A STUDY OF THYROID STATUS IN HYPEREMESIS GRAVIDARUM

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ABSTRACT

Study was undertaken to assess thyroid status in hyperemesis gravidarum. 150 women pregnant with < 20 weeks of gestation were selected randomly and out of these 100 women presenting with hyperemesis formed study group while 50 normal pregnant women served as controls. 53% of hyperemetic pregnant women were primigravidae and 82% of pregnant women presented with vomiting at less than 12 weeks of gestation. Statistically significant, 22% of hyperemetic women had increased serum T_3 levels while T_4 levels were increased in 67% of women in study group as compared to 8% and 16% respectively in control group. TSH levels were decreased in 18% of hyperemetic women as compared to 8% in control group with decrease in mean TSH level statistically significant. 22% of hyperemetic women had electrolyte disturbances and 7% were ketonuric. In clinically euthyroid women, biochemically altered thyroid function can attribute to vomiting and its prolongation to second trimester

KEY WORDS

Thyroid function, Hyperemesis gravidarum, Morning sickness, Thyrotoxicosis

INTRODUCTION

Nausea and vomiting in early pregnancy affects 50% to 90% pregnancies (1) and because of this it is listed as a presumptive symptom of pregnancy (2). Hyperemesis gravidarum affects only 0.3-2% pregnancies (3) and approximately 0.5% of live births (4), once it occurs, is quite serious. Its etiology is obscure. Factors responsible for it vary from social, psychological, allergy to products produced by ovum to dietary deficiency of protein, vitamin B₁ and B₆ (2). It has also been related to high or rapidly rising levels of chorionic gonadotrophins or its effect on steroidogenesis causing increased estradiol concentration (5) or lower body mass index (6). HCG was even thought to be indirectly involved in its etiology by its ability to stimulate thyroid (7) and molecular variants of HCG with greater thyrotrophic activity have been documented in hyperemetic pregnant women (8), even biochemical thyrotoxicosis has been displayed in these women (9,10). Thus, this study was undertaken to evaluate the thyroid status in women with hyperemesis gravidarum.

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MATERIALS AND METHODS

This prospective study was conducted on randomly selected 150 pregnant women at less than 20 weeks of gestation out of these 100 women with excessive vomiting presenting in OPD or admitted in ward constituted study group however, 50 women with normal pregnancy formed control group. Inclusion of outpatients was based on consideration that many patients do suffer from severe degree of vomiting but do not get admitted due to either financial or family restrictions. Women with more than 20 weeks of gestation, multiple pregnancy, hydatidiform mole, known case of thyroid diseases, and vomiting due to any medical or surgical disorder were excluded from the study. After detailed history thorough general physical and systemic examination was done to find the cause, severity and systemic effects of hyperemesis. In every woman routine investigations (Hb, Total & differential leucocytic count, blood group, VDRL, serum electrolytes and urine examination especially for ketone bodies) were sent. Special investigations like lower abdomen ultrasound, liver/kidney function tests were done only if needed & patient could afford. In women of both groups 5ml of venous blood was withdrawn and serum T_3 , T_4 and TSH levels were measured by IMX system in which T_3 and TSH assay was based on microparticle enzyme immunoassay technology (MEIA) whereas T_4 measurement was based on fluorescence polarization immunoassay (FPIA).

All women were treated on outdoor basis symptomatically with assurance, diet modification, vitamins and antiemetic drugs. In case woman did not respond, she was hospitalized where fluids and antiemetic drugs were given parenterally. Antithyroid drugs were given if needed.

RESULTS

Women were comparable in age, socio-economic status and geographic distribution in both study and control group. 32% parous women and 53% Primigravidae (Table 1) presented with excessive vomiting. In the study group, 82% women were pregnant with less than 12 weeks of gestation (Table 2), and in 2% vomiting had prolonged beyond 16 weeks of gestation whereas all the controls were at less than 16 weeks of gestation. In both groups none of the women had clinical enlargement of the thyroid gland. Almost equal number of women (49% in study and 52% in control) were mildly anaemic and Rh+ve (92% vs 90% respectively).

Table 1 : Distribution Of Women According To Obstetrical History

Parity	Study group		Control group		Statistical Comparison	
	No.	%	No.	%	Z Value	P
Primigravida	53	53	21	42	1.23	>0.05
Nullipara with previous abortions	15	15	7	14	0.16	>0.05
Parous	32	32	22	44	1.44	>0.05
Total	100	100	50	100		

Table 2 : Distribution Of Women According To Period Of Gestation

Period of gestation (Weeks)	Study group		Control group		Statistical Comparison	
	No.	%	No.	%	Z Value	P
≤ 8	28	28	15	30	0.26	>0.05
8-12	54	54	25	50	0.46	>0.05
12-16	16	16	10	20	0.61	>0.05
16-20	2	2	0	0	0.01	>0.05
Total	100	100	50	100		

On analyzing thyroid functions, serum T₃ levels were increased i.e. >1.66ng/ml in significant number of hyperemetic women (22% vs 8%) (Table 3). However increase in mean T₃ level (1.70±2.9 vs 1.24 ±0.35ng/ml) was not statistically significant (p > 0.05).

Table 3 : Distribution Of Women According To Serum T₃ Level

Serum T ₃ level ng/ml	Study group		Control group		Statistical Comparison	
	No.	%	No.	%	Z Value	P
0.51-1.65	78	78	46	92	2.14	<0.05
1.66-2.00	13	13	3	6	1.31	>0.05
2.01-2.9	7	7	1	2	1.29	>0.05
≥ 3.00	2	2	0	0	1.01	>0.05
Mean T ₃ ±SD*	1.70±2.9		1.24±0.35			

Normal Serum T₃ level : 0.51-1.65 ng/ml

67% of hyperemetic women (Table 4) as compared to only 16% of normal pregnant women were found to have raised serum T₄ level i.e. >12.00ng/dl. Mean T₄ level was significantly higher (14.10 ± 3.28 vs 9.89 ± 2.46 ng/dl) in study group (p < 0.001).

Table 4 : Distribution of women according to serum T₄ level

Serum T ₄ level ng/dl	Study group		Control group		Statistical Comparison	
	No.	%	No.	%	Z Value	P
4.5-12.00	33	33	42	84		
12.01-15.00	31	31	5	10	5.89	<0.001
15.01-20.00	30	30	3	6	2.84	>0.05
20.01-25.00	6	6	0	0	3.34	>0.05
Mean T ₄ level ±SD*	14.10±3.28		9.89±2.46		1.77	>0.05

Normal Serum T₄ level : 4.5-12.00 ng/dl

P value of * < 0.001 Highly significant

Serum TSH level was less than normal i.e. <0.47µIU/ml, in 18% women of study group whereas in control group only 8% had TSH less than normal (Table 5). Mean TSH level was significantly lower (1.70 ± 1.16 vs 2.36 ± 1.33) in study group (p < 0.01).

Table 5 : Distribution Of Women According To Serum TSH Level

Serum TSH level µIU/ml	Study group		Control group		Statistical Comparison	
	No.	%	No.	%	Z Value	P
<0.47 ¹	18	18	4	8	1.60	< 0.01
0.47-2.50 ²	63	63	26	52	1.29	>0.05
2.51-5.01 ³	19	19	20	40	2.76	>0.05
>5.01 ⁴	0	0	0	0		
Mean TSH level ±SD*	1.70±1.16		2.36 ±1.33			

Normal Serum TSH level : 0.47-5.01 µIU/ml

P value of * < 0.01 Highly significant

In spite of all hyperemetic women being treated symptomatically on outdoor basis, 37/100 required hospitalization and in 22/100 women (Table 6) vomiting had caused electrolyte disturbances in the form of hyponatraemia, hypokalaemia & hypochloraemia, in 7/100 women ketone bodies were present in urine. On further analyzing these seven ketonuric women, all required hospitalization and had increased serum T_4 level, two women had raised T_3 level and six had deranged electrolytes. On evaluating 18 women

Table 6 : Biochemical Profile

	Study group n =100		Control group n = 50	
	No.	%	No.	%
Serum Electrolytes				
Normal	78	78	30*	
Deranged	22	22	0	0
Urinary Ketones				
Negative	93	93	50	100
Positive	7	7	0	0

* Rest did not agree for electrolyte analysis.

in whom vomiting had prolonged to the second trimester 13 had raised serum T_4 level, one had increased serum T_3 level, four had decreased serum TSH level, five had electrolyte imbalance and seven needed hospitalization. In the study group all women responded to general symptomatic measures, none had any life threatening complication and nor deteriorated or required antithyroid drugs.

DISCUSSION

HCG is a bipeptide, it has an alpha-subunit identical to TSH and beta-subunit with limited sequence homology to TSH and has a weak thyrotrophic activity. In early pregnancy thyroid is under control of both TSH and HCG (10), peak of HCG & nadir of serum TSH almost coincide each other at about 10 weeks of gestation (11). HCG possibly stimulates thyroid activity via its receptors along with LH & HCG receptors (12). This stimulating activity was measured remarkably high ($p < 0.001$) in hyperemetic patients (5). In our study 82% women had vomiting at less than 12 weeks of gestation that coincides with the period of peak HCG levels and 53% were exposed to HCG for the first time. Ganguli et al (13) also reported vomiting in 93.3% of women at less than 12 weeks of gestation.

Hyperthyroidism in hyperemetic women is transient & raised T_3 & T_4 levels normalize by 15 & 19 wks of gestation

respectively (9), in our study also in 18 women vomiting had prolonged up to 20 weeks & all had biochemical hyperthyroidism.

Hyperemesis in current pregnancy has been reported to be associated with fewer pregnancies and deliveries & past unsuccessful obstetrical outcome like more spontaneous abortions (14), however in our study previous abortions and parity had no correlation, as approximately 32 % parous and 15% nulliparous women with previous abortions had excessive vomiting and almost same number with similar history had no vomiting in current pregnancy. Age, parity, racial and marital status, was observed same in hyperemetic patients and general population (15). Which coincides with our observation that in both groups age, blood group and hemoglobin status of women was same.

Pregnancy through HCG stimulates thyroid gland but effect on TSH level is reported to be conflicting i.e. normal (16) or decreased (17,18) between 0.1 to 0.4mU/L during eighth to 14th wks of normal pregnancy (19). This stimulation is more (53.3% vs 6.68%) in hyperemetic women (13); we also observed statistically significant suppression of TSH in hyperemetic women (18% vs 8%). Similar TSH suppression was reported in both Asian and European pregnant women by Price et al (20). With thyroid stimulation, in hyperemetic women both serum T_3 & T_4 level rises but rise of T_4 is observed more significantly and frequently (9,10,18,) than T_3 . Ganguli et al (13) found raised serum T_4 level in 80% of hyperemetic cases as compare to 13.33% controls (mean 12.22µg/dl vs 9.679µg/dl.) & raised T_3 levels in 53.3% hyperemetic & 6.66% of controls (mean 2.13ng/ml vs 1.269ng/ml). Similarly only rise in T_4 level was statistically significant in our study.

Dietary iodine intake also affects thyroid functions even during pregnancy. Our study was conducted in area of adequate dietary iodine intake and all women were clinically euthyroid and none had goiter. In areas of marginally low iodine intake, significant number of women with hypothyroidism and goiter were reported to be associated with gestation (10).

Tan et al (9) had reported transient hyperthyroidism in hyperemesis gravidarum but lacks clinical features of hyperthyroidism. Hyperemesis can lead to dehydration, metabolic disturbances and nutritional deficiencies requiring timely treatment & hospitalization but if left untreated can be fatal (21). Hyponatraemia & hypokalaemia was reported in 66.7% & 59% of hyperemetic women respectively (9). Though our hyperemetic women had various electrolyte disturbances & ketonuria yet none of women had any life threatening

complication while Wernicke's encephalopathy was reported in two women (22). No doubt, hyperthyroidism was observed in our study but it was not to the extent of demanding treatment with antithyroid drugs. In clinically euthyroid women, biochemically altered thyroid function may be the cause of vomiting and may attribute to its prolongation to second trimester.

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