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Evaluation of the Relationship Between Short Femur Length and Preeclampsia

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ABSTRACT

Background & Objective: Preeclampsia is a perinatal and maternal morbidity and mortality-related pregnancy disease. A diagnostic challenge is frequently presented by the finding of a small femur length, especially below the fifth percentile. When the ultrasound was performed, it can be related to fetal growth restriction. This study sought to determine how short femur diaphysis length (FDL) during 32–37 weeks of gestation affected preeclampsia.

Materials & Methods: Between February 2021 and February 2022, pregnant women who received a regular abnormality scan at the Shahid Motahari University Hospital in Urmia, Iran, between 32 and 37 weeks of gestation were included in the study. As part of the abnormality scan, fetal biometry and uterine artery Doppler ultrasound were evaluated, and the mean pulsatility index of the two uterine arteries was noted. From our database system, we gathered information on maternal obstetric features such as ethnicity, age, weight, parity, smoking, and medical history including hypertension and diabetes mellitus.

Results: The present study's findings showed that preeclampsia, maternal age, and the number of prior pregnancies were all connected with multivariate analysis of the fetal femoral length percentile. Additionally, the 50th percentile femoral's sensitivity and specificity for the diagnosis of preeclampsia were 96.88 and 81.88, respectively.

Conclusion: According to our findings, there is a substantial association between PE and short FLduring 32–37 weeks of gestation.

Keywords: Preeclampsia, Short Femur length, Complications of Pregnancy

Introduction

A pregnancy problem known as preeclampsia is marked by elevated blood pressure and symptoms of damage to another organ system, most frequently the liver and kidneys **(1)**. Pre-eclampsia may cause intrauterine fetus growth retardation and early delivery, premature placental detachment, HELLP syndrome, eclampsia, and cardiovascular illness **(2)**. In pregnant women whose blood pressure had previously been normal, preeclampsia typically develops after 20 weeks of pregnancy **(3)**. Along with biparietal diameter, belly circumference, and head circumference, fetal weight estimation is frequently done by measuring the length of the femur. A diagnostic challenge is frequently presented when a short femur length is found, especially if it is below the fifth percentile **(4-6)**. At the time of the ultrasound exam, it can be connected to fetal growth restriction. In a fundamentally small fetus, a short femur is probably a normal deviation, especially if it is an isolated observation. Short femur length has been linked to later placental-related disorders such preeclampsia (PE), small for gestational age (SGA), low birth weight, and preterm birth, according to recent studies. Here, our goal is to ascertain whether an isolated short femur is associated with placenta-related negative outcomes such PE, SGA, and premature delivery. One of the markers for determining gestational age throughout the second and third trimesters of pregnancy is the fetal femur length (FL), which is measured by ultrasound. The length of the femur below the fifth percentile of gestational age is referred to as the fetal femoral length.

Fetal growth restriction (FGR), aneuploidy, low birth weight, placental abruption, and even normal fetuses with a genetic history can all result in short fetal femoral length relative to gestational age. It is linked to various genetic abnormalities, and some writers have identified it as a marker of chromosomal anomalies such trisomy 21 **(7-11)**, trisomy 18 or trisomy 13 **(10)**. However, in a fundamentally small fetus, a short femur is likely to be a normal deviation, especially when it is an isolated observation. The goal of the current study was to examine the connection between fetal femoral length and preeclampsia in light of the correlation between short fetal femoral length and preeclampsia that has been demonstrated by several studies, as well as the relationship between short fetal femoral length and gestational age (SGA), intrauterine growth retardation (IUGR), and low birth weight. Additionally, the beginning of eclampsia was planned and executed.

Methods

In this study, 320 pregnant women who chose not to have their pregnancies referred to Shahid Motahari Hospital participated in an analytical, retrospective case-control investigation. If they matched the requirements for inclusion, they were split into two groups: 160 expectant mothers who were diagnosed with preeclampsia and gave birth at Shahid Motahari Hospital, and 160 expectant mothers who were not diagnosed with the condition but gave birth there. The mother had to be free of endometriosis or Cushing's syndrome and the gestational age had to be greater than 24 weeks. Similarly, Singleton Delivery moms without a smoking history were chosen because of the prevalence of IUGR and its effect on fetal femoral length. The fetus shouldn't have any chromosomal or structural problems, it should be highlighted. The mothers were excluded from the study if, during the examinations, there was evidence of an underlying illness in the mother, such as a history of gestational diabetes, type 2 diabetes, heart disease, a history of macrosomic embryos, or a history of polyhydramnios, all as a result of IUGR or macrosomia in the fetus and changes in femoral length. A sonologist (supervising professor) used a single ultrasound machine of the SAMSUNG SW80 brand (South Korea) to measure the fetal femoral length of the chosen patients and record it in millimeters from the start to the end of the femoral diaphysis. The length of the femur was then calculated using the percentile difference between the gestational age on the day of hospitalization and the gestational age at the time of hospitalization, after which it was assigned to one of the two study groups. Each participating patient has provided their written informed permission. An expert in statistics examined the data.

Results

After removing patients with aberrant karyotype, significant fetal abnormalities, or termination of pregnancy, 320 women with gestational ages>24 weeks were included in the study. The 50th percentile femoral's sensitivity and specificity for the preeclampsia diagnosis were 13.98 and 75.88, respectively. Table 1 compares the obstetric characteristics of patients with PE to women without PE in terms of demographic information. The findings of the current study showed that preeclampsia, maternal age, and the number of prior pregnancies were all associated with multivariate analysis of fetal femoral length percentile. Our findings indicate the correlation matrix between quantitatively measured variables and the comparison of the frequency of femoral length (based on the percentile of gestational age) according to the study groups (Table 2). The findings show a substantial correlation between fetal femur length, birth weight, and height ($r = 0.321$, $p \leq 0.001$). A comparison of the two study groups' femoral length distributions (percentiles less and higher than 50%) is shown in (Table 3). The diagnostic value for the diagnosis of preeclampsia was assessed, with the outcomes shown in (Table 4), taking into account the cut-off point of the 50th percentile for the length of the femur and the prevalence of preeclampsia being equal to 8%. The distribution of the two groups' femoral lengths is compared in (Table 5) (percentiles less and greater than 75%), and the chi-square test result revealed a significant difference ($P \leq 0.001$). Given that preeclampsia is 8% common and that the cut-off point for femoral length is the 75th percentile, the diagnostic value was reassessed in terms of preeclampsia diagnosis. The results are displayed in (Table 6). The average birth weight in the control group was 3121.76±430.52 and in the case group it was 2136.86±958.71. The result of the t-test in (Table 7 and 8) showed that there was a significant difference between the two groups ($P \leq 0.001$).

Table 1. Comparison of the control group and PE group

Variables	Control group	PE group	p- value
	n= 160	n= 160	
Age, Years	7.28 ± 28.94	5.98 ± 30.57	p= 0.036
Conception			
Spontaneous	742 (92.7)	728 (91)	
In Vitro fertilization	58 (7.2)	72 (9)	p= 0.273
Previous hypertension	7 (0.8)	3 (0.3)	p < 0.001

Variables	Control group n= 160	PE group n= 160	p- value
Parity			
Nulliparous	421 (52.6)	495 (61.8)	
Para 1	328 (41)	285 (35.6)	
Para ≥ 2	51 (6.3)	20 (2.5)	p= 0.021
GA at delivery, weeks	1.4 ± 39.2	3.1 ± 37.2	p < 0.001
Delivery			
Vaginal	520 (65)	230 (28.7)	
Elective cersarean section	160 (20)	180 (22.5)	
Urgent cersarean section	120 (15)	390 (48.7)	p < 0.001
Intrauterine death	9 (1.1)	36 (4.5)	

Table 2. **The comparison of the frequency of femoral length (based on the percentile of gestational age)**

		PE group		control group	
		Frequency	Percent	Frequency	Percent
Femur length (percentile for gestational age)	>95%	-	-	15	9.4
	95%	-	-	17	10.6
	90%	-	-	52	32.5
	90%-75%	1	0.6	11	6.9
	75%	4	2.5	35	21.8
	75%-50%	6	3.8	14	8.7
	50%	7	4.4	9	5.6
	25%-50%	5	3.1	3	1.9
	25%	12	7.5	3	1.9
	25%-10%	16	10	1	0.6
	10%	22	13.8	-	-
	5%-10%	3	1.9	-	-
	5%	32	20	-	-
	<2.5%	52	32.5	-	-
	Total	160	100	160	100

χ^2 = 260.51, df=13, p<0.001

Table 3. **A comparison of the distribution of the two groups under study in terms of femoral length (percentile less and higher than 50%).**

		PE group		control group	
		Frequency	Percent	Frequency	Percent
Femur length (percentile for gestational age)	≥50	18	11.2	157	98.1
	≤50	142	88.8	3	1.9
	Total	160	100	160	100

χ^2 = 243.65, df=1, p<0.001

Table 4. Evaluation of the diagnostic value of 50th percentile fetal femoral length for preeclampsia

Sensitivity	98.13%	94.62 % - 99.61 %
Specificity	88.75%	82.80 % - 93.20 %
AUC	0.93	0.90 – 0.96
Positive Likelihood Ratio	8.72	5.64 – 13.49
Negative Likelihood Ratio	0.02	0.01 – 0.07
Disease prevalence	8 %	
Positive Predictive Value	43.13 %	32.91 % - 53.97%
Negative Predictive Value	99.82 %	99.44 % - 99.94 %
Accuracy	89.50 %	85.61 % - 92.64 %

Table 5. A comparison of the distribution of the two groups under study in terms of femoral length (percentile less and higher than 75%).

		PE group		control group	
		Frequency	Percent	Frequency	Percent
femur length (percentile for gestational age)	≥ 75	5	3.1	131	81.9
	< 75	155	96.9	29	18.1
	Total	160	100	160	100

χ^2 = 203.38, df=1, p<0.001

Table 6. Evaluation of the diagnostic value of 75th percentile fetal femoral length for preeclampsia

Sensitivity	96.88 %	92.86 % - 98.98 %
Specificity	81.88 %	75.02 % - 87.51 %
AUC	0.89	0.86 - 0.93
Positive Likelihood Ratio	5.35	3.84 - 7.44
Negative Likelihood Ratio	0.04	0.02 - 0.09
Disease prevalence	8 %	
Positive Predictive Value	31.73 %	26.04 % - 39.28 %
Negative Predictive Value	99.67 %	99.22 % - 99.86 %
Accuracy	83.08 %	78.51 % - 87.02 %

Table 7. The correlation matrix between quantitatively measured variables

		femur length	Age	Maternal weight	Maternal height	BMI	Previous pregnancy	Abortion	Birth weight	Birth height
Femur length	Pearson Correlation	1	-0.033	0.053	0.009	0.044	-0.105	0.043	0.296	0.321
	Sig. (2-tailed)		0.577	0.356	0.878	0.447	0.068	0.457	< 0.001	< 0.001
	N	315	294	308	307	307	302	302	313	314

Age	Pearson Correlation	-0.033	1	0.253	0.054	0.014	0.557	0.249	-0.094	-0.112
	Sig. (2-tailed)	0.577		< 0.001	0.354	0.815	< 0.001	< 0.001	0.105	0.054
	N	294	298	292	291	291	286	286	296	296
Maternal weight	Pearson Correlation	0.053	0.253	1	-0.386	0.679	0.161	0.050	0.010	-0.010
	Sig. (2-tailed)	0.356	< 0.001		< 0.001	< 0.001	0.005	0.384	0.867	0.854
	N	308	292	313	312	312	301	301	311	311
Maternal height	Pearson Correlation	0.009	0.054	-0.386	1	-0.860	0.013	-0.007	0.012	0.022
	Sig. (2-tailed)	0.878	0.354	< 0.001		< 0.001	0.821	0.905	0.829	0.694
	N	307	291	312	312	312	300	300	310	310
BMI	Pearson Correlation	0.044	0.014	0.679	-0.860	1	-0.011	-0.029	0.013	-0.005
	Sig. (2-tailed)	0.447	0.815	< 0.001	< 0.001		0.844	0.617	0.814	0.925
	N	307	291	312	312	312	300	300	310	310
Previous pregnancy	Pearson Correlation	-0.105	0.557	0.161	0.013	-0.011	1	0.621	-0.010	-0.068
	Sig. (2-tailed)	0.068	< 0.001	0.005	0.821	0.844		< 0.001	0.855	0.234
	N	302	286	301	300	300	307	307	305	305
Abortion	Pearson Correlation	0.043	0.249	0.050	-0.007	-0.029	0.621	1	-0.094	-0.102
	Sig. (2-tailed)	0.457	< 0.001	0.384	0.905	0.617	< 0.001		0.101	0.075
	N	302	286	301	300	300	307	307	305	305
Birth weight	Pearson Correlation	0.296	-0.094	0.010	0.012	0.013	-0.010	-0.094	1	0.807
	Sig. (2-tailed)	< 0.001	0.105	0.867	0.829	0.814	0.855	0.101		< 0.001
	N	313	296	311	310	310	305	305	318	316
Birth height	Pearson Correlation	0.321	-0.112	-0.010	0.022	-0.005	-0.068	-0.102	0.807	1
	Sig. (2-tailed)	< 0.001	0.054	0.854	0.694	0.925	0.234	0.075	< 0.001	
	N	314	296	311	310	310	305	305	316	318

Table 8. Comparison of quantitative variables measured of the control group and PE group

		N	Mean	standard deviation	p-value
Age	control group	154	28.94	7.28	t=-2.11, df=296, p=.036
	PE group	144	30.57	5.98	
Mother's weight	control group	154	78.36	11.51	t=-3.20, df=311, p=.002
	PE group	159	82.91	13.49	

		N	Mean	standard deviation	p-value
Mother's height	control group	154	162.99	8.72	t=-.53, df=310, p=.597
	PE group	158	163.48	7.76	
Gravidity	control group	153	2.18	1.56	t=-1.59, df=305, p=.113
	PE group	154	2.49	1.84	
Abortion	control group	153	0.38	0.71	t=-2.70, df=305, p=.007
	PE group	154	0.66	1.06	
Birth weight	control group	159	3121.76	430.52	t=11.82, df=316, p<.001
	PE group	159	2136.86	958.71	
Maternal height	control group	160	49.18	2.15	t=10.39, df=316, p<.001
	PE group	158	41.63	8.93	
Femur length	control group	160	57.56	14.29	t=2.82, df=313, p=.005
	PE group	155	53.46	11.27	
BMI	control group	154	31.09	25.18	t=-0.41, df=310, p=.683
	PE group	158	32.13	19.55	

Discussion

All the body's systems may be impacted by the pregnancy-specific illness known as preeclampsia. Proteinuria and elevated blood pressure are its symptoms after the 20th week of pregnancy **(12-14)**. In the world and Iran, preeclampsia is the second most typical cause of maternal mortalityBased on a wide range of studies, the prevalence of preeclampsia in Iran is estimated to be between 1 and 8%. **(15-17)**. In the present study, the mean age in the control group and the case group was 28.94 ± 7.28 and 30.57± 5.98 years, respectively, suggesting a significant difference between the two groups (p = 0.036). According to Sheen et al, with a changing demographic profile of preeclampsia, older women accounted for an increasing proportion of preeclampsia and related adverse outcomes **(18)**. In the study by Kashanian et al., the mean age of women with preeclampsia (27.74± 6.6) was not significantly different from that of non-preeclamptic women (27.36± 6.5) **(19)**. In the present study, the mean gravidity was 2.18± 1.56 in the control group and 2.49± 1.84 in the case group, however, no significant difference was observed between the two groups (P=0.113). This finding disagrees with those of Kashanian et al. **(19)** The control and case groups' mean abortion were 0.38 ± 0.71 and 0.66± 1.06, respectively, showing that there was a significant difference between the two groups (P = 0.007), a finding agreeing with the results of Kashanian et al. **(19)**. Furthermore, a significant difference was observed between the mean maternal weight in the control and case groups (78.36± 11.51 and 82.91± 13.49, respectively) (P = 0.002).The mean height of mothers in the control group (162.99 ± 8.72 cm) was lower than that of the case group (163.48± 7.76), however, it did not lead to any significant differences between the two groups (P = 0.597).The mean body mass index in the control group (31.09 ± 25.18 kg / m2) was lower than the case group (32.13± 19.55), meanwhile, no significant difference was marked between the two groups (P = 0.683).In the study by Kashanian et al., the body mass index in preeclampsia patients was higher than that of healthy women, yet no statistically significant difference was reported to be in line with the present study **(19)**. Furthermore, in the present study, the two groups had significantly different mean birth weights and birth heights (P <0.001). The results of the present study revealed that the mean fetal femoral length in the control group (57.56±14.29) was higher than that in the group with preeclampsia (53.46± 11.27) and that this difference was statistically significant (P=0.005). Given that this index is affected by different factors such as age at birth etc., a more accurate comparison requires standardization which is why percentiles were used relative to women's age. Thus, the distribution of this index according to the two study groups had a statistically significant difference and clearly, the control group had the highest frequency of percentiles (52.5% above 90th percentile) while the frequency in the case group (preeclampsia group) was zero. Most cases in the preeclampsia group belonged to the lower percentiles (53.4% of the preeclampsia group being in the lower 10th percentile while there was none in the control group), which was also statistically significant (P <0.001). Femoral shortening is one of the factors limiting embryonic growth in the third and second trimesters. Some studies have displayed an association between femoral shortening and intrauterine growth restriction (IUGR) (12, 20). Ventura's study indicated that femoral shortening was not significantly associated with maternal age, gestational age, maternal weight, parity, and history of preeclampsia (11). Femoral shortness was also found to have a significant relationship with birth weight, age at birth, but it had no statistically significant relationship with neonatal sex and preeclampsia. Mailath-Pokorny et al. revealed that femoral length below the fifth percentile was not significantly associated with maternal age, parity, maternal weight, maternal height, maternal body mass index, preeclampsia, and gender, yet it was found to be significantly associated with gravidity, age at birth, and birth weight (21). The femur length showed a significant correlation with birth weight and height in the current study, and a statistically significant difference was found between the two preeclampsia groups and the control group. To account for the impact of various factors on femur length and to make a more informed assessment using percentiles, a multivariate analysis was conducted. The results indicated that, when controlling for other variables and using the 50th percentile as the cut-off point, the mother's age, number of previous pregnancies, and the presence or absence of pre-eclampsia were significantly related to the femur length percentile.

In this study, we tried to evaluate the diagnostic utility of using the femur's percentiles as a measure of preeclampsia. In order to find the 75th percentile cut-off point, different cut-off points were investigated. Two incision points were chosen, and their characteristics included 88.96 sensitivity, 88.81 features, 73.31 positive predictive value, 67.99 negative predictive value, 35.5 positive likelihood ratio, and 0.40 negative likelihood ratio. The positive likelihood ratio was 8.72, and the negative likelihood ratio was 0.02 when the cut-off points of the 50th percentile was taken into account. Similarly, the sensitivity was 98.13, the feature was 88.75, the positive predictive value was 441.13 and the negative predictive value was 99.82. These results suggest that the cut-off point of the 50th percentile would be more appropriate. It would be better to say fifty in a study by Morales-Rosell, the use of the 10th percentile as a cut-off points for IUGR detection had a sensitivity of 66% and a specificity of 67% (22). Given the prominence and status of preeclampsia in the field of women's health, it appears that fetal femoral length is connected to preeclampsia and that growth restriction, particularly femoral length relative to gestational age, can be utilized to quickly predict preeclampsia through imaging.

Conclusion

Our findings imply that there is a significant relationship between PE and Short FDL between 32 and 37 weeks of gestation. Isolated short femur length is associated with placental-related problems including SGA and PE and may be the earliest detectable biometric indicator of placental insufficiency. Furthermore, as short FDL may be an early indicator of placental malfunction, more prenatal monitoring of fetal growth is necessary, including regular blood pressure checks and closer sonographic monitoring. To create accurate counseling and care for these patients, more research is required.

Author contributions

AJ: Project development, data analysis, manuscript writing and editing. JR: Project development, data analysis, manuscript writing and editing. FB: Revision and editing of the trial, data analysis, manuscript editing. SS: Project development, laboratory evaluation and acquisition of data, manuscript editing. All authors were involved in critical revision of the manuscript and approved the final version of the manuscript to be submitted.

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Data availability the datasets used and/or analyzed in the present study are available from the corresponding author upon reasonable request. Code availability not applicable.

Declarations

Conflict of interest the authors have no financial or non-financial interests to disclose. Ethical approval this study with the code of ethics IR.UMSU.REC.1400.088 has been approved by the ethics committee of the University of Medical Sciences

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None.

Conflict of Interest

The authors declare no conflict of interest.

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