CHAPTER 1:
PURPOSE OF THE STUDY
1.1 INTRODUCTION:

A global transition in disease pattern has been observed during recent years, where the relative impact of infectious diseases are decreasing while chronic diseases like cardiovascular diseases (CVD) and diabetes mellitus are increasingly dominating the disease pattern\(^1\). Epidemiologists in India along with experts in WHO have been sounding an alarm on rapidly rising burden of CVDs for past 15 years. It is estimated that by 2020, CVD will be the largest cause of disability and death in India with 2.6 million Indians predicted to die due to CVDs\(^2\).

Various chronic non-communicable diseases in particular cardiovascular diseases, anaemia, diabetes mellitus and cancer are increasingly becoming a significant cause of morbidity and mortality in developing countries\(^3\). World Health Organisation (WHO) projected, by the end of the year 2015, non-communicable diseases will account for over 70% of all deaths with 80% of death occurring in developing countries\(^4\). Rapid urbanization, changing life style, sociocultural factors, poverty and poor maternal, foetal and infant nutrition form the basis of the development of different forms of non-communicable diseases\(^5\).

Cardio metabolic disorders can be predicted by presence of various risk factors in subjects that are represented as a constellation of interconnected physiological, biochemical, clinical and metabolic risk factors including hypertension, dyslipidaemia, central obesity, glucose intolerance, pro-inflammatory and pro-thrombotic states, which reflects an underlying insulin resistance\(^6\). It is a modern day epidemic which predicts total and CVD mortality, the incidence and progression of carotid atherosclerosis and sudden death, independent of other CVD risk\(^7\). Subjects with predominance of such risk factors have three fold probability of suffering from heart attacks or stroke, two fold probability of developing CVD or dying from such events, and five-fold greater probability of developing type 2 diabetes mellitus in both sexes when compared to normal individuals\(^8-10\).
Women share many risk factors for cardiovascular disorders as men and in both the risk are associated with age\textsuperscript{11}. However, sex difference in occurrence of various cardiovascular risk factors exists, suggesting a sex-specific difference in the physiological mechanisms and risk factors for disease occurrence\textsuperscript{12}. During the last decade, researchers all over the world including India, have shown the interest on assessment of burden of cardiovascular metabolic risk in different groups of women.

Menopause is thought to be one of the major contributors for increasing burden of cardiovascular metabolic risk in women\textsuperscript{13}. The biological plausibility of such relationship depends on the fact that menopause brings in various physiological and hormonal changes including increased adiposity, hyperglycaemia, hyperinsulinism and dyslipidaemia which contribute to predominance of such risk in menopausal women\textsuperscript{14}. Limited information is available on cardio metabolic status of pre and postmenopausal Indian women. Moreover, the association among various obesity and atherogenicity markers and traditional cardio metabolic risk factors is not evaluated in this group.

Anaemia is one of the most common types of nutritional problems in women worldwide\textsuperscript{15}. A World Health Organisation estimate suggested that globally up to 500 million women during their reproductive age suffered from anaemia\textsuperscript{16}. As both anaemia and various cardiovascular metabolic risk factors are associated with inflammatory state in the subjects, there is a theoretical possibility that both these conditions are interconnected. Anaemia is common in patients with heart failure\textsuperscript{17}. There has been increasing appreciation of the significance of anaemia in the pathophysiology, treatment and prognosis of heart failure. Once considered a downstream complication of heart failure, anaemia is now emerging as a crucial and potentially modifiable factor in the overall treatment strategy for patients with chronic heart failure\textsuperscript{18}. There are very few reported studies on co-existence of anaemia and cardio metabolic risk factors. It is, therefore, important to assess the prevalence and possible co-existence of the two conditions in a population who are prone to develop above said conditions.

Studies all over the world have shown significant role of ethnicity, life style, socioeconomic and nutritional factors in pathogenesis of many diseases\textsuperscript{19}. According to the United Nations geographical region classifications, India falls under the region-South Asia along with Afghanistan, Bangladesh, Bhutan, Iran, Maldives, Nepal, Pakistan and Srilanka\textsuperscript{20}. Ethnic distribution of South Asian population is complex as it has been invaded and settled by many ethnic groups over the centuries including various Dravidian, Indo-Aryan and
Iranian groups and amalgamation of Dravidian, Indo-Aryan and native societies has produced a composite culture\(^{21}\). Nationally, representative studies comprising of subjects from diverse ethnic and socioeconomic background are generally not available from any South Asian country\(^{22}\). Considering India as a multi-ethnic, multi-racial and multi-cultural country, it is, therefore, pertinent to include subjects from different ethnic and cultural backgrounds to draw a meaningful conclusion from such studies\(^{23,24}\).

Recent evidences, especially from animal models, suggested role of antioxidant defence mechanism in pathogenesis of different diseases\(^{25,26}\). In recent years, number of studies confirmed that oxidative stress, chronic inflammation and angiogenesis all play important role in the pathogenesis of cardio metabolic disorders\(^{27}\). A growing body of evidence now suggests that increased oxidative stress to adipocytes is central to the pathogenesis of different cardio metabolic disorders\(^{28}\). Chronic hyperglycaemia causes oxidative stress in tissues prone to complications in patients with diabetes mellitus\(^{29}\). Oxidative stress occurs in a cellular system when the production of free radical moieties exceeds the antioxidant capacity of that system. If cellular antioxidants do not remove free radicals, radicals attack and damage proteins, lipids and nucleic acids. The oxidized or nitrosilated products of free radical attack have decreased biological activity leading to loss of energy metabolism, cell signalling, transport and other major functions. These altered products are also targeted for proteosome degradation, further decreasing cellular function. Accumulation of such injury ultimately leads a cell to die through necrotic or apoptotic mechanisms. A puzzle of many pieces of evidence suggests that free radical over generation may be considered the key in the generation of insulin resistance, diabetes mellitus and cardiovascular diseases \(^{30}\). However, evidences linking these factors with pathogenesis of cardio metabolic disorders and anaemia in human, especially in women during postmenopausal stage of their life is sparse.

Studies conducted over last decade revealed that burden of cardio metabolic risk is gradually increasing among different populations. Women, especially the menopausal women are found to be more susceptible to such risk. There is considerable biological and epidemiological evidence that suggested presence of different cardio metabolic risk factors increased the probability of future development of cardiovascular diseases and diabetes mellitus. Early detection of such risk might help in planning early intervention through lifestyle modification which might prevent these diseases.
In view of the above fact, the present study is designed to evaluate cardio metabolic risk profile in a representative sample of postmenopausal Indian women consisting of subjects from two different ethnic and non-ethnic groups from two different regions of India and to compare the parameters with premenopausal women from same regions.

The health status, especially of women of the two ethnic groups chosen for the study is still remained unexplored. Reports suggested women from such groups are at the highest risk of developing various kinds of diseases which might be related to their life style and socioeconomic status.

Therefore, this study which aimed to relate the health status of these women with their life style, socioeconomic status and ethnicity is having a great scientific relevance.

The National Health Policy of the country aims to achieve the goal of Health for all by the year 2020. The present study might contribute in achieving the goal by providing a background knowledge regarding the health status of the targeted group to the policy makers.

The present study is designed to investigate the relationship between anaemia and cardio metabolic risk in women. There are very few reports on this approach of simultaneous investigation on both these conditions in women, who are particularly prone to both the conditions.

Moreover, the study aimed to relate oxidative stress and status of some non-enzymatic antioxidants in postmenopausal women. This noble approach will provide insight into the understanding of pathophysiological change associated with various cardio metabolic risk profile in women.

There are limited published data on cardio metabolic risk profile and the effects of different confounding factors on these factors in the targeted study group. It is, therefore, justifiable to conduct the study that describes the cardio metabolic risk profile in a representative sample of Indian postmenopausal women with studies on status of various confounding factors like anaemia and antioxidant status in them.

The study findings might form the basis for future research on cardio metabolic risk among this population.
1.2. **HYPOTHESIS:**

Hypothesis I: The cardio metabolic risk in women is influenced by their menopausal status.
Hypothesis II: Various obesity and atherogenicity markers present in the subjects influence traditional cardio metabolic risk factors of the subjects.
Hypothesis III: There is relationship between anaemia status and cardio metabolic status of the subjects.
Hypothesis IV: Occurrence of cardio metabolic risk in the subjects is influenced by their socio-demographic status and ethnicity.
Hypothesis V: The cardio metabolic risk in women is influenced by oxidative stress and antioxidant defence mechanism of the subjects.
1.3. **OBJECTIVES OF THE STUDY:**

**Broad Objective:**
With above background, the present study aims to evaluate the cardio metabolic risk profile in Indian women comprising of subjects from two different ethnic and non-ethnic communities in relation to their menopausal status, anaemia and status of their antioxidant defence system.

**Specific objectives:**

i) To evaluate cardio metabolic risk profile in both pre and postmenopausal Indian women.

ii) To evaluate association of traditional cardio metabolic risk factors with various obesity markers and atherogenicity markers in the subjects.

iii) To evaluate association of various haematological parameters, specially haemoglobin concentration with various markers of cardio metabolic risk in subjects.

iv) To evaluate role of nutritional status, socio-demographic characteristics and ethnicity on cardio metabolic risk and anaemia in the subjects.

v) To evaluate association between various enzymatic and non-enzymatic antioxidants and cardio metabolic risk profile and anaemia in subjects.
1.4. REFERENCES:


