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# Ischemic Heart Disease - A Haematological, Biochemical and Cytogenetic Study

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**ABSTRACT** Ischemic Heart Disease (IHD) is a condition in which there is lack of oxygen to the heart due to inadequate perfusion. A study was undertaken to correlate IHD with chromosomal abnormalities. As a multifactorial disorder IHD is influenced by both environmental and genetic factors. The lipid profile in IHD was significantly altered. Deletion was a common chromosome aberration noted in the male and female subjects. In addition, aberrations such as inversion and translocation have also been noted and in the case of females 2 of them displayed a satellite chromosome and the rest showed translocation, inversion and mosaicism. The results are discussed pertaining to recent literature.

## INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in industrialized countries where 51% of deaths are related to Ischemic heart disease (IHD). IHD is a complex disorder which is influenced by both environmental and genetic factors. It is now well known that developing countries like India contribute a much larger share to the global CVD burden than that of the developed countries (Reddy et al. 1998 )

Ischemic heart diseases (IHD) is defined as an acute or chronic form of cardiac disability arising from imbalance between myocardial supply and demand for oxygenated blood. Since narrowing or obstruction of the coronary arterial system is the most common cause of myocardial anoxia, the alternate term 'Coronary Artery Diseases' (CAD) is used synonymously with IHD.

Ischemic heart disease among Indians, tends to occur earlier in life, is more severe and extensive and follows a malignant course. This predilection to IHD is attributed to clustering of various traditional and nontraditional risk factors which include insulin resistance with or without glucose intolerance or diabetes mellitus, central obesity, hypertension and dyslipidemia characterised by elevated triglycerides, a high proportion of small dense LDL particles and low HDL levels, smoking, high fat diet, sex, age greater than 45 in male and 55 in female and a previous or a family history of heart disease.

Genetic factors play a significant role in pathogenesis of most diseases of heart. As a multifactorial disorder IHD is caused by an interaction of multiple genes, multiple exogenous or environmental factors. Although IHD has long been known to run in families, the inheritance pattern is complex and unpredictable.

The present study was undertaken to correlate Ischemic Heart Disease with haematological, biochemical alterations and chromosomal abnormalities and to apply this information for further enlightenment of investigation in this field.

## MATERIALS AND METHOD

Samples for the present study were collected from patients comprising of an unrelated heterogeneous group of subjects in the Indian population attending the cardiology department of a private medical science and research institute at Coimbatore city, with the help of a questionnaire and after getting an informed consent. The subjects were categorized based on age as Group I (those with the age of 45 to 54 years) and Group II (those aged 55 years and above). The category also included sex difference (male n = 44 and female n = 34).

Equal numbers of mentally normal and physically healthy subjects were taken as controls. The blood and sera of the experimentals and controls were utilized for analysis of haematological, biochemical parameters and cytogenetic analysis.

## RESULTS

A statistically significant increase in mean

erythrocyte count was observed in all the male subjects, except the subjects of Group I. In controversy to the above results the female subjects exhibited a decrease in mean erythrocyte count when compared to the respective controls. The mean leucocyte count was significantly elevated in the male and female subjects except the Group II female. The mean Haemoglobin content of male subjects expressed a statistically increased value while females showed a statistically decreased value (Table 1).

Significant elevations were observed with regard to Triglycerides, Cholesterol and Low Density Lipoproteins (LDL) with respect to the male and female experimental subjects of Groups I and II. High Density Lipoprotein was significantly decreased in male subjects of Groups I and II while the level increased in the female subjects of Group I and decreased in Group II.

The SGOT values showed a statistically significant increase in all the subjects. The SGPT values also displayed a similar trend, but the increase was statistically significant only for Group I (Table 2).

Out of the 44 male subjects, 3 subjects of Group I showed deletion, addition and satellite chromosome. In Group II, deletions, inversions and a translocation were expressed by 6 subjects. Of the 34 female subjects 2 subjects of Group I displayed addition and a satellite chromosome. In Group II, 6 subjects expressed aberrations such as deletion in two subjects, addition in two, mosaicism in one subject and an inversion in one subject (Table 3).

## DISCUSSION

It has been predicted that CVD will be the most important cause of mortality in India by the year 2015 than any other diseases. Coronary artery diseases or Ischemic heart diseases is the largest killer in developing countries. It has been estimated that approximately one quarter of all deaths in developing countries and almost half of all deaths in developed countries are attributed to IHD (WHO 1993).

The Haematological analysis in this study showed some significant results. According to Sangone (1975) and Smith (1978) smoking is strongly correlated with Polycythemia through increased carboxyhaemoglobin levels. The male subjects with IHD were mostly active smokers. The present study showed the increased mean WBC counts among male and female subjects with IHD and the values were statistically significant, which corroborates with the findings of Gillum et al. (1993) that high WBC counts have been found to be an independent risk factor for IHD. The Hb content showed an increased value in the male subjects.

Lipid abnormalities form an important risk factor for IHD (George 2002). There are a number of factors which influence the formation of plaques due to excess cholesterol. The plaque that are deposited on the walls of the blood vessels narrows the passage through which blood flows to heart muscle and causes Ischemia.

The mean HDL values of both male and female subjects showed decreased values and this decrease was statistically significant. In a major prospective study by Stampher et al. (1995), an association between HDL sub fractions and the risk of acute myocardial infraction was undertaken which confirmed the strong relationship between low serum high density lipoprotein (HDL) levels and an increased infarction risk. A 10 mg increase in HDL was associated with 42% reduction in risk of coronary deaths.

In Indian patients with CAD, high triglyceride levels are found more often than high cholesterol levels. An increase of triglycerides from 90 mg/dl – 180 mg/dl is associated with doubling the incidence of IHD with high LDL-c levels and low HDL levels (Bhatnagar 1995).

Brown et al. (1990) found that increase in small LDL particle is associated with CAD. In the present study mean LDL levels were elevated in both the male and female subjects . From this result it is inferred that high LDL is also an independent risk factor for CAD. Diet has been advanced to reduce LDL cholesterol the majority risk factor for IHD.

The activities of number of enzymes in serum are used as an aid to the evaluation of patients with various diseases. Now this method can also be used to predict cardiovascular diseases. Myocardial infarction causes substantial increase in SGOT as this enzyme is abundantly present in heart muscle (Zimmerman 1970). This may also occur in association with a low cardiac output. In the present study, mean SGOT content of male and female subjects with Ischemic heart disease displayed a significant increase which was statistically significant over their respective controls.

**Table 1: Changes in haematological parameters in various groups of male and female subjects with ischemic heart disease**

| S.No. | Particulars | No. of subjects studied | RBC (million cells/ cu. mm) | WBC (thousand cells/ cu. mm) | Haemoglobin (gm%) |
|---|---|---|---|---|---|
| | *Group I (Male)* | | | | |
| 1 | Controls | 24 | 5.39 ± 0.09 | 10.28 ± 0.16 | 15.08 ± 0.42 |
| | Experimentals | 24 | 6.03 ± 0.17* | 15.40 ± 0.36** | 15.29 ± 0.10** |
| | *Group II* | | | | |
| 2 | Controls | 20 | 5.13 ± 0.09 | 10.21 ± 0.11 | 14.75 ± 0.27 |
| | Experimentals | 20 | 5.33 ± 0.06 | 10.12 ± 0.14* | 15.42 ± 0.10** |
| | *Group I (Female)* | | | | |
| 3 | Controls | 16 | 5.30 ± 0.08 | 10.30 ± 0.23 | 11.71 ± 0.45 |
| | Experimentals | 16 | 4.86 ± 0.10 | 15.04 ± 0.11** | 10.95 ± 0.14** |
| | *Group II* | | | | |
| 4 | Controls | 18 | 5.25 ± 0.06 | 10.58 ± 0.32 | 10.35 ± 0.14 |
| | Experimentals | 18 | 4.89 ± 0.08 | 14.52 ± 0.17 | 9.82 ± 0.24* |

Group I: 45 - 54 years of age
Group II: 55 years and above
* Value significant at 5 % level
* * Value significant at 1% level

**Table 2: Lipid profile and enzyme assay in various groups of male and female subjects with ischemic heart disease**

| S. No. | Particulars | No. of Sub. | Triglycerides (mg/dL) | Cholesterol (mg/dL) | High Density Lipoprotein (mg/dL) | Low Density Lipoprotein (mg/dL) | Mean Value of SGOT (units /L) | Mean Value of SGPT (units /L) |
|---|---|---|---|---|---|---|---|---|
| | *Group I (Males)* | | | | | | | |
| 1 | Controls | 24 | 132.84 ± 2.17 | 212.37 ± 3.11 | 35.79 ± 0.28 | 150.38 ± 3.31 | 30.45 ± 1.07 | 28.12 ± 0.97 |
| | Experimentals | 24 | 185.45 ± 7.96** | 254.00 ± 4.62 | 29.50 ± 1.09** | 187.95 ± 5.18 | 88.45 ± 4.74** | 49.45 ± 2.00** |
| | *Group II (Males)* | | | | | | | |
| 2 | Controls | 20 | 134.45 ± 1.97 | 213.95 ± 3.83 | 34.45 ± 0.31 | 152.61 ± 3.82 | 34.45 ± 1.07 | 27.15 ± 1.49 |
| | Experimentals | 20 | 215.30 ± 8.32* | 255.15 ± 4.26 | 29.05 ± 0.55** | 182.72 ± 4.71 | 81.00 ± 5.87** | 53.35 ± 1.42 |
| | *Group I (Females)* | | | | | | | |
| 3 | Controls | 16 | 136.44 ± 1.72 | 221.06 ± 3.57 | 36.37 ± 0.53 | 155.34 ± 3.34 | 32.75 ± 1.31 | 29.00 ± 0.75 |
| | Experimentals | 16 | 200.31 ± 9.52** | 260.44 ± 5.99** | 31.33 ± 1.18* | 188.0 ± 6.12** | 87.75 ± 7.99** | 53.50 ± 1.55** |
| | *Group II (Females)* | | | | | | | |
| 4 | Controls | 18 | 132.44 ± 1.72 | 221.78 ± 3.37 | 36.05 ± 0.36 | 158.90 ± 3.49 | 32.77 ± 1.19 | 30.00 ± 0.56 |
| | Experimentals | 18 | 197.61 ± 6.71* | 253.28 ± 5.30 | 30.83 ± 0.93* | 183.13 ± 5.50 | 87.05 ± 4.93** | 53.27 ± 1.84** |

Group I: 45 - 54 years of age
Group II: 55 years and above
* Value significant at 5 % level
* * Value significant at 1% level

**Table 3: Details of chromosomal aberrations in male and female subjects with ischemic heart disease**

| *S.No.* | *Case ID* | *Particulars* | *Chromosomal Aberration (Males)* |
|---|---|---|---|
| 1 | HGIHD3 | Group I | 46,XY, del ( Xq-) |
| 2 | HGIHD6 | Group I | 46,XY, 22 s+ |
| 3 | HGIHD13 | Group I | 46,XY, t (14 q-; 21 q+) |
| 4 | HGIHD2 | Group II | 46,XY, del (18 q-) |
| 5 | HGIHD7 | Group II | 46,XY, del (11 q- ) |
| 6 | HGIHD10 | Group II | 46,XY, inv ( 9 ) |
| 7 | HGIHD28 | Group II | 46,XY, t (5p-; 12 q+) |
| 8 | HGIHD34 | Group II | 46,XY/ 46 XY, t (5p-; 12 q+) |
| 9 | HGIHD37 | Group II | 46,XY, inv (11) |
| *S.No.* | *Case ID* | *Particulars* | *Chromosomal Aberration (Females)* |
| 1 | HGIHD12 | Group I | 46,XX / 46,XX, t (14q-; 22q+) |
| 2 | HGIHD17 | Group I | 46,XX, 14 s+ |
| 3 | HGIHD30 | Group II | 46,XX / 45, XO |
| 4 | HGIHD27 | Group II | 46,XX, (4q-) |
| 5 | HGIHD22 | Group II | 46,XX, del (1q-) |
| 6 | HGIHD1 | Group II | 46,XX, t (11p-; Xq+) |
| 7 | HGIHD50 | Group II | 46,XX, t (5p-; 12q+) |
| 8 | HGIHD31 | Group II | 46,XX, inv (9) |

Chromosomal analysis revealed many aberrations, both minor and major, some of which were corroborative to the findings of few earlier reports. A male subject with IHD displayed the chromosomal complement 46, XY, del(18q-), which corroborates with the findings of Pankow et al.(2001) who found significant evidence for the presence of possible locus on 18q influencing blood pressure response, a major risk factor for IHD. Some female subjects displayed a chromosomal complement 46, XX /45, XO. According to Gerald (1976) and Nora (1970) 35-50% of all patients with this complement are affected with Cardiovascular abnormalities.

## CONCLUSION

In most families which seem to be genetically predisposed to coronary artery disease by history, the nature of genetic factors underlying this predisposition is obscure. Most patients with coronary artery disease have inherited multiple predisposing genes that interact with multiple factors to produce the disease. In these patients atherosclerosis does not have a single cause. Yet treatment of one or predisposing factors, such as diet rich in animal fat, hypertension, hypercholesterolemia, regular exercise, diabetes mellitus, obesity or smoking and drug therapy will slow the progression of the disease.

Due to the extreme severity and prematurity of IHD in Asian Indians, an intensive programme of early identification of individuals at high risk as a result of genetic predisposition, primary prevention and alteration of all modifiable risk factor is urgently required.

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