CHAPTER V

Summary and Conclusion

The studies till today have showed many revolutionary turns in the field of diagnosis, treatment and therapy of various types of malignancies. The inventions started long back from Shushruta by identifying the cancer cells till today with advanced techniques for treating the various cancers or malignancies. However the final goal is to be achieved in total eradication of the malignancies.

The present study was carried out to evaluate and correlate the organ function test [related to the renal profile and the liver profile] and the status of serum antioxidant /oxidative stress indicators in various forms of cancer. Main focus of the study was on the malignancies occurring commonly in the females. In this category, the breast cancer, cervix cancer and ovarian tumour patients were considered as the test group. Age and sex matched control cases comprised of healthy subjects free of obvious systemic disease.

The renal profile (blood urea, serum creatinine and serum uric acid), the liver profile (serum bilirubin, serum alkaline phosphatase, serum glutamate oxaloacetate transaminase SGOT, serum glutamate pyruvate transaminase SGPT, serum total proteins and serum albumin) values were evaluated. Serum Thiobarbituric acid Reactive Substance, (TBARS) or malondialdehyde (MDA) and Sensitivity of Erythrocytes for lipid Peroxide Heamolysis (SEPH) values were assessed as indicators of oxidative stress / lipid peroxidation. Serum Vitamin A levels and serum reduced glutathione levels indicated antioxidant status in patients with above said malignancies.
The results were statistically analysed by performing students ‘t’ test. The biochemical parameters were estimated using standard procedures. The methodology is described in Chapter II.

**Chapter III : Breast Cancer, Cervix Cancer and Ovarian Cancer.**

The evaluation of Renal profile assists in correlating the prognosis of the disease i.e. the metastasis or the severity of the disease with relation to the kidney functioning. The assessment of liver profile enables to study the enzymatic alteration due to the changes in metabolism because of the diseased condition. The combination of evaluation of these two profiles along with the valuation of oxidative stress/ antioxidant status may result in a definitive way for the assessment and treatment of the patients.

By considering the importance of evaluation of these biochemical parameters in cancer, the present study was planned to evaluate the correlation of these biochemical parameters in various types of malignancies.

**A) Breast Cancer :**

Patients diagnosed for breast cancer in the studied cases were mostly coming from the rural areas. The lack of awareness of the diagnosed condition as compared to the areas leaded the disease to advanced stages. Self screening for breast cancer is a good major if taken advertised to the interiors to peripheries to minimize the expanded number of the breast cancer patients.

The observations of the present study in Breast Cancer patients were :

1. The levels of blood urea, serum creatinine and uric acid in healthy controls were 20.6±3.410 mg/dl, 0.77±0.008 mg/dl and 4.47±0.654 mg/dl respectively.
The patient group showed elevated values of these parameters. All values were higher with mean values 23.58±5.719 mg/dl, 1.17±0.06 mg/dl and 7.25±0.27 mg/dl for blood urea, serum creatinine and serum uric acid respectively. These findings of elevated mean level will provide new dimensions to the role of renal profile in Breast cancer patients.

2. The assessment of liver profile in breast cancer patients showed that serum bilirubin and SGPT were within normal limits. Being non-icterus the serum in these patients did not suggest any jaundice condition. The elevated mean values of serum alkaline phosphatase and serum glutamate oxaloacetate transaminase (SGOT) and lowered serum protein levels in the breast cancer patients suggested that these alterations are due to the malignant stage of the patients.

3. Lipid peroxidation has been postulated to be the destructive process of liver injury. The increase in TBARS (MDA) levels suggest enhanced lipid peroxidation/ oxidative stress leading to tissue damage and failure of antioxidant defense mechanism to prevent formation of excessive free radicals. The antioxidant status (serum vitamin A and reduced Glutathione) in the breast cancer patients exhibited decrease; vitamin A and reduced glutathione evaluated values being 7.520±20.960 µg/dl and 12.793±1.664 mg/dl respectively, compared to the control (37.10±3.674 µg/dl and 30.16 ±0.493 mg/dl), respectively.

4. Some special cases of breast cancer patients showed elevated mean levels of reduced glutathione, 46.509±19.825mg/dl compared to the control group mean level 28.711±0.441mg/dl which needs a particular / special consideration. This correlates with the glutathione study that the elevated levels of glutathione in turnover cells are able to protect the cancerous cells in bone marrow, breast, colon, larynx and lung cancers. These patients also showed elevated
TBARS (MDA) mean values, 22.80±11.889 nmol/ml as compared to the control mean value 5.305±7.347 nmol/ml. This suggests that the defense mechanism reacts to minimize the cancerous cell growth. Similarly the lower levels of serum vitamin A concentration in these patients suggested the deficiency of that vitamin was created due to impairment in the systemic conditions.

*The oxidative stress resulting from an imbalance between pro-oxidant and antioxidants seems to play an important role in human breast carcinogenesis.*

**B) Cervix Cancer**

Patients diagnosed/screened for cervix cancer in the studied cases were found to be reporting very lately. But still the percentage deaths have been minimized crediting to the Pap smear technology. It was seen that by the time the subject patient reaches for diagnosis, the systemic organs have been affected. The disease has already onset the metastasis. **Most of the patients of cervix cancer succumb due to the malfunctioning of the organs related to the spread of metastases occurred.**

The kidney function test and liver function test were carried out in the cervix cancer as that in breast cancer patients. Accordingly the present study was planned to evaluate the biochemical correlation of these biochemical parameters and the antioxidant/oxidative stress status in the cervix cancer patients.

The results of the study of the biochemical markers in the patients screened for cervix cancer were as follows:

1. The blood urea level and serum creatinine levels were within normal levels of patients with recent detection of the disease. *However, some cases showed elevated renal profile levels. These patients were diagnosed for advanced cancer stages. As aforesaid the spread of the malignancy seemed to have affected the organ metastases.* The blood urea mean level and serum
creatinine mean level were comparatively elevated in these patients, 47.4±9.154 mg/dl and 1.80±0.071 mg/dl respectively as compared to the controls. The uric acid was showing elevated mean level 8.92±0.779 mg/dl as compared to control mean level 4.54±0.963 mg; implying that uric acid may be acting as an enzymatic antioxidant to minimize the enzymatic alteration due to metastasis.

2. The liver profile showed elevated SGOT mean levels suggesting the malfunctioning of the liver, the patients may be having hypertension and cardiac relative abnormalities.

   The serum proteins were decreased in the test group; may be due to alterations in the metabolism.

3. The antioxidant status in these cervix cancer patients showed decreased levels of vitamin A and reduced glutathione. This correlates well with the free radical scavenging activity of the reduced glutathione. The increase in the oxidative stress indicator TBARS mean level suggested the competing capability of the TBARS with the cancer cells growth to necrosis. SEPH mean levels were also elevated; which may be due to red blood cells haemolysis because of their osmotic fragility.

C) Ovarian Cancer

One of the leading causes of deaths among gynecologic malignancies is the ovarian cancer. The renal profile, liver profile and the antioxidant/oxidative stress status was evaluated in these patients with ovarian tumour.

The findings of the biochemical markers studied in these malignancies were as follows.

1. Renal profile of the ovarian tumour patients (the blood urea and serum creatinine mean levels) was within the normal limits. This suggested that there was no involvement of the kidney functioning
in ovarian tumour patients. Nevertheless, the serum uric acid level were decreased.

2. The liver profile showed highly elevated values of serum alkaline phosphatase and the SGOT enzyme activity. This proposes that there was liver malfunctioning due to involvement of bone resorption. Elevated values of SGOT suggested the muscle involvements (which are rich in this enzyme). Both the parameters showed highly elevated mean value levels, 38.4±2.510 KAU and 26.4±4.278 IU/L respectively compared to the controls 11.0±1.0 KAU and 10.4±1.517 IU/L, respectively; implying that the oxidative stress due to free radical generation and subsequent lipid peroxidation of hepatocyte membrane may be involved in toxic induced liver injury.

3. The oxidative stress indicator TBARS showed highly elevated mean levels, 22.7±0.332 nmol/ml against 4.81±2.678 nmole/ml of control. Antioxidant status showed decreased vitamin A and reduced glutathione levels to be significant. This suggested that the changes in liver enzymes, reduced glutathione and lipid peroxidation may be due to free radical induced damage to the liver.

**Chapter IV : Oral and Oral Related Cancers**

The parameters of renal profile, liver profile, oxidative stress indicators and antioxidant status were studied in the oral and oral related cancers. This test group consisted of cancers of cervical nodes, pyriform fossa, maxilla, parotid tumour, larynx and oesophagus.

Oral cancer is characterized by a high degree of local invasiveness and a high rate of metastasis to cervical lymph nodes. Death is often as the result of local recurrence or regional and/or systemic metastasis. The metastasis is the strenuous problem in successful cancer treatment. Considering oral malignancy as one of the leading malignancies in India
which is engulfing today’s youth, study of better markers for the prediction of oral cancer progression is needed.

The observations and findings of the biochemical markers studied in these oral and oral related malignancies were as follows:

1. The malignancies of **cervical nodes, pyriform fossa and maxilla** showed elevated values of renal profile. This suggested that the malfunctioning of the kidney, may be due to the metastasis by the disease.

The other malignancies viz that of **parotid tumour, larynx** and **oesophagus** did not have much impact on the kidney functioning. *The uric acid parameter showed upper mean levels suggesting its antioxidant activity due to diseased condition.*

2. The liver profile (serum bilirubin, SGOT and SGPT levels) was within the normal limits in the studied test group. *The oral related malignancies showed elevated serum alkaline phosphatase levels*; especially the malignancy of **maxilla and parotid tumour** test group showed highly elevated serum alkaline phosphatase mean levels being 306.2±529.339 IU/L and 244.5±21.246 IU/L in test group respectively against the control values being 187.2±8.719 IU/L and 180.95±1.041 IU/L. *This suggested that the prime location of the metastasis was bone involvement.*

3. The oxidative stress parameter TBARS product (MDA), was increased in all the above said malignancies. The oxidative stress indicator SEPH also showed elevated levels There was a significant decrease in the antioxidant status values of Vitamin A and reduced glutathione. *This indicated that the antioxidant defense system has been altered due to the cancerous status.*
The present study **signified** that the renal profile and liver profile evaluations may be considered in the progression and treatment of the malignancies along with other established routine explicit parameters.

The present results implied that the evaluation of oxidative stress indicators and the antioxidant status of the related malignancies may be helpful and useful in the context of metabolic disturbances associated with the disease status. The overall results of the present study, demonstrated that the findings of oxidative stress indicators and antioxidant status/may be of novel importance in treating and monitoring the malignancies.