

# Determination of risk factors and cumulative effects of the maternal and neonatal risk factors in relation to preterm labor

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## ABSTRACT

**Background:** Preterm labor is the leading cause of neonatal morbidity and mortality this study aimed to determine single and combined effects of all risk factors in relation to preterm labor. **Methods:** This was a case-control study that included patients from a teaching hospital affiliated to Tehran University of Medical Sciences. Women who came to this hospital for delivery were divided into two groups: 200 in preterm delivery (before 37 weeks) and 195 in term delivery (after 37 weeks). **Results:** In all 409 pregnant women were delivered. 217 were preterm (group A) and 192 were term (group B). The mean age of mothers in group A was  $30.04 \pm 5.74$  and the mean age of mothers in group B was  $27.28 \pm 5.90$  ( $P < 0.001$ ). The risk of preterm labor was 4.22 higher in mother with any risk factor before or during pregnancy ( $P < 0.001$ ), it was 3.67 higher in mother with complication of pregnancy ( $P < 0.001$ ) and it was 3.40 higher in neonate with any complication ( $P = 0.002$ ) compared to mother without any risk factors. For each mother, we calculated risk score for preterm labor by counting the number of risk factors. The risk of preterm labor was significantly higher in mother with risk factors compared to those without any risk factors ( $P$  for trend = 0.002). Mother with two risk factors had a 5.60 ( $P = 0.01$ ) and mother with three or more risk factors had a 23.48 ( $P = 0.001$ ) times higher risk for preterm labor than those who did not have any risk factors. **Conclusion:** The screening and identification of mothers with risk factors for preterm delivery can increasing mother's attention and participation to better manage of these condition to have more safe pregnancy period.

**Keywords:** Delivery, neonate, premature labor

## Introduction

Preterm birth defines as all births before 37 completed weeks of gestation,<sup>[1]</sup> or fewer than 259 days from the first date of a woman's last menstrual period.<sup>[2]</sup> Despite advanced information on the risk factors and mechanisms, preterm birth has led to the rise in number of these births in all countries.<sup>[3]</sup> It is the leading

cause of mortality, morbidity, and impaired motor and cognitive development in childhood than infants born at term.<sup>[4]</sup> In fact, about 15 million babies (5% to 18%) are born prematurely each year and in many countries the rate of preterm birth has increased from 1990 to 2015. Nevertheless, its complications' have risen from 1.57 million in 1990 to 0.81 million in 2015. Preterm neonates who survive are at greater risk of a range of short-term and long-term complications such as high rates of respiratory distress syndrome, bronchopulmonary dysplasia, necrotizing enterocolitis sepsis, periventricular leukomalacia, seizures, intraventricular hemorrhage, cerebral palsy, infections, feeding difficulties, hypoxic-ischemic encephalopathy, and visual and hearing problems.<sup>[5-13]</sup>

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Received: 08-06-2020

Revised: 09-09-2020

Accepted: 20-12-2020

Published: 29-04-2021

### Access this article online

#### Quick Response Code:



Website:  
www.jfmpc.com

DOI:  
10.4103/jfmpc.jfmpc\_1118\_20

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**How to cite this article:** Tavoli Z, Tajdar A, Kheiltash A, Rabie M. Determination of risk factors and cumulative effects of the maternal and neonatal risk factors in relation to preterm labor. J Family Med Prim Care 2021;10:1747-53.

Preterm birth is a complex cluster of problems with a set of overlapping risk factors including individual and psycho-social factors, medical conditions such as diabetes, obesity, hypertension, multi gestational pregnancy, vaginal infections. Many of these factors occur in combination.<sup>[14]</sup> Determination of the maternal and neonatal risk factors can help the Pediatrics primary care physicians to have a released a further categorization of the levels in the neonatal care unit consisting of basic, specialty, and subspecialty care levels reflecting the important role of applying a suitable physical space, equipment, proper personnel, and organization in achieving a better prognosis in preterm neonates. Therefore, we investigated the combined effect of risk factors in relation to preterm birth in a case-control study.

## Methods

### Study design

This is a prospective case-control study prepared between September 2018 and January 2019 at a teaching hospital affiliated to Tehran University of Medical Sciences. In all 395 pregnant mothers admitted for delivery, 200 pregnant women were below 37 weeks (preterm delivery) as case group and 195 patients more than 37 weeks gestational age (term deliveries) at the same time interval as the control group.

### Data collection

Initially by referring to the medical records that made on the day of admission for each mother, the required information was extracted from the medical records of patients prepared and completed by the medical staff, including obstetricians and midwifery experts. The questionnaires were then completed by referring to the mother's bedside after the delivery and interviewing with mothers. Finally, the remaining missing data were completed by telephone contact with the mother during the review phase. Pregnant mothers were selected in the case group. And in the control group, it was completely random and based on the inclusion criteria of the study (pregnant mother  $\geq$  37 weeks gestational age at Days for delivery).

The data collection form includes the personal and demographic information of the mothers, including nationality (Iranian and Afghan), age, gender, weight and height, body mass index (BMI), education level, occupation, and BMI in addition to gender, age, and weight of neonate at birth. Moreover, we collected information about risk factors affect delivery during pregnancy from the mothers including mother's working hours, average maternal weight gain, maternal systolic and diastolic blood pressure at the time of last visit for delivery, receiving prenatal and maternal care during recent pregnancy, medication used and smoking during pregnancy.

Further, we gathered information regarding neonates (such as gestational age based on LMP and ultrasound, and Apgar score at 1 and 5 minutes) and also risk factors that may affect term pregnancy (including Gravidity, Parity and Abortion, Number of

Live children and Outcome of delivery during recent Pregnancy, Fetal Presentation, History of Fall or Abdominal trauma During Recent Pregnancy, Chronic Blood Pressure, Gestational Hypertension and Preeclampsia, Diabetes Pre-gestational and gestational diabetes, placenta previa, oligohydramnios, history of stillbirth, premature rupture of membrane, urinary tract infection, history of miscarriage, placental abruption, history of curettage and cervical surgery, vaginal bleeding and finally the time interval between this pregnancy and the last pregnancy).

### Data analysis

Descriptive tests including frequency and percentage were used to describe qualitative data using the Chi-square test and Fisher Exact test for low number of variables. Since the assumptions of the T-Test include the normal distribution of the quantitative variable, the normal distribution of the quantitative variable was examined by Kolmogorov–Smirnov test. The non-parametric Mann–Whitney *U* test was used for quantification of blood pressure because of no normal distribution. Logistic regression was used to compare the association of risk factors in mothers with of preterm delivery compared to term delivery. We considered term delivery as reference group.

To assess the cumulative effect of risk factors for preterm delivery, a factor called “cumulative risk score” was defined based on the risk factors reported in Table 1. All analyses were performed using the SPSS for Windows software package, version 20.0.

## Results

In all 409 pregnant mothers admitted for delivery, 217 pregnant women were below 37 weeks (preterm delivery) as case group and 192 patients more than 37 weeks gestational age (term deliveries) at the same time interval as the control group. General characteristics of mothers with preterm and term delivery were compared between two groups. There was not a significant difference in nationality, maternal education level, maternal occupation, drug addiction between mothers with preterm labor and term labor ( $P > 0.05$ ) [Table 2]. The mean maternal age of the participants was 30.04 years for the preterm group and 27.28 years for the full-term group, which was significant ( $P < 0.001$ ). The risk of preterm birth was just 3.64 times greater than that of mothers aged 20 to 25 years. Mothers between 30 and 35 years were 1.89 times more likely to have preterm labor than mothers aged 20 to 25 years that was statistically significant, this risk was 1.51 for mothers aged 25-30 years compared to mothers aged 20-25 [Figure 1].

**Table 1: Cumulative effect of risk factors for preterm delivery**

	OR (95% CI)	P
No risk factor	1	0.002*
Risk Factor $\leq$ 2	5.60 (2.08-15.09)	0.001**
Risk Factor $\geq$ 3	23.48 (8.94-61.65)	0.001

OR denotes to odds ratio and CI denotes to confidence interval. \*P for trend. \*\* compared with reference group with no risk factor

There was not a significant association between preterm and term delivery groups in terms of maternal care before and during pregnancy as well as body mass index, and drug use [Table 2].

Maternal medical conditions were compared in mothers with term and preterm delivery. Chronic hypertension was observed in 3.7% of mothers with preterm delivery whereas this was presented only a 0.5% of mothers with term delivery ( $P = 0.04$ ). Of note, all diabetic mothers had preterm labor ( $P = 0.008$ ).

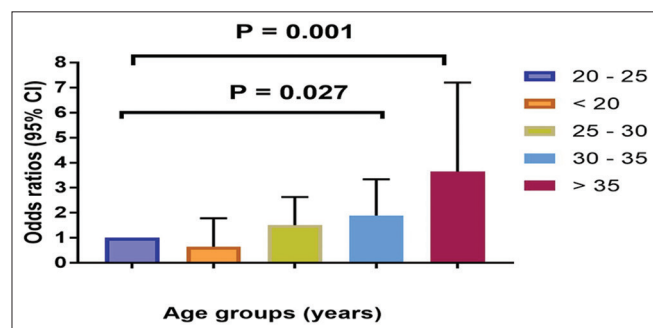


Figure 1: Risk of preterm delivery by age group

Table 2: General Characteristics of Mothers Participating in the study with Term and Preterm delivery denotes to number and % denotes to percentage

	Term (n=192) n (%)	Preterm (n=217) n (%)	P
Age			0.001
< 20	15 (7.8)	6 (2.8)	
20-25	64 (33.3)	46 (21.2)	
25-30	52 (27.1)	62 (28.6)	
30-35	43 (22.4)	59 (27.2)	
> 35	18 (9.4)	44 (20.3)	
Nationality			0.717
Iranian	178 (92.7)	198 (91.2)	
Afghan	14 (7.3)	19 (8.8)	
Education			0.12
Illiterate	36 (18.8)	40 (18.4)	
Intermediate	45 (23.4)	35 (16.1)	
High school	90 (46.9)	104 (47.9)	
University	21 (10.9)	38 (17.5)	
Job			0.415
worker	181 (94.3)	206 (94.9)	
Employee	6 (3.1)	3 (1.4)	
housewife	5 (2.6)	8 (3.7)	
Mothers care			0.421
Before Pregnancy	75 (39.1)		
Mothers care			0.689
During pregnancy	190 (99.0)		
Maternal weight gain	11.94±4.51	11.54±4.91	
BMI			0.234
Under weight	13 (6.8)	9 (4.1)	
normal	87 (45.3)	84 (38.7)	
Over weight	64 (33.3)	82 (37.8)	
Obese	28 (14.6)	42 (19.4)	
Smoking	0	1 (0.5)	1
Drug use	1 (0.5)	3 (1.4)	0.625

Mothers with preterm delivery had higher percentage of hypertension (14.3%) and preeclampsia (22.1%) compared with mothers with term labor (2.1%, 2.1%, respectively,  $P < 0.0001$ ). It was a significant difference in prevalence of gestational diabetes in mothers with preterm delivery (24.9%) compared with mothers with term delivery (10.9%) ( $P < 0.0001$ ). Although, mothers with preterm delivery had higher percentage of urinary tract infection during the third trimester than those with preterm, this difference was not statistically significant ( $P = 0.112$ ). [Table 3]

Pregnancy complications and risk factors in mothers with term and preterm delivery were compared between two groups [Table 3]. Placenta Previa, oligohydramnios, premature rupture of the membranes, and bleeding during pregnancy of preterm delivery were statistically significantly higher than that of term delivery ( $P < 0.05$ ). Although percentage of placental abruption was higher in mothers with preterm delivery compared with term delivery. This difference was not significant ( $p > 0.05$ ). Interestingly mother with previous history of miscarriage, cervix surgery, or abdominal trauma had significantly higher frequency of preterm labor compared with term labor ( $P < 0.05$ ). Prevalence of stillbirths in previous pregnancy was higher in mothers with preterm delivery than term but this difference was not significant ( $p > 0.05$ ). [Table 3]

Multiple gestation had a significant impact on preterm delivery ( $p < 0.0001$ ) [Table 4].

Notably, frequency of low birth weight infants was higher in mothers with preterm delivery and this difference was

Table 3: Association of Pregnancy complications and risk factors in mothers with term and preterm delivery

	Term (n=192) n (%)	Preterm (n=217) n (%)	P
Maternal diseases before pregnancy			
History of Chronic hypertension	1 (0.5)	8 (3.7)	0.04
History of Diabetes	0	8 (3.7)	0.008
Maternal diseases during pregnancy			
Hypertension	4 (2.1)	31 (14.3)	<0.0001
Preeclampsia	4 (2.1)	48 (22.1)	<0.0001
Gestational Diabetes mellitus	21 (10.9)	54 (24.9)	<0.0001
UTI in the third Trimester of Pregnancy	29 (15.1)	46 (21.2)	0.112
Pregnancy Complications			
Trauma to the abdomen during pregnancy	2 (1)	11 (5.1)	0.023
Placenta Previa	0	7 (3.2)	0.016
Oligohydramnios	1 (0.5)	38 (17.5)	<0.0001
PROM	3 (1.6)	13 (6)	0.021
Placental abruption	1 (0.5)	5 (2.3)	0.221
Pregnancy Bleeding	20 (10.4)	47 (21.7)	0.003
History of pregnancy complications			
History of Abortion	43 (22.4)	71 (32.7)	0.021
History of stillbirth	6 (3.1)	14 (6.5)	0.167
History of Curettage	9 (4.7)	34 (15.7)	<0.0001
History of Cervical Surgery	2 (1)	12 (5.5)	0.014

statistically significant ( $P < 0.0001$ ). There was no significant difference between the gender of neonates in two mother groups ( $P = 0.322$ ). [Table 4]

Interestingly all term neonates had Apgar scores equal to and above 7 and had cephalic presentation ( $P < 0.0001$ ). [Table 4]

The chances of having preterm labor increased with increasing maternal age from 20 to 25 years, and mothers over 35 had a 3.64-fold risk of preterm delivery compared to term delivery, which was statistically significant (95% CI: 1.84-7.20, ( $P = 0.001$ )). Although the risk of preterm delivery increased with body mass index more than that of term delivery, this difference was not significant ( $p. 0.635$ ). Risk of preterm delivery with gravidity in preterm delivery was more than term delivery but this difference was not significant. Mother with preeclampsia had 14.46 times, hypertension 9.34 times and diabetes 2.66 times higher risk of preterm delivery compared with term delivery ( $P < 0.05$ ) [Table 5].

The risk of preterm delivery based on maternal illnesses before and during pregnancy, complications of pregnancy, pregnancy history, and neonatal characteristics were compared [Figure 2]. Mother with any maternal illnesses before and during pregnancy had 4.22 times, mother with complications of pregnancy had 3.67 times and mother with neonatal issues had 3.40 times higher risk of preterm delivery than that of term delivery ( $P < 0.05$ ) [Figure 2].

We found the risk of preterm birth was 5.60 times higher in mothers having at least 1 to 2 risk factors compared with those with no risk factors ( $P = 0.001$ ). Interestingly, mothers who had more than 3 risk factors had a 23.48 times higher risk of preterm delivery than of those with no risk factors, suggesting a cumulative effect of these risk factors. [Table 1]

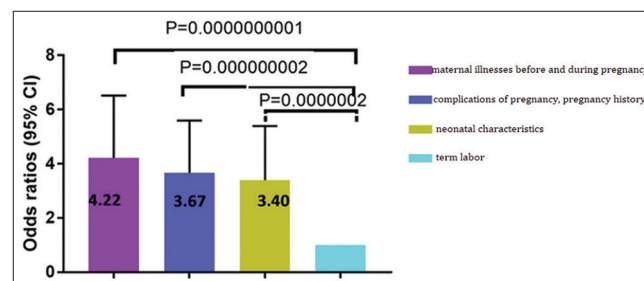
## Discussion

This study demonstrates that mother risk factors such as maternal illnesses before and during pregnancy are strongly associated with preterm birth compared with complication of pregnancy or neonatal issues. Furthermore, we observed that risk of preterm delivery was increased substantially in mother who had 3 or more risk factors. This study indicates that despite the fact that the individual risk factors revealed small effects; the combinations of risk factors may more clearly predict susceptibility of a pregnant mother to have preterm delivery.

To our knowledge, the present study is the first to study the cumulative effects of the maternal risk factors, pregnancy risk factors, as well as neonatal risk factors, in relation to preterm delivery. There was no significant difference in the nationality, education, maternal Occupation, BM, tobacco and drug use of mothers with preterm labor and term labor. According to the accumulation of frequencies of obesity and overweight, 57.2% and 47.9%, respectively, of the

**Table 4: Association of neonatal characteristics in mothers with Term and Preterm delivery**

	Term (n=195) n (%)	Preterm (n=200) n (%)	P
Distance from previous pregnancy			0.676
<6 months	67 (34.9)	71 (32.7)	
>6 months	125 (65.1)	146 (67.3)	
History of Multiple Pregnancy			<0.0001
singleton	192 (100)	187 (86.2)	
twin	0	30 (13.8)	
Neonate gender			0.322
Girl	89 (46.4)	112 (51.6)	
Boy	103 (53.6)	105 (48.4)	
Birth weight (g)			<0.0001
Normal $\geq 2500$	188 (97.9)	96 (44.2)	
1500 < LBW < 2500	4 (2.1)	74 (34.1)	
1000 < VLBW < 1500	0	23 (10.6)	
ELBW < 1000	0	24 (11.1)	
Apgar score 5 min			
0-3	0	22 (10.1)	
4-6	0	14 (6.5)	
7-10	192 (100)	181 (83.4)	
Live baby birth	192 (100)	189 (87.1)	
Birth of a dead baby		28 (12.9)	
Presentation of the fetus at delivery			
Cephalic	192 (100)	182 (83.9)	
Breech	0	31 (14.3)	
Other	0	4 (1.8)	



**Figure 2:** Shows the risk of preterm delivery based on maternal illnesses before and during pregnancy, complications of pregnancy, pregnancy history, and neonatal characteristics compared to term labor

mothers with preterm delivery and term, no significant relationship was found between BMI and preterm labor but in other studies there was a statistically significant relationship<sup>[15]</sup>

Therefore, approximately 50% of mothers are overweight. It seems that weight control and lifestyle modification programs in women of childbearing age can be helpful in reducing cases such as preterm labor in future pregnancies.<sup>[16]</sup>

In the case of cigarettes and drugs use, the result of this study may be due to the mothers' unwillingness to say the right answers. In other studies, it has been suggested that smoking is responsible for 15% of all preterm deliveries and 20% to 30% of low birth weight infants.<sup>[17]</sup> In this study, smoking was listed as one of

Table 5: Maternal risk factors and risk of preterm delivery

	OR (95% CI)	P
Age (years)	1.49 (1.24-1.78)	0.00002
20-25	1	0.394
<20	0.64 (0.23-1.78)	0.147
25-30	1.51 (0.86-2.63)	0.027
30-35	1.89 (1.10-3.34)	0.001
>35	3.64 (1.84-7.20)	
Maternal body mass	1.20 (0.94-1.53)	0.149
Normal	1	0.635
Under weight	1.25 (0.50-3.08)	0.327
Over weight	1.58 (0.63-3.94)	0.291
Obese	1.70 (0.63-4.57)	
Gravidity	1.13 (0.88-1.45)	0.337
Before pregnancy		
Chronic maternal hypertension before pregnancy	15.62 (0.89-272.46)	0.059
Maternal Diseases During Pregnancy		
Diabetes	2.66 (1.51-4.66)	0.001
Hypertension during pregnancy	9.34 (3.22-27.03)	0.00004
Preeclampsia	14.46 (5.08-41.18)	<0.000001
Pregnancy infection (UTI in third trimester)	1.53 (0.90-2.59)	0.114
	3.11 (0.32-30.21)	0.327
Pregnancy Complications		
Placental abruption	5.25 (0.61-45.35)	0.132
Premature rupture of the membrane	4.71 (1.32-16.80)	0.017
Oligohydramnios	37.96 (5.12-281.16)	0.0004
Pregnancy Bleeding	1.98 (1.10-3.60)	0.023
Baby features		
Baby gender	1.25 (0.83-1.87)	0.283
History of pregnancy complication		
History of Cervical Surgery	4.25 (3.89-20.26)	0.07
Curettage history	3.43 (1.57-7.51)	0.002
History of trauma or fall in Pregnancy	5.94 (1.30-27.16)	0.02167
Abortion history	1.72 (1.09-2.71)	0.01989
0	1	0.11846
1	1.48 (0.90-2.43)	0.01919
2	3.18 (1.21-8.37)	
History of stillbirth	2.51 (0.94-6.67)	0.065

OR denotes to odds ratio and CI denotes to confidence interval

the most important and modifiable risk factors associated with adverse prenatal outcomes.

In the case of occupation, a study of standing, stressful and hard work was associated with preterm labor<sup>[18]</sup> In this study, there was no significant relationship between pre and postnatal maternity cares, while in other studies there was a significant relationship between had or had not maternity care during pregnancy<sup>[14]</sup>

Frequency of prenatal care was 43.3% in pre-term and 39.1% in term group. Overall, about 40 percent of mothers have received pre-natal care. Considering the presence of maternal diseases before pregnancy (such as heart disease) that can not only have exacerbated during pregnancy but also they may adversely affect maternal and fetal normal pregnancy. Given the comprehensiveness of the health care system, especially the maternal care system, 40% of mothers have received pre-natal care do not appear to be satisfactory. Therefore, educating women of childbearing age it is most likely to increase their care

during pregnancy, and subsequently increasing the chances of having a safe and healthy pregnancy.<sup>[19]</sup>

Several studies have shown that the relationship between maternal age and preterm delivery is more at the two ends of the age spectrum, in less than 18 years and greater than 35 years<sup>[20,21]</sup> But in this study the risk of preterm delivery increased with increasing maternal age from 20 to 25 years and in mothers over 35 years old they had 3.64 times higher risk of preterm delivery compared to term delivery, which is in line with previous studies. In mothers less than 20 years old, the risk of preterm birth was 0.64, indicating a protective effect of the age under 20, although this difference was not significant, probably because of the low frequency of this age group (6 persons or 2.8% in preterm and 15 persons or 7.8% in term labor). While, in one study younger than 20 years of age was reported as a protective factor.<sup>[22]</sup> The risk of preterm delivery with the number of maternal pregnancies (gravidity) in preterm delivery was higher than that of term delivery, but this difference was not significant. However, in the other study, the number of maternal pregnancies was the risk factor for preterm delivery.<sup>[14]</sup>

In this study the presence of chronic maternal hypertension, gestational hypertension, preeclampsia, pre-gestational diabetes and diabetes mellitus, frequency of pregnancy complications such as placenta previa, oligohydramnios, premature rupture of membrane, and prenatal bleeding in mothers with preterm labor was greater than term mothers and the difference was statistically significant, and confirming other studies.<sup>[14,23-25]</sup>

In this study, the frequency of placental abruption was higher in mothers with preterm delivery but this difference was not significant but in other studies there was a significant relationship between placental abruption and preterm labor.<sup>[14]</sup>

Urinary tract infection (UTI) has also been reported to be associated with preterm labor<sup>[14,22,26]</sup> However, in this study the frequency of UTI in third trimester was higher in mothers with preterm delivery than in mothers with term labor, but this relationship was not statistically significant. In this study, the frequency and history of abortion and abdominal trauma in mothers with preterm labor were significantly higher than mothers with term labor, which confirms other studies.<sup>[14]</sup> Prevalence of stillbirths was higher in mothers with preterm delivery but this difference was not significant. But there is a significant relationship between the history of stillbirth and preterm labor in other studies.<sup>[14]</sup>

In our study, neonatal characteristics such as low birth weight infant, a stillborn baby is born at this time, fetal breech presentation and twin pregnancies were higher in women with preterm labor than in women with term labor and this difference was statistically significant similar to previous studies.<sup>[27]</sup>

There was no significant difference in terms of neonatal gender between term and preterm delivery, despite a study that showed that fetuses with male sex were more prone to preterm delivery and fetuses with male sex more likely to have early premature birth.<sup>[28]</sup>

Our study also has some limitations. We had a limited access to the records of mothers and their infants who had been not prenatal cared in this hospital and we prepared variables with asking with a questionnaire.

Maternal risk factors had highest contribution to increase the risk of preterm delivery. identification of risk factors specially mother's risk factors play more important rule than neonatal risk factors and consequently the screening and identification of mothers with risk factors for preterm delivery can increasing mother's attention and participation to better manage of these condition to have more safe pregnancy period. despite the fact that the individual risk factors revealed small effects; the combinations of risk factors may more clearly predict vulnerability of a pregnant mother to have preterm delivery and may require intensive and frequent follow-up during their pregnancy.

## Ethical consideration

The study protocol and all the procedures were reviewed and approved by the Research Ethics Committee of Tehran University of Medical Sciences. Ethical cod No IR.TUMS.REC.1397.478.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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