

Has the Incidence of Molar Pregnancy Changed Over the Last 10 Years?

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Abstract

A retrospective audit was conducted at the Rotunda hospital, Dublin to assess the incidence of partial molar pregnancies and complete molar pregnancies over a 10-year period from the 1st of January 1997 to 31 of December 2006.

Methods: Records from the pathology department were accessed for the number of molar pregnancies from 1997 to 2006. Each pathology result was then retrieved to differentiate between complete moles and partial moles. The annual reports published by the hospital were used to obtain the number of deliveries and live births per year.

Results: The incidence of partial molar pregnancies at the Rotunda Hospital from 1997 to 2006 was 1 in 328 live births. The incidence of complete molar pregnancies from 1997 to 2006 was 1 in 1105 live births. The incidence of a molar pregnancy in the study period was 1:253.

Conclusion: The incidence of a molar pregnancy was estimated to be 1: 512 in 1993 and was 1: 253 in this study, indicating a significant rise. The incidence of complete and partial molar pregnancies has also doubled. The Rotunda hospital caters to a large proportion of Dublin's noncaucasian population which might account for an increase. But it is still possible that there is an over diagnosis of cases as diagnosis is only by histology and flow cytometry is not routinely performed in all cases.

Keywords: Complete molar pregnancy, partial molar pregnancy, B-human chorionic gonadotrophin, flow cytometry, p57kip2.

INTRODUCTION

Molar pregnancies also known as gestational trophoblastic neoplasia are a result of abnormal fertilization and can be classified as three types, complete, partial and indeterminate. Complete molar pregnancies are a result when the products of conception consist of strictly only paternal chromosomes (usually 46XX) which commonly result from duplication of the paternal chromosomes inside an empty egg. Occasionally the genotype might be 46XY when an empty ovum is fertilized by two sperms. A partial molar pregnancy on the other hand results when two sperms fertilize a single egg resulting in the genotype being 69XYY. Molar pregnancies are premalignant and have significant bearing on the patients' psychology and fertility. Not only does the patient have to bear the loss of a pregnancy but they need to avoid conception again for six months from the time the HCG is normal again. The couple also have to deal with the possibility that it is a premalignant condition.

Surgical pathologists often encounter hydropic villi in products of conception at the first trimester and must determine whether the villi represent complete hydatidiform mole, partial hydatidiform mole, or hydropic abortion.¹ The distinction between these is important for determining the appropriate treatment of patients. The partial mole differs from the complete mole in the proportion of the villi that are vesicular. It is not

uncommon for a fetus to be present, and it may be abnormal. Histologically a proportion of the villi are edematous with sometimes a central cistern. Some enlarged villi may show a degree of trophoblastic hyperplasia but usually less marked than that seen in a complete mole.

Whilst women from the far east and those that are at the extreme ages of child bearing are more likely to have a molar pregnancy, so are those women with a previous history of a molar pregnancy, it is important for clinicians to be able to inform the patient of her probability of having a molar pregnancy.

AIMS

A retrospective audit was conducted from 1.1.1997 to 31.12.2006 at the Rotunda hospital. The aim was to obtain the incidence of hydatidiform moles, both partial and complete over the time period. The aim was also to assess the changing trends from previous audit conducted at the Rotunda hospital in 1993 and compare it with international figures.

METHODS

All products of conception from first and second trimester miscarriages in hospital are sent for histopathology. Tissue obtained following evacuation of retained products of

conception, are also routinely referred for histological examination. Hematoxylin and eosin (H and E) stained sections were examined in cases of spontaneous miscarriage, evacuation of retained products of conception, or surgery following ectopic pregnancy. P57kip2 was not performed on all the cases, but was done on cases where the microscopic diagnosis was ambiguous. Flow cytometry was done prior to the availability of p57kip2.

Records from the pathology department were accessed for the number of molar pregnancies from 1997 to 2006. Each pathology result was then retrieved to differentiate between complete moles and partial moles. The annual reports published by the hospital were used to obtain the number of deliveries and live births per year.

RESULTS

Over the 10 years period there were a total 262 molar pregnancies. In the study period 202 (77%) were partial molar pregnancies and 60 (23%) were complete moles. Over the 10 years there were a total of 66,296 births at the Rotunda hospital. As seen in Figure 1, there is a steady rise in the number of births over the 10 years period. The total number of births was 6223 in 1997, and there were 7325 births in 2006.

Table 1 represents the yearly distribution of the number of molar pregnancies. The incidence of molar pregnancies has been relatively static averaging to be around 0.41%. An increase in incidence was seen in the year 2000 where the number of cases was 44 (0.78%) and in the year 2001 where the number of cases was 37(0.62%).

Partial molar pregnancies were 3.37 times more common than complete molar pregnancies over the 10-year period. There was also an increase in the number of partial molar pregnancies in the years 2000 and 2001. As seen in Table 2 there were 39 partial molar pregnancies the year 2000 and 33 partial molar pregnancies in the year 2001.

Similar trends were not seen when the numbers of complete molar pregnancies was analyzed. The incidence in the number of complete molar pregnancies (Fig. 2) was relatively stable with an overall incidence of 1: 1105. There was a maximum of 11 cases in the year 2004, with the least number, three, in 2005. Table 3 illustrates the number of complete molar pregnancies year by year, over the 10-year period.

The incidence of partial molar pregnancies at the Rotunda hospital from 1997 to 2006 was 1 in 328 live births (Fig. 3). The incidence of complete molar pregnancies from 1997 to 2006 was 1 in 1105 live births. The incidence of a molar pregnancy in the study period was 1: 253.

DISCUSSION

Clinical signs associated with hydatidiform mole include disproportionately large uterine dimensions, serum hCG levels that rise after the 14th week of gestation, (a fall is usual at this stage in normal pregnancies), and toxemia, (manifesting as hypertension, proteinuria, and edema) in the early stages of pregnancy.²

Histologically, hydatidiform moles are characterized by swelling of the trophoblastic villi. They are categorized as pre-malignant (complete or partial), and malignant.² Diagnostic

Table 1: Total molar pregnancies from 1997 to 2006

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	Total
Molar Pregnancies	31	16	24	44	37	31	16	27	18	18	262
Total births	6223	6387	6334	6310	6600	6793	6789	6731	6802	7325	66296
Incidence	0.5% 1:200	0.25% 1:400	0.38% 1:263	0.78% 1:128	0.62% 1:161	0.49% 1:204	0.25% 1:400	0.40% 1:250	0.29% 1:344	0.25% 1:250	0.418% 1:240

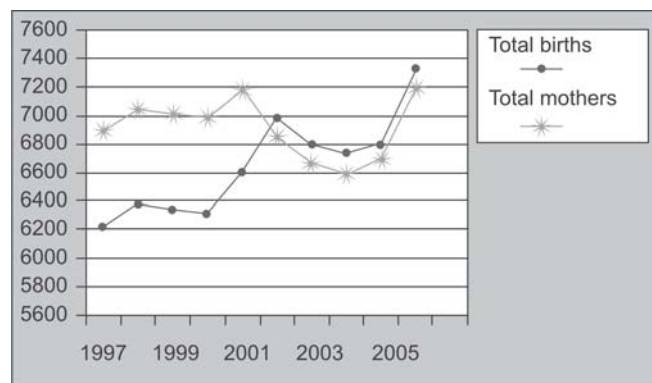


Fig. 1: Yearly distribution of the member of births per year from 1997 to 2006

Table 2: Partial molar pregnancies from 1997 to 2006

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	Total
Partial molar pregnancies	24	10	19	39	33	25	9	16	15	12	202
Total births	6223	6387	6334	6310	6600	6793	6789	6731	6802	7325	66296
Incidence	1:259	1:637	1:334	1:162	1:200	1:279	1:755	1:420	1:455	1:610	1:328

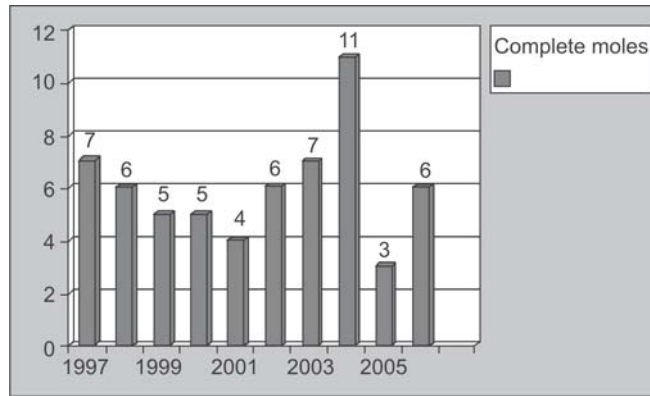


Fig. 2: Yearly distribution of complete molar pregnancies

Table 3: Complete molar pregnancies from 1997 to 2006

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	Total
Complete molar pregnancies	7	6	5	5	4	6	7	11	3	6	60
Total births	6223	6387	6334	6310	6600	6793	6789	6731	6802	7325	66296
Incidence	1:909	1:1063	1:1266	1:1266	1:1667	1:1163	1:1000	1:625	1:2273	1:1220	1:1105

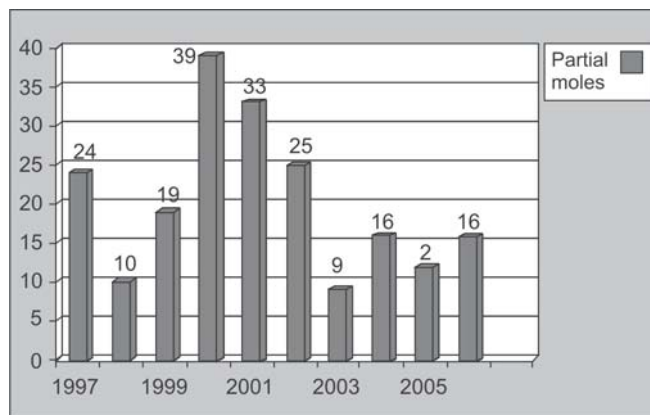


Fig. 3: Yearly distribution of partial molar pregnancies

accuracy on histological grounds alone can reach 95%.³ Constraints are commonly related to low submitted volumes of placental material, and to necrotic change in submitted material. Most hydatidiform moles are now evacuated in early pregnancy.³

Partial moles demonstrate an irregular or "dentate" villus outline with patchy mild to moderate hydrops, stromal

karyorrhectic debris and collapsed blood vessels, stromal fibrosis, mild focal villus trophoblast hyperplasia, scattered trophoblastic pseudo inclusions, and often the presence of amnion or fetal tissue.

Early histological signs of complete mole include the absence of amnion and embryonic tissue, with excessive

trophoblastic proliferation. Morphological abnormalities of chorionic villi occur, including "budding" of the villus outline. If the pregnancy proceeds beyond 12 weeks, generalized excessive trophoblastic proliferation suggests the diagnosis.⁴

Immunohistochemical staining can assist morphological examination in differentiating complete and partial moles. The immunohistochemical marker p57kip2 is a protein product of a gene located on chromosome 11p15. It inhibits cyclin dependent kinase, and thereby serves to inhibit cell proliferation, and suppress tumor growth. The marker p57kip2 is absent or expressed at low levels in the villous cytotrophoblast and villous stromal cells of complete hydatidiform mole. In contrast, p57kip2 expression is normal in partial hydatidiform moles, and in normal placental tissue.⁵

The partial hydatidiform mole conceptus is abnormal, by the addition of an extrahaploid quota of paternal chromosomes, giving 69 in total. This contrasts with the complete mole, which has a 46 chromosome androgenic karyotype. Flow cytometry has proved useful in distinguishing complete and partial hydatidiform moles in a research setting.⁶

A previous smaller retrospective study was conducted at the Rotunda hospital⁷ over 3-year period. There were 19,457 pregnancies in that study and a total of 38 confirmed cases of molar pregnancy. Ten were complete molar pregnancies and 28 were partial molar pregnancies.⁷ It was observed that the number of partial molar pregnancies outnumbered the number of complete molar pregnancies as seen in the authors study with the partial moles being almost three times more common. The incidence of a molar pregnancy in the study by Jeffers et al was estimated to be 1:512 pregnancies (complete mole, 1:1,945: partial mole 1:695).⁷ It is apparent that the number of molar pregnancies has increased since 1993. It is also noticeable that it is not proportional to the increase in number of births. The incidence of a complete molar pregnancy has almost doubled from 1:1,945 as published in 1993 to 1:1105 (1997-2006). The statistics for partial moles is much the same. The incidence has increased from 1: 695 to 1:328 (1997-2006). The incidence of complete moles has also apparently doubled from 1:512 (1993) to 1:253.

The question we must ask ourselves is why has the incidence doubled over the last 10 years? It is known that the incidence of molar pregnancies is higher in people of ethnic descent from the East Asia. It is also known that molar pregnancies are more common in women who conceive at the extremes of age. The population attending the Rotunda hospital consists of a large proportion of non ethnic Irish people but the

incidence described here is much higher than that illustrated for these races of people.

In the study by Jeffers et al, ploidy was estimated by flow cytometry.⁷ Quantitatively imprecise morphologic criteria contribute to the inaccuracy in reporting of partial mole; analysis of ploidy is useful in the evaluation of problem cases.⁷

So are we over diagnosing partial molar pregnancies? Are the hydropic miscarriages being diagnosed as molar pregnancies? The increased number of diagnosed molar pregnancies has implications for the mothers. Women are advised not to get pregnant for 6 months after the hCG is normal.⁸ She is informed of the 0.5% risk of recurrence with a partial mole and 15% recurrence with a complete mole. There are also cost implications of follow-up. The current practice would be to carry out weekly B-hCG levels till normal then monthly for 6 months.

If the incidence of molar pregnancies is rising, then it is essential to inform women of the current incidence of a molar pregnancy. In the event of a possibility of over diagnosis the true incidence can be ascertained by checking for discrepancy between flow cytometry and pathological diagnosis. It may well be that there is genuine pathological over diagnosis of molar pregnancies. If this is the case it may be prudent to use flow cytometry as the gold standard in all cases.

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