

Thyroid Hormone Levels and Its Relationship with Human Chorionic Gonadotropin in Patients with Hydatidiform Mole

Nankali Anisodowleh¹, Keshavarzi Farahnaz¹, Jalilian Nasrin^{1*}, Hematti Maryam², Basami Elaheh³

¹Maternity Research Center, Department of Obs & Gyn, Imam Reza Hospital, Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran

²Kermanshah University of Medical Sciences (KUMS), Kermanshah, Iran

³Clinical Research Development Unit, Department of Obs & Gyn, Imam Reza Hospital, Kermanshah University of Medical Sciences(KUMS), Kermanshah, Iran.

Email: *njalilian@yahoo.com

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Abstract

Objective: Hydatidiform pregnancy occurs in 1:1000 pregnancies worldwide; incidence is higher in Asian countries. In approximately 5% of cases of hydatidiform mole, clinical hyperthyroidism is present. The aim of this study was to examine the relation between HCG level and thyroid function test. **Methods:** During 5 years (2009-2013) we included 146 cases of molar pregnancies into the study at Imam Reza teaching hospital. The demographic and clinical data as well as serum initial HCG level and thyroid function test (TSH T3 T4) were retrieved and entered into prepared proformas. $p < 0.05$ was considered significant. **Result:** The mean age of patients was 29.31 years; mean of gestational age was 11.71 weeks; mean of gravidity was 2.32; mean of serum BHCG was $3.88E4$; mean of T4 was 11.07 and mean of T3 was 1.97. In this study significantly inverse relation was observed between B-HCG and TSH ($p = 0.05$). We also found a significantly direct correlation between B-HCG and T3 ($p = 0.01$) and T4 ($p = 0.01$). **Conclusion:** We concluded significantly meaningful relationship between BHCG and T3, T4, TSH.

Keywords

Molar Pregnancy, TSH, BHCG, T3, T4, Hyperthyroidism

*Corresponding author.

1. Introduction

Hydatidiform pregnancy occurs in 1:1000 pregnancies worldwide; incidence is higher in Asian countries [1] [2]. Hyperthyroidism is rare complication of molar pregnancy. Thyroid storm occurs even less frequently [3]. Prevalence of hyperthyroidism during complete molar pregnancy is as high as 7% [1]. Thyroid hyper function in molar pregnancy is attributed to excess of human chorionic gonadotropin which has a weak intrinsic thyroid stimulating activity and molar thyrotrophic hormone, differing from Human Chorionic Gonadotropin (HCG) by being larger in molecular size and longer in duration of action [4] clinical hyperthyroidism because trophoblastic disease is cured by evacuation of molar tissue [5]-[8].

The severity of trophoblastic disease-associated hyperthyroidism can vary from clinically asymptomatic elevations of thyroid hormones to life threatening thyrotoxicosis [9]. Studies indicate the analogy between HCG and thyrotrophic hormone (TSH), as well as among their receptors. The high levels of HCG seen in molar pregnancy may cause secondary hyperthyroidism [10]. In approximately 5% of cases of hydatidiform mole, clinical hyperthyroidism is present [11] and occasionally severe thyrotoxicosis may develop [12] [13]. The association between elevated HCG and TSH concentration during pregnancy has been known for many years [14] [15]. Numerous studies have documented the thyrotrophic effect of HCG [14] [16] [17]. It has been demonstrated that HCG can bind TSH receptors and suppress TSH production [18]. The aim of this study was to examine the relation between HCG level and thyroid function test (thyroid hormone TSH T3 T4) in patients with the diagnosis of molar pregnancies.

2. Material and Methods

This was a retrospective analytic descriptive study carried out on the cases of molar pregnancies who admitted at the department of gynecology in Imam Reza teaching hospital study during 5 years (2009-2013). It was approved by Imam Reza Hospital Clinical Research development unit. Molar pregnancies were diagnosed based on sonographic findings and histological studies. Those with incomplete molar pregnancy and choriocarcinoma excluded from the study. Medical records were reviewed for each subject to establish the subjects clinical thyroid status and document the presence of molar pregnancy. The demographic and clinical data as well as serum initial HCG level and thyroid function test (TSH T3 T4) were retrieved from Patient records and entered into prepared proformas. In 146 registered the patients with hydatidiform mole HCG in blood and thyroid function test was analyzed in our institute. TSH level (0.35 - 6.5 MIU/ml) was considered normal. Normal T4 level was considered 4.8 - 11.6 µg/dl. Normal T3 level was considered 0.6 - 2.1 ng/ml. Minimum sample size with confidence interval 95% and power of 80% was considered 119 cases. But we included all the patients during our study period (146 cases). SPSS version 20 was used for statistical analysis. To compare the relation between thyroid hormones and HCG Pearson or Spearman correlation was used. $p < 0.05$ was considered significant.

3. Results

67 cases of 155 study group (43%) were 25 - 34 years old and 31% were 15 - 24 years old and 38% were more than 35 years old. Regarding gravidity near to 80% of patients had gravidity one and two. In our study most of patients had subclinical hyperthyroidism 76 cases (49%) and no patients had clinical hyperthyroidism, and 79 cases (51%) were euthyroidism. The basic characteristics are shown in **Table 1**.

25 patients of 155 cases had B-HCG < 10,000 when they admitted, 40 patients had B-HCG = 10,000, 23 patients had B-HCG between 10,000 - 40,000, 10 patients had B-HCG between 40,000 - 100,000, 34 patients had B-HCG = 100,000, 5 patients had B-HCG > 100,000. 65 cases (41.9%) of 155 population study had B-HCG levels up to 10,000, and 90 cases (58.1%) had B-HCG levels more than 10,000. **Table 2** shows frequency of normal and abnormal levels of TSH, T4 and T3 in population study.

In this study the most common presenting symptom was vaginal bleeding, occurring in 81 out of 155 (52%). Lower abdominal pain was reported in 21 out of 155 cases (13%). Among 155 cases of molar pregnancy 32 cases was recognized just after doing abdominal sonography for prenatal care and they were asymptomatic (**Table 3**).

In this study significantly inverse relation was observed between B-HCG and TSH ($p = 0.05$). We also found a significantly direct correlation between B-HCG and T3 ($p = 0.01$) and T4 ($p = 0.01$) (**Figure 1**).

Mean of B-HCG level in subclinical hyperthyroidism group (76 cases) was 50,000 and in 79 cases without subclinical hyperthyroidism was 20,000, which shows a higher level with subclinical hyperthyroidism.

4. Discussion

Hydatidiform mole is the most common form of gestational trophoblastic disease that originates from the placenta and includes complete and partial site trophoblastic tumors [19]. Clinical hyperthyroidism is relatively common, occurring in about 1 in 100 pregnant woman. This is explained by the similarity of the α -subunit of HCG to TSH [20]-[23]. Thyroid storm although rare has a mortality rate as high as 15% [24]. Subclinical hyper-

Table 1. Basic demographic characteristics of patients.

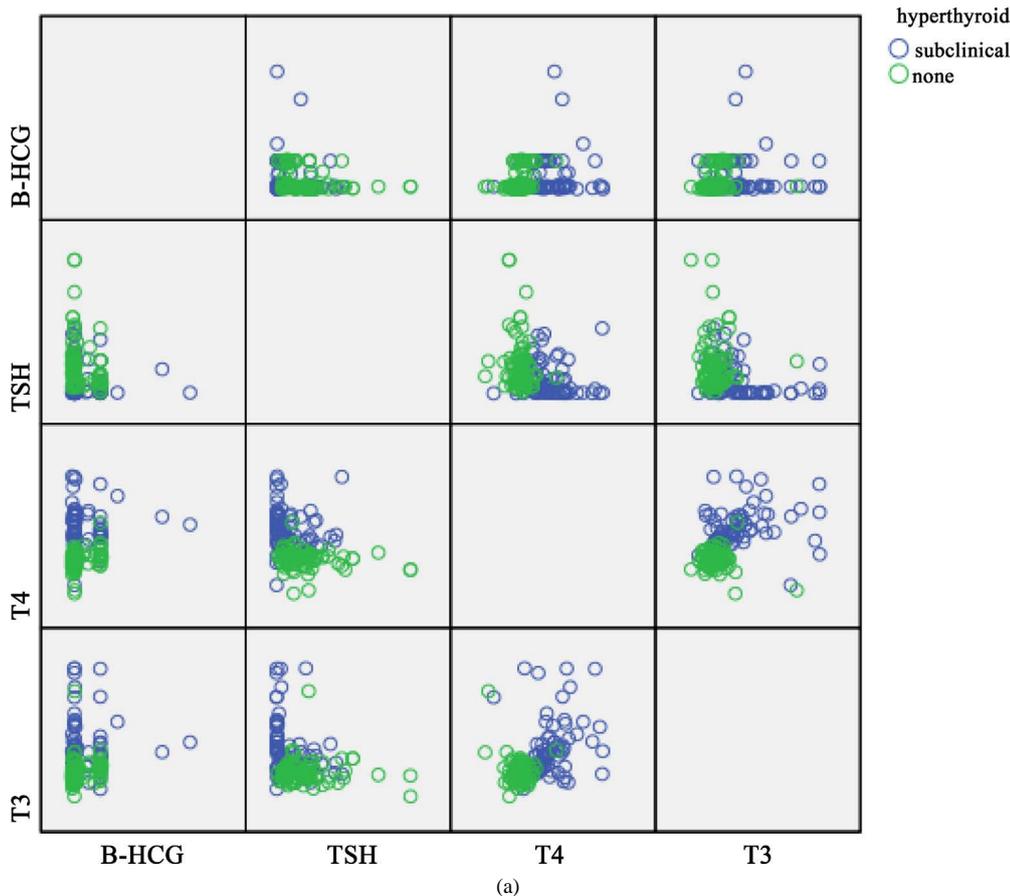
	Age (year)	gestational age (week)	Gravidity (NO)	B-HCG (IU/L)	TSH (MIU/ml)	T4 (μ g/dl)	T3 (ng/ml)
Mean	29.31	11.71	2.33	3.88E4	1.42	11.07	1.97

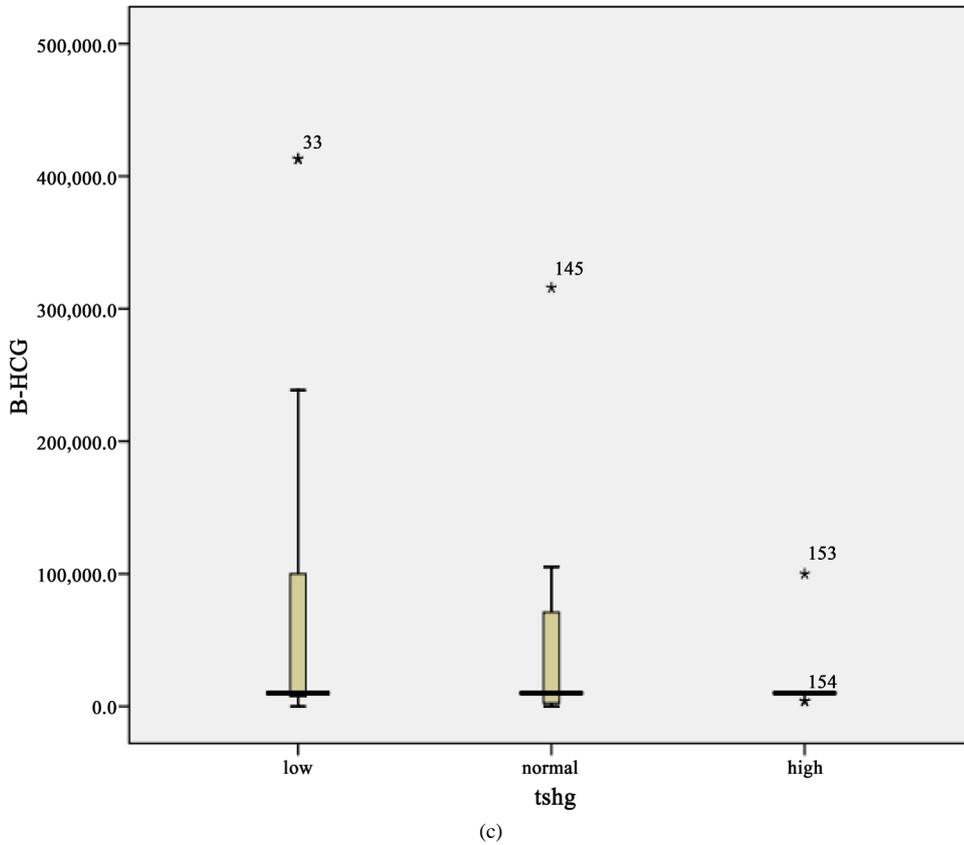
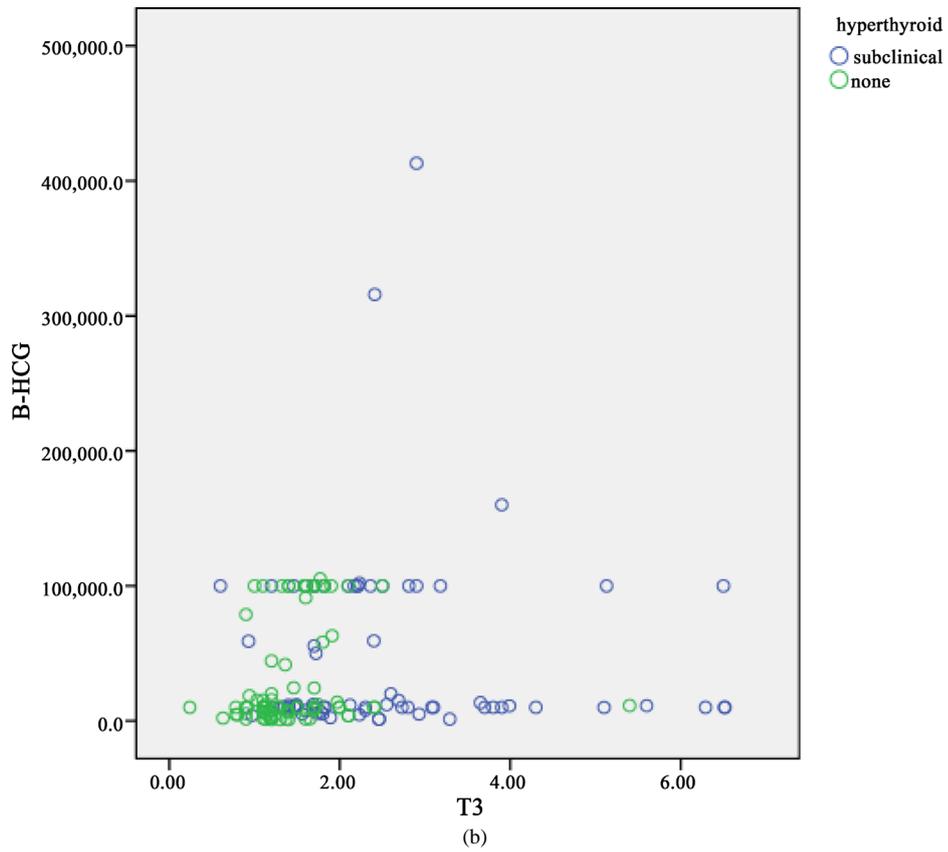
Table 2. Levels of TSH, T4 and T3 in patients.

	Number of patients with normal levels	Number of patients with less than normal levels	Number of patients with more than normal levels
TSH	104 (67%)	42 (27%)	9 (6%)
T4	93 (60%)	3 (1.9%)	59 (38.1%)
T3	110 (71%)	-	45 (29%)

Table 3. The common sign and symptom of patients with molar pregnancies.

	Vaginal bleeding	Abdominal pain	No symptom	Other symptoms
Number (percent)	81 (52%)	21 (13%)	32 (22%)	21 (13%)





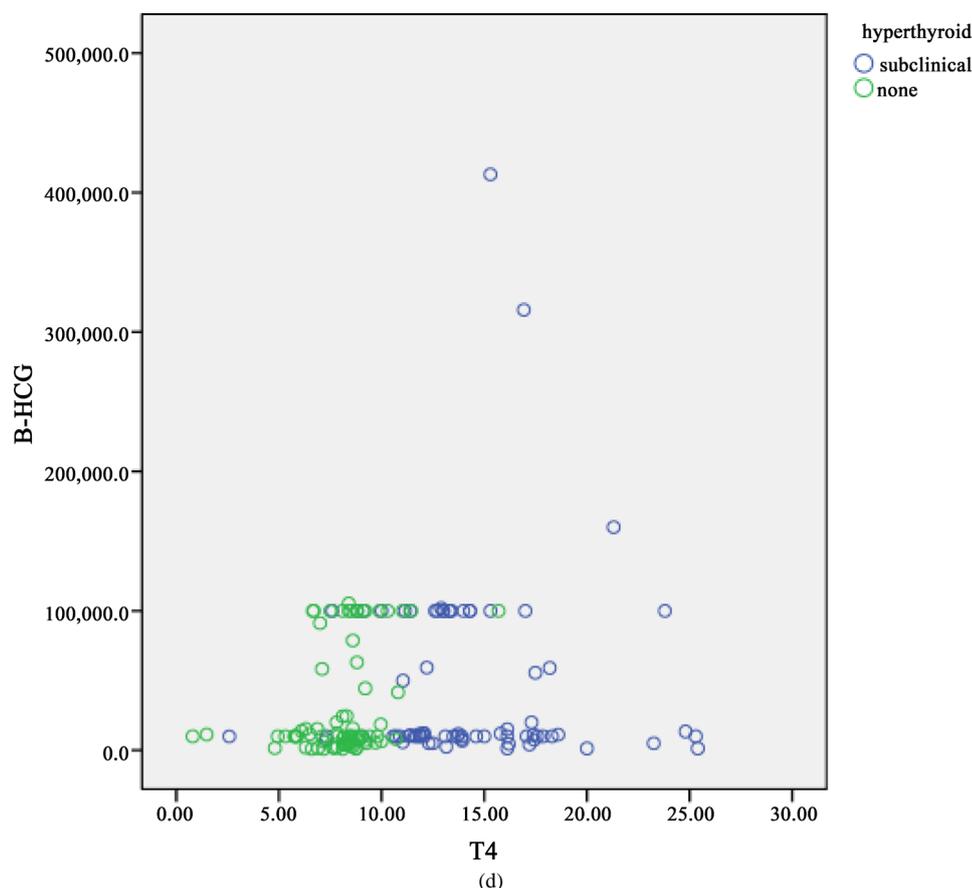


Figure 1. Relation between the hormone levels BHCG, TSH, T4 and T3.

thyroidism is well documented in pregnancy. At the time of peak HCG levels in normal pregnancy, serum TSH falls and bears a mirror image to the HCG peak. This fall in TSH suggests that it is HCG that causes increased secretion of T3 and T4 [25]. When there are clinical features of thyrotoxicosis, as in some cases of hyperemesis gravidum, anti-thyroid treatment may be given, but is rarely required beyond 22 weeks gestation.

Human chorionic gonadotrophin is a glycoprotein composed of α and β subunits. The α subunit is almost identical to that found in TSH, luteinising hormone (LH) and follicle-stimulating hormone [25]. The subunit consists of a 92-amino-acid chain containing two nitrogen-linked oligosaccharide side chains. *In vitro* testing has shown low-affinity cross-reactivity between these hormones [25] [26].

Thyroid-stimulating activity in serum of normal pregnant women shows a significant correlation with levels of serum HCG levels. It is likely that the thyrotrophic activity of HCG during first trimester peak secretion overrides the normal operation of the hypothalamic-pituitary-thyroid feedback system [27]. An association has been reported in certain pathologies of pregnancy, where there is increase in HCG, as in hyperemesis gravidarum, with an increase in thyroid function [28]. In some cases, the gestational trophoblastic disease is complicated with hyperthyroidism. This is believed to occur because of molecular mimicry between HCG and TSH causing cross-reactivity of the molecule of HCG with the TSH receptor. Treating gestational trophoblastic disease normalizes the HCG levels and hyperthyroidism is resolved [29].

The aim of this study was to explore the relation between HCG level with TSH, T3 and T4 in patients with molar pregnancies. HCG shares a common α -subunit with TSH, possessed thyroid stimulating activity [30]. Lack wood *et al.* reported that HCG concentration higher than 400,000 IU/L suppresses TSH level and most patients with HCG higher than 200,000 IU/L lack overt hyperthyroid syndrome [31]. In the present study no patient had clinical hyperthyroid syndrome. This may be due to less HCG level than 200,000 IU/L. But among 76 patients with subclinical thyroid syndrome the mean serum HCG level was 50,000 and in those without subclinical hyperthyroid syndrome was 20,000 which shows a correlation between HCG level and subclinical hyper-

thyroid syndrome. The HCG levels in present study ranged from 20,000 - 50,000 MIU/L and there is a significantly inverse correlation between the HCG and TSH levels ($p = 0.05$). Correlation between HCG and T3 was also significant and directly ($p = 0.01$) and there was direct correlation between HCG level and serum T4 level ($p = 0.01$). We found higher HCG level in subclinical hyperthyroid syndrome group than in normal group (50,000 versus 20,000 MIU/L).

Lindhome and flan [32] from Sweden have reported on 75 patients with complete mole and 60 with partial moles. In the complete mole group the mean gestational age at the time of sonography was 12.4 weeks which is near to the present study 11.71 weeks. In their study 77% of patients had vaginal bleeding. In the present study also the most common symptoms was vaginal bleeding 52% (81 cases). Pain was observed in 13% (21 cases) of our patients versus 23% in Lindhome study. In the present study 22% (32 cases) had no symptom but in Lindhome study 12 patients had experience no symptoms. This may be due to early request for doing ultra sonography. In view of the controversy regarding the role of human chorionic gonadotropin as the stimulator of thyroid function in patients with trophoblastic tumors, especially hydatidiform mole, we concluded that relationship between HCG and T4 and T3 was direct and meaningful but relationship between HCG and TSH was inverse and meaningful. Regarding this syndrom, Amir [33] found a weakly positive correlation ($p < 0.05$, $r < 0.35$, $n = 47$) between the serum human chorionic gonadotropin levels and serum total thyroxine concentrations. However he found no correlation between HCG levels and free thyroxine index values ($p > 0.05$, $r = 0.32$, $n = 34$). Also in that study there was no correlation between serum HCG levels and either serum total 3,5,3'-triiodthyronine concentrations ($p > 0.1$, $r = 0.32$, $n = 17$). This is against our study which showed a meaningful relationship. The present study support the premise that human chorionic gonadotropin per se is the thyroid stimulator of molar pregnancy.

5. Conclusion

We concluded significantly meaningful relationship between BHCG and T3, T4, TSH. Thyroid function tests should be mandatory in all women with hydatidiform mole and these women should be stabilized with β blockers and antithyroid medication prior to induction of anesthesia for their surgical evacuation. Vigilant monitoring and intensive care should be extended into the postoperative period because there is a likelihood of occurrence of cardiopulmonary complications, thyroid storm, and disseminated intravascular coagulation.

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Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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