ACTA ONCOLOGICA
2018, VOL. 57, NO. 8, 1094–1099
https://doi.org/10.1080/0284186X.2018.1438653

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Temporal trends in incidence and outcome of hydatidiform mole: a retrospective cohort study

Urika Joneborg[a], Yasin Folkvaljon[b], Nikos Papadogiannakis[c], Mats Lambe[b,d] and Lena Marions[e]

[a]Department of Women's and Children's Health, Division of Obstetrics and Gynaecology, Karolinska University Hospital/Institutet, Stockholm, Sweden; [b]Regional Cancer Centre, Uppsala University Hospital, Uppsala, Sweden; [c]Department of Laboratory Medicine, Division of Pathology, Karolinska University Hospital/Institutet, Stockholm, Sweden; [d]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; [e]Department of Clinical Science and Education, Division of Obstetrics and Gynaecology, Karolinska Institutet Södersjukhuset, Stockholm, Sweden

ABSTRACT

Background: Reported incidence rates of hydatidiform mole (HM) show wide geographic and temporal variations, making reliable international comparisons difficult. The aim of the current study was to examine temporal trends in the incidence of HM and post-molar gestational trophoblastic neoplasia (GTN) in Stockholm County.

Material and methods: Data of all women with a diagnosis of HM in Stockholm County 1991–2010 was collected. The incidence of HM was assessed both in relation to number of births and viable conceptions (births and pregnancy terminations). The risk of post-molar GTN was analysed for all HM, as well as for the subtypes complete (CHM) and partial hydatidiform mole (PHM). Temporal trends were analysed by stratifying the study period into five-year intervals.

Results: The overall incidence rate of HM was 2.08/1000 deliveries and 1.48/1000 viable conceptions. A significant temporal increase in the incidence rate of HM, as well as in the total number and proportion of PHM, was seen. Among 956 women with HM, 77 (8%) progressed into post-molar GTN. There was evidence of a slight, but non-significant increase in the risk of malignancy in the two last five-year periods under study.

Conclusions: We found evidence of a significant temporal increase in the incidence rate of HM, which could not fully be explained by an increase in maternal age over time. Changes in diagnostic methods probably contributed to the increased incidence rate of PHM. The risk of post-molar GTN remained constant over time.

ARTICLE HISTORY
Received 24 October 2017
Accepted 6 February 2018

Introduction

Gestational trophoblastic disease (GTD) encompasses the pre-malignant hydatidiform mole (HM) and the malignant forms invasive mole, choriocarcinoma, placental site trophoblastic tumor and epithelioid trophoblastic tumor. The term gestational trophoblastic neoplasia (GTN) includes all the malignant forms [1–3]. HM can be divided into two morphologically and genetically different groups, complete (CHM) and partial hydatidiform mole (PHM) [4,5]. The risk of a post-molar GTN is approximately 15% after CHM and 1% following PHM [6–10].

The associations between increasing maternal age and the incidence of both HM and post-molar GTN are well established [11–14]. In Sweden, like in the rest of the western world, there is a marked trend of delayed childbearing to older age [15]. The mean age at first childbirth in Sweden increased from 26.3 to 28.9 years between 1990 and 2010. The trend in urban areas has been even more pronounced. In the Stockholm area, with a population of 2.2 million inhabitants, representing about one-fifth of the Swedish population, the mean age at first birth is on average two years higher, increasing from 28.3 years in 1990 to 31.2 years in 2010 [16].

Incidence rates of HM show wide geographic variations, with reported estimates ranging from 1/500–1000 pregnancies in Europe and North America to 1–12/1000 pregnancies in some areas of Asia and the Middle East [17,18]. More recent reports indicate a decreasing trend in Asia, while some European countries demonstrate an increasing rate of GTD over time [12,19–21]. Various methods have been used to determine incidence rates, precluding reliable international comparisons.

Since 1970, incidence rates of HM in Sweden have been estimated in three reports [22–24]. These reports are based on information from different population-based registers to identify molar conceptions, and different denominators have been used to calculate incidence rates, which make direct comparisons difficult (Table 1). Furthermore, a documented under-registration of GTD in the Swedish Cancer Register adds to the challenge to correctly determine incidence rates [24,25].

CONTACT Ulrika Joneborg ulrika.joneborg@sll.se Department of Women's and Children's Health, Division of Obstetrics and Gynaecology, Karolinska University Hospital/Institutet, Stockholm SE-171 76, Sweden

Table 1. Comparison of four Swedish studies on the incidence rate (IR) of HM.

	Ringertz et al., Sweden1958–1965	Flam et al., Stockholm 1975–1988	Salehi et al., Sweden 1973–2004	Joneborg et al, Stockholm 1991–2010
HM (*n*)	654	393	3844	956
IR (per 1000 deliveries)	0.74	1.46	1.20	2.08
IR (per 1000 viable conceptions)	0.64	0.99	–	1.48
IR (per 1000 pregnancies)	–	0.9	–	–
Information Cancer Register	Yes	Yes	Yes	Yes
Information In-Patient Register	–	Yes	Yes	Yes
Information SymPathy	–	–	–	Yes
Post-molar GTN	3.5	5.9	–	8.1

The aim of this study was to investigate temporal trends in the incidence rates of HM and post-molar GTN in Stockholm County. For this purpose, we retrieved information from the regional pathology database, in addition to the regional and national registers used in the previous studies, to avoid the problem of under-registration of molar conceptions. The number of births as well as viable conceptions (births and pregnancy terminations) was used to optimize the estimation of the risk of HM at different ages.

Material and methods

The data was extracted from five regional or national registers.

Regional Cancer Register (RCR)

Since the start of the Swedish Cancer Register (SCR) in 1958, reporting of all newly diagnosed cancer cases has been mandated by law. Reports are made separately by clinicians and pathologists or cytologists [26]. Some pre-malignant conditions, including HM, are also reported to the SCR, but earlier studies have shown an under-reporting of approximately 20% of all cases of HM [24,25]. The SCR does not differentiate between the two subtypes of molar pregnancies, nor does it contain information on recurrences, treatment data or cases of post-molar GTN. The SCR is based on information retrieved from six regional cancer registers. The RCR of Stockholm-Gotland was used to identify women diagnosed with HM in Stockholm County, using the International Classification of Diseases (ICD)-7: 173 and pathoanatomical diagnosis (PAD): code 801 for HM.

Regional pathology data base – SymPathy

There is no nationwide central pathology register in Sweden. The pathology database SymPathy (Tieto AB, Malmö, Sweden) contains information on results reported by pathology departments at the five regional and university hospitals with gynaecological in-patient and emergency wards in Stockholm County. Information in the SymPathy database distinguishes between CHM and PHM, but does not contain information on cases of post-molar GTN, since this diagnosis is based on criteria rather than histopathology. Application of ancillary immunohistochemical techniques (mainly antibody p57) has been routinely in use in primary molar diagnosis at the main pathology departments in Stockholm since 2003, while cytometry for DNA ploidy has been reserved to the Karolinska University Hospital.

The SymPathy database was used to identify women with a diagnosis of CHM and PHM, using the Systematized Nomenclature of Medicine (SNOMED): m91000 (CHM), m91001 (invasive mole) and m91030 (PHM).

Karolinska University Hospital Discharge Register

The Karolinska University Hospital in Stockholm is the referral center for all women with GTN in Stockholm County and neighboring regions. The Karolinska University Hospital Discharge Register was used to identify women with a diagnosis of post-molar GTN, using discharge codes ICD-9: (236.1, 181) and ICD-10: (D39.2A, C58.9) for invasive mole and choriocarcinoma.

The Swedish Medical Birth Register (MBR)

Established in 1973, the Swedish MBR holds records of more than 98% of all births in Sweden with information on maternal characteristics, reproductive history and complications during pregnancy, delivery and the neonatal period [27]. Births were registered from gestational week 28 until 2008, and since then from gestational week 22. For the purpose of the present study, all deliveries in Stockholm between 1991 and 2010 were identified in the MBR.

Swedish National Board of Health and Welfare

The current Swedish legislation on termination of pregnancy was passed in 1975, and permits termination of pregnancy at the request of the woman until the 18th week of gestation. Thereafter, termination of pregnancy can be granted under certain circumstances. The Swedish National Board of Health and Welfare holds descriptive statistics on all pregnancy terminations, including information on women's age, gestational age and method of termination. No personal identification is possible, precluding record linkage to other national registers. For the purpose of this study, we collected regional descriptive data on calendar year of pregnancy termination and maternal age.

Study population

All cases of HM registered in the Stockholm RCR and SymPathy system were retrieved for our cohort. The hospital discharge register of the Karolinska University Hospital was used to identify women with post-molar GTN. Information on deliveries was retrieved from the MBR and information on the number of pregnancy terminations from the Swedish National Board of Health and Welfare. The incidence of HM was calculated by the number of deliveries as well as viable conceptions, and reported per 1000 births and per 1000 viable conceptions. The number of deliveries was defined as the number of women giving birth, including stillbirths and counting multiple births as one delivery. Viable conceptions were defined as the number of deliveries and pregnancy terminations. The cohort of women with a diagnosis of HM was stratified into seven age groups (<20, 20–24, 25–29, 30–34, 35–39, 40–44 and ≥45), and into the subgroups CHM and PHM for additional information. For assessment of temporal trends, the study period was stratified into four 5-year intervals, 1991–1995, 1996–2000, 2001–2005 and 2006–2010. The incidence of post-molar GTN was defined as the number of post-molar GTN divided by the number of HM at risk during each period.

Table 2. Demographics.

Period	HM (*n*)	Mean age (years)	Range	*p*
1991–1995	197	30.3	14.1–51.8	ref
1996–2000	199	30.3	16.5–55.3	n.s
2001–2005	254	32.4	14.3–57.8	$p < .01$
2006–2010	306	33.5	16.1–55.5	$p < .01$

Period	GTN (*n*)	Median age* (years)	Range
1991–1995	15	34.8	21.6–51.8
1996–2000	12	30.6	24.2–55.3
2001–2005	25	30.1	21.7–53.5
2006–2010	25	39.0	19.4–55.5

*Median age chosen and no statistical tests performed due to small numbers.

Statistical analysis

Student's *t*-test was used to compare means and Fisher's exact test was used to analyse the proportion of women progressing into post-molar GTN. Incidence rates of HM were calculated for each five-year time period between 1991 and 2010. In order to assess whether the incidence rates were confounded by different age distributions across time periods, age-standardised incidence rates were also calculated in a sensitivity analysis. Poisson regression models were used to compare age-specific incidence rates, by interpreting incidence rate ratios (IRR) as relative risks of HM, with the youngest women (<20 years) as the reference group. Poisson models were stratified by time period. Logistic regression was employed to analyse odds ratios (OR) of GTN after CHM, adjusting for time period and age, using the lowest level of each covariate as the reference category. The two-sided significance level was set to $\alpha = 0.05$ in all analyses.

Results

A total of 956 women with HM were identified in the RCR and the SymPathy database between 1991 and 2010. The Karolinska University Hospital Discharge Register yielded 102 women with post-molar GTN. After excluding 25 women referred for treatment from other regions, we identified 77 women subsequently diagnosed with post-molar GTN from the Stockholm County cohort of HM. The demographics are shown in Table 2. There was a significant temporal increase in age at diagnosis of HM. Figure 1 illustrates the change in age distribution between time periods.

We identified 460,635 deliveries and 184,901 pregnancy terminations (645,536 viable conceptions in total) between 1991 and 2010. Because of missing data on maternal age, 2270 deliveries and 54 terminations were excluded from the age-stratified analyses, but were included in the overall analyses.

For the entire period under study, the incidence of HM was 2.08/1000 deliveries and 1.48/1000 viable conceptions.

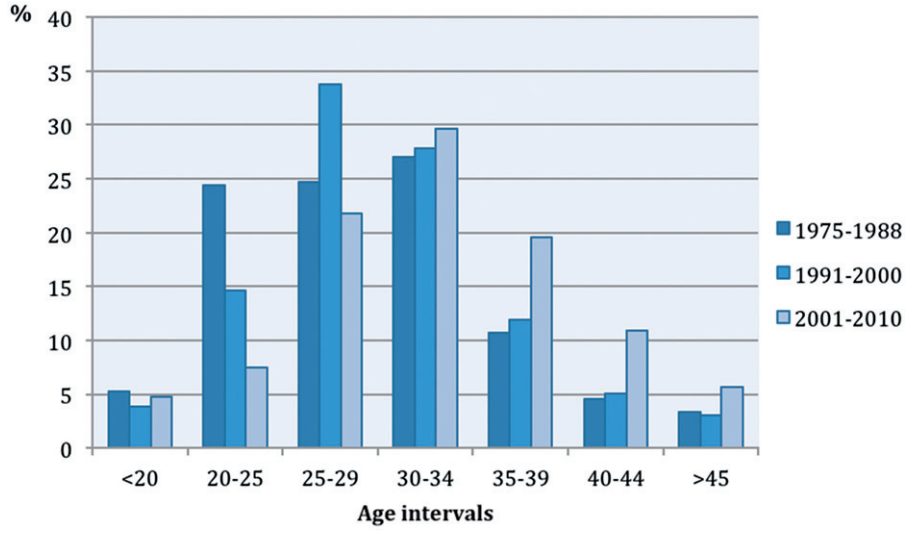

Figure 1. Temporal changes in the age distribution of women with HM. Data 1975–1988 from Flam et al. [23].

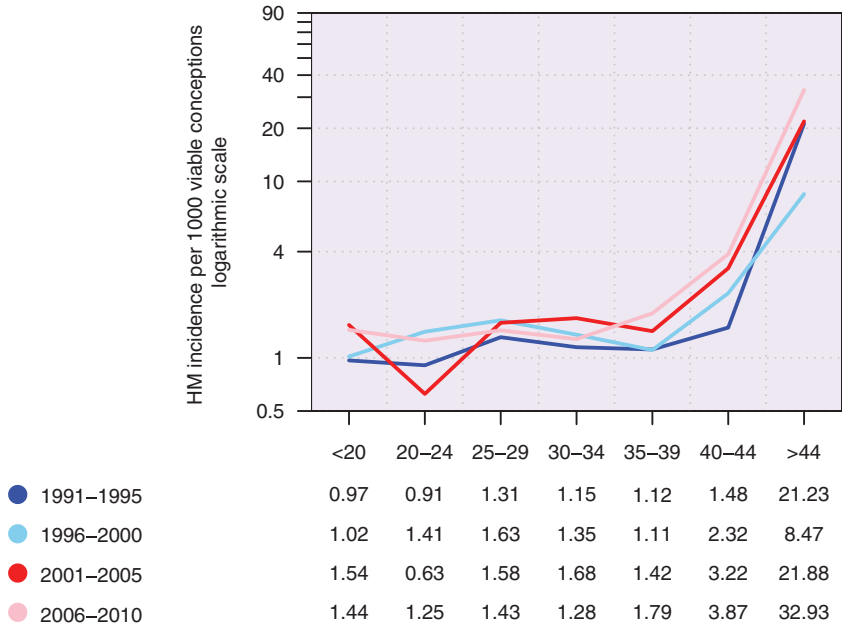

Figure 2. Age specific incidence of HM per 1000 viable conceptions, logarithmic scale.

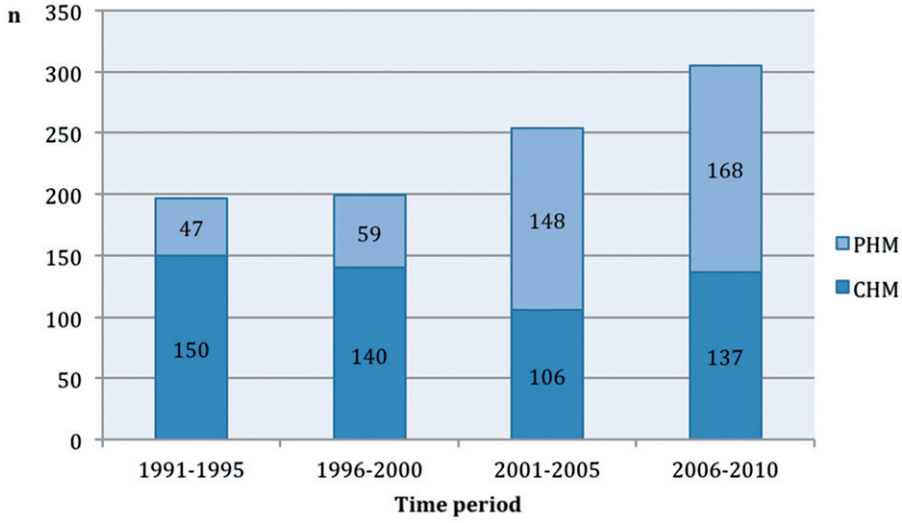

Figure 3. Temporal changes of CHM and PHM.

After stratifying into five-year intervals, the incidence increased from 1.66/1000 deliveries and 1.21/1000 viable conceptions in 1991–1995 to 2.31/1000 deliveries and 1.66/1000 viable conceptions in 2006–2010 ($p < .01$). The highest incidence was observed in women above the age of 40. Compared to younger women, women of 45 years and above demonstrated a considerably higher risk of a molar conception, 1 in 17 deliveries and 1 in 43 viable conceptions. The age-specific incidence of HM is illustrated in Figure 2.

In the cohort of women with HM, 533 were diagnosed with a CHM and 422 with a PHM. One HM was not possible to subtype, and was included in the analyses of HM overall, but was excluded in the subgroup analyses of CHM and PHM. The temporal change in the proportion of CHM and PHM is shown in Figure 3 ($p < .01$).

The overall risk of post-molar GTN was 8%. The risk varied between 6% and 10%, with some evidence of a trend of a higher risk in the two later five-year periods. The proportion of progression into post-molar GTN after CHM and PHM was 13% and 2%, respectively. The number of GTN was small and the rates varied, but did not change significantly over time, except in the years 2001–2005, when the proportion of post-molar GTN after a CHM was significantly higher and reached 21%.

The proportion of HM reported to the Cancer Register increased steadily over time, from 55% (109/197) in 1991–1995 to 84% (246/306) in 2006–2010.

Discussion

Main findings

This population-based cohort study demonstrates a continuous temporal increase in the incidence rate of HM. While both the mean maternal age at first child, and the mean age at diagnosis of a HM increased markedly during the study period, as well as compared to earlier assessment in the

same population [23], these changes could not fully explain the increased incidence rate of HM. There was also a significant increase in the absolute number as well as proportion of PHM, which may have contributed to the increased incidence rate of molar pregnancies. A trend towards an increased risk of post-molar GTN was seen, which, however, did not reach statistical significance.

Strengths and limitations

Strengths of the present study included its comprehensive approach using data from several different population based register sources. By use of record linkages, a virtually complete follow-up was ensured, including the development of post-molar GTN. Estimates of incidence rates were based not only on number of births, but also viable conceptions, giving a more accurate estimate of the risk of HM at different ages

Several weaknesses need mentioning. Since this study was restricted to information retrieved from registers, no re-evaluations of pathological slides were performed. Thus, it cannot be excluded that some women recorded with a molar pregnancy were misdiagnosed. This could possibly explain the difference in the proportion of CHM and PHM between the earliest and latest five-year intervals under study.

Another potential weakness was that the study was restricted to women reported with HM and post-molar GTN to the available registers. It is possible that a few HM were neither reported to the Cancer Register, nor diagnosed at a pathology department connected with the SymPathy system.

Interpretation

World-wide reports of incidence rates of molar pregnancies have shown marked geographic and ethnic differences, with sometimes 10–20 fold variations. The highest rates have been reported in the Asian population [17,18,28]. Discrepancies in the use of hospital-based or population-based data can partly explain the variations. Furthermore, there have been differences in the use of denominator to calculate incidence rates. Whether a HM will develop or not will be determined at the time of conception. The ideal denominator would therefore be all conceptions. Since it is not possible to calculate total conceptions in a population, reported estimates of incidence rates have been based on known pregnancies, viable conceptions, total births and live births, which may further explain observed differences in incidence rates. Estimating the incidence of HM using births as the reference will over-estimate the risk in the extremes of reproductive age, since a higher proportion of pregnancies in very young and older women will end in pregnancy terminations or miscarriages.

The estimated overall incidence rate of HM of 2.08/1000 deliveries and 1.48/1000 viable conceptions in our study is consistent with reports from England, a region with an established central registration of all women with a diagnosis of GTD [12]. However, our estimates are higher than those reported from the Netherlands, Finland and Denmark, where rates have ranged from 1–1.42/1000 deliveries and 1.1/1000 pregnancies [19,29,30]. Corroborating results from previous Swedish studies [24,25], we observed an under-registration of HM to the SCR. In the present study, we combined information from all available register resources of HM in Stockholm County, including the pathology diagnostic database. Altogether, this is likely to have contributed to the higher incidence rate of HM observed in our cohort compared to the previous Swedish studies, which were based on data from central registers only (Table 1). It may also explain some of the differences compared to the reports from the geographically close countries Denmark and Finland, where data from national registers were used. Of special note is that Danish and Finnish estimates of incidence rates are comparable to those reported by previous Swedish studies based on similar data sources.

Our finding of a temporal increase of HM may partly be explained by increasing maternal age. The overall incidence of HM related to viable conceptions increased from 1 in 833 to 1 in 595 between the first and last five-year period of study. At the same time, the number of viable conceptions in the older age groups 40–44 and $\geq$45 increased by 82% and 57%, respectively. The absolute number of HM also increased in the age group 40 and above, and in the last five-year period almost one-third (28%) of all cases of CHM occurred in women of age 40 and above. A temporal increase in the incidence rate of HM has also been reported from England and the Netherlands [12,19], while other countries have demonstrated stable or decreasing rates [20,21,29,31].

There was also a significant increase in the absolute number as well as proportion of PHM, which probably contributed to the increased incidence rate of molar pregnancies. It is difficult to find a plausible biological explanation for this increase of PHM, which is more likely to depend on external factors, such as diagnostic methodology, increased usage of complimentary diagnostic methods and increased use of early obstetric ultrasound for detection and sequential diagnosis of pathological pregnancies. The distinction between the subtypes of HM, and also non-molar specimens, can be difficult, especially in early gestation, when the molar morphology has not yet fully developed. The addition of different ancillary diagnostic methods, based on the genetic constitution of HM, has increased the diagnostic accuracy. During the period under study, different complimentary diagnostic methods were introduced, which may have led to a different distribution of CHM and PHM in the earlier study periods compared to more recent time. This reflects a difficulty in epidemiological studies, and in the future, much of our understanding of gestational trophoblastic disease may be based on molecular biology. With the continuous development of molecular methods and tumour sequencing, it may even be possible to diagnose a gestational trophoblastic tumour, and predict the risk of malignant transformation, by identifying its specific genetic features.

We found evidence of an overall, but non-significant, trend towards an increased risk of post-molar GTN. The risk of malignant progression overall was 8%, which is low compared to most other reports, but consistent with recent data from England and previous Swedish data [13,23]. A reason for the relatively low risk of malignancy in our report may be the complete data acquisition of HM in the utilized registers. In the subgroup of CHM, a significant increase in malignant

progression between 2000 and 2005 was noted, and may be attributed to the relatively low number of CHM diagnosed this time period compared to the other three (Figure 2). The total number of CHM was constant during three of the four 5-year calendar periods, while the total number of PHM differed. However, during the 2000–2005 period, the total number of CHM dropped while the number of PHM increased. Since the complimentary diagnostic methods were not yet fully established, this might have led to an over-diagnosis of PHM in the group of early CHM, something which may have been corrected in the latest time period under study, when the pathology departments more fully had introduced the complimentary methods. Since CHM leads to GTN to a much higher extent than PHM, the low total number of CHM 2000–2005 might explain the higher rate of malignancy.

Conclusion

In conclusion, the incidence rate of HM in Stockholm County showed a significant temporal increase between 1991 and 2010, while the incidence rate of post-molar GTN remained constant. The absolute number and proportion of PHM also increased over time, which together with rising maternal age may have contributed to the increase in registered molar pregnancies. The observation of an increasing proportion of PHM in recent time periods is likely to reflect changes in diagnostic methodology and registration practices.

Disclosure statement

The authors have no disclosures of interests.

Ethical approval

The study was approved by the Research Ethics Committee at Karolinska Institutet, Stockholm, Sweden (Dnr 2010/242-31/1 and 2010/1408 32).

ORCID

Yasin Folkvaljon http://orcid.org/0000-0003-1735-721X

References

[1] Kim S. Epidemiology. In: Hancock B, Newlands ES, Berkowitz RS, editors. Gestational Trophoblastic Disease. London: Chapman & Hall; 1997. p. 27–42.
[2] Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. Lancet. 2010;376:717–729.
[3] Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstet Gynecol. 2010;203:531–539.
[4] Szulman AE, Surti U. The syndromes of hydatidiform mole. I. Cytogenetic and morphologic correlations. Am J Obstet Gynecol. 1978;131:665–671.
[5] Sebire NJ, Makrydimas G, Agnantis NJ, et al. Updated diagnostic criteria for partial and complete hydatidiform moles in early pregnancy. Anticancer Res. 2003;23:1723–1728.
[6] Bagshawe KD, Dent J, Webb J. Hydatidiform mole in England and Wales 1973–83. Lancet. 1986;2:673–677.
[7] Newlands E, editor. Presentation and management of persistent gestational trophoblastic disease and gestational trophoblastic tumors in the UK. London: Chapman&Hall; 1997.
[8] Seckl MJ, Fisher RA, Salerno G, et al. Choriocarcinoma and partial hydatidiform moles. Lancet. 2000;356:36–39.
[9] Hancock BW, Nazir K, Everard JE. Persistent gestational trophoblastic neoplasia after partial hydatidiform mole incidence and outcome. J Reprod Med. 2006;51:764–766.
[10] Golfier F, Raudrant D, Frappart L, et al. First epidemiological data from the French Trophoblastic Disease Reference Center. Am J Obstet Gynecol. 2007;196:172e1–175.
[11] Sebire NJ, Foskett M, Fisher RA, et al. Risk of partial and complete hydatidiform molar pregnancy in relation to maternal age. BJOG. 2002;109:99–102.
[12] Savage P, Williams J, Wong SL, et al. The demographics of molar pregnancies in England and Wales from 2000–2009. J Reprod Med. 2010;55:341–345.
[13] Savage PM, Sita-Lumsden A, Dickson S, et al. The relationship of maternal age to molar pregnancy incidence, risks for chemotherapy and subsequent pregnancy outcome. J Obstet Gynaecol. 2013;33:406–411.
[14] Altman AD, Bentley B, Murray S, et al. Maternal age-related rates of gestational trophoblastic disease. Obstet Gynecol. 2008;112(2 Pt 1):244–250.
[15] RCOG statement on later maternal age. Available from: www.rcog.org.uk/en/news/rcog-statement-on-later-maternal-age/2009.
[16] Statistics Sweden. Available from: www.statistikdatabasen.scb.se; 2014.
[17] Altieri A, Franceschi S, Ferlay J, et al. Epidemiology and aetiology of gestational trophoblastic diseases. Lancet Oncol. 2003;4:670–678.
[18] Smith HO. Gestational trophoblastic disease epidemiology and trends. Clin Obstet Gynecol. 2003;46:541–556.
[19] Lybol C, Thomas CM, Bulten J, et al. Increase in the incidence of gestational trophoblastic disease in The Netherlands. Gynecol Oncol. 2011;121:334–338.
[20] Matsui H, Iitsuka Y, Yamazawa K, et al. Changes in the incidence of molar pregnancies. A population-based study in Chiba Prefecture and Japan between 1974 and 2000. Hum Reprod. 2003;18:172–175.
[21] Matsui H, Kihara M, Yamazawa K, et al. Recent changes of the incidence of complete and partial mole in Chiba prefecture. Gynecol Obstet Invest. 2007;63:7–10.
[22] Ringertz N. Hydatidiform mole, invasive mole and choriocarcinoma in Sweden 1958–1965. Acta Obstet Gynecol Scand. 1970;49:195–203.
[23] Flam F, Lundstrom-Lindstedt V, Rutqvist LE. Incidence of gestational trophoblastic disease in Stockholm County, 1975–1988. Eur J Epidemiol. 1992;8:173–177.
[24] Salehi S, Eloranta S, Johansson AL, et al. Reporting and incidence trends of hydatidiform mole in Sweden 1973–2004. Acta Oncol. 2011;50:367–372.
[25] Flam F, Rutqvist LE. Under-registration of gestational trophoblastic disease in the Swedish Cancer Registry. Eur J Epidemiol. 1992;8:683–686.
[26] Barlow L, Westergren K, Holmberg L, et al. The completeness of the Swedish Cancer Register: a sample survey for year 1998. Acta Oncol. 2009;48:27–33.
[27] Cnattingius S, Ericson A, Gunnarskog J, et al. A quality study of a medical birth registry. Scand J Soc Med. 1990;18:143–148.
[28] Tham BW, Everard JE, Tidy JA, et al. Gestational trophoblastic disease in the Asian population of Northern England and North Wales. BJOG. 2003;110:555–559.
[29] Loukovaara M, Pukkala E, Lehtovirta P, et al. Epidemiology of hydatidiform mole in Finland, 1975–2001. Eur J Gynaecol Oncol. 2005;26:207–208.
[30] Olsen JH, Mellemkjaer L, Gridley G, et al. Molar pregnancy and risk for cancer in women and their male partners. Am J Obstet Gynecol. 1999;181:630–634.
[31] Salerno A. The incidence of gestational trophoblastic disease in Italy: a multicenter survey. J Reprod Med. 2012;57:204–206.