Student's Journal of Health Research Africa
Vol. 4 No. 6 (2023): June 2023 Issue
https://doi.org/10.51168/sjhrafrica.v4i6.503
Original article

A META-ANALYSIS ON COMPLETE AND PARTIAL MOLAR PREGNANCY.

Emrana Rahman*
Janm IVF Centre, Bhagalpur, Bihar, India.

Abstract

Background :

The hydatidiform mole is an uncommon gynaecological condition that arises from trophoblastic cells. Post-molar pregnancies can result in multiple abortions, stillbirths, preterm deliveries, or live births, or they can recur in subsequent molar pregnancies. The literature on the obstetric outcomes of molar pregnancies is limited, frequently consisting of monocentric studies and national database data. This review and meta-analysis aim to examine the obstetric outcomes of complete (CHM) and partial (PHM) molar pregnancies managed conservatively. Following MOOSE and PRISMA, the meta-analysis was conducted.

Methods :

Six studies met inclusion criteria. Included were 13,129 complete (52,1%) and 12,093 incomplete (47.9%) molar pregnancies out of a total of 25,222 patients.

Results:

The rate of live births after CHM was significantly higher (p = 0.002) than after PHM (53.6% vs. 51.0%, 3266 vs. 1807 cases, respectively). I2 = 57.7%, the pooled proportion = 0.2%, and the 95% Confidence Interval (CI) ranged from 0.6 to 0.9. There was no statistically significant difference between CHM and PHM with regard to ectopic pregnancies (p = 0.633), miscarriage (p = 0.637), preterm birth (p = 0.865), stillbirth (p = 0.911), termination of pregnancy (p = 0.572), or complete molar recurrence (p = 0.580). Partial molar recurrence was more common following PHM than CHM (0.4% vs. 0.3%, 52 vs. 37 cases, p = 0.002).

Conclusion:

Patients desiring additional pregnancies should receive careful counselling on the outcomes of subsequent obstetric pregnancies, and further research is required to confirm these results.

Keywords: A Meta-Analysis, Complete and Partial Molar Pregnancy, Submitted: 2023-06-23
Accepted: 2023-06-26

1. Introduction:

The hydatidiform mole, also known as molar pregnancy, is a rare gynaecological disease arising from trophoblastic tissue, with an incidence spanning from 0.6 to 11.5 per 1000 births [1, 2]. Complete hydatidiform mole (CHM) occurs when an enucleated egg is fertilised by two spermatozoa or one haploid duplicating spermatozoon; partial hydatidiform mole (PHM) occurs when a haploid egg is fertilised by two spermatozoa or one haploid duplicating spermatozoon [3]. CHM is typically diploid, with 90% of cases having a karyotype of 46 XX and only paternal DNA expression, whereas PHM is triploid, with 90% of cases

*Corresponding author.
Email address: emrana.bgp@gmail.com (Emrana Rahman)

having a karyotype of 69 XXX and paternal and maternal DNA expression [4]. CHM is characterised by a fatal placental development defect resulting from aberrant genomic imprinting and loss of the maternal counterpart [5]. This atypical imprinting results in a generalised methylation defect, which causes the trophoblastic component to overdevelop [6]. NLRP7 and KHDC3L [7] are two important autosomal recessive genes implicated in the pathogenesis process. The first gene, located on chromosome 19q13.4, encodes proteins involved in inflammatory and apoptotic processes; the second gene, located on chromosome 6q13, encodes proteins of the KHDC1 family, which are typically oocyte gene regulators [8, 9]. The most common clinical manifestations are metrorrhagia and an enlarged uterus with an abnormal human chorionic gonadotropin (HCG) level for gestational age [10].

Histological analysis is the gold standard for diagnostic purposes, and transvaginal ultrasound is a useful instrument in the diagnostic algorithm, displaying snowstorm-like patterns with grape-like cysts in the absence of a distinct embryonic structure [11]. The diagnosis is frequently made by accident following suction dilation and curettage, the treatment of preference [12]. In the absence of a desire for fertility, nonconservative management including hysterectomy and bilateral salpingectomy is indicated, while chemotherapy is recommended for extrauterine disease according to international guidelines [13].

In the majority of instances, conservative management with serial HCG dosages until hormone levels normalise is sufficient. The course of postmolar pregnancies is exceedingly variable, ranging from multiple abortions, stillbirths, preterm births, and live births to recurrence in subsequent molar pregnancies [14]. Due to the rarity of the disease, the literature on obstetric outcomes following molar pregnancy is limited, frequently consisting of monocentric studies and national database data [15]. To the best of our knowledge, an obstetrics outcomes meta-analysis of patients with a prior molar pregnancy has never been conducted. This review and meta-analysis aimed to examine the obstetric outcomes of complete and partial molar pregnancies managed conservatively. We believe that this study may be a useful tool for more precise counselling of patients of childbearing age who seek a subsequent pregnancy following a molar pregnancy.

2. Materials and methods:

From March to July 2020, a systematic literature review was conducted on Pubmed, Medscience, Google Scholar, and Scopus. The following essential phrases have been chosen: 'hydatidiform mole'; 'complete mole'; 'partial mole'; and 'trophoblast diseases'. The authors CVA and DB conducted their bibliographic investigation in double-blind. Afterward, a third author (RB) oversaw the selected studies. The meta-analysis was conducted using MOOSE [16] and PRISMA [17] guidelines. All studies reporting obstetric outcomes of patients treated conservatively for partial or total hydatidiform mole were included in the analysis. Pregnancies with live-borns, ectopic pregnancies, miscarriage, preterm birth (37 gestational weeks), stillbirth, complete mole recurrence, partial mole recurrence, and termination of pregnancy were considered obstetric outcomes. By conservative management, dilation and curettage or systemic chemotherapy were intended. Excluded from the analysis were patients undergoing hysterectomy. The authors, study type, number of complete moles, number of partial moles, average age, and obstetric outcomes were analysed for each study. Excluded from this meta-analysis were case reports, non-English language articles, studies that did not report the required outcomes, and those that were irrelevant to the purpose of this analysis.

2.1. Statistical Analysis:

All values were presented as either figures (percentages) or means. For categorical variables, the Chi-square or Fisher exact test was used, while the t-test and Mann–Whitney non-parametric equivalent test were used for continuous variables. The I 2 test was used to assess the studies' heterogeneity. I2 > 50% indicated a high level of heterogeneity among the analysed studies. The

random effect model was utilised [2] regardless of the I test. A p-value of <0.05 was statistically significant. Version 3.0.0 of Prometa Software was used for statistical analysis.

3. Results:

Six investigations met inclusion criteria [16]. The electronic research yielded 349 studies, including 312 articles irrelevant to the current meta-analysis, 14 case reports, 2 articles written in a language other than English, and 15 studies with incomplete data. Included were 13,129 complete (52,1%) and 12,093 incomplete (47.9%) molar pregnancies out of a total of 25,222 patients. The median age ranged from 29.0 to 29.7 years. After molar disease, there were 7802 subsequent pregnancies, of which 4674 (66%) occurred after CHM and 2408 (34%) after PHM. Of all post molar pregnancies, 5073 (71.6%) live births (3266 and 1807 cases in the CHM and PHM group, respectively), 40 (0.6%) ectopic pregnancies, 31 (0.4%) stillbirths, 1194 (16.9%) miscarriage, 265 (3.7%) pregnancy terminations, 125 (1.8%) recurrences complete molar pregnancy, 76 (1.1%) partial molar pregnancy recurrence, and 298 (4.2%) preterm births had occurred (results reported in Table 1).

4. Discussion:

Molar pregnancy most frequently affects women between the ages of 20 and 30 [17]. In this reproductive age, patients frequently desire additional pregnancies, and a history of molar pregnancy negatively impacts their quality of life [18]. Patients desiring a subsequent pregnancy should be counselled carefully on the obstetric outcomes of consecutive pregnancies in this situation.

Surprisingly, the current meta-analysis of 25222 M cases and 7082 subsequent pregnancies revealed a substantially higher rate of live births after complete molar pregnancy than after partial molar pregnancy (53.6% vs. 51.0%). No published study has evaluated this aspect of molar disease to date. Contradictory results were obtained regarding the role of Cyclin E and p57kip2 proteins in the pathogenesis of CHM [19]. By regulating the cell cycle, these proteins could affect not only the persistence of molar disease but also subsequent pregnancies [20]. However, the function of cyclin E in subsequent pregnancies is only a hypothesis; additional research is required to confirm these findings. In addition, none of the studies included in the meta-analysis specified whether subsequent pregnancies were spontaneous or the result of assisted reproduction techniques, whether the same partner was involved, or how much time had elapsed since the previous molar pregnancy. All of these inaccessible variables should be analysed, as they may have impacted successive pregnancies in both the complete and partial mole groups.

Our meta-analysis also revealed a higher rate of partial mole recurrence in PHM versus CHM. This result was consistent with the literature, which reported a higher recurrence rate (2%) in patients with a history of molar pregnancy compared to those with a silent anamnesis [21]. Our study was unique in that, for the first time, we observed a higher correlation between recurrent partial moles and previous partial moles, but not with previous complete moles (p = 0.002). However, this correlation was not observed between the recurring complete mole and the preceding complete mole (p = 0.580). Several factors relating to the characteristics of women with recurrent molar disease have been studied in the literature. Young age (range 21–25 years), Indian / Pakistani women (relative risk 2.4, 95% CI 0.95–5.78), blood group B, and the interval from the initial molar pregnancy (highest incidence in the second year after the initial molar event) were characteristics of patients with recurrent molar pregnancy [22]. In addition, multiple authors have reported that the risk of recurrence increases with the number of previous molar pregnancies [1]. In these instances, an autosomal recessive pattern of molar recurrence was described.

In terms of ectopic pregnancy (0.1-4%), miscarriage (2-15%), stillbirth (0.1-0.2%), preterm birth (1-8%), termination of pregnancy (2-10%), and complete mole recurrence (0.1-06%), there was no difference between the partial and complete

mole groups; in addition, the incidence of these events after molar pregnancy was comparable to that of the general population. Patients with a single previous molar pregnancy should therefore be reassured about the outcomes of their subsequent pregnancies. Despite the lack of statistical significance, the Forest Plot analysis revealed a high degree of heterogeneity among the included studies.

5. Conclusion:

The meta-analysis revealed that the rate of surviving births after a complete mole was statistically higher than after a partial mole. In addition, patients with partial molar pregnancy had an increased risk of developing a subsequent partial molar pregnancy. In terms of ectopic pregnancies, stillbirths, preterm birth, abortion, and miscarriage, the incidence of adverse obstetric outcomes was comparable to that of the general population among patients with molar pregnancy.

6. Acknowledgement:

None

7. List of abbreviations:

CHM- Complete molar pregnancies
PHM- Partial molar pregnancies
DNA- Deoxyribonucleic acid
HCG- Human chorionic gonadotropin

8. Conflict of Interest:

None declared.

9. Source of funding:

Nil

10. Publisher details:

Publisher: Student's Journal of Health Research (SJHR)
(ISSN 2709-9997) Online
Category: Non-Governmental & Non-profit Organization
Email: studentsjournal2020@gmail.com
WhatsApp: +256775434261
Location: Wisdom Centre, P.O.BOX. 148, Uganda, East Africa.

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Author biography

Emrana Rahman Director, Janm IVF Centre, Bhagalpur, Bihar, India.