International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article.

A Comparative Study of Newer and Conventional Risk Factors of Coronary Artery Disease in Young Patients: A Case-Control Study from a Centre in Uttar Pradesh, India

Mastakim A Mazumder[1], Manzoor A Parry[2*], Hamad Jeelani[2], Shahzad Alam[3]

[1]DM Student, Department of Nephrology, Gauhati Medical College and Hospital, Guwahati, Assam, India. [Ex PG Resident, Department of Medicine, Jawaharlal Nehru Medical College, AMU, UP, India]
[2]DM Student, Department of Nephrology, Gauhati Medical College and Hospital, Guwahati, Assam, India. [Ex PG Resident, Department of Medicine, SKIMS, Srinagar, J & K, India]
[3]DM Student, Department of Nephrology, Gauhati Medical College and Hospital, Guwahati, Assam, India. [Ex PG Resident, Department of Medicine, Sarojini Naidu Medical College, Agra, UP, India]

ABSTRACT

Aim: To analyze the young patients with coronary artery disease in relation to the levels of Apolipoprotein A-I and B, Lipoprotein (a), and hs-CRP and to study their relation with other conventional risk factors.

Methods: We conducted a case-control study on 156 subjects who were younger than 45 years of age. All the subjects underwent a detailed clinical history and examinations followed by biochemical investigations underlining th risk factors of coronary artery disease (CAD). 78 of these subjects were confirmed cases of CAD and the rest were normal controls. Statistical analysis was done using unpaired t-test and chi-square test. A value of p <0.05 was considered significant.

Result: The levels of Serum Apolipoprotein A-I were significantly low and the levels of Serum Apolipoprotein B and Serum Lipoprotein (a) were significantly elevated in young CAD patients. The hs-CRP levels were elevated but it did not show any significant correlation with the presence of CAD in young individuals.

Conclusion: Apolipoprotein A-I, Apolipoprotein B and Lipoprotein (a) are significant risk markers for CAD in young.

Keywords: Coronary Artery Disease, Lipoprotein, Apolipoprotein, Lipid Profile.

***Correspondence to:**

Dr. Manzoor A Parry
Department of Nephrology
Gauhati Medical College and Hospital,
Guwahati, Assam, India.

Article History:

Received: 25-09-2018, **Revised:** 22-10-2018, **Accepted:** 28-11-2018

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2018.4.6.022	

INTRODUCTION

Coronary artery disease (CAD) has a multifactorial etiology and the incidence of disease increases with age,[1] but in recent years CAD has been recognized more frequently in the young.[2] Premature CAD is defined as cardiac events occurring before the age of 55 in men and 65 in women.

Sixty percent of the cardiovascular disease burden around the globe is contributed by South Asia (India, Pakistan, Bangladesh, Sri Lanka, and Nepal) although it comprises only 25% of the world population. In India, the incidence of CAD in young is 12-16% as compared to only 5% in the Western population.[3,4] Indians also show higher incidence of hospitalization, morbidity, and mortality than other ethnic groups.[5]

In India, 52% of the CVD-related deaths occur below the age of 50 years and about 25% of acute myocardial infarction (MI) occurs under the age of 40 years.[6,7] Primary prevention of CAD requires identification of an at-risk population and, more important, at-risk individuals, so that effective intervention can be implemented. Unfortunately, traditional Framingham risk assessment factors predict only 60% to 65% of hard cardiac events—acute myocardial infarction (MI) or sudden cardiac death.[8] In up to 50% of patients with CAD the first manifestation of the disease is MI or death,[8] exemplifying the acute need to improve risk prediction. A significant number of young patients with CAD do not have any of the conventional risk factors such as dyslipidemia, hypertension, DM, and smoking.[9] Dyslipidemia and inflammation are key mechanisms in the pathogenesis of atherosclerosis. Apolipoprotein B and Apolipoprotein A-I levels are implicated in the pathogenesis of CAD.[10-12] There is possibility that these measures might be superior to traditional lipid measures for CAD risk prediction based on the premise that Apo B levels better reflect the number of atherogenic lipoprotein particles in a given volume of plasma.[13,14] In comparison to Low-Density Lipoprotein

Cholesterol (LDL–C), the ApoB / ApoA-I ratio is a better indicator of the risk of coronary heart disease.[15] Lp(a) is a powerful risk factor for premature coronary artery disease in both sexes,[16] and elevated serum levels of Lp(a) have been associated with rapid progression of atherosclerosis.[17] This risk, which appears to be limited to premature vascular disease, is strongest before age 45, declines after age 55, and often disappears after age 65.[18]

CRP has been examined as a surrogate marker of other inflammatory mediators such as IL-6 and TNF-α to better understand the inflammatory component of atherosclerosis.[19,20] Although levels of serum CRP is influenced by environmental factors such as obesity, smoking, and hormone therapy, genes play an important role in determining serum CRP levels.

MATERIALS AND METHODS

This was an open-labelled, observational, hospital based, case-control study. A total of 156 subjects were included in the study out of which 78 were confirmed cases of CAD and the rest were controls. The current study was conducted during January 2014 to October 2015, in a tertiary care hospital of Aligarh, Uttar Pradesh. Institutional ethical approval was obtained for the study protocol and written informed consent was taken from all participants.

78 patients of either sex admitted to the Intensive Coronary Care with acute coronary syndrome were taken as cases. The main inclusion criteria for the study were: 1) Age less than 45 years. 2) Patients giving consent to participate in the study. 3) Confirmation of CAD by ECG, specific enzymes like serum CPK-MB & Troponin, stress testing or echocardiography. An equal number of subjects were selected as controls for comparison. Controls were patients younger than 45 years who presented to Medicine OPD for non-cardiac complaints. The exclusion criteria for controls were diabetes, hypertension, history of smoking and a family history of CAD. All 156 subjects underwent detailed history, clinical examination, biochemical tests (Blood sugar- fasting and post prandial , fasting lipid profile, complete blood counts, Apo A-I, Apo B, Lp(a) and hs-CRP). Statistical analysis was done using unpaired t-test and chi-square test.

RESULTS

The baseline characteristics of cases and controls were comparable and there was no statistically significant difference (Table 1). The mean age of cases was 39.74 ± 4.403 years and that of controls was 38.64 ± 4.643 years.

Among the 78 cases of CAD, 68 (87.2%) were males and only 10 (12.8%) were females. The male: female ratio was 6.8: 1. All cases were diagnosed with ACS out of which 42% had STEMI, 29.5% had USA and 28.2% had NSTEMI. 47 (60.3%) were smokers, 19 (24.4%) were obese (BMI ≥ 25 kg/m^2), 18 (23.08%) were hypertensive, 9 (11.5%) were diabetic and 14 (17.9%) had a family history of CAD.

HDL level was lower than the gender adjusted reference range (<40 mg/dl in males and <50 mg/dl in females) in 46 out of 78 (58.97%) cases of young CAD. LDL level was above the normal reference range (100mg/dl) in 42 out of 78 (53.84%) cases of young CAD. TG level was above the normal reference range (130mg/dl) in 23 out of 78 (29.49%) cases of young CAD. T. Cholesterol level was above the normal reference range (200mg/dl) in 9 out of 78 (11.54%) cases of young coronary artery disease.

As reported in Table 2, the mean apoB level and apo B/apoA-I ratio was significantly higher in obese CAD patients. In young CAD patients with raised LDL levels (>100mg/dl), the mean apo B and apo B/apoA-I ratio was significantly higher than those with normal LDL levels. Young CAD patients with low HDL levels (gender adjusted) had significantly lower mean apoA-I level compared to those with normal HDL levels. In young CAD patients with raised total cholesterol levels (>200mg/dl), the mean apoB level was significantly higher than those with normal total cholesterol levels.

Lp(a) was elevated above the reference range i.e. 30 mg/dl in 36 cases (46.15%) and only in 20 controls (25.63%). The higher serum LP(a) levels in CAD cases as compared to the controls was found to be statistically significant (P<0.05). In young CAD patients with raised TG levels, Lp(a) was elevated significantly (p<0.01).

Table 1: Baseline characteristics of cases and controls

	CASE	CONTROL
Mean Age	39.74 ± 4.403	38.64 ± 4.643
Number of males	68	10
Number of females	10	10
26-30 years age group	5 (6.4%)	5 (6.4%)
30-35 years age group	10 (12.8%)	12 (15.4%)
35-40 years age group	24 (30.8%)	26 (33.3%)
40-45 years age group	39 (50.0%)	35 (44.9%)

Table 2: Comparison of the means of Apolipoprotein A-I and B between cases and controls

	CASES (n=78)	CONTROLS (n=78)	p-value
Apo A-I	113.78 ± 30.26	125.33 ± 23.01	<0.01
Apo B	117.76 ±50.52	105.18 ±22.53	<0.05
Apo B/Apo A-I ratio	1.06 ± 0.42	0.87 ± 0.28	<0.01

Table 3: Comparison of mean Apo A-I and Apo B levels among cases with other risk factors

		Apo A-I	Apo B	Apo B/Apo A-I
Smoking status	**Smoker**	111.68±27.94	119.92±54.89	1.09±0.43
	Non-smoker	116.97±33.69	114.48±43.73	1.02±0.40
	p-value	0.47 (NS)	0.64(NS)	0.45 (NS)
Family History	**Present**	105.07±25.54	126.18±54.51	1.22±0.43
	Absent	115.69±31.05	115.92±49.87	1.03±0.41
	p-value	0.24 (NS)	0.49(NS)	0.13(NS)
Type 2 DM	**Diabetic**	105.11±29.37	119.00±11.94	1.21±0.35
	Non-diabetic	114.91±29.37	117.60±53.60	1.04±0.43
	p-value	0.36(NS)	0.85(NS)	0.27(NS)
BMI	**Obese(BMI ≥ 25)**	112.63±32.68	161.98±73.58	1.45±0.51
(kg/m²)	**Non-obese**	114.15±29.72	103.55±29.40	0.94±0.29
	p-value	0.85(NS)	<0.01	<0.01
HDL	**Low (<40 in males and <50 in females)**	105.46±25.37	111.35±47.33	1.08±0.44
(mg/dl)	**Normal**	125.75±33.01	126.98±54.22	1.03±0.39
	p-value	<0.01	0.18(NS)	0.59(NS)
LDL	**Raised (>100)**	120.00±29.45	139.78±57.73	1.19±0.47
(mg/dl)	**Normal**	106.53±29.96	92.07±21.86	0.91±0.28
	p-value	0.60(NS)	<0.01	<0.01
TG	**Raised (>130)**	120.26±36.31	132.89±64.00	1.16±0.54
(mg/dl)	**Normal**	111.07±27.26	111.44±42.81	1.02±0.36
	p-value	0.28(NS)	0.08(NS)	0.27(NS)
T. Cholesterol	**Raised (>200)**	123.10±42.60	150.30±71.12	1.27±0.55
(mg/dl)	**Normal**	112.41±28.17	112.97±45.53	1.03±0.39
	p-value	0.46(NS)	<0.05	0.10(NS)

Table 4: Comparison of Lipoprotein (a) levels between cases and controls

Lp(a) (mg/dl)	CASES(n=78)	CONTROLS(n=78)	TOTAL(n=156)
<5	14 (17.95%)	13 (16.67%)	27
5-30	28 (35.90%)	45 (57.70%)	73
>30	36 (46.15%)	20 (25.63%)	56

Table 5: Comparison of number of cases with elevated Lp(a) levels having other risk factors

		Number of cases with Lp(a) > 30 mg/dl	p-value (using Chi-square test)
Smoking status	**Smoker (n=47)**	20 (42.55%)	0.58
	Non-smoker (n=31)	16 (51.61%)	
Family History	**Present (n=14)**	7 (50%)	0.13
	Absent (n=64)	29 (45.31%)	
T2DM	**Diabetic (n=9)**	5 (55.56%)	0.33
	Non-diabetic (n=69)	31 (44.92%)	
BMI	**Obese(BMI≥25kg/m²) (n=19)**	13 (68.42%)	0.06
	Non-obese (n=59)	23 (38.98%)	
HDL	**Low (<40 mg/dl in males and <50 mg/dl in females) (n=46)**	17 (36.95%)	0.1
	Normal (n=32)	19 (59.37%)	
LDL	**Raised (>100mg/dl) (n=42)**	24 (57.14%)	0.08
	Normal (n=36)	12 (33.33%)	
TG	**Raised (>130mg/dl) (n=23)**	17 (57.14%)	<0.01
	Normal	19 (33.33%)	
T. Cholesterol	**Raised (>200mg/dl) (n=10)**	7 (70%)	0.10
	Normal	29 (42.64%)	

DISCUSSION

In the present study, the prevalence of dyslipidemia in young CAD patients was very high. A previous study conducted in young patients with CAD showed that 90% patients had dyslipidemia. Amongst them, 29% had high serum cholesterol levels [>200 mg %], 72.2% patients had high levels of serum triglycerides [>150 mg%], 72.2% showed decreased HDL-C fraction [<40 mg %] and 77.8% had high levels of LDLC [>100 mg%].[21]

The lower ApoA-I levels and higher apoB levels and the apoB/apoA-I ratio in young CAD subjects is consistent with the finding of many previous studies. Apolipoprotein-related Mortality Risk Study [AMORIS*]* demonstrated that apoB, apoA-I and apoB/apoA-I ratio were all highly significant predictors of MI in both sexes [after adjusting for age, total cholesterol and triglycerides].[22] ApoB was also more significant than LDL cholesterol in prediction of risk of MI in both men and women. Second Northwick Park Heart Study [NPHSII] demonstrated higher risk ratio for ApoB, ApoA-I and ApoB/ApoA-I ratio compared to LDL.[23] Also, the ApoB/ApoA-I ratio conferred the highest relative risk of CAD. Health Professionals Follow-up Study also concluded that the risk ratio for apoB was higher than those for LDL cholesterol.[24] The INTERHEART Study demonstrated that the ratio of ApoB to ApoA-I [OR 3.25, 95%CI 2.82–3.76] was the strongest risk factor in predicting MI.[25] The significant association of ApoA-I with HDL; ApoB with LDL and T. Cholesterol; and that of ApoB/ApoA-I ratio with LDL is consistent with a previous study.[26]

The higher level of Lp(a) in young individuals suffering from CAD compared to controls is in agreement with some previous studies.[27,28] Although it has been reported that hypertriglyceridemia and elevated Lp(a) are independent risk factors for major coronary events in middle-aged men,[29] the higher level of Lp(a) in patients of hypertriglyceridemia was in contrast to the results of a previous study which showed that hypertriglyceridemia is associated with lower levels of Lp(a).[30] The INTERHEART study also reported that high TG level is more prevalent than high cholesterol levels in Indian CAD patients.

Several prospective trials in apparently healthy individuals have shown that elevated hs-CRP is positively correlated with cardiovascular morbidity and mortality.[31,32] According to a study, hs-CRP was better predictor of cardiovascular risk than LDL cholesterol and added prognostic information to the Framingham score.[33] However, there is no complete consensus regarding these findings. Several other studies have concluded that the predictive power of hs-CRP alone and in association with conventional risk factors is relatively low and the focus in clinical practice should continue to be on classic risk factors such as BP, lipids, and smoking.[34-36]

CONCLUSION

The levels of Serum Apolipoprotein A-I were low and the levels of Serum Apolipoprotein B and Serum Lipoprotein (a) were elevated in young patients presenting with CAD therefore making the ratio of Apo B/Apo A-I an important marker in young individuals having CAD. The hs-CRP levels were elevated but it did not show any significant correlation with the presence of CAD in young individuals.

There is still a paucity of Indian data on newer biomarkers for risk stratification of CAD in the younger population. Our study will add to the pool of data, as CAD in the young is becoming a major health concern in our country. Although it is a small study, and cannot be extrapolated to the general population of the country, but it can be used to highlight the significance of these factors in North India. Since, larger randomized studies are requested to expand the findings of the current study and to include testing of these biomarkers as part of risk stratification for CAD in young patients.

ACKNOWLEDGEMENTS

The authors want to thank the patients who were included in the study for the consent for inclusion in the study.

REFERENCES

1. Kannel WB, Abbott RD, Incidence and prognosis of unrecognized myocardial infarction, An Update on the Framingham study, N Engl J Med, 1984; 311:1144-47.

2. Perski A, Olsson G, Landou C, de Faire U, Theorell T, Hamsten A. Minimum heart rate and coronary atherosclerosis: independent relations to global severity and rate of progression of angiographic lesions in men with myocardial infarction at a young age. Am Heart J. 1992;123:609–16.

3. Mammi MVI, Pavithran P, Rahman PA et al. Acute MI in North Kerala. A 20-year hospital based study. Indian Heart J 1991; 43: 93-6.

4. Negus BH, Williard JE, Glamann DB et al. Coronary anatomy and prognosis of young asymptomatic survivors of myocardial infarction. Am J Med 1994; 96: 354-8.

5. Enas EA, Dhawan J, Petkar S. 1996. Coronary artery disease in Asian Indians: lessons learnt and the role of lipoprotein-a. Indian Heart J, 49:25–34.

6. Murray CJL, Lopez AD. 1994. Global comparative assessments in the health sector. Geneva, Switzerland: World Health Organization.

7. Enas EA, Senthilkumar A. 2001. Coronary artery disease in Asian Indians: an update and review [online]. Internet J Cardiol,1. http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijc/vol1n2/cadi.xml. Accessed 15 Feb 2005.

8. Budoff MJ. Atherosclerosis imaging in calcified plaque: Coronary artery risk assessment. Prog Cardiovasc Dis 2003;46:135-148.

9. Seedat YK, Mayet FG, Khan S, Somers SR, Joubert G. Risk factors for coronary heart disease in the Indians of Durban. S Afr Med J 1990;78:447-54.

10. Lamarche, B., Moorjani, S. and Lupien, P.J. et al. 'Apolipoprotein AI and B levels and the risk of ischemic heart disease during a five-year follow-up of men in the Quebec cardiovascular study'. Circulation 1996; 94, 273–8.

11. Sharrett, A.R., Ballantyne, C.M. and Coady, S.A., et al. Coronary heart disease prediction from lipoprotein cholesterol levels, triglycerides, lipoprotein(a), apolipoproteins A-I and B, and HDL density subfractions: The Atherosclerosis Risk in Communities (ARIC) Study'. Circulation 2001; 104, 1108–13.

12. Shai, I., Rimm, E.B. and Hankinson, S.E., et al. 'Multivariate assessment of lipid parameters as predictors of coronary heart disease among postmenopausal women. Potential implications for clinical guidelines'. Circulation 2004; 110, 2824–30.

13. Pischon T, Girman CJ, Sacks FM, Rifai N, Stampfer MJ, Rimm EB. Non-high-density lipoprotein cholesterol and apolipoprotein B

in the prediction of coronary heart disease in men. Circulation. 2005;112(22):3375-83.
14. Benn, M. 'Apolipoprotein B levels, APOB alleles, and risk of ischemic cardiovascular disease in the general population, a review.' Atherosclerosis 2009, 206(1),17-30.
15. Walldius G, Jungner I. Apolipoprotein A-I versus HDL cholesterol in the prediction of risk for myocardial infarction and stroke. Curr Opin Cardiol. 2007;22(4):359-67.
16. Maher VMG, Brown BG. Lipoprotein (a) and coronary artery disease. Curr Opin Lipidol.. 1995;6:229–35.
17. Enas EA, Mehta J, Malignant coronary artery disease in young Asian Indians: thoughts on pathogenesis, prevention, and therapy. Coronary Artery Disease in Asian Indians (CADI) Study. Clin Cardiol, 1995; 18:131–35.
18. Enas EA, Chacko V, Senthil kumar A, Puthumana N, Mohan V. Elevated lipoprotein(a)–a genetic risk factor for premature vascular disease in people with and without standard risk factors: a review. Dis Mon. Jan 2006;52(1):5-50.
19. Rus HG, Vlaicu R, Niculescu F. Interleukin-6 and interleukin-8 protein and gene expression in human arterial atherosclerotic wall. Atherosclerosis 1996;127:263–71.
20. Sukovich DA, Kauser K, Shirley FD, DelVecchio V, Halks-Miller M, Rubanyi GM. Expression of interleukin-6 in atherosclerotic lesions of male ApoE-knockout mice: inhibition by 17b-estradiol. Arterioscler Thromb Vasc Biol 1998; 18: 1498–505.
21. Suman B Sharma, Seema Garg, Abhinav Veerwal and Sridhar Dwivedi. hs-CRP And Oxidative Stress In Young CAD Patients: A Pilot Study. Indian Journal of Clinical Biochemistry, 2008; 23 (4); 334-36.
22. Walldius G, Jungner I, Holme I, Aastveit A, Kolar W, Steiner E. High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study. Lancet 2001; 358: 2026–33.
23. Talmud PJ, Hawe E, Miller GJ, Humphries SE. Nonfasting apolipoprotein B and triglyceride levels as a useful predictor of coronary heart disease risk in middle-aged UK men. Arterioscler Thromb Vasc Biol 2002; 22: 1918–23.
24. Meisinger C, Loewel H, Mraz W, Koenig W. Prognostic value of apolipoprotein B and A-I in the prediction of myocardial infarction in middle-aged men and women: results from the MONICA/KORA Augsburg cohort study.EurHeartJ 2005;26:271-8.
25. Yusuf S, Hawken S, Öunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004; 364: 937-52.
26. G. Kannan, N. N. Rajendran, J. S. N. Murthy, N. Vanitha Rani. The Predictability of APO B, APO A, APO B/APO AI as Better Markers for CAD in South Indian Population. International Journal of Science and Research (IJSR) 2014 June; 3(6): 240-49.
27. L Chen, MR Chester, S Redwood, J Huang, EW Leatham, JC Kaski. Rapid angiographic disease progression in patients with stabilised unstable angina. Circulation, 91 (1995), 2319–2324.
28. Gupta, R., Kastia, S., Rastogi, S., Kaul, V., Nagar, R. and Enas, E.A. (2002) Lipoprotein(a) in Coronary Heart Disease: A Case-Control Study. Ind. Heart. J. 52, 407- 10.
29. Gerd Assmann, Helmut Schulte, Arnold von Eckardstein. Hypertriglyceridemia and elevated lipoprotein (a) are risk factors for major coronary events in middle-aged men. The American Journal of Cardiology. 1 June 1996; 77(14), 1179–84.
30. Werner Bartens, Daniel J. Rader, Glenda Talley, H.Bryan Brewer Jr.Decreased plasma levels of lipoprotein(a) in patients with hypertriglyceridemia. Atherosclerosis August 1994; 108(2), 149–57.
31. Koenig W, Sund M, Frohlich M, Fischer HG, Lowel H, Doring A, et al. C-Reactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men: results from the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Augsburg Cohort Study, 1984 to 1992. Circulation 1999;99:237–42.
32. Kuller LH, Tracy RP, Shaten J, Meilahn EN. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case control study. Multiple Risk Factor Intervention Trial. Am J Epidemiol 1996;144:537–47.
33. Ridker P, Rifai N, Rose L, et al. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N Engl J Med. 2002;347:1557---65.
34. Wang TJ, Gona P, Larson MG, et al. Multiple biomarkers for the prediction of first major cardiovascular events and death. N Engl J Med. 2006 Dec 21. 355(25):2631-9.
35. Lloyd-Jones DM, Liu K, Tian L. Assessment of C-reactive protein in risk prediction for cardiovascular disease. Ann Intern Med. 2006;145:35---42.
36. Danesh J, Wheeler JG, Hirschfield GM. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. N Engl J Med. 2004;350: 1387---97.

Source of Support: Nil. **Conflict of Interest:** None Declared.

Cite this article as: Mastakim A Mazumder, Manzoor A Parry, Hamad Jeelani, Shahzad Alam. A Comparative Study of Newer and Conventional Risk Factors of Coronary Artery Disease in Young Patients: A Case-Control Study from a Centre in Uttar Pradesh, India. Int J Med Res Prof. 2018 Nov; 4(6):109-13.
DOI:10.21276/ijmrp.2018.4.6.022