UDC: 618.3-06:616.12-008.331.1]- 037:577.175.8.088
DOI: 10.24061/2413-4260. XIV.1.51.2024.13

ROLE OF MATERNAL SERUM FIBROBLAST GROWTH FACTOR 21 LEVEL IN PREDICTION OF PREECLAMPSIA

A. Karim El-din, M. Hassan, G. Sayed, A. Helmy

Ain Shams University (Cairo, Egypt)

Summary

Pregnancy complications resulting from hypertensive disorders are a serious problem that impact 2-10 % of all pregnancies globally. Preeclampsia is defined as new onset hypertension and proteinuria after 20 weeks of gestation which may be associated with other maternal organ dysfunction, such as liver or renal insufficiency, hematological or neurological complications, uteroplacental dysfunction and fetal growth restriction.

Aim of the Work: *Primary outcome is to determine the correlation between fibroblast growth factor 21 level and preeclampsia & significance of serum fibroblast growth factor 21 levels as a predictive tool for preeclampsia. Secondary outcome is to establish the relationship between maternal serum fibroblast growth factor 21 level and Maternal complictions:*

- *Eclampsia (tonic clonic fits after 20 weeks with elevated blood pressure and proteinuria)*
- *HELLP syndrome (hemolysis, elevated liver enzymes and low platelet occur as a complication of severe preeclampsia)*
- *placental abruption (bleeding after 20 weeks gestation due to premature separation of a normally situated placenta)*

Patients and Methods: *This was a Nested case-control study that was conducted on 90 primigravidas at Ain Shams University maternity hospital from April 2021 to April 2022. Ethical approval was obtained from the ethical committee at Ain-Shams university maternity hospital. Data was recruited from patient attending obstetric clinic at Ain Shams University Maternity Hospital. Blood samples were collected after 20 weeks to 28 weeks gestation. Patients was followed up until delivery and grouped according to development of preeclampsia.*

Random samples from 45 patients (group who develop PE) and 45 random samples from control group were assessed for fibroblast growth factor 21. Serum fibroblast growth factor 21 levels were measured by a commercially available enzyme-linked immunosorbent assay kit.

Results: *our study showed that there was a significant difference in FGF21 levels between the groups, patients with preeclampsia having higher levels than controls, 15.9 % of patients with preeclampsia experienced maternal complications compared to none in the control group. Meanwhile, 18.2 % of patients with preeclampsia experienced fetal complications compared to 0 % in the control group.*

Conclusion: *Serum FGF-21 levels are significantly higher in preeclamptic pregnant women compared to healthy normotensive pregnant women. So, it can be used as a predictor for preclampsia and maternal complications*

Funding information: *The article was written and published without any financial support.*

Conflict of interest disclosure: *The authors of the article have noconflict of interest related to the publication of the article*

Key words: *Serum Fibroblast 21; Preeclampsia; Primigravida.*

Introduction

Up to 10 % of pregnancies in developing countries result in complications due to preeclampsia (PE), where emergency care is frequently insufficient or nonexistent. [1]

The measurement of maternal blood pressure and proteinuria is essential for the diagnosis of PE; however, these parameters have poor predictive power for unfavorable outcomes for both the mother and the fetus. Thus, there is a pressing need for broadly applicable, reasonably priced tests that can reliably identify women who are at risk and identify which fetus may have complications. By giving these patients and their offspring the best prenatal care possible, we can prevent morbidity and improve the outcome of the newborn. [2]

Preeclampsia shares many risk factors with cardiovascular, chronic kidney disease and metabolic diseases. The relationship between preeclampsia and the level of fibroblast growth factor 21 has been rarely studied. [3]

Fibroblast growth factor family are responsible for cell growth and differentiation, wound repair, embyrogensis and angiogenesis. As a member of this family, fibroblast growth factor 21 is a metabolic regulator with beneficial effects on lipid and glucose metabolism, it also plays a role in many disease such as cardiovascular and chronic kidney disease. [4]

The study was to explore the possible role of fibroblast growth factor 21 in preeclampsia and provide new theoretical basis for the prevention and treatment of preeclampsia. [5]

Patient and methods

After ethical committee approval and informed consent from patients**,** this was a nested case-control study that was conducted on 500 healthy pregnant women, recruited from the Obstetrics outpatient clinic at Ain Shams University Maternity hospital from April 2021 to April 2022. Participants included in this study were 18-40 years old primigravida pregnant ladies in single viable fetus 20-28 weeks gestional age, with BMI (20-30) kg/m2. Pregnant ladies aged less than 18 or more than 40 years old, or with previously diagnosed maternal disease e.g DM, chronic hypertension, thrombophilias were excluded from the study. Any participant with fetal comorbidity e.g CFMF were excluded too.

All women included are subjected to detailed medical history including past medical history and the date of the first day of LMP to calculate the gestational age. They

ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)

also underwent physical examination including BMI, blood pressure measurement and abdominal examination to assess the fundal level and the viability of the fetus. Obstetric ultrasound was done to all of the women included in the study to assess fetal biometry and exclude any fetal abnormalities in addition to CBC and Serum fibroblast growth factor 21 analysis for samples of target patients.

Blood samples were withdrawn from healthy pregnant primigravidas 20-28 weeks gestational age. Samples were centrifuged and then the supernatant were freezed at –80 °C. Patients were followed up until delivery and grouped according to development of preeclampsia. It targeted reaching a sample of (45) initially healthy primigravidas who subsequently develop preeclampsia and (45) healthy primigravidas who continued their pregnancies without any maternal or fetal complication. Criteria for the diagnosis of preeclampsia are illustrated in Fig1 and 2. Serum fibroblast growth factor 21 levels were measured by a commercially available enzyme-linked immunosorbent assay kit. The detection range was 31 ng/L –200 ng/L. The main outcome of the study is to determine the correlation between maternal serum fibroblast growth factor 21 level and preeclampsia & significance of serum fibroblast growth factor 21 levels as a predictive tool for preeclampsia.Secondary outcome is to establish the relationship between maternal serum fibroblast growth factor 21 level and maternal and fetal morbidities e.g. IUGR, oligohydraminos, abruptio placentae.

Criteria for the diagnosis of preeclampsia

Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two occasions at least four hours apart after 20 weeks of gestation in a previously normotensive patient
If systolic blood pressure is ≥160 mmHg or diastolic blood pressure is ≥110 mmHg, confirmation within minutes is sufficient
and
Proteinuria ≥0.3 grams in a 24-hour urine specimen or protein (mg/dL)/creatinine (mg/dL) ratio ≥0.3
Dipstick ≥1+ if a quantitative measurement is unavailable
In patients with new-onset hypertension without proteinuria, the new onset of any of the following is diagnostic of preeclampsia:
Platelet count <100,000/microliter
Serum creatinine >1.1 mg/dL or doubling of serum creatinine in the absence of other renal disease
Liver transaminases at least twice the normal concentrations
Pulmonary edema
Cerebral or visual symptoms

Adapted from: Hypertension in pregnancy: Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013; 122:1122.

Figure 1: Diagnostic criteria of Preclampsia [6]

The presence of one or more of the following indicates a diagnosis of "preeclampsia with severe features"

Symptoms of central nervous system dysfunction:
New onset cerebral or visual disturbance, such as: ▪ Photopsia, scotomata, cortical blindness, retinal vasospasm ▪ Severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy ▪ Altered mental status
Hepatic abnormality:
Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥ twice normal, or both
Severe blood pressure elevation:
Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg on two occasions at least four hours apart while the patient is on bedrest (unless the patient is on antihypertensive therapy)
Thrombocytopenia:
<100,000 platelets/microL
Renal abnormality:
Progressive renal insufficiency (serum creatinine >1.1 mg/dL or doubling of serum creatinine concentration in the absence of other renal disease)
Pulmonary edema

In contrast to older criteria, the 2013 criteria do not include proteinuria >5 grams/24 hours and fetal growth restriction as features of severe disease.

Adapted from: Hypertension in pregnancy: Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013; 122:1122.

Figure 2: Criteria of severity of Preclampsia [6]

Results

Table (1) shows that there was no significant difference in age and BMI between the groups, but there was a significant difference in GA, with patients with preeclampsia having a lower GA than controls.

Table 2 shows that15.9 % of patients with preeclampsia experienced maternal complications compared to 7 % in the control group. Meanwhile, 18.2 % of patients with preeclampsia experienced fetal complications compared to 8 % in the control group (table 2).

Table 1

Comparison between control and cases regarding age, GA and BMI

	Control		cases		t test		
	Mean	SD	Mean	SD	t	p value	sig.
Age	24.55	2.98	24.18	5.39	0.392	0.697	NS
GA	38.16	2.21	34.97	2.82	5.902	<0.001	S
BMI	26.53	2.18	26.28	2.31	0.528	0.599	NS

Table 2

Comparison between groups regarding secondary outcome

Mean		Cases	
		SD	
Maternal comp	No	37	84.1 %
	Yes	7	15.9 %
Fetal comp	No	36	81.8 %
	Yes	8	18.2 %

Table 3

Median levels of fibroblast growth factor 21 (FGF21) between patients with preeclampsia and controls using Mann Whitney's test.

	Controls		Cases		Mann Whitney's test		
	Median (IQR)	Range	Median (IQR)	Range	z	p value	sig
FGF21	131.7 (108.9-174.9)	59.78-216.5	585.5 (446.95-791.15)	229.1-1447	-8.08	<0.001	S

Table (3) shows the results of a Mann Whitney's test comparing the median levels of fibroblast growth factor 21 (FGF21) between patients with preeclampsia and controls. The median and interquartile range (IQR) are reported for both groups. The Mann Whitney's test was used to assess the statistical significance of the differences between the groups. The results indicate that there was a significant difference in FGF21 levels between the groups, with patients with preeclampsia having higher levels than controls.

Table 4

Median levels of fibroblast growth factor 21 (FGF21) between patients with and patient without maternal complication using Mann Whitney's test.

	No maternal complication		Maternal complication		Mann Whitney's test		
	Median (IQR)	Range	Median (IQR)	Range	z	p value	sig
FGF21	537.2 (350.9-674.6)	229.1-1353	1062 (1019-1264)	996.8-1447	-3.96	<0.001	S

Table (4) shows the results of a Mann Whitney's test comparing the median levels of fibroblast growth factor 21 (FGF21) between patients with and patient without maternal complication among cases. The median and interquartile range (IQR) are reported for both groups. The Mann Whitney's test was used to assess the statistical significance of the differences between the groups. The results indicate that there was a significant difference in FGF21 levels between the groups, with patients with maternal complication having higher levels than those without.

Table 5

Median levels of fibroblast growth factor 21 (FGF21) between patients with and patient without fetal complication using Mann Whitney's test.

	No fetal complication		Fetal complication		Mann Whitney's test		
	Median (IQR)	Range	Median (IQR)	Range	z	p value	sig
FGF21	574.4 (398.55-855.3)	229.1-1353	632.55 (542.85-682)	294.3-1447	-0.578	0.563	NS

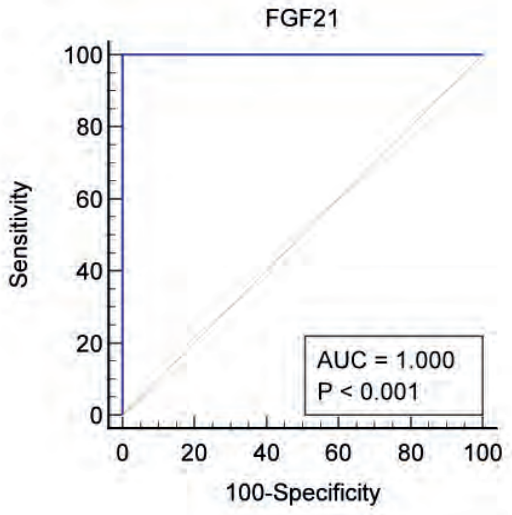
Table (5) shows the results of a Mann Whitney's test comparing the median levels of fibroblast growth factor 21 (FGF21) between patients with and patient without fetal complication among cases. The median and interquartile range (IQR) are reported for both groups. The Mann Whitney's test was used to assess the statistical significance of the differences between the groups. The results indicate that there was no significant difference in FGF21 levels between the groups.

Table 6

Correlation between fibroblast growth factor 21 (FGF21) levels with age, gestational age (GA), body mass index (BMI), and cell-free fetal DNA (CFFDNA) in patients with preeclampsia and controls

	Control		Cases	
	FGF21		FGF21	
	rs	p value	rs	p value
CFFDNA	0.011	0.956	0.994	<0.001
Age	0.12	0.438	-0.074	0.632
GA	-0.093	0.548	-0.42	0.005
BMI	0.306	0.043	-0.06	0.7

Table (6) shows the Spearman correlation coefficients and p-values for the association between fibroblast growth factor 21 (FGF21) levels with age, gestational age (GA), body mass index (BMI), and cell-free fetal DNA (CFFDNA) in patients with preeclampsia and controls. The results show that there was a significant positive correlation between FGF21 levels and CFFDNA in patients with preeclampsia (rs = 0.994, p < 0.001) but not in controls. There was also a significant negative correlation between GA and FGF21 levels in patients with preeclampsia (rs = –0.42, p = 0.005) but not in controls (rs = –0.164, p = 0.385).



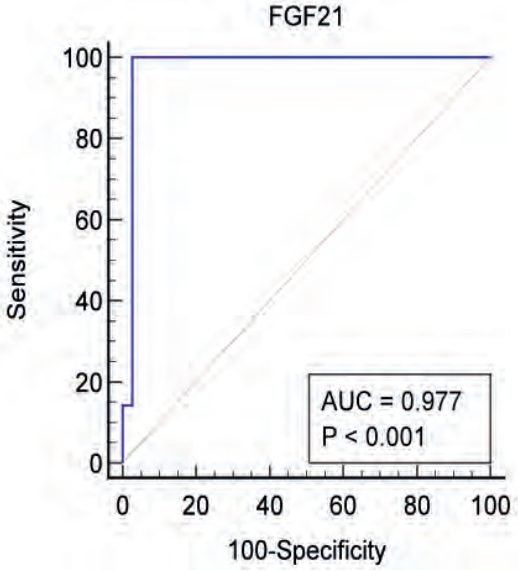
	AUC	95 % CI	p value	sig.	cutoff point	Sensitivity	Specificity	+PV	-PV
FGF21	1	0.959 to 1.000	<0.0001	S	>216.5	100	100	100	100

Figure 3: ROC Curve of FGF21 to differentiate cases from controls

Figure (3) shows the results of a receiver operating characteristic (ROC) curve analysis for cell-free fetal DNA (FGF21) to differentiate between patients with preeclampsia and controls. The area under the curve (AUC) is a measure of the accuracy of the test, the results indicate that FGF21 has an AUC of 1.0, indicating perfect discrimination between patients with preeclampsia and controls.

Figure (4) also shows the optimal cutoff point for FGF21, which is >97, sensitivity of 100 %, meaning that it correctly identifies all patients with preeclampsia. It also has a specificity of 100 %, meaning that it correctly identifies all controls without preeclampsia. The +PV and -PV are also 100 %, meaning that there are no false positives or false negatives in the test.

The table shows the results of a receiver operating characteristic (ROC) curve analysis for fibroblast growth factor 21 (FGF21) to detect maternal complications among patients with preeclampsia. The area under the curve (AUC) is a measure of the accuracy of the test, the results indicate that FGF21 has an AUC of 0.977, indicating excellent discrimination between patients with and without maternal complications. It also shows the optimal cutoff point for FGF21, which is >918.5, with a corresponding sensitivity of 100 %, meaning that it correctly identifies all patients with maternal complications. It also has a specificity of 97.3 %, meaning that it correctly identifies most of the patients without maternal complications. The +PV and -PV are 87.5 % and 100 %, respectively, meaning that there are few false positives and no false negatives in the test.



	AUC	95 % CI	p value	sig.	cutoff point	Sensitivity	Specificity	+PV	-PV
FGF21	0.977	0.879 to 0.999	<0.0001	S	>918.5	100	97.3	87.5	100

Figure 4: ROC curve of FGF21 to detect maternal complications among cases.

Discussion

Preeclampsia (PE) complicates up to 10 % of pregnancies in developing nations, despite the fact that emergency care is often inadequate or nonexistent in these areas. [7]

While measuring maternal blood pressure and proteinuria is necessary for the diagnosis of PE, these indicators have a relatively low sensitivity and specificity in terms of predicting adverse outcomes for the mother and the fetus. [8]

Thus, there is a pressing need for tests that can reliably identify women who are at risk and predict which fetus may have complications. These tests also need to be widely applicable and reasonably priced. By guaranteeing that these patients and their offspring receive the best prenatal care available, this will enable the prevention of morbidity and the improvement of neonatal outcome. [8]

Many of the risk factors for preeclampsia are also associated with cardiovascular disease, chronic renal disease, and metabolic disorders. Preeclampsia and the level of fibroblast growth factor 21 have only seldom been examined in conjunction with one another as a link. [7]

Our study was done among Egyptian primigravidas pregnant in single fetus 20-28 weeks gestational age attending to maternity hospital – Ain shams university, Measuring the maternal serum fibroblast growth factor 21 and establishing the relationship between maternal serum fibroblast growth factor 21 and preeclampsia.

We concluded that there was no significant difference in age and BMI between the groups, but there was a significant difference in GA, with patients with preeclampsia having a lower GA than controls (Table 1).

Our study's findings concurred with those of Jiang et al. [7], who investigated the relationship between PE and the serum level of fibroblast growth factor (FGF) 21. His study included 80 cases in total, including 49 cases in the PE group and 31 cases in the control group (normal pregnancy). PE was split into two groups: late-onset PE (LOPE) and early-onset PE (EOPE). Prior to delivery, biochemical parameters and the serum level of FGF21 were measured. Regarding mother age, the multipara ratio, and pre-pregnancy BMI, there were no statistically significant differences between the groups ($P > 0.05$).

Our study showed that there was a significant difference in FGF21 levels between the groups, patients with preeclampsia having higher levels than controls. The median level of FGF21 in patients with preeclampsia was 585.5 pg/ml, while the median level of FGF21 in the control group was 131.7 pg/ml (Table 3).

The findings of Stepan et al. [9] were consistent with our study, which demonstrated that the serum FGF21 level in PE patients was significantly higher than that of a normal pregnancy (maternal FGF-21 serum concentrations in PE patients were nearly three times higher (309.6 ng/l) than in healthy age-matched pregnant women (105.2 ng/l).

Similarly, Buell et al. [8] sought to examine the serum FGF-21 profile during each trimester of pregnancy in healthy and mildly preeclamptic pregnant women. In a nested case-control study within a longitudinal cohort study comprising healthy (n = 54) and mildly preeclamptic (20) pregnant women, women three months postpartum (n = 20), and eumenorrheic women during the menstrual cycle (n = 20), serum FGF-21 levels were ascertained by ELISA. They demonstrated that during the three trimesters of pregnancy, maternal levels of FGF-21 were significantly higher in preeclamptic pregnant women than in healthy normotensive pregnant women. Moreover, FGF-21 serum levels peak in the third trimester of pregnancy after being considerably lower in the first and second trimesters of pregnancy in both healthy ($p < 0.0000$) and preeclamptic pregnant women ($p < 0.0036$).

Jiang et al. [7] likewise demonstrated that serum FGF21 level of PE group (462.53 ± 188.00 ng/L), EOPE group (510.76 ± 172.26 ng/L) and PE group with complication (517.26 ± 195.88 ng/L) was respectively higher than that of control group (366.85 ± 191.49 ng/L). FGF21 level of EOPE group was significantly higher than that of LOPE group (403.33 ± 193.36 ng/L). When compared with PE

ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)

group who had no complication (376.11 ± 139.84 ng/L), PE group with complication had higher FGF21 level.

Also, Abd Elmagid et al. [10] examined the serum levels of fibroblast growth factor-21 in patients with mild and severe preeclampsia; the severe group showed a significant increase, nearly two times higher than the control group and 1.5 times higher than the mild group.

In contrary to our research, Nitert et al. [11] found no significant difference in serum FGF21 level between PE patients and normal pregnant women(Circulating FGF21 was examined in maternal and cord blood samples of 10 mother-baby dyads in each group. FGF21 levels in maternal blood were comparable in women with and without PE (PE 0.44(0.3-1.00) ng/ml vs. control 0.38(0.21-0.66), P=0.38). In most cord blood samples, FGF21 was below the detection threshold (0.03ng/ml), but in two cord blood samples from normotensive pregnancies and four cord blood samples from PE pregnancies, it was slightly above the detection threshold. This contradictory results could be explained by variations in characteristics of the study participants such as BMI, insulin resistance, gestation of blood sampling and parity.

Our study showed that 15.9 % of patients with preeclampsia experienced maternal complications compared to none in the control group. Meanwhile, 18.2 % of patients with preeclampsia experienced fetal complications compared to 0 % in the control group (Table 2).

We used the results of a receiver operating characteristic (ROC) curve analysis for FGF21 to differentiate between patients with preeclampsia and controls. The area under the curve (AUC) is a measure of the accuracy of the test, the results indicate that FGF21 has an AUC of 1.0, indicating perfect discrimination between patients with preeclampsia and controls. The table also shows the optimal cutoff point for FGF21, which is >97, sensitivity of 100 %, meaning that it correctly identifies all patients with preeclampsia. It also has a specificity of 100 %, meaning that it correctly identifies all controls without preeclampsia. The +PV and -PV are also 100 %, meaning that there are no false positives or false negatives in the test (Fig 3).

We also found that there was a significant difference in FGF21 levels between the groups, patients with maternal complication having higher levels of FGF21 levels than those without(median level of FGF21 537.2pg/ml for patient without maternal complication, but 1062pg/ml for patient with maternal complication (Table 4) but there was no significant difference in FGF21 levels between patients with and patient without fetal complication among cases.(median level of FGF21 574.4 pg/ml for patient without fetal complication, 632.55 pg/ml for patient with fetal complication (Table 5).

The results of our study were in accordance with Jiang et al. [7] 49 PE patients, 30 cases had maternal complications, 19 cases had no complications. Considering that early-onset preeclampsia is more strongly associated with placental factors and may have a more severe disease course than late-onset preeclampsia, the proportion of small for gestational age (SGA) in patients with EOPE was significantly higher than that in LOPE (9/27 vs 1/22, $P < 0.05$).

Our study showed that the results of a receiver operating characteristic (ROC) curve analysis for fibroblast growth factor 21 (FGF21) to detect maternal complications among patients with preeclampsia. The area under the curve (AUC) is a measure of the accuracy of the test, the results indicate that FGF21 has an AUC of 0.977, indicating excellent discrimination between patients with and without maternal complications. The table also shows the optimal cutoff point for FGF21, which is >918.5, with a corresponding sensitivity of 100 %, meaning that it correctly identifies all patients with maternal complications. It also has a specificity of 97.3 %, meaning that it correctly identifies most of the patients without maternal complications. The +PV and -PV are 87.5 % and 100 %, respectively, meaning that there are few false positives and no false negatives in the test (Fig 4).

The results of our study were in accordance with Buell et al. [8] showed that the area under the receiver operating characteristic curve (AUC ROC) for predicting the development of the adverse maternal outcome of mild preeclampsia (dependent variable) from serum levels of FGF-21 levels (independent variable) was determined in the 1st (0.681 (95 % confidence interval 0.537-0.826)), 2nd (0.644 (95 % confidence interval 0.501-0.788)) and 3rd (0.680 (95 % confidence interval 0.523-0.836)) trimesters of pregnancy.

In correlation with our study, there were other studies done among primigravidas pregnant in single fetus 20-28 weeks gestional age measuring cell free fetal DNA and establishing its relation to preeclampsia [10-20]. The Spearman correlation coefficients and p-values for the association between fibroblast growth factor 21 (FGF21) levels with age, gestational age (GA), body mass index (BMI), and cell-free fetal DNA (CFFDNA) in patients with preeclampsia and controls was shown in Table 6. The results showed that there was a significant positive correlation between FGF21 levels and CFFDNA in patients with preeclampsia ($rs = 0.994$, $p < 0.001$) but not in controls. There was also a significant negative correlation between GA and FGF21 levels in patients with preeclampsia ($rs = –0.42$, $p = 0.005$) but not in controls ($rs = –0.164$, $p = 0.385$).

The cut-off points in the levels of FGF-21 obtained through the different ROC curves in each trimester of pregnancy could contribute to the risk prediction of preeclampsia and further studies are needed to confirm a relationship between FGF-1 and Log (sFlt-1)/Log (PlGF) ratio and the outcome of preeclampsia [21-26].

Conclusion

Finally, our results showed that serum FGF-21 levels are significantly higher in preeclamptic pregnant women compared to healthy normotensive pregnant women. So, it can be used as a predictor for preclampsia and maternal complications

References:

1. Timofeeva AV, Gusar VA, Kan NE, Prozorovskaya KN, Karapetyan AO, Bayev OR, Chagovets VV, Kliver SF, Iakovishina DY, Frankevich VE, Sukhikh GT. Identification of potential early biomarkers of preeclampsia. Placenta. 2018; 61: 61-71. doi: 10.1016/j.placenta.2017.11.011

2. Foo L, Tay J, Lees CC, McEniery CM, Wilkinson IB. Hypertension in pregnancy: natural history and treatment options. Current hypertension reports. 2015; 17(5): 36. doi: 10.1007/s11906-015-0545-1

3. Nair A, Savitha C. Estimation of serum uric acid as an indicator of severity of preeclampsia and perinatal outcome. J Obstet Gynecol India. 2017; 67: 1-10. doi: 10.1007/s13224-016-0933-8

4. Gathiram P, Moodley J. Pre-eclampsia: its pathogensis and pathophysiology. Cardiovasc J Afr. 2016; 27: 71-78. doi: 10.5830/CVJA-2016-009

5. Witcher PM. Preeclampsia: Acute complications and management priorities. AACN Adv Crit Care. 2018; 29: 316-326. doi: 10.4037/aacnacc2018710

6. ACOG. Hypertension in pregnancy: Report of the American College of Obstetricians and Gynecologists' Task force on Hypertension in Pregnancy. Obstet Gynecol. 2013; 122:1122. doi: 10.1097/01.AOG.0000437382.03963.88

7. Jiang, L, Zhou, Y, & Huang Q. Serum fibroblast growth factor 21 level is increased in pre-eclampsia patients: Association with blood pressure and lipid profile. Journal of Obstetrics and Gynaecology Research. 2021;47(1), 375-381. doi: 10.1111/jog.14534

8. Buell-Acosta JD, Garces MF, Parada-Baños AJ, Angel-Muller E, Paez MC, Eslava-Schmalbach J, Escobar-Cordoba F, Caminos-Cepeda SA, Lacunza E, Castaño JP, Nogueiras R, Dieguez C, Ruiz-Parra AI, Caminos JE. Maternal Fibroblast Growth Factor 21 Levels Decrease during Early Pregnancy in Normotensive Pregnant Women but Are Higher in Preeclamptic Women-A Longitudinal Study. Cells. 2022; 11(14): 2251. doi: 10.3390/cells11142251

9. Stepan H, Kley K, Hindricks J, Kralisch S, Jank A, Schaarschmidt W, Schrey S, Ebert T, Lössner U, Kratzsch J, Blüher M, Richter J, Fasshauer M. Serum levels of the adipokine fibroblast growth factor-21 are increased in preeclampsia. Cytokine. 2013; 62(2):322-6. doi: 10.1016/j.cyto.2013.02.019

10. Abd Elmagid AM, Elewa HA, Elawady R, Abd Eltawab WA. Role of fibroblast growth factor-21 in women with pre-eclampsia. Al-Azhar Medical Journal. 2017; 46(3),689-698. Available from: https://api.semanticscholar.org/CorpusID:214631686

11. Nitert MD, Scholz-Romero K, Kubala MH. Placental fibroblast growth factor 21 is not altered in late-onset preeclampsia. Reprod Biol Endocrinol. 2015; 13: 1-8. doi: 10.1186/s12958-015-0006-3

12. Yuan D, Wu BJ, Henry A., Rye KA, Ong KL. Role of Fibroblast Growth Factor 21 in Gestational Diabetes Mellitus: A Mini-Review. Clin Endocrinol. 2019;90:47-55. doi: 10.1111/cen.13881. doi: 10.1111/cen.13881

13. Darka Aslan I, Sel G, Barut F, Baser Acikgoz R, Balci S, Ozmen U, Barut A, Harma M, Harma MI. Investigation of CD56, ADAM17 and FGF21 Expressions in the Placentas of Preeclampsia Cases. Medicina (Kaunas). 2023 Jun 14;59(6):1145. doi: 10.3390/medicina59061145

14. Li Q, Zhang Y, Ding D, Yang Y, Chen Q, Su D, Chen X, Yang W, Qiu J, Ling W. Association Between Serum Fibroblast Growth Factor 21 and Mortality Among Patients With Coronary Artery Disease. J Clin Endocrinol Metab. 2016 Dec;101(12):4886-4894. doi: 10.1210/jc.2016-2308

15. Dalamaga M, Srinivas SK, Elovitz MA, Chamberland J, Mantzoros CS. Serum Adiponectin and Leptin in Relation to Risk for Preeclampsia: Results from a Large Case-Control Study. Metabolism. 2011;60:1539-1544. doi: 10.1016/j.metabol.2011.03.021

16. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis Model Assessment: Insulin Resistance and Beta-Cell Function from Fasting Plasma Glucose and Insulin Concentrations in Man. Diabetologia. 1985;28:412-419. doi: 10.1007/BF00280883

17. Zhang X, Hu Y, Zeng H, Li L, Zhao J, Zhao J, Liu F, Bao Y, Jia W. Serum Fibroblast Growth Factor 21 Levels Is Associated with Lower Extremity Atherosclerotic Disease in Chinese Female Diabetic Patients. Cardiovasc. Diabetol. 2015;14:32. doi: 10.1186/s12933-015-0190-7

18. Alvino G, Cozzi V, Radaelli T, Ortega H, Herrera E, Cetin I. Maternal and Fetal Fatty Acid Profile in Normal and Intrauterine Growth Restriction Pregnancies with and Without Preeclampsia. Pediatr Res. 2008;64:615-620. doi: 10.1203/PDR.0b013e31818702a2

19. Gómez-Sámano MÁ, Grajales-Gómez M, Zuarth-Vázquez JM, Navarro-Flores MF, Martínez-Saavedra M, Juárez-León ÓA, Morales-García MG, Enríquez-Estrada VM, Gómez-Pérez FJ, Cuevas-Ramos D. Fibroblast Growth Factor 21 and Its Novel Association with Oxidative Stress. Redox Biol. 2017;11:335-341. doi: 10.1016/j.redox.2016.12.024

20. Tanajak P, Chattipakorn SC, Chattipakorn N. Effects of Fibroblast Growth Factor 21 on the Heart. J Endocrinol. 2015;227: R13–R30. doi: 10.1530/JOE-15-0289

21. Grygiel-Górniak B. Peroxisome Proliferator-Activated Receptors and Their Ligands: Nutritional and Clinical Implications – A Review. Nutr J. 2014;13:17. doi: 10.1186/1475-2891-13-17

22. Powe CE, Huston Presley LP, Locascio JJ, Catalano PM. Augmented Insulin Secretory Response in Early Pregnancy. Diabetologia. 2019;62:1445-1452. doi: 10.1007/s00125-019-4881-6

23. Phillips MI, Kagiyama S. Angiotensin II as a Pro-Inflammatory Mediator. Curr Opin Investig Drugs. 2002;3:569-577. Available from: https://www.researchgate.net/publication/11284419_Angiotensin_II_as_a_pro-inflammatory_mediator

24. Forrester SJ, Booz GW, Sigmund CD, Coffman TM, Kawai T, Rizzo V, Scalia R, Eguchi S. Angiotensin II Signal Transduction: An Update on Mechanisms of Physiology and Pathophysiology. Physiol Rev. 2018;98:1627-1738. doi: 10.1152/physrev.00038.2017

25. Mallick R, Duttaroy AK. Modulation of Endothelium Function by Fatty Acids. Mol Cell Biochem. 2022;477:15-38. doi: 10.1007/s11010-021-04260-9

26. Pan X, Shao Y, Wu F, Wang Y, Xiong R, Zheng J, Tian H, Wang B, Wang Y, Zhang Y, et al. FGF21 Prevents Angiotensin II-Induced Hypertension and Vascular Dysfunction by Activation of ACE2/Angiotensin-(1-7) Axis in Mice. Cell Metab. 2018;27:1323-1337.e5. doi: 10.1016/j.cmet.2018.04.002

РОЛЬ МАТЕРИНСЬКОГО РІВНЯ СИРОВАТКОВОГО ФАКТОРА РОСТУ ФІБРОБЛАСТІВ 21 У ПРОГНОЗУВАННІ ПРЕЕКЛАМПСІЇ

А. Карім Ель-дін, М. Хасан, Г. Сайєд, А. Хелмі

Університет Айн Шамс
(Каїр, Єгипет)

Резюме.

Вступ. Ускладнення вагітності внаслідок гіпертонічних розладів є серйозною проблемою, яка стосується 2-10 % усіх вагітностей у світі. Прееклампсія визначається як гіпертонія та протеїнурія, які виникли після 20 тижнів вагітності, що можуть бути пов'язані з дисфункцією інших органів матері, наприклад, печінковою або нирковою недостатністю, гематологічними або неврологічними ускладненнями, матково-плацентарною дисфункцією та обмеженням росту плода.

ISSN 2226-1230 (PRINT) ISSN 2413-4260 (ONLINE)
KEY TITLE: NEONATOLOGÌÂ, HÌRURGÌÂ TA PERINATAL'NA MEDICINA (ONLINE)
ABBREVIATED KEY TITLE: NEONATOL. HÌR. PERINAT. MED. (ONLINE)

Мета роботи: встановити зв'язок між рівнями сироваткового фактора росту фібробластів 21 матері та прееклампсією у якості предиктору прееклампсії.

Пацієнти та методи: дослідження типу «випадок-контроль», яке було проведено на 90 першовагітних у пологовому будинку університету Айн Шамс з квітня 2021 року по квітень 2022 року.

Результати: наше дослідження показало, що існувала значна різниця в рівнях FGF21 між групами, а саме, пацієнтки з прееклампсією мали вищі рівні, ніж у контрольній групі, 15,9 % пацієнток з прееклампсією мали материнські ускладнення порівняно з відсутністю жодного випадку у контрольній групі. Водночас у 18,2 % пацієнток із прееклампсією спостерігалися ускладнення у плода порівняно з 0 % випадків у контрольній групі.

Висновок: рівень FGF-21 у сироватці крові значно вищий у вагітних жінок з прееклампсією порівняно зі здоровими вагітними жінками, які мають нормальний тиск. Отже, його можна використовувати як предиктор розвитку преклампсії та ускладнень у матері.

Ключові слова: сироватковий фібробласт 21; прееклампсія; приміравіда.

Contact information:
Alaa Mohamed Atef Karim El-din – MD, Lecturer of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University (Cairo, Egypt).
e-mail: Alaa@yahoo.com

Magdy Hassan Kolib – MD, Professor of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, (Cairo, Egypt).
e-mail: magdy@yahoo.com

Gehad Sayed Abdel-Rahman Bakhat – MD, Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University (Cairo, Egypt).
e-mail: Bakri__pedi91@outlook.com

Amr Helmy Yehia – MD, Assistant Professor of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, (Cairo, Egypt).
e-mail: Amr@yahoo.com,

Контактна інформація:
Алаа Мохамед Атеф Карім Ель-Дін – доктор медичних наук, викладач акушерства та гінекології, кафедра акушерства та гінекології, медичний факультет, Університет Айн Шамс (Каїр, Єгипет).
e-mail: Alaa@yahoo.com

Магді Хассан Коліб – доктор медичних наук, професор кафедри акушерства та гінекології, кафедра акушерства та гінекології, медичний факультет, Університет Айн Шамс (Каїр, Єгипет).
e-mail: magdy@yahoo.com

Гехад Сайед Абдель-Рахман Бахат – доктор медичних наук, кафедра акушерства та гінекології, медичний факультет, Університет Айн Шамс (Каїр, Єгипет).
e-mail: Bakri__pedi91@outlook.com

Амр Хелмі Єхія – доктор медичних наук, доцент кафедри акушерства та гінекології, кафедра акушерства та гінекології, медичний факультет, Університет Айн Шамс (Каїр, Єгипет).
e-mail: Amr@yahoo.com

Received for editorial office on 11/01/2024
Signed for printing on 18/02/2024