ACH Med J
(2025) 1: 015-021
ISSN:2822-5872
Doi : 10.5505/achmedj.2025.08379

RESEARCH ARTICLE

Investigation of Prohibitin Levels in Preeclampsia Cases: A Case Control Study from a Tertiary Hospital

Hasan Burak Keser[1], Funda Gulcu Bulmus[2], Salih Burcin Kavak[3], Ebru Celik Kavak[4]

[1]Turkish Ministry of Health, Elazığ Fethi Sekin City Hospital,department Of Obstetrics And Gynecology
[2]Balıkesir University, Faculty of Health Sciences, Departmant of Nutrition and Dietetics
[3]Turkish Ministry Of Health,Medical Faculty Hospital Of Fırat University,Department Of Obstetrics And Gynecology
[4]Kavak Medical Center Of Obstetrics And Gynecology

Article Info

Received Date: 09.01.2025
Revision Date : 09.02.2025
Accepted Date: 11.02.2025

Keywords:
Prohibitin,
Preeclampsia,
Pregnant,
Oxidative stress,
Apoptosis

ORCIDs of the authors:
HBK :0000-0001-7445-2366
FGB :0000-0002-2514-4559
SBK :0000-0002-6318-5175
ECK :0000-0002-7447-8264

Abstract

Introductıon: To evaluate the relationship between the effects of prohibitin at the cellular level and the pathophysiology of preeclampsia.

Methods: This study included a total of 120 patients who presented to our clinic at 20–41 weeks of gestation. The participants were divided into three groups: 40 pregnant women with preeclampsia with severe features, 40 pregnant women with preeclampsia, and 40 healthy pregnant women. To measure serum prohibitin levels, 10 cc of venous blood was collected from each participant, and comparisons were made between the groups.

Results: Serum prohibitin levels were significantly higher in pregnant women with preeclampsia with severe features and preeclampsia compared to the control group ($p<0.001$ for both).

Conclusion: Prohibitin levels were found to be significantly increased in pregnant women with preeclampsia with severe features and those with preeclampsia compared to healthy pregnant women, suggesting that prohibitin may serve as a marker of preeclampsia.

Correspondence Address: Adnan Kahveci Bul. Çaydaçıra Mah. Rüyampark Sitesi Elazığ- Türkiye
Phone: +90 539 607 01 49 / **e-mail:** brkksr23@gmail.com

Introduction

Preeclampsia is among the most significant complications encountered in obstetrics, affecting approximately 2–7% of all pregnancies.[1] Defined as hypertension and proteinuria occurring after the 20th week of pregnancy, preeclampsia is, in fact, a multisystemic and complex syndrome that extends beyond hypertension and proteinuria, affecting the entire body.[2] Annually, approximately 50,000 maternal and 900,000 infant deaths globally are attributed to preeclampsia and its complications, accounting for around 12% of all maternal fatalities.[3] The onset and clinical course of the disease are unpredictable; therefore, robust tools are needed for accurate diagnosis and treatment. Preeclampsia with severe features characterized by severe hypertension, symptoms of central nervous system dysfunction, new onset headache unresponsive to medication,hepatocellular injury, thrombocytopenia, renal insuffiency, pulmonary edema, and cerebrovascular events.[4]

PHB is a pleiotropic protein belonging to the SPFH (stomatins, flotillins and HflK/C) protein family, sharing the SPFH domain that plays a role in both adipocytes and immune cells.[5] It derives its name from prohibitin, which was found in a search for anti-proliferative genes. Later, a homologous protein with almost 50% sequence homology to PHB was identified as a repressor of estrogen activity (REA, also known as PHB2). After the discovery of PHB2, PHB received the alternative name PHB1.[6,7]

Prohibitins have been reported to perform numerous functions across various cellular localizations and cell types. The functions attributed to prohibitins include their roles in nuclear transcription, their presence as lipid skeleton proteins in the plasma membrane, their function as mitochondrial morphogenesis proteins within mitochondria, and their regulation of apoptosis.[8] Furthermore, induced oxidative stress has been associated with prohibitin expression.[9] In endothelial cells, down-regulation of prohibitin has been shown to result in increased production of mitochondrial reactive oxygen species (ROS) and cellular aging.[10,11] Given the sequence of activities undertaken by prohibitin proteins, they have been identified as promising therapeutic targets in diverse disease states, including inflammation, obesity, and cancer, although a deeper understanding of their cell-specific functions remains essential.[12]

Considering the pathophysiology of preeclampsia and the cellular-level effects of prohibitin, prohibitin has been found noteworthy in elucidating the pathophysiology of preeclampsia. This study aimed to investigate prohibitin (PHB1) levels in cases of preeclampsia-complicated pregnancies and preeclampsia with severe features as compared to healthy pregnancies.

Material and Methods

Following approval from the local ethics committee (meeting number: 12, decision number: 21, date: August 1, 2019), the study was conducted with a total of 120 pregnant women who presented to the Obstetrics and Gynecology Clinic of Fırat University Medical Faculty Hospital. The study was designed as a prospective case control study, with participants selected using quota sampling. During blood sample collection, medical consent was obtained from all participants in accordance with the ethical guidelines of the Declaration of Helsinki. The participants were at gestational ages ranging from 20 to 41 weeks and were divided into three groups for evaluation: 40 patients with preeclampsia with severe features, 40 patients with preeclampsia, and 40 healthy pregnant women.

The preeclamptic patient group included individuals with blood pressure measurements of 140/90 mmHg or higher recorded at least twice with intervals of six hours or more, along with proteinuria of 300 mg/24 hours or higher, or a dipstick reading of +1 or greater. Preeclamptic patients were further evaluated in two subgroups according to the severity of preeclampsia based on the criteria specified in the introduction section. The control group included normotensive pregnancies with no significant pathology in their obstetric history (e.g., placenta previa, intrauterine growth restriction, or placental abruption) in both their current and previous pregnancies. Pregnant women with a history of diabetes mellitus, chronic hypertension, thromboembolism, thrombophilia, liver or renal disease, fetal anomalies, or multiple gestations were excluded from the study.

Detailed medical histories and obstetric evaluations were obtained for all participants. Data recorded included maternal age, body mass index (BMI), gravidity, parity gestational week, gestational week at birth, systolic/diastolic blood pressure and mean arterial pressure (MAP) measurements.

For the determination of serum prohibitin (PHB1) levels, 10 cc of venous blood was collected

in plain tubes. After the diagnosis of preeclampsia with severe features or preeclampsia, 10 cc of venous blood was taken from the patients, centrifuged at 5,000 rpm for 10 minutes, and stored at -86°C in Eppendorf tubes until analysis. Healthy pregnancies were verified through the absence of elevated blood pressure on routine examination cards, and further blood pressure measurements were taken before blood samples were collected and appropriately prepared for storage. Serum prohibitin levels were subsequently measured using the human prohibitin enzyme-linked immunosorbent assay kit [Shanghai Sunredbio Technology Co. Ltd., Catalog No.: 201-12-2131, China], following the kit instructions. Absorbance values were read spectrophotometrically at 450 nm using the Multiskan FC Microplate Photometer [Thermo Scientific, USA], and test results were reported in ng/ml, with a sensitivity of 0.0724 ng/ml and a measurement range of 0.1-30 ng/ml.

Statistical analysis

Statistical analyses were conducted using IBM SPSS Statistics version 22.0. Categorical variables were summarized as numbers and percentages, while continuous variables were presented as means and standard deviations. The Kolmogorov-Smirnov test was used to assess whether continuous variables met the normal distribution assumption. A one-way analysis of variance was used for the general comparison of continuous measures among more than two groups. The statistical significance level was accepted as 0.05 for all tests.

Results

The study included a total of 120 pregnant women, aged 18–44 years, comprising 40 women with preeclampsia with severe features, 40 with preeclampsia, and 40 healthy controls. There were no statistically significant differences in maternal age, body mass index, or mean gestational age between the three groups ($p > 0.05$). However, systolic, diastolic, and mean arterial blood pressure values were statistically significantly higher in the preeclampsia with severe features group compared to the preeclampsia and control groups ($p < 0.001$ and $p < 0.05$, respectively). Additionally, there were significant differences in systolic, diastolic, and mean arterial blood pressure values between the preeclampsia and control groups [Table 1].

Table1. Demographic and obstetric data of the study groups

	Group			
	Preeclampsia with severe features (n=40)	**Preeclampsia (n=40)**	**Control (n=40)**	**p-value**
Maternal age	30.7 ± 6.8	30.8 ± 5.7	30.1 ± 5.1	>0.05
BMI	28.9 ± 4.1	30.9± 4.0	29.3 ±4.3	>0.05
Gravidity	1 ± 1	2 ± 2	2 ± 2	0.417
Parity	1 ± 1	1 ± 1	2 ± 1	0.289
Gestational week	29 ± 4	29.5 ± 5	30 ± 4	0.216
Gestational week at birth	32.83 ± 4.27	35.11 ± 3.84	38 ± 2	<0.001
Systolic BP[mmHg]	168.46 ±12.88	141.87 ±7.90	107.5±11.93	<0.001
Diastolic BP[mmHg]	113.20 ± 6.73	92.12 ± 5.97	71.36 ± 7.42	<0.001
MAP[mmHg]	132.85 ±7.7	109.1 ± 4.2	82.86 ± 8.4	<0.001

Values are given as mean ± standard deviation.
n: number, BMI: body mass index, BP: blood pressure, MAP: mean arterial pressure

When comparing serum prohibitin levels across groups, the preeclampsia with severe features group showed statistically significantly higher levels compared to the control group [$p < 0.001$]. Similarly, prohibitin levels in the preeclampsia group were significantly elevated compared to the control group [$p < 0.001$]. However, no statistically significant difference was observed between the preeclampsia with severe features and preeclampsia groups ($p > 0.05$) [Table 2].

Table2. Comparison of the laboratory test results and prohibitin values between the study groups

	Prohibitin(ng/ml)	**Min**	**Max**	**p-value***
Preeclampsia with severe featuresa (n=40)	5.3988 ± 7.63748	.10	26.50	>0.05 a-b
Preeclampsiab (n=40)	5.0051 ± 6.59079	.59	30.00	
Contr (n=40)	2.6079 ± 2.35926	.10	9.95	<0.001 a-c b-c
Total [n=120]	4.3373 ± 6.05898	.10	30.00	

*One-way analysis of variance. Values are given as mean ± standard deviation.
n: number, min: minimum, max: maximum.

Discussion

This study showed that pregnant women with preeclampsia with severe features and preeclampsia had higher serum prohibitin levels than healthy pregnant women. The underlying biological mechanisms linking organ dysfunction in preeclampsia are not yet clear, and as a result, preeclampsia remains a disease of theories. While the precise cause of hypertensive disorders in pregnancy remains unclear, several hypotheses suggest that issues in placental implantation and trophoblastic invasion are key contributors to the disease.[13,14] The initial step are inadequate or abnormal trophoblastic invasion of the uterine decidua and spiral arteries during early pregnancy is generally considered a primary etiological factor in the development of preeclampsia and restriction of intrauterine growth. Predisposing genetic, immunological and preexisting maternal risk factors may affect this abnormal placentation.[15] As stated in many studies, impaired placental vascularity causes inadequate placental perfusion, which in turn causes the release of antiangiogenic factors into the systemic circulation and endothelial dysfunction occurs.[16] There is no curative treatment for PE, except the delivery of the placenta. As a result, management protocols for PE are supportive, including hypertension management, seizure prophylaxis, delivery at the optimal time, prevention of maternal and fetal mortality/morbidity due to the disease.[17] In the current study, the preeclampsia with severe features and preeclampsia group had significantly higher negative perinatal outcomes, such as preterm birth and maternal systolic, diastolic and mean blood pressures.

Apoptosis, although essential for normal placental development, can also play a role in pathological conditions of the placenta. The presence of these cells is associated with various stages of placental development, such as trophoblast attachment and invasion, trophoblast differentiation and cycle, spiral artery transformation, and parturition.[18,19] Furthermore, apoptosis has been shown to be essential in establishing maternal immune tolerance to paternal antigens expressed by trophoblasts.[20,21] Complicated pregnancies, such as those with preeclampsia or intrauterine growth restriction, show a high incidence of trophoblast apoptosis. Changes in the regulation of trophoblast apoptosis may contribute to the pathophysiology of these disorders.[22,23]

It has been reported that prohibitins have multiple functions, including roles in nuclear transcription across various cellular localizations and cell types, anti-oxidation, anti-inflammation, functioning as a lipid cytoskeletal protein within the plasma membrane, acting as a mitochondrial morphogenesis protein within the mitochondria, and serving as a regulatory protein in apoptosis.[24] Prohibitin expression has also been associated with induced oxidative stress. Nuell et al. reported that the downregulation of prohibitin in endothelial cells resulted in increased production of mitochondrial reactive oxygen species (ROS) and led to cellular senescence.[25] Under normal conditions, low ROS concentrations play essential roles in cell signaling and homeostasis.[26] However, oxidative stress can occur when the balance between ROS formation and the detoxification actions of antioxidant proteins is disrupted. The overproduction of reactive oxygen molecules as a result of placental oxidative stress in preeclampsia has an effect on endothelial dysfunction.[27] This data supports the idea that prohibitin is a factor of oxidative stress.

Mishra et al. determined that prohibitin protected cells and tissues against the induction of apoptosis.[28] Thus, it is plausible that increased levels of prohibitin in preeclampsia may function to prevent trophoblast apoptosis. In a study by Allaire et al., trophoblast apoptosis was shown to be elevated in pregnancies complicated by preeclampsia.[29]

The association of prohibitin with oxidative stress was further investigated by Jupe et al., who observed that prohibitin overexpression in intestinal epithelial cells reduced oxidative stress in inflammatory bowel disease.[30] In another study undertaken by Rusterholz et al., inflammation was found to be markedly increased in preeclampsia, and factors triggering inflammatory responses [such as infections and rheumatic diseases] were suggested to raise the likelihood of developing preeclampsia.[31] While this finding may contradict our results, it is possible that elevated prohibitin levels in our study reflect a compensatory mechanism to mitigate oxidative stress.

Studies showing that prohibitin expression is increased in autoimmune diseases.[32] It has been shown that preeclamptic pregnant women have autoantibodies that activate the angiotensin receptor and that autoantibody-mediated receptor activation contributes to the pathophysiology associated with

preeclampsia. This pathophysiology strengthens the possibility that preeclampsia is a pregnancy-related autoimmune disease.[33] Similarly, in the current study, the serum prohibitin level was found to be higher in the preeclampsia with severe features and preeclampsia group than in the control group and it was statistically significant. High serum prohibitin levels in preeclampsia patients suggest that there is a relationship between prohibitin and angiotensin reseptor systems, and this finding is in agreement with the literature.

Conclusion

To our knowledge, this is the first study to evaluate serum prohibitin levels in pregnant women with preeclampsia. This study revealed that prohibitin levels were significantly elevated in the severe preeclampsia and preeclampsia groups compared to the control group, highlighting prohibitin as a noteworthy biomarker. This novel biomarker appears to hold potential for managing pregnant women with preeclampsia. The relatively low number of cases and single-center experience can be considered as the major limitations of the research. To elucidate the role of prohibitin levels in the prediction of preeclampsia, as well as to evaluate their potential as a biomarker for clinical practice, it is essential to conduct studies with large patient cohorts.

References

1. Higgins JR, de Swiet M. Blood-pressure measurement and classification in pregnancy. Lancet. 2001;357(9250):131-5. doi: 10.1016/s0140-6736(00)03552-2. PubMed PMID: 11197413.

2. Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: Pathophysiology, Challenges, and Perspectives. Circ Res. 2019;124(7):1094-112. doi: 10.1161/circresaha.118.313276. PubMed PMID: 30920918.

3. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. Lancet. 2005;365(9461):785-99. doi: 10.1016/s0140-6736(05)17987-2. PubMed PMID: 15733721.

4. Wu P, Green M, Myers JE. Hypertensive disorders of pregnancy. Bmj. 2023;381:e071653. Epub 20230630. doi: 10.1136/bmj-2022-071653. PubMed PMID: 37391211.

5. McClung JK, Danner DB, Stewart DA, Smith JR, Schneider EL, Lumpkin CK, et al. Isolation of a cDNA that hybrid selects antiproliferative mRNA from rat liver. Biochem Biophys Res Commun. 1989;164(3):1316-22. doi: 10.1016/0006-291x(89)91813-5. PubMed PMID: 2480116.

6. Osman C, Haag M, Potting C, Rodenfels J, Dip PV, Wieland FT, et al. The genetic interactome of prohibitins: coordinated control of cardiolipin and phosphatidylethanolamine by conserved regulators in mitochondria. J Cell Biol. 2009;184(4):583-96. Epub 20090216. doi: 10.1083/jcb.200810189. PubMed PMID: 19221197; PubMed Central PMCID: PMC2654118.

7. Mishra S, Murphy LC, Murphy LJ. The Prohibitins: emerging roles in diverse functions. J Cell Mol Med. 2006;10(2):353-63. doi: 10.1111/j.1582-4934.2006.tb00404.x. PubMed PMID: 16796804; PubMed Central PMCID: PMC3933126.

8. Ande SR, Nguyen KH, Nyomba BLG, Mishra S. Prohibitin in Adipose and Immune Functions. Trends Endocrinol Metab. 2016;27(8):531-41. Epub 20160613. doi: 10.1016/j.tem.2016.05.003. PubMed PMID: 27312736.

9. Coates PJ, Nenutil R, McGregor A, Picksley SM, Crouch DH, Hall PA, et al. Mammalian prohibitin proteins respond to mitochondrial stress and decrease during cellular senescence. Exp Cell Res. 2001;265(2):262-73. doi: 10.1006/excr.2001.5166. PubMed PMID: 11302691.

10. Nijtmans LG, de Jong L, Artal Sanz M, Coates PJ, Berden JA, Back JW, et al. Prohibitins act as a membrane-bound chaperone for the stabilization of mitochondrial proteins. Embo j. 2000;19(11):2444-51. doi: 10.1093/emboj/19.11.2444. PubMed PMID: 10835343; PubMed Central PMCID: PMC212747.

11. Theiss AL, Idell RD, Srinivasan S, Klapproth JM, Jones DP, Merlin D, et al. Prohibitin protects against oxidative stress in intestinal epithelial cells. Faseb j. 2007;21(1):197-206. Epub 20061129. doi: 10.1096/fj.06-6801com. PubMed PMID: 17135366.

12. Scherz-Shouval R, Elazar Z. Regulation of autophagy by ROS: physiology and pathology. Trends Biochem Sci. 2011;36(1):30-8. Epub 20100820. doi: 10.1016/j.tibs.2010.07.007. PubMed PMID: 20728362.

13. Abbas Y, Turco MY, Burton GJ, Moffett A. Investigation of human trophoblast invasion in vitro. Hum Reprod Update. 2020;26(4):501-13. doi: 10.1093/humupd/dmaa017. PubMed PMID: 32441309; PubMed Central PMCID: PMC7473396.

14. Melchiorre K, Giorgione V, Thilaganathan B. The placenta and preeclampsia: villain or victim?

Am J Obstet Gynecol. 2022;226(2s):S954-s62. Epub 20210324. doi: 10.1016/j.ajog.2020.10.024. PubMed PMID: 33771361.
15. Tomimatsu T, Mimura K, Matsuzaki S, Endo M, Kumasawa K, Kimura T. Preeclampsia: Maternal Systemic Vascular Disorder Caused by Generalized Endothelial Dysfunction Due to Placental Antiangiogenic Factors. Int J Mol Sci. 2019;20(17). Epub 20190830. doi: 10.3390/ijms20174246. PubMed PMID: 31480243; PubMed Central PMCID: PMC6747625.
16. Leijnse JEW, de Heus R, de Jager W, Rodenburg W, Peeters LLH, Franx A, et al. First trimester placental vascularization and angiogenetic factors are associated with adverse pregnancy outcome. Pregnancy Hypertens. 2018;13:87-94. Epub 20180411. doi: 10.1016/j.preghy.2018.04.008. PubMed PMID: 30177079.
17. Tanacan A, Fadiloglu E, Beksac MS. The importance of proteinuria in preeclampsia and its predictive role in maternal and neonatal outcomes. Hypertens Pregnancy. 2019;38(2):111-8. Epub 20190402. doi: 10.1080/10641955.2019.1590718. PubMed PMID: 30939965.
18. Smith SC, Leung TN, To KF, Baker PN. Apoptosis is a rare event in first-trimester placental tissue. Am J Obstet Gynecol. 2000;183(3):697-9. doi: 10.1067/mob.2000.106555. PubMed PMID: 10992195.
19. Ashton SV, Whitley GS, Dash PR, Wareing M, Crocker IP, Baker PN, et al. Uterine spiral artery remodeling involves endothelial apoptosis induced by extravillous trophoblasts through Fas/FasL interactions. Arterioscler Thromb Vasc Biol. 2005;25(1):102-8. Epub 20041021. doi: 10.1161/01.Atv.0000148547.70187.89. PubMed PMID: 15499040; PubMed Central PMCID: PMC4228192.
20. Abrahams VM, Straszewski-Chavez SL, Guller S, Mor G. First trimester trophoblast cells secrete Fas ligand which induces immune cell apoptosis. Mol Hum Reprod. 2004;10(1):55-63. doi: 10.1093/molehr/gah006. PubMed PMID: 14665707.
21. Huppertz B, Frank HG, Kingdom JC, Reister F, Kaufmann P. Villous cytotrophoblast regulation of the syncytial apoptotic cascade in the human placenta. Histochem Cell Biol. 1998;110(5):495-508. doi: 10.1007/s004180050311. PubMed PMID: 9826129.
22. Genbacev O, DiFederico E, McMaster M, Fisher SJ. Invasive cytotrophoblast apoptosis in pre-eclampsia. Hum Reprod. 1999;14 Suppl 2:59-66. doi: 10.1093/humrep/14.suppl_2.59. PubMed PMID: 10690801.
23. Crocker IP, Cooper S, Ong SC, Baker PN. Differences in apoptotic susceptibility of cytotrophoblasts and syncytiotrophoblasts in normal pregnancy to those complicated with preeclampsia and intrauterine growth restriction. Am J Pathol. 2003;162(2):637-43. doi: 10.1016/s0002-9440(10)63857-6. PubMed PMID: 12547721; PubMed Central PMCID: PMC1851173.
24. Mishra S, Nyomba BG. Prohibitin: A hypothetical target for sex-based new therapeutics for metabolic and immune diseases. Exp Biol Med (Maywood). 2019;244(2):157-70. Epub 20190204. doi: 10.1177/1535370219828362. PubMed PMID: 30717609; PubMed Central PMCID: PMC6405819.
25. Nuell MJ, Stewart DA, Walker L, Friedman V, Wood CM, Owens GA, et al. Prohibitin, an evolutionarily conserved intracellular protein that blocks DNA synthesis in normal fibroblasts and HeLa cells. Mol Cell Biol. 1991;11(3):1372-81. doi: 10.1128/mcb.11.3.1372-1381.1991. PubMed PMID: 1996099; PubMed Central PMCID: PMC369408.
26. Sosa V, Moliné T, Somoza R, Paciucci R, Kondoh H, ME LL. Oxidative stress and cancer: an overview. Ageing Res Rev. 2013;12(1):376-90. Epub 20121031. doi: 10.1016/j.arr.2012.10.004. PubMed PMID: 23123177.
27. Chiarello DI, Abad C, Rojas D, Toledo F, Vázquez CM, Mate A, et al. Oxidative stress: Normal pregnancy versus preeclampsia. Biochim Biophys Acta Mol Basis Dis. 2020;1866(2):165354. Epub 20181224. doi: 10.1016/j.bbadis.2018.12.005. PubMed PMID: 30590104.
28. Mishra S, Murphy LC, Nyomba BL, Murphy LJ. Prohibitin: a potential target for new therapeutics. Trends Mol Med. 2005;11(4):192-7. doi: 10.1016/j.molmed.2005.02.004. PubMed PMID: 15823758.
29. Allaire AD, Ballenger KA, Wells SR, McMahon MJ, Lessey BA. Placental apoptosis in preeclampsia. Obstet Gynecol. 2000;96(2):271-6. doi: 10.1016/s0029-7844(00)00895-4. PubMed PMID: 10908776.
30. Jupe ER, Liu XT, Kiehlbauch JL, McClung JK, Dell'Orco RT. Prohibitin antiproliferative activity and lack of heterozygosity in immortalized cell lines.

Exp Cell Res. 1995;218(2):577-80. doi: 10.1006/excr.1995.1194. PubMed PMID: 7796893.
31. Rusterholz C, Hahn S, Holzgreve W. Role of placentally produced inflammatory and regulatory cytokines in pregnancy and the etiology of preeclampsia. Semin Immunopathol. 2007;29(2):151-62. doi: 10.1007/s00281-007-0071-6. PubMed PMID: 17621700.
32. Wang D, Tabti R, Elderwish S, Abou-Hamdan H, Djehal A, Yu P, et al. Prohibitin ligands: a growing armamentarium to tackle cancers, osteoporosis, inflammatory, cardiac and neurological diseases. Cell Mol Life Sci. 2020;77(18):3525-46. Epub 20200215. doi: 10.1007/s00018-020-03475-1. PubMed PMID: 32062751; PubMed Central PMCID: PMC11104971.
33. Jung E, Romero R, Yeo L, Gomez-Lopez N, Chaemsaithong P, Jaovisidha A, et al. The etiology of preeclampsia. Am J Obstet Gynecol. 2022;226(2s):S844-s66. doi: 10.1016/j.ajog.2021.11.1356. PubMed PMID: 35177222; PubMed Central PMCID: PMC8988238.