Journal of Obstetrics, Gynecology and Cancer Research | ISSN: 2476-5848

Relationship between Adenosine Deaminase with Ectopic Pregnancy in Pregnant Women Referred to Motahari Hospital in Urmia (2017-2018)

Tahereh Behrouzi lak*, Behrouz Ilkhanizadeh, Somayeh Ghasemzadeh, Sahel Khalilzadeh

Reproductive Health Research Center, Urmia University of Medical Sciences, Urmia, Iran

Article Info

10.30699/jogcr.7.1.15

Received: 2021/04/22;
Accepted: 2021/06/07;
Published Online: 09 Sep 2021;

Use your device to scan and read the article online

Corresponding Information:
Tahereh Behrouzi lak,
Reproductive Health Research Center, Urmia University of Medical Sciences, Urmia, Iran
Email: t.behrooz2@yahoo.com

ABSTRACT

Background & Objective: One of the most common causes of maternal mortality in the first trimester of pregnancy is ectopic pregnancy (EP). Adenosine deaminase (ADA) plays an essential role in production, maturation and function of lymphoid cells, which is produced in all tissues of the body. Total serum adenosine deaminase levels decrease during normal pregnancy. Considering the importance of early detection of EP, this study aimed to investigate the relationship between adenosine deaminase and EP in pregnant women referred to Motahari Hospital in Urmia from 2017 to 2018.

Materials & Methods: This study consisted of two groups of patients including patients with EP as a case group and patients with normal pregnancy confirmed by sonography as a control group. The level of βHCG and serum ADA levels were compared in the two groups. P-values less than 0.05 were considered as significant.

Results: In this study, 94 pregnant women were enrolled, including 47 patients as control group with normal pregnancy and 47 patients as case group with EP. The mean ADA level in patients with EP and the control group were 12.21±8.17 IU/L and 8.44±6.21 IU/L (P=0.01), respectively. The mean βHCG level in women with EP was 3215.60±1400.71 mIU/mL. In women with normal pregnancy, it was 11926.96±3408.23 mIU/mL (P=0.001).

Conclusion: High levels of ADA can be helpful in the early diagnosis of EP.

Keywords: Adenosine deaminase, Early diagnosis of ectopic pregnancy, Ectopic pregnancy

Introduction

Achieving health promotion and reducing maternal mortality has been introduced as one of the Millennium Development Goals. Currently, one of the most common causes of maternal mortality in the first trimester of pregnancy is ectopic pregnancy (EP) **(1)**. Following fertilization and the passage of the pregnancy product through the fallopian tube, the blastocyst implants in the endometrial lining of the uterine cavity **(2)**. In an EP, the fetus is implanted in a location other than the uterine cavity and mostly in the fallopian tubes **(3)**.

Ectopic pregnancies account for 1 to 2 percent of all first-trimester pregnancies in the United States. This small share accounts for 6% of all pregnancy-related deaths **(2)** and, according to a report by the World Health Organization, 4.9% of maternal deaths are due to ectopic pregnancies **(1)**.

In recent decades, the prevalence of EP has been increasing in different countries due to the improvement of early detection methods and increasing risk factors for EP. The prevalence of EP in the general population of Iran in 2006 was equal to 1.9 per 1000 pregnancies and its prevalence after 2006 was estimated to be 3.7 per 1000 pregnancies, which indicates an increase in the prevalence in the last 10 years.

Despite this apparent increase in the prevalence of ectopic pregnancies, the mortality rate has decreased due to early detection, but its long-term complications are still high **(1)**.

Following a miscarriage, the chances of infertility and subsequent EP increase **(3)**. It also reduces the chance of a successful subsequent pregnancy **(4)**.

The main risk factors for EP vary in different countries depending on habits and social conditions. According to studies, the most important risk factors in Iran include previous EP, history of tubal ligation, use of intrauterine devices, and history of abdominal or pelvic surgery **(3)**.

EP is associated with high morbidity and mortality due to delayed diagnosis **(5)**. Transvaginal ultrasound in combination with serial βHCG levels is commonly used to diagnose EP **(6)**.

Despite the presence of high-resolution transvaginal ultrasound and serial βHCG checks, approximately 40-

50% of cases of EP are not initially diagnosed (7) and early detection of EP is still a major challenge for physicians (8).

Therefore, there is a fundamental need to find new markers and algorithms that are more sensitive and specific to the diagnosis of EP to minimize its life-threatening complications, including abdominal bleeding and the need for surgical intervention (5).

To date, several biomarkers have been studied for the early detection of EP, including implant and inflammatory markers (5). For example, one study evaluated Activin A levels, which were lower in ectopic pregnancies than in normal pregnancies (9). In another study, measurements of FSH, LH, estrogen, progesterone, prolactin, and testosterone were used for early detection of EP (6).

Adenosine Deaminase (ADA) is an enzyme essential for production, maturation, and function of lymphoid cells that are produced in all tissues of the body. ADA originates from the class of macrophages and monocytes and therefore reflects the involvement of the cellular immune system. Studies have shown that the enzymatic activity of ADA changes in response to diseases involving the cellular immune system, such as rheumatoid arthritis and lupus. In fact, this enzyme is considered an indicator of cellular immunity and a non-specific marker of T cell activity. Because there is an immune system adjustment during pregnancy, total serum levels of ADA decrease during normal pregnancy. On the other hand, the decrease in serum ADA activity in a normal pregnancy is probably due to an increase in pregnancy-related hormones such as cortisol and estradiol, which inhibit ADA (8).

Studies have shown that ADA levels in pregnant women with Hyperemesis gravidarum (HEG) and Preeclampsia are higher than normal pregnancies due to increased cellular immunity in preeclampsia and increased lymphocyte count in HEG. Since EP is not considered normal, it is thought that serum ADA levels in EP are higher than in normal pregnancies due to insufficient inhibition of cellular immunity compared to normal pregnancies (8).

In a study by Turkman *et al.* in 2016, the relationship between EP and ADA levels was measured compared to normal pregnancies. They were able to find an effective association between increased ADA activity and EP and found that ADA levels were higher than 10.95 IU/L as the optimal threshold with 56% sensitivity and 67% specificity predicts EP and higher levels of adenosine deaminase are valuable for early detection of EP (8).

Due to the high importance of early detection of EP and the existence of studies on the increasing levels of ADA in EP compared to normal pregnancies in the first weeks of pregnancy, we aimed to measure and compare serum ADA levels in individuals with EP and normal intrauterine pregnancy and to evaluate the role of ADA as a biomarker for early detection of EP.

Materials and Methods

The present study was a case-control study that was performed to compare the serum levels of ADA in individuals with and without EP in Shahid Motahari Medical Center in 2017. Two groups, including patients with non-ruptured EP as the case group and patients with live intrauterine pregnancy confirmed by ultrasound as the control group, were studied. Both groups of patients entered the study with informed consent. Demographic characteristics of patients including weight, body mass index, age, parity, history of previous abdominal surgery, and history of abortion were recorded. All patients underwent clinical examinations and pelvic examinations by the researchers and pregnancy ultrasounds were performed by the expert sonographer of the hospital.

Women with several pregnancies, smoking, any previously known systemic disease, under medication including assisted reproductive drugs, multiple pregnancies, threatened abortion or missed abortion, and no fetal heart rate on ultrasound was excluded from the study. Blood samples of 3 cc were taken from all patients to measure βHCG levels and serum ADA levels. Serum samples were frozen at a temperature of -70°C in the hospital laboratory and after sampling, the serum ADA level was measured using a kit (Diazyme, Germany) by colorimetric method. The two groups were compared in terms of serum ADA level.

Standard patient history forms were used and the required information was collected and reviewed. Before collecting the data, we obtained the informed consent of the participants to accept and cooperate with the appropriate attitude to enter the project, and also in the data checklists, we recorded the name of each patient with the appropriate code to respect the patient's privacy. To compare the mean serum ADA levels, an independent t-test was used and data analysis was performed using SPSS software 20 (SPSS Inc., Chicago, IL., USA).

Results

In this study, 94 pregnant women including 47 as a case group with EP and 47 as a control group with normal pregnancy were included.

The mean age of patients was 28.42±4.71 years and 28.08±5.01 years in the in the case group and the control group, respectively. According to the t-test, there was no significant difference between the ages of patients in the two groups (P=0.73).

The mean weight in the case group was 70.85±11.43 kg and in the control group was 69.94±10.97 kg. Statistical t-test did not show a significant difference between the mean ages of the two groups (P=0.69).

The mean height in the case group was 163.26±6.64 cm and in the control group was 162.04±05.07 cm.

There was no significant difference between the mean height of the two groups (*P*=0.31).

The mean body mass index was 26.51±3.54 kg in the case group and 26.59±3.62 kg/m2 in the control group. According to the t-test, there was no significant difference between the body mass index of the two groups (*P*=0.92) (Table 1).

In the case group, 19 patients (40.4%) had a history of previous surgery and in the control group, 11 patients (23.4%) had a history of previous surgery. According to Chi-square statistical test, there was no significant difference between the history of surgery of the two groups (*P*=0.07) (Table 2).

According to the Pearson correlation coefficient, there was no significant relationship between βHCG level and ADA level in women with EP. Also, according to the same test, there was no significant relationship between βHCG levels and endometrial thickness. Pearson correlation coefficient test showed that ADA level was not significantly related to endometrial thickness (Table 3).

The mean ADA level in patients with EP was 12.21±8.17 IU/L and in the control, group was 8.44±6.21 IU/L. According to the t-test, there is a significant difference between ADA levels of the two groups (*P*=0.01) (Table 4).

The mean βHCG level in women with EP was 3215.60±1400.71 mIU/mL and 11926±3408.23 mIU/mL in women with normal pregnancies. According to the T-test, there was a significant difference between the levels of βHCG in women with EP pregnancy and normal pregnancy (*P*=0.01) (Table 5).

According to the ROC chart, ADA at the level of 10.50 IU/L indicates an abnormal pregnancy. In this study, ADA has a sensitivity of 42% and a specificity of 86% (Figure 1).

Table 1. Comparison of demographic characteristics of patients in the two groups

Variable	Ectopic pregnancy	Normal pregnancy	P-value
Mean age (years)	28.42±4.71	28.08±5.01	0.73
Mean weight (kg)	70.85±11.43	69.94±10.97	0.69
Mean height (cm)	163.26±6.64	162.04±5.07	0.31
Mean body mass index	26.51±3.54	26.59±3.62	0.92

Table 2. Distribution of absolute and relative frequency of surgical history in the two groups

Variable	History of surgery		Total
	Negative	Positive	
Case group	(59.6 %) 28	(40.4 %) 19	47
Control group	(76.6 %) 36	(23.4 %) 11	47
Total	(68.1 %) 64	(31.9 %) 30	94
P-value = 0.07			

Table 3. Relationship between βHCG level and ADA level; ADA levels & βHCG level with endometrial thickness

Variable	Control group		Case group	
	P-value	The correlation coefficient	P-value	The correlation coefficient
βHCG level with ADA level	0.54	0.09	0.95	0.008
βHCG level with endometrial thickness	0.69	0.06	0.65	0.06
ADA level with endometrial thickness	0.4	0.12	0.8	0.03

Table 4. Comparison of the mean and standard deviation of ADA level in the two groups

Variable	Abnormal pregnancy	Normal pregnancy	P-value
Mean ADA	12.21±8.17	8.44±6.21	0.01

Table 5. Comparison of mean and standard deviation of βHCG levels in the two groups

Variable	Abnormal pregnancy	Normal pregnancy	P-value
Mean βHCG	3215.60±1400.71	11926.96±3408.23	0.01

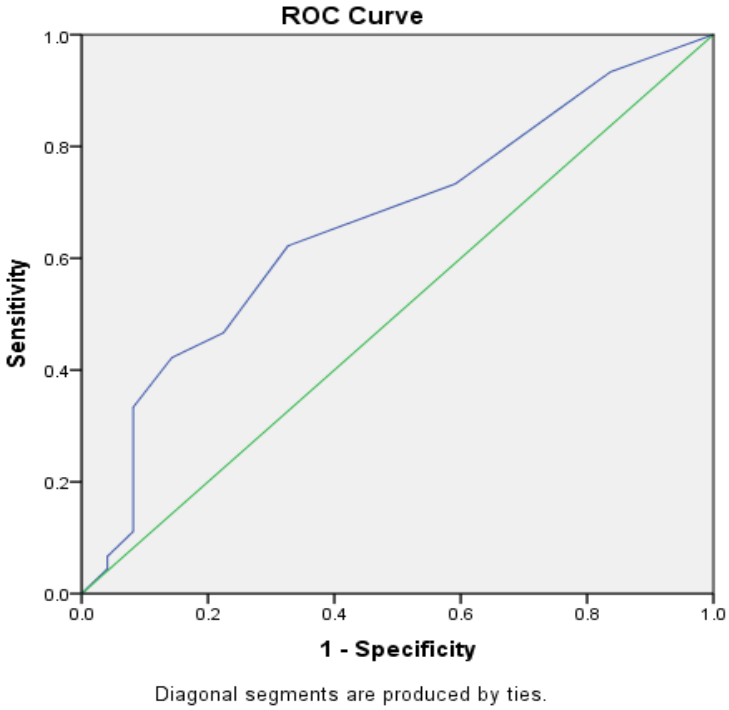

Figure 1. Determination of ADA levels for ectopic pregnancy

Discussion

Due to the high importance of early detection of EP and the existence of studies on the increase of ADA levels in EP compared to normal pregnancies in the first weeks of pregnancy, we decided to measure and compare serum ADA levels in individuals with EP and normal intrauterine pregnancy and to evaluate the role of ADA as a biomarker for early detection of EP.

In this study, 94 pregnant women, including 47 as a control group (normal pregnancy) and 47 as a case group (EP) have participated. The mean βHCG level in women with EP was 3215.60±1400.71 mIU/mL and in women with normal pregnancy was 11926±3408.23 mIU/mL. There was a significant difference between the βHCG level of women with EP and normal pregnancy (P=0.01).

In a study, Kohn *et al.* reported that the distribution of βHCG levels in patients with EPs and abnormal intrauterine pregnancies was similar and much lower than the distribution of βHCG levels in patients with normal intrauterine pregnancies **(10)**.

In another study by Chun Feng and colleagues, patients with EP were reported to have lower levels of βHCG changes than the ones with intrauterine pregnancies **(6)**. In this study, the mean ADA level in patients with EP was 12.21±8.17 IU/L and in the control group was 8.44 ± 6.21 IU/L; there was a significant difference between the ADA level of the two groups (P=0.01).

In a study by Turkman *et al.* ADA's role in the early diagnosis of EP was evaluated. They reported that serum ADA levels were higher in patients with EP (10.9±0.3 IU/L) than in the control group (9.2±3.6 IU/L), (P=0.01). Moreover, ADA levels higher than 10.95 IU/L as the optimal threshold with 56% sensitivity and 67% specificity could predict EP and higher levels of ADA are valuable for early detection of EP **(8)**.

The results of the abovementioned study are in line with the results of ours. Based on the ROC diagram, we examined the ADA level to determine EP and according to the ROC diagram, the ADA level of 9.5 IU/L was identified as the risk of EP with 42% sensitivity and 86% specificity.

In a study by Turkmen *et al.*, the ADA level of 10.95 IU/L was expressed as a risk factor for EP with a sensitivity of 56% and a specificity of 67%, predicting an EP which is consistent with our study.

Conclusion

According to the results, it seems that in women with the EP risk factor, ADA tests should be checked in the first weeks of pregnancy. In case of ADA level disorders, necessary measures should be taken to follow up and terminate the pregnancy to reduce the risk of dangerous complications of EP such as ruptured tubes, bleeding, and death. High levels of ADA can be helpful in the early diagnosis of EP.

Acknowledgments

The authors thank the staff of the obstetrics and gynecology department of Mahzad Hospital, Urmia, for their help and suggestions.

Conflict of Interest

Authors declared no conflict of interest.

References

1. Hasani M, Keramat A, Khosravi A, Oshrieh Z, Hasani M. Prevalence of ectopic pregnancy in Iran: a systematic review and meta-analysis. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2016;19(23):15-23. [DOI:10.5812/ircmj.40856]
2. Cunningham F, Leveno K, Bloom S, Spong CY, Dashe J. Williams obstetrics, 24e: Mcgraw-hill New York, NY, USA; 2014.
3. Parashi S, Moukhah S, Ashrafi M. Main risk factors for ectopic pregnancy: a case-control study in a sample of Iranian women. International journal of fertility & sterility. 2014;8(2):147-54.
4. Asnafi N , Hajian K , Shahriyari M , Taheri B Risk factors in ectopic pregnancy: a case - control study. Journal of Gorgan University of Medical Sciences. 2012;14(2):52-7.
5. Dhiman P, Senthilkumar GP, Rajendiran S, Sivaraman K, Soundararaghavan S, Kulandhasamy M. Serum activin B concentration as predictive biomarker for ectopic pregnancy. Clin Biochem. 2016;49(7-8):609-12. [DOI:10.1016/j.clinbiochem.2015.11.024]
6. Feng C, Chen ZY, Zhang J, Xu H, Zhang XM, Huang XF. Clinical utility of serum reproductive hormones for the early diagnosis of ectopic pregnancy in the first trimester. J Obstet Gynaecol Res. 2013;39(2):528-35. [DOI:10.1111/j.1447-0756.2012.02001.x]
7. Refaat B. Role of activins in embryo implantation and diagnosis of ectopic pregnancy: a review. Reproductive Biology and Endocrinology. 2014;12(1):116. [DOI:10.1186/1477-7827-12-116]
8. Turkmen G, Karçaaltıncaba D, Isık H, Fidancı V, Kaayalp D, Tımur H, et al. Does adenosine deaminase activity play a role in the early diagnosis of ectopic pregnancy? Journal of Obstetrics and Gynaecology. 2016;36(3):347-50. [DOI:10.3109/01443615.2015.1065228]
9. Júnior JE, Oliveira LG, Fernandes Silva MO, Araujo Júnior E, Camano L. Serum activin A levels and tubal ectopic pregnancy. International Journal of Reproductive BioMedicine. 2014;12(3):227-8.
10. Kohn MA, Kerr K, Malkevich D, O'Neil N, Kerr MJ, Kaplan BC. Beta-human chorionic gonadotropin levels and the likelihood of ectopic pregnancy in emergency department patients with abdominal pain or vaginal bleeding. Acad Emerg Med. 2003;10(2):119-26. [DOI:10.1197/aemj.10.2.119].

How to Cite This Article:

Behrouzi lak T, Ilkhanizadeh B, Ghasemzadeh S, Khalilzadeh S. Relationship Between Adenosine Deaminase with Ectopic Pregnancy in Pregnant Women Referred to Motahari Hospital in Urmia (2017-2018). J Obstet Gynecol Cancer Res. 2022; 7 (1) :15-19.

Download citation:
BibTeX | RIS | EndNote | Medlars | ProCite | Reference Manager | RefWorks