CHAPTER - 5

SUMMARY AND CONCLUSIONS
5.1. Summary and conclusions

Breast cancer is the most common cancer among females worldwide. Statistics shows that breast cancer will account for 500,000 deaths annually. The causes of breast cancer are multiple. Hormonal, genetic and environmental factors appear to interplay in the pathogenesis of breast cancer.

The present study was undertaken to study the changes in Hb, RBC count, lipid peroxidation, GSH, GPx, catalase, ACP, ALP, inorganic phosphate, sialic acid, uric acid, iron, copper, mucoproteins, vitamin C and blood sugar levels in the breast cancer patients and to evaluate the use of these parameters as biomarkers in human mammary tumors.

Blood samples obtained from breast cancer patients were analysed together with an equal number of age and sex matched normal healthy subjects.

In present study, we found that the RBC count and Hb levels were decreased in all clinical stages of breast cancer, when compared to the normal control. The extent of decrease in Hb level was markedly increased from stage - I to stage IV indicating the progression of anemia as the disease advances from stage - I to stage - IV. The decrease in Hb was further reflected by corresponding decrease in RBC count. Decrease in RBC count was also intensified from stage - I to stage - IV. The decrease in RBC count in cancer patients compared to controls may be a consequence of enhanced plasma lipid peroxidation observed in these patients.
Serum iron levels were found to be increased in breast cancer patients compared to control. Serum iron levels were not significantly altered in stage-I breast cancer patients, whereas markedly elevated in advanced stages of breast cancer. Increased serum iron levels in breast cancer patients indicate that anemia observed in these patients is not due to iron deficiency. The enhanced serum iron level may enhance the oxidative stress in breast cancer patients.

Blood sugar levels were found to be decreased slightly but not significantly in stage-I breast cancer patients, whereas significantly reduced blood glucose levels were observed in advanced stages of breast cancer. Hypoglycemia induced in breast cancer patients was may be due to increased utilization of glucose to meet the needs of the growing tumors and increased catabolism of glucose.

In the present study, plasma lipid peroxidation was found to be increased significantly in breast cancer patients, compared to control. The enhanced lipid peroxidation may be due to increased serum iron levels in these patients. In our study, the serum iron levels were correlated with the extent of lipid peroxidation at different stages of cancer (Figure 1).

GSH levels were found to be decreased by 9.4% to 68% from stage-I to stage-IV cancer patients compared to controls indicating the % of decrease in GSH advances from stage I to stage IV (9.4%, 37%, 61%, 68%). The decreased GSH levels in different stages of breast cancer correlated positively with the enhanced lipid peroxidation observed in the corresponding stages of the cancer patients (Figure 2).
Vitamin C levels were found to be decreased slightly in first two stages of breast cancer patients, whereas markedly decreased levels were observed in advanced stages of breast cancer. The significant decrease in vitamin C level at stage - III and stage - IV indicates the consequences of vitamin C deficiency leading to cell proliferation and malignant conversion.

GPx and catalase activities were found to be increased significantly from stage - II to IV, whereas no significant change was observed in stage - I breast cancer patients, when compared to control. The elevation of GPx in breast cancer patients and progression of its elevation from stage II to stage IV may be a marker of cell proliferation by eliminating \( \text{H}_2\text{O}_2 \) and other hydroperoxides. The enhanced activity of GPx in the present study also correlated with decreased GSH levels of plasma. Inspite of enhanced GPx and catalase activities, the plasma lipid peroxidation was found to be enhanced in cancer patients indicating that the protection provided by GPx and catalase is not sufficient to counterbalance the oxidative stress observed in these patients.

Sialic acid levels were found to be increased significantly by 14% to 85% from stage - I to stage - IV of breast cancer patients, compared to control. Cancer patients have increased sialic acid concentrations, which correlate positively with the degree of metastasis and are useful in monitoring treatment.

In present study serum copper levels were found to be increased significantly from stage II to stage IV of breast cancer patients,
whereas in stage I serum copper levels were not altered significantly when compared to control.

The enhanced copper and iron levels may induce ascorbic acid oxidation leading to significant decrease in ascorbic acid content in stage III and IV.

Serum uric acid levels were found to be increased significantly in all clinical stages of breast cancer patients compared to control. The high uric acid levels in these patients may be an index of increased antioxidant defense to compensate the loss of other antioxidant mechanisms.

Serum ACP and ALP activities were found to be increased significantly in stage III and stage IV of breast cancer patients, whereas no significant changes were observed in stage-I and II, compared to control.

Serum inorganic phosphate levels were found to be increased gradually from stage-I to stage-IV of breast cancer patients, when compared to control. Increased ACP and ALP activities in breast cancer patients may be a reason for increased serum inorganic phosphate concentrations in breast cancer patients.

The present study leads to conclusion of increased oxidative stress as the disease advances from stage I to stage IV with decreased antioxidant capacity. In order to overcome the oxidative stress the exogenous antioxidant compounds taken concurrently with drugs are beneficial for chemotherapy. In addition the exogenous antioxidants may also reduce the adverse effects of chemotherapy.
Even though anemia was observed in breast cancer patients, elevated serum iron levels were observed. Much evidence indicates that DNA damaging OH\(^-\) are produced through the interaction of H\(_2\)O\(_2\) and O\(_2\)\(^-\) with transition metals. Thus enhanced serum iron levels from stage I to stage IV indicates, increased OH\(^-\) production from stage I to stage IV, compared to controls. Infact metal chelators that block the elaboration of OH\(^-\) can inhibit DNA damage and malignant transformation, and propagation induced by ROS.

In addition to this, higher levels of ALP, ACP, Sialic acid and Copper in the circulation of breast cancer patients and the gradual increase in these parameters from stage I to stage IV may be used in the diagnosis and treatment monitoring of the patients with breast cancer at different stages.