

A PROSPECTIVE OBSERVATIONAL STUDY FOR THE ASSESSMENT OF MEAN PLATELET VOLUME IN ACUTE CORONARY SYNDROME PATIENTS

Divya Lakshmi.V, Ashok Govindaraj , Abishkauf Jenish Beautlin , Binodini

Department of Cardiology, Chettinad Hospital and Research Institute, Kelambakkam- 603103.

ABSTRACT:

BACKGROUND:

Acute coronary syndrome refers to group of clinical signs and symptoms which includes unstable angina, Non ST segment elevation myocardial infarction(NSTEMI), ST segment elevation myocardial infarction(STEMI). Due to rupture of plaque and results in the coronary thrombus formation. Platelet play a major role in initiation of thrombosis. MPV is useful biomarker for the activity of platelets. Elevated MVP is associated with impaired angiographic perfusion in ACS patients.

AIM:

To evaluate the levels of mean platelet volume in ACS patients.

METHODS:

Prospective observational study was done in 500 patients, Complete clinical details of patients were taken. Blood investigations were done as a part of routine investigation. Platelet count and MPV were determined using STKS automated hematology analyzer (Beckman coulter). Mean platelet volume is statistically analyzed using Pearson correlation between ACS and control groups and One way ANOVA test between ACS groups.

RESULT:

A total number of 250 cases with ACS and 250 normal healthy individuals were taken up for the study. About 85% of patients with ACS had significantly elevated MPV value compared with control groups. Among ACS groups significant difference was obtained with elevated MPV in STEMI patients compared to NSTEMI and UA.

CONCLUSION:

MPV value was significantly higher in ACS patients and MPV values vary significantly between ACS groups. Hence it can be used as reliable marker for early risk stratification of ACS.

KEY WORDS:

Mean platelet volume; acute coronary syndrome; acute myocardial infarction

INTRODUCTION:

The spectrum of clinical symptoms of acute coronary syndrome (ACS) encompasses unstable angina (UA), non-ST elevation myocardial infarction (MI), and ST-segment elevation MI (1). The abrupt disruption of atherosclerotic plaque in coronary artery, results in partial thrombosis, is aetiology of ACS, including UA and AMI. The hallmark of UA is a partial obstruction of coronary artery, results in decreased blood flow; the hallmark of AMI is a complete coronary artery blockage, results in cardiomyocyte necrosis(2). The development of thrombus and atherosclerotic plaque is significantly influenced by platelets. The most widely used and trustworthy metric for determining platelet size and activation status is MPV, which is a component of CBC (3). When platelets are activated, they secrete substances like thromboxane A₂ and 5-hydroxytryptamine (5HT), cause vasoconstriction; platelet-derived growth factor (PDGF), β -thromboglobulin (β -TG), and platelet factor 4 (PF4), cause arteriosclerosis; leukotrienes, which intensify inflammatory reactions; and glycoprotein IIb/IIIa receptor, triggers the haemostatic system for aggregation of platelet & formation of thrombus (4,5,6). The mean platelet volume, or MPV, during a routine blood examination positively correlates with

platelet activity in addition to reflecting platelet size. Greater volume of platelets results in higher platelet aggregation capacity, thromboxane production, β -thromboglobulin release, and adhesion surface molecule expression(7). When compared to healthy persons, patients with DM, HTN, hypercholesterolemia, smoking habits, or obese are also have a susceptible risk of cardiovascular disease have increased MPV(8,9,10,11,12). According to several studies, there is a connection between increased MPV and ACS(13) and also the correlation between elevated one and the results of percutaneous coronary intervention, such as stent restenosis and mortality(14,15,16,17). This suggests that MPV is a potential biomarker for ACS diagnosis and a risk factor for patients to develop cardiovascular diseases(18).

METHODS AND MATERIALS:

The current study was prospective observational study conducted in cardiology department in CSSH. The IHEC gave their consent to the study. The study analyses the MPV and platelet count in ACS patients. Inclusion criteria includes the patients presented with the complaints of chest pain, ECG changes such as STelevation, STdepression and T wave inversion, patient with positive cardiac biomarkers.

Both gender, patients with diabetes, hypertension, dyslipidemia were included. Exclusion criteria includes patients who are receiving anti coagulant or anti platelet therapy, patient with bleeding disorder, patient with recent blood transfusion. Patients were informed about the trial and given formal consent. In the questionnaire, relevant history was documented. Hospital based prospective observational study was done in Cardiology department at Chettinad hospital and Research institute, Kelambakkam. Data is collected in the year of Jan2020- April 2020 from the department of cardiology, CARE. To assess the MPV in ACS patients. The study consisted, 250 Acute coronary syndrome patients having diagnostic criteria and 250 controls who were non-ACS patients. ACS patients were diagnosed based on clinical presentation, examination, electrocardiographic changes like ST-T changes, echocardiographic changes with development of regional wall motion abnormality and cardiac biomarkers. Venous blood samples of 2ml were taken in the EDTA containing blood collection tube for the complete blood count

assessment. Platelet count and MPV were determined using STKS automated hematology analyser (Beckman coulter).

STATISTICAL METHODS: Pearson correlation was performed for comparing the MPV statistical data obtained from the controls and ACS patients. A P-value < 0.05 are regarded as statistically significant.

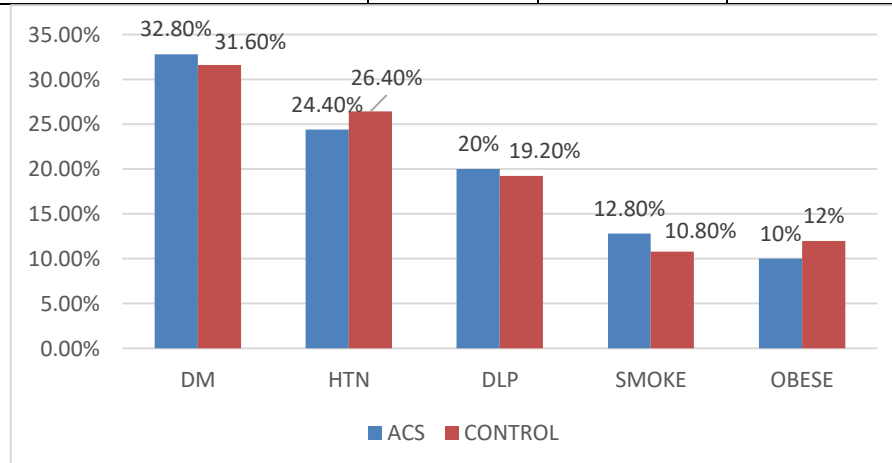
RESULTS:

PRELIMINARY STUDY:

The study participants of 500 patients were divided into two groups: (1) ACS patients; (2) Normal healthy individuals. The clinical profile of patients including Gender, HTN, DM, DLP, smoking, obesity, MPV are listed in the Table 1.. Among ACS group, 32.8% of patients had DM, 24.4% had HTN, 20% had DLP, 12.8% were smokers, 10% were obese patients. In control group, 31.6% patients had DM, 26.4% patients had HTN, 19.2% patients had DLP, 10.8% patients were smokers, 12% patients were obese. Average MPV in ACS and Control was found to be in range of 13 ± 0.71 and 8.75 ± 0.35 respectively.

CLINICAL PROFILE OF STUDY POPULATION

S.no	Variables	ACS-STEMI	ACS-NSTEMI	ACS-UA	CONTROL
1	GENDER M:F	54:42	35:45	38:36	143:107
2	DIABETES MELLITUS	24 (9%)	30 (12%)	28 (11.2%)	79 (31.6%)
3	HYPERTENSION	32 (12.8%)	12 (4.8%)	17 (6.8%)	66 (26.4%)
4	DLP	20 (8%)	15 (6%)	15 (6%)	48 (19.2%)
5	SMOKING	10 (4%)	15 (6%)	7 (2.8%)	27 (10.8%)
6	OBESITY	10 (4%)	8 (3.2%)	7 (2.8%)	30 (12%)
7	MPV Mean \pm SD	12.85 ± 0.49	12.4 ± 0.28	13.65 ± 0.21	8.75 ± 0.35

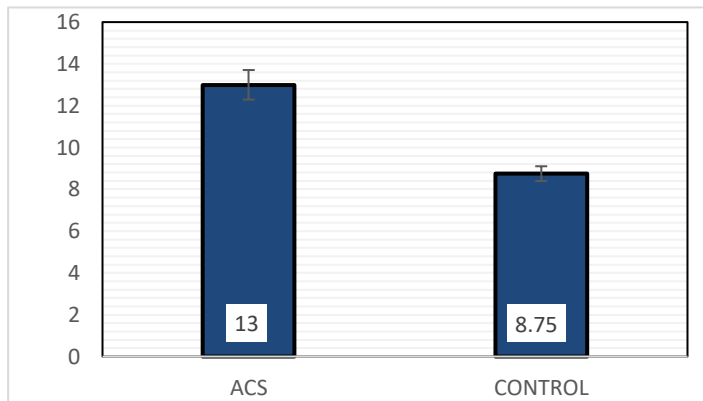


Average MPV was found to be significantly increase in patients compared to control groups (ACS patients (13 ± 0.71) and control groups (8.75 ± 0.35); $P= 0.005$) using pearson correlation. P- value <0.05 are regarded as

statistically significant. About 85% of patients groups showed elevated MPV compared to control groups ($P= 0.005$).

MPV IN PATIENTS VS CONTROLS

	ACS	Control	t-Value	p-Value
MPV mean \pm SD	13 \pm 0.71	8.75 \pm 0.35	2.19	0.02867

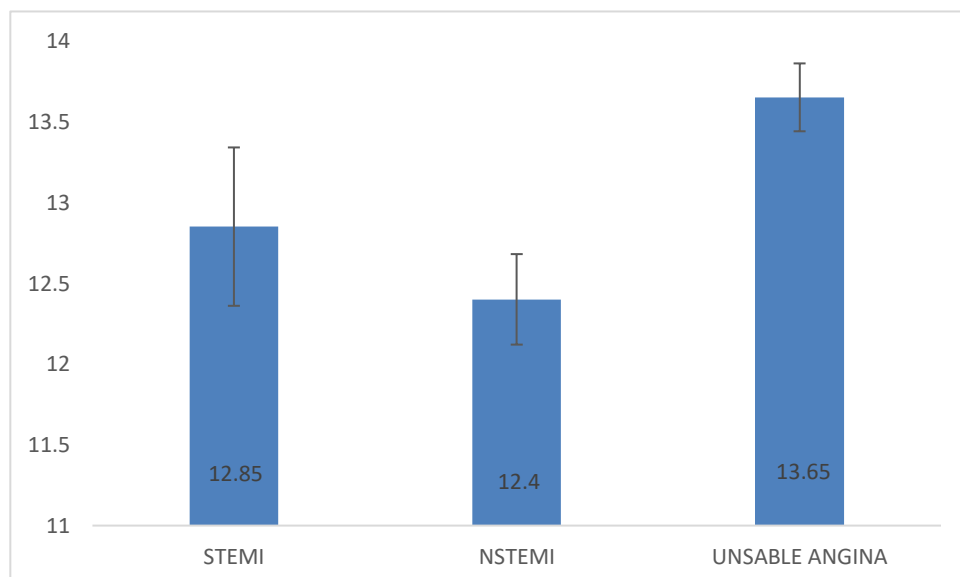


ACS patients were divided into 3 groups (1) Patients with STEMI; (2) Patients with NSTEMI; (3) Patients with UA. Comparing the MPV value of UA, NSTEMI, STEMI significant difference were noted. One way ANOVA test

was used to compare the MPV in ACS groups. MPV value above 8.1 was considered to be elevated. A p-value <0.05 are regarded as statistically significant.

COMPARISON OF MPV PARAMETERS IN ACS : NSTEMI, STEMI AND UA

S.No	Variables	STEMI	NSTEMI	UA	f-Value	p-Value
1	MPV	12.85 \pm 0.49	12.4 \pm 0.28	13.65 \pm 0.21	8.34	0.0003113



DISCUSSION

ACS is caused due to sudden rupture of atheromatous plaque. The diagnosis of ACS is major challenge in cardiovascular medicine because of atypical chest pain, normal electrocardiograms. Cardiac enzymes are used as biomarkers for ACS diagnosis as it indicates the severity of myocardial injury. Many studies have been done to find a better marker which is easily available in the risk stratification ACS patients than with Atypical chest pain. At the earliest stages of ACS, the current cardiac markers are insufficiently sensitive. (40,41). Several studies that have been published recently have identified MPV as a risk factor for long-term mortality & cardiovascular disease in individuals with ACS(35,36,37). The aetiology, morbidity, and mortality of ACS are significantly influenced by platelets(19). Cardiovascular disease (CAD), peripheral artery disease (PAD), and transplant vasculopathy are linked to elevated platelet activation (20,21,22,23). More mediators, including adhesive proteins (fibrinectin, thrombospondin, & fibrinogen), growth factors (PDGF, transforming growth factor- β , basic FGF), chemotactic and mitogenic factors (PF4), coagulation factors (factor V, factor XI), and cytokine-like factors (IL-1, CD40 ligand), are secreted and expressed by larger platelets than by smaller ones (24,25,26). Active platelets release chemokines that activate smooth muscle cells and cause atherogenesis & inflammation. (27,28). The existence of 1. bigger PLTs is correlated with a higher risk of MI & coronary thrombosis because they are hemostatically more active. In the biggest study to date, researchers found that 2. MPV was separate risk factor for death or recurrent ischemia after a myocardial infarction(38,39). According to Klovaite et al., regardless of established cardiovascular risk factors, the chance of MI has risen by 38% in people with 3. MPV 7.4 vs < 7.4fl (29). MPV was observed to be higher in Endler et al.'s study comparing AMI patients to stable AP (30). In their research, Martin et al. hypothesised that elevated MPV may function as a separate risk factor for 4. mortality and post-MI recurrence of coronary events. (31). In our study, MPV was considerably higher in ACS patients than in control groups. (ACS patients (13 ± 0.71) and control groups (8.75 ± 0.35); $P = 0.005$). Among ACS groups elevated MPV was found in STEMI patients 5. compared to NSTEMI and UA. Jan Budzianowski et al. in their meta analysis study suggested that to find the hematological indices in acute coronary syndrome and 6. concluded that inflammatory process play a major role in atherosclerosis and inflammatory markers like NLR, MPV, PLR, PDW and RDW have significance in the ACS diagnosis(32). Study conducted in university by Lippi et al 7. reported that MPV was found to be higher in patients with ACS than control groups. MPV in patients with ACS (8.0 ± 5 , $P < 0.001$) and without ACS (7.4 ± 5 , $P < 0.001$)(33). In our prospective observational study there was significant difference in the MPV value between ACS and non ACS patients and also between the ACS

groups. In a study conducted at Jabalpur MPV value was found to be significantly increased in ACS patients. Larger platelet activity is mainly involved in thrombus formation and is expressed in mean platelet volume. As MPV is part of routine hematological study and is noninvasive can be used a risk factor in prediction of ACS development (34).

CONCLUSION:

The main aim of this observational study is to consider the role of MPV as a predictor of CAD. Several common factors such as diabetes, hypertension, obesity are also being compared here. Diagnosis of ACS patients is still challenging in cardiovascular medicine. MPV values in 250 ACS patients and 250 normal healthy individuals were statistically analyzed. The MPV value was significantly elevated in ACS patients and MPV value varies significantly between ACS groups. About 85% of patients showed elevated MPV value compared with control groups. I conclude that with enough evidence obtained from this study and previous other studies, it can be concluded that the role of MPV as a marker of ACS is inevitable. Further research, with emphasis laid on effective drug discovery and diagnostic methods, of ACS, using MPV, may contribute to a revolution in the field of ACS diagnosis.

REFERENCES:

1. S.A. Achar, S. Kundu, W.A. Norcross, Diagnosis of acute coronary syndrome. *Am Fam Physician*, 72 (2005), pp. 119-126.
2. C.W. Hamm, M. Bertrand, E. Braunwald. Acute coronary syndrome without ST elevation: implementation of new guidelines. *Lancet* (London, England), 358 (2001), pp. 1533-1538.
3. S.G. Chu, R.C. Becker, P.B. Berger, et al., Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *J Thromb Haemost*, 8 (2010), pp. 148-156.
4. J.A. Coppinger, G. Cagney, S. Toomey, T. Kislinger, O. Belmont, J.P. McRedmond, et al. Characterization of the proteins released from activated platelets leads to localization of novel platelet proteins in human atherosclerotic lesions. *Blood*, 103 (2004), pp. 2096-2104.
5. M. Gawaz, H. Langer, A.E. May. Platelets in inflammation and atherogenesis. *J Clin Invest*, 115 (2005), pp. 3378-3384.
6. S. Willoughby, A. Holmes, J. Loscalzo. Platelets and cardiovascular disease. *Eur J Cardiovasc Nurs: J Work Group Cardiovasc Nurs Eur Soc Cardiol*, 1 (2002), pp. 273-288.
7. P.M. Bath, R.J. Butterworth. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis: Int J Haemost Thromb*, 7 (1996), pp. 157-161.
8. E. Coban, M. Ozdogan, G. Yazicioglu, F. Akcıt. The mean platelet volume in patients with obesity. *Int J Clin Pract*, 59 (2005), pp. 981-982.

9. K. Kario, T. Matsuo, K. Nakao. Cigarette smoking increases the mean platelet volume in elderly patients with risk factors for atherosclerosis. *Clin Lab Haematol*, 14 (1992), pp. 281-287.
10. S. Nadar, A.D. Blann, G.Y. Lip. Platelet morphology and plasma indices of platelet activation in essential hypertension: effects of amlodipine-based antihypertensive therapy. *Ann Med*, 36 (2004), pp. 552-557.
11. N. Papanas, G. Symeonidis, E. Maltezos, G. Mavridis, E. Karavageli, T. Vosnakidis, et al. Mean platelet volume in patients with type 2 diabetes mellitus. *Platelets*, 15 (2004), pp. 475-478.
12. R. Pathansali, N. Smith, P. Bath. Altered megakaryocyte-platelet haemostatic axis in hypercholesterolaemia. *Platelets*, 12 (2001), pp. 292-297.
13. M.M. Khandekar, A.S. Khurana, S.D. Deshmukh, et al. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. *J Clin Pathol*, 59 (2006), pp. 146-149.
14. Z. Huczek, J. Kochman, K.J. Filipiak, et al. Mean platelet volume on admission predicts impaired reperfusion and long-term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention. *J Am Coll Cardiol*, 46 (2005), pp. 284-290.
15. S.C. Goncalves, M. Labinaz, M. Le May, et al. Usefulness of mean platelet volume as a biomarker for long-term outcomes after percutaneous coronary intervention. *Am J Cardiol*, 107 (2011), pp. 204-209.
16. H. Vakili, R. Kowsari, M.H. Namazi, et al. Could mean platelet volume predicts impaired reperfusion and in-hospital major adverse cardiovascular event in patients with primary percutaneous coronary intervention after ST-elevation myocardial infarction. *J Tehran Heart Cent*, 4 (2009), pp. 17-23.
17. M.H. Seyyed-Mohammadzad, R. Eskandari, Y. Rezaei, et al. Prognostic value of mean platelet volume in patients undergoing elective percutaneous coronary intervention. *Anadolu Kardiyol Derg* (2014) [Epub ahead of print].
18. Huang HL, Chen CH, Kung CT, Li YC, Sung PH, You HL, Lin YH, Huang WT. Clinical utility of mean platelet volume and immature platelet fraction in acute coronary syndrome. *biomedical journal*. 2019 Apr1;42(2):107-15.
19. Thaulow E, Erikssen J, Sandvik L, Stormorken H, Cohn P.F. Blood platelet count and function are related to total and cardiovascular death in apparently healthy men. *Circulation*. 1991; 84: 613-617.
20. Willoughby S, Holmes A, Loscalzo J. Platelets and cardiovascular disease. *Eur J Cardiovasc Nurs*. 2002; 1: 273-288.
21. Fateh-Moghadam S, Bocksch W, Ruf A, Dickfeld T, Scharlt M, Pogátsa-Murray G, Hetzer R, Fleck E, Gawaz M. Changes in surface expression of platelet membrane glycoproteins and progression of heart transplant vasculopathy. *Circulation*. 2000; 102: 890-897.
22. Fateh-Moghadam S, Li Z, Ersel S, Reuter T, Htun P, Plöckinger U, Bocksch W, Dietz R, Gawaz M. Platelet degranulation is associated with progression of intima media thickness of the common carotid artery in patients with diabetes mellitus type 2. *Arterioscler Thromb Vasc Biol*. 2005; 25: 1299-1303.
23. Elsherbiny I.A, Shoukry A, El Tahlawi M.A. Mean platelet volume and its relation to insulin resistance in non-diabetic patients with slow coronary flow. *J Cardiol*. 2012; 59: 176-181.
24. Kaya M.G, Yarlioglues M, Gunebakmaz O, Gunturk E, Inanc T, Dogan A, Kalay N, Topsakal R. Platelet activation and inflammatory response in patients with non-dipper hypertension. *Atherosclerosis*. 2010; 209: 278-282.
25. Gawaz M, Langer H, May A.E. Platelets in inflammation and atherogenesis. *J Clin Invest*. 2005; 115: 3378-3384.
26. Varol E, Akcay S, Ozaydin M, Erdogan D, Dogan A, Altinbas A. Mean platelet volume is associated with insulin resistance in non-obese, non-diabetic patients with coronary artery disease. *J Cardiol*. 2010; 56: 154-158.
27. Gawaz M, Langer H, May A.E. Platelets in inflammation and atherogenesis. *J Clin Invest*. 2005; 115: 3378-3384.
28. Gawaz M. Role of platelets in coronary thrombosis and reperfusion of ischemic myocardium. *Cardiovasc Res*. 2004; 61: 498-511.
29. Klovaite J, Benn M, Yazdanyar S, Nordestgaard BG. High platelet volume and increased risk of myocardial infarction: 39 531 participants from the general population. *J Thromb Haemost*. 2011; 9: 49-56.
30. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C, et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. *Br. J. Haematol*. 2002; 117:399- 404.
31. Martin JF, Bath PM, Burr ML. Influence of platelet size on outcome after MI. *Lancet*. 1991;338:1409-11.
32. Budzianowski J, Pieszko K, Burchardt P, Rzeźniczak J, Hiczkiewicz J. The role of hematological indices in patients with acute coronary syndrome. *Disease Markers*. 2017 Jan 1;2017.
33. Lippi G, Filippozzi L, Salvagno GL, Montagnana M, Franchini M, Guidi GC, Targher G. Increased mean platelet volume in patients with acute coronary syndromes. *Archives of pathology & laboratory medicine*. 2009Sep;133(9):1441-3.
34. Ranjith MP, Divya R, Mehta VK, Krishnan MG, KamalRaj R, Kavishwar A. Significance of platelet volume indices and platelet count in ischaemic heartdisease. *Journal of clinical pathology*. 2009 Sep1;62(9):830-3.
35. Sansanayudh N, Numthavaj P, Muntham D, et al. Prognostic effect of mean platelet volume in patients with coronary artery disease. A systematic review and meta-analysis. *Thromb Haemost* 2015; 114(06):1299-1309.
36. Sansanayudh N, Anothaisintawee T, Muntham D, McEvoy M, Attia J, Thakkestian A. Mean platelet volume and coronary artery disease: a systematic review and meta-analysis. *Int J Cardiol* 2014;175(03):433-440.

37. Lai HM, Chen QJ, Yang YN, et al. Association of mean platelet volume with impaired myocardial reperfusion and short-term mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Blood Coagul Fibrinolysis* 2016;27(01):5–12.
38. Martin JF, Bath PM, Burr ML. Influence of platelet size on outcome after myocardial infarction. *Lancet* 1991;338(8780):1409–1411 15.
39. Burr ML, Holliday RM, Fehily AM, Whitehead PJ. Haematological prognostic indices after myocardial infarction: evidence from the diet and reinfarction trial (DART). *Eur Heart J* 1992;13(02): 166–170.
40. Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin; the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J*.2002;23(15):1190-201.
41. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. *Heart*.2008;94:16-26.