

Assessment of Epidemiological and Hormonal Parameters among patients with Hydatidiform Mole

Dana Abdulkhaleq Khorshed, Pathological Analysis in West Erbil Emergency Hospital, Email: drdanababani@gmail.com, Mobile: +9647503814680
ORCID: <https://orcid.org/0000-0002-9454-1689>.

Zaid Nabeel Elia, Medical Laboratory Department, Erbil Technical Health College, Erbil Polytechnic University, Email: zaidbio82@yahoo.com; Mobil: +9647507668497, ORCID: <https://orcid.org/0000-0003-4993-1159>
Nabeel Elia Wahed, Clinical Immunology, College of Medicine, Hawler Medical University, Email: newlab2004@yahoo.com, Mobile: +1 6196338462
ORCID: <https://orcid.org/0000-0003-2980-2405>

Correspondence author: Zaid Nabeel Elia
Medical Laboratory Department, Erbil Technical Health College, Erbil Polytechnic University. Email: zaidbio82@yahoo.com; Mobil: +9647507668497.

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Abstract

Background: Gestational trophoblastic disease encompasses several disease processes that originate in the placenta. These include complete and partial moles, placental site trophoblastic tumors, choriocarcinomas and invasive moles.

Aim: This study was aimed to evaluate best marker for diagnosis and follow up of Hydatidiform mole (HM) and evaluate some immunological parameters.

Materials and Methods: Forty patients with Hydatidiform Mole (HM) attended Hawler Maternity Teaching Hospital were enrolled in this study in addition to 10 healthy pregnant women in 1st trimester served as a control group, the sampling period lasted one year. In this study, many epidemiological, hormonal and immunological parameters were evaluated.

Results: This study shows relation between risk factors and development of HM. Among these factors is age, it revealed that the most frequent age group for HM was between (25-34) year when compared with other age groups. The frequency of development HM among the housewives was [37/40 (92.5%)] and more than the official or educated women which was [3 (7.5%)]. The frequency of HM among patients with blood group B and O, [14 (35%) & 14 (35%) respectively] were higher than those with blood group A and AB. The results showed that the number of patients with body mass index (BMI) of (18.50 - 24.99 kg/m²) were higher. The highest frequency (90%) of HM was among patients whom married at period "between" (1993 - 2010). The percentage of patients with HM having history of abortion was higher (87.5%) than in those without abortion. There were no relation between HM and history of using oral contraceptive (40%). Mean concentration of β -HCG hormone in sera of patients showed a significant elevation before dilatation and curettage (D&C) as compared to mean concentration of β -HCG in control group (healthy pregnant women in 1st Trimester). After D & C, the mean concentration in sera of the same patients significantly decreased after 10 days as compared with

mean concentration of β -HCG in sera of patients before D & C. However, no significant change recorded between mean concentration of β -HCG in patients sera after D&C and control group ($P = 0.5$).

The mean concentration of Inhibin-A hormone in the sera of patients before D&C was significantly higher as compared to control group. However, after D&C the mean concentration of Inhibin-A sharply decreased in sera of same patients after 10 days ($P = 0.0001$) as compared with mean concentration of Inhibin-A in patients sera before D&C and control group. No significant change ($P = 0.41$) recorded in mean concentration of Carcino Embryonic Antigen (CEA) before and after D&C. While, there was significant difference between mean concentration of CEA in patients after D&C and control group ($P = 0.003$).

Conclusion: The best diagnostic and follow up marker for HM was Inhibin-A. Blood group B and O, BMI of (18.50 - 24.99 kg/m²), (25-34) year's age group and women who married at period "between" (1993 - 2010) were highest frequency of HM.

Keywords: Inhibin-A, β -HCG, CEA, Hydatiform mole.

Introduction:

Gestational Trophoblastic Disease (GTD) is a rare pre-malignant condition that occurs in approximately one in 500 to 2000 pregnancies. On pathologic examination, trophoblastic hyperplasia and hydropic swelling of the chorionic villi are predominantly present. These villous malformations of trophoblast can be subdividing in partial moles (both paternally and maternally genetic) and complete moles (solely paternally genetic). After evacuation of the hydatidiform mole, serum human chorionic gonadotropin (HCG) monitored to detect the malignant development of persistent trophoblastic disease (PTD) which classified patients as having low or high lethal risk, and they must treated immediately [1,2]. Patients with recurrent molar pregnancy indicate that dysregulation of parentally imprinted genes is important in the pathogenesis of complete hydatidiform mole (CHM). CHM is now being diagnosis earlier in pregnancy in the first trimester changing the clinical presentation and making the histological appearance more similar to partial hydatidiform mole (PHM) and hydropic abortion. While the classic presenting symptoms of CHM are less frequent, the risk of developing GTN remains unchanged. Flow Cytometry and immunostaining for maternally expressed genes are helpful in distinguishing early CHM from PHM [2,3].

Gestational trophoblastic neoplasia (GTN) refers to a subset of GTD with a persistently elevated serum HCG in the absence of a normal pregnancy and with a history of normal or abnormal pregnancy. Lethal disease, GTN is considered today the curable gynecologic cancer. However, a delay in the diagnosis may increase the patient's risk of developing malignant GTN, and therefore the prompt identification of GTN is important [1,2]. Serum HCG is closely monitoring in all patients with GTD and PTD after the evacuation of the hydatidiform mole. All patients with GTD are advising not to conceive within 6 to 12 months after normalization of serum HCG. It remains to be elucidating which patients with GTD will develop PTD. The main objective of strategies is early identification of PTD and critical analysis of its treatment [1, 2].

HCG test is essential for detection of GTN. It has emerged that there are problems with HCG tests. In addition to regular HCG, at least five major variants of HCG are present in serum samples. False-positive HCG (phantom HCG) can occur in the absence of GTN. Low-level real HCG may occasionally persist in the absence of clinical evidence of pregnancy or GTD. alternatively; low-level real HCG may be

due to pituitary HCG. Other placental hormone was human placental lactogen (HPL), Inhibin, Activin and progesterone been evaluated as tumor markers and follow-up for GTD. In cases where low-level HCG persists, it must be differentiate whether it is real or false. Real-HCG may be due to quiescent gestational trophoblastic disease or Pituitary HCG [1, 2].

The risk for post molar tumor increased in older patients. Women older than 40 and 50 years of age developed persistent GTT after molar evacuation in 37% and 56%, respectively. Patients with repetitive molar pregnancy have been observed to have a threefold to fourfold increased risk of developing persistent tumor in their later [2].

After development of complete hydatidiform mole, about 20% of patients develop persistent GTT. The risk of developing persistent GTT after complete mole is increase to 40-50% among patients with signs of marked trophoblastic proliferation, high HCG level, excessive uterine enlargement, and prominent theca lutein ovarian cyst [2, 3].

Treatment strategies need to be optimizing, in order to obtain cure in individual patients as soon as possible, with a minimum of side effects and dose of chemotherapy in a population of patients who are often anxious to conceive. Triple therapy with methotrexate, actinomycin D, and cyclophosphamide was once the preferred treatment for patients with high risk metastatic GTT but induced remission in only about 50%. Treatment with etoposide, methotrexate, actinomycin D, cyclophosphamide, oncovin EMA/CO is now the preferred regimen for treatment of high risks metastatic GTT was been shown to induce remission in about **70%** of patients [2,3].

Present study was aimed to evaluate best marker for diagnosis and follow up of Hydatidiform mole (HM) and evaluate some immunological parameters as:

1. Evaluation of beta human chorionic gonadotropin (β -HCG) and Inhibin-A hormone in sera of patients having (HM) before dilatation and curettage (D&C) and 10 days of study after evacuation.
2. Assessment of Carcino Embryonic Antigen (CEA), in sera of patients having (HM) before (D&C) and 10 days of study after evacuation.

Material & method

During 1 October 2010 to third of September 2011, 40 patients suffering from Complete Hydatidiform Mole (CHM) with age range (17-50) year attended to Hawler Maternity Teaching Hospital. Control group composed of ten apparently healthy looking pregnant women in the 1st Trimester. Blood samples were collected from above patients having HM before and after Dilatation and Curettage (D & C) and control group and separated to obtain serum, which is stored in deep freeze (- 20 C°) until estimation for the following parameters by Enzyme Linked Immunosorbent Assay (ELISA) technique: Beta Human Chorionic Gonadotropin (β -HCG), Inhibin-A hormone & Carcino Embryonic Antigen (CEA). The research protocol was approved by the Ethical Committee of Erbil Technical Health College, Erbil Polytechnic University and informed consent taken from each woman before enrollment in the study.

Statistical analysis

Data analysis were performed using statistical software (SPSS) version 17. One way ANOVA analysis was used to test the significant difference between treatments , $p < 0.05$ was set a significant level .

Results**Distribution of patients with hydatidiform mole (HM) according to age range group.**

Table (1) categorized patients suffering from HM according to age range groups (year) into four major group (15-24), (25-34), (35-44) and (45-54). The results revealed that the number and percentage of patients with age group (25-34) and (15-24) were higher, 18 (45%), 13 (32.5%) respectively, than the number and percentage of patients with age groups (35-44) and (45-54), 6 (15%), 3 (7.5%) respectively.

Table 1. Distribution of patients with HM according to age range groups (year).

Age range group of patients (year)	No. of Patients	Percentage %
15-24	13	32.5
25-34	18	45
35-44	6	15
45-54	3	7.5
Total	40	100

Distribution of patients according to occupation.

Table (2) revealed that the number and percentage of housewife patients were higher 37 (92.5%), when compared with the number and percentage of official patients 3 (7.5%).

Table 2. Distribution of patients according to occupation.

Occupation	Number of Patients	Percentage %
Housewife	37	92.5
Official	3	7.5
Total	40	100

Distribution of patients according to type of blood group.

The number and percentage of patients with Blood group (B and O) were higher, 14 (35%), 14 (35%) respectively when compared with the number and percentage of patients with blood group (A and AB), 9 (22.5%), 3 (7.5%) respectively as demonstrated in Table (3).

Distribution of patients according to categories of body mass indexes (BMI)

Table (4) categorized patients suffering from HME into four major groups of (BMI) (kg/m^2), under weight ($<18.5 \text{ kg/m}^2$), normal range ($18.50\text{--}24.99 \text{ kg/m}^2$), over weight ($\geq 25.00 \text{ kg/m}^2$) and obese ($\geq 30.00 \text{ kg/m}^2$). The result demonstrated that the number and percentage of patients with BMI ($18.50 - 24.99 \text{ kg/m}^2$) and (≥ 25.00

kg/m²) were higher 23 (57.5%) 11 (27.5%) respectively when compared with the number and percentage of patients with BMI (≥ 30.00 kg/m²) and (< 18.5 kg/m²) 4 (10%) 2 (5%) respectively.

Distribution of patients according to date of marriage .

The number and percentage of patients who married since (1993 - 2010) were higher 36 (90%) when compared with patients who married since (1977 - 1984) and (1985 - 1992), 2 (5%), 2 (5%) respectively, as illustrated in Table (5)

Table 3. Distribution of patients according to type of Blood Group.

Blood Group	No. of RH+	No. of RH-	No. of Patients	Percent
A	7	2	9	22.5
B	12	2	14	35
O	13	1	14	35
AB	3	0	3	7.5
Total			40	100

Table 4. Distribution of patients according to categories of Body Mass Index (BMI).

Categories of BMI	No. of Patients	Percent
Underweight (< 18.50 kg/m ²)	2	5
Normal range (18.50 - 24.99 kg/m ²)	23	57.5
Overweight (≥ 25.00 kg/m ²)	11	27.5
Obese (≥ 30.00 kg/m ²)	4	10
Total	40	100

Table 5. Distribution of patients according to date of marriage (year).

Date of Marriage (year)	No. of Patients	Percentage %
1977-1984	2	5
1985-1992	2	5
1993-2010	36	90
Total	40	100

Distribution of patients according to history of abortion and times of abortion.

Table (6) and Figure (23) showed that the number and percentage of patients having history of abortion were higher, 35 (87.5%) than the number and percentage of patients with history of no Abortion 5 (12.5%). The same table and figure showed that the number and percentage of patients having history of one of abortion was higher, 19 (47.5%) than the 2 and 3 previous abortion, 9 (22.5%), 7 (17.5%) respectively.

Table 6. Distribution of patients according to history of abortion and times of abortion.

Abortion	Times of Abortion			No. of Patients	Percent
	One abortion	2 Abortions	3 abortions		
Present	19 (47.5%)	9 (22.5%)	7 (17.5%)	35	87.5
Absent	-	-	-	5	12.5
Total				40	100

Distribution of patients according to history of oral contraceptive use.

The number and percentage of patients using oral contraceptive before afflicting HM were 16 (40%), while the number and percentage of patients have not use oral contraceptive were 24 (60%) as illustrated in Table (7) .

Table 7. Distribution of patients according to history of oral contraceptive use.

Oral contraceptive use	No. of Patients	Percentage
Yes	16	40
No	24	60
Total	40	100 %

Mean concentration of β -HCG hormone in sera of patients with HM before, after dilatation and curettage (D&C) and control group.

Table (8) showed that there were significant differences between mean concentration of β -HCG (674540 pg/ml) in sera patients before D&C and mean concentration of β -HCG (381380 pg/ml) in sera of Control group ($P < 0.001$). The same Table showed that there were no significant differences between mean concentration of β -HCG (386590 pg/ml) in sera of patients after D&C and mean concentration of β -HCG (381380 pg/ml) in sera of Control group ($P < 0.5$). There were a significant differences between mean concentration of β -HCG (674540 pg/ml) in sera of patients before (D&C) and mean concentration of β -HCG (386590 pg/ml) after D&C within 10 days follow up of the study ($P < 0.001$).

Table 8. Mean concentration of β -HCG hormone (pg/ml) in sera of patients with HM before, after dilatation and curettage and control group.

Study group		No. of Patient	Range concentration β -HCG pg/ml	Mean concentration β -HCG pg/ml	Difference in means	S.D	P
B	Before D&C	40	324000 - 858600	674540	B-C 293160	136075	B×C <0.001
A	After D&C	40	38150 - 790500	386590	A-C 5210	222675	A×C 0.5
C	Control Group	10	221800 - 627900	381380	B-A 287950	138945	B×A <0.001

Mean concentration of Inhibin-A hormone in sera of patients with HM before, after dilatation and curettage (D&C) and control group.

Table (9) showed that there were a significant extreme elevation of mean concentration of Inhibin-A (479.71 pg/ml) in sera of patients before D&C than the mean concentration of Inhibin-A (53.41 pg/ml) in sera of Control group within 10 days follow up of the study ($P < 0.0001$). In addition, there were a significant decrease of mean concentration of Inhibin-A (12.75 pg/ml) in sera of patients after D&C than the mean concentration of Inhibin-A (53.41 pg/ml) in sera of Control group within 10 days follow up of the study ($P < 0.0001$). Also there was strong a significant differences between mean concentration of Inhibin-A (479.71 pg/ml) in sera of patients before D&C and mean concentration of Inhibin-A (12.7 pg/ml) in sera of same patients after D&C within 10 days follow up of the study ($P=0.0001$), Table 9.

Table 9. Mean concentration of Inhibin-A hormone (pg/ml) in sera of patients with HM before, after (D&C) and control group.

Study Group		No. of Patient	Range concentration Inhibin-A pg/ml	Mean concentration Inhibin-A pg/ml	Difference in means	S.D	P
B	Before D&C	40	12- 2593	479.71	B-C 426.3	760	B×C <0.0001
A	After D&C	40	0.0 - 91	12.7	A-C 40.65	19.0	A×C <0.0001
C	Control group	10	8 - 286	53.41	B-A 466.95	82.65	B×A 0.0001

Mean concentration of Carcino Embryonic Antigen (CEA) hormone in sera of patients with HM before , after dilatation and curettage (D&C) and control group.

Table (10) showed that there were no significant differences between mean concentration of CEA (3374.3 pg/ml) in sera of patients before (D&C) and mean concentration of CEA (2606 pg/ml) in sera of Control group ($P=0.37$). Additionally, there were a significant differences between mean concentration of CEA (3661

pg/ml) in sera of patients after (D&C) and mean concentration of CEA (2606 pg/ml) in sera of Control group ($P=0.003$). There were no significant differences between mean concentration of CEA (3374.3 pg/ml) in sera of patients before (D&C) and mean concentration of CEA (3661 pg/ml) after (D&C) ($P=0.41$), Table 10.

Table 10. Mean concentration of (CEA) (pg/ml) in sera of patients with HM before, after D&C and control group.

Study group		No. Of Patient	Range concentration CEA pg/ml	Mean concentration CEA pg/ml	Difference in means	S.D	P
B	Before (D&C)	40	0.0 - 13090	3374.3	B-C 768.3	3732.7	B×C 0.37
A	After (D&C)	40	0.0 - 48580	3661	A-C 1055	8081.6	A×C 0.003
C	Control group	10	0.0 - 8270	2606	B-A 286.7	3462.8	B×A 0.41

Discussion

Distribution of patients with hydatidiform mole (HM) according to age range group.

The results revealed that the number and percentage of patients with age group (25-34) and (15-24) were higher, 18 (45%), 13 (32.5%) respectively. This result agrees with previous studies done in Maternity teaching hospital, Erbil city, Kurdistan region that found the incidence rate of the disease was between (20-39) years [4]. In other studies, the maternal age group (25-40) year has proven to be a risk factor for a complete mole. The postulated hypothesis is that the ova from the older women may be more susceptible to abnormal fertilization [2,5-7].

A study done in Saudi Arabia revealed that the youngest (less than 20 years of age) had significantly higher than expected incidence [8]. Another study done in USA about GTD by maternal age showed the highest rate among women aged (15-19) year, due to early reproductive system development in their early teenage [9].

This study disagrees with a study done in the state of Victoria/ Australia, overall it was found that across all studies of different type of GTD, mothers over the age of 40 have 5-10 times greater chances of GTD. Women per menopausal year are most at risk.[10,11].

Distribution of patients according to occupation .

Results revealed that the number and percentage of housewife patients were higher 37 (92.5%), when compared with the number and percentage of official patients or educated women 3 (7.5%). Women who have lower income or education level have an increased risk [2]. Researchers have suggested that diet and low education may play a role [4].

The high incidence of molar pregnancy in some populations has been attributing to nutritional and socioeconomic factors. It was reporting that regions with a high incidence of molar pregnancy correspond to the geographic areas with a high frequency of vitamin A deficiency. A dietary factor such as beta-carotene (vitamin A precursor) intake has been suggesting in some studies in Italy as being a protective factor [2,6]. However, these results disagree with Jonathan *et al* study

which stated that there were no significant differences in educational level of the women, or their partners, and the racial groups of the case and HM [12].

Distribution of patients according to type of blood group.

The number and percentage of patients with Blood group (B and O) were higher 14 (35%) 14 (35%) respectively when compared with the number and percentage of patients with blood group (A and AB)

There was a slight excess in-group AB and a slight deficiency in-group O in patients with HM. However, there was a significant decrease in blood group A and a slight excess in groups O, B and AB in patients with malignant trophoblastic disease compared with the distribution in healthy pregnant women. A higher mortality rate observed in-group B in patients with malignant trophoblastic disease. ABO blood group of patients with malignant trophoblastic disease can be an important prognostic factor in the diagnosis and treatment of the trophoblastic disease [13].

In second study, blood group type "O" was more in both groups, which might be due to its predominance in the population [14]. While in another study, the blood type "B" was more in HM patients. The differences are because of different environmental and genetic differences as well as different distribution of various blood types in the regions [15].

Women with blood type A or AB are at slightly higher risk than those with type B or O [16]. Another study represented; an increased risk is evident for HM for women with blood group A and men with group O or A [2,6].

Distribution of patients according to categories of body mass indexes (BMI)

The result demonstrated that the number and percentage of patients with BMI (18.50 - 24.99 kg/m²) were higher 23 (57.5%) than the other BMI categories.

It has been reported that ovulating subfertile women with a BMI (18-29kg/m²) have lower pregnancy and higher risk rates of GTDs when compared with the other BMI categories [17].

Total plasma peroxides were positively associated with BMI; this indicated that increasing BMI might be a risk factor for increased oxidative stress and the associated deleterious effects on the general body system. Oxidative stress has been implicating in the pathogenesis of more than 100 disease conditions including GTD, Breast cancer and infertility. This finding suggests that BMI may increase oxidative stress and its influence on infertility in the defect or absence of an ovulation [18].

Distribution of patients according to date of marriage .

The number and percentage of patients who married since (1993 - 2010) were higher 36 (90%) when compared with patients who married in the other date.

The annual incidence of gestational trophoblastic disease from (1991 - 1999) in the northern part of England and Wales averaged 1/714 live births. The frequency and incidence of gestational trophoblastic disease registered in Weston Park Hospital over the nine years of study showed that incidence was higher than other year. This result disagrees with a study, which stated that use of oral contraceptive pills (OCP), is generally associated with increased risk of afflicting HM. Hydatidiform mole incidence among multiparous women who used OCP was more [6,19,20].

Second study reported that oral contraceptives use was in correlation with increase risk of GTD. Previous use of OCP has increased the risk two times as much and it seems that a longer term of using pill is positively in correlation with the risk. One possibility is that long-duration oral contraceptive use may damage the ova or interfere with meiosis and thus yield ova with absent or inactivated nuclei [16,21,22].

Mean concentration of β -HCG hormone in sera of patients with HM before , after dilatation and curettage (D&C) and control group.

There were significant differences between mean concentration of β -HCG (674540 pg/ml) in sera patients before D&C and mean concentration of β -HCG (381380pg/ml) in sera of Control group ($P < 0.001$). In addition, there was a significant difference between mean concentrations of β -HCG (674540 pg/ml) in sera patients before D&C and mean concentration of β -HCG (386590 pg/ml) after D&C within 10 days follow up of the study ($P < 0.001$). However, there were no significant differences between mean concentration of β -HCG (386590 pg/ml) in sera of patients after D&C and mean concentration of β -HCG (381380pg/ml) in sera of Control group ($P < 0.5$).

After D&C, the test was repeated every 2 weeks to check β -HCG level in studies patients. Once patient's level is normal, the tests will become less frequent. Patients was followed for at least 6 months.

Markedly elevated serum (B-HCG) level that produced by the trophoblastic tissue [2]. Some studies, which stated that Serum HCG level, are usually extremely higher in patients with CHM than in normal pregnancy [23-26].

There have been reports of false-negative urine, serum and both urine and serum B-HCG pregnancy tests in HM. In each of these reports, the serum B-HCG levels were determined to be greater than (1000000 mIU/ml), and the likely because for false negative results were reported to be the "high-dose hook effect due to excessive heterophilic anti B-HCG antibodies and cause false negative results. This phenomenon called (Phantom HCG) [27-29].

Mean concentration of Inhibin-A hormone in sera of patients with HM before , after dilatation and curettage and control group.

There were a significant increase in mean concentration of Inhibin-A (479.71 pg/ml) in sera of patients before D&C and mean concentration of Inhibin-A (53.41 pg/ml) in sera of Control group within 10 days follow up of the study ($P < 0.0001$). In addition, there was a significant decrease in mean concentration of Inhibin-A (12.75 pg/ml) in sera of patients after D&C and mean concentration of Inhibin-A (53.41 pg/ml) in sera of Control group within 10 days follow up of the study ($P < 0.0001$). But there were strong a significant differences between mean concentration of Inhibin-A (479.71 pg/ml) in sera of patients before D&C and mean concentration of Inhibin-A (12.7 pg/ml) in sera of same patients after D&C within 10 days follow up of the study ($P=0.0001$).

The data obtained from this study is similar to that study which stated that serum Inhibin-A concentrations are substantially; increased in patients with HM and may provide an important diagnostic marker of the condition [30].

Women with HM had significantly higher serum levels of Inhibin-A and activin-A than healthy pregnant women, several fold higher than the control values. After evacuation, the levels of both Inhibin-A and Activin-A, declined significantly to the levels of nonpregnant controls [23-25]. Other researchers showed in compared between Inhibin-A and β -HCG before evacuation that the serum Inhibin-A concentrations were significantly greater than normal women were at the same stage of pregnancy, and Inhibin-A in molar tissue was present in high concentrations (158-1162 U/ml). Seven to 10 days after evacuation Inhibin-A concentrations in serum samples from the same patients declined significantly to values (1-4 U/ ml) similar to those seen in the follicular phase of normal menstrual cycles. Serum β -hCG concentrations declined after evacuation, but remained far higher than in non-pregnant women. The exceptionally high concentrations of Inhibin-A in molar tissue and the dramatic fall in concentrations in the serum after evacuation strongly support

the mole as the source of the circulating Inhibin-A. The findings are consistent with the localization of Inhibin-A to the cytotrophoblast of normal placenta [30,31].

Mean concentration of Carcino Embryonic Antigen hormone in sera of patients with HM before , after dilatation and curettage and control group.

There were no significant differences between mean concentration of CEA (3374.3 pg/ml) in sera of patients before D&C and mean concentration of CEA (2606 pg/ml) in sera of Control group ($P=0.37$). The result showed that there were a significant differences between mean concentration of CEA (3661 pg/ml) in sera of patients after D&C and mean concentration of CEA (2606 pg/ml) in sera of Control group ($P=0.003$). There were no significant differences between mean concentration of CEA (3374.3 pg/ml) in sera of patients before (D&C) and mean concentration of CEA (3661 pg/ml) after (D&C) ($P=0.41$). Carcinoembryonic antigen (CEA) is a glycoprotein involved in cell adhesion. It normally produced during fetal development, unlike HM that there was no fetal formation [31].

This study agrees with study that showed no significant and no affects of CEA, CA 125, CA 19-9, CA 15-3 markers, the source of CEA marker are amnion cells with amniotic fluid and colo-rectal carcinoma cells [33-35].

Conclusions

The epidemiological study of HM patients in Erbil city conclude that the most susceptible age group for HM in Erbil city is (25-34) years, most frequent blood groups in HM patients are B and O group and the most BMI among patients are (18.50 - 24.99 kg/m²) and (≥ 25.00 kg/m. The high percentage of HM among patients who married since date (1993 - 2010) and among patients having history of abortion especially one abortion. Concentration of β -HCG in sera of patients significantly increase before D&C and significant decrease after (D&C), but there were no significant change between mean concentration of β -HCG after D&C and control, also there were no relationship between HM and history of using OCP. There were no significant differences between mean concentration of CEA in sera of patients before and after D&C, but there were significant differences between mean concentration of CEA in sera of patients after D&C and Control group. The better diagnostic and follow up marker for HM was Inhibin-A. There were strong significant increase in mean concentration of Inhibin-A in sera of patients before D&C, and sharply decreased after D&C, and declined to normal value in non pregnant women within 10 day of study follow up.

References

- 1- Bentley RC. Pathology of gestational trophoblastic disease. Clin Obstet Gynecol 2003; 46:513-22.
- 2- Berkowitz RS, Goldstein DP. Molar Pregnancy. N Engl J Med. 2009; 360 (16): 1639.
- 3- Cotran RS, Kumar V, Fausto N, Nelso F, Robbins SL, Abbas AK. pathologic basis of Gestational trophoblastic disease (7th ed.). St. Louis, Mo: Elsevier Saunders. 2005; p. 1110.
- 4- Al-Alaf SK, Omer DI. Prevalence and clinical observations of Gestational Trophoblastic Diseases in Maternity Teaching Hospital in Erbil City. WSEAS Transaction Bio Biomed 2010;7(3):190-199
- 5- Shapter A P, McLellan R. Gestational Trophoblastic Disease. Obstet Gynecol Clin Nort. 2001; 28: 805-17.
- 6- Altieri A, Franceschi S, Ferlay J, Smith J, La Vecchia C. Epidemiology and aetiology of gestational trophoblastic diseases. Lancet Oncology, 2003;4(11):670–678.

- 7- Loh KY. Epidemiological study in Molar pregnancy, Department of Family Medicine, IMU Clinical School, Jalan Rasah, 70300 Seremban, Negeri Sembilan. *Med J Malaysia*. 2004; 59:697-703.
- 8- Hayash KI, Bracken MB, Freedman DH, Hellenbrand K. Hydatidiform mole in the United States, a statistical and theoretical analysis. *Am J Epidemiol*. Jan 2003;115(1):67-77.
- 9- Chattopadhyay SK, Sengupta BS, ALGhreimil M, Edrees WB, Lmbourne A. Cohn D E, Herzog TJ. Gestational trophoblastic disease: New standards for therapy. *Curr Opin Oncol*. 2000; 12: 492-96.
- 10- Morrow C. The natural history of theca lutein cysts. *Obstet-Gynecol*. 2003;72(2):247-51.
- 11- Beischer NA, Bettenger HF, Fortune DW, Pepperell R. Hydatidiform mole and its complications in the state of Victoria/ Australia. *J Obstet Gynecol Br Common* 2005; 77(3):263-276.
- 12- Buckley JD, Henderson BE, Morrow CP, Hammond CB, Kohorn EI, Austin DF. Case-Control Study of Gestational Choriocarcinoma. *Cancer Res* 1988; 48:1004-1010.
- 13- Sasaki K, Hata H, Nakano R. ABO blood group in patients with malignant trophoblastic disease. *Gynecol Obstet Invest*. 1985; 20(1):23-6.
- 14- Rezavand N., M. Kamravamanesh¹, Z. Safdari, F. Ghodsi. Study on hydatidiform mole frequency and some of its relevant factors. *Int J Academic Res* 2011; 3(2):834-837.
- 15- Talat N. The pattern of benign Gestational trophoblastic disease in Katachi. *JMP A J Pakistan Med Association*. 1998; 48 (10): 226-300.
- 16- Palmer JR, Driscoll SG, Rosenberg L, Berkowitz RS, Lurain JR, Soper J, et al. Oral contraceptive use and the risk of gestational trophoblastic tumors. *J Natl Cancer Inst*. 1999; 91:635-640.
- 17- Steeg Van der JW, Steures P, Eijkemans MJ, Habbema JD, Hompes PG, Burggraaff JM, *et al*. Obesity affects spontaneous pregnancy chances in subfertile, ovulatory women. *Hum Reprod*. 2008;23(2): 324-328.
- 18- Agarwal A, Gupta S, Sharma KR. Role of oxidative stress in female reproduction. *Rep Biol Endocrinol* 2005; 3: 28-49.
- 19- Khabouze S, Erchidi J, Bouchikhi C, Chahtane A. Gestational trophoblastic disease. *Gynecol Obstet Fertile*. 2002; 30(1):42-49.
- 20- Famouri S, Yarendi F, Mallahian M. Survey on epidemiology characteristics among gestational trophoblastic disease in the selected Tehran hospitals during 1992-2002. *Scientific Res J Med Sci Univ I.R. Iran Army*. 2006;4(4):1023-1026.
- 21- Schorge J, Schaffer J, Halvorson L, Hoffman B, Bradshaw K, Cunningham F, Williams Gynecology. New York: McGraw Hill CO. 2008; 755-756.
- 22- Palmer JR, Driscoll SG, Rosenberg L, Berkowitz RS, Lurain JR, Soper J, et al. Oral Contraceptive Use and Risk of Gestational Trophoblastic Tumors. *J National Cancer Institute*, 1999; 91(7):635-640.
- 23- Seckl MJ, Sebire NJ & Berkowitz RS. Gestational trophoblastic disease. *Lancet*. 2010; 376(9742):717-729.
- 24- Florio P, Cobellis L, Luisi S, Ciarmela P, Severi FM, Pocchi C, Petraglia F. Changes of inhibins and activin secretion in healthy and pathological pregnancy. *Mol Cell Endocrinol*. 2001; 180: 123–130.
- 25- Florio, P. Severi, F. Cobellis, L. Danero, S. Bomè, A. Luisi, S. Petraglia, F. Serum activin A and inhibin. A New clinical markers for hydatidiform mole. 2002; 94(10): 2618–2622.

- 26-Smith HO. Gestational trophoblastic disease epidemiology and trends. Clin Obstet Gynecol. 2003; 46:541–56.
- 27-Rotmensch S. & Cole LA. False diagnosis and needless therapy of presumed malignant disease in women with false-positive human chorionic gonadotropin concentrations. Lancet. 2000; 355: 712–5.
- 28-Er TK, Tsai EM, Hung CL, Chou HW, Zheng BH, Tsai LY. False-negative pregnancy test in hydatidiform mole. Clin Chem. 2006; 52:1616-7.
- 29-Davisson CM, Kaplan RM, Wenig LN, Burmeister D. Qualitative β -hCG urine assay may be misleading in the presence of molar pregnancy: a case report. J Emerg Med. 2004; 27:43-7.
- 30-Petraglia F, Sawchenko P, Lim ATW, Rivier J, Vale W. Localisation, secretion and action of inhibin in human placenta. Science 1987; 237(4811):187-9.
- 31- Paoloni-Giacobino A. Epigenetics in reproductive medicine. Paediatr Res. May 2007; 61 (5 Pt 2): 51R–57R.
- 32-Thomas SN, Tong Z, Stebe KJ, Konstantopoulos K. Identification, characterization and utilization of tumor cell selectin ligands in the design of colon cancer diagnostics. Biorheology. 2009; 46 (3): 207–25.
- 33-Hegab HM, Schindler AE, Rizk M, Ramadan M. Evaluation of tumour markers in molar pregnancy. Arch Gynecol Obstet.,2003;268(3):151-154
- 34-Ahmad AE, Dehaghani AS, Shaker M, Fattahi MJ. Clinical value of tumor markers in gestational trophoblastic diseases. J Reprod Med. 2008; 53(12):930-4
- 35-Schindler AE. The value of gonadotropin-releasing hormone-agonists together with other drugs for medical treatment and prevention. Gynecol Endocrinol. 2009; 25(12):765-7.