Original Article

Gestational Trophoblastic Diseases. An Overview of Patients visiting Sheikh Zayed Medical Hospital, Rahim Yar Khan

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ABSTRACT

Background: gestational trophoblastic disease is an important obstetric condition which if untreated, can result in serious and harmful consequences. Objective of this study was to determine incidence and pattern of gestational trophoblastic disease in tertiary care hospital of Rahim Yar khan.

Methods: This prospective observational cohort study was conducted at Sheikh Zayed Medical Hospital, Rahim Yar Khan, from January 2019 to December 2022. Patients presented with gestational amenorrhea and vaginal bleeding were suspected to be cases of molar pregnancy based on certain distinct clinical factors. These indicators included a large-for-date symphysio-fundal height (SFH), a snow storm appearance on ultrasonography, and significantly higher serum β-hCG levels. Data for these specific cases was collected from molar pregnancy registers maintained in Obstetrics and Gynecology department of Sheikh Zayed Medical Hospital, Rahim Yar Khan. Final diagnosis of molar pregnancy was confirmed by histopathology of the tissue removed from uterine cavity by suction and evacuation.

Results: A total of 33,494 pregnant women were admitted during the study period. Among this population, 197 were diagnosed with a molar pregnancy, representing a 0.58% rate. This equates to an overall incidence of 5.8 per 1,000 obstetric admission. Complete hydatidiform mole was the most common type, diagnosed in 127 females (64.4%). Partial mole occurred in 58 females (29.4%), while choriocarcinoma was found in 12 females (6.1%). Among 12 women with choriocarcinoma, four presented with pulmonary metastasis, received multiagent chemotherapy in liaison with oncology department.

Conclusion: High sensitivity pelvic ultrasonography may have led to early detection of abnormal pregnancies, before we can detect classical symptoms or identify patients with advanced disease.

Keywords: Gestational trophoblastic disease (GTD); Partial mole (PM); Complete mole (CM); Choriocarcinoma; β-hCG

INTRODUCTION

Hydatidiform mole and Gestational Trophoblastic Disease (GTD) both term can be used side by side. Pathophysiology involves abnormal trophoblastic proliferation associated with villous enlargement (moles) or neoplasm with absent villi (choriocarcinoma, placental site trophoblastic tumor). Hydatidiform mole (HM) incidence is 1-2 per 1000 pregnancies in Europe and the United States. Frequency of GTD in much higher in some Asian countries.[1] Approximately, 15-20% of cases of complete moles may need future treatment with chemotherapy post evacuation.[2] To determine which molar pregnancy will be completely cured after evacuation or in which, further treatment will be required, no evidence is available currently. Fortunately, Beta-HCG secretion from trophoblasts gives a very accurate assessment of the level of disease activity and this forms the tumor maker having diagnostic role and basis of the follow-up protocol. [3,4] Genetically, complete mole (CM) are consequence of fertilization of an `empty' egg by a haploid sperm or two sperms, making karyotype of 46, XX or 46, XY of purely paternal origin (androgenic). Majority of partial moles (PMs) are formed by fertilization of an apparently normal oocyte by two sperms, and giving it triploid (69, XXX or 69, XXY) karyotype.[4] The incidence of GTD revelead marked geographic and ethnic variation, ranging from the highest incidence of 1 in 120-400 pregnancies in Asian countries such as Taiwan, Philippines and Japan, to the lowest incidence of 1 in 1000 to 2000 in Europe and the USA.[5] In 2009 of Pakistan survey, the incidence of GTD was 28 per 1000 live births and 70% of these turned out to be Hydatidiform mole.[6] Main stay of treatment is by suction evacuation. The important aspect is follow-up of all the cases as it can be changed to other forms of GTD which may need chemotherapy, so early detection and treatment of HM is important. Those cases requiring chemotherapy are generally cured with very low toxicity regimen. Unlike

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other gynecological malignancies, fertility preservation and normal pregnancy outcome are much better in these cases. Good prognosis with this disease is a milestone of success in the history of medicine.[7,8] Objective of this study was to determine incidence and pattern of gestational trophoblastic disease in tertiary care hospital of Rahim Yar khan.

PARTICIPANTS AND METHODS

This prospective observational study was conducted in Sheikh Zayed Hospital, Rahim Yar Khan, from January 2019 to December 2022, after obtaining approval from the Institutional Ethical Review Board (No.03/RDSU/ SZMC). Consecutive non-probability sampling was employed. All patients presenting during the study period who fulfilled the inclusion criteria; gestational amenorrhea with vaginal bleeding and a clinical suspicion of molar pregnancy based on one or more of the following: uterine size greater than the period of gestation, characteristic "snowstorm" appearance on ultrasonography, and/or elevated serum β-human chorionic gonadotropin (β-hCG) level were enrolled. A total of 197 eligible patients were included in the study. Diagnosis of molar pregnancy was confirmed by histopathology of the tissue removed from uterine cavity by suction and evacuation and serum β-hCG was used for fortnightly 6 months follow up to detect relapse or persistent gestational trophoblastic disease. Patients were categorized as cases of partial mole, complete mole, invasive mole and choriocarcinoma from report of histopathology. Each follow-up was maintained in molar Pregnancy register. Demographic data of patients like age, parity, gestational amenorrhea, presenting symptoms, pre-evacuation serum β-hCG, chest X-ray and histopathology report all were entered in proforma and results was analyzed in percentages. Incidence of molar pregnancy was calculated and percentage of type of molar pregnancy and need of chemotherapy among patients was calculated.

RESULTS

In our study 128 females (64.9%) were primigravida and 69 (35.0%) were >P4. Average age of females presented was 23.5 years. In all 197 patients presenting complaint was gestational amenorrhea and vaginal bleeding. Twenty-eight patients were presented with heavy bleeding and hypovolemic shock, where immediately suction evacuation was done. All 197 patients were having, symphysio-fundal height large than gestational age. 154 (78.1%) were having anemia (HB <11 g/dl) and received blood transfusion during suction evacuation. Seven (3.5%) patients with theca luteal cyst of size more than 6cm managed conservatively. None of our patient developed hyperemesis or preeclampsia. Pre-evacuation β-hCG was between 50,000 to 100,000mIU/ml in 148 (75.1%) females, and in 49 (24.9%) serum β-hCG was >100,000 mIU/ml. Total pregnant females were admitted during the study period from January 2019 to December 2022 were 33,494. Out of this pregnant population, total 197 (0.58% cases of molar pregnancy during study time admitted. This makes the incidence of 5.8 per 1000 patients admitted in our department. Suction evacuation was done in 185 (93.9%) cases successfully, one of our patients underwent emergency hysterectomy due to massive hemorrhage during suction evacuation, 23 (12.5%) patients needed re-evacuation for incomplete evacuation. Twelve patients who were suspected choriocarcinoma due to β-hCG value >500,000 mIU/ml and highly vascular mass

Table 1: Incidence of GTD, and Demographic Data

Category	No. of Cases	Percentage
Gestational trophoblastic disease		
Total cases	197	0.58%
Rate per 1000 obstetric admissions	~5.8	Per 1000 admissions
Parity		
Primigravida	128	64.9
Para >4	69	35.0
Age		
15–20 years	117	59.3
21–25 years	40	20.3
26–30 years	30	15.2
>30 years	10	5.0
Size of luteal cyst (>6 cm but <10 cm)	7	3.5
SFH		
10–14 weeks	139	70.5
15–30 weeks	58	29.5
Anemia (Hb <11 g/dL)	154	78.1
Year-wise cases of molar pregnancy		
2019	35	17.7
2020	31	15.7
2021	57	28.9
2022	74	37.5

Table 2: diagnosis, management and complications

Category	No. of Cases (n=197)	Percentage
β-hCG level		
50,000–100,000 mIU/mL	148	75.1
>100,000 mIU/mL	49	24.9
Treatment		
Suction evacuation	185	93.9
Hysterectomy	13	6.1
Re-evacuation	23	12.2
Histopathological diagnosis		
Partial mole	58	29.4
Complete mole	127	64.4
Choriocarcinoma	12	7.1
Persistent trophoblastic disease after complete mole	23	12.5
Chemotherapy for persistent trophoblastic disease		
Single-agent chemotherapy	23	12.5
Multi-agent chemotherapy	4	33.3

in uterine cavity underwent elective hysterectomy. A total of 197 patients with gestational trophoblastic disease were included in the study. Of these, 127 (64.5%) were diagnosed with complete hydatidiform mole**,** 58 (29.4%) with partial hydatidiform mole**,** and 12 (6.1%) with choriocarcinoma. Among, the 12 patients with choriocarcinoma, 4 (33.3%) had pulmonary metastases at the time of diagnosis and were managed with multi-agent chemotherapy in collaboration with the Department of Oncology.

The remaining 185 patients with hydatidiform mole (complete and partial mole) underwent suction evacuation followed by serial serum β-hCG monitoring every two weeks**.** Persistent gestational trophoblastic disease (GTD) developed in 23 patients (12.4%), as evidenced by plateaued serum β-hCG levels over four consecutive weeks according to standard diagnostic criteria. These patients received single-agent methotrexate. Among the 23 patients who developed persistent GTD, 9 (39.1%) achieved complete normalization of serum β-hCG levels after four cycles of methotrexate therapy, whereas the remaining 14 (60.9%) achieved remission after three cycles of methotrexate. Of the 185 patients with hydatidiform mole, 161 (87.0%) experienced spontaneous normalization of serum β-hCG levels within 56 days following suction evacuation without requiring chemotherapy.

DISCUSSION

In the present study, the incidence of hydatidiform mole (HM) was 5.8 per 1,000 obstetric admissions, which is comparable to the incidence reported by Fatima et al. from Pakistan (approximately 5 per 1,000 pregnancies) but lower than the 7 per 1,000 pregnancies reported by Almasi et al. from Iran.[8-10] Recent FIGO recommendations acknowledge substantial geographical variation in HM incidence, with rates of 0.57–2 per 1,000 pregnancies in Europe and North America compared with considerably higher rates reported from several Asian countries. These differences reflect variations in population characteristics, study methodology, and healthcare systems rather than ethnicity alone.[11-14]

Maternal demographic characteristics further support these observations. Nearly 60% of patients in our study were between 15 and 20 years of age, similar to previous Pakistani studies demonstrating that HM predominantly affects younger women.[15] According to the FIGO 2021 guidelines, both extremes of maternal age, particularly women younger than 20 years and older than 35-40years, are well-recognized risk factors for complete mole. Early marriage and adolescent pregnancy remain relatively common in Pakistan compared with Europe, potentially contributing to the higher incidence observed in our population.[14-17]

Comparison with other Asian countries demonstrates considerable regional variation. Studies from Pakistan and Iran have reported incidences comparable to those observed in our study, whereas Malaysia has reported a higher proportion of partial moles than complete moles. Conversely, long-term population-based studies from Japan have demonstrated a gradual decline in HM incidence over recent decades, approaching that reported in Europe. Improvements in maternal nutrition, universal healthcare access, widespread early ultrasonography, and comprehensive antenatal care have been proposed as major contributors to this decline. These findings suggest that healthcare infrastructure and socioeconomic development substantially influence HM epidemiology in addition to genetic factors. Complete mole accounted for 64.4% of all cases in the present study, whereas Humaira et al. and Malaysian investigators reported a predominance of partial mole.[18-20] This discrepancy may reflect differences in referral patterns, pathological expertise, availability of ancillary diagnostic tools such as p57 immunohistochemistry and molecular genotyping, and evolving histopathological classification systems. Recent international recommendations

advocate ancillary molecular techniques in diagnostically difficult cases to improve diagnostic accuracy and reduce inter-observer variability.[20-22,]

A gradual increase in the annual number of diagnosed molar pregnancies was observed during the study period. Although this trend may represent a genuine increase in disease occurrence, it is more likely attributable to improved availability of high-resolution ultrasonography, increased clinician awareness, enhanced referral pathways, routine histopathological evaluation of products of conception, and improved documentation of GTD cases. Similar improvements in early diagnosis have been reported in recent international reviews, where widespread use of first-trimester ultrasonography has substantially altered the clinical presentation of molar pregnancy.[17-18]

The comparatively higher incidence observed in our study may, in part, be explained by referral bias. Our institution is a tertiary care referral center receiving patients from secondary and primary healthcare facilities, resulting in an overrepresentation of complicated pregnancies and suspected gestational trophoblastic disease (GTD). Consequently, hospital-based studies often report higher incidences than population-based registries because they preferentially capture high-risk patients. Similar observations have been highlighted in recent FIGO recommendations and international epidemiological reviews of GTD.[21,22] Socioeconomic factors are also likely to contribute to the increased disease burden in Pakistan. Poverty, limited female education, delayed initiation of antenatal care, inadequate access to specialist obstetric services, and financial barriers frequently result in delayed presentation. Women therefore commonly seek medical attention only after developing significant vaginal bleeding, anemia, hyperemesis gravidarum, or excessive uterine enlargement. In contrast, most European countries have well-established early pregnancy assessment services and routine first-trimester ultrasonography, facilitating earlier diagnosis before classical clinical manifestations develop. Consequently, disease severity and referral rates are generally lower in developed countries.[18]

Nutritional deficiencies may further explain the higher incidence of HM in developing countries. Deficiency of vitamin A and β-carotene has long been associated with abnormal trophoblastic proliferation and an increased risk of complete hydatidiform mole. Women from low-income populations remain at greater risk of micronutrient deficiencies because of inadequate dietary intake, which may partly account for the persistently higher incidence observed in South Asia compared with Europe and North America. Although nutritional status was not directly assessed in the present study, it remains a biologically plausible contributing factor supported by previous epidemiological studies.[20-22]

Persistent gestational trophoblastic neoplasia developed in 12.5% of patients following evacuation, diagnosed according to plateaued serum β-hCG levels over four consecutive weeks. This proportion is consistent with contemporary literature reporting progression to GTN in approximately 13–20% of complete moles and 0.5–5% of partial moles**.** Considering the considerable risk of loss to follow-up in our setting, affected patients received single-agent methotrexate according to institutional protocol. No significant methotrexate-related adverse effects were observed, supporting the safety and effectiveness of timely chemotherapy combined with structured β-hCG surveillance, as recommended by current FIGO and Society of Gynecologic Oncology guidelines.[21] Overall, the higher incidence of hydatidiform mole observed in Pakistan compared with Europe is probably attributable to the combined effects of referral bias, delayed presentation, socioeconomic disparities, nutritional deficiencies, younger maternal age, and differences in healthcare infrastructure**,** rather than a single etiological factor. Future multicenter prospective population-based studies incorporating nutritional, socioeconomic, and molecular risk factors are required to determine the true disease burden and identify modifiable determinants of gestational trophoblastic disease in Pakistan.[21,22]

CONCLUSION

The incidence of hydatidiform mole, particularly complete mole, has shown an increasing trend at our institution over the study period. This rise may reflect a combination of factors, including referral bias to a tertiary care center, improved case detection through widespread use of high-resolution ultrasonography, and the persistence of demographic and socioeconomic risk factors within the study population. Younger maternal age, primiparity, and lower socioeconomic status were commonly observed among affected women and may have contributed to the disease burden. Early diagnosis, prompt referral, and timely management have substantially improved clinical outcomes and reduced the risk of progression to persistent gestational trophoblastic neoplasia. Further multicenter, population-based studies are warranted to better define the underlying epidemiological trends and identify modifiable risk factors to facilitate effective prevention and early intervention strategies.

Author Contributions

MN: Concept, Design, Analysis, Data interpretation, Literature review, Critical review, Accuracy, Integrity of work, Final approval
BN: Conception, Analysis, Drafting the article, Accuracy of data, Final approval
SS: Data collection, Analysis, Data interpretation, Drafting the article
FS: Acquisition of data, Conception, Design, Analysis and interpretation

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