Research Paper

Volume : 3 | Issue : 6 | June 2014 • ISSN No 2277 - 8179

Fibrinogen and Ischaemic Heart Disease

Medical Science

KEYWORDS : Ischaemic Heart Disease, fibrinogen, coronary artery disease

Dr. Aashka M Shah MD (Biochemistry), 4th year Resident Doctor, Department of Biochemistry, B.J. Medical College, Ahmedabad.

ABSTRACT

Fibrinogen has been identified as an independent risk factor for Ischaemic Heart Disease (IHD) and has been associated with traditional cardiovascular risk factors. Also, the role of elevated fibrinogen in thrombosis suggests that it may be on the causal pathway for certain risk factors to exert their effect. The aims of present study are to estimate levels of plasma fibrinogen in patients of IHD and in controls and to evaluate its role as a thrombotic risk factor for IHD. Plasma fibrinogen levels were determined in cases and controls by functional Clauss method. Significant elevation in Plasma Fibrinogen levels was observed in cases as compared to controls with significant p value. (p value <0.001). Fibrinogen is a risk factor for CAD and it may be a useful screening tool to identify persons at increased thrombotic risk.

INTRODUCTION:

There is a rapidly escalating Coronary artery disease (CAD) epidemic among Asian Indians. Asian Indians have low rates of standard risk factors but the highest rates of premature CAD. Recently, Shojaie et al(2009)[16] and Pineda et al(2009)[14] introduced high levels of fibrinogen as a risk factor for premature CAD in subjects <55 years. Green et al (2009) attributed this acute phase protein a role in subclinical atherosclerosis.[4] Supportive data had previously shown that fibrinogen is involved in the subclinical phase of extracoronary and coronary atherosclerosis and may add to the atherogenic effect of hyperlipidemia.[9]

Plasma fibrinogen is an independent and newer risk factor for IHD. Normal plasma fibrinogen levels are 2 to 4.5 gm/L.[2] Fibrinogen increases the blood viscosity and plays a key-role in thrombosis.[5] Fibrinogen is an acute phase reactant that is increased in inflammatory states. It represents an inflammatory marker that appears to be implicated in the pathophysiology and prognosis of CAD. Its presence contributes to the formation of atheromatous plaque.[12]

MATERIALS AND METHODS:

This is a case control study conducted on 60 cases of IHD who were admitted at Civil hospital, Ahmedabad during the period of January 2013 to December 2013 and 50 age and sex matched healthy control subjects. IHD was defined as the occurrence of Myocardial infarction (MI) or characteristic symptoms of angina pectoris based on location, character and duration of pain and Treadmill test (TMT) positive or Coronary Angiography (CAG) proven cases of IHD. A diagnosis of MI required the presence of at least two of the following criteria: characteristic chest pain, elevated cardiac enzymes, electrocardiographic changes indicative of MI.

The clinical details of patients were recorded in a performa. About 3-4 ml of patient's blood sample was collected by a clean venipuncture in 3.2% trisodium citrate vacutainer and analyzed on StaCompact autoanalyzer. Plasma fibrinogen levels were determined by the functional Clauss method**.** The results were analyzed by student's t-test and p value was calculated by using graphpad software.

OBSERVATION AND RESULTS:

Mean age of cases is 44.43 ± 9.46 years and that for controls is 45.88 ± 10.56 years. The mean levels of plasma fibrinogen in both the cases and controls are as shown in table 1.

Table 1: Plasma Fibrinogen levels (Mean ± SD) in gm/L in cases and controls along with the p value

Cases (Mean ± SD)	Controls (Mean ± SD)	p value
3.2 ± 0.31	2.7 ± 0.29	< 0.001

Plasma Fibrinogen levels were found to be significantly elevated in cases as compared to controls with significant p value (p value <0.001).

DISCUSSION:

Elevation in Plasma Fibrinogen levels in IHD as observed in the present study correlates well with other similar studies[1,6,11,13]. This has been clearly depicted in table 2.

Table 2: A comparative study of plasma fibrinogen levels (gm/L) in IHD

Study	Cases (Mean)	Controls (Mean)	p value
Panwar et al(2011)[13]	2.8	2.31	<0.001
Assmann et al.(1996)[1]	3.3	2.6	<0.001
Stec et al(2000)[6]	3.28	3.03	<0.001
Meade et al(1986)[11]	3.15	2.9	<0.001
Present study	3.2	2.7	< 0.001

The above findings demonstrate a strong correlation between plasma Fibrinogen levels and Ischaemic Heart Disease.

In my present study, mean fibrinogen levels in cases is significantly higher than the mean fibrinogen levels in controls (p <0.001) but the mean fibrinogen levels in both the cases and controls fall within its normal reference range. Similar results were reported by Lima et al(2012)[10] and Giannitsis et al(1999)[3] who found that the mean values for the plasma levels of fibrinogen increased progressively as the CAD became more severe, although these values remained within the normal range.

The Framingham Study by Kannel et al (1997) found that plasma fibrinogen is a consistent risk factor for coronary artery disease.[7] Thompson et al (1995) found fibrinogen to be a strong predictor of coronary events in patients with angina pectoris. In those subjects with high total cholesterol, a high fibrinogen level conferred added risk compared with those with low fibrinogen.[17] Panwar et al(2011) showed that premature coronary artery disease in Indians is due to combination of thrombotic (high fibrinogen) and atherogenic risk factors (high LDL, low HDL and high Triglycerides).[13]

However, conflicting data has also been reported by Lawlor et al(2005) and he showed no association between fibrinogen levels and CAD. Lawlor et al found that adjustment for all potential confounding factors attenuated the association between fibrinogen and CAD.[8]

CONCLUSION:

The present study identifies the association of raised plasma fibrinogen levels with IHD. Fibrinogen acts as a link between inflammation and Coronary Artery Disease. Fibrinogen is an important mediator of cell–cell interaction, adhesion and

inflammation.[15]Fibrinogen participates in the formation of atherosclerotic plaque during the first stages of CAD, suggesting that it is a causative factor rather than a result.[12]

Thus, it can be concluded that fibrinogen is a risk factor for CAD and it may be a useful screening tool to identify persons at increased thrombotic risk.

REFERENCE

1. Assmann G, Cullen P, Heinrich J et al. Hemostatic variables in the prediction of coronary risk: results of the 8 year follow-up of healthy men in the Munster Heart Study (PROCAM). Prospective Cardiovascular Munster Study. Isr J Med Sci 1996; 32:364–370. | 2. Fody, Schoeff, Bishop. Clinical Chemistry-Techniques, Principles, Correlations; 6th edition: Chapter 10, Page no: 239. | 3. Giannitsis E, Siemens HJ, Mitusch R et al. Prothrombin fragments F1+2, thrombin-antithrombin III complexes, fibrin monomers and fibrinogen in patients with coronary atherosclerosis. Int J Cardiol. 1999;68(3):269-274. | 4. Green D, Chan C, Kang J et al. Longitudinal assessment of fibrinogen in relation to subclinical cardiovascular disease: the CARDIA Study. J Thromb Haemost. 2009;13: 95-99. | 5. HS Rissam, S Kishore, N Trehan. Coronary Artery Disease in Young Indians – The Missing Link. Journal of Indian Academy of Clinical Medicine 2001; 2(3):128-132. | 6. James J. Stec, Halit Silbershatz, Geoffrey H. Tofler et al. Association of Fibrinogen With Cardiovascular Risk Factors and Cardiovascular Disease in the Framingham Offspring Population. Circulation. 2000; 102: 1634-1638. | 7. Kannel et al. Influence of Fibrinogen on Cardiovascular Disease. Drugs 1997; 54: 32–40. | 8. Lawlor DA, Smith GD, Rumley A et al. Associations of fibrinogen and C-reactive protein with prevalent and incident coronary heart disease are attenuated by adjustment for confounding factors. British Women's Heart and Health Study. Thromb Haemost. 2005; 93: 955-963. | 9. Levenson J, Giral P, Megnien JL et al. Fibrinogen and its relations to subclinical extracoronary and coronary atherosclerosis in hypercholesterolemic men. Arterioscler Thromb Vasc Biol. 1997; 17: 45-50. | 10. Lima LM, Carvalho MG, Sousa MO. Plasminogen and fibrinogen plasma levels in coronary artery disease. Rev Bras Hematol Hemoter. 2012; 34(4):298-301. | 11. Meade TW, Mellows S, Brozovic M et al. Haemostatic function and ischaemic heart disease: principal results of the Northwick Park Heart Study. Lancet 1986; 2: 533–537. | 12. Nikolaos Papageorgiou, Dimitris Tousoulis, Gerasimos Siasos, Christodoulos Stefanadis. Is Fibrinogen a Marker of Inflammation in Coronary Artery Disease? Hellenic J Cardiol 2010; 51: 1-9. | 13. Panwar, Gupta,Raja et al. Atherothrombotic risk factors & premature coronary heart disease in India: A case-control study. Indian J Med Res 2011; 134: 26-32. | 14. Pineda J, Marín F, Marco P et al. Premature coronary artery disease in young (age <45) subjects: interactions of lipid profile, thrombophilic and haemostatic markers. Int J Cardiol. 2009; 136: 222-225. | 15. S. Kamath and G.Y.H. Lip. Fibrinogen: biochemistry, epidemiology and determinants. Q J Med 2003; 96:711–729. | 16. Shojaie M, Pourahmad M, Eshraghian A et al. Fibrinogen as a risk factor for premature myocardial infarction in Iranian patients: a case control study. Vasc Health Risk Manag. 2009; 5: 673-676. | 17. Thompson et al. Hemostatic Factors and the Risk of Sudden Death in Patients with Angina Pectoris. European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study Group, N. Engl. J. Med.1995; 332: 635–641. |