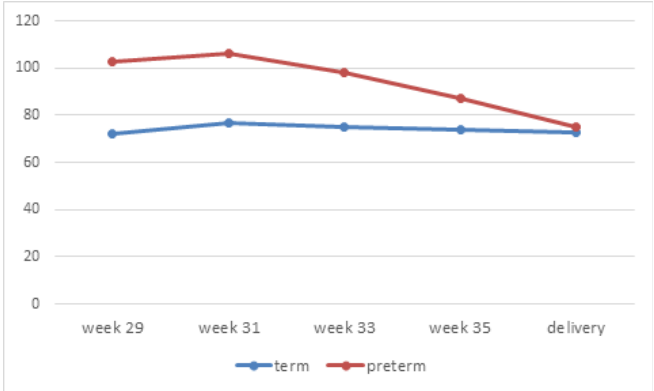

Fig. 1. β-HCG levels in women at risk of preterm delivery

Table 1. Factors related to preterm and term delivery in the studied subjects.

Maternal factors		preterm	Term	P-value*
Age > 35 years	Yes	28	210	0.003
	No	185	1570	
BMI kg/m^2	< 18	8	95	0.035
	18 – 25	180	1346	
	25<	25	321	
History of thyroid diseases	Yes	20	270	0.046
	No	193	1510	
History of high blood pressure (before pregnancy)	Yes	65	310	0.015
	No	148	1470	
Previous miscarriage history (at least one miscarriage)	Yes	18	145	0.8
	No	195	1635	
History of intrauterine fetal death (IUFD)	Yes	5	58	0.15
	No	208	1722	
History of diabetes	Yes	35	420	0.333
	No	178	1360	
Ectopic pregnancy	Yes	3	45	0.457
	No	210	1735	
Pre-labor rupture of membranes	Yes	11	54	0.002
	No	202	1726	
Pre-eclampsia	Yes	21	187	0.412
	No	192	1593	
Parity	Null parity	154	950	0.002
	Multi parity	59	830	
Twin or multiple pregnancy	Yes	8	38	0.003
	No	205	1742	
History of caesarean section	Yes	105	1152	0.6
	No	108	628	
Decreased amniotic fluid volume	Yes	12	74	0.004
	No	201	1706	

*P-value chi-square .

Table 2. Cervicovaginal β-HCG levels in women at risk of preterm delivery.

β-HCG	Term	preterm	P-value*
29 weeks	72.06 ± 2.1	103 ± 4.11	0.001
31 weeks	77.22 ± 1.47	106 ± 3.21	0.001
33 weeks	75.85 ± 8.41	98.36 ± 6.23	0.001
35 weeks	74.33 ± 4.35	87.67 ± 3.66	0.001
Delivery	73.44 ± 2.47	75.41 ± 5.52	0.74

*P-value t-test.

Table 3. Factors affecting preterm in the studied subjects

risk factors	OR, CI (95%)	P-Value*
Age > 35 years	1.36, (1.15 – 1.75)	0.002
History of high blood pressure (Before pregnancy)	2.65, (1.52 – 3.69)	0.001
Pre-labor rupture of membranes	1.44, (1.22 – 1.54)	0.001
Parity	2.23, (1.54 – 3.87)	0.001
Twin or multiple pregnancies	1.64, (1.32 – 1.95)	0..001
Decreased amniotic fluid volume	2.21, (1.32 – 3.74)	0.001
β-HCG level	2.11, (1.54 – 3.64)	0.001

*P-value regression logistic

risk of preterm delivery (64%) than women with a history of singleton birth OR (1.64) (P-Value ≤ 0.001 CI: 1.32 to 1.95). In this study, it was also shown that the risk of preterm delivery for women who had reduced amniotic fluid was 2.21 times higher than for women who did not have a history of reduced amniotic fluid. Higher β-HCG level increased the risk of preterm birth by 2.11 times OR (2.11) (P-Value ≤ 0.001 CI: 1.54 to 3.64). (Table 3)

4. Discussion

Preterm birth is one of the most serious and significant complications in obstetrics. On the one hand, the birth of a premature baby leads to an increase in infant mortality, and on the other hand, problems related to disabilities and high costs associated with the treatment of premature babies cause many problems for families and the health care system of society. Therefore, solutions to reduce the preterm birth rate and identify the factors of preterm birth and preterm delivery are essential [23]. In this study, the factors influencing preterm birth in mothers were investigated. The prevalence of preterm birth in this study was found to be 10.68%, while in other studies the prevalence of preterm birth was reported differently from this study. In the study by P Wagura et al (2018) [5], the prevalence of preterm birth was reported as 18.3%. In contrast, in other studies, this value was reported as 5.33% [24] and 9% [25]. Also, the global mean value of preterm births is reported to be 11% [1], and the value obtained in this study is consistent with the global mean value.

Several studies have identified different maternal factors in preterm birth. In this study, maternal age was identified as a factor influencing the occurrence of preterm birth. Various studies have also shown that the risk of preterm birth increases with increasing maternal age, which is consistent with the findings of the present study [26, 27]. It has been determined that giving birth at an older age is not only associated with preterm birth but may also cause physiological and physical problems for the baby. Barbuscia et al (2020) showed that age over 40 years leads to a higher risk of preterm birth [28].

Rupture of the amniotic sac can occur at any time before delivery, which occurs in approximately 10% of pregnancies. In this study, a significant association was found between (PROM) and preterm births, which has also been shown in many other studies. The rupture of the amniotic sac was identified as one of the main factors for preterm labor [29, 30].

High BMI during pregnancy has been identified as an important risk factor for fetal health. This study showed a significant correlation between BMI and the incidence of preterm birth. Slack et al. (2019) and Su et al. (2020), showed that the higher the BMI, the higher the incidence of preterm birth, which is consistent with the results of the present study [31, 32]. Untreated thyroid disease in pregnant mothers is associated with severe complications such as preterm birth, miscarriage, and stillbirth. In this study, a significant association was found between thyroid disease and the incidence of preterm birth, confirming the results of previous studies [33, 34].

High blood pressure during pregnancy can prevent blood flow in the placenta. If the baby does not receive enough nutrients or oxygen, there is a risk of low birth weight or preterm labor. Our results showed that a history of hypertension is a risk factor for preterm birth. This result is also seen in the study by Kornfeld et al (2019) [35]. Also, the study by Jones et al. (2019) [36] showed that pregnant mothers at a younger age who have uncontrolled blood pressure have a higher risk of preterm birth.

Previous studies have shown that parity is related to preterm labor, with this correlation being most prevalent in the first birth and less so in the second birth. In this study, parity was found to be an important factor for preterm labor, which is consistent with the results of previous studies [37, 38]. In the present study, there was a significant association between the lack of amniotic fluid and the occurrence of preterm birth, confirming the results of previous studies [39, 40]. In addition, this study showed that twin and multiple births had a significant correlation with preterm births, which is consistent with previous studies [39].

In this study, the history of previous miscarriage did not show a significant correlation with preterm delivery, and this finding is not consistent with the results of Li et al. (2021) study that did not show a direct correlation between the history of miscarriage and preterm delivery [39]. In this study, there was no significant correlation between the history of intrauterine death of the fetus and the history of diabetes, which is not consistent with other studies, while most of the previous studies showed a significant correlation [41, 42]. In other studies, the history of ectopic pregnancy, preeclampsia, and history of cesarean section have been shown as risk factors and an important factor in preterm delivery, while the results of this study did not show this correlation [11, 43].

The results of the β-HCG variable investigation showed that β-HCG can be a useful marker for the diagnosis of preterm labor. In the study of Adefashola et al. (2021), it was shown that the level of β-HCG at 24-36 weeks of pregnancy and in those with preterm delivery is higher than those with term delivery; These results are consistent with the results of the present study [13]. Also, in a study conducted by Gupta et al. (2020), the results showed that β-HCG in high-risk women can be used as a sensitive marker [44].

5. Conclusion

Overall, the findings of this study about maternal factors affecting preterm are confirmed by other studies. Considering the importance of educating mothers on the factors affecting the occurrence of preterm labor in order to know and refer faster to prevent or control it, it is emphasized to investigate such cases. Therefore, prospective studies with larger sample sizes and more efforts to increase the accuracy of the studies are recommended. By considering the conditions of the mother in terms of factors such as age, and BMI, as well as a regular examination of amniotic fluid volume and other controllable factors of the fetus, including the occurrence of preeclampsia, reducing the risk of multiple births, controlling diabetes and primary blood pressure, thyroid diseases, and paying attention to determining the cause of IUFD as influential factors in the preterm, it is possible to reduce this problem.

Maternal factors including the age of 35 and above, BMI, history of thyroid disease, blood pressure, PROM, parity, twin and multiple births, and decreased amniotic fluid volume were identified as factors affecting preterm labor.

Limitations

Failure to examine maternal problems and how to control them. Improvement of maternal problems and lack of follow-up on infants.

Conflict of interests

All authors declare no conflict of interest.

Consent for publications

All authors read and approved the final manuscript for

publication.

Ethics approval and consent to participate
The research was designed and approved by the ethical review board of the Wasit University, Baghdad, Iraq(WU/2022-13/12).

Informed Consent
Written consent was obtained from all the participants and they were assured of the confidentiality of the information.

Availability of data and material
The authors guarantee that the data of this research will be provided at the request of other researchers.

Authors' contributions
HA; ASA; Conceived and designed the study: AA; MA: collected and analyzed the data, interpreted the results, and wrote the manuscript.; MSA: Contributed to the study design, data analysis, interpretation of results, and manuscript revision

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References

1. Walani SR (2020) Global burden of preterm birth. Int J Gynecol Obstet 150:31–33. doi: 10.1002/ijgo.13195
2. Vogel JP, Chawanpaiboon S, Moller AB, Watananirun K, Bonet M, Lumbiganon P (2018) The global epidemiology of preterm birth. Best Pract Res Clin Obstet Gynaecol 52:3–12. doi: 10.1016/j.bpobgyn.2018.04.003
3. Krieger N, van Wye G, Huynh M, Waterman PD, Maduro G, Li W, et al (2020) Structural racism, historical redlining, and risk of preterm birth in New York City, 2013-2017. Am J Public Health 110:1046–1053. doi: 10.2105/AJPH.2020.305656
4. da Fonseca EB, Damião R, Moreira DA (2020) Preterm birth prevention. Best Pract Res Clin Obstet Gynaecol 69:40–49. doi: 10.1016/j.bpobgyn.2020.09.003
5. Wagura P, Wasunna A, Laving A, Wamalwa D, Ng'ang'a P (2018) Prevalence and factors associated with preterm birth at kenyatta national hospital. BMC Pregnancy Childbirth 18:1–8. doi: 10.1186/s12884-018-1740-2
6. Teoh PJ, Ridout A, Seed P, Tribe RM, Shennan AH (2018) Gender and preterm birth: Is male fetal gender a clinically important risk factor for preterm birth in high-risk women? Eur J Obstet Gynecol Reprod Biol 225:155–159. doi: 10.1016/j.ejogrb.2018.04.025
7. Jiang M, Mishu MM, Lu D, Yin X (2018) A case control study of risk factors and neonatal outcomes of preterm birth. Taiwan J Obstet Gynecol 57:814–818. doi: 10.1016/j.tjog.2018.10.008
8. Armanian AM, Barekatain B, Sohrabi F, Salehimehr N (2018) The prevalence of complications of prematurity among 1000 newborns with weight of less than 1500 grams in university hospitals in Isfahan city, Iran. J Isfahan Med Sch 35:1974–1979. doi: 10.22122/jims.v35i464.9473
9. Woo J, Giurgescu C, Wagner CL (2019) Evidence of an Association Between Vitamin D Deficiency and Preterm Birth and Preeclampsia: A Critical Review. J Midwifery Women's Heal 64:613–629. doi: 10.1111/jmwh.13014
10. Magro Malosso ER, Saccone G, Simonetti B, Squillante M, Berghella V (2018) US trends in abortion and preterm birth. J Matern Neonatal Med 31:2463–2467. doi: 10.1080/14767058.2017.1344963
11. Chouinard M, Mayrand MH, Ayoub A, Healy-Profitós J, Auger N (2019) Ectopic pregnancy and outcomes of future intrauterine pregnancy. Fertil Steril 112:112–119. doi: 10.1016/j.fertnstert.2019.03.019
12. Cobo T, Kacerovsky M, Jacobsson B (2020) Risk factors for spontaneous preterm delivery. Int J Gynecol Obstet 150:17–23. doi: 10.1002/ijgo.13184
13. Adefashola OR, Fabamwo AO, 0yedele OY (2021) Cervicovaginal fluid beta human chorionic gonadotropin assay as an early predictor of spontaneous preterm delivery among antenatal patients. Niger Heal J 21:45–59.
14. Ranjbar-Navazi Z, Fathi M, Abdolahinia ED, Omidi Y, Davaran S (2021) MUC-1 aptamer conjugated InP/ZnS quantum dots/nanohydrogel fluorescent composite for mitochondria-mediated apoptosis in MCF-7 cells. Mater Sci Eng C 118:111469. doi: 10.1016/j.msec.2020.111469
15. Ziaei S, Bahadori A, Faghihzadeh S (2005) Relationship between β-hCG levels in cervicovaginal secretions and labor. Int J Gynecol Obstet 90:99–102. doi: 10.1016/j.ijgo.2005.03.029
16. Ikeoha CC, Anikwe CC, Umeononihu OS, Okorochukwu BC, Mamah JE, Eleje GU, et al (2022) Fetal Fibronectin as a Predictor of Preterm Delivery: A Nigerian Cohort Study. Biomed Res Int. doi: 10.1155/2022/2442338
17. Haque MM, Merchant M, Kumar PN, Dutta A, Mande SS (2017) First-trimester vaginal microbiome diversity: A potential indicator of preterm delivery risk. Sci Rep 7:1–10. doi: 10.1038/s41598-017-16352-y
18. Glass HC, Costarino AT, Stayer SA, Brett CM, Cladis F, Davis PJ (2015) Outcomes for extremely premature infants. Anesth Analg 120:1337–1351. doi: 10.1213/ANE.0000000000000705
19. Caughey AB, Robinson JN, Norwitz ER (2008) Contemporary diagnosis and management of preterm premature rupture of membranes. Rev Obstet Gynecol 1:11–22.
20. Swiatkowska-Freund M, Traczyk-Los A, Partyka A, Obara K, Damdinsuren A, Preis K (2019) Perinatal outcome in preterm premature rupture of membranes before 37 weeks of gestation. Ginekol Pol 90:645–650. doi: 10.5603/GP.2019.0109
21. Zaccara TA, Paganoti CF, Mikami FCF, Francisco RPV, Costa RA (2022) WHO criteria for diabetes in pregnancy: a retrospective cohort. BMC Pregnancy Childbirth 22:1–8. doi: 10.1186/s12884-022-04708-w
22. Fox R, Kitt J, Leeson P, Aye CYL, Lewandowski AJ (2019) Preeclampsia: Risk factors, diagnosis, management, and the cardiovascular impact on the offspring. J Clin Med 8:1625. doi: 10.3390/jcm8101625
23. Riley C, Roy B, Herrin J, Spatz E, Silvestri MT, Arora A, et al (2019) Do pregnant women living in higher well-being populations in the USA experience lower risk of preterm delivery A cross-sectional study. BMJ Open 9:e024143. doi: 10.1136/bmjopen-2018-024143
24. Alamneh TS, Teshale AB, Worku MG, Tessema ZT, Yeshaw Y, Tesema GA, et al (2021) Preterm birth and its associated factors among reproductive aged women in sub-Saharan Africa: evidence from the recent demographic and health surveys of sub-Sharan African countries. BMC Pregnancy Childbirth 21:1–11. doi: 10.1186/s12884-021-04233-2
25. Anto EO, Ofori Boadu WI, Opoku S, Senu E, Tamakloe VCKT,

Tawiah A, et al (2022) Prevalence and Risk Factors of Preterm Birth Among Pregnant Women Admitted at the Labor Ward of the Komfo Anokye Teaching Hospital, Ghana. Front Glob Women's Heal 3:70. doi: 10.3389/fgwh.2022.801092

26. Esposito G, Mauri PA, Cipriani S, Franchi M, Corrao G, Parazzini F (2022) Correction to: The role of maternal age on the risk of preterm birth among singletons and multiples: a retrospective cohort study in Lombardy, Northern Italy (BMC Pregnancy and Childbirth, (2022), 22, 1, (234), 10.1186/s12884-022-04552-y). BMC Pregnancy Childbirth 22:1–11. doi: 10.1186/s12884-022-04695-y
27. Fuchs F, Monet B, Ducruet T, Chaillet N, Audibert F (2018) Effect of maternal age on the risk of preterm birth: A large cohort study. Obstet Gynecol Surv 73:340–342. doi: 10.1097/01.ogx.0000541308.53092.4a
28. Barbuscia A, Martikainen P, Myrskylä M, Remes H, Somigliana E, Klemetti R, et al (2020) Maternal age and risk of low birth weight and premature birth in children conceived through medically assisted reproduction. Evidence from Finnish population registers. Hum Reprod 35:212–220. doi: 10.1093/humrep/dez275
29. Ali M, Abd-El-Kader A, Mansour M (2020) Prevalence, Fetal and Maternal Outcomes of Premature Rupture of Membranes Among Pregnant Women Attending Minia Maternity University Hospital: a prospective study. Minia J Med Res 31:329–333. doi: 10.21608/mjmr.2022.220312
30. Wang K, Tian Y, Zheng H, Shan S, Zhao X, Liu C (2019) Maternal exposure to ambient fine particulate matter and risk of premature rupture of membranes in Wuhan, Central China: A cohort study. Environ Heal A Glob Access Sci Source 18:1–9. doi: 10.1186/s12940-019-0534-y
31. Slack E, Best KE, Rankin J, Heslehurst N (2019) Maternal obesity classes, preterm and post-term birth: A retrospective analysis of 479,864 births in England. BMC Pregnancy Childbirth 19:1–9. doi: 10.1186/s12884-019-2585-z
32. Su XJ, Huang SJ, Li X, Du QL (2020) Prepregnancy Overweight and Obesity Are Associated with an Increased Risk of Preterm Birth in Chinese Women. Obes Facts 13:237–244. doi: 10.1159/000506688
33. LaFranchi SH (2021) Thyroid Function in Preterm/Low Birth Weight Infants: Impact on Diagnosis and Management of Thyroid Dysfunction. Front Endocrinol (Lausanne) 12:666207. doi: 10.3389/fendo.2021.666207
34. Mahadik K, Choudhary P, Roy PK (2020) Study of thyroid function in pregnancy, its feto-maternal outcome; a prospective observational study. BMC Pregnancy Childbirth 20:1–7. doi: 10.1186/s12884-020-03448-z
35. Kornfeld BD, Finer G, Banks LE, Bolanos L, Ariza AJ (2019) Does History of Prematurity Prompt Blood Pressure Evaluations at Primary Care Visits? Glob Pediatr Heal 6:2333794X19828314. doi: 10.1177/2333794X19828314
36. Skudder-Hill L, Ahlsson F, Lundgren M, Cutfield WS, Derraik JGB (2019) Preterm Birth is Associated With Increased Blood Pressure in Young Adult Women. J Am Heart Assoc 8:e013109. doi: 10.1161/JAHA.119.012274
37. Delnord M, Blondel B, Prunet C, Zeitlin J (2018) Are risk factors for preterm and early-term live singleton birth the same? A population-based study in France. BMJ Open 8:e018745. doi: 10.1136/bmjopen-2017-018745
38. Koullali B, Van Zijl MD, Kazemier BM, Oudijk MA, Mol BWJ, Pajkrt E, et al (2020) The association between parity and spontaneous preterm birth: A population based study. BMC Pregnancy Childbirth 20:1–8. doi: 10.1186/s12884-020-02940-w
39. Li S, Gao J, Liu J, Hu J, Chen X, He J, et al (2021) Perinatal Outcomes and Risk Factors for Preterm Birth in Twin Pregnancies in a Chinese Population: A Multi-center Retrospective Study. Front Med 8:657862. doi: 10.3389/fmed.2021.657862
40. Weiner E, Barrett J, Zaltz A, Ram M, Aviram A, Kibel M, et al (2019) Amniotic fluid volume at presentation with early preterm prelabor rupture of membranes and association with severe neonatal respiratory morbidity. Ultrasound Obstet Gynecol 54:767–773. doi: 10.1002/uog.20257
41. Crump C, Sundquist J, Sundquist K (2020) Preterm birth and risk of type 1 and type 2 diabetes: a national cohort study. Diabetologia 63:508–518. doi: 10.1007/s00125-019-05044-z
42. Muin DA, Kollmann M, Blatterer J, Hoermann G, Husslein PW, Lafer I, et al (2021) Cardio-pathogenic variants in unexplained intrauterine fetal death: a retrospective pilot study. Sci Rep 11:6737. doi: 10.1038/s41598-021-85893-0
43. Zhang Y, Zhou J, Ma Y, Liu L, Xia Q, Fan D, et al (2019) Mode of delivery and preterm birth in subsequent births: A systematic review and meta-analysis. PLoS One 14:e0213784. doi: 10.1371/journal.pone.0213784
44. Gupta R, Mukherjee P, Kaur H, Singhal S (2020) Role of cervicovaginal β-hCG in prediction of preterm delivery: a prospective observational study. Int J Reprod Contraception, Obstet Gynecol 9:3677. doi: 10.18203/2320-1770.ijrcog20203839