J Biochem Tech (2018) Special Issue (2): 52-56
ISSN: 0974-2328

Comparison of Serum Level of Type 70 Heat Shock Protein in Mothers with Complicated and Uncomplicated Preeclampsia

Roghayeh Dargahi, Hajar Memar, Afshan Sharghi, Fatemeh Mallah*

Received: 28 March 2018 / Received in revised form: 06 Jun 2018, Accepted: 11 June 2018, Published online: 05 September 2018

Abstract

Introduction: heat shock proteins (HSPs) refer to intracellular proteins expressed in stress conditions in cell. In normal pregnancy, the level of HSP70 is reduced and an increase in the level of these proteins is associated with several complications of pregnancy. The role of HSP70 in normal and pathologic pregnancies is not well known. This research was conducted to evaluate the relationship between the level of type 70 heat shock protein in mothers with preeclampsia and complications caused by it. Methodology: This cohort study was conducted on 80 patients with preeclampsia in Alavi Hospital in Ardabil in 2017. These subjects were followed up during the study until the end of pregnancy. HSP70 level was measured in serum samples of patients using ELISA method. The collected data were analyzed by SPSS19 software and statistical tests. P -value less than 0.05 was considered significant.Results: In this study, the mean total of gestational age in patients was 33.99 ± 3.53 (32.30 ± 2.88 in the complicated group and 36.06 ± 3.17 in the uncomplicated group), and the difference between the two groups was statistically significant. In this study, 6.3% (n=5) of the patients had HELLP syndrome, 20% (n=16) had intrauterine growth retardation complication, 28 % (n=23) had preterm delivery and 45% (n=36) had no complication. The serum level of HSP70 was 22.69 ± 11.72 in the complicated group and 14.77 ± 3.32 in the uncomplicated group. There was a statistically significant difference between the two groups in terms of serum level of HSP70.Conclusion: Serum level of HSP70 was higher in preeclampsia patients than that in people with normal pregnancy. HSP70 can not only be a marker for these conditions, but also can play an important role in the preeclampsia pathogenesis.

Keywords: Preeclampsia, Type 70 Heat Shock Protein, Eliza

Introduction

Preeclampsia is one of the most serious complications of high-risk pregnancies, threatening the health of women at global level, especially in developing countries. Based on the diagnostic criteria and the population studied in these countries, the prevalence of preeclampsia is between 1.8 to 16.7 percent (Reyes et al., 2012). Annually, 8 million women die due to preeclampsia around the world (Williams & Morgan, 2012). It seems that preeclampsia, in addition to short-term complications, causes long-term complications in the later stages of maternal and neonatal life such as the risk of cardiovascular disorders (Garovic & August, 2013; Heidrich et al., 2013). Despite the developments made in control of this disease in recent years, the exact cause of the disease and its prevention has not been diagnosed yet (Mohaupt, 2007; Chadha & Sood, 2009). Although symptoms of preeclampsia emerge 12 weeks after the pregnancy, it is believed that the disease is caused by a series of molecular events. As a result, proteomics of the disease can help to early diagnose of this disease (Kalkunte et al., 2009). Diagnosis of risk factors of a disease before clinical manifestations or before turning into mild to severe cases to diagnose the patients who need special care and attention is an essential.

Heat shock proteins (HSPs) refer to total proteins expressed in stress conditions in the cell. The role of these proteins is to prevent

Rogayeh Darghahi and Hajar Memar

Obstetrics and Gynecology, Ardabil University of Medical Sciences, Ardabil, Iran.

Afshan Sharghi

Associate Professor of Community Medicine Social Determinant of Health Research Center, Ardabil University of Medical Sciences, Ardabil, Iran.

Fatemeh Mallah*

Obstetrics and Gynecology, Women's Reproductive Health Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.

***Email**: fatima_m815@yahoo.com

changes in composition of cells in stress conditions. These proteins are found in all living cells in a status binding to protein or non-binding to protein. The synthesis of HSPs is induced by several types of stressors such as fever, alcohol, inflammation, oxidative stress, heavy metals, as well as conditions causing injury and necrosis (Ekambaram, 2000). These proteins have been named based on their molecular weight (such as kilodalton 70-60-90 HSP). Heat shock protein 70 (HSP70) in involved in bloodstream of healthy pregnant and non-pregnant people. In normal pregnancy, HSP70 level shows a positive association with gestational age (Walker & Pre-eclampsia, 2000). In addition, HSP70 level is associated with pregnancy complications (Ekambaram, 2000; El-Said et al., 2009).

Its level increases in systemic inflammation, oxidative stresses, preeclampsia, and damage to liver cells. HSP70 serum level increase in HELLP syndrome indicates tissue damage and severity of the disease, and its increase in HELLP syndrome is much higher than that in HELLP syndrome without preeclampsia. Increased level of HSP70 may not be just a marker of this condition, but also plays role in its pathogenesis (Ekambaram, 2000; Molvarec et al., 2006).

Serum HSP70 level is high in preterm delivery, especially in patients who have resistance to treatment, and may be a useful indicator for predicting response to treatment. Its high level at term time may be a sign of labor onset (El-Said et al., 2009). However, enough studies have not been conducted on the predictive ability of HSP70 on complications of pregnancy and preeclampsia, and different studies have yielded different results. The objective of this study was to evaluate the level of type 70 heat shock protein in mothers with complicated and uncomplicated preeclampsia.

Methodology

This research was conducted in years 2017-2018 on all pregnant women with preeclampsia admitted to the educational and therapeutic center of Alavi hospital in Ardebil. Eighty people were included in the study. The research inclusion criteria included gestational age of 28 weeks with preeclampsia diagnosis (blood pressure equal to or greater than 140.190 mmHg after 20 weeks of gestation or proteinuria 300 mg or more in 24 hours or +1 or (in the urine test) in randomized urine samples or thrombocytopenia, sudden weight gain, impaired LFT, headache or epigastric pain). They were included into study using convenient sampling method.

A checklist was prepared from the people included into study. Based on the informed consent of the subjects, 3 cc of blood was collected. After separating the serum, samples were stored at -20 ° C until after the completion of the sampling. Then, it was measured in the same conditions of plasma level of HSP70 by ELISA method. They were followed up by the end of pregnancy. Finally, a group was candidate for termination of pregnancy due to simple preeclampsia, and one group was candidate for termination of pregnancy due to the complications considered in the study (fetal death, preterm labor, IUGR, HELLP and eclampsia). Then, the level of HSP70 measured at the beginning of the study was compared in both groups at the same gestational age (gestational age at the beginning of study).

In the first section of checklist, the characteristics of subjects such as the gestational age and the patient's age were determined separately if had any of preeclampsia criteria (high pressure, headache, blurred vision, chest pain). The HSP70 level was also measured and recorded. In the second section of the checklist, preeclampsia complications such as fetal growth retardation (neonates whose birth weight is below 10% of community weight at reproductive age), fetal death, eclampsia (the onset of seizure in pregnant women with preeclampsia), HELLP (hemolysis, high liver enzymes and low platelet) and preterm delivery (deliveries before the 37th week) were determined and recorded.

Data were analyzed by SPSS16 software, independent t-test and Mann-Whitney test. The significance level for all tests was considered $p < 0.05$.

Results

In this study, the total mean of gestational age at termination of pregnancy was 33.99 ± 3.54 weeks (32.30 ± 2.88 in complicated group and 36.06 ± 3.17 in the uncomplicated group). The lowest and highest gestational age of the subjects was 28 and 40 weeks, respectively. A significant difference was found between two groups in terms of gestational age at termination of pregnancy using independent t-test ($p = 0.001$). Table 1 shows the pregnancy age of the subjects at termination of pregnancy.

Table 1: Comparison of gestational age of the subjects at termination of pregnancy (week)

gestational age		28	29	30	31	32	33	34	35	36	37	38	39	40
n	complicated	2	5	10	3	3	5	6	7	0	0	1	1	1
	uncomplicated	1	1	1	2	0	1	2	3	6	9	3	0	7
total		3 (8.3%)	6 (5.7%)	11 (8.13%)	5 (3.6%)	3 (8.3%)	6 (5.7%)	8 (10%)	10 (5.12%)	6 (5.7%)	9 (3.11%)	4 (5%)	1 (3.1%)	8 (10%)

In this study, 80 patients were studied, which 5 patients (3.6%) had HELLP syndrome, 16 patients (20%) had intrauterine growth retardation (28%), 23 patients (28%) had preterm labor, and 36 patients (45%) had no complication. Fetal death and eclampsia were not seen in our study. The results showed that serum level is significantly associated with HELLP syndrome and intrauterine growth retardation. The results of Kruskal Wallis test revealed a significant difference between the groups studied (p = 0.001). The results are presented in Table (2).

Table 2: Distribution of complications in patients studied

Complications		n	%
Complicated	HELLP	5	3/6
	IUGR	16	20
	Preterm labor	23	28
Uncomplicated		36	45

In this research, the mean serum level of HSP70 was 18.95 ± 9.84 in patients (22.69 ± 11.72 in complicated group and 14.37 ± 3.32 in uncomplicated group). The lowest and highest level was 10.32 and 70.118, respectively. The results of the Mann-Whitney test showed that there was a statistically significant difference between the two groups in terms of serum level of HSP70 (p = 0.001). Tables 3 and 4 present the serum level of HSP70 in the groups studied.

Table 3: Serum level of HSP70 s in the groups studied (ng / ml)

	Group	Lower limit	Upper limit	Mean and SD
Serum level of HSP70	HELLP	9.23	14.54	87.12±19.41
	IUGR	34.14	514.36	15.5±708.20
	Preterm delivery	63.12	12.70	50.11±05.20

Table 4: Serum level of HSP70 in complicated preeclampsia groups (ng / ml)

	Group	Lower limit	Upper limit	mean	SD	median
Serum level of HSP70	complicated	627.12	118.70	69.22	72.11	49.19
	uncomplicated	32.10	189.27	37.14	32.3	06.13

The results of post hoc non-parametric test also showed a significant difference between the groups of patients with and without complication (Table 5).

Table 5: Comparison of the studied groups in terms of serum level of HSP70

Preterm labor	IUGR	HELLP	
0.018	0.012	0.001	significance

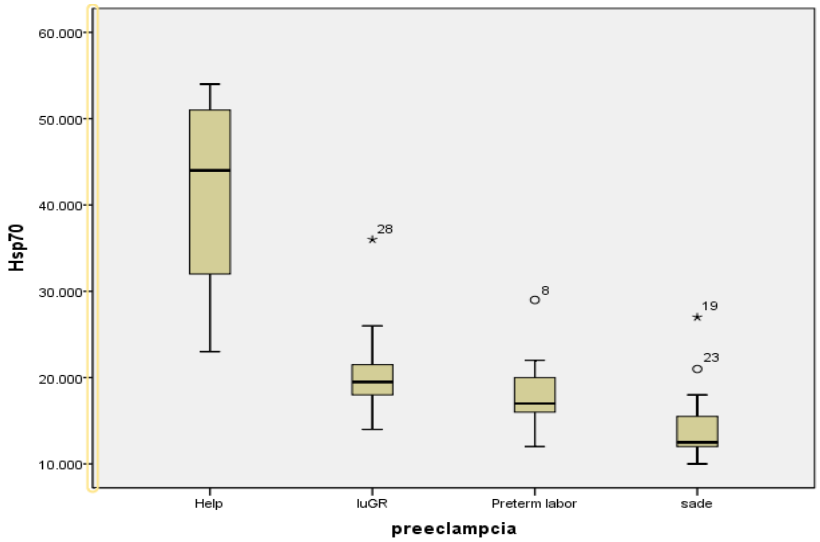

Diagram 1: The mean serum level of HSP70 in the studied groups (ng / ml)

Discussion

Delivery is a definite cure for preeclampsia and the main goals of treatment are as follows: prevention of seizures, prevention of intracranial hemorrhage and prevention of severe injury to other vital organs and the birth a healthy neonate. If the fetus is certainly or probably premature, physicians will tend to postpone the delivery, hoping that adding a few weeks to intrauterine life will reduce the risk of neonate's death or severe disability. Adopting this approach is certainly wise in mild cases (Cuningham et al., 2005). In this study, the mean gestational age in patients was 33.99 ± 3.54 (32.30 ± 2.88 in the complicated group and 36.06 ± 3.17 in the uncomplicated group) and this difference was statistically significant. This difference can be attributed to higher number of preterm deliveries in the complicated group compared with that in uncomplicated group. In a study conducted by Yang et al. (2006) in China, the results showed that early onset of severe preeclampsia, as a result, termination of pregnancy in the 32nd week are associated with poor maternal and perinatal outcomes (Yang et al., 2006).

Out of 80 patients, 6.5% (n=5) had HELLP syndrome, 20% (n=16) had intrauterine growth retardation, 28% (n=23) had preterm labor and 45% (n=36) had no complication.

Preeclampsia, especially in advanced stages associated with is associated with severe reduction in uterine placental perfusion, is associated with higher prevalence of small for gestational age (SGA) (Prakash et al., 2006; XU-xiong, 2000). In a study conducted by Jaquin Min et al, it was found that LBW level in people with hypertension was higher than that in people with normal blood pressure. It should be noted that hypertension before 26 weeks of gestation had no effect on fetus weight. Since 26th week onwards, preeclampsia is involved in low birth weight, while gestational hypertension between the weeks 28 and 34 causes weight loss in the fetus and does not affect before and after it. Preeclampsia added in the weeks 28 to 34 affects birth weight. In patients with gestational hypertension or preeclampsia during term, both birth weight gain and birth weight loss have been seen (Jacquemyn et al., 2006).

The serum level of HSP70 was 22.69 ± 11.72 in the uncomplicated group and 14.37 ± 3.32 in the uncomplicated group. There was a statistically significant difference between the two groups in terms of serum level of HSP70. In addition, Ekambaram et al (2011) estimated 35 patients with preeclampsia and 35 healthy pregnant women and stated that the level of HSP70 in endothelial cells in patients with preeclampsia is significantly higher than that in healthy subjects (Ekambaram, 2011). This result is consistent with that of this study.

In the study conducted by Cirque et al. (2002), serum level of HSP70 was measured in both case and control groups and a higher serum level of HSP70 was observed in patients with severe preeclampsia, so that HSP 70 level was 2.82 in patients with serum preeclampsia, but it was reported to be 10.1 ng / mL (Jirecek et al., 2002) in control group. This result is consistent with that of our study, but the serum level of HSP70 in our study was slightly higher than that obtained in the Cirque study, which was probably due to the greater severity and complication of the patients in our study as well as difference resulted from laboratory kits and equipment.

One of the studies inconsistent with our study is Livingstone et al. (2002), which examined the serum level of HSP70 in two case (47 patients with severe preeclampsia) and control (51 healthy pregnant women) groups. The higher serum level of HSP70 in preeclampsia patients was not observed and the difference between the two groups was not statistically significant (Livingston et al., 2002), which might be due to the low sample size in the mentioned study. In a study conducted by Akbarzadeh et al (2015) on 31 patients with preeclampsia and 31 healthy pregnant women, serum level of HSP70 was not significantly different between the two groups (Akbarzadeh et al., 2015). In this research, no significant association was found between gestational age and serum level of HSP70. In a study conducted by Mulvarak et al. (2006), the serum level of HSP70 increased with increasing gestational age. It was also reported that increasing the serum level of HSP70 by increasing the gestational age may be due to increased loss of protein by growing placental trophoblastic villus (130, 25). However, this association was not found in the study conducted by Sogafi, which is in line with the result of our study (Saghafi et al., 2013).

Conclusion

Based on the results of this study, the complications of preeclampsia in patients can be reduced by evaluating the serum level of HSP70 in preeclampsia diagnosis time and with a higher number of pregnancy visits and fetus health tests.

References

Akbarzadeh-Jahromi M, Daneshyar Z, Aslani FS, Asadi N, Zare HR. Circulating Levels of Heat Shock Protein 70 in Women With Preeclampsia and Healthy Controls. Shiraz E-Medical Journal. 2015 Jun;16(6).

Chadha G, Sood D. Hellp Syndrome-Revisited. Apollo Medicine. 2009; 6(3): 242-6.

Cuningham F Gary, Hauth C John, Leveno J Kenneth. Hypertensive disorders: Williams obstetrics, 22th ed. New York: Mccraw-Hill; 2005: 768.

Ekambaram P. HSP70 expression and its role in preeclamptic stress. Indian J Biochem Biophys 2011;48(4):243-55. Review.

El-Said MH, El-Ghaffar Mohamad NA, Ahmad S. Serum heat shock protein 70 levels in pre-eclampsia and adverse pregnancy outcomes. Med J Cairo Univ 2009; 77(1):409-15.

Garovic VD, August P. Preeclampsia and the future risk of hypertension: the pregnant evidence. Curr Hypertens Rep 2013 Apr;15(2):114-21.

Heidrich MB, Wenzel D, von Kaisenberg CS, Schippert C, von Versen-Hoynck FM. Preeclampsia and longterm risk of cardiovascular disease: what do obstetrician-gynecologists know? BMC Pregnancy and Childbirth 2013 Mar 9;13:61.

Jacquemyn Y, Osmanovic F, Martens G. Preeclampsia and birthweight by gestational age in singleton pregnancies in Flanders, Belgium: a prospective study. Clin Exp Obstet Gynecol, 2006; 33(2):96-8.

Jirecek S, Hohlagschwandtner M, Tempfer C, Knöfler M, Husslein P, Zeisler H. Serum levels of heat shock protein 70 in patients with preeclampsia: a pilot-study. Wien Klin Wochenschr 2002 Aug 30;114(15-16):730-2.

Kalkunte S, Lai Z, Norris WE, Pietras LA,Tewari N, Boij R, et al. Novel approaches for mechanistic understanding and predicting preeclampsia. J Reprod Immunol 2009; 83(1-2):134-8.

Livingston JC, Ahokas R, Haddad B, Sibai M, Awaads R. Heat shock protein 70 is not increased in women with severe preeclampsia. Hypertens Pregnancy 2002;21(2):123-6.

Mohaupt M. Molecular aspects of preeclampsia. Mol Aspects Med. 2007; 28(2): 169-91.

Molvarec A, Prohaszka Z, Nagy B, Szalay J, Fust G, Karadi I, et al. Association of elevated serum heat-shock protein 70 concentration with transient hypertension of pregnancy, preeclampsia and superimposed preeclampsia: a case-control study. J Hum Hypertens 2006; 20(10):780-6

Prakash J, Pandey LK, Singh AK, Kar B. Hypertension in pregnancy: hospital based study.J Assoc Physicians India, 2006;54:273-8.

Reyes LM, Garcia RG, Ruiz SL, Camacho PA, Ospina MB, Aroca G, et al. Risk factors for preeclampsia in women from Colombia: a case-control study. PlLos One 2012;7(7):e41622.

Saghafi N, Hoseini Hoshyar A; Amel Jamedar S, Ghazanfari S; Namani H. Comparison of Serum Heat-Shock Protein 70 Levels in Pre-Eclampsia with Normal Pregnancy. Iranian Journal of Obstetrics, Gynecology and Infertility.2013; 16(17): 1-8

Walker JJ. Pre-eclampsia. Lancet .2000 ;356(9237):1260-5. Review.

Williams PJ, Morgan L.The role of genetics in pre-eclampsia and potencial pharmacogenomic interventions. Pharmacogenomics Pers Med 2012;5.37-51.

XU-xiong MB-Drph. Association of preeclampsia with high birth weight for gestational age. Am J Obstet and Gynecol; 2000, 183:148.

Yang Z, Wang JL, Huang P, Shi LY, Li R, Ye RH, et al. Study on different onset patterns and perinatal outcomes in severe preeclampsia. Z honghua Fu Chan Ke Za Zhi, 2006 May; 41(5):302-6.