Chapter 1
Introduction

Breast cancer is the commonest female malignancy worldwide with nearly 1.15 million new cases were recorded in 2002, representing over 23% of all female malignancies. Globally, in high-income countries, the overall incidence rates of this disease are nearly three times higher than in middle to low-income countries. It has been estimated that breast cancer incidence rates (age-standardized) range from 75-100 per 100,000 women being observed in North America, Northern Europe and Australian populations, whereas low rates (less than 30 per 100,000 women) being observed in African and Asian populations (Globocan 2002).

The reason for the strong regional differences in breast cancer incidence rates is likely be due to lifestyle, reproductive, hormonal and nutritional factors, although the relative contribution of each of these factors and their interplay are unclear. Factors associated with breast cancer have been extensively studied in developed countries, although little studied in developing countries, and direct comparisons are therefore not possible.

Breast cancer is the first leading cancer among women in almost all the cancer registries in India. It has been estimated that in 2001 there were approximately 80,000 new breast cancer patients in India. This malignancy accounted for 19-34% of all cancer cases among women in the country. The age-standardized incidence rates vary between 8-29 per 100,000 women (NCRP, 2006). The cumulative incidence (life-time risk) of breast cancer up to the age of 74 years is 2-3%. Thus it is estimated that in India 1 out of 30 to 42 women would develop breast cancer during her lifetime.

Most cancers result from the multi-factorial etiology, having several causes (risk factors) for the development of disease, which ranges from genetic to lifestyle factors. Based on studies mostly from developed countries, a number of risk factors such as nulliparity, late age at first child birth, early menarche, late menopause, less breast-fed
duration; anthropometric factors like increased body mass index or overweight or obesity, increased body fatness, reduced physical activity, genetic and family history of breast or ovarian cancer, use of exogenous estrogen, oral contraceptive use, and benign breast diseases have been identified for the development of breast cancer. Although not consistently reported in the literature, dietary factors such as increased consumption of alcohol, diary fat and red meat, decreased consumption of fruits and vegetables are reported as associated factors for the development of breast cancer. Some other factors such as pesticide use, organochlorine exposure, ionizing radiation and cigarette smoking are also reported as risk factors for the development of breast cancer.

Risk estimates (probability) for the development of breast cancer according to the above factors are varied. Also, it is reported that the etiology of this disease may be different for pre and post-menopausal women. Further, the association between risk factors of interest or exposures of interest and breast cancer may be confounded by other factors. Confounding occurs when the risk estimate of a particular exposure is mixed-up with the real effect of another exposure on the same outcome. Also the joint effect of several risk factors may influence the development of disease, and are termed as interaction or effect modification.

Regression models are used to calculate risk estimates for development of disease. The models are also be used to estimate the risk after adjusted for potential confounders and possible interactions between risk factors. In the present thesis, breast cancer risk estimates by menopausal status were obtained using the binary logistic regression model. The same model is used for adjustment of confounding factors and assessment of interaction between risk factors. The population excess fraction or attributable risk (assuming causality, the proportion of the new cases of disease observed in the study population attributed due to the risk factor) according to the risk factors is further estimated.

Factors for risk assessment were obtained using a case-control study conducted at the Regional Cancer Centre, Trivandrum during 2003-2004. The risk factors considered
In the present thesis were life style factors such as reproductive factors, anthropometric factors and level of household and occupational physical activities. In India, there are only a few risk factor studies have been carried out and most of the studies have focused only on the association between reproductive factors and breast cancer risk. No study has been carried in India to assess the risk factors related anthropometric factors and level of physical activity. Factors related to the above two aspects have been recently received more importance in the etiology of breast cancer.

The specific objectives of the present thesis are the following.

**Specific objectives**

(i) To estimate the risk for development of breast cancer in pre and post-menopausal women according to the reproductive factors such as, age at menarche, age at marriage, age at first pregnancy, age at last pregnancy, parity (number of live births), age at first childbirth, breast feeding status and lifetime duration of breast feeding and age at menopause.

(ii) To estimate the risk for development of breast cancer in pre and post-menopausal women according to the anthropometric factors such as height, weight, body mass index (weight in kg/height in m$^2$), waist size, hip size, waist-to-hip ratio and body size at different ages.

(iii) To estimate the risk for development of breast cancer in pre and post-menopausal women according to the levels of household and occupational physical activities.

(iv) To assess the degree of confounding and interaction between the risk factors.

(v) To estimate the population attributable risk (etiologic fraction) for the development of breast cancer according to the risk factors.

In the next chapter, a detailed review of literature on the disease burden and risk estimates of various factors associated with the development of breast cancer in pre and post-menopausal women are provided.