

Serum adenosine deaminase and its isoenzyme activities in pregnancy

Gebelerde serum adenozin deaminaz ve izoenzim aktivitesi

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Abstract

Objective: ADA is widely distributed in human tissues, which may contribute to the maturation of the immunological system, especially the proliferation and differentiation of lymphoid cells, and seems to be critical at different stages of the maturation process. The activity of ADA changes in diseases characterized by the alteration of cell-mediated immunity. In this study we examined changes in serum total ADA activity and the patterns of two ADA isoenzymes, ADA-1 and ADA-2, in healthy pregnant women, and evaluated the possible role of the alteration of cell-mediated immunity during pregnancy as causes of changes in ADA activity.

Materials and Methods: We measured serum activities of total ADA, ADA-1 and ADA-2 in healthy pregnant women (n=129) and age-matched healthy nonpregnant women (n=42). We divided the study group into three different subgroups: first trimester, second trimester and third trimester.

Results: Serum ADA, ADA-1 and ADA-2 activities in healthy pregnant women were significantly lower than in nonpregnant women (p<0.001, p<0.001 and p<0.01 respectively). ADA (p<0.001) and ADA-2 (p<0.001) activities in the first trimester were significantly lower than in the control group. However, there were no significant differences between the first trimester and control group according to their ADA-1 activities (p=0.016). ADA (p<0.001), ADA-1 (p<0.001) and ADA-2 (p<0.008) activities in the second trimester were significantly lower than in the control group. Combined trisomy 21 risk, biochemical trisomy 21 risk, age risk and trisomy 18 + Nuchal translucency (NT) risk were calculated using a first trimester screening test in 63 pregnant women. Furthermore, trisomy 21 risk, age risk and trisomy 18 risk were calculated by triple test in 52 pregnant women. ADA, ADA-1 and ADA-2 activities were not significantly correlated with risks in the first trimester screening test. ADA-1 activity was slightly significantly negative correlated with age risk (r= -0.314, p<0.05) and trisomy 18 risk (p<0.05) in the triple test. ADA (p<0.05) and ADA-2 (p<0.05) activities were slightly significantly correlated with gestational age, while there was no significant correlation between ADA-1 activity and gestational age.

Conclusion: Serum ADA activity may be useful for clinical diagnosis and observation of high-risk pregnancies in which cell-mediated immunity has been altered. (J Turkish-German Gynecol Assoc 2011; 12: 209-13)

Key words: Adenosine deaminase, immunity, pregnancy

Received: 13 May, 2011

Accepted: 16 September, 2011

Özet

Amaç: ADA insan dokularında yaygın bir dağılım göstermektedir. ADA immünolojik sistemin olgunlaşmasına, özellikle lenfoid hücrelerin çoğalma ve farklılaşmasına katkıda bulunur ve olgunlaşma işleminin farklı aşamalarında kritik bir rol oynar. ADA aktivitesi hücre-aracılı immünitenin değiştiği hastalıklarda değişmektedir. Bu çalışmada sağlıklı gebe kadınlarda serum total ADA ve ADA izoenzim (ADA-1 ve ADA-2) aktivitelerini inceledik ve gebelik boyunca ADA aktivitesinde değişikliklere neden olan hücre-aracılı immünitedeki değişikliklerin olası rollerini değerlendirdik.

Gereç ve Yöntemler: Sağlıklı gebe kadınlarda (n=129) ve yaşça uyumlu sağlıklı gebe olmayan kadınlarda (n=42) serum total ADA, ADA-1 ve ADA-2 aktivitelerini ölçtük. Çalışma grubunu 1. trimester, 2. trimester ve 3. trimester olmak üzere üç farklı gruba ayırdık.

Bulgular: Gebe grubunun ADA, ADA-1 ve ADA-2 değerleri, kontrol grubunun değerlerine göre anlamlı olarak daha düşük bulundu (ADA ve ADA-1 için p<0.001, ADA-2 için p<0.01). 1. trimester'e ait ADA (p<0.001) ve ADA-2 (p<0.001) değerleri, kontrol grubunun değerlerinden anlamlı olarak düşük bulundu. Fakat ADA-1 değerleri açısından kontrol grubu ile 1. trimester arasında anlamlı bir fark bulunamadı (p=0.016). 2. trimester'e ait ADA (p<0.001), ADA-1 (p<0.001) ve ADA-2 (p<0.008) değerleri, kontrol grubunun değerlerinden anlamlı olarak düşük bulundu. 63 gebe kadında, 2'li test kullanılarak kombine trizomi 21 riski, biyokimyasal trizomi 21 riski, yaş riski ve trizomi 18 + Nuchal translucency (NT) riski hesaplandı. Ayrıca, 52 gebe kadında 3'lü test kullanılarak trizomi 21 riski, yaş riski ve trizomi 18 riski hesaplandı. 2'li test riskleri ile ADA, ADA-1 ve ADA-2 arasında bir ilişki bulunamadı. 3'lü teste ait yaş riski (r= -0.314, p<0.05) ve trizomi 18 riski (r= -0.314, p<0.05) ile ADA-1 arasında negatif yönde zayıf bir ilişki tespit edildi. 3'lü teste ait diğer riskler ile ADA, ADA-1 ve ADA-2 arasında anlamlı bir ilişki bulunamadı. Gestasyonel yaş ile ADA (r=0.201, p<0.05) ve ADA-2 (r=0.195, p<0.05) arasında zayıf bir ilişki tespit edildi fakat gestasyonel yaş ile ADA-1 arasında anlamlı bir ilişki tespit edilemedi.

Sonuç: Serum ADA aktivitesi hücre-aracılı immünitenin değiştiği yüksek riskli gebeliklerin teşhis ve incelenmesinde faydalı olabilir.

(J Turkish-German Gynecol Assoc 2011; 12: 209-13)

Anahtar kelimeler: Adenozin deaminaz, immünite, gebelik

Geliş Tarihi: 13 Mayıs 2011

Kabul Tarihi: 16 Eylül 2011

Introduction

Adenosine deaminase (adenosine aminohydrolase, EC 3.5.4.4.; ADA) is an enzyme in the purine salvage pathway which is primarily responsible for the intracellular disposition of transported adenosine (1). ADA catalyzes the irreversible hydrolytic deamination of adenosine and 2-deoxyadenosine to inosine and 2-deoxyinosine, respectively (2). ADA is an important enzyme that participates in the degradative pathways of adenosine monophosphate (AMP), a purine nucleotide (3). Patients who inherently lack this enzyme have defects in both humoral and cellular immunity that are manifested as severe combined immunodeficiency disease (1). When ADA fails to catalyze the deamination of adenosine, those compounds that accumulate are readily converted into their respective nucleotides. Deoxyadenosine triphosphate (dATP) is one of the nucleotides generated in this way. In ADA deficiency, deoxyadenosine accumulates intracellularly as dATP. dATP has been recognized as the toxic metabolite in the immunodeficiency disease associated with ADA deficiency. This compound is a potent inhibitor of DNA replication, because it prevents the synthesis of deoxyribonucleotides from ribonucleotides by interference with ribonucleotide reductase (3).

ADA is widely distributed in human tissues, and it is detected in high levels particularly in lymphoid tissues (4). Furthermore, ADA may contribute to the maturation of the immunological system, especially the proliferation and differentiation of lymphoid cells, and seems to be critical at different stages of the maturation process (1). Thus it has been considered as an indicator of a nonspecific marker of T-cell activation (5). ADA has been used for monitoring several diseases in which immunity has been altered. As an indicator of cellular immunity, the serum activity of this enzyme has been suggested to be altered in diseases that cause a cell-mediated immune response such as rheumatoid arthritis, systemic lupus erythematosus and tuberculosis (5). On the other hand, it has been shown that serum ADA activity was increased in several diseases where cellular immunity is stimulated. Lymphocytes or the monocyte-macrophage cell system have been assumed to contribute to changes in serum ADA activity, however, the exact mechanisms by which serum ADA activity is altered has not been elucidated (2, 5).

Human ADA exists in at least three molecular isoforms, ADA-1, ADA-2 and ADA-1 and ADA-complexing protein. Although ADA-1 is present in almost all human tissues and cells, ADA-2 is the predominant isoenzyme in the serum of normal subjects. The majority of ADA activity is derived from ADA-1. Most human cells contain very small amounts of ADA-2 and its tissue sources may be lymphocytes or the monocyte-macrophage cell system (2). It is assumed that ADA-1 arises mainly from injured tissues or cells, while ADA-2 primarily derives from stimulated T-cells (4). Adenosine and 2-deoxyadenosine are molecules with many effects on human cells. Thus, the homeostasis of these substances and the activity of the isoenzymes, ADA-1 and ADA-2, in human cells are of extreme importance (6).

Pregnancy is an immunological balancing act in which the maternal immune system has to remain tolerant of paternal

human leucocyte antigens (HLA) expressed by the fetus and yet maintain normal immune competence for defense against microorganisms (7, 8). Immunologically, the human fetus has always been considered as an allograft to the pregnant mother (8). Despite being biological allografts, fetuses are not normally rejected by the maternal immune system. One likely explanation for this phenomenon is that the fetoplacental unit is an immunologically privileged site that creates a mechanical barrier which reduces interactions between fetal tissues and maternal lymphocytes, and/or functionally impairs the maternal immune response (9). Cytokine-secreting T cells play a central role in the immune response and have been classified into subsets based on their type of cytokine production. T helper 1 cells synthesize mainly interleukin-2 (IL-2) and interferon gamma, which induce cellular immunity. T helper 2 cells produce predominantly IL-4, -5, -6 and -10, which promote humoral immunity. The shift of Th1/Th2 balance to Th2 predominance occurs in normal pregnancy and appears to protect the fetus and placenta from being rejected and to aid in the maintenance of normal pregnancy (10). The deviation of the immune response from Th1 to Th2 may leave the mother more open to infection whose control is Th1-dependent, but increased production of Th1 cytokines has been linked to spontaneous abortion and small-for-date babies (7). Not only T cells, but also B cells, decrease during pregnancy, and serum levels of IgG, IgM and IgA also decrease during pregnancy (11). In this study, we analyzed changes in serum total ADA activity and the patterns of two ADA isoenzymes, ADA-1 and ADA-2, in healthy pregnant women and evaluated the possible role of the alteration of cell-mediated immunity during pregnancy as causes of changes in ADA activity. We also performed prenatal screening tests in pregnant women and calculated prenatal risks by the Prisca package program, and studied a possible correlation between prenatal risks and serum ADA activity and its isoenzyme pattern in pregnant women.

Materials and Methods

One hundred and twenty-nine healthy pregnant women from the department of gynecology and obstetric of Haseki Education and Research Hospital, were analyzed. Among the 129 healthy pregnant women, 38 were in the first trimester, 79 were in the second trimester, and 12 were in the third trimester. The inclusion criteria for eligibility were as follows; a singleton fetus, normal fetal anatomy, well-established gestational age corroborated by ultrasonography, nonsmoker, no evidence of recent infection, no prescribed medication and no maternal medical complications. In this study, 42 age and sex-matched healthy nonpregnant women with no known history of any disease were taken as controls. The informed written consents were obtained from each patient and healthy controls.

A blood sample was taken from the antecubital vein, which was then centrifuged at 3000xg for 10 min. within half an hour and stored at -20°C until assay. Stability of the ADA enzyme in the serum lasts 24 hours at 25°C, 7 days at 4°C and 3 months at -20°C. ADA, ADA-1 and ADA-2 activities of all serum samples were measured. Furthermore, pregnancy associated plasma

Table 1. Demographic characteristics of subjects

	All pregnant (n=129)	1. Trimester (n=38)	2. Trimester (n=79)	3. Trimester (n=12)	Control (n=42)
Age (year)	26.5±5.44	25.7±4.50	26.9±5.96	26.5±4.54	28.1±6.99
Weight (kg)	63.6±11.95	59.8±9.71	64.2±11.66	71.3±16.21	62.5±11.59

Table 2. Serum total ADA, ADA-1 and ADA-2 activities in healthy pregnant women and nonpregnant women (controls). Data are presented as mean±SEM

		All Pregnant (n=129)	1. Trimester (n=38)	2. Trimester (n=79)	3. Trimester (n=12)	Control (n=42)
ADA	Mean±SEM	33.93±0.47	32.97 ±0.76	34.10 ±0.64	35.91±1.45	39±0.99
IU/L	Median (min-max)	34 (23-51)	33 (25-42)	34 (23-51)	35 (26-45)	39 (28-55)
ADA -1	Mean±SEM	4.14±0.18	4.42 ±0.36	4±0.21	4.25±0.91	5.78±0.32
IU/L	Median (min-max)	4 (1-12)	4.5 (1-9)	4 (1-11)	4 (1-12)	5.5 (1-11)
ADA -2	Mean±SEM	29.79±0.44	28.55±0.70	30.10±0.58	31.66±1.65	33.21±0.92
IU/L	Median (min-max)	29 (20-44)	29 (20-37)	29 (21-44)	31 (25-43)	31.5 (22-45)

protein-A (PAPP-A) and free β -human chorionic gonadotropin (free β -hCG) used for the first trimester prenatal screening test were measured in the first trimester pregnant women. Alpha-fetoprotein (AFP), free estriol (FE3) and β -hCG used for triple test were measured in the second trimester pregnant women. Concentrations of PAPP-A, free β -hCG, AFP, FE3 and β -hCG were assayed using an automatic analyzer (Immolute 2500) with a commercial kit according to the instructions of the manufacturer (Siemens Medical Solutions Diagnostics Limited, Llanberis, Gwynedd. LL55 4EL United Kingdom). Measurement of these parameters were performed by a chemiluminescent immunometric assay which is based on the antibody sandwich complex method. Prenatal screening tests were evaluated using the Prisca package program (version 4.0.20.4) obtained from Siemens.

The manual kinetic ADA activity assay was optimized for the automated analyser (Konelab 60 I). For the determination of ADA activity, the ammonia produced by the enzymatic activity was coupled to 2-oxoglutarate by glutamate dehydrogenase. 2-oxoglutarate was activated by adenosine diphosphate (ADP). In this reaction, NADH was used as indicator and the reaction was followed by the decrease of absorbance at 340 nm. This method was developed by Ellis (12). To distinguish ADA-1 from ADA-2, the activity was measured using the same techniques with Erythro-9 (2-hydroxy-3-nonyl) adenine (EHNA) which is a potent inhibitor of only ADA-1 isoenzyme, showing the ADA-2 activity. The activity of ADA-1 was calculated by subtracting the ADA-2 activity from total ADA activity. All chemicals for ADA assay were obtained from Sigma.

Statistical analysis

Statistical analyses were carried out using the SPSS 17.0 (SPSS Inc., Chicago, IL, USA) software. Results were expressed as the mean±standard error of the mean (SEM) and as the median and range. Distributions of the groups were analyzed with the Kolmogorov-Smirnov test. Because all groups did not show normal distribution, nonparametric statistical methods were

Table 3. Serum total ADA, ADA -1 and ADA -2 activities in pregnant and control group

	All Pregnant (n=129)	Control (n=42)	p
ADA	33.93±0.47	39±0.99	<0.001
ADA -1	4.14±0.18	5.78±0.32	<0.001
ADA -2	29.79±0.44	33.21±0.92	<0.01

used to analyse the data. The Kruskal-Wallis test was used for skewed data, and data obtained from the study groups were compared by the nonparametric Mann-Whitney U test. Bonferroni's test was used to evaluate the repeated measurements. Spearman correlation analysis was performed to evaluate relations between variables.

Results

Demographic data are given in Table 1. Serum total ADA, ADA-1 and ADA-2 activities are shown in Table 2. Serum ADA, ADA-1 and ADA-2 activities in healthy pregnant women were significantly lower than those of nonpregnant women ($p<0.001$, $p<0.001$ and $p<0.01$, respectively). Table 3 summarizes the ADA activities in both pregnant and nonpregnant groups. ADA ($p<0.001$) and ADA-2 ($p<0.001$) activities in the first trimester were significantly lower than those in the control group. However, there was no significant difference between the first trimester and control group according to their ADA-1 activities ($p=0.016$). ADA ($p<0.001$), ADA-1 ($p<0.001$) and ADA-2 ($p<0.008$) activities in the second trimester were significantly lower than those of the control group. There was no significant difference between the third trimester and control group, and between each trimester of pregnancy with respect to their ADA, ADA-1 and ADA-2 activities. These comparison results are given in Table 4.

Combined trisomy 21 risk, biochemical trisomy 21 risk, age risk and trisomy 18 + Nuchal translucency (NT) risk were calculated

Table 4. Comparison of results between each trimester of pregnancy and control group, and among each trimester of pregnancy according to their ADA, ADA -1, and ADA -2 activities

	ADA	ADA -1	ADA -2
Control - 1. Trimester	<0.001	0.016	<0.001
Control - 2. Trimester	<0.001	<0.001	<0.008
Control - 3. Trimester	0.166	0.040	0.478
1. Tri - 2. Tri	0.417	0.291	0.196
1. Tri - 3. Tri	0.086	0.542	0.118
2. Tri - 3. Tri	0.230	0.877	0.356
Differences were considered significant a $p < 0.008$ according to Bonferroni's correction			

using the first trimester screening test in 63 pregnant women. Furthermore, trisomy 21 risk, age risk and trisomy 18 risk were measured by the triple test in 52 pregnant women. ADA, ADA-1 and ADA-2 activities were not significantly correlated with risks in the first trimester screening test. ADA-1 activity was slightly significantly negative correlated with age risk ($r = -0.314$, $p < 0.05$) and trisomy 18 risk ($r = -0.314$, $p < 0.05$) in the triple test. ADA, ADA-1 and ADA-2 were not significantly correlated with other risks in the triple test. Results in the correlation analysis are shown in Table 5 and Table 6. ADA ($r = 0.201$, $p < 0.05$) and ADA-2 ($r = 0.195$, $p < 0.05$) activities were slightly significantly correlated with gestational age, while there was no significant correlation between ADA-1 activity and gestational age.

Discussion

ADA is an essential enzyme for the differentiation of lymphoid cells, so changes in ADA activity reflect alterations in immunity (2). This enzyme is widely distributed in human tissues, especially in the lymphoid tissues (5). Normal pregnancy is characterized by depressed cell-mediated immunity in conjunction with enhanced humoral immunity, so serum ADA activity may be altered (10). In this study, we examined changes in serum total ADA activity and the patterns of two ADA isoenzymes, ADA-1 and ADA-2, in healthy pregnant women and they were compared with those of age-matched healthy nonpregnant women. We divided the study group into three different subgroups: first trimester, second trimester and third trimester. Serum ADA, ADA-1 and ADA-2 activities in healthy pregnant women were significantly lower than those of nonpregnant women ($p < 0.001$, $p < 0.001$ and $p < 0.01$ respectively). ADA ($p < 0.001$) and ADA-2 ($p < 0.001$) activities in the first trimester were significantly lower than those in the control group. However, there was no significant difference between the first trimester and control groups according to their ADA-1 activities ($p = 0.016$). ADA ($p < 0.001$), ADA-1 ($p < 0.001$) and ADA-2 ($p < 0.008$) activities in the second trimester were significantly lower than that in the control group. There was no significant difference between the third trimester and control groups and between each trimester of pregnancy according to their ADA, ADA-1 and ADA-2 activities. Jaqueti et al. found similar results (13). Our results were thus compatible with the literature.

Table 5. Correlation between risk in the first trimester screening test and ADA, ADA -1, and ADA -2

	r	p
ADA - Combined Trisomy 21 Risk	-0.045	0.72
ADA - Biochemical Tri. 21 Risk	-0.044	0.724
ADA - Age Risk	0.076	0.546
ADA - Trisomy 18 + NT Risk	-0.159	0.204
ADA 1- Combined Trisomy 21 Risk	-0.012	0.921
ADA 1-Biochemical Tri. 21 Risk	0.097	0.438
ADA 1- Age Risk	-0.043	0.734
ADA 1- Trisomy 18 + NT Risk	-0.161	0.197
ADA 2 - Combined Trisomy 21 Risk	-0.022	0.863
ADA 2 - Biochemical Tri. 21 Risk	-0.09	0.471
ADA 2- Age Risk	0.136	0.276
ADA 2- Trisomy 18 + NT Risk	-0.094	0.451

Table 6. Correlation between risk in the triple test and ADA, ADA -1, and ADA -2

	r	p
ADA - Trisomy 21 Risk	0.01	0.942
ADA - Age Risk	-0.028	0.844
ADA - Trisomy 18 Risk	-0.028	0.844
ADA 1- Trisomy 21 Risk	-0.228	0.101
ADA 1- Age Risk	-0.314	0.022
ADA 1- Trisomy 18 Risk	-0.314	0.022
ADA 2- Trisomy 21 Risk	-0.07	0.618
ADA 2- Age Risk	0.058	0.68
ADA 2- Trisomy 18 Risk	0.058	0.68

Yoneyama et al. (2) measured serum activities of total ADA, ADA-1 and ADA-2 in normal pregnant women in the third trimester and age-matched healthy nonpregnant women. The authors found that, in normal pregnant women, serum total ADA and ADA-2 activities were lower than those of the nonpregnant women, while there was no difference in ADA-1 activity. In the light of these results, they concluded that reduced serum total ADA activity might be reflected by decreased ADA-2 activity, which may be in part associated with depressed cell-mediated immunity during normal pregnancy (2). In our study, there was also no difference between third trimester and control groups according to their ADA-1 activity. Because no significant difference was found in ADA and ADA-2 activities between third trimester and control groups, our results differed from the findings of Yoneyama et al. (2). Therefore, we believe that this current study contributes to the literature. In a different study performed by Yoneyama et al. (10), they found results that were similar to ours.

Serum ADA activity in normal pregnant women was significantly lower than that in nonpregnant women. In addition, Oladipo

et al. (14) demonstrated that the mean serum ADA level in nonpregnant women was higher than that of normal pregnant women. Lee et al. (5) measured the catalytic values of serum ADA from normal pregnant women, who were divided into four groups according to the gestational age in weeks (Gwks) (Group I: 5-9 Gwks; Group II: 15-20 Gwks; Group III: 24-30 Gwks; Group IV: 30-39 Gwks). The serum ADA activity of group III was significantly higher than the other groups. The significant increase in ADA activity which was detected in Lee et al.'s study (5) during 24 to 30 gestational weeks may be associated with the fact that the increase in maternal cardiac output reaches its peak during the late second trimester to early third trimester and decreases in late pregnancy. In contrast, in the present study there was no significant difference among each trimester of pregnancy according to their ADA, ADA-1 and ADA-2 activities. Jaqueti et al. found results that were similar to ours (13). Our study were slightly different from Lee et al.'s study (5). However, the study population differed from that of our study, which may account for the discrepancy in the results. Lee et al. did not find significant correlation between the serum ADA activity and gestational age in normal pregnant women (5). On the contrary, in our study ADA and ADA-2 activities were mildly significantly correlated with gestational age, but there was no significant correlation between ADA-1 activity and gestational age.

Similar results for ADA activity have been reported in an animal study carried out by Chaudhry et al. (15). In this study, total serum ADA and ADA-2 activities were lower in pregnant than in nonpregnant buffaloes. However, ADA-1 activity did not differ between the pregnant and nonpregnant buffaloes. Similarly, the activities of total ADA, ADA-1 and ADA-2 did not differ among pregnant buffaloes of three trimesters. Our study is supported by these results.

Uslu et al. measured serum ADA activity in the second trimester pregnant women who were of advanced age and Down syndrome risk as compared with nonpregnant women (16). In this study, serum ADA activity was lower in pregnant women with low Down syndrome risk, in all pregnant women and in pregnant women with high age risk and higher in pregnant women with high Down syndrome risk when compared to the control group. Since there were a few pregnant women with high Down syndrome risk in our study, we could not perform such comparison. However, in the present study, ADA, ADA-1 and ADA-2 activities were compared to the prenatal risks. ADA, ADA-1 and ADA-2 activities were not significantly correlated with risks in the first trimester screening test. ADA-1 activity was slightly significantly negatively correlated with age risk and trisomy 18 risk in the triple test. ADA, ADA-1 and ADA-2 were not significantly correlated with other risks in the triple test.

In conclusion, normal pregnancy is characterized by depressed cell-mediated immunity, so serum ADA activity and its isoenzyme pattern alter in normal pregnancy. That is, changes in serum ADA activity reflect changes in the immune system during pregnancy. Moreover, the clinical significance of changes in

ADA activity and the regulatory mechanisms that alter the activity of serum ADA have not been elucidated. Serum ADA activity may be useful for clinical diagnosis and observation of high-risk pregnancies in which cell-mediated immunity has been altered. Further studies are needed to evaluate the usage of ADA activity in pregnancy for prenatal screening test and to determine the relationship between ADA activities and preeclampsia.

Conflict of interest

No conflict of interest was declared by the authors.

References

1. Yagawa K, Okamura J. Role of adenosine deaminase in activation of macrophages. *Infect Immun* 1981; 32: 394-7.
2. Yoneyama Y, Suzuki S, Sawa R, Otsubo Y, Miura A, Kuwabara Y, et al. Serum adenosine deaminase activity and its isoenzyme pattern in women with normal pregnancies. *Arch Gynecol Obstet* 2003; 267: 205-7.
3. Kutlar I, Aksoy F, Koyluoglu O, Ugur MG, Balat O, Tarakcioglu M. Adenosine deaminase activity in serum and placenta of patients with anembryonic pregnancies and missed abortions. *Arch Gynecol Obstet* 2005; 272: 124-6. [\[CrossRef\]](#)
4. Kurata N. Adenosine deaminase. *Nippon Rinsho* 1995; 53: 1178-83.
5. Lee SJ, Hwang HS, Kim BN, Kim MA, Lee JW, Park YW, et al. Changes in serum adenosine deaminase activity during normal pregnancy. *J Korean Med Sci* 2007; 22: 718-21. [\[CrossRef\]](#)
6. Gakis C. Adenosine deaminase (ADA) isoenzymes ADA-1 and ADA-2: diagnostic and biological role. *Eur Respir J* 1996; 9: 632-3. [\[CrossRef\]](#)
7. Weetman AP. The immunology of pregnancy. *Thyroid* 1999; 9: 643-6. [\[CrossRef\]](#)
8. Kumar V, Medhi B. Emerging role of uterine natural killer cells in establishing pregnancy. *Iran J Immunol* 2008; 5: 71-81.
9. Marzi M, Vigano A, Trabattini D, Villa ML, Salvaggio A, Clerici E, et al. Characterization of type 1 and type 2 cytokine production profile in physiologic and pathologic human pregnancy. *Clin Exp Immunol* 1996; 106: 127-33. [\[CrossRef\]](#)
10. Yoneyama Y, Sawa R, Suzuki S, Yoneyama K, Doi D, Araki T. Relationship between adenosine deaminase activity and cytokine-secreting T cells in normal pregnancy. *Obstet Gynecol* 2002; 100: 754. [\[CrossRef\]](#)
11. Shimaoka Y, Hidaka Y, Tada H, Nakamura T, Mitsuda N, Morimoto Y, et al. Changes in cytokine production during and after normal pregnancy. *Am J Reprod Immunol* 2000; 44: 143-7. [\[CrossRef\]](#)
12. Ellis G, Goldberg DM. A reduced nicotinamide adenine dinucleotide linked kinetic assay for adenosine deaminase activity. *J Lab Clin Med* 1970; 76: 507-17.
13. Jaqueti J, Martinez-Hernández D, Hernández-García R, Navarro-Gallar F, Arenas-Barbero J. Adenosine deaminase in pregnancy serum. *Clin Chem* 1990; 36: 2144.
14. Oladipo O, Afolabi B, Okorodudu A. Adenosine deaminase activity in subjects with normal pregnancy, pregnancy induced hypertension and pre-eclampsia. *West Afr J Med* 2009; 28: 161-4.
15. Chaudhry SM, Naseer Z, Rabbani S and Alrokayan SA. Activity of adenosine deaminase and its isoenzymes in serum of pregnant buffaloes. *Pakistan Vet J* 2007; 27: 152.
16. Uslu S, Sütken E, Güçlüer Z, Çolak Ö, Alataş Ö. Yüksek yaş ve Down Sendromu riski taşıyan gebelerde, seruloplazmin ve adenosin deaminaz aktiviteleri. *Türk Klinik Biyokimya Dergisi* 2004; 2: 121-6.