

# Adenosine Deaminase Activity in Iraqi Patients with Myocardial Infarction

Shatha Abdul Wadood<sup>1</sup>, Shaema Saadon Fadel<sup>2</sup>

<sup>1</sup> Ph.D in Clinical Biochemistry, Assistant Professor  
Department of Chemistry, College of Science, University of Baghdad  
Baghdad, Iraq

<sup>2</sup> MSc in Biochemistry, Assistant Lecturer  
Department of Chemistry, College of Science, University of Baghdad  
Baghdad, Iraq

---

**ABSTRACT**— Adenosine deaminase (ADA) activity increases during antigenic and mitogenic responses of lymphocytes; therefore it is considered as an important immunoenzyme marker for assessing cell mediated immunity in diseases characterized by T lymphocyte proliferation and maturation. Myocardial Infarction (MI) is a term used to describe acute necrotic changes in the myocardium due to sudden deprivation of coronary blood supply. Since a relationship exists between adenosine deaminase and cell mediated immunity we have undertaken a preliminary study to determine its activity and highlight its importance in the immunopathogenesis of MI, also searching for a new biochemical marker.

**METHODS:** 25 cases all diagnosed with MI at admission to AL-Yarmook Hospital /Iraq. The control group consisted of 25 age and sex matched normal healthy individuals. Serum biochemical parameters were estimated by spectrometric methods such as: ADA activity, Aspartate aminotransferase (AST), lipid profile, and total protein. Statistical analysis was made by SPSS version 15 and student T- Test was used.  $P < 0.05$  was considered significant.

**RESULTS:** There were significant differences ( $p < 0.05$ ) in ADA levels ( $43.14 \pm 10.8U/L$ ) in patients than controls ( $20.71 \pm 3.54U/L$ ). Significant increase ( $p < 0.05$ ) were found in AST activity, total cholesterol, TG, and LDL-C, while level HDL-C show a significant decrease ( $p < 0.05$ ).

**CONCLUSIONS:** ADA levels may be increased to compensate the increase in adenosine levels due to MI. Also the observations of the study provide evidence for T lymphocyte activation and proliferation in MI.

**GENERAL SIGNIFICANCE:** We suggest that ADA may be one of the markers to elucidate the pathogenesis of MI, and may be used as drugs target.

**Keywords**— Adenosine deaminase, Aspartate aminotransferase, Lipid profile, Myocardial Infarction, Biochemical marker.

---

## 1. INTRODUCTION

Myocardial infarction is a common presentation of ischemic heart disease/coronary artery disease. The World Health Organization estimated in 2004, that 12.2% of worldwide deaths were from ischemic heart disease; with it being the leading cause of death in high or middle income countries and second only to lower respiratory infections in lower income countries [1].

In Myocardial Infarction there is ischemic necrosis of a variable amount of myocardial tissue as a result of an abrupt acute decrease in coronary flow or an equivalent abrupt increase in myocardial demand for oxygen, which cannot be supplied by an obstructed coronary artery. Coronary flow may be impaired by a thrombus in one of the coronary arteries or hemorrhage within or beneath an atherosclerotic plaque [2].

The role of immunological mechanisms in the progression of atherosclerosis and its thrombotic complications has been an active area of research during the last two decades. The presence of both lymphocytes and macrophages in human atheroma suggests the contribution of immunological process in the pathogenesis of atherosclerotic lesions. Adenosine deaminase (E.C. 3.5.4.4) (ADA) is a polymorphic enzyme that is involved in purine metabolism through the salvage pathway. ADA catalyzes the irreversible deamination of adenosine and deoxy adenosine to produce inosine and deoxyinosine, respectively [3]. It is widely distributed in human tissues and shows highest activity in lymphoid tissues. It is necessary for the proliferation, maturation and function of lymphocytes, specifically for T lymphocytes [4].

The use of biomarkers can undoubtedly assist in several different clinical specialties, as well as add prognostic information regarding acute short-term or chronic long-term risk and severity. Biomarker, such as troponin, is highly sensitive but has decrease specificity for myocardial infarction [5, 6].

In the present study we have measured the activity of adenosine deaminase in MI patients and compared with that of healthy subjects serving as control to understand a possible role of the enzyme in myocardial infarction.

## **2. METHOD**

25 Iraqi male patients, admitted to the cardiology unit of AL-Yarmook Hospital, Iraq, from September 2012 to April 2013. The diagnosis of AMI was established according to clinical criteria: chest pain, which lasted for up to 3 hours, ECG changes (ST elevation of 2 mm or more in at least two leads).

Inclusion criteria: The inclusion criteria were male patients with MI, (mean age  $45.8 \pm 10.3$  years), with BMI < 25 kg/m<sup>2</sup>.

Exclusion criteria: The following criteria were used to exclude patients from the study: hepatic or renal disorder; other ailments, like tuberculosis, rheumatoid arthritis, and gout, pregnancy, alcoholic, and smoker subjects.

Control group consisted of 25 age and sex matched healthy individuals (mean age  $47.6 \pm 9.0$  years) with no known history of any disease. All patients and control subjects were volunteers for the study. An informed consent was obtained from all subjects and an ethical approval was also obtained.

All the subjects were examined clinically and information pertaining to age, sex, Body mass index BMI, habits and health status were recorded in special case Performa.

Five ml of blood sample were collected from each subject by vein puncture from both control and patients. The blood samples were centrifuged at 3000 rpm for 10 minutes after allowing the blood to clot at room temperature. The serum was assayed immediately for ADA activity as described by Guisti and Galanti [7], based on the Bertholet reaction, that is, the formation of colored indophenol complexes from ammonia liberated from adenosine and quantitated spectrophotometrically at 630 nm in a Shimadzu UV-240 spectrophotometer. Measurement of serum AST activity level was performed by using colorimetric techniques with kit assay systems (Randox, Japan) in Olympus AO 600 auto-analyzer system (Olympus, Japan), and performed as described by manufacturers. Results were expressed as international unit (IU) of enzyme activity of serum. Lipid profile levels: triglycerides (TG), total cholesterol (TC), HDL cholesterol (HDL-C) were measured by spectrophotometric methods using (Randox, Japan) kits. Protein was estimated by the method of Lowry et al. [8] using Folin phenol reagent. Bovine serum albumin was used as the standard.

## **3. STATISTICAL ANALYSIS**

Statistical analysis was performed using SPSS version 15.0 for Windows (Statistical Package for Social Science Inc., Chicago, IL, USA). Descriptive analysis was used to show the mean and standard deviation between variables. The significance of difference between mean values was estimated by student T- Test. The probability  $P < 0.05 =$  significant,  $P > 0.05 =$  non significant.

## **4. RESULTS**

The base line characteristics of the patients and control group are shown in Table I. The mean age of both the controls and patients were  $47.6 \pm 9.0$  and  $45.8 \pm 10.3$  years respectively. BMI was also almost similar in the both groups with the values not greater than 25.

Mean ADA levels estimated in patients with MI and controls are presented in (Table 2). The mean  $\pm$  SD of ADA levels in serum of MI patients was  $43.14 \pm 10.8$  U/L and that of controls was found to be  $20.71 \pm 3.54$  U/L. The difference in the mean values was statistically significant at 0.05.

All other biochemical parameters of MI patients like cholesterol, LDL-cholesterol, triglycerides, and AST activity show significant increase ( $p < 0.05$ ) when compared with control. Levels of HDL- cholesterol of MI patients show a significant decrease ( $p < 0.05$ ) than control, while total protein shows no significant difference (Table 2).

## **5. DISCUSSION**

The major mechanisms by which T cells contribute to the pathogenesis of inflammatory disease are via the release of specific patterns of cytokines. Evidence is indicated for an LDL- induced pathway of type 1 cytokine activation in atherosclerosis, which is regulated by the local production of IL-12 and IL-10. Thus the degree of T-cell and macrophage infiltration in atherosclerotic plaques has been shown to correlate with the occurrence of plaque rupture [9].

It was reported that the ADA levels are elevated whenever cell mediated immunity is stimulated and thus reflects the activity of stimulated T-lymphocytes and reflect the changes in the immune response. Cytokines produced by T – helper1 and T–helper 2 cells also regulate membrane adenosine deaminase on human lymphocytes. Interferon-

gamma producing cells IFN-g activates the monocyte -macrophage cell system, which may also contribute to the regulation of plasma ADA activity [10].

In the present study we observed a significant elevation in the adenosine deaminase levels in MI when compared to controls. Serum Adenosine deaminase activity was also found to be high in myocardial infarction [11], and unstable angina [12] suggesting the contribution of immunological and inflammatory process in the pathogenesis of coronary heart disease. Also ADA was considered as an inflammatory molecule in acute MI [13].

Elevated levels of ADA have also been reported in other diseased conditions like tuberculosis [14], acute nephrotic syndrome[15], leukemia, Behcet's Disease[16],and in typhoid[17].

Shiva Prakash et.al [18] concluded that the use of adenosine deaminase is a cost-effective process and the elevated adenosine deaminase activity may be an important indicator in the immuno-pathogenesis of type 2 diabetes mellitus. The high adenosine deaminase activity might be due to abnormal T-lymphocyte responses or proliferation [19]; may point towards a mechanism that involves its release into circulation as suggested by Hovi et al. [20].

Previously, Chang and Shaio [20] , have demonstrated that impaired cell mediated immunity was associated with abnormal lymphocyte proliferation, and as adenosine deaminase is associated with T- lymphocyte activity [18], its altered blood levels may help in predicting immunological dysfunction in type 2 diabetic individuals and might be one of the important biomarkers in predicting the disease.

MI is a term used to describe necrotic changes in the myocardium due to sudden deprivation of coronary blood supply (i.e., acute coronary occlusion or hemorrhage), which causes hypoxia or anoxia, forcing the cardiomyocyte metabolism to change from aerobic to anaerobic. During this process, oxygen free radicals and cellular acidosis are generated and high-energy phosphates are rapidly consumed [21].

Elevation of ADA activity in IM may be explained to be due to the damage of cells resulting in the release of intracellular components into the blood, hence elevation its level in the blood [22].

Adenosine is a purine nucleoside that, once released from cells or being formed extra-cellularly, diffuses to the surface of surrounding cells, where it binds specific membrane receptors [23]. Although adenosine is present at low concentrations in the extracellular space stressful conditions, such as inflammation, can markedly increase its extracellular levels [24]. Recent evidence indicates that adenosine helps to maintain tissue integrity by reducing energy demand, increasing nutrient availability, and modulating the immune system [25]. Accordingly, adenosine can play a beneficial role as immunomodulator in tissues subjected to injurious stimuli, including ischemia and inflammation [26].

Several reports have demonstrated the ability of adenosine to exert anti-inflammatory actions in a variety of experimental models. In particular, this nucleoside can interfere with the biosynthesis of proinflammatory cytokines [27], and it down-regulates neutrophil functions, decreasing their adhesion, degranulation, and oxidant activity [26, 28].

Under conditions of tissue damage, endogenous adenosine concentration rapidly raises; furthermore, the activation of G protein-coupled adenosine receptors is responsible for changes such as vasodilatation, inhibition of inflammation, modulation of the sympathetic nervous system activity, and protection against the deleterious consequences of ischemia-reperfusion [29]. Adenosine levels are regulated by the activity of the enzyme adenosine deaminase (ADA), the physiological role of ADA is not entirely clear; however, various studies indicate that ADA activity in plasma of patients with chronic hypoxia is higher as compared with healthy patients, indicating that induction of ADA activity represents a physiological adaptation to high levels of adenosine during hypoxia [30]. This lead Riksen [29] and his colleagues to propose that intensity of cellular hypoxia correlated with elevated serum ADA activity during AMI. Adenosine, as is reported, is an endogenous activator of cellular antioxidants [29]. The depletion of adenosine by adenosine deaminase may lead to enhanced production of free radicals which are implicated in the pathogenesis of myocardial ischemic injury. The significance of adenosine deaminase in ischemic myocardial syndromes were shown earlier [31,32].

Adenosine has been suggested to be critical regulator of inflammation and increased adenosine release could be utilized to diminish inflammation [33]. The ADA catalyzes the deamination of adenosine to inosine contributing to the regulation of intracellular and extracellular concentrations of adenosine, and probably modulates energy metabolism. Systemic administration of an ADA inhibitor produce clear anti-inflammatory effects [34, 35].

It is noteworthy that inosine, the metabolite produced by adenosine deaminase, is also effective in reducing the severity of inflammation [36] and protecting against endotoxin-induced shock [37]. Therefore, the blockade of

adenosine deaminase could hamper the anti-inflammatory potential resulting from inosine production, but at the same time this deficiency seems to be overcome by the concomitant adenosine accumulation that ensures a significant and more effective anti-inflammatory activity, as shown in the previous studies [25].

Kuddusi et al. [38] suggested that there is a correlation between pro-oxidative stress and antioxidative defence with ADA activity, as an indicator of T-cell activation, and it can be considered as significant supportive diagnostic indicators, especially in active disease.

Another study suggested that ADA could be considered a prognostic marker only in those patients with no ST segment elevation EKG and receiving no thrombolytic therapy. The elevation of serum ADA activity in patients receiving thrombolytic treatment could reflect the ADA release from its endothelium attachment by the action of thrombolytic enzymes[39].

Although traditional treatments have focused on nonspecific suppression of inflammation, advances in the knowledge of the immunopathogenesis of inflammation have paved the way to targeted therapies, allowing a selective blockade of the inflammatory cascade and modulation of key cytokines. The adenosine system represents an attractive target for novel therapies against inflammatory diseases. According to the present results, the blockade of adenosine deaminase allows an effective control of experimental inflammation, and adenosine deaminase inhibitor can provide a basis for development of anti-inflammatory drugs suitable for treatment of inflammatory disorders. Further studies on ADA activity in lymphocytes is required to consider ADA as an effective prognostic and pathological marker.

## 6. CONCLUSIONS

ADA levels may be increased to compensate for the increase in adenosine levels due to MI and its product (inosine) effect in reducing the severity of inflammation. Also the observations of the present study provide evidence for T lymphocyte activation and proliferation in MI patients and suggest ADA as one of the markers to elucidate the pathogenesis of MI. We support the suggestion that ADA act as an inflammatory molecule in acute MI.

The study suggests the inclusion of another easily measurable and cost effective marker ADA along with other biomarkers for better management and for the development of new treatment strategies.

### **Conflict of interest statement**

#### **Authors' conflict of interest disclosure:**

The authors stated that there are no conflicts of interest regarding the publication of this article. Research funding played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

**Employment or leadership:** None declared.

**Honorarium:** None declared.

**Table 1:** Baseline characteristics of the both groups.

Mean ± SD	Patients	Controls
Number of samples	25	25
Age	45.8± 10.3	47.6± 9.0
BMI	24.29± 0.45	24.55 ± 0.21
Blood pressure		
a. Systolic	118 ± 2	119± 3
b. Diastolic	80 ± 3	79 ±5

**Table 1:** Biochemical parameters of the both groups.

Parameters	Patients	Controls	P value
ADA (U/L)	43.14 ± 10.8	20.71 ± 3.54	0.047
AST (U/L)	15.98 ± 4.88	17.81 ± 3.29	0.044
Cholesterol (mg/dl)	430.73 ± 9.6	165.53±7.17	0.001
LDL- C (mg/dl)	231.95± 7.8	134 ± 9.3	0.001
Triglyceride (mg/dl)	245.34± 7.95	98.42 ±18.588	0.0001
HDL- C (mg/dl)	56 19± 6.61	185.62 ± 11.05	0.005
Total protein (g/dl)	6.75 ± 0.62	7.15 ± 0.72	non

## 7. REFERENCES

- [1] World Health Organization (2008). *The Global Burden of Disease: 2004 Update*. Geneva: World Health Organization.
- [2] Chesebro JH, Rauch U, Fuster V, Badimon JJ. “Pathogenesis of thrombosis in coronary artery disease” *Haemostasis*, 1997, vol. 2, pp.12-18.
- [3] Reuter H, Burgess LJ, Carstens ME, Doubell AF “Adenosine deaminase activity – more than a diagnostic tool in tuberculous pericarditis”, *Cardiovasc J South Afr*; 2005, vol. 16, no. 3, pp.143–147.
- [4] Franco R, Valenzuela A, Lluís C, Blanco J. “Enzymatic and extra-enzymatic role of ecto-adenosine deaminase in lymphocytes”. *Immunol Rev*. 1998, vol. 161, pp. 27-42.
- [5] de Lemos JA, Drazner MH, Omland T, Ayers CR, Khera A, Rohatgi A, and et al. “Association of Troponin T detected with a highly sensitive assay and cardiac structure and mortality risk in the general population”. *J Am Med Assoc*. 2010, vol. 304, pp. 2503 – 2512.
- [6] Giuseppe Lippi, Mario Plebani, Salvatore Di Somma, Valter Monzani, Marco Tubaro, and et al. “Considerations for early acute myocardial infarction rule-out for emergency department chest pain patients: the case of copeptin” *Clin. Chem. Lab. Med*. 2012, vol. 50, no.2, pp. 243–253.
- [7] Giusti G, Galanti B, Colorimetric Method. Adenosine deaminase. Bergmeyer HU, (ed). *Methods of enzymatic Analysis*, 3rd ed. Weinheim: Verlag chemie,; 315-323, 1984.
- [8] Lowry O.H., Rosebrough N.J., Farr A.I., Randall R.J. “Protein measurement with the Folin phenol reagent” *J. Biol. Chem*. 1951, vol. 193. pp. 265-275.
- [9] Haruyo Yamashita, Kazunori Shimada, Eriko Seki, Hiroshi Mokuno, Hiroyuki Daida,. “Concentrations of interleukins, interferon, and C-reactive protein in stable and unstable angina pectoris” *The American Journal of Cardiology* 2003 vol. 91, no, 2, pp. 133–136.
- [10] Yoneyama Y, Sawar, Suzuki, Miura A, Kobayashi H, Doi D, and et al. “Relation between adenosine deaminase activities and cytokines producing T cells in women with preeclampsia”. *Clin Biochem*. 2002, vol. 335, pp. 303-306.
- [11] Jyothy.A, Surekha Rani H, Dayasagar Rao.V, Reddy PP. “Serum adenosine deaminase activity in Myocardial Infarction” *Int J Hum Genet*. 2003, vol. 3, no.1, pp. 65-67.
- [12] Surekha Rani H, Dayasagar Rao V, Shiva Prakash M, Jyothy A. “Serum Adenosine deaminase activity and C-reactive protein levels in unstable angina” *Ind J Hum Genet*, 2003, vol.9, no.1, pp.17-20.
- [13] Neela Patil, Vishwas Chavan, N.D.Karnik, Antioxidant status in patients with acute myocardial, *Indian Journal of Clinical Biochemistry*, 2007, vol 22. no. 1, pp.45-51.
- [14] Sharma SK, Suresh V, Mohan A., Kaur P, Saha P, Kumar A, Pande JN. “A prospective study of sensitivity and specificity of adenosine deaminase estimation in the diagnosis of tuberculosis pleural effusion”. *Indian J Chest Dis Allied Sci*. 2001, vol.43, pp.149-155.
- [15] Mishra OP, Rajiv G, Ali Z, Usha “Adenosine deaminase activity in nephrotic syndrome”. *J Trop Pediatr*; 1997, vol.43, pp.33-37.
- [16] Kose K, Yazici C, Asciglu O “The Evaluation of lipid peroxidation and adenosine deaminase activity in patients with Behcet's disease” *Clin Biochem*. 2001, vol. 34, pp.125-129.
- [17] Ungerer JPG, Oostuizen HM, Bissbort SH, Vermaak WJH “Serum adenosine deaminase: isoenzyme and diagnostic application” *Clin Chem*. 1992, vol. 38, pp.1322-1326.
- [18] Shiva M Prakash, Chennaiah S, Murthy YSR, Anjaiah E, Ananda Rao S, Suresh C “Altered Adenosine Deaminase Activity in Type 2 Diabetes Mellitus”. *Journal Indian Academy of Clinical Medicine* 2006, vol. 7, no.2, pp.34-39.

- [19] Sullivan JL, Oxborne WRA, Wedgewood RJ “Adenosine deaminase activity in lymphocytes”. *Br J Haematol.* 1977, vol. 37, pp. 157-158.
- [20] Hovi T, Smyth JF, Allison AC, Williams SC “Role of adenosine deaminase in lymphocyte proliferation”. *Clin Exp Immunol.* 1976, vol. 23, pp.395-403.
- [21] Chang FY, Shaio MF “Decreased cell-mediated immunity in patients with non-insulin-dependent diabetes mellitus”. *Diabetes Res Clin Pract.* 1995, vol. 28, pp.137-146.
- [22] Cave AC, Ingwall JS, Friedrich J, Liao R, Saupe KW, Apstein CS, and et al. “ATP synthesis during low-flow ischemia: Influence of increased glycolytic substrate”. *Circulation* 2000, vol. 101, pp. 2090-2096.
- [23] Brichman ,A.S.,Coburn, J.W, Massry, S.G.“Adenosine Deaminase activity in tuberculosis pleural effusions, *American journal of Medicine* 1974, vol. 57, pp.156-161.
- [24] Ralevic V and Burnstock G “Receptors for purines and pyrimidines”. *Pharmacol Rev.* 1998, vol.50, pp.413–492.
- [25] Kuno M, Seki N, Tsujimoto S, Nakanishi I, Kinoshita T, and et al. “Anti-inflammatory activity of non-nucleoside adenosine deaminase inhibitor FR234938”. *Eur J Pharmacol.* 2006, vol. 534, pp. 241–249.
- [26] Siegmund B, Rieder F, Albrich S, Wolf K, Bidlingmaier C, and et al. “Adenosine kinase inhibitor GP 515 improves experimental colitis in mice”. *J Pharmacol Exp Ther.* 2001, vol. 296, pp. 99–105.
- [27] Haskó G and Cronstein BN “Adenosine: an endogenous regulator of innate immunity”. *Trends Immunol.* 2004, vol. 25, pp.33–39.
- [28] Naganuma M, Wiznerowicz EB, Lappas CM, Linden J, Worthington MT, Ernst PB “Cutting edge: critical role for A 2a adenosine receptors in the T cell-mediated regulation of colitis”. *J Immunol.* 2006, vol. 177, pp. 2765–2769.
- [29] Riksen NP, Rongen GA, Yellon D, Smits P “Human in vivo research on the vascular effects of adenosine”. *Eur J Pharmacol.* 2008, vol.13, pp.220-222.
- [30] Eigler A, Matschke V, Hartmann G, Erhardt S, Boyle D, Firestein GS, Endres S “Suppression of TNF-alpha production in human mononuclear cells by an adenosine kinase inhibitor”. *J Leukoc Biol.* 2000, vol. 68, pp.97–103.
- [31] Eltzschig HK, Faigle M, Knapp S, Karhausen J, Ibla J, Rosenberger P, and et al. “Endothelial catabolism of extracellular adenosine during hypoxia: the role of surface adenosine deaminase and CD26”. *Blood* 2006, vol.108, pp.1602-1610.
- [32] Kaul A, Chandra M, Misra MK. “Adenosine deaminase in ischemia reperfusion injury in patients with myocardial infarction. *J Enz Inhib Med Chem* 2006, vol. 21, pp. 543-546.
- [33] Kaul A, Sethi R, Misra MK. “ Evaluation of the roles of adenosine deaminase and xanthine oxidase in reperfusion injury in patients with myocardial infarction”. *Clin Chim Acta* 2007, vol. 380, pp. 225-227.
- [34] Sawynok J, Liu XJ. “Adenosine in the spinal cord and periphery: release and regulation of pain” *Prog Neurobiol* 2003, vol. 69, pp. 313-340.
- [35] Adanin S, Yalovetskiy IV, Nardulli BA, Sam AD , Jonjev ZS, and et.al. “Inhibiting adenosine deaminase modulates the systemic inflammatory response syndrome in endotoxemia and sepsis. *Am J Physiol Regul Integr Comp Physiol*2002, vol.282, pp. R1324-1332.
- [36] Mabley JG, Pacher P, Liaudet L, Soriano FG, Haskó G, and et.al. “Inosine reduces inflammation and improves survival in a murine model of colitis”. *Am J Physiol.* 2003b, vol. 284, pp.138–144.
- [37] Haskó G, Kuhel DG, Ne´meth ZH, Mabley JG, Stachlewitz RF, and et al. “Inosine inhibits inflammatory cytokine production by a posttranscriptional mechanism and protects against endotoxin-induced shock”. *J Immunol.* 2000, vol. 164, pp.1013–1019.
- [38] Kuddusi Erkiliç, Cem Evereklioglu, Mustafa Çekmen, Abdullah Özkiris, Fuat Duygulu, Hakki Dogan, “Adenosine deaminase enzyme activity is increased and negatively correlates with catalase, superoxide dismutase and glutathione peroxidase in patients with Behçet's disease: original contributions/clinical and laboratory investigations” *Mediators of Inflammation*, 2003, vol.12, no.2, pp. 107-116.
- [39] Torrellas, Yulan, Ramos Belkis, Useche Antonio Franco, Pérez-Aguilar Mary Carmen, and et.al. “Increased adenosine deaminase serum activity in patients with acute myocardial infarction” *Revista Latinoamericana de Hipertensión* 2010, Vol. 5, no. 2, pp. 38-42.