

A STUDY OF ENDOMETRIAL CARCINOMA

by

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The incidence of endometrial carcinoma in India and other Asian countries is low as compared to that in the Western countries. In the Christian Medical College Hospital, Vellore, during 8 years (1966-1973), 45 cases of endometrial carcinoma were diagnosed. During the same period there were 1,866 cases of cervical carcinoma, giving a ratio of 1:41.4. This paper is a study of the 45 cases of endometrial carcinoma.

Material and Methods

The clinical features, epidemiological factors including fertility index, age at first intercourse and intercurrent disease, diagnostic procedures and type of tumour have been analysed. The staging of the tumour and the treatment given have also been studied.

The staging used was based on that established by the International Federation of Obstetricians and Gynaecologists at the Sixth World Congress in 1970 (Kottmeier 1971).

Observations

Presenting Symptoms

Postmenopausal bleeding or a blood stained discharge was the presenting symptom in 32 cases (71.4 per cent). Carmichael and Bean (1967) and Lees (1969) found 89.2 per cent and 80 per

cent respectively in this group. Milton and Metters (1972) however found postmenopausal bleeding in 69.5 per cent in their series.

The remaining 13 cases (28.8 per cent) presented with menstrual irregularity, which emphasizes the need for curettage in all cases of irregular pre and perimenopausal bleeding. Milton and Metters (1972) found 19.1 per cent of patients presenting with menstrual irregularities.

Age

In this series the maximum incidence of endometrial carcinoma was between 45 to 54 years, and 55 to 64 years, being 15 patients in each group (33.3 per cent each). There were 10 patients (22.2 per cent) under the age of 45 years, which is much higher than that found by Dobbie *et al* (1965) and Milton and Metters (1972) which was 6.2 per cent and 10.7 per cent respectively in the same age group. There were only 5 patients (11.1 per cent) above 65 years in contrast to 26.4 per cent found by Milton and Metters (1972). The median age was 51.6 years which was significantly lower than the median age of 60.4 years found by Sall *et al* (1970). Table I shows the age distribution of the patients with endometrial carcinoma.

Fertility Index

All the patients were married in this series. The fertility rate was found to be markedly low. There were 15 nulliparous patients (33.3 per cent) and another

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TABLE I
Age Distribution

Age (Years)	No. of Cases	Percentage
Below 45	10	22.2
45 — 54	15	33.3
55 — 64	15	33.3
65 and above	5	11.1

15 patients were para 2 and less, again showing low fertility.

The causes of infertility were varied. Ten patients (22.2 per cent) however showed evidence of endocrinal imbalance, suggestive of anovulatory cycles. One case had secondary amenorrhoea at the age of 25 years, and 27 years later developed endometrial carcinoma. Early widowhood was noted in 7 cases (15.5 per cent).

Sherman and Woolf (1959), Boutselis *et al* (1963) and Dunn and Bradbury (1967) also observed low fertility in their series. In the study of Sall *et al* (1970), 42 per cent of the patients were nulliparous which was significantly higher than the 17.8 per cent nulliparity rate for the general population. Dunn and Bradbury (1967) found the average parity for endometrial carcinoma patients was 2.05 births per patient as compared to 4.6 births in the control patients.

Table II shows the parity of the patients with endometrial carcinoma. Most of the parous patients had a long

TABLE II
Incidence in Relation to Parity

Parity	No. of Cases	Percentage
0	15	33.3
1	5	11.1
2	10	22.2
3	2	4.4
4 and above	13	28.8

period of infertility after their last child birth and before the age of menopause.

Associated Medical Conditions

(a) Obesity

Fourteen patients (31.1 per cent) were obese. Dunn and Bradbury (1967) also found a significant difference in their series as compared to the controls. Lynch *et al* (1966), Lees (1969) and Milton and Metters (1972) reported 80 per cent, 51 per cent (marked obesity) and 37.1 per cent respectively in their series. The higher incidence of obesity affects the choice of therapy, curtailing extensive surgical procedures, as they may be nullified by increased incidence of postoperative complications leading to death.

(b) Diabetes

In this series there were 10 patients (22.2 per cent) who had diabetes mellitus. Lees (1969) and Milton and Metters (1972) found only 5 per cent and 4.6 per cent respectively, of diabetes in their study. Lynch *et al* (1966) however noted 42 per cent diabetic patients in their series.

(c) Hypertension

Eight patients (17.7 per cent) had moderate to severe hypertension, two of these had ischaemic heart disease also. The increased prevalence of hypertension can be explained due to obesity and older age group of the patients. Lees (1969) gave an incidence of 68 per cent of patients having blood pressure over 150/90 mm of Hg. Lynch *et al* (1966) had 65 per cent hypertensive patients in their series.

Previous Irradiation

Four patients (8.8 per cent) had been previously irradiated with radium or external irradiation to induce menopause.

There is a much higher incidence of endometrial carcinoma in the irradiation patients as compared to the general population. This has been reported by Taylor and Backer (1947) and Milton and Metters (1972).

Age of First Intercourse

There was a high incidence of coitus at any early age in this study. Twenty-seven patients (60.0 per cent) were married below the age of 16 years, and another 8 (17.7 per cent) were between 16-20 years. Early age of first intercourse was high in patients with corpus carcinoma as reported by Masubachi and Nemoto (1972). Biologically immature sexual organs are said to be highly sensitive to carcinogenic factor (s) that invades these organs through sexual intercourse has been stated by Moghissi and Mack (1968). The susceptibility of the endometrium to carcinogenic agents occurs after ovulation as stated by Stein-Werblowsky (1973). Table III shows the age of marriage of the 45 cases of endometrial carcinoma.

TABLE III
Age of Marriage

Age	No. of Cases	Percentage
Under 16	27	60.0
16 — 20	8	17.7
21 — 25	5	11.1
Above 25	1	2.2
Not mentioned	4	8.8

Vaginal Cytology

Vaginal Cytology was done in 15 cases and was positive in 2 cases only and was suspicious of malignancy in 1 case. Poor pick up rate of endometrial carcinoma by vaginal cytology has been reported by other authors. Milton and Metters (1972) obtained 11.9 per cent positive smears by vaginal cytology in their series.

Histology

Table IV shows the histological pattern of the endometrial carcinoma. There were 91.0 per cent (39 cases) adenocarcinomas, out of which 17.7 per cent (8 cases) were adenoacanthomas. Four tumours (8.8 per cent) were anaplastic.

TABLE IV
Histology of Endometrial Carcinomas

Histological pattern	No. of Cases	Percentage
Adenocarcinoma	33	73.3
Adenoacanthomas	8	17.7
Anaplastic	4	8.8

Stage of Growth

Table V shows the stage of growth. The incidence of Stage I was only 55.5 per cent (25 cases). Thirteen patients (28.8 per cent) were in Stage II. In comparison Lees (1969) and Milton and Metters (1972) had 70 per cent and 67.7 per cent respectively of Stage I carcinoma of the endometrium. In Stage I there were 6 cases, with myometrial infiltration of the tumour. Advanced disease was chiefly due to long duration of symptoms before the patient sought medical aid.

TABLE V
Stage of Growth

Stage	No. of Cases	Percentage
I	25	55.5
II	13	28.8
III	1	2.2
IV	4	8.8
Unstaged	2	4.4

Treatment and Prognosis

The line of treatment followed at our hospital was preliminary radiation followed 6-8 weeks later by surgery consisting of total hysterectomy and bilateral salpingo-oophorectomy with removal of cuff of vagina. Alternatively, surgery

was performed initially and postoperative radiation given when there was myometrial infiltration or undifferentiated tumour. Combined treatment of radiation and surgery was given to 15 patients. Two patients had Wertheim's hysterectomy and 8 patients were treated with surgery alone. Seventeen patients were treated by radiation alone, 5 patients failed to come for surgery after initial radiotherapy. The rest were advanced cases with medical conditions contraindicating extensive surgical procedures. Five patients refused treatment or went elsewhere for treatment. Table VI shows the various types of treatment given. Long acting progestational agents were given to patients with advanced disease, recurrence or treated with radiation only.

TABLE VI
Treatment of Endometrial Carcinoma

Treatment	No. of Cases	Percentage
Radiation	17	37.7
Total hysterectomy, bilateral salpingo-oophorectomy and vaginal cuff	8	17.7
Radiation and Total hysterectomy bilateral salpingo-oophorectomy and vaginal cuff	13	28.8
Wertheim's hysterectomy and Radiation	2	4.4
Not treated	5	11.1

There was one (2.2 per cent) operative mortality. The patient died on the 10th postoperative day due to septicaemia. Nineteen patients have been treated over 5 years ago, at the time of writing the paper, but very few have come for follow up. Four patients have, come with recurrence 6 months-3 years later, all were treated with radiation only. One patient who had an anaplastic tumour,

Stage II, was treated with Wertheim's hysterectomy and postoperative radiation died 3 years later of widespread metastases.

Five patients have survived for 5 years and more, four of them received combined therapy and one surgery alone.

Discussion

Endometrial carcinoma was found in only 2.4 per cent of uterine carcinomas. In Japan also the incidence was approximately 4 per cent of uterine carcinomas as reported by Boyd and Doll (1964). This is in distinct contrast to the incidence of corpus carcinoma in the western countries where the ratio is on the increase.

The commonest presenting symptom of endometrial carcinoma was postmenopausal bleeding, 71.4 per cent of the patients being postmenopausal. The mean age in this study was 51.6 years. Sall *et al* (1970) in America, and Masubachi and Nemoto (1972) in Japan reported higher mean ages which were 60.4 and 55.2 years respectively. This difference is probably due to the low life expectancy in India, patients may not survive to develop endometrial carcinoma.

The predisposing factors which predominate the disease were nulliparity and patients with low fertility. In this study 66.6 per cent (30 cases) of patients were in this group, and 22.2 per cent (10 cases) showed an endocrinal factor causing infertility. It was, however, noted that 15.5 per cent (7 cases) with nulliparity or low parity were probably due to early widowhood.

There was a high incidence of obesity (31.1 per cent) and diabetes mellitus (22.2 per cent) in the patients with endometrial carcinoma. These two medical associations again point to an endocrinal or metabolic abnormality.

Previous irradiation (8.8 per cent) was

also high in the patients with endometrial carcinoma. The inference to this is two-fold. Firstly, these patients were in the high risk group as they had excessive uterine bleeding and associated obesity and/or diabetes mellitus for which reason artificial menopause was induced by irradiation. Secondly, it is well-documented that radiation induced carcinomas can occur.

The reason for the overall low incidence of endometrial carcinoma can be explained due to the lower life expectancy and high parity rates in our country. There is a definite decline in the incidence of endometrial carcinoma with increasing parity as shown by Dunn and Bradbury (1967), Sall *et al* (1970), and the present study.

Endocrinal factors may have a role in producing infertility and endometrial carcinoma. It was however seen that no or less childbearing may be due to the single status or early widowhood of the patients. In these women also the risk of endometrial carcinoma is high. Dobbie *et al* (1965) found that the incidence of endometrial carcinoma in single women was significantly greater. In the present study also there were 15.5 per cent (7 cases) of patients with low fertility due to early widowhood.

All evidence indicates that the treatment of choice in endometrial carcinomas is mainly surgical. Surgery was carried out in 23 patients only. This was due to the fact that there were only 55.5 per cent (25 cases) with Stage I carcinoma. Some of the patients refused surgery after preliminary radiation and others were unfit for surgery due to associated medical conditions or extensive disease.

It was noted that in the few patients

who reported for follow up that the 5 year survival was better in patients with Stage I, well differentiated carcinomas. Radiation alone had very poor results. These observations concurred with the views of Milton and Metters (1972) who analysed 355 cases of endometrial carcinoma and had an adequate follow up. They also found that the prognosis is better in well differentiated Stage I endometrial carcinomas that were treated with surgery.

Summary and Conclusions

Forty-five consecutive cases of endometrial carcinoma have been studied. The incidence of endometrial carcinoma was 2.4 per cent of uterine carcinomas. Postmenopausal bleeding (71.4 per cent) was the commonest presenting symptom, and the mean age was 51.4 years. The maximum incidence of the disease was between 45-64 years in this study.

Women who are nulliparous or with low fertility, obesity and diabetes mellitus are more prone to develop endometrial carcinoma. Artificial menopause with irradiation also increases the tendency to develop endometrial carcinoma.

Early diagnosis and surgical treatment are important for prognosis. Patients in the high risk category should have diagnostic curettage and greater vigilance to diagnose the disease early.

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