INTRODUCTION
1. INTRODUCTION

Cancer of uterine cervix is the leading malignancy affecting the women in developing countries. Of the total 459,400 cases occurring worldwide, 354,300 arise in the developing world (Parkin, 1984). India, alone accounts for approximately 16% of the global incidence (WHO Bulletin, 1986; Luthra et al., 1987). It has been further estimated that in absence of any control programme, this load will increase by 1.6 fold by turn of this century (Murty et al., 1990). 80-85% of cervical cancer are squamous cell carcinoma arising around the transforming zone. Majority of the cancers of uterine cervix do not arise from a normal epithelium but are preceded by a spectrum of abnormal epithelium changes known as "dysplasia" which is an important precancerous lesions. The comparative risk of development of carcinoma in situ (CIS) from different grades of dysplasia has been found to be 1:20 for mild dysplasia, 1:4 for moderate dysplasia and 1:2 for severe dysplasia (Luthra et al., 1987). Progression to invasive cancer has been found to be highest in severe dysplasia and lowest in mild dysplasia.

The etiology of cervical cancer has been thought to be multifactorial and complex (Frency & Winkler, 1987). The epidemiologic studies suggest that the development of cervical cancer is strongly linked with
the sexual behaviour and the sexually transmitted infections like HPV, HSV, Chlamydia (Rotkin, 1973; zur Hausen, 1977). The current consensus indicates that the viral integration into the host DNA in presence of other unknown carcinogens may produce the neoplastic transformation. Further it has also been speculated that free radicals generated during phagocytosis (Babior, 1982) as a consequence of viral infections may be one of the contributory factor in the pathogenesis of cervical cancer. Glutathione (GSH) is known to quench free radicals and others carcinogens that have the potential to cause significant cellular damages.

Glutathione (GSH), in which N-terminal glutamate (Glu) is linked to cystein (Cys) via a non-\(\varepsilon\)-peptidyl bond, is a non-protein thiol widely distributed in all the living cells. It is involved in several biological functions including the function as a coenzyme, its function in the activation of thiol requiring enzymes and its role in the protection of cells against the oxidative damages (Meister, 1975). The importance of GSH in carbohydrate metabolism arises as it supplies NADP required by glucose 6-phosphate dehydrogenase (G6PD) and 6-phosphogluconate dehydrogenase (6PGD), the key regulatory enzymes of PP pathway. Recently increasing attention has been paid to the presence of GSH and its related enzymes activities in
carcinogenesis and in most of the cases differences in the activities of several GSH metabolising enzymes and in the levels of GSH have been found between normal and malignant cells (Peskin et al., 1977; Bauer & Wendel, 1980; Bozzi et al., 1979; Siegers et al., 1984). Decreased plasma GSH content has been reported in several malignancies (Beutler & Gilbert, 1985). Administration of certain carcinogens have been found to increase the levels of GSH and τ-GTP (Cameron et al., 1978).

Fortunately, cancer of uterine cervix is preventable if detected in early stage. The organised cytology screening programme in the developing countries have demonstrated that incidence and mortality from cervical cancer has fallen. GSH and its related enzymes have also been studied during cervical carcinogenesis and the alteration in some of the enzymes like GST, G6PD, 6PGD have been used as a marker for the detection of precancerous and early cancerous lesions of uterine cervix (Satoh et al., 1985; Kodate et al., 1986; Dutu et al., 1980; Palaoro et al., 1988). Most of the investigations on GSH in relation to cervical cancer have been carried out in the areas where the frequency of cervical cancer is low (Basu et al., 1990). However, no such report has appeared from India where the incidence of this malignancy is the
highest in the world (WHO Bulletin, 1986). Therefore it is worthwhile to examine the role of GSH redox system during cervical carcinogenesis among Indian women. Therefore a case-control study has been carried out and the GSH related indices have been investigated in women with varying degree of CIN (precancerous lesions) and with invasive cancer and the values have been compared with the age matched normal women. Since the measurement of tissue GSH and its related variables is difficult due to small size of tissue biopsy, all the analysis of GSH related variables have been carried out in the blood samples of the study women. Others have also measured the blood GSH in the several malignancies and reported altered GSH redox system (Beutler & Gilbert, 1985; Engin, 1975). The broad objective of this study is to find out any significant changes in the GSH related parameters and to explore the possibility of using these changes as an objective systemic biochemical marker(s) for early detection of cervical lesions.

The present study encompasses the following aims and objectives-

1. To investigate the role of erythrocyte GSH content during cervical carcinogenesis.
(i) Measurement of erythrocyte reduced and oxidized GSH and their ratio (GSH/GSSG) in women with precancerous and cancerous lesions of uterine cervix.

2. To examine the role of GSH related enzymes viz GR, GST and GPX during cervical carcinogenesis.
   (i) Measurement of baseline activities of these enzymes in the erythrocytes.
   (ii) To find out any difference in the enzyme activities between the cervical precancer/cancer cases and control women.

3. To find out any association between the plasma total GSH (GSH plus GSSG) and various stages of uterine cervical carcinoma.

4. To examine the relationship between the erythrocyte Se content and the risk of cervical precancerous and cancerous lesions.

5. To establish the role of G6PD and 6PGD, the key enzymes of PP pathway in cervical neoplasia.
   (i) To find out the baseline activities of G6PD and 6PGD in human erythrocytes.
   (ii) The comparison of the activities of G6PD and 6PGD between cervical precancer/cancer cases and control women.