OBSTETRICS

Hydatidiform mole and subsequent pregnancy outcome: a population-based cohort study

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OBJECTIVE: The objective of the study was to investigate whether a history of hydatidiform mole (HM) is associated with an increased risk of adverse outcomes in subsequent pregnancies.

STUDY DESIGN: This was a nationwide cohort study with data from population-based registers. The study population consisted of all children registered in the Swedish Medical Birth Register 1973-2009 (n = 3,730,825). Odds ratios (ORs) with 95% confidence intervals (CIs) were estimated for adverse maternal and offspring pregnancy outcomes by maternal history of HM prior to the delivery, with children to women with no maternal history of HM as the reference. Risk estimates were adjusted for maternal age at delivery and maternal country of birth.

RESULTS: A history of HM was not associated with an increased risk of adverse maternal outcomes in subsequent pregnancies (n = 5186). Women exposed to a molar pregnancy prior to the index birth were at an almost 25% increased risk of preterm birth (OR, 1.23; 95% CI, 1.06–1.43), whereas women with at least 1 birth between the HM and the index birth were at an increased risk of a large-for-gestational-age birth and stillbirth (OR, 1.35; 95% CI, 1.10–1.67 and OR, 1.81; 95% CI, 1.11–2.96, respectively). The risk of repeat mole was 0.4%.

CONCLUSION: Women with a history of HM are at no increased risk of adverse maternal outcomes in subsequent pregnancies but have an increased risk of large-for-gestational-age birth, stillbirth, and preterm birth. However, in absolute terms, the risk of subsequent adverse offspring outcomes is very low.

Key words: gestational trophoblastic neoplasia, hydatidiform mole, pregnancy outcome, repeat mole, subsequent pregnancy

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Hydatidiform mole (HM) is a genetically abnormal conception occurring in about 1 of 500-1000 pregnancies.[1,2] The most important risk factors for the development of HM are maternal age, geographical factors including ethnicity, and a previous molar pregnancy.[1,3-5] Molar pregnancies are classified as complete or partial hydatidiform mole based on different histopathological and cytogenetic features.[6,7]

An HM is considered to be a premalignant condition, with approximately 15% of complete and 1% of partial moles progressing into a malignant gestational trophoblastic neoplasia (GTN).[2,8-10] To ensure early recognition of a postmolar GTN, levels of human chorionic gonadotropin are monitored following a diagnosis of HM. During the surveillance period, women are recommended to refrain from a new pregnancy.

Previous studies have documented long-standing psychosocial consequences, including future fertility fears, in women with a diagnosis of HM, and women who do not conceive subsequent to a diagnosis of gestational trophoblastic disease have been shown to have poorer psychosocial outcome and are at greater need of support.[11-14]

Results from earlier studies indicate that women with a history of HM can expect a normal future reproductive outcome, except for a slightly increased risk of a repeat mole.[4,5,15,16] Similarly, women treated for a GTN appear not to be at increased risk of adverse subsequent pregnancy outcomes, although there have been reports of an increased risk of stillbirth, possibly reflecting an effect of chemotherapy rather than of factors associated with the gestational trophoblastic disease.[5,17]

However, because most earlier studies have focused on the likelihood of a live birth vs the risk of spontaneous abortion and stillbirth, the aim of this nationwide cohort study encompassing more than 3.7 million singleton births was to examine the risk of subsequent adverse maternal and offspring outcomes in women with a history of HM.

Materials and Methods

Data sources

Data were obtained from 3 nationwide Swedish population-based registers. Record linkage between registers is made possible by use of an individually unique national registration number assigned

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to all Swedish residents at birth or first permanent residency.[18]

The Swedish Medical Birth Register

The Swedish Medical Birth Register (MBR) was established in 1973 and contains more than 98% of all births in Sweden and records information on maternal characteristics, reproductive history, and complications during pregnancy, delivery, and the neonatal period.[19] For the purpose of the present study, all births in Sweden between 1973 and 2009 were identified in the MBR.

The Swedish Cancer Register

The Swedish Cancer Register (SCR) was established in 1958 to monitor the cancer burden in the Swedish population. Reporting of all newly diagnosed cancer cases and some premalignant conditions, including HM, is mandatory. Reports are made separately by both a clinician and a pathologist or cytologist.[20] No treatment data are available in the SCR. Earlier studies have shown an underreporting of approximately 20% of all cases of HM to the SCR.[21,22] The SCR does not differentiate between complete and partial hydatidiform mole, and cases of postmolar GTN are not registered. The SCR was used to identify women diagnosed with HM.

The Multi-Generation Register

The Multi-Generation Register (MGR) encompasses all individuals in Sweden born in 1932 or later, who resided in Sweden at some point after 1961. It allows the identification of family structures, including information on reproductive history. Information from the MGR allowed the identification of births before 1973, not encompassed in the MBR (Figure).

Study population

A total of 3,730,789 births were identified in the MBR between 1973 and 2009. From these, we excluded multiple births (n = 90,128), children with missing data on maternal country of origin (n = 169), and children born to a woman with a childbirth and a diagnosis of HM registered the same date (suggesting a twin molar pregnancy or a third-trimester partial molar pregnancy) (n = 17, referring to 7 unique women). To be able to perform a complete case analysis, children with missing data on small for gestational age (SGA) or large for gestational age (LGA) were also excluded (n = 18,063). In this way, the analyses encompassed 3,622,412 children and 1,878,917 mothers.

Exposure variable

Our exposure variable was maternal history of HM prior to childbirth. Information on exposure was extracted from the SCR, using the *International Classification of Diseases* (ICD)-7: 173 and pathoanatomical diagnosis: 801 codes to identify all recorded cases of HM. In this way, a total of 4940 cases of HM were identified in the SCR since 1958, 20 of which were identified as a repeat mole.

By means of record linkage between the MBR and the SCR, we found 3709 unique women with a first diagnosis of HM during the period that was included in the analysis. Of these, 3071 women had a diagnosis of HM prior to at least 1 of their childbirths, with a total of 5186 exposed births. The study population was further stratified into a maternal history of HM prior to the index pregnancy, defined as no birth between the HM and the index pregnancy (n = 2867), and a maternal history of HM and at least 1 birth between the HM and the index pregnancy (n = 2319). Information on births occurring prior to 1973 was retrieved from the MGR.

Outcome variables

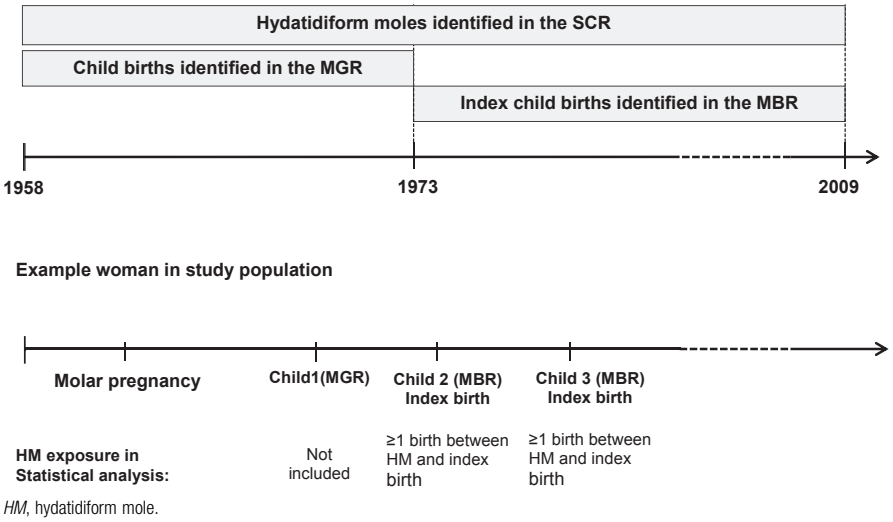
Outcomes of interest included adverse maternal pregnancy outcomes (maternal preeclampsia [PE]; ICD-8: 63703, 63704, 63709, 63799; ICD-9: 642E, 642F, 642H; ICD-10: O11, O14; maternal hypertension; ICD-8: 63701; ICD-9: 642D, 642X; ICD-10: O13, O16; placental abruption; ICD-8: 6514; ICD-9: 641C; ICD-10: O45 and premature rupture of membranes [PROM]; ICD-8: 6610; ICD-9: 658B, 658C; ICD-10: O42; and adverse offspring outcomes [congenital malformations; ICD-9: 740-759; ICD-10: Q30-Q99, preterm birth (delivery <37 gestational weeks), stillbirth, neonatal mortality (child died <28 days' postpartum), SGA, and LGA]).[23,24]

Statistical analysis

An unconditional logistic regression analysis was used to estimate the

FIGURE

Identification of HM and subsequent births in 3 nationwide Swedish population-based registers



HM, hydatidiform mole.

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