Study the Association of Plasma Homocysteine, Retinol Binding Protein, Pre Albumin, and Albumin In Partial Hydatidiform Mole

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(Received: Oct 2017 Revised: Dec 2017 Accepted: Feb 2018)

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ABSTRACT

Introduction and Aim: The Hydatidiform mole is one of a group of diseases referred to as gestational trophoblastic disease (GTD), and the commonest type of GTD. Classification of a hydatidiform mole into complete and partial depends on histopathological and cytogenetic features. An H mole is considered to be a premalignant condition, with approximately 15% of complete and 1% of partial moles progress to a malignant gestational trophoblastic neoplasia (GTN). The objectives of the study were to assess nutritional status as a possible cause of Hydatidiform mole. In addition, to investigate the changes in the homocysteine, Retinol binding protein, Pre albumin, and albumin in the first-trimester pregnant women compared to non-pregnant.

Materials and Methods: This was a case-control study which included (75) subjects,(25) of them were patients group, the other (25) were pregnant women in the first trimester (first control group), and the remainder (25) were nonpregnant women were (second control group). The sera obtained from the fasting blood of subjects were used to measure the level of homocysteine, Retinol binding protein, pre-albumin, and albumin).

Results: The results of the present study showed that The mean age of patients group was (27.44 ± 5.36) years, ranging from 18-39 years and the peak incidence of PHM between 22-29 years. The majority (76%) of a patient with hydatidiform mole came from the rural area. Accident finding at ultrasonography was the commonest way of presentation (44%) followed by vaginal bleeding (40%) while (16%) hyperemesis gravidram. The Pre albumin level was significantly lower in the Pregnant women with mole compared with healthy pregnant women control group ($P < 0.001$), but the homocysteine level was not significantly different ($P = 0.146$). The levels of homocysteine and albumin were found significantly different between first-trimester pregnant women and non-pregnant ($P < 0.001$).

Conclusion: The highest incidence of PHM was found in the age group between 22-29 years, belonging to the rural city. PHM was more common in nulliparous and low parous patients having 1-2 children. The accidental finding of ultrasonography was the commonest way of presentation followed by vaginal bleeding. This is the first report to suggest that there may be an association between pre-albumin and PHM. But it is also suggesting that there may be no association between homocysteine and PHM.

Key Words: Hydatidiform mole, Homocysteine, Retinol binding protein, Pre albumin, Albumin

INTRODUCTION

A variation Hydatidiform mole or molar pregnancy is one of a group of diseases referred to as gestational trophoblastic disease (GTD), H mole is the commonest type of GTD (1). Most of the molar pregnancies are benign but on rare occasions, they have the tendency for local and distant metastasis. Classification of the hydatidiform mole into complete and partial depends on histopathological and cytogenetic features (2). An H mole is considered to be a premalignant condition, with approximately 15% of complete and 1% of partial moles progress to a malignant gestational trophoblastic neoplasia (GTN) (3). Several potential etiologic risk factors have been evaluated for the development of H mole. These include the extreme of maternal age, prior history of H mole, deficiency of Beta-carotene and animal fat intake (4). Vaginal bleeding is the most common presenting symptom.

During the second trimester, the diagnosis of molar pregnancy is usually made, and the classical signs and symptoms include toxemia, large uterine size, hyperemesis, anemia, hyperthyroidism, and respiratory distress (3). The clinical presentation of molar pregnancy has changed largely in recent years; the diagnosis of H mole occurs at earlier gestational age owing to the ultrasonographic examination made at early pregnancy (3).

MATERIALS AND METHODS

This study was conducted in Babylon Maternity and Pediatrics Teaching Hospital in Babylon Province and Al Zahraa teaching hospital in Al Najaf Province from the first of September 2016 to the end of March 2017.

This was a case control study which included 75 subjects,twenty-five were patients diagnosed with partial H mole, the other twenty-five pregnant women in the first trimester were healthy subject (first control group), and the remainder twenty-five non pregnant womenwere healthy subject (second control group). patients who suffered from metabolic or endocrine disease, renal dysfunction, and BMI > 30were excluded. The sera obtained from the fasting blood of subjects were used to measure the level of homocysteine and Retinol binding protein by (ELISA), pre albumin by Nephlometry, and albumin by Spectrophotometry).

Statistical Analysis

All Statistical analysis had been done by using (SPSS) version 20th for social sciences. Categorical variables had been presented as percentages, frequencies. Contentious variables had been presented as mean and standard deviation (SD). The t-test had been used to determine the mean statistically significant difference between two groups. P value less than (0.05) had been considered to be significant.

RESULTS

Table (3.1) showed that the mean age of patients group was (27.44 ± 5.36) years, ranging from 18-39 years and the mean BMI of patients group was (23.58 ± 2.27), ranging from18.2-26.5 Kg/m2 and also showed that the mean level of B HCG was (15815.6 ± 14442.12), ranging from(2160-54354.0) (mIU/ml).

Table 3.1: Demographic characteristics of patients group including (age, BMI and HCG level).

Study variable	(Means ± SD)	Range
Age (years)	(27.44 ± 5.36)	(18-39)
BMI (Kg/m2)	(24.58 ± 2.27)	(20.2-27.5)
β- HCG (mIU/ml)	(15815.6 ± 14442.12)	(2160-54354.0)

Figure 3.1 showed that the majority (76%) of patient with hydatidiform mole came from rural area. While only (24%) of patient with hydatidiform mole came from urban area.

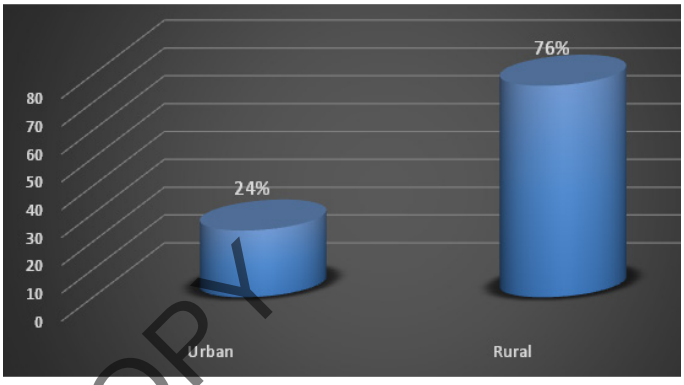

Figure 3.1: The distribution of patients according to residence

Figure 3.2 showed that (34%) of patients presented with blood group A+ve and (31%) of patients presented with blood group O+ve and (20%) of patients presented with blood group AB+ve, the reminder Only (15%) of patients presented with blood group-B+ve.

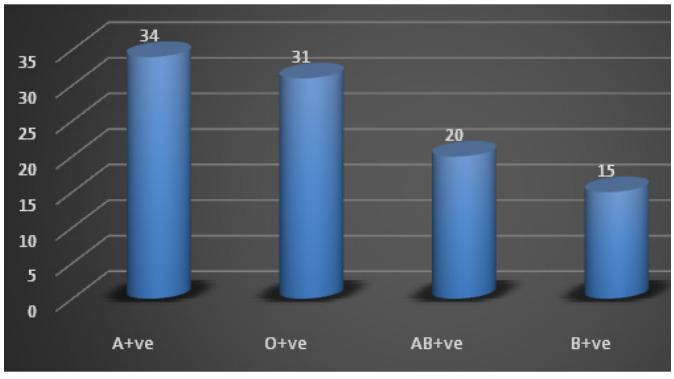

Figure 3.2: Distribution of patients according to blood group

Table 3.2 showed the distribution of patients according to study variables including (gestational age, history of mole, family history of mole, clinical presentation, number of miscarriage and parity).

Table 3.2: The Distribution of patients according to clinical history

Study variables	Number	%
Gestational age		
≤ 9 weeks	14	66%
>9-13 weeks	11	44%
Total	25	100%
History of mole		
Present	2	8%
Absent	23	92%
Total	25	100%
Family history of mole		
Present	1	4%
Absent	24	96%
Total	25	100%
Way of presentation		
Hyperemesis gravidram	4	16%
Ultrasound	11	44%
Vaginal bleeding	10	40%
Total	25	100%
Number of miscarriage		
Nill	20	80%
Once	2	8%
Twice	3	12%
Total	25	100%
Parity		
0	8	32%
1-2	9	36%
3-4	5	20%
5-6	2	8%
7 or more	1	4%
Total	25	100%

Table 3.3 showed that there was no significant difference in the mean of serumHomocysteine,Retinol binding protein, and Albumin betweenpatient'spregnant women with mole and healthy pregnant women, while serum Pre albumin level was found to be significantlydifferent(p<0.05).

Table 3.3: The mean differences of study markers between patients and control pregnant women

Study markers	Group	N	Mean ± SD	P value
Homocysteine (mmol/l)	Pregnant women with mole	25	7.3 ± 2.03	0.146
	healthy pregnant women	25	6.5 ± 1.92	
Retinol binding protein (ng/ml)	Pregnant women with mole	25	326.5 ± 109.4	0.222
	healthy pregnant women	25	366.4 ± 118.2	
Pre albumin (mg/dl)	Pregnant women with mole	25	18.71 ± 5.08	<0.001*
	healthy pregnant women	25	23.40 ± 2.39	
Albumin (g/dl)	Pregnant women with mole	25	3.98 ± 0.56	0.337
	healthy pregnant women	25	4.10 ± 0.25	

Figure 3.3 showed that there was a significant difference in the mean of serum homocysteine level (mmol/l) between patient's pregnant women with mole and non-pregnant women (p<0.05).(P= <0.001*).

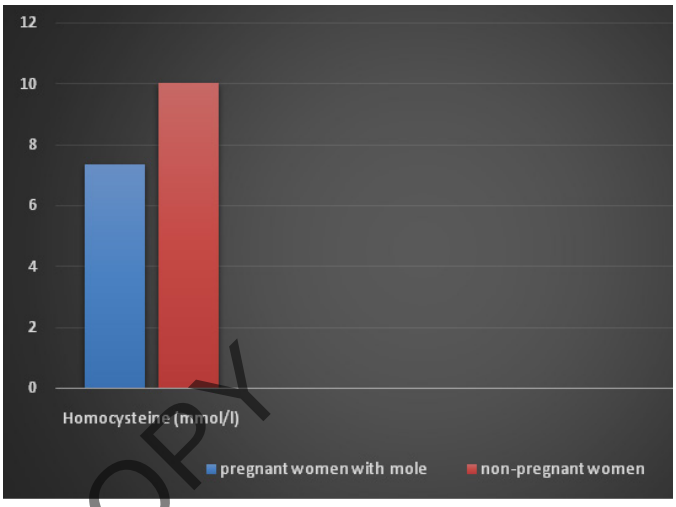

Figure 3.3 Mean differences of homocysteine level between patients and control non-pregnant group

Figure 3.4 showed that there was no significant difference in the mean of serum Retinol binding protein level (ng/ml) between patient's pregnant women with mole and non-pregnant women (p<0.05).(P= 0.07).

Figure 3.4 Mean differences of retinol binding protein level between patients and control non pregnant group

Figure 3.5 showed that there was a significant difference in the mean of serum pre albumin level (mg/dl) between patient's pregnant women with mole and non-pregnant women (p<0.05).(P= <0.001*).

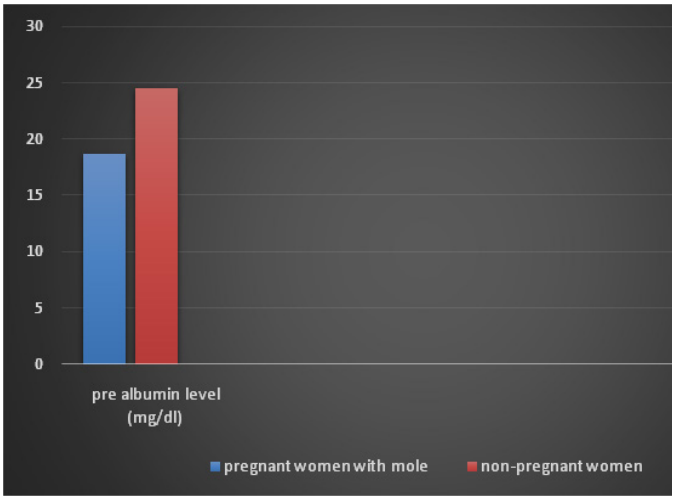

Figure 3.5 Mean differences of pre albumin level between patients and control non pregnant group

Figure 3.6 showed that there was a significant difference in the mean of serum albumin level (g/dl) between patient's pregnant women with mole and non-pregnant women (p<0.05).(P= <0.001*).

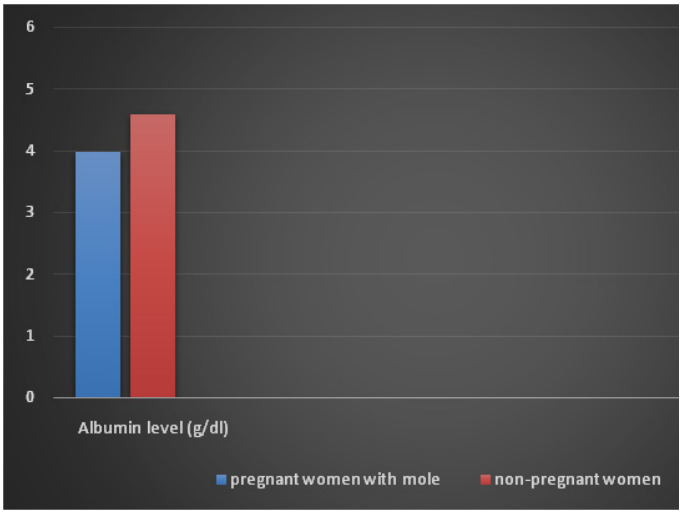

Figure 3.6 Mean differences of albumin level between patients and control non pregnant group

Table 3.4 showed that there was significant decrease in the mean of serumHomocysteine and Albumin-between healthy pregnant women and non-pregnant women (p>0.05), while there was no significantde-creasein the mean ofserum Retinol binding protein, and Pre albumin level.

Table 3.4: The mean differences of study markers according between healthy pregnant and non-pregnant women

Study markers	Group	N	Mean ± SD	P value
Homocysteine (mmol/l)	healthy pregnant women	25	6.5 ± 1.92	<0.001*
	Non pregnant women	25	10.02 ± 2.48	
Retinol binding protein (ng/ml)	healthy pregnant women	25	366.4 ± 118.2	0.639
	Non pregnant women	25	381.45 ±106.7	
Pre albumin (mg/dl)	healthy pregnant women	25	23.40 ± 2.39	0.149
	Non pregnant women	25	24.49 ± 2.85	
Albumin (g/dl)	healthy pregnant women	25	4.10 ± 0.25	<0.001*
	Non pregnant women	25	4.58 ± 0.44	

***P value ≤ 0.05 was significant.**

DISCUSSION

In the present study, the highest incidence was found in the age group 22–29 years and similar results were reported from Sadiq S *et al*. (5). The overall mean age of patients was 27.44±5.3 years, nearly similar results have been reported by Moodley M *et al* (6).The result of the pre-evacuation β- HCG in this study was nearly similar with study conducted by Agrawal N *et al*. in 2015 (7).The highest percentage of patients belonging to the rural city, these results may be attributed to low socioeconomic status and malnutrition (8). Nutritional and socioeconomic factors appear to be important risk factors for molar pregnancy in some populations (9). Another study conducted by Taboo ZA *et al*. (10) concluded that Sixty-five percent of cases were of low socioeconomic state, while 35% of the cases were of high socioeconomic status (10). Our finding in this study that blood group A and O were commonly associated with HM, are compatible with other study Abdelrub AS *et al*. (11). However, the data regarding such association are conflicting. Nevertheless, the number of studies that have found a positive association with blood group makes this issue worthy of further studies.All of the patients in this study were diagnosed at first trimester with gestational age ranging from (7-12) weeks. In a study done in Malaysia by aye and karate (2009) revealed that 75% of cases of GTD were diagnosed at first trimester (12), which nearly coincide with the result of the current study. Both CM and PM are now mainly diagnosed in the first trimester. A first-trimester fetal ultrasound scan is now recommended and commonly performed; this may have contributed to the earlier diagnosis of PM (13).

Two of the patients (8%) had a previous history of molar pregnancy. similar results have been reported from Ocheke AN *et al*. (1). A previous history of molar pregnancy has consistently been shown to influence the risk of HM (4). Also in this study, we found only one of the patients (4%) had a family history of molar pregnancy. Very rarely, several women in the same family have one or more molar pregnancies. It is a rare autosomal recessive condition in which the affected women have a predisposition to pregnancy losses, but most of which are CM (14). In the current study, we found that accidental finding of ultrasonography was the commonest way of presentation in PHM followed by vaginal bleeding. The increased use of Ultrasound scan has significantly improved the diagnosis and promoted prompt uterine evacuation of molar pregnancy (15). Ultrasonography aided the diagnosis of hydatidiform mole in most cases. Ultrasonography plays a critical role in the diagnosis of both complete and partial mole, it has virtually replaced all other means of preop-

erative diagnosis (15). It can be said that patients with molar pregnancy are increasingly being diagnosed earlier in pregnancy and treated before they develop the classic clinical signs and symptoms as a result of widespread use of Ultrasonography (4). In this study the most frequency was seen in the women who were experiencing their second pregnancy 36% and nulliparous 32%. In Ocheke AN *et al*. a large proportion of the hydatidiform mole patients (64%) were of low parity (0-2) (1). In MoodleyM *et al*. study, hydatidiform mole pregnancy was seen more among nulliparous women (6). Although this is at variance with reports from some authors where most patients were of high parity (16), But also, other authors have reported that hydatidiform mole has no significant association with parity (17). The present study showed that there was no statistically significant mean difference of plasma homocysteine between partial moles and healthy pregnant women. These result disagree with Kokanali MK *et al*. study that reported statistically significant mean difference in the levels of plasma Hcy was found between partial moles and healthy pregnant women (18).

Regarding Retinol binding protein in the present study, the mean level was little bit higher in the control group but the difference was not statistically significant. This may be explained by the relationship between the Retinol binding protein and pre albumin. The retinol-RBP compound is secreted into the blood flow, where it is bound to PA (19). Therefore, the observed correlations between PA and RBP levels (20). Interestingly, in this study Pre albumin levels were significantly lower in the Pregnant women with mole compared with healthy pregnant women control group This may be explained by the fact that the pre albumin has short half-life (2-3) days, this make it showed a much higher degree of sensitivity to the change in nutritional status (21). In the present study pregnant women have been found to have lower levels of plasma Hcy, the mean plasma homocysteine levels between first trimester pregnant women and non-pregnant was found statistically difference. This result was nearly similar to study conducted by Muhammad K *et al*. (22). It is interesting to note that Hcy concentration in plasma actually decreases in normal pregnancy. Various hypotheses have been proposed to explaining the decrease in Hcy concentration during pregnancy. Among these are hormonal influences on Hcy metabolism, maternal dietary protein intake during pregnancy, pregnancy-associated hemodilution, and fetal utilization (23). The mean Serum albumin levels between first trimester pregnant women and non-pregnant was found statistically significant difference. Serum albumin was decreased in first and third trimester of pregnancy than in non-pregnant women and maximum decrease seen in third trimester. This study affirms with that of the study done by Gohel *et al*. in 2013 and Zannat MR *et al*. in 2016 (24, 25). They found that serum albumin level is significantly lower in all three trimester compared to non-pregnant women.

CONCLUSION

- This study demonstrates that the highest incidence of PHM is found in the age group between 22-29 years.
- The highest percentage of Patients with PHM belonging to the rural city, nutritional and socioeconomic factors appear to be important risk factors for molar pregnancy.
- Accidental finding of ultrasonography was the commonest way of presentation followed by vaginal bleeding, routine first trimester ultrasound has made diagnosis of Molar pregnancy easier and earlier before any complications arise.
- PHM was more common in nulliparous and low parous patients having 1-2 children.
- This is the first report to suggest that there may be an association between pre albumin and PHM, pre albumin is sensitive to change in nutritional status due to short half-life (2-3) days.
- It is also suggesting that there may be no association between homocysteine and PHM.

Recommendations

- Future studies should focus on the association between Retinol binding protein, and Pre albumin in PHM.
- The main weakness of this study is small numbers of the patients, other studies should focus not only on the association between homocysteine and PHM but also on the association between homocysteine and CHM.
- Providing health education of community with regards to the importance of nutrition may decrease the incidence of HM.

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