

Pregnancy, gestational diabetes, thyroid function: our experience

T. IZZO¹, G. LO DICO¹, P. RICHIUSA²

SUMMARY: Pregnancy, gestational diabetes, thyroid function: our experience.

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This is a retrospective study of 112 patients with GDM. The purpose is to evaluate the relationship between GDM and impaired thyroid function. All the patients were evaluated: TSH, FT4 and glycosylated hemoglobin (HbA1c). The normal range for TSH is between 0,45 and 2,5 μ U/ml; for FT4 is instead between 0,9 and 1,8 ng/dl; for HbA1c is less than 6%. Patients with elevated TSH and low levels of free thyroxine were diagnosed as "hypothyroid"; those with elevated TSH and FT4 in the standard as "subclinical hypothyroid"; pregnant women who had high TSH and low FT4 were diagnosed as "hyperthyroid"; women with low TSH and normal FT4 as "subclinical hyperthyroid". Patients who had normal levels of both thyrotropin and free thyroxine were considered "euthyroid". Based on the values of TSH and FT4 we obtained the following results: 77 patients (68,75%) euthyroid; 18 (16,1%) subclinical hypothyroidism; 12 (10,7%) hypothyroid; 5 patients (4,4%) subclinical hyperthyroidism. Our study confirms the association between thyroid disease and gestational diabetes.

In addition, the hypothyroid patients insulin-treated, compared with euthyroid, increased the insulin requirement. The results show that women with GDM have a risk greater for both clinical and subclinical hypothyroidism; for this reason it is advisable to carry out a program of screening for thyroid function.

RIASSUNTO: Gravidanza, diabete gestazionale, funzione tiroidea: la nostra esperienza.

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Il nostro è uno studio retrospettivo condotto su 112 pazienti affette da GDM. Esso valuta la relazione tra GDM e alterazioni della funzione tiroidea. In tutte le pazienti è stato esaminato: TSH, FT4 ed emoglobina glicosilata (HbA1c). Il range di normalità di TSH è tra 0,45 e 2,5 μ U/ml; il range di FT4 è tra 0,9 e 1,8 ng/dl; il range di HbA1c è inferiore al 6%. Le pazienti con TSH elevato e bassi valori di tiroxina libera sono state diagnosticate come "ipotiroidiche", quelle con TSH elevato e valori di FT4 nella norma come "ipotiroidiche subcliniche", le gestanti che presentavano TSH bassi e alti valori di FT4 sono state diagnosticate come "ipertiroidiche"; le donne con TSH bassi e normali valori di FT4 come "ipertiroidiche subcliniche". Le pazienti che presentavano normali valori sia di tirootropina, sia di tiroxina libera sono state considerate "eutiroidiche". Sulla base dei valori di TSH e di FT4 abbiamo ottenuto i seguenti risultati: 77 pazienti (68,75%) eutiroidiche; 18 (16,1%) ipotiroidiche subcliniche; 12 (10,7%) ipotiroidiche; 5 pazienti (4,4%) ipertiroidiche subcliniche. La nostra indagine conferma l'associazione tra disfunzioni tiroidee e diabete gestazionale. Inoltre, le pazienti ipotiroidiche insulino-trattate presentano, rispetto alle eutiroidiche, un maggiore fabbisogno insulinico. I risultati ottenuti mostrano che le donne affette da GDM sono a maggior rischio per ipotiroidismo sia clinico sia subclinico; per tale ragione è consigliabile eseguire un programma di screening per la funzione tiroidea.

KEY WORDS: Pregnancy - Gestational diabetes - Thyroid disease.
Gravidanza - Diabete mellito gestazionale - Alterazioni tiroidee.

Introduction

Pregnancy brings many endocrine and metabolic changes that derive from physiological changes on the borderline between mother and fetus.

The prevalence of the thyroidal dysfunctions in pregnancy is: 0,2% for hyperthyroidism (with serious and frequent fetal and neonatal complications), 2,5% for hypothyroidism, 4-5% for thyroidal nodules (1).

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Gestational diabetes mellitus (GDM) has a prevalence that varies from 5 to 6%.

Many recent studies suggest that even slight maternal deficits of thyroid hormones (subclinical hypothyroidism and ipotiroxinemia maternal isolated) during pregnancy may affect the neuropsychological development of newborn (5-12).

Physiological changes of TBG in pregnancy make the dosage of the whole T4 of inadequate value in the diagnosis of hypothyroidism, unlike the high sensitivity attributed to TSH. The latter, in fact, represents the most sensitive index to notice, in a reliable way, abnormalities of the thyroid function (13).

Today, the reference range for serum TSH in the general population is 0,45 to 2,5 μ U/ml.

The condition of insulin resistance in subjects with hypothyroidism clinically overt led to analyze the possible correlation between pancreas and the thyroid gland (14-18).

The observation that the insulin resistance is comparable between patients with clinically overt hypothyroidism and those with subclinical hypothyroidism, indicating that the levels of thyroid hormones, by itself, can not be entirely responsible for the manifestation of this phenomenon.

Materials and methods

The purpose of our study is to evaluate the association between gestational diabetes and alterations of the thyroid function: hypothyroidism, subclinical hypothyroidism, hyperthyroidism and subclinical hyperthyroidism.

This is a retrospective study performed on 112 women with gestational diabetes mellitus, they have been followed at the Observation Clinic of gestational diabetes of the UOC of Obstetrics and Gynaecology of the Hospital "Paolo Giaccone" University of Palermo, over a time interval of 39 months (January 2009 - March 2012).

Gestational diabetes was diagnosed – between the 24th-and 28th week of gestation – on the basis of guidelines recommended by the Italian Society of Diabetology (ISD), using a one-stage procedure (OGTT with 75 g glucose), interpreted according to the criteria of the HAPO Study.

All pregnant women in which it was identified the GDM, were subjected to a venipuncture to determine TSH, FT4 and glycosylated haemoglobin (HbA1c). The normal range for TSH is between 0,45 and 2,5 μ U/ml, the FT4 is between 0,9 and 1,8 ng/dl, and that of HbA1c less than 6%.

Patients with elevated TSH, but with low levels of free thyroxine have been defined as "hypothy-

roid", those with elevated TSH and FT4 in the standard as "subclinical hypothyroid"; pregnant women who had high and low TSH FT4 as "hyperthyroid"; finally, women with low TSH and normal FT4 as "subclinical hyperthyroid". Women who had normal levels of both thyrotropin and free thyroxine were considered "euthyroid".

Age, parity, body mass index and blood pressure were correlated with TSH values.

We also compared the insulin requirement with the thyroid condition.

Results

Our record consists of 112 pregnant women suffering from gestational diabetes mellitus. Patients have an average age of $32,43 \pm 5,43$ (M \pm SD) (range: 19-46 years) and body mass index of $28,28 \pm 6,99$ kg/m² (M \pm SD) (range: 16,94 to 48,44 kg/m²).

Based on the values of TSH and FT4 we obtained the following results: 77 patients (68,75%) are euthyroid, 18 patients (16,1%) are subclinical hypothyroidism, 12 patients (10,7%) are hypothyroid; 5 patients (4,4%) are subclinical hyperthyroidism; it has not be found any cases of hyperthyroidism (Fig. 1).

The average values of FT4 observed in our study are: $1,06 \pm 0,355$ ng/dl (M \pm SD) (Fig. 2); the average values of TSH are: $2,01 \pm 1,282$ μ U/ml (M \pm SD) (Fig. 3).

36 patients (28,57%) were subjected to insulin treatment, of these 23 patients (63,88%) were euthyroid, 12 patients (33,33%) were hypothyroid, one patient (2,7%) was hyperthyroid.

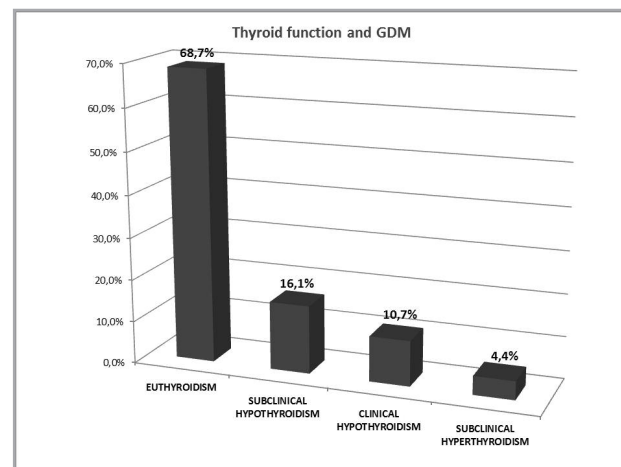


Fig. 1 - Patients distribution in relation to the thyroid function.

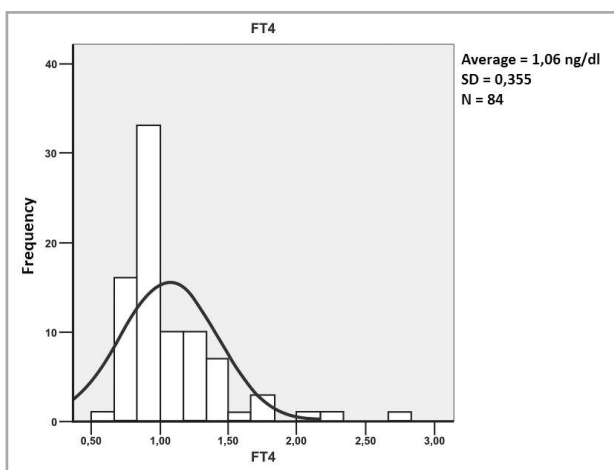


Fig. 2 - FT4 levels [ng/dl] in the cohort of examined patients.

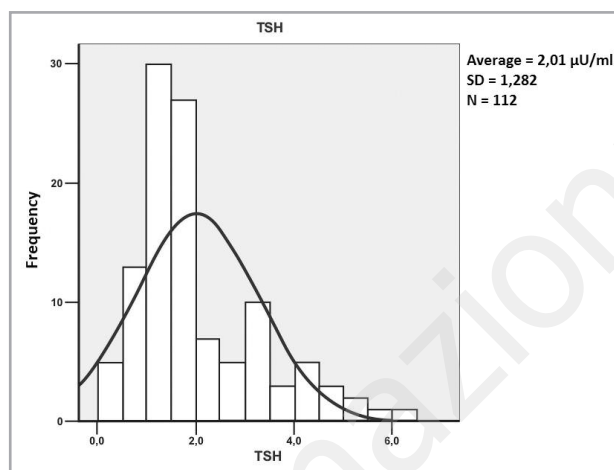


Fig. 3 - TSH levels [µU/ml] in the cohort of examined patients.

Of the 12 patients treated with insulin, classified as “hypothyroid”, 9 (75%) are “subclinical hypothyroid”, 3 (25%) “hypothyroid”.

Hypothyroid patients insulin treated have, compared to the euthyroid ones, an increased need for insulin (Fig. 4).

Age, BMI, HbA1c did not correlate statistically significantly with TSH and FT4 (Table 1).

Debate

This study was conducted to evaluate the possible association between thyroid disorders and gestational diabetes.

Tudela et al. (19) have shown that – in pregnant women with thyroid dysfunction – the risk of devel-

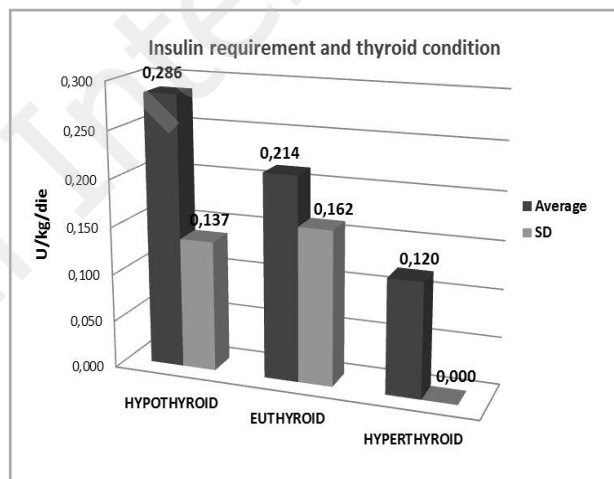


Fig. 4 - Average and standard deviation of quantitative insulin practiced by each group of patients.

TABLE 1 - A: EUTHYROID PATIENTS; B PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM; C: PATIENTS WITH CLINICALLY OVERT HYPOTHYROIDISM. IT HAVE BEEN TESTED THE POSSIBLE CORRELATION WITH AGE, BMI, HBA1C, FASTING PLASMA GLUCOSE LEVELS, SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE. THE TABLE DOES NOT SHOW STATISTICAL SIGNIFICANCE WITH ANY OF THE VARIABLES CONSIDERED.

PATIENTS TYPE	A	B	C	P FOR TREND
N. Patients	77	18	12	
Age	32,79 ± 5,43	32,56 ± 6,47	29,75 ± 2,63	N.S. 0,108
BMI	28,58 ± 7,24	28,07 ± 6,59	26,59 ± 6,01	N.S. 0,374
HbA1c	5,63 ± 0,64	5,47 ± 0,68	5,36 ± 0,74	N.S. 0,545
Fasting glucose	94,69 ± 16,45	90,17 ± 8,30	96,42 ± 22,36	N.S. 0,882
Systolic OBP	118,06 ± 13,25	116,47 ± 13,78	117,92 ± 8,90	N.S. 0,829
Diastolic OBP	72,6 ± 10,66	72,94 ± 9,02	72,50 ± 9,65	N.S. 0,807

oping gestational diabetes increases proportionally with the increase of TSH. This association remains statistically significant even after adjustments for maternal age, weight and race (factors known to have important effects on the incidence of hypothyroidism – subclinical and clinical – and gestational diabetes).

Our investigation, although represented by a small case series, showed an incidence of clinically overt hypothyroidism and subclinical hypothyroidism, respectively of 16% and 10%, confirming the association between thyroid disorders and gestational diabetes.

The high incidence of subclinical hypothyroidism in the second trimester of gestation is independent from age and BMI of pregnant women.

Mild or subclinical hypothyroidism in pregnancy, when untreated, is associated with obstetric complications (gestational hypertension, placental abruption, preterm delivery) and fetal (fetal mortality, congenital malformations, IUGR, delay in the psychomotor and mental development) (5-10).

Today, however, be able to diagnose subclinical/clinical pregnancy is not easy, because symptoms of this endocrine deficit may be masked by the hypermetabolic state generated by the pregnancy itself.

Current guidelines (2011) of the Endocrine Society and the American Thyroid Association does not approve universal screening of pregnant women for thyroid dysfunction, but recommend a case by case approach in high-risk pregnancies (9, 20), suggesting a measurement of circulating TSH during the first visit.

In addition, this measurement should be performed every 6-8 weeks to make sure that the women have a normal thyroid function during the pregnancy.

Others, however, suggest to check the value of TSH of women before they become pregnant (pre-pregnancy counseling) or as soon as pregnancy is confirmed.

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A disadvantage of the screening during pregnancy is that fetal nervous system depends on the values of T4 maternal before conception, while the first prenatal visit occurs at about 14 weeks, period in which the damage may have already occurred.

Even if it is necessary a deeper investigation in this area, it is hoped that in the next years, screening strategies will be applied in different centers.

The results reported from the study conducted by Tudela MC et al. (19) have shown a relationship between the increase of serum levels of thyrotropin in women with normal serum concentrations of free T4 and an increased risk for gestational diabetes.

These results suggest that women with subclinical hypothyroidism have a higher risk for gestational diabetes than euthyroid women, however, informations also found in our study (the percentage of patients with subclinical hypothyroidism in our records is higher than in patients with hypothyroidism).

In the end we observed that, among the patients insulin treated the hypothyroid ones present, compared to the euthyroid ones, a greater insulin requirement.

Conclusions

The results obtained from our study, in agreement with the majority of the informations reported in literature, have shown an important relationship between the increased of serum levels of thyrotropin and a higher risk of gestational diabetes. Women with GDM, therefore, are at greater risk for both clinical and subclinical hypothyroidism.

So we observe that the screening for the thyroid function in GDM it must be taken seriously and that the thyroid hypofunction of pregnant women should be diagnosed and corrected as quickly as possible.

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