Patient Safety & Quality Improvement Journal
http://psj.mums.ac.ir
PSQI

The Relationship between Preeclampsia and Quadruple Screening Test in Nuliparous

Farnaz Zand Vakili[1] (MD); Masomeh Rezaie[1] (MD); Sirous Shahsavari[2] (MD); Roonak Niazi[1]* (MD)

[1.] Department of Gynecology, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran.
[2.] Department of Public Health, Faculty of Health, Kurdistan University of Medical Sciences, Sanandaj, Iran.

ARTICLEINFO

Article type:
Original Article

Article history:
Received: 14-May-2016
Accepted: 05-June-2016

Keywords:
Preeclampsia
Pregnant women
Quadruple screening test

ABSTRACT

Introduction: Early diagnosis and prediction of preeclampsia needs appropriate obstetric care. Preeclampsia predicting methods are important. This study was designed to determine the correlation between preeclampsia and quadruple screening test in the nulliparous.

Materials and Methods: This case - control study was conducted on 54 pregnant women with preeclampsia (case group) and 108 healthy pregnant women (control group) who referred to health centers in Sanandaj, Iran. Ultrasonography was performed to determine the gestational age by a radiologist. Maternal serum levels of Alpha-fetoprotein (AFP), human Chorionic Gonadotropin (hCG), unconjugated estriol (uE3), and inhibin-A were measured in the second trimester of pregnancy. Data were analyzed using SPSS statistical software and Chi-square test, T-test, sensitivity, specificity, positive and negative predictive values.

Results: The results showed that the sensitivity and specificity for the diagnosis of preeclampsia in pregnant women for hCG were 35.2% and 79.6 respectively. These findings for estriol were 20.4% and 88.9%, for inhibin-A were 38.8% and 88% and for alpha-fetoprotein were 38.8% and 74.1%. The positive predictive value for hCG, estriol, inhibin-A and alpha-fetoprotein were 46.3%, 47.8%, 61.8% and 42.9% respectively. The negative predictive value for hCG, estriol, inhibin-A and alpha-fetoprotein were also 71%, 69.1%, 74.2% and 70.8% respectively.

Conclusion: There was a relationship between preeclampsia and high levels of inhibin-A and hCG. Further studies on these markers and evaluating their usefulness in the diagnosis and management of preeclampsia are recommended.

► ***Please cite this paper as*:**
Zand Vakili F, Rezaie M, Shahsavari S, Niazi R. The Relationship between Preeclampsia and Quadruple Screening Test in Nuliparous. Patient Saf Qual Improv. 2017; 5(1):493-496.

Introduction

Hypertensive disorders occur in 5 to 10 percent of pregnancies that along with bleeding and infections constitute a deadly triad.

Among hypertensive disorders, preeclampsia syndrome either alone or as added on chronic hypertension is the most dangerous mode. Hypertensive disorders are responsible for16 per cent of maternal deaths in developed countries (1).

Preeclampsia is a pregnancy-specific syndrome which can affect almost all organs of the body.

This syndrome was described in two stages. The first stage is created due to improper penetration of placenta into the vessels. This process leads to the second stage which includes hypertension, proteinuria and damage to the end organs such as liver, kidneys, and brain (2).

Pathophysiology of preeclampsia is not precisely known, but one of the main factors is vasospasm which can lead to vascular damage, localized hypoxia, bleeding, necrosis and end-organ dysfunction (1).

In preeclampsia the synthesis of nitric oxide and prostacyclin 12 reduce significantly and Thromboxane A2 rises. These changes happen from week 22 of pregnancy in women who later suffer from preeclampsia (3).

Endothelial cell dysfunction is probably the main cause of preeclampsia. In pregnancies complicated by preeclampsia, 30 to 50 percent of uterine blood flow is reduced which leads to compensatory increases in the number of placental capillaries in order to increase blood flow to the uterus. The increase in placental villi

***Corresponding Author:** Roonak Niazi, Department of Gynecology, Faculty of Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran. Email: mahmoodreza.mohajer@gmail.com

can be placenta early maturation factor (4). Risk factors for preeclampsia include nulliparity, family history, age over 40 years, chronic hypertension, chronic kidney diseases, Diabetes and multiple pregnancies (2). Early diagnosis and prediction of preeclampsia require appropriate obstetric care. Preeclampsia predicting methods are important (4).

In recent years more than 100 biochemical and clinical tests to predict preeclampsia have been developed, but so far the method with high sensitivity and specificity has not been determined (5).

Various types of biological, biochemical and biophysical markers have been introduced in order to predict the occurrence of preeclampsia. Researchers have tried to identify markers of dysfunction in placentation, reduction in placental perfusion and coagulation (6). Quadruple tests are the second trimester screening tests which predict congenital defects. Approximately 75 to 80 percent of the problems related to the crebrospinal development as well as genetic disorders would be determined by blood test. High levels of Alpha-fetoprotein (AFP) indicate cerebrospinal problems or twin fetus and its low levels than normal show the risk of having a baby with Down syndrome. The higher levels of hCG and Inhibin-A, which are hormones produced by the placenta also show the risk of this syndrome and lower than normal levels of estriol also determines risk of this genetic defect (7). Some studies have indicated the HCG serum levels measurement as a tool for diagnosis and clinical management of preeclampsia (8), but some studies have rejected (9, 10).

Since the gestational hypertension and preeclampsia in pregnant women are relatively common complications which leads to maternal and perinatal mortality and morbidity (11) this study was designed to determine the correlation between preeclampsia and quadruple screening test in the nulliparous.

Materials and Methods

This case - control study was conducted on 54 pregnant women with preeclampsia (case group) and 108 healthy pregnant women (control group) who referred to health centers in Sanandaj, Iran in 2015. The two groups were matched for age, gestational age and body mass index.Inclusion criteria included primigrvidity and living in Sanandaj.

Exclusion criteria included; multiple pregnancies, history of chronic hypertension, diabetes, polycystic ovary syndrom, thyroid dysfunction, fetus genetic diseases and consuming medications (steroids, thyroid, gonadotropin and ACTH). Ultrasonography was performed to determine the gestational age by a radiologist.

Maternal serum levels of Alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), unconjugated estriol (uE3), and inhibin-A were measured in the second trimester of pregnancy.

For all study participants a questionnaire was completed that included demographic information and lab test results. Data were analyzed using SPSS statistical software and Chi-square test, T-test, sensitivity, specificity, positive and negative predictive values.

Results

The mean ages of pregnant women in case and control groups were 29.53±4.37 and 29.42±5.10 years respectively. Gestational age in case and control groups were33.05±2.08 and 33.05±2.07 which was the same.

Body mass index was similar in both case and control groups and there was no significant difference statistically (p=.05).

The results showed that the sensitivity and specificity for the diagnosis of preeclampsia in pregnant women for hCG were 35.2% and 79.6 respectively. These findings for estriol were 20.4% and 88.9%, for inhibin-A were 38.8% and 88% and for alpha-fetoprotein were 38.8% and 74.1%. (Table 1)

The positive predictive value for hCG, estriol, inhibin-A and alpha-fetoprotein were 46.3%, 47.8%, 61.8% and 42.9% respectively. The negative predictive value for hCG, estriol, inhibin-A and alpha-fetoprotein were also 71%, 69.1%, 74.2% and 70.8% respectively.

Table: Comparison of the results of Lab tests in case and control groups

Lab Test	Groups	Case No (%)	Control No (%)	Sensitivity	Specificity	Positive predictive values	Negative predictive values	OR (CI 95%)
HCG	Abnormal	19(46.3)	22(53.7)	35.2	79.6	46.3	71	2.1(1.02-4.4)
	Normal	35(28.9)	86(71.1)					
Estriol	Abnormal	11(47.8)	12(52.2)	20.4	88.9	47.8	69.1	2.05(.84-5)
	Normal	43(30.9)	96(69.1)					
Inhibin A	Abnormal	21(68.1)	13(38.2)	38.8	88	61.8	74.2	4.65(2.96-10.3)
	Normal	33(25.8)	95(74.2)					
Alpha fetoprotein	Abnormal	21.(42.9)	28(87.1)	38.8	74.1	42.9	70.8	1.83(.91- 3.65)
	Normal	33(29.2)	80(70.8)					

Discussion & Conclusion

The findings of this study showed that quadruple tests for the diagnosis of preeclampsia in pregnant women in the second trimester had low sensitivity.

Although Inhibin A and Alpha-fetoprotein (AFP) compared to the estriol, and HCG had better situation.

Specificity of all 4 tests to reject preeclampsia in pregnant women was also relatively in better situation.

Inhibin A test had positive and negative predictive values of higher value than other three tests.

In a study by Florio, Inhibin A achieved a sensitivity of 39% and a specificity of 92% as a marker for prediction of preeclampsia (12). Muttukrishna reported Inhibin-A 67% sensitivity for preeclampsia in 19-15 weeks and 89% in 21-25 weeks of gestation (13). Walt reported in the pregnancies that went on to develop preeclampsia, early second trimester inhibin-A and hCG values were significantly raised and uE(3) values were significantly lowered, while AFP values were not significantly altered. They concluded that preeclampsia screening performance using the Quadruple test markers was materially better than that using the Triple test markers (14). In Yazdani study a correlation between preeclampsia and higher levels of Inhibin A was found, but no association between preeclampsia and Alpha-fetoprotein (AFP) was observed (15). There was no relationship between preeclampsia and Alpha-fetoprotein (AFP) in Wald study (16). Kang reported statistically significant relationship between preeclampsia with Inhibin A, but the relationship between preeclampsia with Alpha-fetoprotein (AFP) and estriol was not reported (17). In a study in second-trimester inhibin A and hCG levels were significantly but modestly elevated in women who later developed preeclampsia. A combination test of maternal age plus inhibin A and hCG predicted 23% of cases of preeclampsia with 95% specificity (18). In a review study inhibin A was introduced as the best predictor for preeclampsia (19). Although there are differences in the determined sensitivity and specificity for Inhibin A, the findings of this study are largely consistent with our findings.

In present study, the sensitivity and specificity of HCG was close to Inhibin A. Yaron reported as with increased second-trimester maternal serum alpha-fetoprotein levels, increased serum beta-human chorionic gonadotropin and low unconjugated estriol levels were significantly associated with adverse pregnancy-induced hypertension (20). Wald showed a reversed correlation between the increase of hCG and decrease of estriol (16), but there was no correlation in Yazdani`s study (15). Gagnon in a review study showed that elevation of HCG In the second trimester is associated with Gestational hypertension and proteinuria (21). Ong demonstrated that reducing maternal serum protein levels and increased levels of beta hCG at 10-14 weeks of pregnancy is associated with increased complications of pregnancy (22). Lee also showed that women with mild pre-eclampsia had a 2.61-times greater chance, while women with severe pre-eclampsia had a 6.13-times greater chance of having MShCG exceeding 2.0 multiples of the median than did women with a normal pregnancy (23). In a study by Hui Alpha-fetoprotein (AFP) and HCG level was increased in preeclampsia (11). In some other studies high levels of Alpha-fetoprotein (AFP) was associated with preeclampsia (24, 25). These studies also confirmed findings of our study, because in our study the frequency of abnormal estriol were less than Alpha-fetoprotein (AFP) and hCG .

Wald et al showed that adding PlGF to the Quadruple test improves preeclampsia screening performance in the second trimester of pregnancy (26). Michael and Dugoff introduced combined markers and its relationship with disorders during pregnancy.

Simultaneous increase of these markers may increase the risk of pregnancy adverse outcomes. Because of low sensitivity and low positive predictive value of screening tests, detection of adverse pregnancy outcomes is not possible definitely (24-27).

There was a relationship between preeclampsia and high level of inhibin-A and hCG. Further studies on these markers and evaluating their usefulness in the diagnosis and management of preeclampsia are recommended. Currently there is no serum marker for preeclampsia as a screening test before 24 weeks of gestation. Large cohort studies with standard screening test parameters are required.

References

1- F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. SpongJodi S. Dashe, Barbara L. Hoffman, Brian M. Casey, Jeanne S. Sheffield . Williams Obstetrics, 24e.

2- Camille E,Powe CE, Seely EW, Rana S, Bhan I, Ecker J, Karumanchi SA, Thadhani R. First trimester vitamin D, vitamin D binding protein, and subsequent preeclampsia. Hypertension. 2010 Oct;56(4):758-63. Epub 2010 Aug 23.

3- Chavarria ME, Lara-Gonzalez L,Gonzalea- Gleason A, Garcia-paleta Y,Vital-Reyes VS, Reyes A. Prostacyclin,thromboxane early changes in pregnancies that are complicated by preeclampsia. Am J obstet gynecal. 2003;188: 986-999.

4- Ghazizadeh S, Lessan-Pezeshki M, Pirzad R. Mean arterial pressure and calcium creatinin ratio in the early prediction of preeclampsia. Daneshvar 2000;29:39-40. [In Persian]

5- Gharekhani P, Sadatian SA. Principles of Obstetrics and Pregnancy. 2nd ed. Tehran: Noure Danesh. 2005. p.416-22. [In Persian]

6- 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): 151-162.
7- Wapner R, Thom E, Simpson JL, Pergament E, Silver R, Filkins K. First trimester screening for trisomies 21 and 18. N Eng J Med. 2003;349:1405–1413.
8- Gurbuz A, Karateke A, Mengulluoglu M, Gedikbasi A, Ozturkmen M, Kabaca C,et al. Can serum hCG values be used in the differential diagnosis of pregnancy complicated by hypertension. pregnancy. 2004; 23: 1-12.
9- Hietala R, Pohja-Nylander P, Rutanen EM, Laatikainen T. Serum insulin-like growth factor binding protein-1 at 16weeks and subsequent preeclampsia.Obstet Gynecol 2000; 95: 185-189.
10- Aquilina J, Maplethorpe R, Ellis P,Harrington K. Correlation between second trimester maternal serum inhibin-A and human chorionic gonadotrophin for the prediction of pre-eclampsia.Pleacenta 2000; 21: 487-492.
11- Hui D, Okun N, Murphy K, Kingdom J, Uleryk E, Shah PS. Combinations of maternal serum markers to predict preeclampsia, small for gestational age, and stillbirth: a systematic review. J Obstet Gynaecol Can. 2012 Feb;34(2):142-53.
12- Florio P, Reis FM, Pezzani I, Luisi S, Severi FM, Petraglia F. The addition of activin A and inhibin A measurement to uterine artery Doppler velocimetry to improve the early prediction of pre-eclampsia. Ultrasound Obstet Gynecol. 2003;21:165–169.
13- Muttukrishna S, North RA, Morris J, Schellenberg JC, Taylor RS, Asselin J, Ledger W, Groome N, Redman CWG. Serum inhibin A and activin A are elevated prior to the onset of pre-eclampsia. Hum Reprod. 2000;15:1640–1645.
14- Wald NJ, Morris JK, Ibison J, Wu T, George LM. Screening in early pregnancy for pre-eclampsia using Down syndrome quadruple test markers. Prenat Diagn. 2006;26:559–564.
15- Yazdani S, Rouholahnejad R, Asnafi N, Sharbatdaran M, Zakershob M, Bouzari Z. Correlation of pregnancy outcome with quadruple screening test at second trimester. Med J Islam Repub Iran. 2015 Oct 19;29:281. eCollection 2015.
16- Wald NJ, Morris JK. Multiple marker second trimester serum screening for pre-eclampsia. J Med Screen 2001; 8(2):65-8.
17- Kang, J, Farina A, Park J, Kim S, Kim J, Rizzo N, et al. Down Syndrome biochemical markers ndscreening for preeclampsia at first and second trimester:Correlation with the week of onset and severity. Prenatal Diagnosis 2008; 28: 704-709.
18- Lambert-Messerlian GM, Silver HM, Petraglia F, Luisi S, Pelzani I, Maybruck WM, Hogge WA, Hanley-Yanez K, Roberts JM. Second-trimester levels of maternal serum human chorionic gonadotropin and inhibin a as predictors of preeclampsia in the third trimester of pregnancy. J Soc Gynecol Investig. 2000;7:170–174.
19- Rachel K Morris, Jeltsje S Cnossen, Marloes Langejans, Stephen C Robson, Jos Kleijnen, Gerben ter Riet, Ben W Mol, Joris AM van der Post, and Khalid S Khan .Serum screening with Down's syndrome markers to predict pre-eclampsia and small for gestational age: Systematic review and meta-analysis .BMC Pregnancy Childbirth. 2008; 8: 33. Published online Aug 4, 2008.
20- Yaron Y, Cherry M, Kramer RL, O'Brien JE, Hallak M, Johnson MP, Evans MI. Second-trimester maternal serum marker screening: maternal serum alpha-fetoprotein, beta-human chorionic gonadotropin, estriol, and their various combinations as predictors of pregnancy outcome. Am J Obstet Gynecol. 1999;181:968–974.
21- Gagnon A, Wilson RD, Audibert F, Allen VM, Blight C, Brock JA, Désilets VA, Johnson JA, Langlois S, Summers A, Wyatt P.Obstetrical complications associated with abnormal maternal serum markers analytes. J Obstet Gynaecol Can. 2008 Oct;30(10):918-49.
22- Ong CY, Liao AW, Spencer K, Munim S, Nicolaides KH. First trimester maternal serum free beta human chorionic gonadotrophin and pregnancy associated plasma protein A as predictors of pregnancy complications. BJOG. 2000;107:1265–1270.
23- Lee LC, Sheu BC, Shau WY, Liu DM, Lai TJ, Lee YH, Huang SC. Mid-trimester beta-hCG levels incorporated in a multifactorial model for the prediction of severe pre-eclampsia. Prenat Diagn. 2000;20:738–743.
24- Dugoff L, Hobbins JC, Malone FD, Vidaver J, Sullivan L, Canick JA, et al. Quad screen as a predictor of adverse pregnancy outcome.Obstet Gynecol 2005;106:260-7
25- Dehghani-Firouzabadi RTN, Ghasemi N,Tahmasbi, Z. The association between secondtrimester maternal serum alpha-fetoprotein in 14-22weeks and adverse pregnancy outcome. Acta Medica Iranica 2010; 48:234-238.
26- Wald NJ, Bestwick JP, George LM, Wu T, Morris JK. Screening for pre-eclampsia using serum placental growth factor and endoglin with Down's syndrome Quadruple test markers. Med Screen. 2012 Jun;19(2):60-7.
27- Michael R, Byron c, Luis A, et al. The ability of the guadruple test to predict adverse Perinatal outcomes in a high-risk Obstetric population. J Med Screen 2009; 16: 55-59.