

# Maternal and fetal complications of the hypothyroidism-related pregnancy

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## ABSTRACT

*Thyroid pathology worsens during pregnancy. Hypothyroidism can be pre-existent or may begin during pregnancy period. Most of the patients who presented hypothyroidism during pregnancy have a history of thyroid disease for which they have undergone treatment (medical, surgical or radioisotopes). Hypothyroidism is difficult to be diagnosed during pregnancy as the signs can belong to pregnancy itself. Changes in thyroid function have a major negative impact on both mother and fetus.*

*Complications that arise depend on the severity of hypothyroidism, on how appropriately and early the treatment will be initiated, on other obstetrical and extragenital pathologies associated with the present pregnancy. Clinical symptoms are polymorphic, often nonspecific, and are related mainly to the time of occurrence and to the severity of thyroid hormone deficiency. The appropriate, early administered treatment and maintenance of a normal level of thyroid hormones minimize the risk of maternal and fetal complications and make it possible that the pregnancy may be carried to term without severe complications.*

**Key words:** hypothyroidism, maternal complications, fetal complications

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## INTRODUCTION

**P**regnancy is seen as a risk factor in the occurrence of thyroid dysfunctions. In recent years, we can notice a more frequent association between thyroid gland pathology and pregnancy, with a frequency of thyroid pathologies on women that has increased approximately sixfold, according to some statistical data. (1)

Moreover, hormonal changes and metabolic needs during pregnancy result in profound alterations of biochemical and clinical parameters which characterize the thyroid gland, changes that express themselves through a state of thyroid hyperstimulation and a relative hypothyroxinemia or a subclinical hypothyroidism, a limiting form between normality and pathology, but nevertheless closer to the pathology during pregnancy. (2,3)

When pregnancy overlaps maternal endocrine imbalance, undesirable consequences for both mother and fetus may appear. It is acknowledged that hypothyroidism in pregnancy is associated with an increased risk of abortion, habitual abortion, premature delivery, intrauterine fetal death, fetal retardation and fetal congenital anomalies, congenital hypothyroidism, postpartum bleeding, anemia, postpartum depression and cardiac dysfunction, which leads to increased maternal morbidity, perinatal morbidity and mortality. (3-5) □

## PURPOSE OF THE PAPER

**T**he study of the evolutionary specific features of the maternal-fetal complications during pregnancy, labor and post-partum period presents a special importance in contemporary obstetrics. □

## MATERIAL AND METHOD

**T**he obstetrical files of the pregnant women with thyroid gland pathology and the medical files of the newly-born were studied and analyzed; the diagnosis algorithm consists of using some multiple elements: anamnesis, general clinic examination and genital examination, echographic examination of the pregnancy, the cardiotocographic registration; the uterus dynamic was also examined through the manual method; determinations (during childbirth and on the first routine examination after

birth), of TSH, FT4, ATPO (the laboratory of the Bucharest University Hospital – made by biologist Belintan), echographic check-up of the patient's thyroid gland volume during childbirth.

It is a retrospective clinical-statistical study; the patients are between 18-35 years old, and presented themselves during January 1st, 2005 – December 31, 2008 at the Obstetrics-Gynecology Clinic of the Bucharest University Emergency Hospital, the Obstetrics-Gynecology departments of Pitesti County Hospital, Câmpulung-Muscel Hospital and Curtea de Arges Hospital. The "t Student" test, which is a common test in biology and medicine, was used in order to perform the statistical calculations in order to establish the various correlations.

Selection of the working material – consists of a sample containing a group of pregnant women who were associating a thyroid problem that was known or diagnosed during pregnancy, a group of women in childbirth and a group of newly-borns; the selected group of 60 pregnant women with premature delivery diagnosis (between 28-37 weeks of gestation, with alive newly-born and a weight < 2500 gr) and a control group of 40 pregnant women with on-term delivery diagnosis (between 38-40 weeks of gestation); these groups were also examined during childbirth period.

The criteria of exclusion from the study are multiple: prophylaxis with iodine, the presence of thyroid nodules at the echographic examination, the existence of a child birth in a period less than 12-18 months, other major medical problems which can interfere with the thyroid status, chronic medication which contains iodine, hepatitis history or HIV congenital anomalies, refuse of giving formal consent, history of surgical intervention which needed local painting with iodine. The criteria of inclusion in the study were represented by the diagnosis given by the obstetrician and endocrinologist and the detection of the hormonal profile through lab tests. □

## RESULTS AND DISCUSSIONS

**A**nalyzing the results, by comparing the two analyzed groups, we can notice a clear prevalence of the maternal and fetal complications during labor and childbirth within the first group as compared to the group with on term child birth (TABLE 1, FIGURE 1, FIGURE 2).

Complications	Premature delivery		Normal delivery	
	Abs no.	Percent	Abs no.	Percent
Labor abnormalities (hypokinesia, hypotony)	10	16.6%	5	12.5%
Fetal suffering	24	40%	12	30%
Respiratory distress, IA<8	12	20%	6	15%
Vicious pelvis	4	6.66%	3	7.5%
Pelvic presentation	2	3.33%	1	2.5%
Postpartum thyroiditis	7	11.6%	1	2.5%
Postpartum haemorrhage	11	18.3%	5	12%
Hypogalactia	11	18.3%	2	5%
Postpartum depression	3	33.3%	1	2.5%

TABLE 1. Various maternal-fetal complications with the two groups

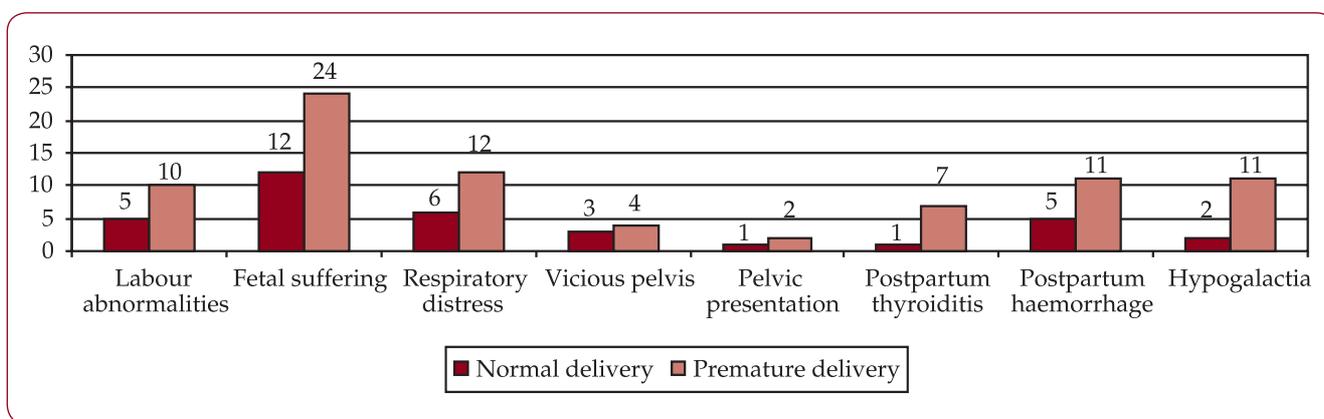


FIGURE 1. Incidence of occurred maternal complications depending on the group type under study

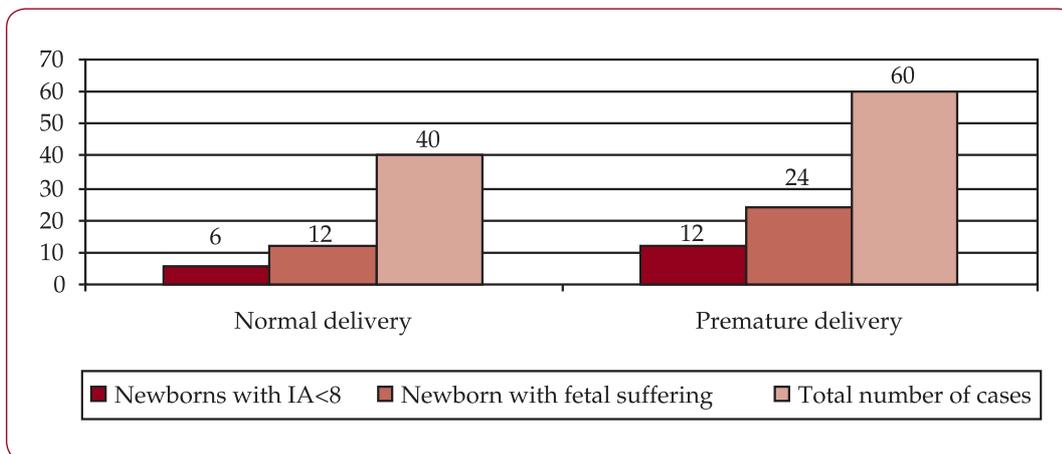


FIGURE 2. The incidence of fetal complications that occurred depending on the group type under study

We have faced the following complications:

- Labor – diskinetik, longer due to the existence of the hypomyotonia and the simultaneous cardio-breathing problems; hypokinesia
- Anomalies of fetus cardiac rhythm (FCR) – fetal suffering; alterations of the basic cardiac rhythm (tachycardia, bradycardia), of FCR variability (diminution until their loss or periodical variations of FCR)

in relation with the uterus contractions, a type of belated slow-ups)

- APGAR mark – frequently lower at pregnant women who continued to be hypothyroidic until the due term
- Vitiated pelvis (limit pelvis) which can be the reason of various cephalic-pelvis disproportions
- Presentations that are close to distocia – pelvic presentation
- Post-partum haemorrhages occur through uterus hypotony and through coagulation disorders (problem of the plaque adhesiveness)
- Post-partum depression, post-partum thyroiditis, hypogalactia

The causes of the hypotony and hypocontractions in hypothyroidism are multiple; among them there are the endogen intoxications, the change of muscular tissue, the myxedema impregnation, the hypovitaminosis (B1 vitamin), affecting the transmission of the nervous influx, affecting the endocrine metabolism, water-electrolitic change which leads to the change of the functional biometrical schemes and to the change of the interaction between actin and myosin: the K and the intracellular Mg decrease due to the metabolic acidosis and therefore the contraction is more difficult, Ca decreases and the equilibrium of P, bicarbonate and H ions is disturbed; on the other hand, the metabolic acidosis also modifies the extracellular distribution of Na, Ca, Mg and K and has a negative influence on the contractions through the decrease of the membrane potential, which leads to insufficient contraction.

Hypotonia, having a tonus less than 10 mmHg, usually accompanies a hypokinesis. There are hypocontractions of frequency and of intensity. Hypokinesis (contractions which are rarer than two within 10 minutes with the contraction value of less than 25mmHg) is the most frequent. Generally, hypocontraction is combined with two types of possibilities. Labour is slow or long, with possibilities of interruption, leading to real uterus inertia, which can be primitive (ante-partum determined) or secondary (intra-partum determined).

The insufficient labour or the discordant labour is present in literature in a variable percentage; recent studies show a percentage of

35.2% at the pregnant women, who remained with hypothyroidism at the end of pregnancy.

APGAR score depends of the uterus-placenta circulation and the proper oxygenation of the fetal-placenta complex during pregnancy and it is frequently lower at pregnant women who continued to have hypothyroidism until the due term. In hypothyroidism, the cardiac debit is not adequate and the uterus-placenta circulation becomes insufficient, which induces a moderate and chronic fetal hypoxia, fetal bradycardia, fetal hypotrophy, diminution of fetal moves and an insufficient tolerance of the delivery by the fetus. The intrauterine chronic hypoxia of the newborn can be met in the literature at variable percentages between 14%-22% at pregnant women with hypothyroidism.

A series of studies, with recent reconfirmed results, showed that the treatment with T4 can improve the obstetrical prognosis but it does not modify the neurological development of the newborn on the long term, the cognitive performances being changed; the maternal hypotiroxinemy on early term pregnancies can have irreversible negative effects on the newborn's state and placenta. Some antioxidants (retinol, tocopherol etc.), are usually used in the treatment of the fetal-placenta insufficiency.

During hypothyroid pregnancy, cephalic-pelvis disproportions can also occur with the vitiated pelvis (limit pelvis). There are a lot of intricate mechanisms (direct and indirect effects of the thyroid hormones) since the very beginning of the pre-gestation period, which can affect the pelvic bones (lower bone density, even osteoporosis), of the spine (multiple deformations), problems of the articulations through the specific infiltration, various artropaties, inflammatory or non-inflammatory, poliartitis, artrosis. Excessive deposits of mucous polysaccharides and glucose in the tissues, affecting protein synthesis, diminution of the insulin level, as a growth factor, can lead to various muscles and skeleton symptoms. A clear mechanism is not established, but a decrease in the proliferation of the cartilage cells and bone tissue and chondrocalcinosis (depositing the hydrates crystals and the calcium pyrophosphates).

The pelvic presentation (complete or incomplete with some types: buttocks type, knee type, legs type) is considered a presentation

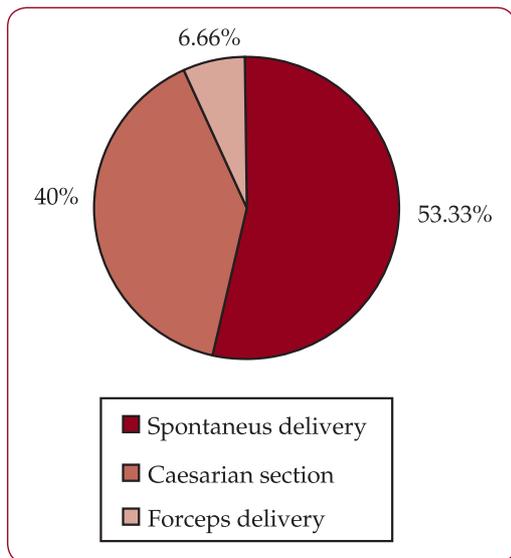


FIGURE 3. Birth completion practice in the abortive birth group

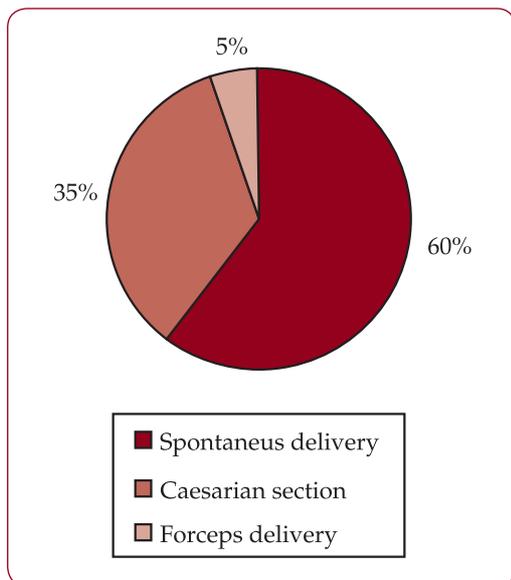


FIGURE 4. Birth completion practice in the on-term birth group

close to distocia, which is frequent at the premature delivery, due to the small dimensions of the newborn cranium, and which predisposes it at its deflection during the labour period. The literature confirms variable percentages for the pelvic presentation: 1/30 of the premature deliveries and 1/60 of the on-term deliveries.

We should remark the fact that in both groups (FIGURE 3 and FIGURE 4), but especially in the group with pregnant women who had premature delivery, the percentage of the caesarean operations is high and known as an existing situation at present time, both on the global level as well as in our country (FIGURE 5).

This can be explained by the fact that, in the modern obstetrics, the indications for the caesarean operation are wider, due to the improvement of the means of fetal investigation, especially cardiotocography (CTG), which tracks the modifications of the fetal cardiac rhythm (FCR) on time, which evokes fetal suffering. As to the assistance of the premature delivery, in the pelvic presentation, the majority of the authors, especially in the U. S. A., generally agrees on the caesarean operation, with prophylactic character. The reasons for this intervention could be: special pregnancy, the impossibility of developing normal labour, important changes at the pelvic level, the pelvic presentation. Post-partum haemorrhages in hypothyroidism are produced both through the uterus hypotony and coagulation problems, with plaque adhesiveness problem. Various studies (Leung, Buckshee, Davis) from the literature indicate a percentage between 7% and 19%.

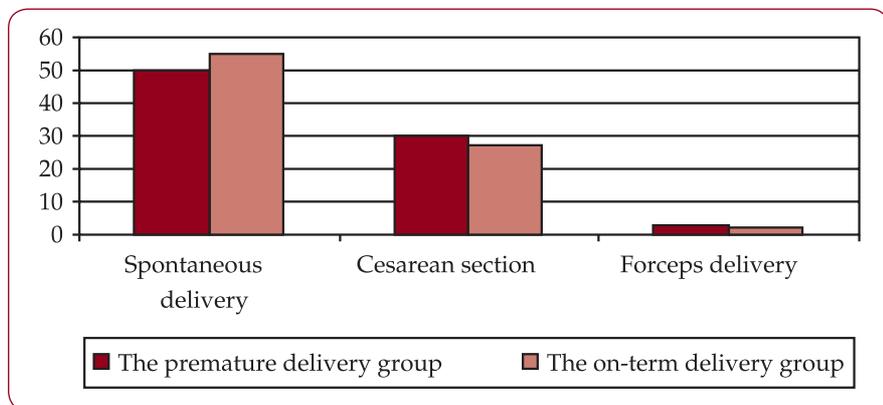


FIGURE 5. Comparison chart of the birth completion types

The etiology of the post-partum thyroiditis has not been well-understood yet but a problem in the self immunity can be probably caused by a constant increase of the level of anti-microzomes antibody in the first trimester of the pregnancy. Post-partum thyroiditis affects 2-7% of the pregnant women. The hypothyroid phase follows a hyperthyroid phase and it manifests after 5-7 months in post-partum.

The hypothyroid can remain permanent (12-61%) and euthyroiditis appears in 5% of the cases. According to recent studies, the incidence has very wide limits, between 1.1-2.1%, within the first year after delivery; the presence of the thyroid antibodies during the first trimester of the pregnancy determines an increase by 35% of the incidence and the risk of developing a post-partum thyroid is of 50%; if they are still present in the third trimester, the risk increases by 80%; the relapse, with a similar evolution and intensity, usually appears after future pregnancies.

The studies which examined a possible association of HLA-DR with post-partum thyroiditis sustain the involvement of a genetic etiology. There is a significant increase of the frequency in HLA B8, DR3, HLA A1, B8, DR 3 antigenes. These haplotypes were also recognized within other self-immune diseases with organs specificity.

There is a close connection between the post-partum thyroiditis and post-partum depressions. The logical association between the self immune thyroiditis and post-partum depressions is the fact that the hypothyroidism is associated with the depression not only in post-partum.

The specialized literature indicates an incidence of about 10% of the post-partum depressions among an unselected population, Nicolaides having obtained a percentage of 30% for the women with positive ATPO. Recent studies show that there is no benefit by the treatment with thyroxine in order to prevent the post-partum depression. Various studies attest a high incidence, especially between the 4th and the 12th post-partum week, for women with positive ATPO (30,31)

It is necessary to consider the puerperal psychosis as an entity with an origin of various factors. Some observations suggest that the level of hormone production by the placenta has a major role in the development of psychological disequilibrium in puerperium. The depression

of pituitary function and the reduction of adrenaline and thyroid hormones production may be included among the potential pathogenic factors; low levels of progesterone or free tryptophan from the plasma, the free usage of agents having vasoactive potential during intrapartum and postpartum and the chronic lack of beta-endorphine along with the increase of the dopaminergic activity may be responsible for these changes. During post-partum, the adrenocorticotrophic-hormone and the arginine-vasopressin are being released, and carried through the portal circulation system until reaching the hypophysis where they induce the production of ACTH, which reacts upon the corticoadrenal and releases cortisol. At the same time with these neuro-humoral releases, cytokine, chemokines, neuropeptides and various monoamines are also set free, with the help of complex mechanisms, their function being that of regulatory agents in the inflammatory processes (cytokine is an important proinflammatory agent), as well as promediators in signal communication between the immune cells. (32-34)

Depression, seen as a chronic reaction to stress, implies a foreground contribution of the hypothalamic-hypophysio-corticoadrenal axes, with all the correlative components of a complex coordination system, as the one foreseen by the studies of Heim and Nemeroff (2001) under the name of BEISA (brain, endocrine, immune and sympathoadrenal axes), whose disfunction generates significant desynchronization in the various signaling and transduction systems. Hypothyroidism is incriminated in the light of the latest studies and in the etiology of hypogalactia which are considered today as a first stage of the hypophysis, thyroid and corticoadrenal insufficiency. The proof is the favourable reaction to the treatment with thyroid hormones in hypogalactia. In the literature, this percentage varies around 19%.

We should take into account that in a reduced number of cases we also came upon other complications as anemia and high blood pressure induced by pregnancy, explained by the fact that we made our study on selected groups. □

## CONCLUSION

There is a multitude of studies in the specialized literature which examine the types and

the incidence of the complications in pregnancy, delivery and on the newborn. The increase of the preeclampsia incidence, of the premature delivery, of the post-partum depressions and haemorrhages could be explained through a maturation process of the placenta and they appear especially if there is a severe hypothy-

roidism, but they have been also signalled in the cases of subclinic hypothyroidism. (35)

Complications in the pregnancies associated with hypothyroidism are complex and serious, with an important increase of the maternal morbidity, and perinatal morbidity and mortality.

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