

# CHORIOCARCINOMA—A STATISTICAL ANALYSIS OF 50 CASES

by

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## Introduction

An increased incidence of trophoblastic tumours is well documented in Asian countries. Reports from various centres in India show a higher incidence in this part of the continent (Das P. C. 1938; Bhasker Rao 1961; Daftery 1963; Reddy D. J. *et al* 1963; Paranjothy 1968; and Sreenivasa Rao 1969). The study of these tumours presents more peculiar problems than any other neoplastic process. Lot of literature on the various aspects of these tumours, especially in the field of chemotherapy of choriocarcinoma have been published in recent years. This paper is a statistical analysis of 50 cases of choriocarcinoma in S.A.T. Hospital, Trivandrum, over a period of 6 years from 1966 to 1971.

## Material and Methods

Total number of pregnant women admitted to the hospital, the number of deliveries conducted and the number of cases of choriocarcinoma occurring during a period of six years from 1966-1971 was taken to study the incidence. The total

number of abortions during the year were taken and related to the incidence of choriocarcinoma. Detailed study of 50 cases of choriocarcinoma seen during the period was made regarding their clinical history, obstetric history, age, parity management and follow-up. Various methods of treatment were compared and results analysed.

## Results

During the period under study medical care was provided for a total of 4,9730 pregnant women. The hospital recorded 35,071 deliveries, 5,698 abortions and 50 cases of choriocarcinoma, giving an incidence of 1 in 995 pregnancies and 1 in 710 deliveries.

Table I shows the age distribution of choriocarcinoma. The maximum age incidence was between 20-34 years, comprising 58 per cent of all cases.

Incidence of choriocarcinoma in relation to parity is seen in Table II. Choriocarcinoma is seen more in lower parity group, 70 per cent in the parity group of 4 or below.

The type of preceding pregnancy and time interval between the end of preceding pregnancy and occurrence of choriocarcinoma is seen in Table III. 54% of the cases followed hydatidiform mole evacuation, 24% followed abortion and 20% followed term pregnancy. Chorio-

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Received for publication on 5-4-1973.

TABLE I  
Incidence of Choriocarcinoma in Different Age Groups

No.	Age Groups	Total No.	Percentage
1	15-19	2	4
2	20-24	9	18
3	25-29	12	24
4	30-34	8	16
5	35-39	7	14
6	40-44	3	6
7	45-49	8	16
8	50-55	1	2

TABLE II  
Incidence of Choriocarcinoma in Relation and Parity

Parity	No. of Cases	Percentage	Parity	No. of Cases	Percentage
0	8	16	6	3	6
1	5	10	7	3	6
2	7	14	8	4	8
3	5	10	9	0	0
4	10	20	10	1	2
5	3	6	Above		
			10	1	2

TABLE III  
Type of Preceding Pregnancy and the Interval Between it and the Development of Choriocarcinoma

Time Interval	Preceding pregnancy				Percentage
	Vesicular Mole	Abortion	Normal Pregnancy	Ectopic	
1 month	12	3	-	1	Following a V. mole = 54%
1-2 months	9	3	1	-	
2-4 months	-	2	1	-	Following abortion } = 24%
5-6 "	1	2	-	-	
7-8 "	1	1	-	-	Following a normal pregnancy } = 20%
9-10 "	-	-	-	-	
11-12 "	-	-	-	-	Following Ectopic } = 2%
1-2 years	2	-	2	-	
2-4 years	2	1	1	-	
4 yrs. and above	-	-	5	-	



carinoma following hydatidiform mole manifests within 2 months time in majority of cases (21 out of 27) and within 6 months in those following abortion (10 out of 12). In cases of choriocarcinoma following term pregnancy 80% was seen occurring after two years of which one occurred after 13 years and another ten years after delivery. 2% of cases followed after an ectopic pregnancy.

Various complaints seen in these cases are summarised in Table IV. The

Table VI shows the site of metastasis seen in these cases. Lung was the commonest site of metastasis; others in the orders of frequency being, suburethral region, brain, bones, etc.

The treatment given to these cases were either chemotherapy alone, chemotherapy with hysterectomy or hysterectomy alone as shown in Table VII. The overall results are better with the combined treatment of chemotherapy and hysterectomy than with other methods

TABLE IV  
*Incidence of Various Complaints in Choriocarcinoma*

No.	Complaints	No. of cases	Percentage
1	Bleeding P/V following vesicular mole evacuation	23	46
2	Irregular bleeding P/V	10	20
3	Bleeding P/V following amenorrhoea	2	4
4	Bleeding P/V following abortion	5	10
5	Pain Abdomen	3	6
6	Chest Pain and cough	3	6
7	Haemoptysis	2	4
8	Haemoplegia	1	2
9	Retention of urine	1	2
10	Bleeding from suburethral nodule	4	8
11	Irregular fever	1	2

most common presenting feature was bleeding per vaginam after molar evacuation.

Table VIII. Patients without demonstrable metastasis gave better results

TABLE V  
*Size of Uterus in Choriocarcinoma*

Size of Uterus	No. of Cases	Percentage
Normal	5	10
Upto 8 weeks	19	38
9-12 weeks	10	20
13-16 weeks	5	10
17-20 weeks	3	6
21-24 weeks	4	8
Not known	4	8

Table V shows the size of the uterus in these cases. In 78% of cases the size of uterus varied from normal to 16 weeks.

TABLE VI  
*Metastatic Lesions in Choriocarcinoma*

Size of Metastasis	No. of cases	Percentage
Pulmonary secondaries	20	40
Suburethral nodule	12	24
Cervix	2	4
Parametrium	5	10
Pelvic bones	2	4
Spine	1	2
Tibia	1	2
Liver	4	8
Brain	4	8
Bladder	3	6
Skin	1	2
No secondaries	20	40

TABLE VII  
Methods of Treatment in Choriocarcinoma

Methods	No. of cases	Methotrexate alone		Combination Methotrexate and			Percentage
		Oral	Injection	Dactinomycin	Vinblastine	Irradiation	
Chemotherapy alone	13	6	5	1	1	—	26
Chemotherapy and hysterectomy	27	17	6	2	1	1	54
Hysterectomy alone	7						14
No treatment (expired before treatment gone home against medical advice, etc.)	3						6

TABLE VIII  
Results of Various Forms of Treatment in Choriocarcinoma

	Number of patients	Complete remission		Dead or Moribund	Unknown
		No.	Percentage		
<i>Chemotherapy alone</i>					
All patients	13	3	23		
Patients with clinically demonstrable metastasis	10	1	1	8	1
Patients without clinically demonstrable metastasis	3	2	66.6		1
<i>Chemotherapy and Hysterectomy</i>					
All patients	27	15	55.5		
Patients with clinically demonstrable metastasis	16	6	37.5	6	4
Patients without clinically demonstrable metastasis	11	9	82		2
<i>Hysterectomy alone</i>					
All patients	7	3	42.8		
Patients with clinically demonstrable metastasis	3			1	2
Patients without clinically demonstrable metastasis	4	3	75		1



than those with metastasis in all forms of treatment. Choriocarcinoma following hydatidiform mole responded in a better way than those following pregnancy Table IX.

*Ages* The average age in the present study was 31.5 years the youngest being 18 years and oldest 54 years. The highest incidence is seen between the age groups of 20-40 only 4% of cases were seen below

TABLE IX  
Results of Treatment According to Type of Preceding Pregnancy from which Choriocarcinoma Developed

Type of Preceding Pregnancy	Number of patients	Remission		Dead of moribund	Unknown
		Number	Percentage		
Hydatidiform mole	27	15	55.6	6	6
Abortion	10	3	31.5	4	3
Term pregnancy	9	3		5	1
Ectopic	1				1
All	47	21		15	11

#### Discussion

Incidence of choriocarcinoma varies in different part of the world. A higher incidence is seen in Asian countries. The present study shows an incidence of 1 in 995 pregnancies. The incidence in the present study is compared with other reported series in Table X. The higher

the age of 20 years. Novak and Seah (1954) found 10.8% in their series below the age of 20 years. In Paranjothy's series 18% were below the age of 20 and 64% between 20-30 years. The youngest patient with choriocarcinoma reported in literature was in a 14 year old (Paranjothy 1968). The joint project for the

TABLE X  
Incidence of Choriocarcinoma Reported by Various Authors

Author	Year	Country	Incidence
Acosta Sison	1939	Philippines	1: 1332 Pregnancies
Hertig	1950	U.S.A.	1: 4000 "
King	1956	Hongkong	1: 2708 "
Hasegava	1959	Japan	1: 271 "
Bhaskar Rao and Shetty	1961	Madras	1: 2958 "
Ping Yen Wei	1963	Taiwan	1: 483 "
Reddy D. J.	1963	Guntur	1: 648 "
Paranjothy	1968	Vellore	1: 645 "
Sreenivasa Rao	1969	Visakapatnam	1: 950 "
Kalyanikutty and Nalini	1970	Trivandrum	1: 826 "
Present Series	1972	Trivandrum	1: 995 "

incidence of choriocarcinoma seen in the present series agrees with the higher incidence in this country as well as others Asian countries.

study of choriocarcinoma and hydatidiform mole in Asia found the average age of Asian patients to be older than the age of patients from United States. There

is striking resemblance between their values and that found in the present study (Table XI).

mole has got a greater potentiality to produce chorionic malignancy. Park and Dees observed (1967) that a patient has

TABLE XI

*Comparative Analysis of the Age Group of Choriocarcinoma in U.S. Asia and Present Study*

Geographical Area	Average Age	Range of Age
U.S.	28	18-48
Asia	33	18-53
Present Series	31	18-54

*Parity:* Hector Marques (1963) found that 32.8% of his cases occurred in primiparas and 18.7% during second pregnancy. In Bhaskar Rao's series (1961) 25% were seen in primiparae and 33% were over the parity group 5. In the present study only 30% were seen above the 4th parity group. 70% were seen in lower parity group with only 16% in primiparae.

*Preceding pregnancy:* 54% of cases followed hydatidiform mole, 24% followed abortion 20% followed term pregnancy and 2% followed an ectopic gestation in the present series. Similar results were observed in most of the reports from Asian countries and from India (see Table XII). Undoubtedly hydatidiform

got 2000-4000 times higher chances of developing choriocarcinoma from hydatidiform mole than from normal pregnancy. Acosta Sison (1961) and Tow (1966) found that the incidence of choriocarcinoma after hydatidiform mole increased dramatically if the patient was over 40 years. They advocate prophylactic hysterectomy in hydatidiform mole in patients above the age of 40 years, especially if the patients is multiparous. However, our study showed that 70% of cases in which choriocarcinoma developed following hydatidiform mole, were seen in the age group below 40 years and in the lower parity group.

The interval between previous pregnancy and the development of tropho-

TABLE XII

*Type of Preceding Pregnancy Reported by Various Authors*

Author	Country	No. of cases	H. M. %	Abortion %	Term pregnancy %	Ectopic pregnancy %
Novak and Seah	U.S.	74	39.2	37.8	23	
Hertig	U.S.	—	50	25	22.5	2.5
Acosta Sison	Philippines	27	63	18	4	
Hasegawa	Japan	257	67.9	25.4	63	
HSU et al	Taiwan	22	81.2	9	4.5	4.5
Bhaskar Rao	Madras	27	40.75	40.75	18.5	
Narayana Rao	Kurnool	16	12.5	56.25	25	6.25
Wei and Ouyang	Taiwan	23	50	19.2	15.4	7
Paranjothi	Vellore	50	46	30	18	4
Present Study	Trivandrum	50	54	24	20	2



blastic growth is usually short. 58% of cases of choriocarcinoma followed within 2 months and 70% within 6 months of preceding pregnancy. One case had two molar pregnancies, the second being 3 years after the first. She developed choriocarcinoma 2 months after the second molar evacuation. In two cases choriocarcinoma developed 2 years after, and in one case 3 years after hydatidiform mole. This clearly indicates that the patient should be under strict observation as long as possible after a molar pregnancy. The interval between term pregnancy and development of choriocarcinoma is found to be comparatively long. 60 per cent of cases developed choriocarcinoma after a period 2-3 years. In one case the interval was 13 years and in another 10 years after the normal pregnancy. The former case was admitted for bleeding, per vaginam. The size of uterus was about 12 weeks. The clinical impression was fibroid uterus. Hysterectomy was done and the histopathology report was choriocarcinoma. The latter had a full term normal delivery 10 years back and presented with retention of urine, swelling of the external genitalia, fever, and cough with expectoration. X-Ray chest showed typical cannon ball shadows. The biopsy taken from the vaginal ulceration proved to be choriocarcinoma. The biological test was strongly positive. These two cases are typical examples of trophoblastic cells remaining dormant for many years and giving rise to malignancy.

#### *Signs and Symptoms*

The main complaints in cases of choriocarcinoma are irregular bleeding per vaginam following hydatidiform mole and bleeding per vaginam following amenorrhoea. Cases presenting with evidence

of secondaries and associated signs and symptoms of it were also seen in some cases. Depending on the site of secondaries choriocarcinoma can at times be mistaken for a medical or surgical emergency. 70 per cent of cases in this study showed metastases, the most common sites being lung followed by brain, liver and bones. Suburethral nodule was seen 24% of cases. One case developed haemorrhagic nodules in the skin over the right iliac crest and tip of right big toe during the terminal stage of the disease.

#### *Treatment*

Till recently, the treatment for choriocarcinoma was mainly surgical. Success of surgical management depends mainly on the presence or absence of metastases. The results are most satisfactory when the lesion is localised to the uterus. The five year survival varies 5% (Mathieu 1939) 28.5% (Sison 1939) and 27.5 per cent (Manahan 1964).

During the last decade marked success was attained in the treatment of choriocarcinoma due to the detected sensitivity of the tumour to chemotherapeutic substances like methotrexate 6-mercaptopurine nitrogen mustard, cyclophosphamide, chlorambucil, vincalucoblastine, and antibiotics like Aactinomycin-D, most authors agree that methotrexate gives the best result. It acts by combining with folic acid reductase and inhibits conversion of folic acid to folinic acid thus preventing nucleic acid synthesis.

In the present study the results of chemotherapy alone, in cases with demonstrable metastases, were found to be unsatisfactory, whereas chemotherapy combined with hysterectomy gave 37.5 per cent remission. In patients without demonstrable metastasis, chemotherapy



alone or combined with hysterectomy gave equally beneficial results, the latter appeared to be more encouraging with 82 per cent remission. Our results with chemotherapy alone were not encouraging when compared to the better response reported by various other workers. (Hertz *et al* 1959, Bhashawe 1963, Lamb *et al*, 1964. The failure in our series may be due to the institution of the treatment in the later stage of the disease. The duration of the disease prior to the starting of treatment appears to be the most vital factor in the ultimate response to chemotherapy. Hertz *et al*, (1961) found a complete remission in 85 per cent of 27 patients treated within 4 months of illness, compared with 61% of 23 patients treated after 4 months of illness.

Tow and Cheng (1968) found that selective hysterectomy combined with chemotherapy gave the best overall results in both metastatic and non metastatic tumours. In the present study an overall complete remission of 85.5% was seen with combined chemotherapy and hysterectomy.

Response to therapy was less favourable in patients who developed choriocarcinoma following pregnancy (31.5%) than in patients who developed the disease in association with hydatidiform mole (55.6). This has been the findings in Brewers series (1964) also.

The maximum total dose of methotrexate given in the present study was 700 mgms. This is low when compared to the dosage given by other workers. We found that our patients did not tolerate a high dose.

#### Summary and Conclusions

A statistical analysis of 50 cases of choriocarcinoma seen among 322 tropho-

blastic tumours during a period of six years from 1966 to 1971 in S.A.T. Hospital, Trivandrum, is presented.

The incidence of choriocarcinoma was found to be 1 in 995 pregnancies and 1 in 700 deliveries.

The average age was found to be 31.5 years with a range between 18-50 years. The highest incidence is seen between 20-40 years.

70 per cent of cases were seen below the 4th parity group, only 16 per cent being in the primis.

Hydatidiform mole was the most common type of preceding pregnancy.

The interval between development of choriocarcinoma and the preceding pregnancy was short in cases of hydatidiform mole and longer in term pregnancy.

Combination of chemotherapy and surgery gave an overall good result when compared to other methods of treatment in choriocarcinoma with or without metastasis.

The response to chemotherapy was higher in cases of choriocarcinoma developing from hydatidiform mole than from pregnancy.

#### References

1. Acosta Sison, H.: Am. J. Obst. & Gynec. 58: 125, 1939.
2. Acosta Sison, H.: Am. J. Obst. & Gynec. 81: 715, 1961.
3. Bagshawe, K. D.: Brit. Med. J. 1303, 1963.
4. Bhaskar Rao, K.: J. Obst. & Gynec. India, 12: 141, 1961.
5. Bhaskar Rao, K. and Shetty, B. M. V.: J. Obst. & Gynec. India, 12: 75, 1961.
6. Brewer, J. I., Gerbie, A. B., Dolkart, R. E., Skom, J. H., Nagle, R. G. and Torok, E. E.: Am. J. Obst. & Gynec. 90: 566, 1964.
7. Daftary, S. N.: J. Obst. & Gynec. India, 12: 8, 1963.
8. Das, P. C.: J. Obst. & Gynec. Brit. Emp. 45: 265, 1938.



9. Hasegawa, T.: Quoted by Wei and Ouyang.
10. Hertig, A. T.: Progress in Gynecology by Meigs, J. V., Sturgis, S. H., Vol. 2, New York, 1950, Grune & Straton Inc. Page 372.
11. Hertz, R., Bergenstal, M., Lipsett, M. B., Price, E. B. and Hilbish, T. F.: Ann. N.Y. Acad. Sci. 80: 262, 1959.
12. Hertz, R., Lewis, J. and Lipsett, M. B.: Am. J. Obst. & Gynec. 82: 631, 1961.
13. Hsu, C. T., Chen, T. Y., Chiu, W. H., Yang, C. C., Lai, C. H., Chan Cheng, C. H., Tung, P. H. and Chen, C. C.: Am. J. Obst. & Gynec. 90: 308, 1964.
14. Kalyanikutty, P. and Nalini, V. I.: J. Obst. & Gynec. India, 20: 480, 1970.
15. King, G.: Am. J. Obst. & Gynec. 65: 856, 1956.
16. Lamb, E. J., Morton, D. G. and Byron, R. C.: Am. J. Obst. & Gynec. 90: 317, 1964.
17. Manahan, C. P., Benitez, I. and Estrella, F.: Am. J. Obst. & Gynec. 82: 641, 1961.
18. Marquez-Monter, H., Alfaro, G., Robles, M. and Bolio-Cicerio, A.: Am. J. Obst. & Gynec. 85: 856, 1963.
19. Mathieu, A.: International Abstracts. Surg. 68: 52, 1939.
20. Narayana Rao, A. V.: J. Obst. & Gynec. India, 16: 685, 1966.
21. Novak, E. and Seah, C. S.: Am. J. Obst. & Gynec. 67: 933, 1954.
22. Park, W. W. and Lees, J. C.: Arch. Path. 49, 75, 208.
23. Paranjothy, D.: J. Obst. & Gynec. India, 18: 967, 1968.
24. Reddy, D. J. et al: Quoted by Sarojini and Reddy.
25. Sarojini, P. and Reddy, D. J.: J. Obst. & Gynec. India, 12: 382, 1963.
26. Sreenivasa Rao, K. and Ray, B.: J. Obst. & Gynec. India, 19: 353, 1969.
27. Tow, W. S. H. and Cheng, W. C.: Vol. of papers and Absts, Ed. Sc. Sub. Committee, 1968, P. 78.
28. Tow, W. S. H.: J. Obst. & Gynec. Brit. Cwlth. 773: 1000, 1966.
29. Wei, P. Y. and Ouyang, P. C.: Am. J. Obst. & Gynec. 85: 844, 1963.