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Original Research Article

The frequency of hydatidiform mole in a tertiary care hospital from central India

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ABSTRACT

Introduction: The gestational trophoblastic disease (GTD) is a group of pregnancy related tumours encompassing complete and partial mole, invasive moles, choriocarcinomas and placental site trophoblastic tumours. Amongst all GTD, hydatidiform moles are the most common form. Hydatidiform mole is a relatively common gynecological condition which could presents like spontaneous abortion, one of the most common gynecological emergencies.

Materials and Methods: Present study is a retrospective analysis to determine incidence of hydatidiform mole for eight years duration.All women who were diagnosed of molar pregnancy by estimation of beta hCG and histopathological examination during1st Jan 2010 to 31st Dec 2017 were enrolled in this study. During the study period, there were 84 cases of Molar pregnancy out of 33856 total deliveries.

Results: The total number of deliveries reported in the study period was 33856 out of which 84 cases were of gestational trophoblastic disease (GTD). The prevalence of GTD in this tertiary care hospital was 2.48 per 1000 deliveries. During the study period, we had received 55 samples of products of conception and 3079 hysterectomy specimens. Out of 3134 cases, 84 cases were diagnosed as GTD. Out of these 84 cases 81cases were hydatidiform mole. There were two cases of choriocarcinomas and one case of placental site trophoblastic tumour.

Conclusion: The prevalence of hydatidiform mole was higher among all entities of gestational trophoblastic disease. The serum beta hCG levels are very sensitive and specific for diagnosis. Histopathological examination is helpful for confirming diagnosis.

1. Introduction

The gestational trophoblastic disease (GTD) is a cluster of pregnancy related tumours which includes complete and partial mole, invasive moles, choriocarcinomas and placental site trophoblastic tumours. Amongst all GTD, hydatidiform moles are the most common form. Hippocrates was the first to describe the formation of moles. He stated that the consumption of dirty water which originated from the marshes, by the pregnant women led to the formation of these moles.[1]

Hydatidiform mole is one of the most common gynecological emergencies which could present like spontaneous abortion and is a relatively common gynecological condition. The risk factors of persistent trophoblastic disease include extreme reproductive age, multiparity, an earlier molar pregnancy, prior miscarriages, ABO blood group, smoking and alcohol consumption, diet deficient in animal fat and carotene.[2,3]

A homozygous nonsense mutation in the NLRP7 gene (c.584G A; p.W195X) in a patient that appears to be linked with recurrent hydatidiform was recently identified by Japanese investigators.[4]

There is wide disparity in the incidence reported worldwide and it is attributed to various genetic, demographic, environmental and host related factors.[5] The incidence rate is highest in Indonesia (1 per 77 pregnancies and 1 per 57 deliveries)[6,7] In India and middle east incidence is believed to be one per 160 pregnancies.[8]

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In developed countries incidence of complete Hydatidiform mole (CHM) is of approximately 1-3 per 1000 pregnancies and those of the partial Hydatidiform mole (PHM) is about 3 per 1000 pregnancies.[9]

Reduction in number of these cases were noted which may be due to advancement in early monitoring and better availability of food.[10]

These moles are generally sporadic in occurrence with exception of rare cases known as singleton case (when the single family member has recurrent HM). Familial recurrent HMs is considered when at least 2 women have one or several HMs. It has a genetic origin with mutation in NLRP7 and rarely KHDC3 genes which corresponds to an autosomal recessive disease.[11,12]

There is 1-2 percent chance of complete or partial mole in second pregnancy after first being molar one.

The risk of third molar pregnancy increases by 15-30 percent which is not decreased by change in partner and may be linked to familial and sporadic bi-parental molar disease.[9,13] Higher frequency of molar pregnancy are seen in upper and lower extremes of maternal age, that is younger than 13-18 years or older than 45-50 years. The ratio of complete to partial mole changes significantly with age. It is 55 to 93 percent for age 41-50 years and 63 percent for those aged between 13-18 years respectively.[14]

As there is lack of clear and precise definition of this disease, over reporting of pregnancies with gestational trophoblastic disease and different denominators were used in different published series. Hence, incidence of hydatidiform mole varies greatly around the world.[15]

There are two different forms of molar pregnancy, partial and complete, which differ in appearance and etiology. Complete mole shows cystic dilatation of all villi with absence of embryonic development. It is always due to absence of maternal chromosome and has exclusively paternal origin of genetic material.

In partial mole there is genetic defect of triploidy with embryonic development being observed along with normal to abnormal cystic villi.

The most sensitive and specific marker for the diagnosis of trophoblastic-related conditions like GTD is serum beta hCG. It is vital for early detection of post molar persistent gestational trophoblastic disease.

The occurence of hydatidiform mole is not much in local population from this part of country. But literature is very limited as far as study of frequency of hydatidiform mole is concerned in Indian population. Considering the varied incidence rates reported from Asian countries, there is a need to determine the incidence rate of in central Indian population.

2. Material and Methods

Present study is a retrospective analysis to determine the incidence of hydatidiform mole over a period of eight years. All women who were diagnosed of molar pregnancy by estimation of beta hCG and histopathological examination during 1st Jan 2010 to 31st Dec 2017 were enrolled in this study.

During the study period, there were 84 cases of Molar pregnancy out of 33856 total deliveries reported.

The data for total deliveries conducted in the hospital was retrieved from the hospital information system and all information collected was kept confidential. The details of maternal characteristics noted for each case were maternal age, parity and period of gestation at the time of presentation, clinical presentation, and diagnostic tools. The detail s regarding past obstetric history such as previous history of molar pregnancy was also noted.

Incidence rate was calculated by the number of cases of molar pregnancies reported to the institution for treatment during the study period for every 1000 pregnancies delivered during the same period.

This study was approved by Institutional Ethical Committee.

All statistical analyses was performed using SPSS version 16.0.

3. Results

The total number of deliveries reported in the study period was 33856 out of which 84 cases were of gestational trophoblastic disease (GTD). The prevalence of GTD in this tertiary care hospital was 2.48 per 1000 deliveries.

During the study period, we had received 55 samples of products of conception and 3079 hysterectomy specimens. Out of 3134 cases, 84 cases were diagnosed as GTD. Out of these 84 cases 81cases were hydatidiform mole. There were two cases of choriocarcinomas and one case of placental site trophoblastic tumour.

Age and gestation al age wise distribution has been mentioned in table number 1 and 3 respectively. (Tables 1, 2 and 3)

In our study, parity one and above were 48(57.14%) cases. Majority of the cases belonged to B (33.33%) blood group followed by A (32.14%), O (25%) and AB (9.5%) blood group respectively (Table 2) Bleeding per vagina in second trimester was the most common clinical presentation. (Table 4)

4. Discussion

The complete hydatidiform mole is mainly diploid in nature with two usual sets of paternal chromosomes. In around 80.0-90.0% of cases, it is the consequence of fertilization of an empty egg with a sperm which then gets reduplicated in the homozygous diploid genome. In such cases, as 46,

Table 1: Different types of GTD according to age

Age	HD CM	PM	Invasive	CC	PSTT	Total
<20	2	0	0	0	0	2
21-25	12	2	0	0	0	14
26-30	28	7	1	0	0	36
31-35	20	4	2	1	0	27
>35	0	2	1	1	1	5

CM: Complete mole, PM: Partial mole, CC: Choriocarcinomas, PSTT: Placental site trophoblastic tumor

Table 2: Different types of blood group with various GTD type

Diagnosis	Blood group A		AB+	AB Neg	O +	O Neg
CM	22	22	5	1	10	2
PM	3	5	0	0	6	1
IM	1	0	0	0	2	0
PSTT	1	0	0	0	0	0
CC	0	1	1	1	0	0
Total	27	28	8		21	

Table 3: Distribution of GTD according to trimester of pregnancy

Trimester	HD CM	PM	Invasive	CC	PSTT	Total
I	25	7	0	0	0	32
II	27	8	1	0	0	46
III	0	0	0	0	0	0
Total	0	0	0	0	0	0
Post Gestation	0	0	3	2	1	6

Table 4: Different clinical presentation of GTD

Clinical features	HD CM	PM	Invasive	CC	PSTT	Total
Bleeding PV	58	12	4	2	1	77
Amenorrhea	56	14	1	0	0	71
Abdominal Pain	22	7	4	2	1	36
Vomiting	6	2	0	0	0	8
Fever	4	1	0	0	0	5
Clots	2	1	0	0	0	3

YY is non-viable therefore the karyotype is always 46, XX. But rarely the karyotype can be 46, XY or 46, XX when the complete mole results as a result of dispermic fertilization (diandricdiploidy) of an empty egg.

However, there are rare cases of tetraploid or biparental diploid complete moles and this is to be considered while evaluating products of conception, as the diagnosis of complete mole should not be excluded based on molecular analysis alone.[16–19]

Accurate diagnosis and classification of molar pregnancy becomes very crucial as the risk of gestational trophoblastic disease including choriocarcinomas is significantly high. The CHM and PHM show 10-30% and 0.5- 5 % risk of choriocarcinomas respectively.[20]

Pathological analysis of the product of conception is considered as the "gold standard" in the diagnosis of molar pregnancies.[21]

There is a clearly defined histopathological criterion for diagnosis of partial and complete mole but they are not always evident in histological slides, especially in case of early molar pregnancy.

There are numerous studies showing significant intra-observer and inter-observer variability, even among experienced pathologists, on the issue of final diagnostic decision which is based on tissue slide examination for both partial and complete molar pregnancies.[22]

As persistence of trophoblastic disease can occur in 15-25% of complete mole, it becomes important not to miss a

case of complete mole.[23]

Majority of GTD in our study were of hydatidiform mole comprising 96.42%. Similar results were reported in many studies.[24,25] Complete mole is most common entity, comprising 73.80% while partial mole was second most common entity with 17.85% cases. These results were in concordance with other studies.[24,26]

During the study period, 84 cases of uterine GTD were observed. The incidence of GTD in present study was 2.48 /1000 which is lower than those reported by other studies done by Jagtap et al[27] showing incidence as 4/1000, Agrawal N et al,[28] and Koiral A et al[29] showing incidence as 4.17/1000 and 3.94/1000 respectively.

Genetic, environmental and host related factors have attributed to a wide variation in incidence reported worldwide. There is 50 % risk of persistent disease with uterine size 4 weeks larger than the date with presence of theca lutein cyst with size more than 6 cm.[30] According to some studies, higher incidence of molar pregnancy is seen in maternal age below 20 years while others reported it to be over 35 years.[31–33]

As 80% of hydatidiform moles are self-limiting and non-invasive, there are around 7-17% cases that show transformation into invasive mole and rarely into choriocarcinomas in 2-5% of cases.[34,35]

The present study revealed cases of GTD ranged between 19 to 39 years with majority in age group of 26-30 years of age group.(36; 42.85%), followed by 31-35 years (27; 32.14%) and 21-25 years(14; 16.66%) respectively.

This differs from the study of Kumar N et al which reported majority of patients in age group of 20-25 years comprising 66% cases.[36]The mean age of presentation in our study was 29 years among all the cases, which showed concordance with study conducted by Agrawal N et al and Mayun AA who noted mean age of 23.9 and 25.7 years respectively.[28,37]

There were 25(29.76%) cases out of 84 cases in primigravida, 35 cases of second gravida and 12 cases of third gravida. Present study showed that prevalence was more common in second trimester as followed by first and third trimester. Most of the studies showed that prevalence was more common in first trimester.[24,38]

WHO prognostic scoring system for GTD included ABO blood group as one of its prognostic factors. If female and male partners are with either blood group O or A, A or O; it carries better prognosis when compared with female having blood group B or AB.[39] Present study showed high incidence of GTD in patients with blood group 'B' followed by blood group 'A' and blood group 'O'. Amongst them 79 (94.04%) were Rh positive. A study done by Parazzini F et al., found that ABO blood groups were linked with higher risk of GTD. Compared to women with blood group O or B, women with blood group A and AB had high relative risk of benign mole.[40] Lurain et al stated that GTD was more prevalent with blood group A which contradicts with our study.[3]

The most sensitive and specific for diagnosis of the trophoblast-related conditions, i.e., pregnancy and the GTD is serum beta hCG. It is of utmost importance to measure beta hCG level on regular basis in women diagnosed with complete and/or partial mole. An escalating level of total beta hCG is diagnostic of invasive disease and choriocarcinomas. It also helps to decide treatment response and recurrence of tumour. Most of the GTD cases showed beta hCG levels between 50,000- 1, 00,000mIU/ml.

In the present study the most frequent presentation was bleeding per vagin a in 77 (91.66%) cases, followed by amenorrhea in 71 (84.52%) cases. Our results are in agreement with many other studies, like Taboo ZA, Fatima et al.[26,24]

P lacental site trophoblastic tumour (PSTTs) are very rare tumours. They represent a rare form of GTD. Out of the 84 GTD cases in our study ; we noted one case (1.20%) of PSTTs and two cases (2.40%) of choriocarcinomas.

5. Limitations

One of the limitations of this study is that the incidence of subsequent pregnancies after complete treatment of molar pregnancies was not studied. The cytogenetic and molecular diagnosis in gestational disorders could not be performed in our study due to the cost of investigations and most of the cases were retrospective.

6. Conclusion

Among all entities of gestational trophoblastic disease, the prevalence of hydatidiform mole was higher. Complete hydatidiform mole was the most common type in this study. The serum beta hCG levels are very sensitive and specific for diagnosis. Histopathological examination is valuable for confirming diagnosis. Follow up of such patients is crucial for early detection of malignant trophoblastic tumours and also to minimize the mortality rate. Because of rarity of this condition multi-centric studies are required in India to determine the true incidence and overall outcome of gestational trophoblastic diseases. This will help to comprehend the burden of this disease and to devise treatment strategy to get optimal outcome.

7. Source of funding

None.

8. Conflict of interest

None

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