

# CARCINOMA OF CERVIX

(A Statistical Study Based on a Review of 3081 Cases)

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Carcinoma of the cervix is a disease which was well-known in India and Egypt, years before the birth of Christ (1500 B.C.). It has gained great importance in the last half a century, because of the various facilities and methods available for its diagnosis. In Andhra Pradesh, the incidence is very high as studied by workers from these areas, compared to the rest of South India. Subhadra Devi (1961), from Visakhapatnam, has studied the distribution pattern of these cases attending the Cervical

Cancer Clinic of the King George Hospital, from Andhra Pradesh, and reported that the majority of cases come from the neighbouring districts. Our study consisted of 644 cases from Cervical Cancer Clinic, King George Hospital, 2408 cases from biopsy material and 29 cases from autopsy material of Pathology Department, Andhra Medical College, Visakhapatnam. This material was analysed with a view to draw conclusions regarding the etiology, pathology and mode of spread of cancer cervix.

TABLE I

*Incidence of Uterine Cancer among Total Malignancies in Females  
(Biopsy Statistics 1950-62)*

	Total	Percentage
Total malignancies in females .. .. .	3469	
Total uterine cancer .. .. .	2465	71.05
(a) Total number of cervical cancer .. .. .	2408	69.41
(b) Total number of cancer of corpus uteri .. .. .	57	1.64

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## Incidence

The incidence of uterine carcinoma as observed by us from the analysis of the biopsy material during the period 1950-62 is recorded in Table 1.

Subhadra Devi (1961), in her study, has come across 1359 cases out

of 2505 total malignancies in females, giving an incidence of 50%; 4.6% of these cases showed carcinoma of corpus uteri, giving an incidence of 1.83% of total malignancies in the female, which compares well with our findings.

It is observed from the above Tables (1, 2, 3) that carcinoma of the cervix ranks first among all female malignancies as recorded by various workers.

A series of 3294 autopsies from the Department of Pathology, Andhra

TABLE II  
*Incidence of Malignancies in Various Sites of the Female Genital Tract (Biopsy Statistics 1950-62)*

	Total	Percentage
Total malignancies of the female genital tract .. .. .	2736	
Carcinoma of the cervix .. .. .	2408	88.01
Carcinoma of corpus uteri .. .. .	57	2.08
Sarcoma of the uterus .. .. .	9	0.32
Chorion-epithelioma of the uterus .. .. .	33	1.20
Malignant ovarian tumours .. .. .	140	5.11
Carcinoma of the vagina .. .. .	42	1.35
Carcinoma of the vulva .. .. .	46	1.68
Carcinoma of Bartholin's gland .. .. .	1	0.03

Table 3 shows the incidence of uterine cancer as compared with the observations of other workers from India. Medical College, Visakhapatnam, from the years 1926-1962 (36 years period) have been analysed. The incidence of cancer of the uterus is

TABLE III  
*Incidence of Cancer Uterus among Total Malignancies of the Female Genital Tract compared with Other Authors*

Author	Total No. of cases	Cancer cervix		Can. Corp. Uteri	
		Total	Percentage	Total	Percentage
Syamasundara Rao et al. (1959) Guntur	758	659	86.9	22	2.9
Reddy, D. B. and David Edward (1960) Visakhapatnam	1506	1263	84.28	32	2.68
Subhadra Devi and Prabhavathy (1961) Visakhapatnam	1648	1359	81.63	46	2.08
Anasuya Dass and Mukerjee (1961) Delhi	695	590	84.89	25	3.6
Paramjothy (1961) Vellore	486	407	83.9	33	6.6
Present series	2736	2408	88.01	57	2.08
Subodh Mitra (1957) Calcutta		Out of 3623 total malignancies in females observed, 1868 uterine cancer with a percentage of 51.55.			

shown in Table 4. Only adult autopsies have been considered for further analysis of these cases, as carcinoma of the cervix rarely occurs in children.

TABLE IV  
Incidence of Carcinoma of Cervix and Corpus Uteri, out of total of 3,294 Autopsies

	Total No. of cases
Total number of autopsies ..	3294
Total number of female autopsies ..	567
Total cancer deaths (M & F.M.) ..	395
Total cancer deaths among females ..	104
Total deaths due to cancer cervix ..	29
Total deaths due to cancer corpus uteri .. .. .	2

The incidence of cancer uterus among all autopsies is 0.94%. This is a very low figure when compared with other countries, the reason being the ratio of males to females in our general autopsy incidence is 4:1; whereas, if only malignancies are taken into consideration it is 3:1. Probably if more female autopsies are conducted, it may compare well with that of other authors, because the corrected incidence of cancer uterus among all tumours is 7.84%, which compares well with that quoted by Steiner ranging from 7.3—12.7% among whites, Caucasoids and Negroids, being highest among Negroids. The autopsy incidence of malignancies of female genital tract lesions as compared with all female malignancies is recorded in Table 5.

It is observed from Table 5 that out of 69 malignancies of the female genital tract 29 are due to cervical cancer giving an incidence of 42.03%

TABLE V  
Autopsy Statistics, A.M.C. (1926-61) showing the Incidence of Female Genital Malignancies

	Total	Percentage
Malignancies in females ..	104	
Malignancies in female genital tract .. .. .	69	66.34
Cancer cervix .. .. .	29	27.88
Cancer body of uterus ..	2	1.92
Chorion-epithelioma ..	4	3.84
Malignant ovarian tumours .. .. .	17	16.34
Primary malignant ovarian tumours .. ..	11	12.57
Secondary malignant ovarian tumours .. .. .	6	5.77

and 27.28% among all malignancies in female which is a fairly high incidence.

Age Incidence

*Carcinoma in situ.* Only six cases could be obtained from the biopsy material after a critical review although 13 cases had been diagnosed (Fig. 1). Seven cases were discard-



Fig. 1  
Photomicrograph illustrating intraepithelial carcinoma of the cervix. The sharp line of demarcation is seen as an oblique line in the left lower corner. (H & EX 100).

ed after a review of the previous slides as they showed only epidermidisation and were mistakenly diagnosed as carcinoma in situ.

The age pattern of our 6 cases was: 20 years, 28 years, 28 years, 40 years, 42 years, 48 years and 50 years. The average age was 37.6 years. The youngest patient was 20 years old and the oldest patient was 50 years old. Similar observations have been made by Hertig and Mansell and Young et al and their average age incidence was 38 and 38.7 years respectively.

In our series 2 patients were below the age of 30 years, whereas there were no cases between the ages of 30-40 years. Young, Hertig and Armstrong found 17% of cases under 30 years of age, and 41.4% under 35 years.

*Invasive Carcinoma.* The age incidence as observed by us in invasive carcinoma is recorded in Table 6. The youngest patient was 18 years old and the oldest patient was 75 years old. The average age was 38.47 years.

TABLE VI  
Age Incidence of 3081 Cases of Cervical Carcinoma in Decades

Age Group	Total No. of cases	Percentage
15-19 years .. ..	2	0.06
20-29 years .. ..	228	7.39
30-39 years .. ..	913	29.63
40-49 years .. ..	1253	40.66
50-59 years .. ..	471	15.28
60-69 years .. ..	117	3.79
70-79 years .. ..	12	0.38
Age not recorded ..	85	2.75

The maximum number of cases is in the age group of 40-49 years, but it is also seen that fairly good number

of these cases occur in the age group of 20-40 years. Carcinoma of the cervix can occur from 7 months of age onwards, but the peak incidence seems to fall in the 4th and 5th decades.

#### *Etiological Factors*

*Racial Incidence.* It is generally considered that carcinoma of the cervix is of a lower incidence among the circumscised races as compared with the uncircumscised. There is good evidence that cancer of the cervix is less frequent in Jews than in non-Jews of the same community. In India we have the Muslims as the circumscised races for comparison with the Hindus and other uncircumscised communities.

In our 644 cases of cervical carcinoma, 6 patients or 0.9% were Muslims. In India, Nath and Grewal (1935, 1937, 1939) and Syamasundara Rao et al (1959) reported a higher incidence of cervical carcinoma among the Hindus when compared with the Muslims. Subodh Mitra (1957) studied the racial susceptibility on etiological basis and concludes that the difference between the Hindus and Muslims was not statistically significant. Paranjothy (1961) in her study of 486 cases in Vellore reports that 87.3% of the cases were Hindus, 11% were Christians and 1.7% were Muslims. Syamasundara Rao et. al. (1959) reported difference in the incidence of carcinoma of the cervix in different religious groups. In areas where the number of Muslims is more, the incidence of carcinoma cervix is higher, thereby proving that the difference may

diminish or disappear completely if the population of the circumcised population rises to that of the uncircumcised.

Uterine cancer among Indians, according to Subodh Mitra, is dependent mainly upon the habits and environments, social status and assaults upon the cervix due to repeated childbirth rather than etiological difference in one or other communities.

*Marital Status.* The marital status of our cases is shown in Table 7. All the 644 cases were married.

is a significant factor and not pregnancy, perhaps due to excessive endocrine stimulation at this age.

The average age at marriage of our patients is 13.24 years which may be also considered to be the age of first coitus, thereby indicating the greater susceptibility of our patients to cancer cervix.

*Role of Smegma and Circumcision.* The example of the Jewish women with circumscised male partners having a low incidence of cervical carcinoma has been studied exten-

TABLE VII  
Details of Marital Status of 644 Cases

Average age at menarche	.. .. .	13.11 years
Average age at marriage	.. .. .	13.24 years
Circumcisional status of male partner:		
Uncircumscised	.. .. .	99.07%
Circumscised	.. .. .	0.93%
Average duration of married life preceding illness: (Excluding period of widowhood and separation, divorce, etc.)		
	.. .. .	24.25 years
Duration of abstinence after delivery:		
In 57.54% of cases average duration of abstinence	.. .. .	2.08 months
In total number of cases average duration of abstinence	.. .. .	4.88 months

*Vulnerability of Cervix in Puerperium.* When the effect of cohabitation after delivery is taken into consideration for all cases, the average period of 4.88 months is not of any significance, but 57.54% of the cases have early cohabitation at a period of 2.08 months, which may have some significance regarding the vulnerability of the cervix to coital trauma.

*Coitus.* Early coitus plays an important role in cancer cervix (Wynder et. al. 1955). Coitus at the age of 16 years or younger doubles the risk over that of the first coitus at the age of 20-24 years. Doll (1957) concludes that marriage or regular cohabitation

sively using the Muslims as examples, who are circumscised between 3-13 years of age. Subodh Mitra did not find any significant statistical difference in the incidence of cancer cervix among the Hindu and Muslim population.

Syamasundara Rao et. al. (1959) in his excellent study of the role of smegma has been able to establish the relationship of smegma accumulation over the prepuce of the male partners and cancer of the cervix in the female partner.

In our laboratory, Reddy and Baruah have studied the effect of human smegma on the cervix of mice

and came to the conclusion that carcinogenic potentiality of human smegma, if there is any, is of a very weak nature and is subjected to modification by genetic constitution of experimental animals. Cooray (1954) is of the opinion that cancer of the cervix and penis are the commonest sites for cancer in Ceylon and attributes it to acquired phimosis due to the use of a tight perineal binder and resultant ineffective cleanliness; this is also the practice among the poorer class in India.

No definite conclusions can be reached of its low incidence among the Muslim race in India unless a general population survey and population incidence is worked out, as has been done by Subodh Mitra.

*Marital Status and Parity.* It has been long recognised that carcinoma

child-bearing have been a feature in 90-95% of cases, and in our series 92.25% were parous. The factors such as child-birth trauma and infection of the cervix acting as chronic irritative lesions, are responsible for the high incidence of carcinoma in this part of the body. Certain workers believe in endocrinal factors being responsible for the causation of cancer cervix. Gagnon found cervical cancer a nonentity among Canadian nuns. Maliphant stresses the increased risk with each pregnancy when compared with controls of the same age groups having no children and having one child. Maliphant is of the opinion that with every pregnancy a married woman has double the risk than a married woman without children and runs 10 times the risk over an unmarried woman.

TABLE VIII

*Incidence of Parity compared with Other Authors*

Authors	Percentage of nullipara cases	Percentage of multipara cases	Not recorded
Cullen	2	98	
Clayton et al.	9	91	
Our series	4.34	92.25	3.41

of the cervix is less frequent in single and in nulliparous women than in parous women. In our series of 644 cancer cervix cases studied, 4.34% were nulliparous women, 92.25% were multiparous and in 3.41% parity was not recorded.

According to Maliphant (1949), 98.5% of the women are married and the risk of developing cancer as calculated against the total population in the age group increases till 55-59 years and then diminishes.

*Child-bearing.* Pregnancy and

TABLE IX  
*Details of Parity of 644 Cases*

Parity	Total No. of cases	Percentage of incidence
Nullipara .. ..	28	4.34
1st para .. ..	60	9.31
2nd para .. ..	98	15.21
3rd para .. ..	77	11.95
4th para .. ..	91	14.13
5th para .. ..	91	14.13
6th para .. ..	62	9.62
7th para .. ..	31	4.81
8th para .. ..	24	3.72
9th para .. ..	60	9.31
Not recorded ..	22	3.41

In our series 55.42% of the cases had 3-5 children; 71.6% of our cases fall into the age group of 31-50 years showing that the majority of the patients bearing 3-5 children are into this age group. We agree with Maliphant (1949) that pregnancy definitely increases the risk of developing cancer of the cervix.

*Socio-economic Status.* Amongst our patients all were of a low income group. Kennaway quotes from the Registrar General's statistical review (1936) where there is a higher incidence of cancer cervix among the working classes. At the same time the fertility rate is higher among these people and so cervical cancer is also commoner in this group when compared with the professional class.

*Symptoms*

The symptomatology as observed in 644 cases is recorded in Table 10, together with menstrual disturbances.

TABLE X

*Symptomatology of 644 Cases of Cancer Cervix pertaining to Menstrual History*

Symptoms	Total No. of cases	Percentage of incidence
Red and white discharge	579	89.90
Normal menstrual flow	306	47.51
Menorrhagia	285	41.14
Post-menopausal bleeding	177	27.50
Post-coital bleeding	55	8.54
Irrgular bleeding	45	6.83
Lactational amenhorrea	8	1.24
Continuous bleeding	8	1.24
Oligomenhorrea	5	0.77

As seen in Table 10, red and white discharge formed the most important symptom in 89.90% of cases. In 55

cases there was a history of post-coital bleeding; in 177 cases post-menopausal bleeding was present.

*Pathology*

The gross lesions as met by us varied from fungating ulcerating growth to diffuse infiltrating type. Most often the patients reported to the hospital very late and atypical cauliflower like growth was visualised. Microscopically two types of carcinoma — squamous-cell carcinoma and adenocarcinoma — were observed. In our series we found 98.44% were cases of squamous-cell carcinoma and 1.56% were of the adenocarcinomatous pattern.

In the squamous-cell pattern, buds and columns of the surface epithelium cells are seen penetrating into the stroma and invading the glands at times. In transverse section these columns appear like nests of cells. Stromal invasion with chronic inflammatory cells is invariably present. The cells show loss of stratification, increase of abnormal mitosis and may be highly differentiated or undifferentiated. Pleomorphism is marked with hyperchromatic cells and giant cells often of degenerative nature. Central degeneration of cancer cell nests produced a pseudo-glandular appearance which may be mistaken for adenocarcinoma. The cells may be highly differentiated or highly anaplastic. The proportion of the cells to the stroma may vary considerably.

*Adenocarcinoma.* Arises from the tall 'picket' cells of the cervical canal or cervical gland epithelium. The orderliness of the glands as well as

the lining epithelium is lost. The tall 'picket' cells become smaller and rounded and increase in layers from a few layers to sheets of undifferentiated cells. There may be an inflammatory stromal reaction. Rarely the highly differentiated cells may retain mucus producing properties and give rise to a mucoid pattern.

TABLE XI

*Various Types of Histological Patterns in Carcinoma of Cervix*

	Total No. of cases	Percentage
Total biopsies of carcinoma cervix	2408	
Squamous-cell carcinoma	1790	74.33
Keratinisation	124	5.15
Transitional cell	440	18.24
Anaplastic	14	0.58
Adenocarcinoma	40	1.66

Spread and metastases have been studied in 29 cases of our autopsy cases and are recorded in Table 12.

TABLE XII

*Autopsy Statistics, A.M.C. (1926-1961) showing Incidence of Spread and Metastases in 29 Cases of Cancer Cervix*

Viscera	Total No. of cases	Percentage
Bladder .. ..	17	58.62
Vagina .. ..	16	55.11
Parametrium ..	16	55.11
Body of uterus ..	10	37.48
Lymph nodes ..	10	37.48
Rectum .. ..	6	20.68
Ovary .. ..	3	10.34
Tube .. ..	1	3.44
Liver .. ..	3	10.34
Intestine .. ..	3	10.34
Lung .. ..	1	3.44

Direct spread by contiguity into the vagina, parametrium, pelvic walls

with ureteric obstruction is the commonest mode of spread (Fig. 2). An-

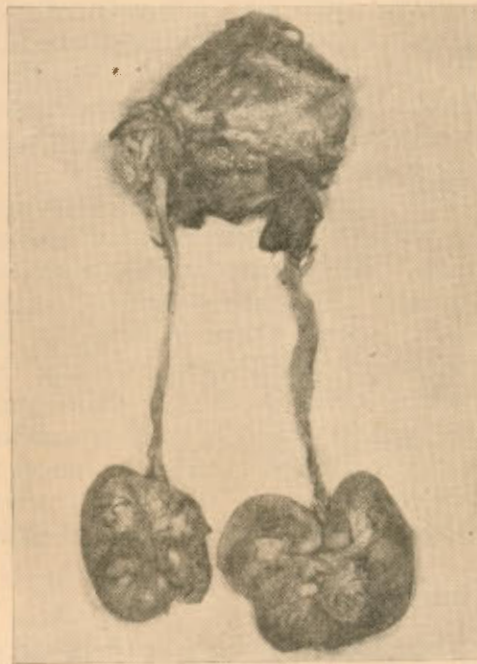


Fig. 2

Photograph of the female genital tract showing cervical growth, hydro-ureter and hydronephrosis, more marked on the right side.

terior and posterior spread to the bladder and rectum is common. Rarely, spread from the parametrium to ovary, tube or intestines may occur. We have observed direct method of spread to the bladder in 17 cases, vagina 16 cases, parametrium 16 cases, rectum 3 cases, ovary 3 cases and tube 1 case.

Lymphatic spread usually occurs into parametrial glands and from these glands the spread extends higher up along the para-aortic lymphatics to lumbar, regional and rarely thoracic and cervical glands, which has been observed in 6 of our cases (20.62%).



Metastases by blood stream were present in 25% of Willis cases. They can occur in the liver, lungs and rarely in the bones. We have encountered 3 cases of metastases in the liver, 3 cases of metastases in the large intestine (Fig. 3) and one in the lung.

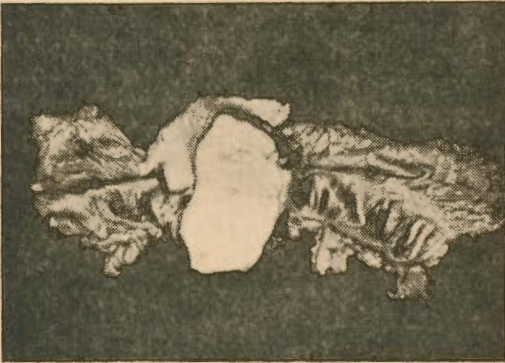


Fig. 3  
Photograph showing secondary nodule in the colon.

### Summary

1. A total of 3081 cases of carcinoma of the cervix have been studied and statistically analysed. Its incidence among malignancies in female is 69.41% in our biopsy series and 27.88% in our autopsy series.

2. Carcinoma of the cervix has the highest incidence and ranks first among all malignancies in females and in the female genital tract.

3. The average age incidence of 3081 cases of carcinoma of the cervix is as 38.47 years. Our oldest case was 75 years old.

4. Various etiological factors concerning marital status, age at marriage, at first coitus, parity, circumcision of the male partner, vulnerability of the cervix after delivery and racial incidence have been studied

and it has been inferred that no single factor is responsible for cancer cervix and together they may be significant.

5. The histological types of carcinoma of the cervix, as analysed by us in 2,408 biopsy cases revealed 74.33% squamous-cell carcinoma, 5.15% showed keratinisation, 18.24% were of the transitional cell type, 0.58% showed an anaplastic pattern 1.66% were adenocarcinoma.

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