ORIGINAL ARTICLE

In Hospital outcome of Prediction of Peripheral Arterial disease In Diabetic Tobacco User Patients

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ABSTRACT

Background: Peripheral artery disease (PAD) is a distinct atherosclerotic disorder marked by stenosis of the arteries common in tobacco users. Here we investigate prediction of unknown peripheral arterial disease (PAD) amongst patients with diabetic tobacco user and diabetic without tobacco user.

Methodology: This prospective observational study was conducted in the Department of Cardiology, Ibrahim Cardiac Hospital and Research Institute, Dhaka, Bangladesh. A total of 60 patients were enrolled in this study who were presented with chest pain associated with lower limb claudication. They were diabetic population, constituted tobacco user in group-I and without tobacco user in group-II.

Results: Hypertension was the leading risk factor in both groups (76.7% vs. 80%). 80% of patients of group I and 46.7% of patients of group II had mild form of ABI value. 3.3% of patient of group II had severe form of ABI value. There was no statistical significant difference between two group of patients (p=0.053). 93.3% patients of group I and 96.7% patients of group II had coronary artery disease. Twenty three patients of tobacco user group (n=30) had peripheral artery disease, whereas ten patients of without tobacco user group (n=30) had peripheral artery disease which was statistically significant (p=0.003). Three quarters (76.7%) of group I developed PVD as compared to 33.3% of group II. The risk of developing PVD in diabetic smokers was observed to be more than 6 fold (95% CI: 2.109-20.479) higher than that in non tobacco user were diabetics. 16.7% patients of group I atherosclerosis in femoral artery and the value is 10% in case of group-II, which is statistically in significant(p=0.433).

Conclusion: The awareness and implementation of ABI in general clinical practice is poor. A simple, inexpensive test like ABI can improve the diagnosis of PAD in clinical practice and thus help in preventing CAD and consequent death by a range of medical therapies.

Key Words: Peripheral artery disease; Diabetes; Risk factors; Tobacco.

Introduction

During the 20th century, use of tobacco products contributed to the deaths of 100 million persons worldwide[1], approximately 6 million additional deaths were linked to tobacco use, the world's leading underlying cause of death, responsible for more deaths each year than human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), tuberculosis, and malaria combined.[1] PAD affects 8 to 10 million individuals in the United States[2,3] and is associated with

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reduced functional capacity[4,5] and increased risk for cardiovascular morbidity and mortality.[6,7] Peripheral arterial disease affects some 12% to 14% of the general population. The prevalence of peripheral arterial disease is age-dependent, reaching 10% in people aged over 60 years[8,9], and some 20% aged over 75 years10-12. Peripheral vascular disease is estimated to affect some 27 million people in Europe and North America.[13] Despite its widespread prevalence and negative associations with quality of life, morbidity, and mortality, PAD remains under diagnosed and undertreated.[3,15,16] Preventable or treatable risk factors for PAD are generally thought to mirror other forms of cardiovascular disease and include tobacco (both smoker and smokeless) user, type 2 diabetes, and clinically elevated levels of blood pressure and cholesterol, which are the main therapeutic targets in clinical and prevention guidelines.[17,18] However, their respective associations with risk of PAD and the extent to which they are jointly associated with the incidence of PAD are not well established.

Peripheral arterial disease is considered to be a set of chronic or acute syndromes, generally derived from the presence of occlusive arterial disease, which cause inadequate blood flow to the limbs. On most occasions, the underlying disease process is arteriosclerotic disease, mainly affecting the revascularization to the lower limbs; From the physiologic point of view, ischemia of the lower limbs can be classified as functional or critical. Functional ischemia occurs when the blood flow is normal at rest but insufficient during exercise, presenting clinically as intermittent claudication. Critical ischemia is produced when the reduction in blood flow results in a perfusion deficit at rest and is defined by the presence of pain at rest or trophic lesions in the legs. In this situation, precise diagnosis is fundamental, as there exists a clear risk of loss of the limb if adequate blood flow is not reestablished, either by surgery or by endovascular therapy. Differentiating between the two concepts is important in order to establish the therapeutic indication and the prognosis in patients with PAD. The degree of clinical involvement depends on two factors: the chronologic evolution of the process (acute or chronic) and the localization, and extension of the disease (involvement of 1 or more sectors).[19]

Tobacco is the most important, preventable risk factor for PAD. Smoker has a significantly greater risk of developing PAD than people who have never smoked. Some types of peripheral arterial disease are almost exclusively found in tobacco user. Tobacco smoking currently kills five million people a year worldwide and, according to estimates, will probably kill eight million people a year between now and 2030 and one billion over the course of the 21st century.[20,21] The World Health Organization projects that the number of smokers worldwide will increase from 1.3 billion today to about 1.7 billion in 2025. In 2010, the World Health Organization (WHO) chose as the theme of "World No Tobacco Day" the relation between gender and tobacco, with an emphasis on marketing cigarettes to women. This theme was chosen "to draw particular attention to the harmful effects of tobacco marketing towards women and girls".[22]

In Bangladesh, tobacco use has become not only a major contributor to the country's high morbidity, but also the biggest drains to the nation's economy. Several national studies in Bangladesh have shown high prevalence of both smoking (e.g., cigarettes, bidis) and use of smokeless tobacco (e.g., betel quid with tobacco, khoini, gul, zarda).[23] In Bangladesh 43.3% of adults (41.3 million) currently use tobacco in smoking or smokeless form. Among them 26.4% of men, 28% of women and 27.2% overall (25.9 million adults) currently use smokeless tobacco.[23]

Methodology

Study population and design

This prospective observational study was conducted in the Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Dhaka for a period of 4 months starting from January, 2016 to April, 2016. A total of 60 patients who were presented with chest pain and diabetic with and without tobacco user followed up during hospital period. Patients were categorized into two groups on the basis of tobacco use. Group I (diabetic with tobacco user) had 30 patients and Group II (diabetic without tobacco user) had 30 patients.

Ankle Brachial Index

The ankle-brachial pressure index (ABPI) or ankle-brachial index (ABI) is the ratio of the blood

pressure at the ankle to the blood pressure in the upper arm (brachium). Compared to the arm, lower blood pressure in the leg is an indication of blocked arteries due to peripheral artery disease (PAD). The ABPI is calculated by dividing the systolic blood pressure at the ankle by the systolic blood pressure in the arm.[24]

$$ABPI_{Leg} = \frac{P_{Leg}}{P_{Arm}}$$

Where P_{Leg} is the systolic blood pressure of dorsalis pedis or posterior tibial arteries

And P_{Arm} is the highest of the left and right arm brachial systolic blood pressure

The ABPI test is a popular tool for the non-invasive assessment of PVD. Studies have shown the sensitivity of ABPI is 90% with a corresponding 98% specificity for detecting hemodynamically significant (Serious) stenosis > 50% in major leg arteries, defined by angiogram.[25] ABPI value of under 0.50, is considered as severe arterial disease.[26]

Statistical Analysis

The age and gender differences and hypertension, diabetes, dyslipidaemia, smoking habit, family history of IHD, CKD, peripheral artery and coronary artery profile were statistically analyzed. Influence of these parameter with standard deviation (SD) was investigated. Data were entered in computer using SPSS for windows version 16.0 (SPSS Inc., Chicago, IL). Results were cross-tabulated to find out the relationships between the variables. Statistical analysis was performed using χ^2-square for test of association and Fisher's exact test as appropriate. A p-value of less than 0.05 was considered significant in all statistical analysis.

Result

Standard deviation (SD) of age in group I and group II patients were respectively 55.57 ± 9.601 and 55.47 ± 8.224 years. No significant difference was observed between two groups (0.428). In group-I patients 93.33 percent was male and rest was female. In group- II 73.30 percent patients was male and rest was female. No statistically significant difference was found between the group of patients $p = 0.531$.

Twenty three (76.7%) patients of group-I and twenty four (80%) patients of group-II had hypertension. There was no statistically significant difference in hypertension between the two groups ($p = 0.120$).Twenty five (83.3%) patients of group-I and twenty four (80%) patients of group-II had dyslipidaemia. There was no statistically significant difference in dyslipidemia between the groups ($p = 0.254$). Nineteen (63.3%) patients of group-I and twenty five (83.3%) patients of group-II had positive family history of IHD. Statistically significant difference was observed both the two groups ($p = 0.003$). Regarding the obesity no significant difference was observed (Table-1).

Table-1: Risk Factors of the study population

Risk Factors	Group-I (n=30) diabetic with tobacco user n(%)	Group-II (n=30) diabetic without tobacco user n(%)	p- value
Hypertension			
Present	23(76.7)	24(80)	0.120^{NS}
Absent	7(23.3)	6(20)	
Dyslipidaemia			
Present	25(83.3)	24(80)	0.254^{NS}
Absent	5(16.7)	6(20)	
Family History			
Present	19(63.3)	25(83.3)	$*0.003^{S}$
Absent	11(36.7)	5(16.7)	
BMI(Obesity)			
Obese (30-34.9kg/m²)	5(16.7)	1(3.3)	
Overweight (25-29.9kg/m²)	12(40.0)	18(60)	0.093^{NS}
Normal (18.5-24.9kg/m²)	13(43.3)	11(36.7)	

*S= Significant; NS=Not significant, *p value reached from X^2 test, p value significant ⩽ 0.05*

Most of the patients in both groups presented with NSTEMI (36.7% in group-I and 46.7% in group-II). STEMI incidence was 26.7% and 30% in group I and group II respectively. Rest of the patients in group-I & group-II were unstable angina (36.7% in group-I and 23.3% in group-II). Analysis found statistical significant ($p = 0.031$) difference considering clinical diagnosis between three groups (Table-2).

Table-2: Clinical diagnosis of the study pati ents by group (n=60)

Clinical diagnosis	Group-I (n=30) diabetic with tobacco user		Group-II (n=30) diabetic without tobacco user		p Value
	Frequency	Percentage	Frequency	Percentage	
STEMI	8	26.7	9	30	
NSTEMI	11	36.7	14	46.7	*0.031^{S}
Unstable angina	11	36.7	7	23.3	

*S= Significant; NS=Non significant, *p value reach from X^2 test, p value significant ⩽0*

Sixty patients underwent coronary angiogram. Among hem thirty one patients had Triple Vessel Disease (TVD), fifteen patients had Double Vessel Disease (DVD). Eleven had Single Vessel Disease (SVD) and rests were of normal epicardial coronaries (Figure-1).

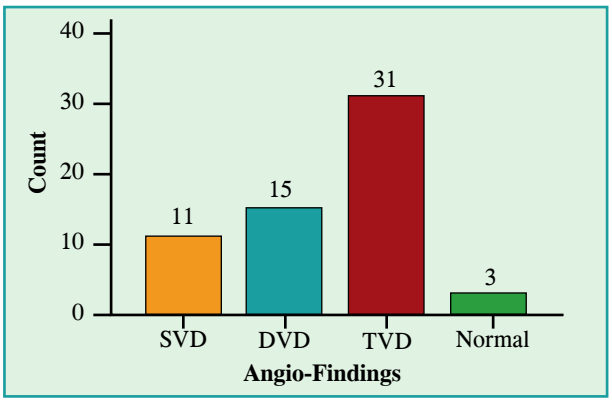

Fig-1: Coronary Angiogram findings of the study patients (n=60)

80% of patients of group I and 46.7% of patients of group II had mild form of ABI value. 3.3% patient of group II had severe form of ABI value. There was no statistical significant difference between two group of patients (p=0.053) (Table-3).

Table- 3: The distribution of ankle brachial index values in both lower limbs and their relation to severity of peripheral artery disease.

Severity (ABI value)	Group-I (n=30) diabetic with tobacco user	Group-II (n=30) diabetic without tobacco user	p Value
Mild (0.80-0.89)	24(80%)	14(46.7%)	
Moderate (0.50-0.79)			
Severe (>0.50)		1(3.3%)	0.053^{NS}
Normal	6(20%)	15(50%)	

S= Significant; NS=Non significant

Twenty three patients of tobacco user group (n=30) had peripheral artery disease and ten patients of nonsmoker group (n=30) had peripheral artery disease, statistically significant (p=0.003) difference was found between the two groups of population (Table-4).

Table-4: Relation of tobacco use to peripheral artery disease

Tobacco Habit	PAD		p Value
	yes	no	
Smoking habit	18	6	
Smokeless tobacco	5	1	*0.003 ^{S}
Nonsmoker	10	20	

*S= Significant; NS=Non significant, *p value reach from X^2 test, p value significant ≤0.05*

Over three quarters (76.7%) of group I developed PVD as compared to 33.3% of group II. The risk of developing PVD in diabetic smokers was observed to be more than 6 fold (95% CI: 2.109-20.479) higher than that in diabetic with non tobacco user (Table-5).

Table: 6 Association of age group and PVD with ADP

Age group	PVD		p Value	PVD		p Value
	Yes	No		Yes	No	
25-45 years	2	4		2	4	
46-65 years	27	19	0.453^{NS}	15	31	0.853^{NS}
66-75 years	4	3		3	4	
76-90 years	0	1		0	1	

16.7% patients of group I had femoral artery atherosclerosis and 10% patients of group II had femoral artery atherosclerosis, which is statistically in significant(p=0.433). 13.3% and 23.3% patients of group I had popliteal and anterior tibial artery atherosclerosis but atherosclerosis of popliteal and ant.tibial artery was not found in group II patients.33.3% patients of group I and 13.3% patients of group II had posterior tibial artery disease which is not statistically significant (p=0.593). 43.5% patients of group I and 23.3% patients of group II had arteria dorsalis pedis disease which is not significant (p=0.089) (Table-7).

Table-7: Distribution of peripheral artery disease in different site between two groups of patients.

Peripheral artery		Group-I (n=30) diabetic with tobacco user		Group-II (n=30) diabetic without tobacco user		p Value
		n	%	n	%	
Femoral artery	yes	5	16.7	3	10	0.433NS
	no	25	83.3	27	90	
Popliteal artery	yes	4	13.3	0		
	no	26	86.7	30	100	
Ant.Tibial artery	yes	7	23.3	0		
	no	23	76.7	30	100	
Post. Tibial artery	yes	10	33.3	4	13.3	0.593NS
	no	20	76.7	26	86.7	
Arteria Dorsalis pedis	yes	13	43.5	7	23.3	0.089NS
	no	17	56.7	23	76.3	

S= Significant; NS=Non significant

Discussion

During the 20th century, use of tobacco products contributed to the deaths of 100 million persons worldwide.[1] In 2011, approximately 6 million additional deaths were linked to tobacco use, the world's leading underlying cause of death, responsible for more deaths each year than human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), tuberculosis, and malaria combined.[1] One third to one half of lifetime users die from tobacco products, and smokers die an average of 14 years earlier than nonsmokers.[27] Tobacco use also is a major risk factor for peripheral arterial disease. PAD is a condition in which plaque builds up in the arteries that carry blood to the head, organs, and limbs. People who have PAD are at increased risk for heart disease, heart attack, and stroke. According to the Centers for Disease Control and Prevention, around 8 million people in the US suffer from PAD, with between 12-20% of these aged 60 and over. But researchers from the UK and US have revealed that the number of people with peripheral artery disease worldwide has risen by 23.5% in the past 10 years, from 164 million in 2000, to 202 million in 2010.

The mean age of studied patients was 56.63±8.95 years. Mean age difference was not statistically significant (p=0. 428). Nearly similar pattern of age distribution was reported by Sharmistha Sarangi, *et al.*[28] in their study in India. This observation was being consistent with the findings of different studies done in foreign countries.[29,30,31,32]

In this present study, there were 93.33% male in group I and 73.33% in group II with no significant difference in gender between the two groups (p=0.531). So the two groups were age and sex matched. In Asia the various studies showed the female patients formed a small percentage.[28-32]

Except for higher prevalence of family history for ischemic heart disease in group I (p=0.003), other cardiovascular risk factors like hypertension (p=0.120), dyslipidemia (p=0.254) and obesity (0.093) were similarly in both group I and group II. The prevalence of risk factors in the present study was comparable with other studies.[28-32]

ST elevation myocardial infarction (STEMI) was diagnosed in 26.7% in group I and 30% in group II. NSTEMI was diagnosed in 36.7% in group I and 46.7% in group II. Unstable angina was diagnosed in 36.7% and 23.3% in group I and group II, which is statistically significant between two group of patients (p=0.031). Similar statistical difference was found in Hasan A. Al Thani, *et al.*.[32]

Coronary angiogram was done both group of patients, out of 60 patients 28(93.3%) patients of group I and 29(96.7%) patients of group II had coronary artery disease. No significant association was found between diabetic tobacco user and CAD severity (p=.500). 24.7% coronary artery disease was found in Sharmistha Saragi, *et al.*.[28]

Twenty three patients of tobacco user group I (n=30) who had peripheral artery disease and ten patients of nonsmoker group II (n=30) had peripheral artery disease which is statistically significant (p=0.003). Gulf RACE (2009) was found statistical significant (p=0.001).[33]

Out of 60 patients twenty three patients of group I and ten patients of group II had peripheral artery disease in this study which was statistically significant (p=0.001),OR for PAD when analyzed by univariate analysis adjusting for confounders like diabetes, family history of ischemic heart disease and tobacco use. DM with tobacco user group showed strong association with adjusted OR was 6.571 (CI 2.109-20.491).

In this study total 33 patients had peripheral artery disease. 27 patients of age 46-65 years group had higher incidence than other groups which was not statistically significant, Shin Yi Jang *et al.*[29] was found similar prevalence but Sharmistha Sarangi, *et al.*[28] was found more prevalence of PAD in more than 65 years age group.16.7% patients of group I had femoral artery atherosclerosis and 10% patients of group II had femoral artery atherosclerosis, which was not statistically significant (p=0.433).13.3% and 23.3% patients of group I had popliteal and anterior tibial artery atherosclerosis but atherosclerosis of popliteal and anterior tibial artery was not found in group II patients. 33.3% patients of group I and 13.3% patients of group II had posterior tibial artery disease which was not statistically significant (p=0.593). 43.5% patients of group I and 23.3% patients of group II had arteria dorsalis pedis disease which was not statistically significant (p=0.089). 15 patients of 46-65 years age group had disease in ADP which was higher than other age group and was not statistically significant.

Conclusion

There is a definite and strong correlation between PAD and CAD. In view of the increasingly aging population and associated increase in atherosclerotic vascular disease, confrontation with patients of PAD will increase, which however, continues to be under diagnosed and under treated. The awareness and implementation of ABI in general clinical practice is poor. A simple, inexpensive test like ABI can improve the diagnosis of PAD in clinical practice and thus help in preventing CAD and consequent death by a range of medical therapies. A further study should be undertaken with larger sample size and involving multiple centers and longer duration of follow-up period will give clear picture of clinical outcome between peripheral artery disease and coronary artery disease among tobacco user diabetic patients.

Conflict of interest: We have no conflict of interest.

References

1. www.who.int/tobacco/mpower/2008/english (WHO report on the global tobacco epidemic 2008), p-7-58.
2. Allison MA, Ho E, Denenberg JO, *et al.* Ethnicspecific prevalence of peripheral arterial disease in the United States. Am J Prev Med. 2007; 32(4): 328-33.
3. Pande RL, Perlstein TS, Beckman JA, *et al.* Secondary prevention and mortality in peripheral artery disease: National Health and Nutrition Examination Study, 1999 to 2004. *Circulation*. 2011; 124(1): 17-23.
4. McDermott MM, Liu K, Greenland P, *et al.* Functional decline in peripheral arterial disease: associations with the ankle brachial index and leg symptoms. *JAMA*. 2004; 292(4): 453-61.
5. McDermott MM, Guralnik JM, Tian L, *et al.* Associations of borderline and low normal ankle-brachial index values with functional decline at 5-year followup: the WALCS (Walking and Leg Circulation Study). *J Am Coll Cardiol*. 2009; 53(12):1056-62.
6. Fowkes FG, Murray GD, Butcher I, *et al.* Ankle Brachial Index Collaboration. Ankle brachial index combined with Framingham risk score to predict cardiovascular events and mortality: ameta-analysis. *JAMA*. 2008; 300(2): 197-208.
7. Steg PG, Bhatt DL, Wilson PW, *et al.*. REACH Registry Investigators. One-year cardiovascular event rates in outpatients with atherothrombosis. *JAMA*. 2007; 297(11): 1197-1206.
8. Criqui MH, Fronek A, Barrett-Connor E, Klauber MR, Gabriel S, Goodman D. The prevalence of peripheral arterial disease in a defined population. *Circulation*. 1985; 71(3): 510-15.
9. Criqui MH. Peripheral arterial disease - epidemiological aspects. *Vasc Med*. 2001; 6(3 uppl): 3-7.

10. Schroll M, Munck O. Estimation of peripheral arteriosclerotic disease by ankle blood pressure measurements in a population study of 60-year-old men and women. *J Chronic Dis*. 1981; 34(6): 261-69.

11. Hiatt WR, Hoag S, Hamman RF. Diagnostic methods for peripheral arterial disease in the San Luis Valley Diabetes Study. *J Clin Epidemiol*. 1990; 43: 597-60.

12. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey 1999-2000. *Circulation*. 2004; 110: 738-43.

13. Belch JJ, Topol EJ, Agnelli G, *et al*. Prevention of atherothrombotic disease network. Critical issues in peripheral arterial disease detection and management: a call to action. Arch Intern Med. 2003; 163: 884-92.

14. Pande RL, Perlstein TS, Beckman JA, *et al*. Secondary prevention and mortality in peripheral artery disease: National Health and Nutrition Examination Study, 1999 to 2004. *Circulation*. 2011; 124(1): 17-23.

15. Hirsch AT, Criqui MH, Treat-Jacobson D, *et al*. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA*. 2001; 286(11): 1317-24.

16. Cacoub PP, Abola MT, Baumgartner I, *et al*. REACH Registry Investigators. Cardiovascular risk factor control and outcomes in peripheral artery disease patients in the Reduction of Atherothrombosis for Continued Health (REACH) Registry. Atherosclerosis. 2009; 204(2): e86-e92.

17. Hirsch AT, Haskal ZJ, Hertzer NR, *et al*. American Association for Vascular Surgery; Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA Task Force on Practice Guidelines Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease; American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; Trans Atlantic Inter-Society Consensus; Vascular Disease Foundation. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; Trans-Atlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation*. 2006;113(11): e463-e654.

18. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FGR. TASC II Working Group. Inter- Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg*. 2007; 45(1) (suppl S): S5-S67.

19. Francisco J. Serrano Hernando *et al*. Peripheral Artery Disease: Pathophysiology, Diagnosis, and Treatment. Rev Esp Cardiol. 2007; 60(9): 969-82.

20. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLo S Med*. 2006; 3: e442.

21. Peto R, Lopez AD. Future worldwide health effects of current smoking patterns. In: Koop CE, Pearson CE, Schwarz MR, editors. Critical issues in global health. San Francisco: Wiley (Jossey-Bass); 2001; pp. 154-61.

22. Tobacco Free Initiative: World No Tobacco Day 2010. Theme: gender and tobacco with an emphasis on marketing to women [Internet]. Geneva: World Health Organization; 2010. Available from: http:// www.who.int /tobacco/wntd /2010 /announcement /en/index.html [accessed 17 November 2010].

23. Global adult tobacco survey (GATS): Bangladesh. World Health Organization; 2009. Available from: http: www. searo.who.int / LinkFiles / Regional Tobacco_Surveillance System GATSBAN FullReport 2009.pdf. Global Adult Tobacco Survey: *GATS Bangladesh Report-2009, Page-19.*

24. Al-Qaisi, M; Nott, DM; King, DH; Kaddoura, S "Ankle brachial pressure index (ABPI): An update for practitioners". Vasc Health Risk Manag. 2009; 5: 833-41.

25. McDermott MM, Criqui MH, Liu King DH, Guralnik JM, Greenland P, Martin GJ, Pearce W "Lower ankle/brachial index, as calculated by averaging the dorsalis pedis and posterior tibial arterial pressures, and association with leg functioning in peripheral arterial disease". J Vasc Surg. December, 2000 32 (6): 1164-71.

26. American Diabetic Association Standard in Medical of Diabetes-2013 Diabetes care, 2013; 36, pp4-10.

27. www.who.int/tobacco/global_report/2013/en, CDC, USA-2008; p.1226-28.

28. Sarangi S, Srikant B, Rao VD *et al*. Correlation between peripheral artery disease and coronary artery disease using ankle brachial index-a study in Indian population. Indian Heart J. 2012; 6401(2012): 2-6.

29. Jang S Yi, Ju YE, Cho S-II, Kim DK *et al*. Comparison of cardiovascular risk factors for peripheral artery disease and coronary artery disease in the Korean population. Korean Circ J. 2013; 43: 316-28.

30. Joosten MM, Pai JK, Bertoia ML *et al*. Association between conventional cardiovascular risk factors and risk of peripheral artery disease in men. JAMA. 2012; vol: 308(16): 1660-67

31. Agarwal AK, Singh M, Arya V, *et al*. Prevalence of peripheral arterial disease in type 2 diabetes mellitus and its correlation with coronary artery disease and its risk factors. J Assoc Physicians India. 2012 Jul; 60: 28-32.

32. Al-Thani HA, El-Menyar A, Zubaid M, *et al*. Peripheral Arterial Disease in Patients Presenting with Acute Coronary Syndrome in Six Middle Eastern Countries. International Journal of Vascular Medicine 2011; Volume 2011, Article ID 815902, 8 pages. (www.hindawi.com)

33. Zubaid M, Rashed WA, Al-Khaja N, *et al*. Clinical presentation and outcomes of acute coronary syndromes in the gulf registry of acute coronary events (Gulf RACE). Saudi Med J. 2008 Feb; 29(2): 251-5.