CHAPTER 5 : DISCUSSION
Presence of several cardio metabolic risk factors especially central obesity and dyslipidemia, places women in high risk for development of insulin resistance and atherosclerosis. Physiological and hormonal changes during menopause acts as an additional risk factor for such diseases. In the present study, 35.52% of women were found to have three or more cardio metabolic risk factors which had values higher than the cut off limits according to consensus statement on Asian Indians. The percentage of subjects with three or more cardio metabolic risk factors were significantly higher in postmenopausal women as compared to premenopausal women in the current study. Pandey et.al. in their study among pre and postmenopausal women from western India also observed a higher prevalence of metabolic syndrome in postmenopausal (56%) than premenopausal (44%) women. Silvaraj et.al. observed 44.2% occurrence of metabolic syndrome among Indian women in the 41-50 years age group and 25.2% occurrence in women in the age group of 30-40 years. Other studies in Austria, China, Germany, Iran and Canada showed a prevalence of 32.6%, 37.34%, 36.1%, 31% and 29.6% respectively which were in agreement with our findings. There were disagreements of findings between our study and some other studies done in Iran, Western India, Argentina and Ecuador with prevalence of 69%, 55%, 22% and 41.5% respectively. These differences in prevalence of cardio metabolic risk factors in different studies can be due to different investigation criteria, socioeconomic and environmental differences, genetic factors and lifestyle of the subjects studied.

Sex difference in the occurrence of cardio metabolic risk and its individual components exists, suggesting sex-specific differences in the physiological mechanisms of occurrence of these risk factors. Particularly in women, reproductive and hormone-related factors such as postmenopausal status, decreased parity and history of maternal gestational diabetes mellitus (GDM) have also been shown to increase the risk of condition. In case of menopause, for example, the biological plausibility of this relationship is explained by the fact that with menopause, women experience changes including increased abdominal adiposity, hyperglycaemia, hyperinsulinism, and dyslipidaemia. Regarding menopausal status, NHANES and other studies had demonstrated strong association between menopause and cardio metabolic risk in women. It has been suggested that the occurrence of cardio metabolic risk after menopause is explained by oestrogen deficiency, because many of the risk factors are more prevalent in postmenopausal women. Also, oestrogen replacement improves insulin sensitivity and reduces the risk of diabetes mellitus. Even though we
did not observe this association, our results are consistent with previous studies performed among postmenopausal women.

Different obesity and atherogenicity markers were found to be significantly higher among both post and premenopausal women with cardio metabolic risk in comparison to those without the risk. The most common cardio metabolic risk factor in our study, was found to be central obesity with a frequency of 79.48% in subjects with cardio metabolic risk in comparison to 38.77% in subjects without cardio metabolic risk. Majrjani et. al. also reported central obesity as the most important cardio metabolic risk factor in women in their study with an Iranian population\textsuperscript{13}. Obesity increases cardio metabolic risk because it induces insulin resistance, increases blood pressure, triglyceride, low density lipoprotein cholesterol (LDL-C) and reduces high density lipoprotein cholesterol (HDL-C)\textsuperscript{14,15}. However, in our study, BMI did not vary significantly between subjects with and without profound cardio metabolic risk. This might be due to the fact that people with normal weight might become metabolically obese due to abnormal distribution of body mass resulting into central obesity\textsuperscript{16}. It is reported that substances released by intra-abdominal fat including inflammatory cytokines like tumour necrosis factor-alpha and interleukin-6 influence glucose metabolism as well as blood lipid profile producing insulin resistance. The second most prevalent cardio metabolic risk factor identified among pre and postmenopausal women, in our study was altered lipid profile. Various studies from different parts of the world have reported altered lipid profile as the main cardio metabolic risk factor in women\textsuperscript{17-19}.

Even though many features of cardio metabolic risk emerge with oestrogen deficiency characteristics of menopause, a considerable percentage of premenopausal women in our study as well as various previous studies were found to be predisposed for development of cardio metabolic risk. Central obesity observed among premenopausal women with cardio metabolic risk might have diluted the protective effect of premenopausal oestrogen level in the women\textsuperscript{20}. Abdominal obesity is quite prevalent in South Asians with females outnumbering males\textsuperscript{21}. Higher abdominal fat is known to be a risk factor for hypertension, hypertriglyceridaemia, hyperinsulinaemia and diabetes mellitus. The central obesity is also associated with changes in many biochemical variables especially with various adipokines like leptin and adiponectin which are found to be associated with insulin resistance and cardio metabolic risk components\textsuperscript{22}.

The second important component of cardio metabolic risk identified in our study was reduced HDL-C and elevated triglyceride. Atherogenic dyslipidaemia is common in South Asians who have lower HDL-C level and higher levels of small, dense and low density
lipoprotein (LDL-C) compared to Caucasians across all strata of the society\textsuperscript{23}. Elevated serum triglyceride is more common in affluent Indians and migrant Indians\textsuperscript{24}. These findings were in agreement with other findings that suggested a strong relationship between TG/HDL-C ratio with insulin resistance leading to cardio metabolic risk. Various studies reported a weak correlation between hypertension and insulin resistance. Consistent with findings of these studies, we also observed a weak correlation between hypertension and cardio metabolic risk in our study\textsuperscript{25,26}.

Studies on association between obesity markers and traditional cardio metabolic risk factors revealed that both waist circumference and waist hip ratio varied with almost all the traditional risk factors in pre and postmenopausal Indian women. Jouyandech et. al.\textsuperscript{27} also observed similar relationship between waist circumference and traditional cardio metabolic risk components in women. The traditional cardio metabolic risk factors were also found to vary significantly with atherogenicity marker TG/HDL-C ratio. Similar observation was reported by Aurther et.al.\textsuperscript{28} in their study with Ghanaian women. Our study showed that all the anthropometric and atherogenic risk factors showed a high risk value in subjects with increased cardio metabolic risk in comparison to subjects without the risk.

Reports suggest that ethnic difference in prevalence of cardio metabolic risk exists\textsuperscript{29,30}. Consequently, we compared the cardio metabolic risk parameters in women from two different ethnic communities of India - Lambani from Vijayapur district of Karnataka state and Riang tribe from Tripura, a North Eastern state of India. For comparison, women from non ethnic population from both the study regions were also included in our study.

It is assumed that traditional societies and population residing in and around rural areas are expected to have lesser cardio metabolic risk as these are not exposed to modernization which is thought to be one of the principal causes of present day epidemic of cardio metabolic disorders\textsuperscript{24}. The ICMR task force collaborative study reported general prevalence of cardio metabolic risk to be 30\% in urban areas of Delhi and 11\% in rural Haryana\textsuperscript{31}. Mishra et. al. reported 30\% prevalence among the urban slum population of Delhi\textsuperscript{32}. Ramchandra et.al., reported 41\% prevalence of cardio metabolic risk in urban area of Chennai among adults of 20-75 years with higher prevalence in women than men\textsuperscript{33}. Kamble et.al., in a study on adult population of Wardha, central India, observed that magnitude of cardio metabolic risk was low among rural adults as compared to urban areas\textsuperscript{34}. Sarkar et. al., in their study with two tribal populations of India, namely Bhutia and Toto, have observed that Bhutia had a relatively more adverse cardio metabolic risk profile compared to Toto, as measured by
blood pressure, blood lipids and blood glucose. Bhutia had higher mean values in majority of the traits considered, except HDL-C, irrespective of age groups and gender. There was difference in cardio metabolic risk factors between urban and rural Toto and Bhutia population\textsuperscript{24}.

Our analysis revealed, overall cardio metabolic risk observed from different ethnic groups varied within a narrow range, where both the ethnic groups showed marginally lesser risk than their corresponding non ethnic counter parts. The risk in premenopausal groups did not show much difference, while in post menopausal groups there was marked difference in prominence of risk factors between the groups. Analysis of cardio metabolic risk indicators in different groups of subjects revealed that central obesity marked by increased waist circumference was most prevalent risk factor in all the groups. In Riang women from Tripura altered lipid profile marked by increased triglyceride level and reduced HDL-C level was more prominent than other groups. This might be connected to non-vegetarian nature of their diet which includes substantial quantity of red meat and other non-vegetarian products. Other risk factors showed similar pattern in all the groups. The cardio metabolic risk in urban subjects was found to be more in comparison to rural subjects, which might be associated with sedentary life style of most of the urban subjects evaluated. Subjects having higher educational level were found to have lesser risk of cardio metabolic disorders. The cardio metabolic risk was found to be highest in subjects from higher family income groups and lowest in subjects with lesser family income. Non-vegetarian subjects were having higher cardio metabolic risk than vegetarian subjects.

Similar findings in regard of influence of socio demographic status on cardio metabolic risk in women were reported from South Korean, Japanese and American studies\textsuperscript{35-37}. Both higher income and educational levels were reported to be protective against different types of chronic diseases. In our study, we observed lesser percentage of subjects with cardio metabolic risk in higher educational but lesser family income groups. This might be explained by the fact that higher educational level increases health awareness, thereby helping in adopting life style modification to prevent cardio metabolic risk. The higher percentage of high income group may be explained by the fact that this group consumes more amount of high energy diet which predisposes such subjects to cardio metabolic risk. The same is true for non-vegetarian group also. Similar findings in regard to influence of family income, educational level and diet were reported by several other workers also\textsuperscript{38,39}.

Results of our study revealed that a good proportion of our subjects with predominant cardio metabolic risk also had lesser hemoglobin concentration. The co-existence of anaemia
and cardio metabolic risk being higher in postmenopausal subjects than premenopausal subjects. Similar observation of higher co-existence of anaemia and cardio metabolic risk in elderly women was reported by various workers\textsuperscript{40}. The high rate of co-existence of anaemia and cardio metabolic risk in women might be explained by the fact that the prevalence rate of anaemia and altered lipid profile is consistently higher in women\textsuperscript{41,42}. There were several studies that had reported positive correlation between anaemia and diabetes mellitus. However, reports on co-existence of anaemia and cardio metabolic risk were very few\textsuperscript{43-45}. Shi et. al. had reported about co-existence of anaemia and cardio metabolic risk in adults for Jiangsu, China and they had suggested that the co-existence might be connected to inflammatory mechanism activated in both the conditions.

We have analysed oxidative stress and antioxidant status among subjects with three or more cardio metabolic risk factors and compared the data with the findings in control subjects without cardio metabolic risk. Our study revealed that lipid peroxidation product malondialdehyde (MAD) levels were higher in subjects with cardio metabolic risk in comparison to control subjects. Increase in MDA could be due to increased generation of reactive oxygen species due to oxidative damage generated in subjects with cardio metabolic risk. Similar study by Romero et.al.\textsuperscript{46} had also reported a significant increase of MDA levels in subjects with cardio metabolic risk. In our study, we also observed a significant decrease in all the antioxidant enzyme levels in subjects with prominent cardio metabolic risk. Studies have shown that many cardio metabolic risk factors including hypertension, hypercholesterolemia, diabetes mellitus and decreased estrogen in postmenopausal women were associated with elevation of oxidative stress\textsuperscript{47}. Oxidative stress phenomena occur, in particular, during the progressive steps of cardiovascular disorders\textsuperscript{48}. Data from study conducted in patients with neurodegenerative disease showed that female patients presented with higher levels of oxidative stress compared to affected males, suggesting a higher susceptibility to oxidative stress in such female subjects\textsuperscript{49}. However, there are very few reported studies on cardio metabolic risk profile of women that also included markers of oxidative stress\textsuperscript{50}.

Our findings are in agreement with the findings of Shrestha et. al., who observed increase in oxidative markers in subjects with cardio metabolic risk from both the sexes\textsuperscript{51,52}. Few earlier studies and a recent study by Vasselleet. al. had reported increase in oxidative stress biomarkers in women associated with cardiovascular events\textsuperscript{53-55}. The levels of antioxidant vitamins E and C, in our study did not show significant difference between the groups. This might be due to the fact that our subjects were apparently healthy and were
taking adequate diet that helped them in maintaining the normal levels of these antioxidant vitamins\textsuperscript{56}. A slight decrease in the levels of these vitamins in subjects with cardio metabolic risk may be explained by the fact that they were being utilized for preventing oxidative damage initiated in this group of subjects. However, the exact role played by the antioxidant vitamins in cardio metabolic risk still remains controversial\textsuperscript{57,58}. 
REFERENCE:


