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Hydatidiform Mole in Kandang Kerbau Hospital – A 5-Year Review

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ABSTRACT

Background: This is a 5-year review of hydatidiform mole in a major maternity hospital.

Patients: A total of 75 patients were studied, with 35 cases of complete hydatidiform mole and 40 cases of partial hydatidiform mole.

Results: The annual incidence of hydatidiform mole was between 1 in 1,601 deliveries and 1 in 721 deliveries. The racial distribution was higher among the Malay and Indian population. Pre-operative diagnosis was made in 53.3% of the cases. Per vaginal bleeding was the main presenting complaint in 89.3% of cases. All patients were treated with vacuum aspiration. All patients with partial hydatidiform mole had spontaneous remission after vacuum aspiration. Three patients with complete mole required chemotherapy. Methotrexate was used. There was a significant number of patients who did not practise contraception in the initial remission period after vacuum aspiration.

Conclusion: Education of these patients is necessary. Prognosis of patients with hydatidiform mole is good with proper follow-up. Setting up of a National Trophoblastic Centre is recommended.

Keywords: hydatidiform mole, vacuum aspiration, prognosis

INTRODUCTION

Hydatidiform mole was first reported in the 6th century. Curry et al[1] described it as a pregnancy usually lacking an intact foetus, in which the placental villi were characterised by oedema and loss of vasculature, and showing varying degrees of trophoblastic proliferation.

Hydatidiform mole may be partial or complete. Its aetiology remains an enigma and its genesis is still uncertain.

Hydatidiform mole is unique among human tumours in its acute oncogenesis and the extremely short interval between the development of the disease and its diagnosis. Sonographic diagnosis and hormonal follow-up have been crucial.

This study looks at the epidemiology and management of patients with hydatidiform mole in a major maternity hospital in Singapore over a 5-year period, from 1988 to 1992. Singapore's population is multi-racial and is made up mainly of Chinese, Malays and Indians.

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MATERIALS AND METHODS

This is a retrospective study of cases of hydatidiform moles seen from 1 January 1988 to 31 December 1992 in Kandang Kerbau Hospital (KKH). Cases were identified through the records of names with the pathological diagnosis of hydatidiform mole, kept at the Women Oncology Centre in the hospital. The case records were then retrieved from the Medical Records Office and the data analysed.

All 75 patients included in the report had serial serum HCG analyses done. Patients with hydatidiform mole were considered to have entered spontaneous remission after evacuation of the molar pregnancies when the HCG levels become undetectable and remained so on follow-up assays.

RESULTS

There were 75 cases of hydatidiform mole from 1988 to 1992.

Incidence

Table I shows the annual incidence for the period 1988 to 1992.

Age distribution

The ages ranged from 17 to 43, with the most number of patients in this age group. Forty-eight patients belonged to the 25 to 34 years category (Fig 1) with only 3 patients (4%) less than 20 years of age and 15 (20%) more than 35 years old.

Racial distribution

The race distribution of patients with hydatidiform mole among the main racial groups in KKH is shown in Fig 2.

There was a proportionately higher number of Malays and Indians with hydatidiform mole in this

Table I – Annual incidence of hydatidiform mole in KKH (n = 75)

Year	Hydatidiform mole cases	Total deliveries	Incidence
1988	9	14,417	1 in 1,601
1989	12	12,291	1 in 1,024
1990	19	13,714	1 in 721
1991	18	14,730	1 in 818
1992	17	15,364	1 in 904

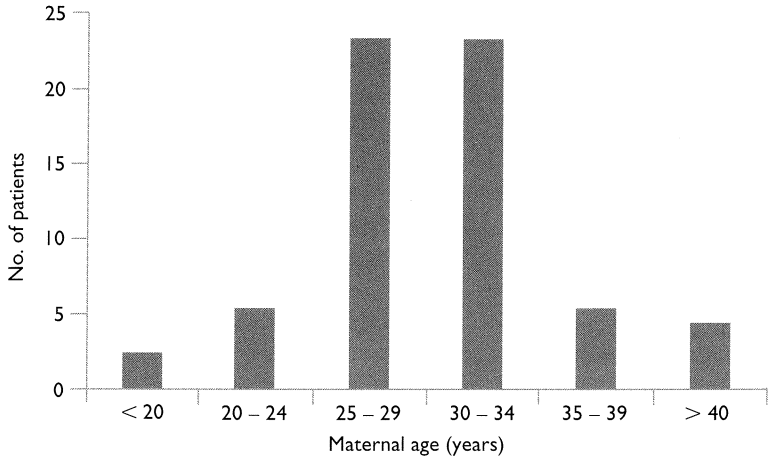

Fig 1 – Age distribution of patients with hydatidiform mole in KKH (1988 – 1992).

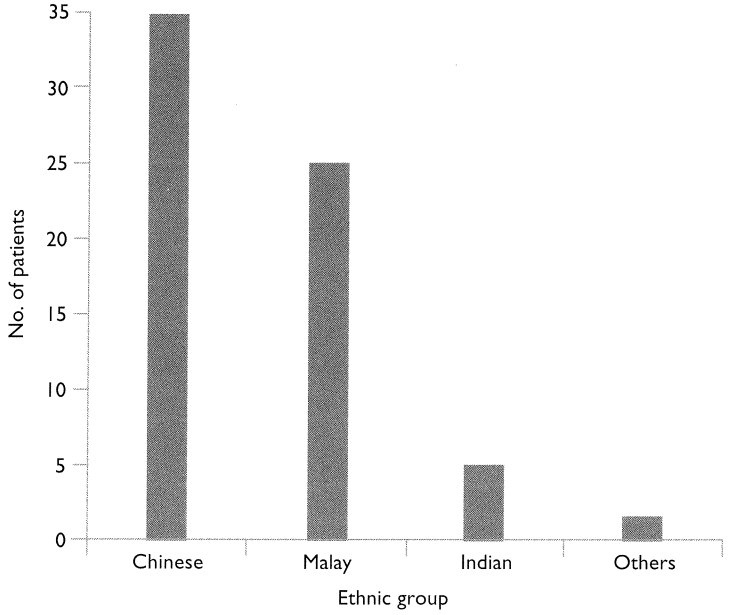

Fig 2 – Racial distribution of patients with hydatidiform mole in KKH (1988 – 1992).

study as compared with their proportion in the general population (Table II). The Malay population which constitutes 12% of the general population, accounted for 36% of patients with hydatidiform mole in this study, and the Indian population which constitutes 9% of the general population, accounted for 13.3% of patients with hydatidiform mole (Fig 3).

Parity

There was an equal proportion of patients in the nulliparous, para 1 and 2 groups. They made up the majority (Fig 4) of patients studied.

Presentation

Bleeding per vaginum was the most common presentation, occurring in 89.3% of the cases (Table III). All patients with symptoms had bleeding per vaginum. Of the 8 asymptomatic patients, molar pregnancy was discovered after a termination of pregnancy by routine histologic examination.

Table II – Racial distribution of patients with hydatidiform mole in KKH (1988 – 1992)

Race	Proportion with hydatidiform mole (%)	Proportion in population (%)
Chinese	46.7	76
Malay	36.0	12
Indian	13.3	9
Other races	4.0	3

Table III – Presenting signs and symptoms of patients with hydatidiform mole

Symptoms	No. of patients (n = 75)	%
Bleeding	67	89.3
Pain	8	10.7
Nausea/vomiting	4	5.3
None (Post-TOP)	8	10.7

Gestation and spontaneous remission

The period of amenorrhoea at diagnosis ranged from 6 to 34 weeks, with a mean of 12.4 weeks. The 10 – 15 weeks of amenorrhoea group was the most common group, making up 54.7% of the cases (Table IV).

Spontaneous remission after vacuum aspiration occurred in all but 3 patients, giving a spontaneous remission rate of 96%. Two of these cases were from the 16 – 20 weeks group and 1 from the 10 – 15 weeks group (at 14 weeks) (Table IV). All patients diagnosed to have hydatidiform mole at gestation less than 14 weeks had spontaneous remission after vacuum aspiration.

Histological types

In our study, there were 35 cases of complete mole and 40 cases of partial mole.

The 8 patients discovered to have molar pregnancy after termination of pregnancy for social reasons had partial hydatidiform mole on routine histological examination.

Forty (53.3%) patients were diagnosed to have molar pregnancy before evacuation of uterus. Of these, 30 had complete hydatidiform mole and 10 had partial hydatidiform mole. All diagnoses were made by ultrasonography.

Twenty-five patients did not have a pre-operative diagnosis of molar pregnancy. Six cases were diagnosed to have missed abortion on ultrasonography. All these 6 cases were found to have partial hydatidiform mole. The remaining 19 cases were diagnosed to have incomplete abortion.

All patients with hydatidiform mole, including the cases for termination of pregnancy had evacuation of uterus by vacuum aspiration. All cases diagnosed pre-operatively had intravenous syntocinon 30 units "cover" intraoperatively and a gentle but thorough check curettage performed after aspiration. No major complications were encountered during vacuum aspiration.

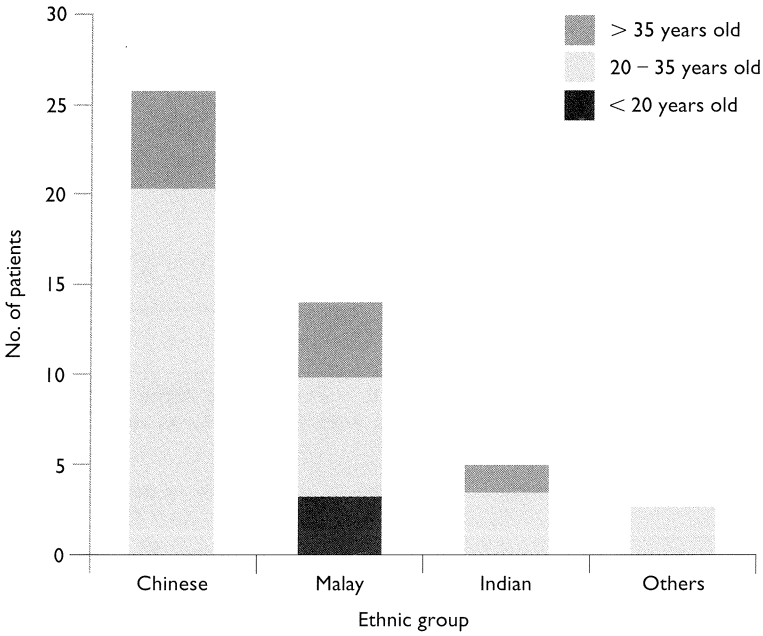

Fig 3 – Age and race distribution of patients with hydatidiform mole

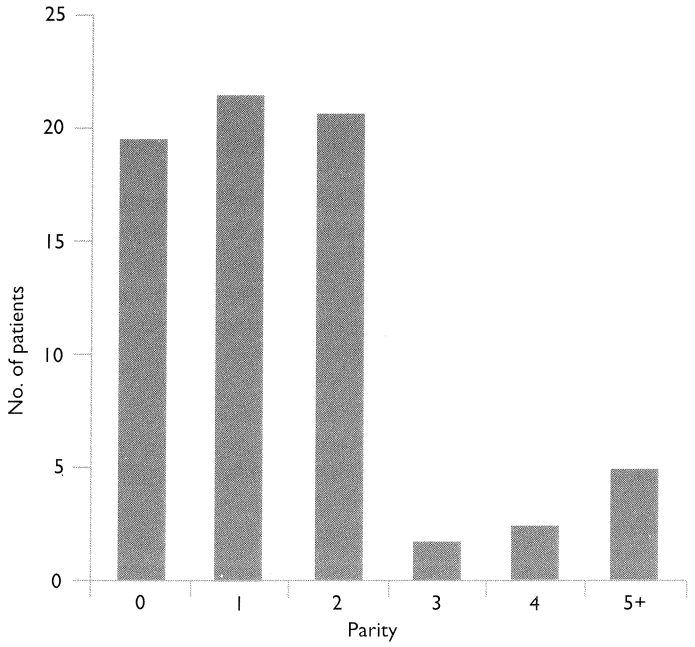

Fig 4 – Parity distribution of patients with hydatidiform mole.

Table IV – Gestation and spontaneous remission after vacuum aspiration in patients with hydatidiform mole

Period of amenorrhoea (weeks)	Number of patients with molar pregnancy	Number of patients with spontaneous remission after vacuum aspiration
< 10	19	19
10 – 15	41	40
16 – 20	8	6
> 20	7	7
Total	75	72 (96%)

A comparison of spontaneous remission and HCG levels between partial and complete hydatidiform mole is shown in Table V.

The gestation at diagnosis for complete hydatidiform mole ranged from 8 to 34 weeks with a mean of 14.8 weeks, and that of partial hydatidiform mole ranged from 6 to 24 weeks, with a mean of 11.8 weeks.

Chemotherapy

Three cases of complete hydatidiform moles had persistently high levels of HCG even after re-evacuation. They were in the low risk group and each was given 6 courses of intramuscular Methotrexate. There was a 100% response to treatment after 3 courses of Methotrexate (50 mg) and an additional 3 courses were given after normalisation of serum HCG levels (Table VI). Metastatic disease was not found.

Contraception

The condom was the only form of contraception used by the patients after evacuation of the uterus and up to 6 months after remission. Data on the number of patients practising contraception was inadequate, but at least 10 patients did not practise any form of contraception.

DISCUSSION

Reports from previous studies have shown that hydatidiform mole is more prevalent in Asia, West Africa and Latin America. The annual incidence of hydatidiform mole in our study ranged from 1 in 721 deliveries to 1 in 1,601 deliveries. If we were to look at the latest 3 years, the incidence would be 1 in 814 deliveries. This figure has remained fairly constant in the last 2 decades.

Djamhoer[2] reported that many experts agree that the risk of having hydatidiform mole is higher in pregnancies under 20 and above 35 years of age, with a progressive increase after 40 years. In our study, only 3 patients (4%) were less than 20 years old and 15 (20%) above 35 years old. The low incidence of hydatidiform mole among teenagers in our study may be due to the fact that Singaporean women are marrying at a later age, and that age of first intercourse is generally higher than in the West. Hence in this study, there was no significant influence of age and parity on the incidence and clinical condition of remission.

In our study, we found a proportionately higher number of Indians and Malays with hydatidiform mole. Majority of the Malays and Indians are of a lower socio-economic status as compared with the Chinese in Singapore and one may draw a link between this and racial incidence of hydatidiform mole. However, this is a hospital-based study and Kandang Kerbau Hospital does see a higher proportion of Malay and Indian patients as compared with their population percentage. Teoh[3] reported that although a higher incidence in Negro and Jewish women in Rhode Island and in Orientals in Hawaii is reported, there is probably no real racial

Table V – Spontaneous remission and HCG levels in patients with hydatidiform mole

Hydatidiform mole	HCG range (IU/L)	Mean HCG (IU/L)	Spontaneous remission (%)	Number with spontaneous remission	
				1 – 2 months	> 2 months
Partial * (n = 32)	15 – 647,360	57,896	100	33 (82.5%)	7 (17.5%)
Complete (n = 35)	21 – 23,330,00	241,969	91.4	21 (60%)	11 (31.4%)

* 8 patients had gone into spontaneous remission when reviewed and had serum HCG level of zero

Table VI – Treatment with methotrexate in 3 patients with persistently raised HCG levels

Patient	A	B	C
Age	43	28	26
Race	Malay	Chinese	Chinese
Parity	1	0	4
Initial HCG level	62,826	137,030	23,330,00
Number of evacuations	2	2	3
Chemotherapy agent	methotrexate	methotrexate	methotrexate
Number of courses before HCG normalised	3	3	3
Response to chemotherapy	100%	100%	100%
Complications of chemotherapy	nil	nil	nil

predisposition to the disease because hydatidiform mole is equally common in many different races, such as Arabs, Japanese and Mexicans.

Bleeding per vaginum was the most common presentation (89.3%) and occurred in all cases with signs or symptoms. This is consistent with other reported series. Other complications of pre-eclampsia, eclampsia, thyrotoxicosis and acute pulmonary oedema were not seen.

Ultrasonography is an important tool in the diagnosis of hydatidiform mole. Twenty-five patients without pre-operative diagnosis of hydatidiform mole had the diagnosis made after routine histological examination. Hence it is important to send all curettings from surgical evacuation for histologic confirmation.

The accuracy of ultrasonography in the diagnosis of hydatidiform mole is user-dependent and is in the region of 98% in good centres. Missed abortions and uterine myoma are important differential diagnosis. Because of the diffuse swelling of chorionic villi, complete moles produce a characteristic vesicular sonographic pattern. As for partial moles, Berkowitz[4] suggested that when:

1. a ratio of transverse to anteroposterior diameter of gestational sac greater than 1.5, and
2. cystic changes in the placenta were present, positive predictive values for partial mole was 87%.

A single HCG determination cannot be diagnostic of molar pregnancy even when the levels are high. Unusually high levels of HCG can occur in normal pregnancies.

Diagnosis of hydatidiform mole should be attempted pre-operatively as it aids in the management of the patient. Once the diagnosis of a mole is suspected, the patient should have her serum estimated for the level of HCG and a chest X-ray taken. Other pre-treatment work-up should include a complete blood count and a coagulation profile.

The treatment of choice of hydatidiform moles is vacuum aspiration, as was used in all our cases. Regardless of the size of the uterus, vacuum aspiration can be performed safely. Use of prostaglandin or oxytocin is not necessary prior to vacuum aspiration. Stone et al[5] reported an increased risk of gestational trophoblastic disease but Flam et al[6] reported no such increase associated with the use of prostaglandin and oxytocin. It is recommended that the mole be evacuated under "oxytoxic cover" (saline drip with 30 units of syntocinon running at 30 drops per minute at the time of evacuation). This minimises the two most common complications of haemorrhage and perforation. After vacuum aspiration, gentle but thorough sharp curettage should be done and the tissue from the decidua basalis studied separately.

The routine use of oxytoxics during vacuum aspiration was criticised on the grounds that they promoted embolisation of molar vesicles, thereby increasing the risk of residual molar tissues. In Singapore, the use of oxytoxics is routine and Teoh[7] found 14.8% incidence of residual trophoblastic disease, choriocarcinoma, or both, when oxytoxics were used, a value comparable to rates reported elsewhere, suggesting that the risk is not increased by oxytoxics. Stone and Bagshawe[5] reported an increased risk of persistent trophoblastic disease when other methods were used as the primary method of evacuation. Other methods of evacuation of the uterus that have been used include syntocinon drip induction, laminaria tent induction, dilatation and curettage, and hysterotomy.

If the patient is older than 40, and no longer desires to maintain fertility, hysterectomy may be the treatment option. Although hysterectomy eliminates the risks of local invasion, it does not prevent metastases, so serial HCG follow-up is still mandatory.

Overall spontaneous remission was seen in 96% of our cases in this study, with 100% spontaneous

remission in partial hydatidiform moles. This figure is higher than other studies which quoted figures of 80% – 85% spontaneous remission for hydatidiform moles. It is noted that the complete hydatidiform mole has higher HCG levels with a mean level more than 4 times that of the partial hydatidiform mole. Also, a higher proportion of the complete hydatidiform mole takes more than 2 months for spontaneous remission; more than twice that of partial mole. Complete moles are also found to be diagnosed at a later gestational age.

Hydatidiform mole has been identified as the most common precursor to choriocarcinoma; 40% – 80% of choriocarcinoma is reported to be preceded by it[8]. The risk of developing choriocarcinoma after a hydatidiform mole is about 1,000 times greater than a normal pregnancy. Histological examination of the mole itself provides a poor guide to the likelihood of malignant sequelae, and although subsequent curettage sometimes provides useful evidence, this is too infrequently the case to provide a general basis for management[9].

Three of our patients who had persistently raised HCG levels and who needed chemotherapy, had complete hydatidiform mole. This appears to suggest that there is a higher risk of complete hydatidiform mole progressing to gestational trophoblastic tumour, invasive mole or choriocarcinoma. It is known that 15% – 20% of complete hydatidiform moles develop invasive moles, choriocarcinoma or gestational trophoblastic tumours. Prognosis is directly related to interval between antecedent pregnancy and the onset of the above diseases. It has also been stated that 5% – 10% of partial mole may require chemotherapy on follow-up (gestational trophoblastic tumour).

A comparison is made with other studies with regards to persistent gestational trophoblastic tumour after partial mole (Table VII). As can be seen, there is generally a low risk of partial hydatidiform mole persisting and our series produced similar results as that of Vassilakos, Ohama and Lawler[4].

Table VII – Persistent gestational trophoblastic tumour after partial mole

Authors[4]	Patients with partial mole	Patients with persistent tumour
Stone and Bagshawe (1976)	194	5
Vassilakos et al (1977)	56	0
Szulman and Surti (1982)	49	2
Czernobilsky et al (1982)	25	1
Wong and Ma (1984)	35	4
Ohama et al (1986)	56	0
Bolis et al (1988)	86	2
Lawler et al (1991)	51	0
Berkowitz et al (1991)	310	17
Chong and Koh (1993) (current series)	40	0
Total	902	31 (3.4%)

Prophylactic chemotherapy remains a controversial issue. It may have a role in those patients with high risk factors (HCG levels > 100,000 IU/L, uterus larger than dates or large theca lutein cysts) and in those in whom hormonal follow-up is unavailable or unreliable.

Prophylactic chemotherapy has no place in the management protocol of molar pregnancy in Kandang Kerbau Hospital where adequate follow-up with serum HCG is possible. With implementation of close follow-up, any increase in HCG can be detected and managed immediately, with little difference to the prognosis. In this study, Methotrexate was used for low risk patients with persistently raised HCG levels with excellent results. There were no metastatic disease in our study. Methotrexate is known to be effective in bringing about retrogression of metastases in the chest and genital tract but metastases in the central nervous system are usually more resistant to this treatment[10].

Bagshawe et al[11] studied HCG regression pattern in 5,124 cases of hydatidiform mole. In 41% of the cases, HCG was undetectable after 56 days. (In this study, in 82.5% of partial moles and 60% of complete moles, HCG levels were undetectable after 2 months). He reported that the risk of recrudescance/chemotherapy if HCG is negative in less than 56 days, is zero, and if HCG is not negative by 56 days but is normal by after more than 6 months, the risk is 1 in 286.

The risk of second mole after complete or partial mole is 10-fold[12], and patients with repeat mole may ultimately have a normal pregnancy. The risk of subsequent pregnancy being molar is 1 in 76[13].

Patients are advised to use reliable contraception for at least 6 months after HCG has become negative. This is mainly to avoid confusion in the diagnosis of recrudescance of the disease based on a positive pregnancy test. In our study, there was a significant number of patients who did not practise any form of contraception even though the data is not complete. In this respect, education of the patient is important. Barrier methods have the least side effects, but compliance is the problem. Oral contraceptives are better because they are more effective in preventing pregnancy. Fear that oral contraceptives increase the risk of chemotherapy is unwarranted.

Close follow-up is important because of the risk of developing choriocarcinoma. This is especially so in the first 2 years and especially the first 6 months[14]. Hormonal follow-up with serial assessment of HCG is the most important aspect of post-treatment follow-up of moles. This is the best way to ensure remission of the disease. Chest X-rays are not indicated if there is a continuous decline in the level of the HCG but is the first investigation of choice if the level plateaus or rises, as the lungs are the most common sites for metastatic disease. In the presence of persistent bleeding during follow-up, a repeat curettage is indicated to exclude incomplete evacuation of the mole or to detect a malignant change.

CONCLUSION

The prognosis following hydatidiform mole is good, especially with good follow-up and serial HCG assessment. Diagnosis prior to evacuation of uterus is important and patients should be educated as to the need for initial contraception after remission. To achieve the best results in its management, a standard protocol and the establishment of a National Trophoblastic Centre is recommended.

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