STUDY OF PROBABLE PRECIPITATING FACTORS OF TROPHOBLASTIC NEOPLASIA

by

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Introduction

Exact etiological factor of trophoblastic tumors is not definitely known even at present. There are some precipitating factors which may act for the variation in the incidences of this disease in different countries and different parts of the same country. They have been throughly scrutinized in the present paper under six different heads as (1) age (2) parity (3) seasonal variation (4) socio-economic status, (5) religion, (6) blood group.

Material and Methods

The material of the present study have been collected from Eden Hospital, Medical College and Hospitals, Calcutta from January 1976 to June 1980. During this four and a half years period total 138 trophoblastic tumor cases have been treated in the institution. The trophoblastic tumors have been classified and described under five different heads as (1) hydatidiform Mole-benign, (2) metastatic mole, (3) invasive or perforating mole, (4) choriocarcinoma, (5) undetermined group.

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Relationship with Age

Reports of different workers varies widely while describing the relation of age to the trophoblastic tumours. Thus William (1969) remarked that age has an important bearing on the incidence of H. mole as indicated by the relatively high frequency among pregnancies at the very beginning and particularly towards the end of the childbearing period. Similarly Ratnam (1975) from Singapore reported that the incidence of H. mole is higher in teenagers and patients above 40 years. While Keir is of opinion (1977) that it may occur at any time of reproductive age, although it is a little more common in older women.

Table I shows the age-wise distribution of the cases in the present series. Here it has been noted that out of 102 benign H.mole cases, 95 (93%) occurred where the age was 30 or less. Of the total cases, 117 (84%) occurred within 21 and 30 (16%) cases were above 30 years of age. Edmonds (1959) reported that moles occurred more frequently than expected in women under the age of 20. Figures from the material of the Albert Mathieu Registry reveal that with benign moles, 15.7% were under 20 years. While Saxena (1971) from India reported that 80% cases of vesicular mole were below the age of 30, which closely agreed with the present findings.

TABLE I
Age-Wise Distribution

	20 or less	21-25	26-30	31-35	36-40	41 and over	Total
Benign H. Mole	28	36	31	5	2	—	102
Metastatic H. Mole	—	2	—	—	2	—	4
Invasive Mole	1	2	2	—	1	3	9
Choriocarcinoma	—	3	5	2	—	4	14
Undetermined	4	1	2	2	—	—	9
	33 (24%)	44 (31.9%)	40 (28.9%)	9 (6.5%)	5 (3.6%)	7 (5.9%)	138
		117 (84%)			21 (16%)		

Mole has been reported in a 12 years old girl and in a 53 years old woman (Novak and Woodruff). In the present paper the minimum age of vesicular mole was in a 12 years old girl and maximum age was 49 years.

The age of choriocarcinoma may be any in the reproductive period or early post reproductive but there is a greater incidence in relation to pregnancies in older age group. It follows that the women most at risk are the elderly primi, who have a chance of getting chorionic carcinoma 15 times higher than average (Scott, 1964). The joint project of study of trophoblastic tumours reported the relationship of these to malnutrition, parity and old age (Acosta Sison, 1959; King, 1956; Hasagawa, 1959). In the present series, it has been also noted that when the age is above 30, incidence of malignancy is very high. Thus there were total 117 cases in below 30 years and 21 cases were above 30. Of these, when the age was above 30, (14%) were malignant and (7%) were benign, whereas when the age was below 30, only 22 cases were malignant and 95 were benign. Thus after 30 all cases of trophoblastic tumours should be taken as potentially malignant.

Radha *et al* (1974) reported that average age of choriocarcinoma in their series was 31.5 years. Novak and Seah (1954) found 10.8% in their series below the age of 20. In Paranjothy's (1970) series, 18% were below 20. The youngest patient with choriocarcinoma reported in the literature was 14 years old (Paranjothy, 1970). On the other side, cases have been reported where choriocarcinoma occurred in women beyond the climacteric, the oldest being 79 years of age (Kair, 1977). In the present series, 36 of malignant tumours occurred when the age was 25 or less. The minimum age of choricarcinoma in the present series was 20 and maximum was 49. No cases were found in post menopausal period.

Relationship with Parity

orr (1977) is of opinion that parity does not appear to have an important influence and in 15-20 per cent cases of H. Mole the patients are primigravidas. Similarly, Hector Marques (1963) found that 32.8 per cent of his cases occurred in primipara and 18.7% during second pregnancy, whereas Bhaskar Rao (1971) found the incidence of H. Mole to be high in the parity group of 5 or more. In a series of 232 cases of H. Mole, Kalyanikutty and Nalini (1970) reported that 25% were primi and 33% were in the parity group of 5 or above. In the present

series of 138 cases, 25% occurred during first pregnancy, 56% between P_1 to P_3 and in 19 per cent the parity was 4 or above. Of 102 benign H. Mole, 29 per cent occurred during first pregnancy and in only 13% the parity was 4 or more. Table II shows the parity distribution.

TABLE II
Parity Distribution

	P_0	P_1-P_3	P_4-P_6	P_7 or more	Total
Benign H. Mole	30	60	10	2	102
Invasive Mole	1	3	4	1	9
Metastatic H. Mole	1	3	—	—	4
Choriocarcinoma	—	5	5	4	14
Undetermined	2	6	1	—	9
	34 (25%)	77 (56%)	20 (14%)	7 (5%)	138

Radha (1974) from India reported that 30% of choriocarcinoma were seen above the 4th para group, 70% were seen in lower parity and only 16% in primi. In the present series, no case of choriocarcinoma was found in primi and 41% of malignant trophoblastic tumour cases occurred in P_1 or more.

Seasonal Variation in Trophoblastic Disease

Ratnam and Cheu (1975) from Singapore reported an increased incidence of trophoblastic tumor cases in May and September. But this increase is however not statistically significant and attempts to correlate it with temperature and rainfall were abortive.

In the present series, during the four and a half years period it has been noted that there was no seasonal variation.

Table III shows month-wise distribution of cases in different years

TABLE III
Month-wise Distribuution of Cases in Different Years

	1976	1977	1978	1979	1980
January	3	—	3	3	1
February	4	1	1	2	3
March	5	2	1	2	1
April	7	3	2	5	3
May	4	1	2	1	1
June	3	7	2	4	—
July	6	2	2	2	—
August	4	3	2	2	—
September	3	2	3	2	—
October	1	—	3	3	—
November	3	2	6	1	—
December	1	1	2	4	—
Total:	44	24	30	31	9 (upto June)

Relation with Socio-Economic Status

Acosta Sison (1959) reported that the high incidence of trophoblastic tumour among the oriental people was mainly due to malnutrition. Chun *et al* (1964), Teoh *et al* (1971) Ratnam (1975) also are of opinion that various international studies have shown that poor countries are affected more than affluent ones. But on the other hand, Srinivas Rao and Ray (1969) mentioned that the incidence is very high in Japan, 1 in 232 pregnancies, where every one is well fed, clean and per capita income is fairly high, whereas the incidence is so low in Brazil i.e. 1:1071 where malnutrition is rampant, thus doubting the etiology to be based on malnutrition. Again McCorriston (1968) from Honolulu found that despite good nutrition amongst orientals hydatiditorm mole was commoner in this racial group than among caucaseans. Hawaieans, however, though having a lower socio-economic and dietary standard had a lower incidence of trophoblastic disease.

Though it is difficult to have an exact idea about the socioeconomic status of the patients, in the present series a gross idea has been made after taking into consideration the income per month of the family. The patients have been grouped into three categories high, medium and low according to the amount of income more than 800 per month (high), between 500 to 800 per month (medium) and less than 500 (low) per month. Basing on these factors, it has been noted that the incidences of hospital patients in high, medium and low group are 14%, 44% and 32% respectively, whereas the incidence among highly affluent are 51%, 44% and 5% respectively. Thus it can not be commented from these figures that the poor people are more affected than the affluent one or in other word there is definite doubt about the question of malnutrition and incidence of tropho tumour. Table IV shows incidence according to Socio-economic status. Again Tow (1966) has remarked that it is not high carbohydrate but actual deficiency of protein which is responsible for the high incidence in Philippines, South East Asia and India etc. In the present series out of total 133 cases, in 98 cases estimation of serum protein, albumin and globin has been performed. These reports show no definite indication of hypoproteneemia among these cases. Table V shows the amount of total protein in various cases.

Table IV shows incidence according to to Socio-economic status

TABLE IV

Incidence According to Socio-economic Status

	High.	Med.	Low	Total
Benign H. Mole	46	52	4	102
Metastatic H. Mole	3	1	—	4
Invasive	7	2	—	9
Chorio carcinoma	9	4	1	14
Undetermined	6	1	2	9
	71 (51%)	60 (44%)	7 (5%)	138

High means — where the family income is more than Rs. 800 per month.
Medium — where the family income is more than Rs. 500 to 800 per month.
Low — where the family income is less than Rs. 500 per month.
Hospital patients 14% 44% 32%.

Table V shows tht amount of total protein

TABLE V

The Amount of Total Protein

Serum Total protein — in 98 cases

	5.1—6 gm.%	6.1—7 gm.%
Tropho-blastic tumour	62 cases (64.5%)	36 cases (35.5%)

Trophoblastic Tumours and Ethnic Group—Racial Influence

Fox and Tow (1966) find definite difference between ethnic groups. Ratnam (1975) from Singapore mentioned that in their previous publication there was a slightly increased incidence of molar pregnancy in Indians as opposed to Chinese and Malays in Singapore. However, the expanded series in 1975 has shown no difference. Kalyanikutty and Nalini (1970) reported that the relative percentage of different communities seeking admission to the S.H.T. hospital are Hindus 82%, Christians 10%, and Muslims 8%. Taking this into account there is no significant predilection for H. Mole to any particular community. But the incidence of malignant tumours is highly significant among the Christians.

In the present series, the hospital patients, though all of them are Indians, they belong to different religions. Thus among the hospital patients 91.6% are Hindus, 7.8 per cent are Muslims and .6 per cent belong to other religions e.g. Christianity, Buddhism etc., whereas among the trophoblastic tumour cases 81% are Hindus, 15.2% Muslims and 3.6% belonged to other group. So it is apparent that the incidence of Muslims is more among trophoblastic tumour cases. Table VI shows the incidence in different religious groups.

Iliya *et al* (1967) stressed about consanguinity as an important etiological factor. They are of opinion that in parts of the oriental countries where choriocarcinoma is prevalent, consanguinous marriages are also most common. In our country also consanguinous marriage is more common among the Muslims. Whether the factor is responsible causing more cases of molar pregnancy among the Muslims is yet to be proved. More expanded series of cases having studied more thoroughly might help to find out this factor.

Table VI shows the incidence of trophoblastic tumour cases among different religious groups.

Relationship of Trophoblastic Disease with Blood Groups

Llewellyn Jones (1967) has reported a shift from 0 towards AB in maternal blood

TABLE VI

Incidence of Trophoblastic Tumour Cases Among Different Religious Groups

	Hindus	Muslims	Others
Benign H. Mole	80	18	4
Metastatic H. Mole	4	—	—
Invasive Mole	8	1	—
Chorio carcinoma	12	2	—
Undetermined	7	1	—
Total:	111 (81%)	22 (15.2%)	5 (3.6%)
Hospital patient's incidence	91.6%	7.8%	.6%

groups among trophoblastic tumour cases. Dawood *et al* (1971) from Singapore reported an increased incidence in group A women and a decrease in group B. Similarly Radha *et al* (1974) reported blood group in 120 cases of H. Mole showed no significant variation in the pattern in blood group distribution of H. Mole patients from the control group.

In the present series, it has been noted that more trophoblastic tumours occur in group A mothers or in other words there is an increase number of group A patient and decreas in group B. Table VII shows the incidences of different blood groups in trophoblastic tumour cases and usual antenatal cases. Among the antenatal patients maximum number belong to Group B (37.5%) while among the trophoblastic tumour cases maximum number (49.2%) belong to group A and lesser number (26.8%) in Group B.

Scott (1964) in a survey of the Albert Mathew Chorionepithelioma registry records found that the blood group of 116 cases of chorionepithelioma showed a shift from 0 to A, B, AB. This may be related to a possible lack of maternal antibody response. Dawood *et al* (1971) while analysing 81 cases found that blood group A was significantly higher in patients with choriocarcinoma. According to them this increased predilection of group A to choriocarcinoma may be related to some factor, perhaps an enzyme where genetic locus is associated with gene for blood group A.

In the present series among the malignant trophoblastic tumour cases (metastatic moles, invasive mole, choriocarcinoma and undetermined group), out of 36 cases in 26 cases (72%) the blood group was A, whereas out of 102 benign moles in 42 cases i.e. 41% cases only the group was A (Table VIII).

Bagshawe *et al* (1971) has drawn attention to the excess incidence of blood group A women married to group 0 men in their series. This excess risk of group A mothers has been shown as being 2.4 with 0 husband as opposed too 0.4 with a group A husband.

In the present series, the blood group of the husband has been collected only in 25

TABLE VII

Distribution of Blood Groups in Trophoblastic Tumour Cases and Antenatal Cases

	Group A.	Group B.	Group O.	Group AB.
Tropho. tumour	68 (49.2%)	37 (26.8%)	24 (17.5%)	9 (6.5%)
Ante natal cases	31%	37.5%	25.5%	6%

TABLE VIII

Distribution of Different Groups Among Malignant Trophoblastic Tumor Cases

Malignant trophoblastic tumour cases	Gr. A.	Gr. B.	Gr. O.	Gr. AB.
Metastatic Mole	3	—	1	—
Invasive Mole	6	2	1	—
Chorio carcinoma	10	1	3	—
Undetermined	7	1	—	1
	26 (72%)	4 (11%)	5 (13.8%)	1 (2.7%)

cases. This number is too small and no comment can be made at this moment regarding that factor.

Summary and Conclusions

Total 138 trophoblastic tumour cases have been studied. 93% of H. Mole occurs where the age in 30 years or less. But invasive mole is common among elderly patients and there is a greater incidence of choricarcinoma in elderly patients. Minimum age of H. Mole found was 12 years and choriocarcinoma 20 years. Maximum age of both of H. Mole and choriocarcinoma was 49 years. 29% of H. Mole cases occur during first pregnancy and in 13% cases only the parity is 4 or more. But 41% of malignant trophoblastic tumours occurs in P_4 or more.

There is no seasonal variation in the incidence of trophoblastic tumours. No relation of the disease with malnutrition has been detected and no definite sign of hypoproteinaemia has been detected in these cases. The incidence of Muslims is more among trophoblastic tumour cases, whether consanguinous marriage among Muslims are responsible for this is yet to be proved. An increased incidence of trophoblastic tumour cases (49.2%) has been detected among Group A women. Among the malignant trophoblastic tumour cases in 72% cases the blood Group is A whereas in the benign H. Mole in 41% only it is Group A.

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