

**PHARMACOVIGILANCE OF ANTI-DIABETIC MEDICATIONS AND CARDIAC  
MEDICATIONS AND THEIR ASSOCIATED STRESS**Durr-e-shehwar Khan<sup>1</sup>, Kisa Fatima Altaf\*<sup>2,3</sup>, Shamoos Noushad<sup>2,3</sup> and Sadaf Ahmed<sup>1,2</sup><sup>1</sup>Psycho-physiology Research Lab, Physiology Dept, University of Karachi.<sup>2</sup>Advance Educational Institute and Research Centre.<sup>3</sup>Dadabhoj Institute of Higher Education.

\*Corresponding Author: Kisa Fatima Altaf

Advance Educational Institute and Research Centre.

Article Received on 01/01/2017

Article Revised on 22/02/2017

Article Accepted on 17/03/2017

**ABSTRACT**

Several chronic diseases such as diabetes and cardiovascular diseases have been declared as the major cause of death and may lead to several mental disorders. The administration of certain chronic medications causes metabolic side effects that include excess weight gain, insulin resistance and hyperlipidemia. In contrast with improved health outcomes, chronic medications can develop a large number of hidden side effects that may lead to worsen the chronic health conditions. The purpose of this study was to analyze the pharmacovigilance of anti-diabetic and cardiac medications by determining significant side effects. Certain complications have been determined by evaluating the effects on nutritional, physical and chemical stress by anti-diabetic and cardiac medications with the help of Sadaf Stress Scale (SSS). A cross sectional study has been conducted in several local hospitals by classifying patients into three groups. All patients were followed by their demographic data Medical History and history of drugs and their dosages. The study showed irritability, hypertension, nausea, vomiting with physical, chemical and nutritional stress in the patients with anti-diabetic medications while the cardiac medications improves heart abnormalities in association with certain side effects like pallor, frequent urination, anorexia, irritability with physical, chemical and nutritional stress. It was concluded that chronic medications are also responsible for the development of chemical stress due to the use of medicine that results in the build-up of chemicals in body, physical due stress due to environmental pressure and demands, while nutritional stress due to the intake of toxin loaded medications, in the chronic patients.

**KEYWORDS:** Sadaf Stress Scale, Chronic diseases, anti-diabetic, cardiovascular diseases, diabetes mellitus, cardiac medications.

**INTRODUCTION**

Chronic disease or non-communicable disease (NCDS) can be controlled but not cured. A study conducted in 2010 revealed two major chronic diseases that have been occurred as the major mortality factor. In 2010, Majority of deaths were caused by seven major chronic diseases that includes severe allergies, breast cancer, asthma, epilepsy, cardio vascular diseases and diabetes. The previous research studies analyzed that cardiovascular disease and diabetes—together accounts for nearly 48% of all deaths around the world. A survey, conducted by ADA (American Diabetes Association) demonstrated diabetes as the major variable for lower limb amputation, certain nephropathies and retinopathies among adults.

The main objective of this study was to analyze the pharmacovigilance of anti-diabetic and cardiac medications, to ascertain side effects of anti-diabetic and cardiac medication and to figure out complications of anti-diabetic and cardiac medications. This study was aimed to evaluate effects on physical, nutritional,

chemical stress by anti-diabetic and cardiac medications and to find out the symptoms caused by anti-diabetic and cardiac medications.

***Diabetes mellitus (DM)***

Diabetes mellitus is not really a single disorder, but rather a constellation of abnormalities of glucose homeostasis that is linked with significant acute and chronic complications and co morbidities. There are 246 million people with diabetes worldwide and the international diabetes federations (IDF) calculated that there would be 380 million people affected by diabetes till the year 2025. Fueling this global explosion of diabetes there are an estimated additional 280 million who would have pre-diabetes or impaired glucose tolerance. Diabetes has been observed to be raised in Pakistan as there are approximately 7.1 million people in Pakistan and it has been estimated to reach 11.4 million people with diabetics and rank 10<sup>th</sup> worldwide in 2030.

Diabetic people are more likely to have poor blood glucose control (Channer K, 2007). Long term physical stress and frustration is caused by prolonged disturbance in blood glucose regulation, and can cause people to be drawn down and cause them neglect their diabetes care. Increased glycoxidation and lipoxidation product in plasma and tissue proteins suggests that oxidative and chemical stress is increased in diabetes. Increased chemical modifications of proteins, carbohydrates and lipids in diabetes are the result of overload on metabolic pathways involved in detoxification of reactive carbonyl compounds formed by both oxidative and non oxidative reaction (JW Bayer, 1999).

### ***Cardio vascular diseases***

Cardiovascular diseases (CVDs) are a group of disorders that involve heart and blood vessels abnormalities. Globally, it has been estimated that the major cause of death in 2012 was due to CVDs, 17.5 million people died from cardiovascular disorders, representing 31% of all global deaths. Of these deaths, about 7.4 million died due to coronary heart disease and 6.7 million were due to stroke. To treat chronic conditions different types of chronic medications have been developed. These medications are used for prolong period of time, along with improving the chronic conditions these medications are responsible for causing different types of side effects and stresses in the patients.

Since years a huge number of medications have been used to treat cardiovascular disorders; these include Diuretics (used to treat pulmonary and systematic fluid overload), Thiazides (used to inhibit the active transport of chloride as well as the passive movement of sodium), K-Sparing Diuretics (used to decrease active sodium re-absorption and potassium excretion), Cardiac Glycosids (improve cardiac performance by improving myocardial contractility), Angiotensin Converting Enzyme (reduces ventricular arrhythmias, decreases end systolic and diastolic dimensions) beta blockers etc.

Prolonged stress is highly disastrous to health, this interrupts with healthy well being. Person with significant mental stress is more prone to have cardiac diseases such as high blood, pressure, chest pain or irregular heartbeats. Studies showed the higher incidence of hypertension among patients with mental stress. Studies also link stress to change in the way blood of clotting, which causes heart attack in mentally upset individuals. To relieve stress, many individuals may

adopt to consume too much alcohol or smoke cigarettes; however these habits can increase blood pressure and may damage the walls of coronaries. In a stress full situation, a chain of events take place that causes a body to release adrenaline, a hormone that temporally cause breathing and heart rate to speed up and blood pressure to raise.

### **MATERIAL AND METHODS**

To check out the side effects and stresses caused by chronic mediations a cross sectional survey based study was conducted at local tertiary care government hospital, the sample population was divided into three groups, Group A included the patients who were dependent on anti-diabetic drugs, patients included in Group B were chronic user of cardiac medications while Group C were using both. The section of questionnaire includes Demographic data, general information, medical history, family history, co-morbidities and Drug use duration and dosage were investigated as well as intensity of Chemical stress, Nutritional stress and Physical stress. The severity of stress was evaluated by using Sadaf Stress Scale (SSS). The patients with severe and psychological and mental illness or any other chronic illness or patients who were failed to provide reliable information were excluded from study. Total number of 114 patients were included in this study Results were analyzed by using latest version of SPSS 20.0.

### **RESULTS**

Results were analyzed by using a structured questionnaire and SSS the results showed that anti-diabetic medications are used to maintain the blood glucose levels within the normal range. The most common classes of anti-diabetic medication include Glucophage, metformin, glimepiride and insulin. Along with the maintaining of blood glucose levels these medication produces a large number of side effects and stresses in these patients. The common side effects include irritability, increased blood pressure, nausea, vomiting and stresses include chemical, physical and nutritional. Cardiac medications are responsible to improve the heart abnormalities; the most important classes include aspirin, atenolol, diuretics and glycosides. Along with improving the heart abnormalities these medications produce a large number of side effects including increase urination, pallor, decrease appetite, irritability and stresses include physical, nutritional and chemical.

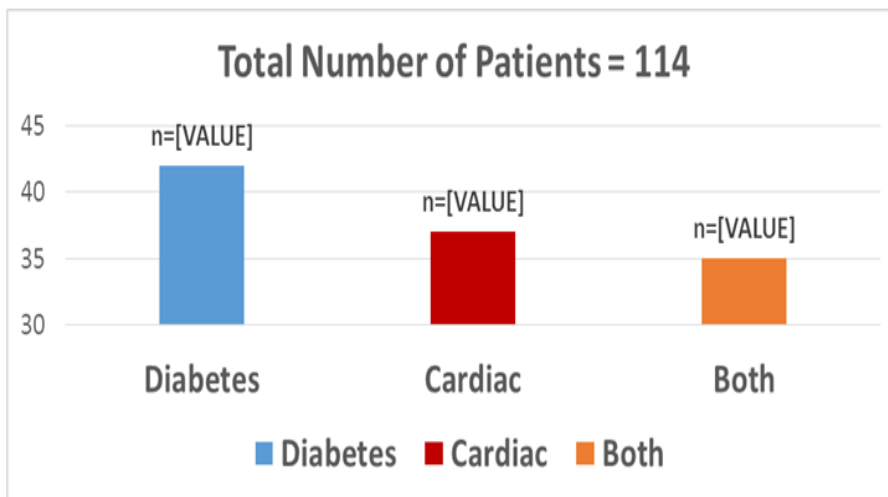


Figure 1 shows the Total Number of Participants, Diabetic Patients i.e. Group A, Cardiac Patients i.e. Group B and Both i.e. Group C Participated.

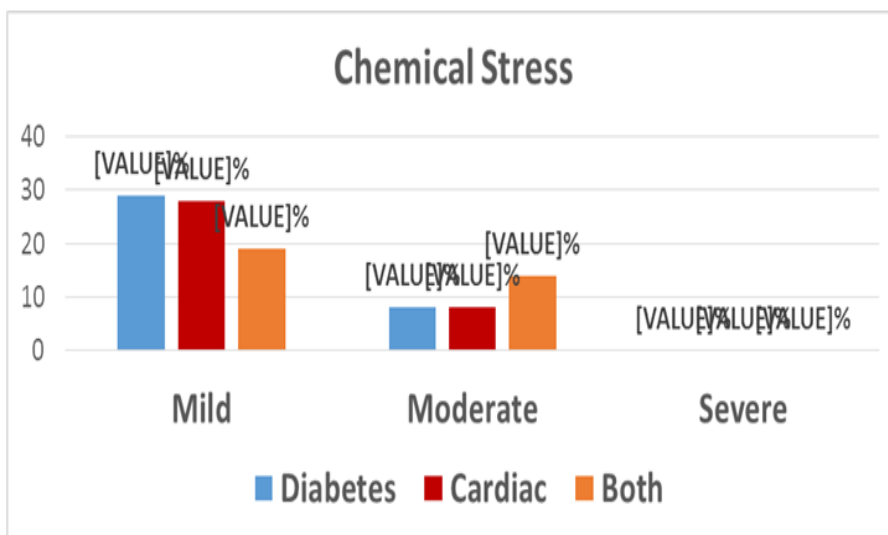


Figure 2 shows the intensities of Chemical Stress calculated in percentages reported in Study Population. Mild and Moderate stress were analyzed whereas no severity reported.

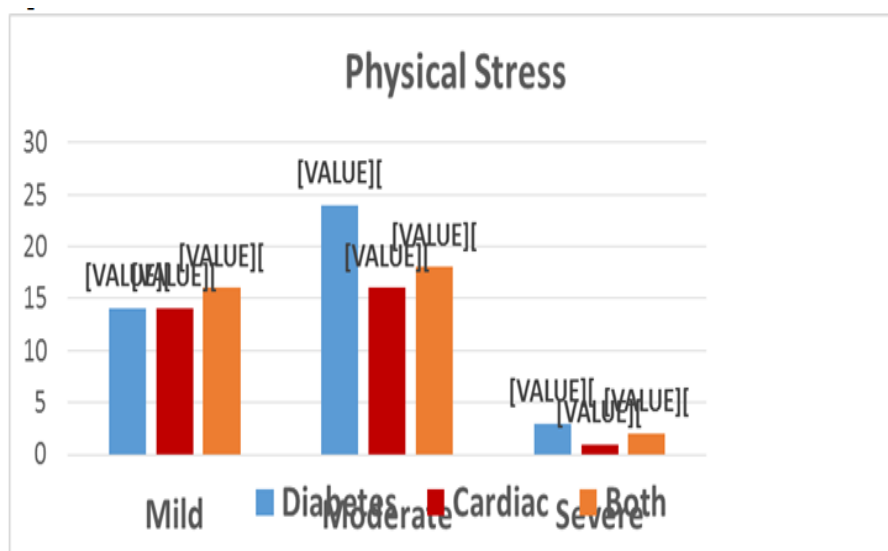


Figure 3 shows the intensities of Physical Stress calculated in percentages reported in Study Population. Mild, Moderate and Severity were reported respectively.

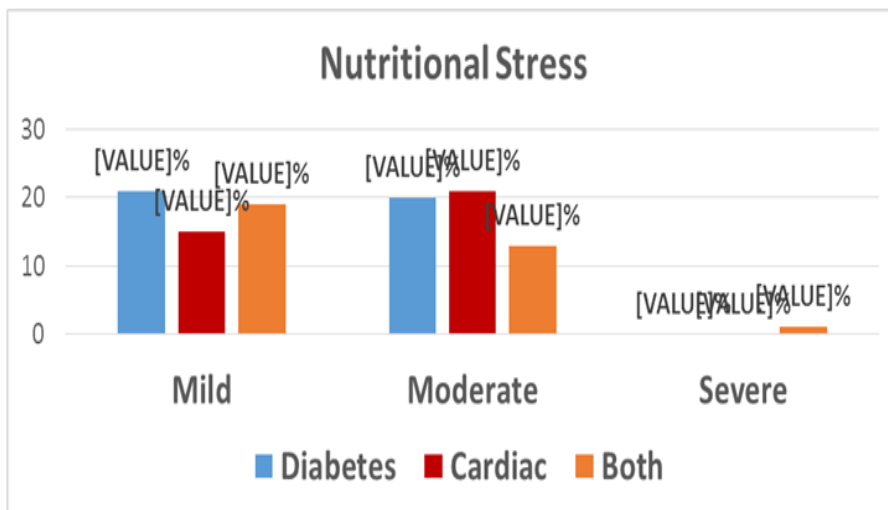


Figure 4 shows the intensities of Nutritional Stress calculated in percentages reported in Study Population. Mild and Moderate stress were reported whereas severity was reported in only 1% of study population taking both medicines.

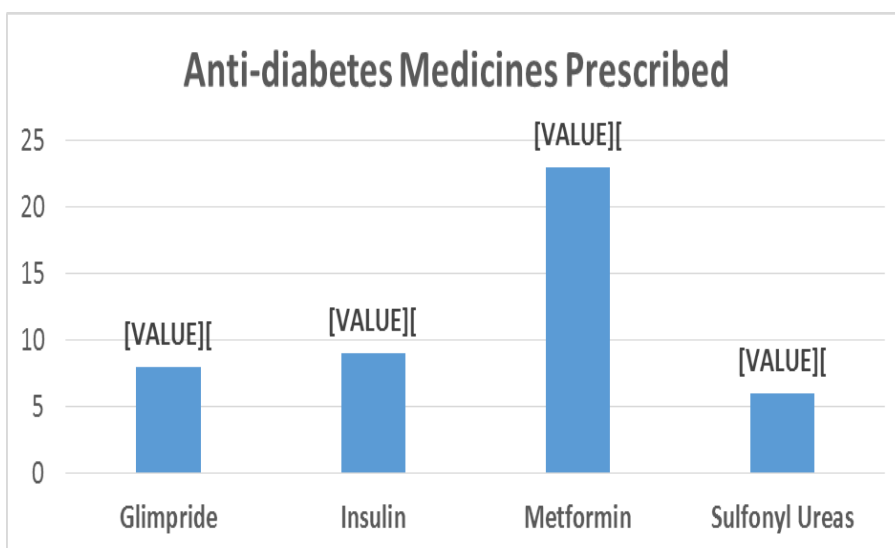


Figure 5 shows the most common drugs prescribed to patients diagnosed with diabetes.

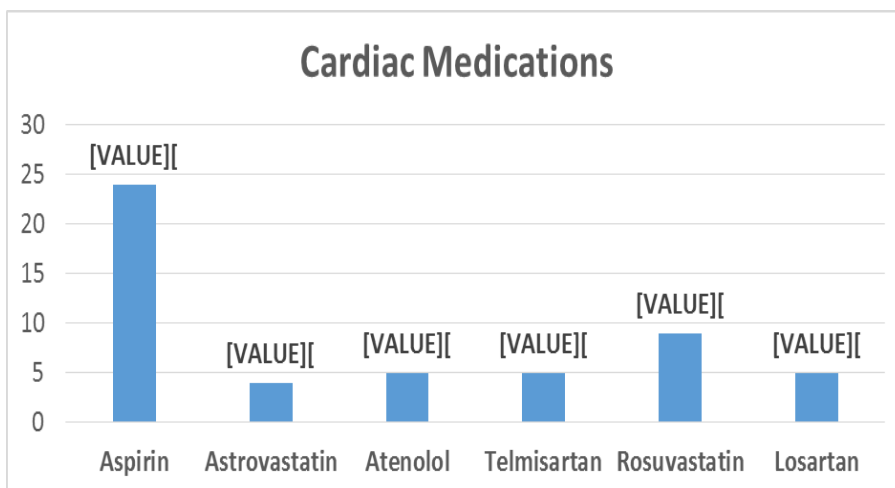


Figure 6 shows the most common drugs prescribed to patients diagnosed with Cardiac Diseases.

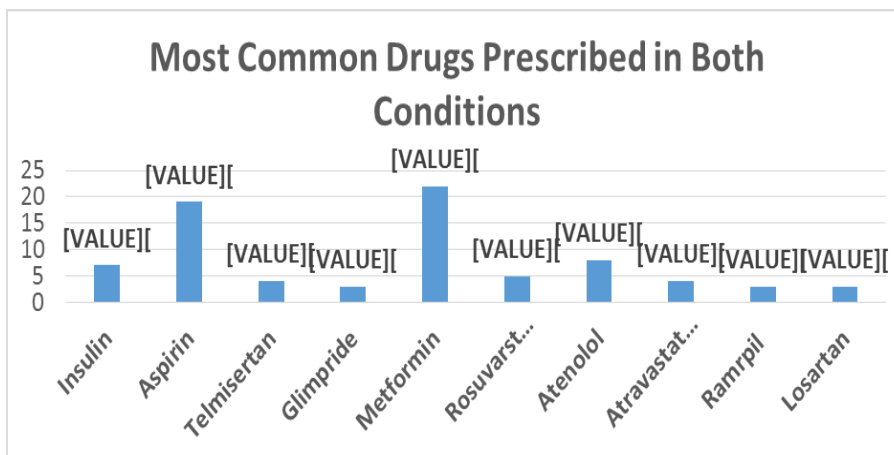


Figure 7 shows the most common drugs prescribed to patients diagnosed with both conditions i.e. Diabetes and Cardiac Diseases.

Table 1: The above Table shows the intensities of symptoms that are most commonly reported in Diabetic Patients.

Symptoms	Intensities in Percentage (%)
Increased BP	10%
Sleep Problem	17%
Mental Fog	25%
Irritability	25%
Fatigue	34%
Indigestion	8%
Abnormal Bowel Movement	6%
Dizziness	19%
Headache	25%
Dry Mouth	25%
Excess Sweating	23%

Table 2: This above table shows the intensities of symptoms that are most commonly reported in Patients with Cardiac Disease.

Symptoms	Intensities in Percentage (%)
Fatigue	36%
Indigestion	33%
Breathlessness	36%
Churning Stomach	37%
Increased Heart Rate	36%
Rapid, Shallow Breathing	36%
Dizziness	37%
Headache	35%
Tingling Sensation	21%
Tremor	14%
Dry Mouth	33%
Excess Sweating	36%
Nausea	29%

Table 3: The Above Table Shows intensities of most common symptoms reported in group C Diabetic and Cardiac Disease.

Symptoms	Intensities in Percentage (%)
Fatigue	16%
Increased BP	22%
Sleep Deficiency	10%
Headache	14%
Dry mouth	10%
Excess Sweating	13%

## DISCUSSION

Concluding the results of this study we can evaluate that chronic medications can improve the chronic health conditions but at the same time they are also responsible to develop a large number of side effects that can be hidden in these patients and in some condition may worsen the chronic health conditions, these side effects includes the symptoms like fatigue, dependency of medicine on regular basis and irritability caused by its prolonged use.

Previous studies reported that the reason which produces higher level of stress in cardiac patients are due to the use the chronic medications that will lead to development of stress, most of the patients uses smoking or drinking that will make heart problems more worst (Micheal H. Crawford, 2003). Our results evaluate the same points which elaborate that much the patient have become dependent on their medication and this have lead them towards stress. The most common symptom observed in patients with diabetes (group A) was dependency on these medicines and fatigue, while abnormal bowel, indigestion and increased blood pressure were observed to a much lesser extent.

Moderate level of physical stress has been found in population with the frequency of 24 individuals out of 42 selected participants, mild chemical stress was found in diabetic and cardiac patients with frequency of 28 and 29 individuals. Similarly, mild and moderate nutritional stress was found in diabetic and cardiac patients included in group A and B respectively. Nutritional stress causes unhealthy eating habits, it has been previously noticed that the poor quality and quantity of nutrients in an individual may cause nutritional stress to a severe level (Sadaf A., 2014) in our study we found much similar results.

In group A the most reported symptom of physical stress is fatigue. Fatigue is not the symptom of diabetes however, this can be the result of physical stress, fatigue also occurs as a result of excessive use of anti-diabetic medication. Medication such as a Pioglitazone hydrochloride, Metformin and Byetta also causes fatigue (Gill, 1991). The most commonly used drug by diabetic patients in this population was metformin, while sulfonyl ureas, insulin and glimpride were equally used. Most of the cardio patients were noticed with using aspirin as the most common drug, however, some of them were also using atrovastatin, atenolol, telmisartan, rosuvastain and losartan.

The lest common side effect observed in cardiac patients included tremor and tingling, while headache, dizziness, excess sweating, nausea, altered breathing pattern, increased heart rate, churning stomach, indigestion and fatigue equally affected these individuals depending upon the condition they are suffering with (Pitt, B, et al., 2000). The C group who were having both the cardiovascular problems and diabetes were observed

with increased use of medicine for their condition. Some of them were facing sleep deficiency, dry mouth and excessive sweating.

## CONCLUSION

By conducting a cross sectional survey on the patient with chronic illness, it has been concluded that chronic medications are also responsible for the development of chemical stress due to the use of medicine that results in the build-up of chemicals in body, physical due stress due to environmental pressure and demands, while nutritional stress due to the intake of toxin loaded medications, in the chronic patients. The patients would get to know about affects and side effects of the medicines, as there are so many people using the prescribed medicines but unaware of the side effects. It is useful for the consultants in their studies of pharmacovigilance of anti-diabetes and cardiac medications. For future recommendation, it is suggested to observe the mechanism by which chronic medications are producing the side effects. And to design such chronic medications that produce least number of side effects.

## REFERENCES

1. Arguedas, JA; Leiva, V; Wright, JM. "Blood pressure targets for hypertension in people with diabetes mellitus." The Cochrane database of systematic reviews, Oct 30, 2013.
2. Goldman L. Approach to the patient with possible cardiovascular disease. In: Goldman L, Schafer AI, eds. *Goldman's Cecil Medicine*. 24th ed. Philadelphia, PA: Saunders Elsevier; 2011: ch. Fisher ND, Williams GH. "Hypertensive vascular disease". In Kasper DL, Braunwald E, Fauci AS; et al. *Harrison's Principles of Internal Medicine* (16th Ed.). New York, NY: McGraw-Hill, 2005; 1463–81. 50.
3. Heric B, Lytle BW, Miller DP et al; Surgical management of hypertrophic obstructive cardiomyopathy. Early and late results. *Thorac Cardiovascular Surge*, 1995; 110: 195.
4. Komajda M, Curitis P, Hanedeld V et al. Effect of addition of rosiglitazone to metformin or sulfonylureas versus metformin/sulfonylurea combination therapy on ambulatory blood pressure in people with type II diabetes: a randomized controlled trial (the RECORD study). *Cardiovasc Dia Beta*, 2008; 7: 10.
5. Maron BJ, Shen WK, Link MS et al: Efficacy of implantable cardioverter-defibrillators for the prevention of sudden death in patients with hypertrophic cardiomyopathy. *N Engl J Med.*, 2000; 342: 365.
6. Micheal H. Crawford. *Current treatment and diagnosis in Cardiology* 2<sup>nd</sup> edition, 2003; 170-187.
7. Perez, MI; Musini, VM (23 January 2008). "Pharmacological interventions for hypertensive emergencies." The Cochrane database of systematic reviews

8. Pocock SJ, Henderson RA, Clayton T et al: Quality of life after coronary angioplasty or continued medical treatment for angina: three- year follow up in the RITA-2 trial *Am Coll Cardiol* 2000; Braunwald E: Instable angina, an etiologic approach to management. *Circulation*, 1998; 98: 221937: 51.
9. Rodriguez A., Reviriego J., Karamanos V., et al. Management of Cardiovascular Risk Factors with Pioglitazone Combination Therapies in type 2 Diabetes: an observational cohort study. *Cardiovascular DiaBeta*, 2011; 10: 18.
10. Shah Pm, Adelman AG, Wigle ED et al: The natural (and unnatural) history of hypertrophic obstructive cardiomyopathy. *Circ Res.*, 1974; 35(9): 95.
11. St. John Sutton M, et al. A comparison of effect of Rosiglitazone and Glyburide on Cardiovascular Function and Glycemic Control in Patients with Type II Diabetes. *Diabetes Care*, 2002; 25: 2058-2064.
12. Thaulow E, Erikessen J, Sandvik L et al: Initial clinical presentation of cardiac disease in asymptomatic men with silent myocardial ischemia and angiographically documented coronary artery disease (the Oslo OIschemia Study). *Am J Cardio*, 1993; 72: 629.
13. U.S. Preventive Services Task Force. "Aspirin for the primary prevention of cardiovascular events: recommendation and rationale". *Ann Intern Med.*, 15 January 2002; **136**(2): 157–60.
14. Pitt, B., Poole-Wilson, P. A., Segal, R., Martinez, F. A., Dickstein, K., Camm, A. J., & Sharma, D. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial—the Losartan Heart Failure Survival Study ELITE II. *The Lancet*, 2000; 355(9215): 1582-1587.
15. Sadaf A. And Shamoon N., *Psychophysiology of Stress*, 2014; 91-100.
16. Micheal H. Crawford . *Current Treatment and Diagnosis in Cardiology 2ndEdition*, 2003; 170-187.