Epidemiological study of complete and partial hydatidiform mole in Abu Dhabi: influence of maternal age and ethnic group

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Abstract

An unmatched case control study of molar pregnancy was carried out at this hospital between 1978 and 1987 to investigate the influence of maternal age and ethnic group on the incidence of complete and partial hydatidiform mole. The age specific incidence of complete mole was minimal between the ages of 30 and 34 years (relative risk 1), showed a minor peak in teenagers (relative risk 3.1, 95% confidence interval 0.5-1.4), and a major peak in those of 35 years and over. Between 35 and 39 years the relative risk was 2.5 (95% CI 0.2-1.0) and at 40 years or more the relative risk was 9.8 (95% CI 2.8-3.3). No age group showed a significantly increased risk of partial mole.

The women of Abu Dhabi had increased risks of both forms of molar pregnancy relative to women in Nottingham, England (relative risk 1): the risk of complete mole was increased threefold (95% CI 1.2-2.2) and that of partial mole twofold (95% CI 1.0-1.2). The increased risk of complete mole was greatest in Gulf Arabs (mainly Omanis and Yemenis) who had a sixfold increase in crude relative risk (95% CI 1.7-3.5). The increased risks of complete mole associated with maternal ethnic group remained after adjustment for maternal age distribution.

The incidence of hydatidiform mole has been studied extensively throughout the world,^{1,2} but only occasional investigations of its prevalence in multiethnic communities have been published.^{3,4} The population of Abu Dhabi forms such a community and its size has increased rapidly over the past two decades as a result of immigration associated with the development of the oil and gas industry. This has provided an opportunity to study the effects of maternal age and ethnic group on the incidence of hydatidiform mole in a community where almost all births take place in hospital.

Methods

The patients who presented with molar pregnancies at this hospital between 1978 and 1987 were retrospectively identified from the records in the pathology laboratory from 1978 to 1984 and then prospectively from 1984 to

1987. Three patients referred with a diagnosis of molar pregnancy from other hospitals were excluded from the study. The gross description of each mole was noted and the histological sections of all moles were reviewed by one of the authors. The diagnosis of molar pregnancy and classification as complete or partial were made according to the morphological criteria of Vassilakos⁵ and Szulman.⁶ Twenty four patients were excluded on morphological grounds. One patient was excluded because her tissue blocks and sections had been lost. The series comprised 116 complete moles and 27 partial ones.

A 1 in a 100 sample of the 70 259 births (live births plus still births) at this hospital between 1978 and 1987 was taken from the labour ward records for purposes of comparison. The sample comprised 697 mothers.

The birthplace and age of each molar and control patient were obtained from hospital records. Molar patients and controls were classified by ethnic group according to birthplace: UAE Arabs (born in any of the Emirates forming the United Arab Emirates), other Arabs (born in Egypt, Jordan, Palestine, Syria, Lebanon, and Iraq), Gulf Arabs (born in Bahrain, Kuwait, Oman, Saudi Arabia, and Yemen), Asians (born in India, Pakistan, Sri Lanka, and Bangladesh), Africans (born in Algeria, Tunisia, Somalia, Sudan, Ethiopia, Kenya, Tanzania, Zaire, and Nigeria), and others (born in Europe, the Americas, Japan, Philippines, Indonesia, and Iran).

We have assumed that all births in this hospital have the same distribution in respect of maternal age and ethnic group as the 1 in a 100 sample (table 1). The ethnic groups of three mothers and the ages of another two were unknown. The ethnic groups of 13 mothers were known, although their birthplaces were not: five were Asians, five were classified as other Arabs, there were two Africans and one a Gulf Arab. In estimating numbers of births such mothers have been assumed to follow the distribution of known cases in respect of the relevant variable.

Birthplace and age were known for all molar patients.

Results

We calculated the age specific incidence of complete and partial mole and estimated the relative risk (RR) with the 95% confidence interval (CI).⁷ The age specific incidence and RR for complete and partial mole are given in table 2.

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Table 1 Distribution of births at Al Corniche (1978–1987) according to maternal ethnic group and age

Maternal ethnic group	Maternal age (years)					Unknown	Total
	Under 20	20–24	25–29	30–34	Over 34		
UAE Arabs	16	28	26	16	18	—	104
Gulf Arabs	4	24	20 (1)*	11	4	—	63
Other Arabs	24 (3)	77 (2)	87	45	19	2	254
Asians	13	66 (1)	70 (2)	34 (2)	4	—	187
Africans	4	20 (1)	24	12 (1)	3	—	63
Others	3	5	7	8	—	—	23
Unknown	—	—	2	1	—	—	3
Total	64	220	236	127	48†	2	697

*Figures in parentheses refer to mothers of known ethnic group but unknown birthplace.

†This includes nine mothers over 39 years.

Table 2 Maternal age specific incidence and RR of complete and partial mole

Maternal age (years)	Numbers			Incidence per 1000 births		RR with 95% CI	
	Births*	Moles					
		Complete	Partial	Complete	Partial	Complete	Partial
Under 20	6470	20	1	3.09	0.15	3.1 (6.5–1.4)	1
20–24	22240	33	10	1.48	0.45	1.5 (2.9–0.7)	2.9 (23.2–0.4)
25–29	23858	31	12	1.30	0.50	1.3 (2.5–0.6)	3.3 [25.5–0.4]
30–34	12839	13	3	1.01	0.23	1	1.5 (14.8–0.2)
35–39	3942	10	1	2.54	0.25	2.5 (6.2–1.0)	1.6 (27.0–0.1)
Over 39	910	9	—	9.89	—	9.8 (28.9–3.3)	—
Total	70259	116	27	1.65	0.38		

*Estimated from a one in a 100 sample of births at Al Corniche Hospital.

Table 3 Incidence and crude RR of complete and partial mole according to maternal ethnic group

Maternal ethnic group	Numbers						
	Births*	Moles		Incidence per 1000 births		RR with 95% CI	
		Complete	Partial	Complete	Partial	Complete	Partial
British	102020	56	18	0.55	0.18	1	1
UAE Arabs	10529	20	—	1.90	—	3.5 (6.1–2.0)	—
Gulf Arabs	6378	21	2	3.29	0.31	6.1 [10.7–3.5]	1.8 (7.9–0.4)
Other Arabs	25714	33	8	1.28	0.31	2.4 (3.7–1.5)	1.8 (4.2–0.8)
Asians	18931	30	11	1.58	0.58	2.9 (4.7–1.8)	3.3 (7.2–1.5)
Africans	6378	7	4	1.10	0.63	2.0 (4.6–0.9)	3.6 (10.9–1.2)
Others	2329	5	2	—	—	—	—
Total at Al Corniche	70259	116	27	1.65	0.38	3.0 (4.2–2.2)	2.2 (4.0–1.2)

*Estimated from a one in a 100 sample of births at Al Corniche Hospital, except in the case of British births.⁸

We calculated the incidence of complete and partial mole for Arab, Asian, and African women and the crude RR for each by comparison with the incidence of complete and partial mole in Nottingham, England, between 1970 and 1981 inclusive.⁸ We calculated the age standardised RR for complete mole at this hospital for each ethnic group by reference to the age specific incidence of molar pregnancy in the Swedish population between 1958 and 1965 inclusive.⁹ The incidence and crude RR

for complete and partial mole are given in table 3; the age standardised risks for complete mole are given in tables 4 and 5.

Discussion

Many epidemiological studies of molar pregnancy have investigated the effects of geography and maternal race and age on its incidence.^{1,2} Some studies showing the highest incidences are considered now to have been flawed by diagnostic inaccuracy and selection bias, the latter being especially likely in hospital based surveys.^{1,2,8,10} The most accurate estimates are derived from population based studies in which diagnosis is cen-

Table 4 Calculation of age standardised RR for complete mole at Al Corniche (1978–1987) with reference to age specific incidence of molar pregnancy in Sweden (1958–1965)

Maternal age (years)	Number of births in Al Corniche (I)	Incidence of moles per 1000 births in Sweden (II)	Expected number of moles in Al Corniche (I × II)
Under 20	6470	0.82	5.31
20–24	22240	0.70	15.57
25–29	23858	0.66	15.75
30–34	12839	0.61	7.83
Over 34	4852	1.15	5.58
Total	70259	—	50.04 (E)
Observed number of complete moles in Al Corniche = 116 (O)			
Age standardised RR = O/E = 2.3 (95% CI 2.9–2.0)			

Table 5 Age standardised RR for complete mole according to maternal ethnic group

Maternal ethnic group	Observed number of complete moles in Al Corniche (O)	Expected number of moles in Al Corniche* (E)	Age standardised RR with 95% CI (O/E)
UAE Arabs	20	8.13	2.5 (3.8–1.5)
Gulf Arabs	21	4.52	4.6 (7.1–2.9)
Other Arabs	33	18.37	1.8 (2.5–1.2)
Asians	30	12.99	2.3 (3.3–1.6)
Africans	7	4.44	1.6 (3.2–0.6)

*Expected number of moles calculated as in Table 4.

Table 6 Birthplace and number of live births in Abu Dhabi medical district (1978-1987)

<i>Birthplace</i>	<i>Number of live births</i>
Al Corniche	69737
Other hospitals	32387
Home	3552
Total	105676

tralised or subject to histological review.^{8,10} The demonstration that moles could be divided into complete and partial forms cytogenetically and morphologically^{5,6} has added to the complexity of epidemiological studies as it is now necessary to incorporate this classification into such investigations.

In this study we tried to minimise diagnostic inaccuracy by reviewing the histology of all the moles and to avoid selection bias by excluding molar patients referred to this hospital from other maternity hospitals. During the period of our study 97% of live births in Abu Dhabi Medical District took place in hospital, two thirds of them in this hospital (personal communication, Dr S M Balasy, Director of Preventive Medicine, Abu Dhabi) (table 6).

Many earlier studies have shown a minor peak in the incidence of molar pregnancy in teenagers and a major one in women of 40 years or more.^{12 10 11} Our results show that this pattern is confined to complete mole and they confirm that the incidence of partial mole does not vary significantly with maternal age, which agrees with the finding of Jacobs *et al* in Hawaii.⁴

In assessing the influence of maternal ethnic group on the risk of molar pregnancy we compared our results with those of Womack and Elston in Nottingham because their findings are representative of those from Europe and North America.^{1 2 9 10} Our studies were partly contemporaneous, both are hospital based and express incidences in terms of births, and in both a histological review was carried out to confirm the diagnosis and to identify complete and partial moles separately. We found it necessary to calculate age standardised risks for complete mole because of the profound influence of maternal age on the incidence of this type of mole and we have done so by using the age specific incidence rates for hydatidiform mole in Sweden.⁹ The Swedish figures do not distinguish between complete and partial mole but we have assumed that all the Swedish moles were complete ones, a conservative assumption which has reduced the size of our age standardised risk estimates. Overall, the

mothers at our hospital show a two to threefold increase in the risk of complete mole and a twofold increase in that of partial mole compared with Europeans, but these figures conceal wide variations in risk depending on maternal ethnic group (table 3). The Gulf Arabs have the highest risk of complete mole, whether this is estimated by the unadjusted or the age standardised method. Ninety per cent (57/63) of Gulf Arab mothers in our sample of births were Omani or Yemeni, and all the complete moles in Gulf Arab women were from Omani or Yemeni patients. The incidence and RR of complete mole among the Omanis and Yemenis are given in table 7.

Published reports of the incidence of molar pregnancy show wide geographical variation which is almost inextricably linked to racial differences. The highest rates have been found in the East and the lowest in the West, the range extending from 4-10 per 1000 deliveries in the Far East, Indonesia, and Iran to about 1 per 1000 in England, Europe, and North America.¹² These values suggest a 10-fold difference in the incidence of mole between East and West, but more recent population based studies from the Far East show rates which approximate more closely to Western ones and to our own estimates. In one such study Ishizuka in Japan calculated an incidence of 2.87 moles per 1000 live births¹² which is in keeping with a three to fourfold increase in risk compared with that of the West. McCorrison made an early attempt at separating the influences of geography and maternal race on the incidence of mole in Honolulu, a multiracial city, and he found that a disproportionately large number of moles occurred in Orientals (Japanese, Chinese, and Filipino) compared with Caucasians or ethnic Hawaiians.³ Such apparently racial differences are not confined to the East; Hayashi investigated racial and geographical differences in the continental United States.¹⁰ He has shown that after standardising for maternal race and age the Rocky Mountain states have an incidence of mole two to six times greater than those found along parts of the Eastern seaboard and the lower Mississippi. He also found that the incidence of mole in whites was twice that in blacks.

There are few studies of the incidence of molar pregnancy in Arabs but that by Ghali in Baghdad showed an incidence of 3.62 moles per 1000 deliveries¹³ which is very similar to that found among the Gulf Arabs in Abu Dhabi. Matalon and Modan showed that the incidence of mole in Jewish women living in

Table 7 Distribution of Omani and Yemeni births by maternal age and calculation of RR for complete mole

Maternal age (years)	Numbers in 1% sample	
Under 20	4	<p>Observed number of complete moles = 21 (O)</p> <p>Incidence = 3.64 per 1000 births</p> <p>Crude RR = 6.7 (95% CI 11.8-3.8)</p> <p>Expected number of moles* = 4.17 (E)</p> <p>Age standardised RR = O/E</p> <p>= 5.0 (95% CI 7.7-3.1)</p>
20-24	22	
25-29	16	
30-34	11	
Over 34	4	
Total	57	

*Expected number of moles calculated as in table 4.

Israel was 0.77 per 1000 live births,¹⁴ a figure closer to that found in Europeans than to that seen in their Arab neighbours. Reddy and Rao have published figures for the incidence of mole in India (2.17 per 1000 pregnancies)¹⁵ which are closely similar to our findings among Asians living in Abu Dhabi.

Earlier studies of molar pregnancy in Africa have described rates ranging from 1.0 to 5.8 per 1000 deliveries.¹² Our findings are closer to the lower end of this range but should be viewed with caution as our African patients are exceptionally heterogeneous and include women from North Africa, West Africa, East Africa and the upper Nile.

The causes of the geographical, racial, and age related variations in the incidence of hydatidiform mole are unknown. Molar pregnancy may progress to choriocarcinoma,¹⁶ and Bracken has reviewed the possible role of some environmental agents and mutagens as risk factors for both conditions.¹ Two of the ethnic groups in the present study who have been shown to have increased risks of complete mole have habits which are almost unique, the Asians chew betel nut mixtures (paan) and many Gulf Arabs chew the leaves of *Catha edulis* (qat or khat). The alkaloids and tannins of betel nut are known mutagens,¹⁷ and it is possible that qat, too, releases mutagens into the saliva.¹⁸⁻²⁰ It is illegal to possess either drug in the Emirates, but investigation of possible associations with molar pregnancy might be worth while where their use is legal and common—India in the case of paan and Yemen or Ethiopia for qat.

- 1 Bracken MB. Incidence and aetiology of hydatidiform mole: an epidemiological review. *Br J Obstet Gynaecol* 1987;94:1123-35.
- 2 Grimes DA. Epidemiology of gestational trophoblastic disease. *Am J Obstet Gynecol* 1984;150:309-18.
- 3 McCorriston CC. Racial incidence of hydatidiform mole. A study in a contained polyracial community. *Am J Obstet Gynecol* 1968;101:377-82.
- 4 Jacobs PA, Hunt PA, Maatsuura JS, Wilson CC, Szulman AE. Complete and partial hydatidiform mole in Hawaii: cytogenetics, morphology and epidemiology. *Br J Obstet Gynaecol* 1982;89:258-66.
- 5 Vassilakos P, Riotton G, Kajii T. Hydatidiform mole: two entities. A morphologic and cytogenetic study with some clinical considerations. *Am J Obstet Gynecol* 1977;127:167-70.
- 6 Szulman AE, Surti U. The syndromes of hydatidiform mole. II. Morphologic evolution of the complete and partial mole. *Am J Obstet Gynecol* 1978;132:20-7.
- 7 Morris JA, Gardner MJ. Calculating confidence intervals for relative risks (odds ratios) and standardised ratios and rates. *Br Med J* 1988;296:1313-6.
- 8 Womack C, Elston CW. Hydatidiform mole in Nottingham: a 12 year retrospective epidemiological and morphological study. *Placenta* 1985;6:93-105.
- 9 Ringertz N. Hydatidiform mole, invasive mole and choriocarcinoma in Sweden 1958-1965. *Acta Obstet Gynecol Scand* 1970;49:195-203.
- 10 Kenji Hayashi, Bracken MB, Freeman DH, Hellenbrand K. Hydatidiform mole in United States (1970-1977): a statistical and theoretical analysis. *Am J Epidemiol* 1982;115:67-77.
- 11 Yen S, MacMahon B. Epidemiologic features of trophoblastic disease. *Am J Obstet Gynecol* 1968;101:126-32.
- 12 Ishizuka N. Studies on trophoblastic neoplasia. *Gann Monograph Canc Res* 1976;18:203-16.
- 13 Ghali FH. Incidence of trophoblastic neoplasia in Iraq. *Am J Obstet Gynecol* 1969;105:992-3.
- 14 Matalon M, Modan B. Epidemiologic aspects of hydatidiform mole in Israel. *Am J Obstet Gynecol* 1972;112:107-12.
- 15 Reddy DB, Rao N. Trophoblastic tumours. I. Hydatidiform mole. *Indian J Med Sci* 1969;23:527-37.
- 16 Bagshawe KD, Dent J, Webb J. Hydatidiform mole in England and Wales 1973-83. *Lancet* 1986;ii:673-7.
- 17 Panigrahi GB, Rao AR. Study of the genotoxicity of the total aqueous extract of betel nut and its tannin. *Carcinogenesis* 1986;7:37-9.
- 18 McKee CM. Medical and social aspects of qat in Yemen: a review. *J Roy Soc Med* 1987;80:762-5.
- 19 Brooke C. Khat (*Catha edulis*): Its production and trade in the Middle East. *Geographical J* 1960;126:52-9.
- 20 Report of a WHO Advisory Group. Review of the Pharmacology of khat. *Bulletin on Narcotics* 1980;32:83-93.