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Association between Maternal Serum Leptin Level and Preterm Birth among Parturients in Lagos, Nigeria

Olubunmi Olufunke Ogein[1,*], Adeyemi Adebola Okunowo[2], Gbenga Olorunfemi[3], Benedetto Osunwusi[1], Omololu Adegbola[2]

[1]Department of Obstetrics & Gynaecology, Lagos University Teaching Hospital, Lagos, Nigeria

[2]Department of Obstetrics and Gynaecology, College of Medicine, University of Lagos/ Lagos University Teaching Hospital, Lagos, Nigeria

[3]Division of Epidemiology and Biostatistics, University of Witwatersrand, Johannesburg, South Africa

*Correspondence should be addressed to Olubunmi O Ogein, olubunmiogein@gmail.com

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Abstract

Background: Preterm birth is one of the major causes of neonatal morbidity and mortality worldwide. The association between occurrence of preterm birth and biomarkers measured in the maternal serum maybe helpful in predicting preterm birth especially in low resource settings.

Aim: We aimed to examine the association between maternal serum leptin level and occurrence of preterm birth.

Materials and Methods: This was an analytical cross-sectional study of women with preterm and term births in Lagos, Nigeria. One hundred and ninety women comprising of 95 women with preterm and term births respectively recruited. Maternal serum leptin levels were determined using Enzyme-linked immunosorbent assay (ELISA) technique. Data was analyzed by Stata version 16 (StataCorp, USA) statistical software with significance level set at p-value <0.05.

Results: The mean serum leptin levels were significantly lower in women with preterm delivery compared to women with term delivery (1.48 ng/ml ± 0.72 vs. 1.75 ng/ml ± 0.67, p-value=0.007). On further analysis, women with very preterm birth had significantly lower serum leptin levels compared with women with moderate to late preterm and term births (1.28 ± 0.73 vs 1.55 ± 0.70 vs 1.75ng/ml ± 0.67, p-value=0.006). There was 57% reduction in the odds of having preterm delivery for every unit increase in serum leptin level on multivariate analysis (adjusted OR: 0.43, 95%CI: 0.26 – 0.71, P-value=0.001).

Conclusion: Serum leptin concentration was significantly lower in women who had preterm births compared to women who had term births. Longitudinal studies are required to determine the predictive value of maternal serum leptin level with regards to preterm birth.

Keywords: Preterm birth, Term birth, Serum leptin levels, Nigeria

Introduction

Preterm birth is defined by the World Health Organization (WHO) as birth prior to 37 completed weeks (259 days). [1] The definition of preterm birth in Nigeria is birth between the age of viability and 36 completed weeks [2]. This could follow spontaneous labour with intact membranes, preterm premature rupture of the membranes (PPROM) and labour induction or caesarean delivery for maternal or fetal indications [3].

It is a global public health problem as it is a major determinant of neonatal mortality and morbidity worldwide. It is also the second most frequent cause of death in children aged <5 years worldwide and has long-term adverse consequences on health [3-5] including cerebral palsy, mental retardation, vision impairment, hearing loss, asthma, learning disabilities, attention deficit disorder, emotional problems [6-10] as well as higher risk of insulin resistance and hypertension in adulthood [11,12].

The average global preterm birth rate (based on 184 countries) was 11%, yielding a total of 14.9 million preterm delivery cases annually [5] with about 60-80% of all preterm birth cases occurring in Africa and Asia [2,5]. In 50% of cases, the cause of preterm labor is idiopathic. In a recent Lagos study, 16.8% of the singleton live-birth deliveries were preterm suggesting that preterm birth rate is still significantly high in our environment [13]. It is associated with financial burden and other difficulties like psychological distress such as anxiety and depression experienced by couples and extended family members [10].

Despite its impact on global health, little is known about the mechanisms underlying spontaneous preterm birth (sPTB) [3,10,14]. Antenatal prevention and prediction of sPTB is therefore crucial to reduce the burden of morbidities associated with this condition [15]. Efforts to predict, prevent, and delay preterm births have had some, but limited success. This includes identifying high-risk patients via risk factors assessment and scoring systems, cervical length assessment, fetal fibronectin assay and the use of progesterone, antibiotics and tocolytics [16]. The use of biomarkers for sPTB could also help to explain the possible mechanisms underlying prematurity, develop predictive tools to identify high-risk pregnancies, decrease the hospital cost, restrict the treatment and identify new targets for intervention [16].

Leptin is a pleiotropic hormone that regulates not only body weight but many other functions including normal physiology of reproductive system [17]. Studies have shown association between maternal serum leptin level and recurrent pregnancy losses, intrauterine growth restriction, preeclampsia, and gestational diabetes mellitus [17,18] However, there is limited information on the association between maternal serum leptin levels and preterm labour as well as its role in prediction of preterm birth. The available literatures were inconclusive on the relationship between maternal serum leptin levels and preterm labour. While some agreed that women with the highest quartile of leptin had reduced risk of sPTB, others reported insignificant differences in leptin levels in relation to preterm birth [16].

These findings were derived from non-Nigerian populations as no study on African population was identified from extensive search of literature. This gap in knowledge and the huge burden of preterm birth in our environment endeared the interest to carry out this study to contribute to the body of knowledge on the relationship between maternal serum leptin level and occurrence of preterm birth among Nigerian women.

Materials and Methods

Study design and site

This was an analytical cross-sectional study conducted at Lagos University Teaching Hospital (LUTH) and Randle General Hospital (RGH) in Lagos, Nigeria over a nineteen month period between 1st September, 2019 to 31st March, 2021. LUTH is a tertiary institution located in Mushin Local Government Area while RGH is a secondary health facility located in Surulere, Lagos State. Both facilities cater for high risk pregnancies and deliveries.

Study population

The study population comprised of two groups of consecutively consenting pregnant women matched for age and parity who met the specified eligibility criteria. The participants in the study group comprised of women with sPTB between gestational ages of 28 and 36 weeks and participants in the comparison group were women with gestational age 37 completed weeks but less than 42 weeks.

Eligibility criteria and sample size determination

The study group included women who had spontaneous preterm vaginal birth who were sure of their last menstrual period or who had early ultrasound scan to date their pregnancy and who gave written informed consent. On the other hand, women who had term birth between gestational ages of 37 and 42 weeks, who were sure of their last menstrual period or who had early ultrasound scan to date their pregnancy and who gave written informed consent were enrolled into the comparison group. Pregnant women with uncertain gestational age, previous and present history of preeclampsia/eclampsia, gestational diabetes mellitus, thyroid diseases, and renal disorders were excluded from the study. In addition, pregnant women with risk factors for preterm birth such as premature rupture of membranes, previous history of preterm birth, multiple gestations, coexisting uterine fibroids, and cervical incompetence were also excluded from the study.

Sample size was calculated using the power analysis formula for comparing means [19]. The calculated minimum sample was one hundred and ninety.

Ethical consideration

The study was approved by the ethical committee of LUTH **(ADM/DCST/HREC/APP/2863)** and written informed consent was obtained from the participants prior to enrollment into the study.

Participants' recruitment, sample, and data collection

Study participants were recruited using convenient sampling method until appropriate sample size was reached from the labour ward. Participants in the comparison group were matched for age (± 2 years) and parity (± 2) with those in the study group.

Information was collected by direct interview and from

the case notes using the data form. The researchers avoided interviewer and response bias by ensuring that the interview was conducted by trained interviewers in a relaxed environment using a structured Proforma so that all the participants answered the same questions. The questions were asked in simple language understood by the participants in a non-leading manner and adequate time was given to respond to the questions without any prompting or urgency in order to allow the respondents offer the correct answers to the questions. The information included socio-demographic data, estimated gestational age determined from the first day of last menstrual period or from an early obstetric scan (within the first 20 weeks) for participants who were unsure of date or expected date of delivery, past obstetric and medical history. The anthropometric measurements such as weight and height were taken and body mass index was calculated by division of body weight by the square of height in kg/m^2. Normal, overweight, and obese mothers were identified based on BMI values of 18.5-24.9, 25.0–29.9, and ≥ 30.0 kg/m^2 respectively [19].

Five millilitres of venous blood were collected by venepuncture at the antecubital vein from each eligible participant into universal (plain) bottles immediately after delivery. Serum leptin levels were estimated using enzyme-linked immunosorbent assay kits manufactured by Elabscience Biotechnology Inc., USA. The sample collection, transport and storage was done accordingly based on the manufacturers' instruction and analysed in a pre-specified standard laboratory.

Statistical analysis

Statistical analysis was done using Stata version 16 (StataCorp, USA) Statistical software for analysis. Continuous variables with normal distribution were expressed as mean ± standard deviation and continuous variables that were not normally distributed were presented as median (interquartile range). Differences in continuous variables among those with preterm birth and those with term birth were assessed using Students' test. Association between preterm birth and categorical socio-biological variables was determined using Chi-square test. Students'-test was used to compare the mean serum leptin levels among the categories of women who had preterm births based on gestational age at delivery. One-way analysis of variance was used to compare the means of maternal serum leptin levels among sub-categories of women who had preterm births based on gestational age at delivery and term birth. Post hoc Bonferroni pair-wise test was conducted to determine where the differences lie. Univariable and multivariable logistic analysis was conducted with preterm delivery as the outcome and the serum leptin level as the primary explanatory variable. The other confounding variables were corrected for in the multivariable analysis using a backward elimination method. Confidence level of 95% was assumed with the level of significance set as P-value of <0.05 for all analysis.

Results

The mean age of the participants in the study group was 31.9 ± 2.6 years. Majority of the participants were within the age range of 30-39 years. There was no statistically significant difference in the socio-demographic characteristics between participants within the study group compared with the comparison group except in the booking status of women, gestational ages and fetal birth weights (P-value ≤ 0.001) (**Table 1**).

Table 1. Comparison of socio-biological characteristics of study participants.

Characteristics	All participants (n=190)	Preterm, n=95 (%)	Term n=95 (%)	P-value
Age(years) Mean ± SD	32.3 ± 3.3	31.9 ± 2.6	32.7 ± 3.8	0.092#
20-29	63 (33.2)	28 (29.5)	35 (36.8)	0.515^
30-39	115 (60.5)	60 (63.2)	55 (57.9)	
≥40	12 (6.3)	7 (7.4)	5 (5.3)	
Marital status				
Single	15 (7.9)	4 (4.2)	11 (11.6)	0.060$
Married	175 (92.1)	91 (95.8)	84 (88.4)	
Educational status				
Primary	4 (2.1)	4 (4.2)	0 (0)	0.129$
Secondary	71 (37.4)	35 (36.8)	36 (37.9)	
Tertiary	115 (60.5)	56 (59.0)	59 (62.1)	

Ethnic groups				
Yoruba	114 (60.0)	60 (63.2)	54 (56.8)	0.166^
Igbo	56 (29.5)	29 (30.5)	27 (28.4)	
Others	20 (10.5)	6 (6.3)	14 (14.7)	
Parity (Median, IQR)	2 (1-3)	2 (1-3)	2 (1-3)	0.521[!]
1	73 (38.4)	34 (35.8)	39 (41.0)	0.456^
>1	117 (61.6)	61 (64.2)	56 (59.0)	
Body mass index kg/m² (Mean ± SD)	29.3 ± 3.8	28.9 ± 3.6	29.7 ± 4.0	0.475[#]
Normal	12 (6.3)	8 (8.4)	4 (4.2)	0.456^
Overweight	104 (54.7)	50 (52.6)	54 (56.8)	
Obese	74 (39.0)	37 (39.0)	37 (39.0)	
Booking status				**<0.001^**
Booked	74 (39.0)	57 (60)	81 (85.3)	
Unbooked	52 (27.4)	38 (40)	14 (14.7)	
Gestational age at delivery (Median, IQR)	36.5 (33-39)	33 (31-35)	39 (38-40)	**<0.001**[!]
Birth weight of baby in kg (Mean ± SD)	2.7 ± 0.86	2.0 ± 0.64	3.3 ± 0.56	**<0.001**[#]
[#]Student's t-test; [$] Fischer's test; ^ Pearson's Chi-square; [!] Mann Whitney U				

The mean serum leptin was significantly higher among the participants who had term birth as compared with those who had preterm birth (1.75 ng/ml ± 0.67 vs 1.48 ng/ml ± 0.72, P-value=0.007). The mean serum leptin levels were lowest among women with very preterm births while women with term babies had the highest mean serum leptin levels. (P-value=0.006) (**Table 2**).

Post-hoc Bonferroni test revealed a statistically significant difference between serum leptin levels among women with very preterm births as compared to the leptin levels among women with term births (P-value=0.007). However, there was no statistically significant difference between the serum leptin level among women with very preterm births and moderate-to-late preterm births (P-value=0.262). Similarly, there was no statistically significant difference between the mean serum level of leptin among women with moderate-to-late preterm births and women with term births (P-value=0.218) (**Table 3**).

Logistic regression analysis of the association between maternal serum leptin and preterm birth showed statistically significant relationship between serum leptin level and the odds of having preterm births. For every unit increase in the serum leptin level, there was 57% reduced odds of having preterm birth among the participants (adjusted OR: 0.43, 95%CI: 0.26 – 0.71, P-value=0.001) implying that, for every

Table 2. Comparison and relationship between Maternal Serum Leptin levels, Preterm and Term Deliveries.

Variable	**Preterm Delivery n=95**		**Term Delivery n=95**	**P-value**
Serum leptin levels (ng/ml) (Mean ± SD)	1.48 ± 0.72		1.75 ± 0.67	**0.007**[*]
	Very preterm (28-31 weeks) n=27	**Moderate-to-Late preterm (32-36 weeks) n=68**		
Serum leptin levels (Mean ± SD)	1.28 ± 0.73	1.55 ± 0.70	1.75 ± 0.67	**0.006**[¥]
[*]Student's T-test; SD: Standard Deviation; [¥]ANOVA: One-way Analysis of Variance				

Table 3. Post-Hoc Bonferroni Test showing the relationship between categories of preterm and term deliveries and maternal serum leptin levels.

	Very preterm (28-31 weeks) n=27	**Moderate-to-Late preterm (32-36 weeks) n=68**	**Term (≥ 37 weeks) n= 95**
Moderate-to-Late preterm (32-36 weeks) n=68	P-value=0.262	-	P-value=0.218
Term (≥37 weeks) n= 95	**P-value=0.007***	P-value=0.218	-
*statistically significant pairwise difference			

Table 4. Logistic Regression of the Association between Maternal Serum Leptin and Preterm delivery.

Variable	**Univariable**			**Multivariable**		
	Odds ratio	**95% Confidence interval**	**P-value**	**Adjusted Odds Ratio**	**95% Confidence interval**	**P-value**
Serum leptin level	0.56	0.37 – 0.86	**0.008***	0.43	0.26 - 0.71	**0.001***
Age (years)						
Mean maternal Age	1.00	0.95 - 1.06	0.904	0.99		
Age category						
20-29	1.00	Reference	Ref	1.00	Reference	Reference
30 – 39	1.36	0.74 - 2.53	0.325	1.35	0.64 - 2.82	0.431
≥ 40	1.75	0.50 - 6.11	0.380	2.91	0.71 - 11.89	0.137
BMI (kg/m²)						
Mean BMI value	0.95	0.88 – 1.02	0.157	0.97		
Normal (18.5 – 24.9)	1.00	Reference	Ref	1.00	Reference	Ref
Overweight (25.0 – 29.9)	0.46	0.13 - 1.63	0.231	0.32	0.08 - 1.31	0.113
Obesity (≥ 30.0)	0.50	0.14 - 1.81	0.290	0.44	0.10 - 1.85	0.262
*statistically significant at P-value<0.05						

unit increase in serum leptin level, there was 2.3 folds odd of having term birth (**Table 4**).

Discussion

Preterm birth remains an unresolved entity [3,10,14] and despite its impact on global health, little is known about the mechanisms underlying sPTB. Although mortality associated with sPTB has been considerably reduced, in the last two decades, preterm birth rates have rapidly increased worldwide especially in Africa & Asia [2,5]. Prediction of sPTB through identification of risk factors and determining the individual risk for pregnant women is crucial to reducing the burden of morbidities associated with this condition [15], as this allows early action for preterm birth in utero transfer to tertiary care centres, administration of corticosteroids necessary for fetal maturity, administration of magnesium sulfate for its neuroprotective effect and antibiotic treatment in case of infection.

Our study aimed to examine the association between maternal serum leptin level and preterm birth among Nigerian women in Lagos, Nigeria. The findings of the study show that maternal serum leptin levels were lower in women who had preterm birth compared with those who had term birth (1.48 ng/ml ± 0.72 vs 1.75 ng/ml ± 0.67; P-value=0.007). This is in agreement with the findings of Fakor et al. and McDonald et al. who reported reduced mean serum leptin levels in pregnancies complicated by preterm birth compared with the term birth [20,21]. They reported that a higher level of leptin in pregnant women could decrease the risk of preterm birth. [20,21]. This was however, contrary to the findings of Kominiarek et al. who concluded that there were no differences in leptin levels when compared with term in a prospective cohort study [16]. The

difference in our finding may be due to the difference in study design and their study population which was predominantly of Caucasian descent.

Studies have documented long-term sequelae of preterm birth occurred mainly in babies delivered at gestational age less than 34 weeks. Therefore, a delay in delivery would contribute significantly to a decrease in neonatal morbidity or mortality. The relationship between serum leptin levels and preterm delivery was analyzed in our study by stratifying the preterm group into two sub-groups: very preterm (28-<32 weeks) and moderate-to-late preterm (32-<37 weeks) based on gestational age at delivery (**Table 3**) [22]. There was no significant difference in the maternal serum leptin levels of the very preterm and moderate-to-late preterm groups (P-value=0.097). The small sample size for sub-analysis may be responsible for this. Further analysis revealed a statistically significant difference in the serum leptin levels of the very preterm and term groups (P-value=0.007). This finding corroborates the documented hypothesis of rising leptin levels over the course of pregnancy especially in the first and second trimester [23,24], however, negates the pattern of leptin level in the third trimester and postpartum in this study thus implying that serum leptin levels may predict preterm delivery in women with preterm contractions/labor before 32 weeks gestation similar to the findings of Fakor et al. [20].

Our study showed that low maternal serum leptin level was an independent predictor of the odds of having a preterm birth among Nigerian women. The odds of having a preterm birth significantly increases by 43% for every unit decrease in the maternal serum leptin level (adjusted OR: 0.43, 95%CI: 0.26 – 0.71, p-value=0.001). Conversely, the odds of preterm birth significantly reduces by 57% for every unit increase in the maternal serum leptin level. This translates to a 2.3 folds increased odd of having a term delivery per unit increase in maternal serum leptin. It is therefore highly likely that leptin played an inhibitory role in spontaneous myometrial contraction as revealed in previous studies [25,26].

Preterm birth remains a significant cause of neonatal morbidity and mortality. Preterm neonates who survive have higher risk of long-term disabilities resulting in significant medical, social, and economic burden on affected families, health care systems and nation in terms of future lost productivity in the household and the labor force [27].

This multicenter study is a relatively new area of research in this environment that will provide evidence that will guide further research on the subject matter. A major limitation of the study is that its findings may not be generalizable and representative of the general population as it is a hospital based study. As a result, a population-based study is recommended to confirm the findings of the study in the population.

In conclusion, our study has shown that maternal serum leptin level is significantly lower in women who had spontaneous preterm deliveries compared with term deliveries. Current data are insufficient to determine the cut off value for prediction of preterm birth in susceptible pregnant women with history of preterm labour. In view of the findings in this study, it is imperative to conduct a large multicenter prospective longitudinal study to further confirm the findings of our study and determine the optimal cut off value of maternal serum leptin that reliably predicts the occurrence of preterm birth among Nigerian women.

Conflicts of Interest

There was no conflict of interest.

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Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Olubunmi O. Ogein, Adeyemi A. Okunowo, Gbenga Olorunfemi, Benedetto Osunwusi, and Omololu Adegbola. The first draft of the manuscript was written by Olubunmi O. Ogein and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References

1. World Health Organization. Manual of the international statistical classification of diseases, injuries, and causes of death. Vol. 1 (9th revision). Geneva (Switzerland): World Health Organization; 1975.

2. Ikechebelu JI, Eleje GU, Ugochukwu EF, Edokwe ES. Should we Re-Define Age of Fetal Viability in Nigeria? A Case Report of Newborn Survival from Pre-Viable Pre-Labor Rupture of Membranes. J Womens Health. 2014, Issues Care 3:3.

3. Goldenberg RL, Culhane JF, Iams JD, Romeo R. Epidemiology and causes of preterm birth. Lancet. 2008. 371(9606): 75-84.

4. Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C. Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. BMC Pregnancy Childbirth. 2010; 10(Suppl 1):S1 (2010).

5. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832): 2162-72.

6. Tronnes H, Wilcox AJ, Lie RT, Markestad T, Moster D. The association

of preterm birth with severe asthma and atopic dermatitis: a national cohort study. Pediatr Allergy Immunol. 2013;24(8):782-787.

7. Aarnoudse-Moens CS, van Goudoever J, Weisglas-Kuperus N, Oosterlaan J. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. Pediatrics. 2009;124(2):717-728.

8. Delobel-Ayoub M, Arnaud C, White-Koning M, Casper C, Pierrat V, Garel M, et al. Behavioural problems and cognitive performance at 5 years of age after very preterm birth: the EPIPAGE Study. Paediatrics. 2009;123(6):1485-1492.

9. Van Lieshout RJ, Boyle MH, Saigal S, Morrison K, Schmidt LA. Mental health of extremely low birth weight survivors in their 30s. Paediatrics. 2015;135(3):452-459.

10. Tsiartas P. Maternal and placental inflammatory biomarkers in spontaneous preterm delivery–Predictive ability, stability and neonatal associations. 2017 Sahlgrenska Academy, Gothenburg University, Gothenburg.

11. Hovi P, Andersson S, Eriksson JG, Järvenpää AL, Strang-Karlsson S, Mäkitie O, et al. Glucose regulation in young adults with very low birth weight. N Engl J Med. 2007;356(20):2053-2063.

12. Rotteveel J, van Weissenbruch MM, Twisk JWR, Delemarre-Van de Waal HA. Infant and childhood growth patterns, insulin sensitivity, and blood pressure in prematurely born young adults. Paediatrics. 2008;122(2):313-321.

13. Butali A, Ezeaka C, Ekhaguere O, Weathers N, Ladd J, Fajolu I, et al. Characteristics and risk factors of preterm births in a tertiary center in Lagos, Nigeria. Pan Afr Med. 2016;24:1.

14. Davey MA, Watson L, Rayner JA, Rowlands S. Risk scoring systems for predicting preterm birth with the aim of reducing associated adverse outcomes. Cochrane Database Syst Rev. 2015;2015(10): CD004902.

15. Lucaroni F, Morciano L, Rizzo G, D'Antonio F, Buonuomo E, Palombi L, et al. Biomarkers for predicting spontaneous preterm birth: an umbrella systematic review. J Matern Fetal Neonatal Med. 2017;31(6): 726–734.

16. Kominiarek MA, Gambala CT, Sutherland M, Varady K. Adipokinins in pregnancies at risk for preterm delivery. GynecolEndocrinol. 2016;32(1):78-81.

17. Perez-Perez A, Toro A, Vilarino-Garcia T, Maymo J, Guadix P, Duenas JL, et al. Leptin action in normal and pathological pregnancies. J Cell Mol Med. 2018;22(2):716-727.

18. Misra VK, Straughen JK, Trudeau S. Maternal Serum Leptin during Pregnancy and Infant Birth Weight: the Influence of Maternal Overweight and Obesity. Obesity. 2013; 21(5): 1064-1069.

19. Gogtay NJ. Principles of sample size calculation. Indian J Ophthalmol. 2010; 58(6):517-518.

20. Fakor F, Sharami SH, Milani F, Mirblouk F, Kazemi S, Pourmarzi D, et al. The association between levels of maternal serum leptin in the third trimester and the occurrence of moderate preterm labour. J. Turk Ger. Gynecol Assoc. 2016;17(4):182-185.

21. Mc Donald CR, Darling AM, Conroy AL, Tran V, Cabrera A, Liles WC, et al. Inflammatory and Angiogenic factors at mid- pregnancy are associated with spontaneous preterm birth in a cohort of Tanzanian women. PLOS ONE. 2015;10(8):e0134619.

22. World Health Organization. Preterm birth. Fact sheet N°363. Geneva (Switzerland): World Health organization; 2018.

23. Misra VK, Trudeau S. The influence of overweight and obesity on longitudinal trends in maternal serum leptin levels during pregnancy. Obesity (Silver Spring) 2011;19(2):416-21.

24. Lacroix M, Battista M, Doyon M, Moreau J, Patenaude J, Guillemette L, et al. Higher maternal leptin levels at second trimester are associated with subsequent greater gestational weight gain in late pregnancy. BMC Pregnancy Childbirth. 2016;(16):62.

25. Wuntakal R, Hollingworth T. Leptin–A tocolytic agent for the future? Med Hypotheses. 2010;74(1):81-82.

26. Moynihan AT, Hehir MP, Glavey SV, Smith TJ, Morrison JJ. Inhibitory effect of leptin on human uterine contractility in vitro. Am J Obstet Gynecol. 2006;195(2):504-509.

27. Hodek JM, von der Schulenburg JM, Mittendorf T. Measuring economic consequences of preterm birth - Methodological recommendations for the evaluation of personal burden on children and their caregivers. Health Econ Rev. 2011;1(1):6.