DISCUSSION

Carcinoma of cervix is the leading cause of cancer death in women. Its incidence is high in developing and underdeveloped world. The worldwide incidence of the disease in developing countries is 80%, whereas its incidence in the developed part of world is about 20%. In India the incidence of cancer cervix is 26%. The various factors influencing its occurrence are multiparity, early marriage, multiple sexual partners and low socio-economic conditions.

The majority of cases of carcinoma of cervix are squamous cell in origin (about 90%). Rests of the cancer cervix are adenocarcinoma. The peak incidence is in women in age group of 30-50 years. The disease is more aggressive in immunosuppressed individuals. Invasive cancer is
highly (40%) associated with human immunodeficiency virus. There are studies which suggest that it is more strongly associated with sexually transmitted diseases, mainly Human Papilloma Virus (HPV) type 16,18,31 and 33. Cervical carcinoma is a locally malignant disease and metastasis occurs mainly by direct extension or lymphatic.

Evaluation of cancer cervix is done by general and pelvic examination, cytological and radiological examination and biochemical tests for function of kidneys and liver. These are of paramount importance in early detection, diagnosis, staging and treatment of the disease. Extensive screening programmes are useful in lowering the mortality rate of the disease.

The primary modalities of treatment of cervical cancer are radiotherapy, chemotherapy
and surgery. Radiotherapy and surgery are employed for stage 0 (pre-invasive), stage IA (micro invasive), stage IB and stage IIA. Patients with stage IIB to IVA stages are treated with radiation therapy.

The aim of giving chemotherapy is to make the tumor radiosensitive and make radiation more effective. The anticancer drugs or chemotherapeutic agents used in treatment of cancer cervix are 5-FU, Mitomycin-C, Cisplatin, Hydroxyurea, Doxorubicin, Camptothecin and Paclitaxel. With chemotherapy the tumor shrinks and makes cure possible and more easy by a second treatment, because there are lesser cells to be killed. Most of the cytotoxic agents exert their effect through inhibition of DNA synthesis and / or its replication. Therefore it is not surprising that their side effects are mainly observed on tissues with a
high self-renewal rate, such as bone marrow and digestive tract (Schwartsmann et al, 1988).

The use of radiotherapy and chemotherapy make it imperative that extensive laboratory support is provided by careful monitoring of various biochemical and immunological changes. This makes it possible to detect toxic effects of the mode of treatment employed.

The present study was carried out with the object of finding out the efficacy of various biochemical and immunological parameters in primary diagnosis and evaluating the therapeutic response of a mode of treatment. The aim was also to find out whether these parameters can be used as a guide in making decision regarding the dose, duration and mode of treatment.

The present study was undertaken on 250 patients of cancer cervix. The study also
included 50 normal healthy females in the age group of 25 to 55 year to serve as control. None of the patients or control had received any drug which can alter the metabolism.

The patients were divided according to the stages of cancer cervix (Table 1). Stage I (n = 41; 16.4%), Stage II (n = 75; 30%), Stage III (n = 107; 42.8%) and Stage IV (n = 27; 10.8%).

The patients were divided according to mode of treatment in four stages (Table 2). Stage I (n = 41) patients underwent surgery and hence were excluded from the study. Stage II patients were further divided into two groups, stage IIa (n = 15) who were treated by radiotherapy following surgery and stage IIb (n =30) patients were treated by radiotherapy only. Stage III patients were also divided into two groups, IIIa and IIIb. The first
group patients of stage IIIa (n = 32) were treated with radiotherapy only whereas stage IIIb patients (n= 75) were given concurrent therapy also, i.e. combination therapy. The stage IV group (n = 27) patients were treated by chemotherapy. The patients of group IIa, IIb and IIIa ( n = 107) were included in one group as they all by chemotherapy (n = 75) comprised of a separate group (Stage IIIb) and the patients who received only chemotherapy only, (n = 27) constituted a single group ( stage IV).

Normal Ranges

Various parameters were estimated in 50 healthy individuals to determine the normal ranges (Table 3). The values mentioned in the literature of the kits matched with these values.
Creatinine: - Serum creatinine value in 50 normal individuals was found to be in the range of 0.2-1.2 (mean 0.95±0.09) mg/dl. The age of the normal control did not make any difference in creatinine value. The normal value reported by Groth et al, (1986) was 88.5 ± 3.35 μmol/l, in healthy persons.

Creatinine clearance: - The 50 individuals of control group showed creatinine clearance in the range of 85-110 (mean 97.9 ± 10.5) ml/min. There was no difference in the range with age of the person. Groth et al, 1986, reported the normal value to be in the range of 117.1 ± 4.03 ml/min in healthy controls.

Urea: - The range of serum urea level in these 50 control group persons was 16-45 (mean 24.6 ± 4.4) mg/dl. There was no major difference in the readings due to age.
**Glucose:** - Serum glucose level ranged from 60-100 (mean 76.6 ± 10.5) mg/dl. There was no variation in the glucose level in different age groups.

**Bilirubin:** - Serum bilirubin in 50 women of control group ranged from 0.5 to 1 (mean 0.87 ± 0.08) mg/dl. All the age group showed similar figures. Trinder (1964) and Dandeker (2000) also reported similar results.

**Alkaline Phosphatase:** - 50 control women in control group had serum alkaline phosphatase in the range of 3-13 (mean 8.3 ± 2.4) K.A.unit. All the age group in control had the same range of alkaline phosphatase. Similar reports were found by King et al, (1965).
**SGPT and SGOT:** - SGPT level in 50 control subjects ranged from 4.5 to 35 (mean 14.3 ± 4.2) U/ml. and SGOT ranged from 5 to 38 (mean 18.0 ± 3.8) U/ml. There was no change in range of different age groups.

**Total Proteins:** - Serum total protein level in 50 normal subjects ranged from 4 to 8 (mean 6.8 ± 1.1) gm/dl. Present study did not show any significant change in different age groups.

**Albumin:** - Control women showed serum albumin level to be in the range of 3.7 to 5.3 (mean 4.2 ± 0.94) gm/dl. Age of the control did not make any difference in albumin level.

**Magnesium:** - The range of serum magnesium level in 50 control women was from 1.6 to 2.6 (mean 2.16
± 0.36) mg/dl. The age of the control was not found to make any impact on serum magnesium level. Ilicin (1971) and Capel et al (1982) reported the normal values to be in the range of 20-25 (21.1 ± 0.4) μg/ml. Sachs et al, (1996) reported this level in the range of 0.80 ± 0.02 mmol/l.

**Calcium**: The serum calcium level in 50 control subjects were found to be in the range of 9 – 12 (mean 10.6 ± 1.3) mg/dl. The results were common in all age groups. Somewhat higher serum calcium level (10.35 ± 0.34 mg/dl) in healthy individuals was reported by De Jorge (1965). Capel (1982) reported normal range as 90-110 μg/ml whereas Sachs et al, (1996) reported 2.17 ± 0.03 mmol/l serum calcium in control women.
Iron: - Serum iron in 50 control women ranged from 32-62 (mean 43.6 ± 7.9) µg/dl. Wester (1973) reported iron level of 1.21 ± 0.78 µg/ml in healthy controls.

Zinc: - Serum zinc ranged from 75 to 115 (mean 95.8 ± 15.42) µg/100 ml. Different age groups had same results in present study. Wester (1973) and Capel (1982) reported similar results.

IgG: - Serum IgG level in 50 control group subjects was in the range of 1000 to 1280 (mean 1145 ± 132.2) mg/dl. The age of control had no significant effect on IgG level. These results coincided with these of Vijaykumar et al, (1986) and Juranic et al (1994).
**IgA:** - 150 to 315 (mean 207.5 ± 38.6) mg/dl was found to be the range of serum IgA level in healthy control. There was no difference in various age groups. Vijaykumar (1986) and Juranic (1994) also reported similar figures in controls.

**IgM:** - Serum IgM level in 50 normal control was in the range of 90 to 160 (mean 126.8 ± 18.2) mg/dl. No difference was observed in different age groups. Similar reports were published by Vijaykumar (1986) and Juranic (1994).

**EFFECT OF RADIOTHERAPY ON RENAL FUNCTION**

(1) Effect of Radiotherapy on Serum Creatinine
When compared to control, the baseline value of serum creatinine was normal 0.95 ± 0.09 mg/dl. [Table 4]. Radiotherapy resulted into rise in serum creatinine level (1.23 ± 0.58 mg/dl; p<0.01). One month after radiotherapy the serum creatinine level decreased (1.17±0.71) (p<0.05). This level returned to normal three months later and remained so after six and nine months. The number of patients undergoing radiotherapy was 107, which remained same after one month but gradually reduced to 88, 75 and 63 after three, six and nine months.

(2) Effect of Radiotherapy on Creatinine Clearance

When compared to control subjects (97.9 ± 10.5 ml/min; Table 4), the baseline serum creatinine clearance in patients suffering from cancer cervix, was normal (96.4 ± 9.9 ml/min, Table 5).
During radiotherapy it reduced significantly to the level of $93.4 \pm 9.02$ ml/min ($p<0.01$). Radiotherapy leading to renal damage could be the cause of fall in creatinine clearance. After one month of therapy there was little increase in the rate of clearance but it attained normal value only after three months of radiotherapy and remained static thereafter.

(3) **Effect of radiotherapy on Serum Urea**

The baseline serum urea ($22.7 \pm 4.1$ mg/dl; Table 5) was within normal range as compared to control subjects ($24.6 \pm 4.4$ mg/dl). It was significantly elevated ($35.2 \pm 8.4$ mg/dl) ($p<0.05$) during radiotherapy and returned to normal after one month, to remain static for the rest of period.

**Effect of Radiotherapy on Serum Glucose**

The serum glucose level was normal at baseline ($77.2 \pm 9.8$ mg/dl; Table 5) when
compared to control (76.6 ± 10.5 mg/dl). During radiotherapy and following months there was no change in serum glucose level.

**EFFECT OF RADIOTHERAPY ON LIVER FUNCTIONS**

(1) **Effect of Radiotherapy on Serum Bilirubin and Alkaline Phosphatase**

Control figures for serum bilirubin and alkaline phosphatase was 0.87 ± 0.08 mg/dl and 6 ±1.3 KAUunit respectively. It was within this normal range at baseline (0.64 ± 0.06 mg/dl and 6.2 ± 1.4 KAUunit, Table 6).

Serum bilirubin was normal (0.71 ± 0.02 mg/dl) and there was no change during or after radiotherapy. Serum alkaline phosphatase on the other hand was raised (9.2 ± 4.2 KAUunit p<0.01) during radiotherapy. This elevation was less at the end of one month (8.3 ± 3.8 KAUunits) and gradually
came to normal level and remained normal after three, six and nine months of radiotherapy.

(2) **Effect of Radiotherapy on Serum Transaminases**

Compared to control group SGPT and SGOT (20 ± 4.2 U/Ml and 18 ± 3.8 U/Ml, Table 7) was normal in baseline patients (18.3 ±4.4 U/Ml and 16.6 ± 2.5 U/Ml). SGPT was significantly elevated during radiotherapy (35 ± 5.6 U/Ml, p<0.05) but SGOT level remained normal throughout the study period.

(3) **Effect of Radiotherapy on Serum Total Protein and Albumin**

There was no difference in the serum protein and serum albumin levels at baseline (6.9 ±1.2 gm/dl and 3.9 ± 0.7 gm/dl) when compared to normal control figures (6.8 ± 1.1gm/dl and 4.2 ± 0.94 gm/dl Table 8). There was no change in serum protein and
albumin levels during radiotherapy and 1, 3, 6, and 9 months later.

One can arrive at a conclusion that radiotherapy in patients with cervical cancer does not disturb the liver functions except the elevation in serum alkaline phosphatase level.

**Effect of Radiotherapy on Minerals**

(1) **Serum Magnesium**

The serum magnesium level at baseline ($2.0 \pm 0.35$ mg/dl) in 107 patients of stage II and IIIa were normal when compared to normal control ($2.16 \pm 0.35$ mg/dl; Table 9) During radiotherapy, the serum magnesium levels were normal and remained so after 1,3,6 and 9 months of treatment. This indicates that radiotherapy does not affect serum calcium levels in patients of cervical carcinoma.

(2) **Serum Calcium**
As against control subjects (10.6 ± 1.4 mg/dl) the serum calcium level in baseline subjects (10.6 ±1.3 mg/dl) were unchanged. Serum calcium levels were within normal range during radiotherapy (10.3 ± 1.2 mg/dl) and remained normal during 1,3,6 and 9 month of follow up. Therefore it can be surmised that radiotherapy alone in cervical malignancy does not affect serum calcium levels.

(3) Serum Iron

The normal range of serum iron was (95.8 ± 7.9 μg/dl; Table 10). There was no change in serum iron level in 107 patients of stage II and IIIa cervical carcinoma, receiving radiotherapy, at baseline (43.9 ± 8.1 μg/dl), during radiotherapy (44.1 ± 8.3μg/dl) and after 1, 3, 6 and 9 months of treatment.
(4) Serum Zinc

Baseline serum zinc levels (95.1 ± 15.2 μg/dl) of 107 patients of stage ii and IIIa cervix carcinoma, who received radiotherapy alone were normal, when compared to normal subjects (95.8 ± 15.42 μg/dl, Table 10). There was no change in serum zinc levels during radiotherapy (94.9 ± 15.9 μg/dl) and 1, 3, 6 and 9 months after radiotherapy. This confirms the findings of other workers that only radiotherapy does not affect serum zinc level in patients of carcinoma cervix.

EFFECT OF RADIOTHERAPY ON IMMUNOGLOBULINS

Cervical carcinoma patients, at their baseline, had significantly raised levels of immunoblobulins, specially IgG (1218.6 ± 166.7 mg/dl p<0.001) and IgA (221.4 ± 34.0 mg/dl,
p<0.01), when compared to normal subjects (1145 ± 132.2 mg/dl and 207.5 ± 38.6 mg/dl). Serum IgM, on the other hand was found to be unchanged throughout (Table 11). As against this finding some other authors, like Check et al (1980), Vasudevan et al (1971) and Adelusi et al (1981) have found that advanced cancer leads to suppressed immunological functions.

Radiotherapy led to increased serum levels of IgG and IgA to 1208 ± 152 mg/dl (p<0.01) and 218 ± 37.5 mg/dl (p<0.05) respectively. This increased level starts regaining normal levels at the end of follow up period. After one month the IgG and IgA levels returned to normal and remained normal after 3, 6 and 9 months. The slow normalization of IgG and IgA levels might reflect the success of therapy. These observations are in concurrence with the finding s of many other studies

This study confirms that radiotherapy alters the cell population, establishing distinctive patterns and that it could be used as clinical and prognostic indicator. The high levels of IgG and IgA in cancer cervix could be due to increase in immunoglobulin synthesis by the solid tumor. May be, this process is enhanced by some immunoglobulin like IgA.

**EFFECT OF CONCURRENT THERAPY ON RENAL FUNCTION**

(1) Effect of Concurrent Therapy on Serum Creatinine

When compared to normal control subjects (0.95 ± 0.09 mg/dl), the baseline value of
serum creatinine, in patients with stage IIIb carcinoma cervix, was normal (0.93 ± 0.08 mg/dl, Table 12). The serum creatinine was elevated during combined therapy (2.1 ± 0.09 mg/dl p< 0.01). It returned to normal within one month of therapy and remained normal after 3, 6 and 9 months. In a report, Reisinger (1996), described similar findings. In his series two patients had to discontinue concurrent therapy due to rise in serum creatinine, following cisplatin intake.

(2) Effect of Concurrent Therapy on Creatinine Clearance

Serum creatinine clearance at baseline was normal (96.5 ± 10.7 ml/min) as compared to healthy controls (97.9 ± 10.5 ml/min, Table 12). It decreased significantly during therapy (92.5 ± 7.9 ml/min, p< 0.01). Within one month the
clearance level became normal and stayed normal till the end of study.

(3) Effect of Concurrent Therapy on Serum Urea

Baseline values of serum urea of stage IIIb patients was normal (20.4 ± 4.0 mg/dl) as compared to healthy controls (24.6 ± 4.4 mg/dl, Table 13). This level increased during concurrent therapy (30.8 ± 6.2 mg/dl, p<0.01) and returned to normal after one month. It remained normal thereafter.

Concurrent therapy, thus causes some renal toxicity but since creatinine, creatinine clearance and urea return to their normal levels within one month, the damage is temporary and reversible. However the toxicity appears to be more in this group as compared to radiotherapy alone.
EFFECT OF CONCURRENT THERAPY ON SERUM GLUCOSE

Serum glucose at baseline was within normal range (77.1 ± 10.5 mg/dl) as compared to healthy controls (76.6 ± 10.3 mg/dl). The serum glucose level remained during therapy and after 1, 3, 6 and 9 months of follow up.

EFFECTS OF CONCURRENT THERAPY ON LIVER FUNCTION

(1) Effect of Concurrent Therapy on Serum Bilirubin

Patients in stage IIIb of cancer cervix had baseline bilirubin level (0.83 ± 0.07 mg/dl) within normal range as compared to control group (0.87 ± 0.08 mg/dl Table 14). There was significant rise in serum bilirubin level during concurrent therapy (0.96 ± 0.09 mg/dl, p < 0.01),
which returned to normal within one month and remained normal after 3, 6 and 9 months.

(2) Effect of Concurrent Therapy on Serum Alkaline Phosphatase

Serum alkaline phosphatase level was normal at baseline (6.1 ± 1.2 KAUunit) in patients with stage IIIb cervical cancer, the control level being 6 ± 1.3 KAUunit. (Table 14). The concurrent therapy made this level to rise noticeably (10.2 ± 2.6 KAUunit, p<0.05). After one month this raised level became normal and there was no change after 3, 6 and 9 months follow up period. The raised level of serum alkaline phosphatase returned to normal even in those cases where treatment was continued in spite of raised levels.

(3) Effect of Concurrent Therapy on Serum Transaminase
Serum SGPT and SGOT levels in stage IIIb cancer cervix patients at baseline were found to be normal (14.6 ± 2.4 U/ML and 12.6 ± 2.5 U/ML) as compared to healthy controls (20 ± 4.2 U/ML and 18 ± 3.8 U/ML, Table 15). SGPT level (28.3 ± 5.9 U/ML, p>0.01) was observed to be more significantly raised than SGPT (25 ± 8.2 U/ML, p<0.05), during therapy. Both SGPT and SGOT levels became normal within one month and stayed normal after 3, 6 and 9 months.

(4) Effect of Concurrent Therapy on Serum Total Protein and Albumin

The serum total protein and albumin levels at baseline (6.2 ± 1.1 gm/dl & 3.8 ± 0.81 gm/dl) were within normal range of controls (6.3 ± 1.1 gm/dl & 4.2 ± 0.90 gm/dl). They were normal during therapy and after 1, 3, 6 and 9 months.
The study shows that concurrent therapy does not affect either total protein or albumin.

**EFFECT OF CONCURRENT THERAPY ON SERUM MINERALS**

(1) Serum Magnesium

In comparison to normal healthy controls (2.16 ± 0.36 mg/dl, Table 17) baseline serum magnesium was normal (2.36 ± 0.45 mg/dl). Slight fall in serum magnesium level was observed during therapy (2.04 ± 0.36 mg/dl). This hypomagnesaemia disappeared within a month and remained normal till the end of study.

(2) Serum Calcium

Baseline serum calcium was normal (10.8 ± 1.6 mg/dl) in stage IIIb cervical carcinoma patients receiving concurrent therapy, as compared to controls (10.6 ± 1.3 mg/dl, Table 17).
Hypocalcaemia (10.13±0.9 mg/dl, p< 0.05) appeared during therapy. The serum calcium level regained normal level in the first month and remained static thereafter. Walder et al (1993) reported similar results.

(3) Serum Iron

The 75 patients of stage IIIb carcinoma cervix receiving concurrent therapy showed normal serum iron level at baseline (44.1 ± 8.1 µg/dl) as compared to control subjects (43.6 ± 7.9 µg/dl, Table 18). Serum iron level remained normal during and after therapy and no deviation from normal level was observed.

(4) Serum Zinc

Like controls (95.8 ± 15.42 µg/dl, Table 18), serum zinc remained normal at baseline, during concurrent therapy, after 1, 3, 6 and 9 months.
Serum magnesium and serum calcium showed some changes due to concurrent therapy in patients of cervical carcinoma but serum iron and serum zinc levels were unaltered.

EFFECT OF CONCURRENT THERAPY ON IMMUNOGLOBULINS

Serum immunoglobulins showed significant elevation in cases of cervical cancer stage IIIb, undergoing concurrent therapy. The normal controls had IgG level of 1145.0 ± 132.2 mg/dl and IgA level of 207.5 ± 38.6 mg/dl whereas the baseline figures for IgG were 1200.7 ± 162.09 mg/dl and for IgA were 292.6 ± 50.18 mg/dl. No change in IgM level was observed (Table 19).

Serum IgG and IgA levels were elevated during concurrent therapy (1192.5 ± 164.8 mg/dl, p<0.01 and 226.7 ± 40.12 mg/dl p<
0.01). IgG and IgA levels returned to normal after month and remained so for the rest of the period. IgM level did not show any change.

Administration of chemotherapy with radiology appears to have certain advantages. Chemotherapy sensitizes the tumor cells to the radiation and reduces the size of tumor so that it becomes easier for radiation to kill the remaining cells. It also reduces the course of radiotherapy and avoids protracting the overall treatment time, thus reducing the time for the cells to proliferate.

It can be concluded from the study that combination of radiotherapy and chemotherapy prevent the rate of progression of the disease and improves the rate of survival.
EFFECT OF CHEMOTHERAPY ON RENAL FUNCTION

(1) Effect of Chemotherapy on Serum Creatinine

Serum creatinine at baseline (0.94 ± 0.08 mg/dl) was within normal limits as compared to control (0.95 ± 0.09 mg/dl) in stage IV cancer cervix patients (Table 20). Serum creatinine was raised significantly during chemotherapy (2.64 ± 1.09 mg/dl, p<0.001). This elevation was still there at the end of one month (1.0 ± 0.07 mg/dl, p<0.01). Daugaard et al (1988), Meijer et al (1983), Stewart et al (1985), Uozumi et al (1993) and Merouani et al (1997) reported similar findings. They also found that serum creatinine was raised at the end of first month. This elevated level returned to normal after one month and remained normal during 3, 6 and 9 month period of follow up. In their study Daugaard et al (1988) found that the serum creatinine level was
still raised at the end of 3 months after the last course of treatment. Sorensen et al (1985) on the other hand did not find any change in serum creatinine levels before, during or after chemotherapy.

(2) Effect of Chemotherapy on Serum Creatinine Clearance

In stage IV carcinoma of cervix, when compared to normal control (97.9 ± 10.5 ml/min), baseline figures (96.4 ± 9.8 ml/min.) were within normal range. It decreased during chemotherapy significantly (88.6 ± 7.2 ml/min, p<0.001). Dentino et al (1978) reported similar findings. This fall persisted, though less (95.12 ± 8.8 ml/min, p<0.01), at the end of one month of chemotherapy. Serum creatinine clearance returned to normal and remained normal at the end of 3, 6 and 9 months. Contradictory to this finding Soernsen et al (1985) did not find any change in serum creatinine clearance before, during or after
chemotherapy. Daugaard et al (1988) reported fall in the rate of creatinine clearance from $109 \pm 3$ ml/min to $68 \pm 3$ml/min after chemotherapy, which persisted even after 24 months.

(3) **Effect of Chemotherapy on Serum Urea**

Baseline serum urea level was normal ($32 \pm 4.1$ mg/dl) when compared to control ($24.6 \pm 4.4$ mg/dl, Table 21). This level, during chemotherapy was elevated to $43 \pm 8.7$ mg/dl ($p<0.001$), after one month $32.2 \pm 5.8$ mg/dl ($p>0.01$) and after 3 months $30 \pm 5.5$ mg/dl ($p<0.05$). It came back to normal after 6 and 9 months. Similar findings were reported by Dentino et al (1978) but Daugaard et al found serum urea to be elevated 3 months after last course of treatment.

This study shows that chemotherapy is nephrotoxic but the initial renal damage recovers after three months.
EFFECT OF CHEMOTHERAPY ON SERUM GLUCOSE

Serum glucose baseline was within normal range \((75.9 \pm 9.9 \text{ mg/dl})\) as compared to normal control \((76.6 \pm 10.5 \text{ mg/dl})\), in the patients of stage IV carcinoma of cervix (Table 21). No change in serum glucose level was observed during and after chemotherapy. Seeckl et al (1999) has reported cases of small cell carcinoma of cervix with hypoglycaemia due to increase in the serum insulin concentration.

EFFECT OF CHEMOTHERAPY ON LIVER FUNCTION

(1) Effect of Chemotherapy on Serum Bilirubin

Baseline serum bilirubin was \((0.78 \pm 0.04 \text{ mg/dl})\) within the normal range in stage IV
cancer cervix patients as compared to normal subjects (0.87 ± 0.08 mg/dl, Table 22). There was significant elevation during chemotherapy (1.1 ± 0.09 mg/dl, p<0.001). After one month the serum bilirubin level was still statistically elevated (.99 ± 0.08 mg/dl, p<0.01) and after 3 months, though less, it was still high (0.95 ± 0.08 mg/dl, p<0.05). Serum bilirubin level came to normal after 6 and 9 months. Similar report was given by Myers et al (1990).

Chemotherapeutic agents, specially methotraxate and bleomycin have been reported to cause acute and chronic hepatotoxicity, hyperbilirubinaemia and elevation of liver enzymes have been described. These toxic effects are usually reversible.
(2) Effects of Chemotherapy on Alkaline Phosphatase

Serum alkaline phosphatase level was normal at baseline (6 ± 1.4 KAUnits) in stage IV carcinoma cervix when compared to normal controls (6 ± 1.3 KAUnits, Table 22). It got elevated (12 ± 2.2 KAUnits, p<0.001) during chemotherapy and was still raised after one month of therapy (11.3 ± 2.3 KAUnits, p<0.05). It returned to normal level after 6 and 9 months. The elevation in the level of serum alkaline phosphatase was also reported by Myers et al (1990) and may indicate effect on bone metabolism.

(4) Effect of Chemotherapy on Serum Total Protein and Albumin

Stage IV cancer cervix patients showed normal baseline total protein (6.8 ± 1.2 gm/dl) and albumin (4.0 ± 0.93 gm/dl) as compared
to controls of total protein (6.8 ± 1.1 gm/dl) and albumin (4.2 ± 0.94 gm/dl, Table 24). During chemotherapy total protein and albumin were normal and remained normal after 1, 3, 6 and 9 months of therapy. Although cisplatin and methotrexate cause proteinurea, the serum level does not reflect it (Dougaard et al, 1988).

(5) Effect of Chemotherapy on Transaminase

Baseline SGPT (14.9 ± 2.5 U/ml) and SGOT (18.9 ± 2.2 U/ml) levels of stage IV patients of Cancer cervix were within normal range when compared to controls (20 ± 4.2 U/ml and 18 ± 3.8 U/ml, respectively, Table 23). SGPT and SGOT were significantly raised during chemotherapy (38.7 ± 4.5 U/ml, p<0.001 and 32 ± 4.1 U/ml, p<0.001). After one month these values were 26.6 ± 3.6 U/ml, (p<0.05) and 25.8 ± 4.1 U/ml, (p<0.050). After 3
months these values returned to normal and remained normal thereafter.

EFFECT OF CHEMOTHERAPY ON SERUM MAGNESIUM AND CALCIUM

(1) Serum Magnesium

Baseline serum magnesium in stage IV patients was within normal range (2.2 ± 0.39 mg/dl) when compared to controls (2.16 ± 0.36 mg/dl). During chemotherapy this level was decreased to value of 1.7 ± 0.26 mg/dl (p<0.001), showing hypomagnesaemia. Though not yet normal, this value rose to 1.95 ± 0.29 mg/dl (p<0.05) after one month, to return to normal level after 3 month and remained same after 6 and 9 months. Schilsky et al (1979), Gonzalez et al (1981), Buckley et al (1984) and Groth et al (1986) also reported hypomagnesaemia after chemotherapy, which returned to normal after one month.
(2) Serum Calcium

Baseline serum calcium level in stage IV patients was within normal range (10.1 ± 1.6 mg/dl) as compared to normal control (10.6 ± 1.3 mg/dl, Table 25). During chemo therapy serum calcium level decreased significantly (7.5 ± 0.96 mg/dl, p<0.001), showing hypocalcaemia. This decrease was less after one month (9.1 ± 1.1 mg/dl, p<0.05). It returned to normal after 3, 6 and 9 months. Gonzalez et al (1981) reported steep fall in magnesium and calcium levels during chemotherapy, sometimes leading to serious medical emergencies. Hypomagnesaemia may itself lead to hypocalcaemia (Lyman, 1980, & Blachley, 1981).

(3) Serum Iron

The 27 patients of stage IV at baseline had serum iron level of 43.1 ± 7.5 μg/dl,
which when compared to control figure of 43.6 ± 7.9 μg/dl, was normal. Insignificant difference in iron level in cancerous and noncancerous tissues was reported by Mulay et al. (1971). Serum Iron levels were found to be normal during and after chemotherapy.

(4) Serum Zinc

Serum zinc at baseline was normal (95.9 ± 15.64 μg/dl) in all 27 cases of stage IV cancer cervix, when compared to control subjects (95.8 ±15.42 μg/dl, Table 26). Capel (1982) reported similar results whereas Mulay et al (1971) reported elevation of zinc level. The serum zinc level remained normal during chemotherapy but showed some decline after one month of therapy. Zinc
deficiency is reported to be associated with loss of acuity of taste (Catalanotto, 1978). Zinc level returned to normal level after 3, 6 and 9 months.

**EFFECT OF CHEMOTHERAPY ON SERUM IMMUNOGLOBULINS**

Immunoglobulins i.e. IgG, IgA, of 27 patients of stage IV cancer cervix showed elevated levels at baseline (1250.8 ± 210.1 mg/dl, p<0.001; 282.6 ± 40.2 mg/dl, p<0.001 respectively) when compared to healthy controls (1145.0 ± 132.2 mg/dl and 207.5 ± 38.6 mg/dl respectively; Table 27). Baseline IgM was normal (129.9 ± 30.2 mg/dl) when compared to healthy controls (126.8 ± 18.2 mg/dl).

IgG and IgA levels of patients were still elevated during chemotherapy (1235.1 ± 212.6 mg/dl; p<0.01; and 231.4 ± 37.5 mg/dl, p>0.01). After 1 month of therapy the IgG and IgA levels
were still high (1214.0 ± 201.1 mg/dl, p<0.05 and 226.9 ± 35.3 mg/dl, p<0.05). This reverted to normal after 3 months and remained normal till the end of study. Vijaykumar et al, (1986) also reported similar results.