Prevalence of gestational trophoblastic disease

A single institution experience

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ABSTRACT

Objective: To study the incidence and time trends of gestational trophoblastic disease in the Kingdom of Saudi Arabia (KSA).

Methods: A retrospective study of medical records of 64,762 pregnancies registered and treated at Security Forces Hospital, Riyadh, KSA, from January 1988 through to December 1998.

Results: Fifty-nine cases of hydatidiform mole (36 complete hydatidiform mole (CHM) and 23 partial hydatidiform mole (PHM) and 2 cases of choriocarcinoma were observed, out of 64,762 pregnancies registered at Security Forces Hospital, Riyadh, KSA, during an 11 year period. The temporal trends exhibited significant reduction in the incidence of GTD during the study period.

Conclusion: The incidence of GTD has declined with the rapid socio-medical development of the KSA, and is now comparable to that of Europe. The optimal management of this disease depends on prompt diagnosis, correct stratification of the risk category and appropriate treatment using various modalities such as chemotherapy and surgery.

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Gestational Trophoblastic Disease (GTD) refers to a wide spectrum of interrelated conditions ranging from benign hydatidiform mole (HM) to malignant choriocarcinoma.[1] They share 3 common characteristics, such as, produce human chorionic gonadotrophin (hCG), origin from chorion which is genetically different from that of host and can be treated successfully with chemotherapy. Hydatidiform mole is an abnormal pregnancy characterized by the presence of hydropic swelling of the chorionic villi and proliferation of the trophoblasts.[2] There are 2 pathological varieties of HM, complete (CHM) and partial hydatidiform mole (PHM). The risk of malignant transformation is much higher with CHM (15-20%) as compared to (<5%) PHM.[3,4] Hydatidiform mole is associated with a substantial risk (5-10%) of subsequent persistent GTD,[5] which includes 3 types; Invasive Mole (IM), Choriocarcinoma (CC) and Gestational Trophoblastic Tumor (GTT).[6] Although the first 2 conditions need histological confirmation but the diagnosis of persistent GTD is made usually on raised serum β-hCG values with or without radiologic evidence.[7] If the serum level of β-hCG during the follow up interval levels plateau for 3 or more consecutive weeks, rise, or do not fall below 20,000 mIU/ml by the first month following evacuation, a diagnosis of persistent GTD is made.[8] Cytogenetic

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studies have shown marked differences in the genetic constitution of molar pregnancies.[9] Complete hydatidiform mole is usually diploid, and androgenetic in origin, having 46, xx or 46, xy karyotype, whereas PM is triploid (69 chromosomes) having an extra haploid set of paternally derived deoxyribonucleic (DNA), achieved by fertilization of normal egg by a duplicated spermatozoon or 2 spermatozoa.[10-12]

The incidence of GTD varies widely between nationalities[13,14] **(Figure 1)**. These regional variations have been reported with many speculative factors as ethnic origin, blood group, age, parity, diet and nutrition, contraception, socio-economic status, immunologic factors and genetic constitution. The socio-cultural background of Saudi population makes the epidemiologic study of GTD very interesting, as consanguinity is common and the society is very conservative towards hysterectomy, considering it defeminization. This attitude provides an opportunity to study the malignant potential of GTD in patients receiving prophylactic chemotherapy. Therefore, the present study was planned to present a report on the incidence and time trends of GTD in the Kingdom of Saudi Arabia (KSA), in consideration of the country's rapid economic development and socio-medical advances, which may have a marked influence on the prevalence of GTD.

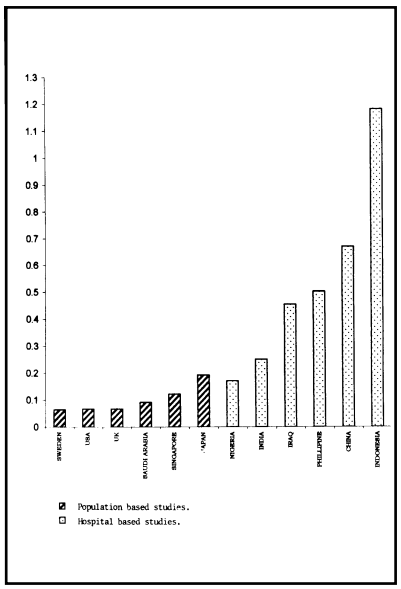

Figure 1 - Incidence of hydatidiform mole per thousand pregnancies for different countries.[8,13,14] USA - United States of America, UK - United Kingdom.

Methods. This study is based on data collected for the period from January 1988 through to December 1998, from Security Forces Hospital, Riyadh, KSA, which serves the employees of the Ministry of interior and their dependants throughout the KSA. The total number of deliveries at the Security Forces Hospital ranges from 6,000-7,000 per year. We retrospectively studied the medical records of 61 cases of GTD, diagnosed by histopathology during the said timeframe. The incidence of CHM, PHM and choriocarcinoma per pregnancy was evaluated using hospital based data on all pregnancies registered (either for delivery, abortion, ectopic gestation or HM) during the study period. Occurrence patterns, distribution of the disease according to the International Federation of Gynecology and Obstetrics (FIGO) and World Health Organization (WHO) scoring system, age distribution (more or less than 40 years), parity, ABO blood group and treatment modalities were evaluated and analyzed from the hospital medical records. The terminology of CHM, PHM, invasive mole, persistent GTD, and choriocarcinoma were defined by the criteria of the WHO scientific working group.[14] The diagnosis of molar pregnancy was based on the pathological criteria defined by Szulman and Surti[10] whereas statistical analysis was carried out using age adjusted incidences and significant analysis by Chi-square test.

Results. Between January 1988 and December 1998, a total of 64,762 pregnant women registered in the Department of Obstetrics and Gynecology, Security Forces Hospital, Riyadh, KSA, 61 Saudi women required treatment for gestational trophoblastic disease. The 59 cases of hydatidiform mole observed among 64,762 deliveries, 36 were CHM while others had PHM, which gives a prevalence rate of 0.94 per 1000 pregnancies or one case in 1098 pregnancies **(Table 1)**. A major proportion (70%) of the molar pregnancies were observed in young patients (Less than 40 years) whereas only 30% of the total cases were above 40 years of age. The average age at the time of molar pregnancy was 25.6 years whereas the mean follow up time for each patient was 5.3 year. Overall, 2 cases of gestational choriocarcinoma were reported among women with previous history of a mole **(Table 1)**. The incidence of HM showed a marked decreasing tendency over the study period **(Figure 2)**. Of the 59 cases of HM, 21% were found in primigravida, 37% in grand-multipara (>5 para) and 42% in Para 1-4. All the patients presented in first or second trimester of pregnancy. Suction evacuation was performed in 87% of the patients, 4% had nalador and suction evacuation, 7% has prostin (PGE2) vaginal tablets followed by suction evacuation and 2% TAH + BSO. Uterine evacuation was followed by serial measurements of hCG in all molar pregnancies. In patients with potential postmolar persistant GTD, a single agent selective chemotherapy and strict contraception was followed by the use of barriers and contraceptive pills. This difficult target was achieved by counseling the families regarding the prospectus and consequences of contraception in GTD.

Table 1 - The incidence of hydatidiform mole and malignant gestational trophoblastic disease (GTD) in a Saudi population.

Year	Total N of deliveries	Hydatidiform mole		Malignant GTD	
		n of cases	Incidence	n of cases	Incidence
1988	**3808**	7	1:544	-	-
1989	**5240**	8	1:655	-	-
1990	**4430**	5	1:886	-	-
1991	**4975**	6	1:829	-	-
1992	**6121**	6	1:1020	-	-
1993	**6411**	5	1:1282	1	1:6411
1994	**6741**	6	1:1123	-	-
1995	**6512**	4	1:1628	-	-
1996	**6543**	4	1:1635	-	-
1997	**6829**	4	1:1707	1	1:6829
1998	**7152**	4	1:1788	-	-
1988-1998	**64,762**	59	1098	2	1:6620

Discussion. Gestational trophoblastic disease is a heterogenous group of rare neoplastic conditions those are highly curable, even in the presence of widespread metastasis.[8] These diseases vary from PHM, which rarely metastasizes and infrequently requires chemotherapy, to highly malignant choriocarcinoma, which requires multi-agent chemotherapy.[15] The incidence of GTD varies widely among different geographic populations of the world, with a maximum incidence in Asia (6-10 per 1000 gestations) and a minimum (less than one per 1000 pregnancies) in North America and United Kingdom.[16-19]

Although the incidence of persistent GTD has not changed, the advent of polymerase chain reaction, transvaginal ultrasonography, and sensitive tests for β-hCG has significantly changed the presentation of molar pregnancy.[20,21] As, both CHM and PHM secrete hCG, the serial measurements of hCG b-subunit core fragment and free β-hCG remains the most efficient and useful tumor markers for diagnosis and follow up after treatment of GTD.[22,23]

The epidemiology and underlying genetics of GTD has been studied widely in all continents of the world except the Arab peninsula.[18,19,24-27] Only a few initial reports are available from the GCC countries. Chattopadhyay et al,[28] published the initial report on the prevalence of hydatidiform mole in Saudi Arabia indicating an alarming incidence of 1:448 pregnancies, very similar to the under developed countries of Asia. Graham and Fajardo[29] documented almost similar trends of this disease in United Arab Emirates. The present study is strikingly dissimilar to these initial reports. A mean incidence of less than one per 1,000 pregnancies (1:1098) for HM, places the Saudi population very close to the Europe and USA rather than Asia. Moreover the time trends in the incidence of GTD has shown obvious decline in the past decade (**Figure 1**). These findings are consistent with the earlier studies suggesting the definite role played by the high protein diet and socio-medical improvement, in lowering the incidence of this disease in developed countries.[30-32] However, no correlation of incidence and progress of GTD with the blood groups, ethnicity and consanguinity were observed. The occurrence patterns

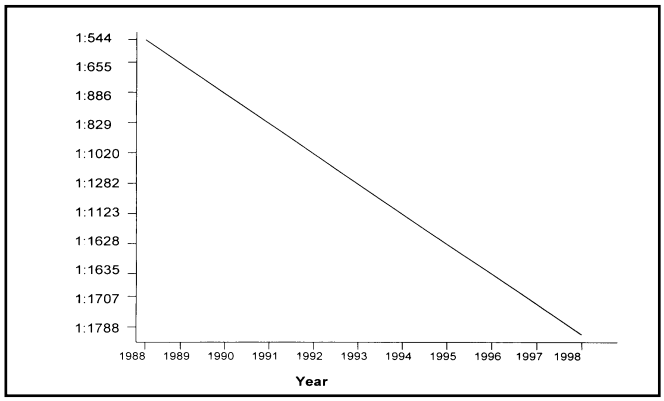

Figure 2 - The incidence of hydatidiform mole and malignant gestational trophoblastic disease (GTD) in a Saudi population.

of GTD at extreme ages of reproductive life in the present study may be the resultant of early marriages and multiparity in early years of reproductive life. In our society, the early marriages are very common and unwed pregnancy extremely rare. So the chances of over reporting of HM or under reporting of pregnancies are minimal. The Saudi culture demands continued reproductive function and contraception is hated.[33] The likelihood of postmolar persistent GTD increases with advancing age, as the ova in older women are more susceptible to abnormal fertilization, possibly due to lowered estrogen levels[8,34-35] hence, primary hysterectomy is the preferred mode of treatment in such high risk patients. This study is limited, however, by a relatively small number of subjects, and short follow up period, 11-years, which may be too short to measure the malignant sequelae of GTD. Modernization of Saudi society is linked to the rapid economic affluence in KSA.[36] Now, Riyadh, the capital of KSA where present study was carried out, has undergone unprecedented changes in its physical as well as social structure. The huge governmental city developmental projects (especially in the health care sector), increase in the size and number of single family dwellings, rise in per capita income and reduction in family size has raised the status of Riyadh residents to that of privileged family.[37] The literacy level, which was estimated to be less than 15% in 1978 and 42% in late 1980s has been raised now to 69.5% in adult Saudi females.[38-39] Lack of literacy profoundly affects many sectors of social development, however efforts promoting health education might be markedly curtailed by it. Patient's illiteracy and an associated low level of comprehension concerning the disease and treatment might limit the effectiveness.[40-42] The role of specialized health care services in improving the health of mothers and children can hardly be disputed, but poorly educated mothers might be less likely to make use of these available medical services.[43-45] The improvement of structured health care system and increased awareness (regarding the disease) in literate Saudi Women has remarkably changed their concept towards hysterectomy in past 2 decades.[46-47] Now it is not resented like the past, however there is an expanding need for awareness of health education especially in high-risk families. As we begin to understand more with regards to the genetics underlying this condition, significant advancement in the prevention, diagnosis and treatment of GTD will be possible.

The present study generates the assumption that the incidence of GTD has declined with rapid socio-medical development of the KSA, and is now comparable to that of Europe. However, this is a single institution experience, which may not reflect the whole country. Therefore a multicentre meta-analysis of the disease is suggested to present the clear picture of the epidemiology of this uncommon disease in the KSA. The optimal management of GTD depends on prompt diagnosis, correct stratification of the risk category and appropriate treatment using various modalities such as chemotherapy and surgery.

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