



HYPEREMESIS IN THE FIRST TRIMESTER OF PREGNANCY: ROLE OF BIOLOGICAL HYPERTHYROIDISM

Endocrinology

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ABSTRACT

Context: Hyperemesis gravidarum (HG) is associated with an important morbidity and a high cost to society. The pathophysiology is not yet well known. Thyroid hormone and human chronic gonadotrophin play an important role in the occurrence of these vomitings.

Objective: The aim of this study was to investigate whether HG was associated with biological hyperthyroidism and to try to clarify the links between biological hyperthyroidism and the severity of hyperemesis.

Design: We reported a retrospective descriptive transversal study.

Methods: We gathered 138 patients who were hospitalized for HG during the first trimester of pregnancy over a period of 3 years (from January 1st 2014 to December 31st 2016) led within the department of obstetrics and gynecology "A" of the Charles Nicolle hospital in collaboration with the endocrinology unit of the department of internal medicine.

Results: The average age of our patients was $29,6 \pm 4,7$ years. The average gestational age was $9,1 \pm 1,6$ weeks. The mean gravidity and parity were $1,9 \pm 1$ and $0,5 \pm 0,7$. Ninety patients (65,2%) had biological hyperthyroidism. These patients were more likely to have fluid and electrolyte disturbances (74,4% against 37,5% for patients with euthyroidism). The same applies to liver function disturbances: 30% for hyperthyroid patients against 12,5% for euthyroid patients. Frequency of severe vomiting was significantly higher for hyperthyroid patients (74,4% vs 41,7%). The TSH was significantly lower and FT4 was significantly higher in patients with severe vomiting compared to patients with non-severe vomiting.

Conclusion: Biological hyperthyroidism is associated to hyperemesis gravidarum and its severity.

KEYWORDS

pregnancy, hyperemesis gravidarum, hyperthyroidism

INTRODUCTION:

Thyroid disorders, taken in aggregate, are common in young women and thus frequently managed in pregnancy. Maternal thyroid changes during pregnancy are substantial, and normally altered gland structure and function are sometimes confused with thyroid abnormalities. That is why some researchers seem to accept the notion that pregnancy may have a role in provoking a new onset of hyperthyroidism or worsening a previously established one [1]. The incidence of thyrotoxicosis or hyperthyroidism in pregnancy complicated by nausea and vomiting is varied and may affect two thirds of those women [2]. The pathophysiological mechanisms of uncontrollable vomiting during pregnancy and their association with hyperthyroidism are still poorly understood [3], which explains the lack of a general consensus on the routine screening for thyroid function during pregnancy even if hyperemesis gravidarum (HG) occurs. We share our experience that was gained from the Department A of obstetrics and gynecology in collaboration with the endocrinology unit of the department of internal medicine in the hospital Charles Nicolle, Tunisia. Besides, we made a review of the literature in an attempt to identify the relation between the biochemical hyperthyroidism and the severity of vomiting.

MATERIALS AND METHODS:

We conducted a cross-sectional, descriptive, and retrospective study involving 138 women, who were hospitalized for severe vomiting occurring during the first trimester of pregnancy, in the Department A Gynecology and Obstetrics in Charles Nicole Hospital during a 3-year period from January 2014 through December 2016 in collaboration with the endocrinology unit of the department of internal medicine A in the same hospital. The women excluded from our study were those with an obvious cause of vomiting or those who previously had a thyroid disorder. We defined hyperemesis gravidarum (HG) by the presence of severe and persistent vomiting associated with at least one of the following abnormalities: hyponatremia, hypokalemia, hypochloremia, and an increase of AST and / or ALT levels. FT4 and TSH 3rd generation were measured by chemiluminescence

immunoassay. We defined hyperthyroidism by a TSH $<0.35 \mu\text{IU} / \text{ml}$ with or without an increase of FT4 $>1.48 \text{ ng} / \text{dl}$.

RESULTS:

Our study involved 138 pregnant women. The mean age of the patients was $29,6 \pm 4,7$ years ranging from 20 to 42 years. Mean gestational age was $9,1 \pm 1,6$ weeks with extremes ranging from 5 to 12 weeks. The mean number of gravidity was $1,9 \pm 1$ with extremes between 1 and 6. The proportion of nulliparas was 58.7%. The majority (60.9%) of patients had no significant previous gynecological or obstetrical history. The remaining patients (N = 54/138 or 39.1%) had a history of miscarriages, premature labour, gestational diabetes mellitus, and preeclampsia.

In order to study the relationship between severe vomiting during the first trimester of pregnancy and biochemical hyperthyroidism, we compared a group of 90 vomiting pregnant patients who had also hyperthyroidism (65,2%) with a group of 48 vomiting pregnant patients who were in euthyroid status (34,8%).

Clinical examination of the patients revealed that only 13.4% of hyperthyroid patients had at least one symptom suggestive of hyperthyroidism. Comparing the two groups with each other, we found some common symptoms which included agitation, palpitations, weight loss and irritability.

On the other hand, clinical signs of hyperthyroidism such as goiter, exophthalmia, tachycardia and tremor, were only found in the hyperthyroid patients. As for ketonuria, we did not find a statistically significant difference between hyperthyroid and euthyroid groups.

As far as the hyperthyroid patients were concerned, electrolyte abnormality (hypokalemia), elevated transaminases or elevated total bilirubin was more encountered in significantly higher proportions compared to the other group. The proportion of women having

hypochloremia or hyponatremia was higher in hyperthyroid group compared to those with euthyroidism. However, this difference was not significant. Regarding the electrolyte abnormalities, they were more likely to occur in the hyperthyroid patients.

Concerning the severity of the vomiting, the proportion of women who suffered from severe and persistent vomiting was found to be more increased in the hyperthyroid patients than the euthyroid ones and this difference was statistically significant ($p < 0.001$). For TSH and FT4 levels in patients with severe vomiting, the mean TSH level was significantly lower and FT4 was significantly higher compared to those with mild or moderate vomiting. We found a statistically significant difference between the two groups of patients in terms of length of hospital stay which was less in the euthyroid group ($p < 0.001$).

DISCUSSION

The association between biochemical hyperthyroidism and hyperemesis gravidarum is clearly illustrated and has been studied by several authors, as shown by the study of Deruelle et al [3]. The incidence of hyperthyroidism in our study was similar to that found in several studies (Table 1). Nausea with or without vomiting is so common in early pregnancy 50 to 75% of pregnancies [3, 4] that mild symptoms may be considered part of the normal physiology of the first trimester. However, these symptoms can significantly impact the quality of life of both the pregnant woman and her family, especially when persistent and/or severe. Hyperemesis gravidarum is the term used to describe the severe end of the symptom spectrum, with an incidence of between 0.3 and 3.6% according to different countries [5, 6].

In our study, the mean age of the patients was 29.6 ± 4.7 years, which was similar to other studies. Younger women appear to be more likely to be affected. Regarding the hyperthyroidism, only 13.4% had symptoms suggestive of thyroid hyperfunctioning as far as our study is concerned. This is comparable to the study of Tan et al. [3] where only 9.1% of hyperthyroid vomiting women were symptomatic. When it comes to Azarian et al [7], the diagnosis of overt hyperthyroidism during pregnancy may be difficult because of the changes in thyroid function that occur during normal pregnancy. Many of the nonspecific symptoms associated with pregnancy are similar to those associated with hyperthyroidism, including tachycardia, heat intolerance, and increased perspiration. The diagnosis of hyperthyroidism during pregnancy is based upon clinical manifestations and thyroid function tests. Specific findings such as goiter and ophthalmopathy suggest Graves' hyperthyroidism. For Mestman, tachycardia is particularly suggestive of hyperthyroidism. [8]. Ketouria, which reflects acute malnutrition, was more common in hyperthyroid group, but this difference was not statistically significant.

Hyperemesis gravidarum is responsible for rapidly developed dehydration associated with electrolyte and acid-base derangements (hyponatremia, hypochloremia and hypokalemia) and abnormal liver enzyme values. In fact, several authors have used this set of criteria for either defining the entity of HG or assessing its severity [3, 9, 10, 11]. Our study illustrated that hyponatremia was more common in women with HG associated with biochemical hyperthyroidism without statistically significant difference between the two groups. The pathogenesis of hyponatremia may be explained by HG and it is associated with the disease severity. In our study as well as Deruelle et al. [3], the proportion of patients having hypochloremia was higher in hyperthyroid group but we did not find a statistically significant difference. The percentage of hyperthyroid vomiting patients with hypokalemia was significantly higher than that of euthyroid patients. Our results are consistent with those of Goodwin et al. [12] and Deruelle et al. [7]. According to the relevant literature, the number of women who had at least one electrolyte and acid-base derangements was expressed as percentage. This allowed us to shed light on a statistically significant relationship between biochemical hyperthyroidism and electrolyte abnormalities. 74.4% of hyperthyroid patients with vomiting had at least one fluid-electrolyte balance disorder compared with 37.5% of euthyroid patients. Similarly, liver enzymes were found to be significantly higher in 30% of hyperthyroid patients against 12.5% in euthyroid patients. The incidence of severe vomiting was significantly higher in hyperthyroid patients (74.4% versus 41.7%). Also, the hospital stay was significantly longer in hyperthyroid group.

TSH was significantly lower and FT4 was higher in patients with severe vomiting than those with mild vomiting.

CONCLUSION:

There appeared to be a correlation between hyperthyroidism and the severity of vomiting. In case of hyperthyroidism superimposed on hyperemesis gravidarum, the electrolyte abnormalities and hepatic cell injury were more encountered. Besides, vomiting was more severe. In case of severe vomiting, the abnormalities of the thyroid functions were of paramount importance. Given the large proportion of asymptomatic types and in the absence of specific clinical signs of biochemical hyperthyroidism, clinicians should take into account the laboratory disturbances in patients suffering from hyperemesis gravidarum rather than depending on indecisive clinical findings. Thus, hyperthyroidism should be suspected in the course of severe nausea and vomiting of pregnancy and therefore be detected.

Table 1: the incidence rate of biochemical hyperthyroidism in the course of hyperemesis gravidarum

Author	Year	incidence of biochemical hyperthyroidism
Goodwin T.M. [19]	1992	66 %
Deruelle et al. [7]	2002	66,7 %
Tan Y.J. [3]	2002	60,9 %
Sun S. [4]	2014	37,9 %
Malek N.Z. [20]	2017	4,8 %
Notre étude	2014 - 2016	65,2 %

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