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Universal Screening for Thyroid Disorders in Pregnancy: Experience of the Czech Republic

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1. Introduction

The role of the thyroid gland in pregnancy and the impact of thyroid disorders on the course of pregnancy and development of the offspring have drawn a considerable interest in the recent years, both in the medical and in the general society. About 10% of pregnant women are positive for autoantibodies against thyroperoxidase (TPOAb) (Glinoer 2007, Lazarus and Kokandi 2000, Springer 2009) and between 2 and 4% suffer subclinical or overt hypothyroidism (Casey 2005; Vaidya 2007, Springer 2009). Dysfunction of the maternal thyroid in pregnancy adversely affects the course of pregnancy and the psychomotor development of the offspring (Haddow 1999, Morreale de Escobar 2004). According to recent findings, even the mere positivity of TPOAb without concomitant thyroid dysfunction in pregnant women may have a negative impact on the psychomotor development of the child (Li 2010). Furthermore, up to one half of the TPOAb-positive (TPOAb+) pregnant women develop postpartum thyroiditis (PPT) which can lead to persistent hypothyroidism in about one third of women (Lazarus and Premawardhana 2008). According to recent findings of Stagnaro-Green, this proportion may be even much higher and persistent hypothyroidism may affect up to one-half of women with history of PPT (Stagnaro-Green 2011b). If unrecognised and untreated, late postpartum thyroid dysfunction, in most cases subclinical (SH) or overt hypothyroidism (OH) may have a long-term negative effect not only on the mother’s health, but also on the next pregnancies.

Since 2006, repeated attempts to implement a universal screening programme for thyroid disorders in the first trimester of pregnancy have been made in the Czech Republic. Moreover, the Czech Endocrine Society initiated a wide informational campaign concerning the importance of correct thyroid function in pregnancy in the media, including TV discussions, seminars and lectures for both the general population and the health professionals. Members of the Czech Endocrine Society together with colleagues from the Czech Society of Biochemistry have initiated several studies focused on various aspects of thyroid disorders among Czech pregnant women. In this review article, we present an overview of the data obtained in the recent years.
Impact of thyroid dysfunction on pregnancy and foetal health

The developing foetus is dependent upon the maternal thyroid hormone synthesis up to the 14th to 16th gestational weeks. Afterwards, its own thyroid gland starts to synthesise thyroid hormones, albeit in insufficient quantities. Thus, the first trimester of pregnancy is crucial in terms of adequate supply of maternal thyroid hormones to the embryo. Numerous retrospective and case-controlled studies confirmed detrimental effects of maternal overt hypothyroidism (OH) on the course of pregnancy and on foetal health.

Severe deficit of thyroid hormones leads to irreversible changes in foetal development. Impairment of neuronal differentiation leads to inadequate development of the central nervous system with resulting mental retardation. It may also lead to somatic defects including congenital cardiac defects and disrupted bone growth. These changes are most prominent in untreated congenital hypothyroidism (cretinism). Moderate thyroid hormone deficit may lead to less pronounced neurocognitive dysfunction. As Haddow et al. have shown in their well-cited study, children of untreated hypothyroid pregnant women had at age 7 to 9 years IQ below 85 points in 19% of cases in comparison with 5% of children of euthyroid or substituted mothers. The average IQ was 7 points lower in children of hypothyroid untreated mothers than in children of hypothyroid mothers substituted by levothyroxine (LT4) (Haddow 1999). Furthermore, iodine-deficient pregnant women are prone to hypothyroxinaemia. As Morreale de Escobar has shown, up to 70% of children of iodine-deficient mothers may suffer from attention deficit hyperactive disorder (Morreale de Escobar 2004a,b).

Apart from neurocognitive foetal impairment, maternal untreated OH is associated with the risk of foetal loss in up to 60% (Abalovich 2002) and the risk of gestational hypertension in 22% (Leung 1993), which was higher than in euthyroid women of women with subclinical hypothyroidism. According to Allan et al, women with OH have also an increased risk of foetal death (Allan 2000). Thus, it is of no doubt that untreated maternal OH may be detrimental for the maternal-foetal unit in the short-term and in the long-term sense.

Pros and cons of universal screening for thyroid disorders in pregnancy

Although maternal autoimmune thyroid disorders (AITD) fulfil many criteria used for identification of diseases subject to universal screening, this issue has been highly controversial. The main arguments for implementation of universal screening are the following: a) the impact of maternal hypothyroidism on the course of pregnancy and the health of offspring has been well described and the treatment is effective and simple; b) the prevalence of hypothyroidism in pregnancy is comparable with other universally screened diseases; c) the method of screening (laboratory measurement of thyroid parameters) is relatively simple and inexpensive – the financial costs depending on the choice of thyroid parameters screened; d) it is cost-effective (on condition that not only OH, but also SH decreases the offspring’s IQ (Dosiou 2008, Thung 2009); e) the risk-benefit ratio of the screening for each individual is acceptable. In the past, some authorities recommended universal screening but not the American Thyroid Association or the Association of American Obstetricians and Gynaecologists, who have consistently advocated a case-finding screening strategy focused on high-risk women (Abalovich 2007, Stagnaro-Green 2011) (Table 1).
Table 1. Overview of recommendations for screening for thyropathy in pregnancy.

<table>
<thead>
<tr>
<th>Authority</th>
<th>Year</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Association of Clinical Endocrinologists</td>
<td>2002</td>
<td>Universal screening</td>
</tr>
<tr>
<td>Expert panel of American Thyroid Association, American Association of</td>
<td>2004</td>
<td>Case-finding</td>
</tr>
<tr>
<td>Clinical Endocrinologists and The Endocrine Society</td>
<td></td>
<td>screening</td>
</tr>
<tr>
<td>Second panel of American Thyroid Association, American Association of</td>
<td>2005</td>
<td>Universal screening</td>
</tr>
<tr>
<td>Clinical Endocrinologists and The Endocrine Society</td>
<td></td>
<td></td>
</tr>
<tr>
<td>British Thyroid Association, Association of Clinical Biochemists, British</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid Foundation. UK guidelines for the Use of thyroid Function Tests</td>
<td>2006</td>
<td>Case-finding</td>
</tr>
<tr>
<td>American College of Obstetrics and Gynecology</td>
<td>2007</td>
<td>Case-finding</td>
</tr>
<tr>
<td>The Endocrine Society</td>
<td>2007</td>
<td>Case-finding</td>
</tr>
<tr>
<td>American Thyroid Association</td>
<td>2011</td>
<td>Case-finding</td>
</tr>
</tbody>
</table>

The main argument of the opponents to universal screening is the lack of randomised controlled trials demonstrating that treatment by LT4 of pregnant women with subclinical hypothyroidism increases the offspring’s IQ. Preliminary results of the first major study “The Control Antenatal Thyroid Screening Study” presented on ITC in Paris 2010 were rather disappointing (Lazarus 2010). The authors found only a non-significant difference in the prevalence of three-year-old children with IQ<85 of women unscreened vs. mothers screened and treated in case of SH in pregnancy (15% vs. 11.5%, p=0.09). However, the major drawback of this study is that pregnant women up to the 16th gestation week were included. Thus, we may suspect that in some women the treatment started too late, after the crucial changes in the embryonic/foetal brain have occurred. Another multicenter randomized placebo-controlled clinical trial is at present being conducted by the Maternal Fetal Medicine Unit of the National Institutes of Health in the USA. The primary outcome will be child IQ at 5 years of age. Results of this study should be available in 2015 and they may give a final answer to the question of universal screening for thyroid disorders in pregnancy.

The case-finding screening strategy

Due to the above-mentioned facts, the latest guidelines of the American Thyroid Association (ATA) recommend a case-finding screening targeted at women at high-risk for hypothyroidism in pregnancy (Stagnaro-Green 2011a). The new guidelines introduce age over 30 years and body-mass index over 40 kg/m2 among the risk factors. The other risk factors include: history of thyroid dysfunction or prior thyroid surgery, symptoms of thyroid dysfunction or the presence of goitre, TPOAb positivity, diabetes type 1 or other autoimmune diseases in history, history of miscarriage or preterm delivery, history of head of neck radiation, family history of thyroid dysfunction, use of amiodarone/lithium or recent administration of iodinated radiologic contrast, infertility and residence in an area of...
known moderate to severe iodine insufficiency. Thus, according to ATA, the first physician dealing with newly pregnant women should consider 12 different risk factors. If any of them were positive, he should order a blood test for thyroid-stimulating hormone (TSH). In our opinion, this form of screening is likely to be neglected due to practical reasons. It has been shown that the case-finding approach may miss up to one half of pregnant women in comparison with universal screening (Vaidya 2007, Horacek 2010, Jiskra 2011a); and it may be difficult to implement in the routine practice (Vaidya 2002). Moreover, in our view, assessment of only TSH is insufficient due to the above-mentioned risks carried by isolated hypothyroxinemia and TPOAb positivity.

2. Prevalence of thyroid disorders in pregnant Czech women

The Czech Endocrine Society together with the Czech Society of Biochemistry has repeatedly attempted to implement universal screening for AITD in the first trimester of pregnancy. In order to gain data on thyroid disorders in Czech pregnant women, two large studies including nearly 8,000 consecutive pregnant women (Springer 2009, Limanova 2011), have been conducted in the Czech Republic in the last years.

The first study by Springer et al. was performed between 2006 and 2008 and examined 5520 consecutive asymptomatic pregnant women in the 9th-11th gestational week. The aim of this study was to evaluate the prevalence of thyroid disorders in pregnant Czech women and to identify optimal reference intervals in evaluation of maternal thyroid function during the first trimester of pregnancy. The screening consisted of laboratory assessment of serum thyroid stimulating hormone (TSH), free thyroxine (FT4, only in those with pathological TSH/TPOAb) and autoantibodies against thyroperoxidase (TPOAb). All measurements were performed by chemiluminometric immunoanalysis on an ADVIA Centaur system (Siemens, Healthcare Diagnostics Inc, Tarrytown, NY, USA) in one centre (Institute of Clinical Biochemistry and Laboratory Diagnostics, General University Hospital in Prague). Women with positive screening result were advised to visit an endocrinologist within a few days. Based on the results obtained, Springer et al. set normal limits for TSH and TPOAb in pregnancy as following: TSH 0.06-3.67 mU/l; TPOAb <143 kU/l; the study did not attempt to set new reference ranges for FT4. In this cohort of pregnant women, 822 (14.9%) had at least one of the parameters outside of the normal range. Suppressed TSH was found in 141 (2.55%) women, while 299 (5.42%) had TSH over the reference interval; elevation of TPOAb was present in 549 (9.95%) women (Jiskra 2011a). The data are shown in detail in Table 2.

Thus, in this study, there was a higher prevalence of pregnant women with TSH elevation (4.48%) as compared to other iodine-sufficient countries, where the prevalence of pregnant women with TSH elevation reaches 2-3% (Casey 2005; Allan 2000; Vaidya 2007). Obviously, these numbers depend on the TSH upper limit of reference range used. In the Czech studies, the cut-off at 3.67 mU/l was used (Springer 2009). This value was determined as the 97.5th percentile of TSH values of 4,337 women in the first trimester of pregnancy with no history of thyroid disease, anti-TPO level lower than 60 kU/l (=negative) and free bhCG lower than triple that of the median (56.6 mg/l). It is interesting to note that the 97.5th percentile in unselected women was higher (Table 3). At present, world authorities recommend to use the upper cut-off at 2.5 mU/l (Stagnaro-Green 2011). Therefore, for the Czech population, this cut-off lies either too low; or there is a
higher prevalence of hypothyroidism among Czech pregnant women; or our analytical method used for TSH measurements gives higher numbers than methods used by others. However, our analysis was performed using a well-established and widely used analyser (Advia Centaur, Siemens). Apparently, the cut-off at 2.5 mU/l would lead to large numbers of pregnant women positive in screening.

<table>
<thead>
<tr>
<th>Number of women screened</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Positive in screening (at least one parameter)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Overt hypothyroidism</td>
</tr>
<tr>
<td>Subclinical hypothyroidism</td>
</tr>
<tr>
<td>TPOAb+ hypothyroidism</td>
</tr>
<tr>
<td>TPOAb- hypothyroidism</td>
</tr>
<tr>
<td>Transient gestational hyperthyroidism</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Overt hyperthyroidism</td>
</tr>
<tr>
<td>Subclinical hyperthyroidism</td>
</tr>
<tr>
<td>TPOAb+ hyperthyroidism</td>
</tr>
<tr>
<td>TPOAb- hyperthyroidism</td>
</tr>
<tr>
<td>TPOAb positivity (&gt;143 kIU/l)</td>
</tr>
<tr>
<td>Euthyroid TPOAb+</td>
</tr>
<tr>
<td>TPOAb+, normal TSH, decreased FT4</td>
</tr>
<tr>
<td>TPOAb+, normal TSH, elevated FT4</td>
</tr>
</tbody>
</table>

Hypothyroidism was defined as TSH >3.67 mIU/l (overt with decreased FT4 and subclinical with TSH >3.67 mIU/l and normal FT4). Hyperthyroidism was defined as decreased TSH <0.06 mIU/l (overt with TSH <0.06 mIU/l and FT4 >23.0 pmol/l and subclinical with TSH<0.06 mIU/l and normal FT4).

Table 2. Results of universal screening for thyroid disorders among Czech pregnant women in the 9th to 11th gestational weeks.

<table>
<thead>
<tr>
<th>TSH mU/l</th>
<th>N</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>2.5th percentile</th>
<th>5th percentile</th>
<th>95th percentile</th>
<th>97.5th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-selected</td>
<td>5520</td>
<td>1.280</td>
<td>0</td>
<td>411.874</td>
<td>0.048</td>
<td>0.147</td>
<td>3.713</td>
<td>4.796</td>
</tr>
<tr>
<td>Selected group</td>
<td>4337</td>
<td>1.213</td>
<td>0</td>
<td>11.534</td>
<td>0.062</td>
<td>0.154</td>
<td>3.144</td>
<td>3.670</td>
</tr>
</tbody>
</table>

Selected group: pregnant women with no history of thyroid disease, anti-TPO level lower than 60 kU/l and free bhCG lower than triple that of the median (56.6 mg/l).

Table 3. Reference ranges for TSH in the 9th to 11th gestational weeks in Czech pregnant women.
After two years of preparations, a joint “Pilot Project” of the Czech Society of Endocrinology, the Society of Clinical Biochemistry and the General Insurance Company of the Czech Republic started in 2009 (Limanova 2011). The Pilot Project was supported by the General Insurance Company. The aim of the Pilot Project was to ascertain the optimal combination and economic feasibility of diagnostic tests, the timing of the blood test and the possibility of connecting the test with genetic-disorder screening in the first trimester of pregnancy. The purpose of the study was also to provide information about cooperation among gynaecologists, laboratories and endocrinologists. In the Pilot Project, TSH, FT4 and TPOAb were measured in 2937 consecutive pregnant women from 13 Czech regions with good laboratory background and cooperative endocrinologists. Contrary to the previous study, measurements were performed in regional laboratories and the reference ranges differed according to each laboratory. In this cohort, 569 (19.4%) woman were screened as positive. Abnormalities of TSH were found in 11% of women: elevation in 7.8% and suppression in 3.2%. Only 15 (0.5%) women with TSH suppression were diagnosed with true hyperthyroidism. Hypothyroxinemia was found in 3.7% and TPOAb positivity in 262 (8.9%) women. One hundred fifty-eight women (5.37%) had positive TPOAb with normal thyroid function. Thus, in this second study, we found an even higher prevalence of abnormally high TSH among pregnant women than in the study of Springer et al. However, due to the different analytical methods, these results cannot be directly compared. Cooperation with gynaecologists wasn’t always optimal despite the fact that they were provided with all necessary information well in advance. On the other hand, laboratories analysed the samples promptly, and many of them took part in providing publicity and further information to other cooperating health care professionals. In conclusion, the Pilot Project study showed that implementation of universal screening for thyroid disorders in pregnancy would be feasible in the Czech Republic, although the general knowledge on importance of correct thyroid function in pregnancy needs to be improved among practical gynaecologists.

The attempts to implement a universal screening programme for AITD in pregnancy in the Czech Republic have suffered a major blow due to the world financial crisis starting in 2009. In the future years, we will probably have to concentrate on implementation of the case-finding approach years among the official risk factors.

3. Ultrasound imaging and risk-assessment of positively screened pregnant women

Most of the studies on AITD in pregnancy deal only with laboratory parameters and it is not clear whether the thyroid ultrasound (TUS) image is of any consequence for the clinical outcomes of the pregnancy. Studies concerning TUS in pregnancy are scarce, mostly aimed at the assessment of thyroid volume. Therefore, in one of our studies, we focused on the relationship between TUS, laboratory parameters and the outcome of pregnancy. Between 2006 and 2009, we performed thyroid ultrasound in 186 pregnant women positively screened for thyroid disorders in the first trimester of pregnancy; i.e. they had abnormal TSH and/or positivity for TPOAb (Jiskra 2011a). The control group consisted of 67 age-comparable non-pregnant women with pathological TSH and/or TPOAb levels. Unexpectedly, we found that these positively screened pregnant women had rather small thyroid glands with the median volume of 8.5 ml. This is smaller than in age-comparable non-selected non-pregnant Czech women in the study of Dvorakova et al. (median 11.8 mL.
in group of women aged 31-35 years) (Dvorakova 2006). Furthermore, the thyroid volume in pregnant women did not differ from controls. This is in contrast to the findings of both Fister and Vila, who showed an increased thyroid volume in pregnancy in iodine-sufficient (Fister 2009) and iodine-deficient areas (Vila 2008). The finding of small thyroids in pregnant Czech women is probably linked to the saturation with iodine. Iodine supplementation of salt has been introduced in Czechoslovakia in 1950. Therefore, the present pregnant women are already the third generation who live in iodine-sufficient conditions.

In our study, we also found that only 49% of the TPOAb+ pregnant women had autoimmune pattern on TUS. This was significantly less than in non-pregnant TPOAb+ controls (74 %) (Fig.1). Apparently, alterations of immune system in pregnancy cause a different manifestation of autoimmunity in the thyroid tissue. Moreover, we found that the thyroid ultrasound pattern was associated with preterm delivery: TPOAb+ women without autoimmune pattern in TUS had significantly lower prevalence of preterm delivery than the TPOAb+ ones with autoimmune pattern (3.1 vs. 15.2 %). Therefore, autoimmune TUS image in TPOAb+ pregnant women seems to be associated with preterm delivery.

![Fig. 1. Ultrasound autoimmune pattern in TPOAb-positive pregnant women and controls.](image)

In the next study from 2011, we focused on the relationship between clinical history, laboratory findings and TUS pattern in positively screened pregnant women (Jiskra 2011b). In this study, 200 of the positively screened women from the cohort of Springer et al. were included (Springer 2009). We regarded women as high-risk if they had any of the following risk factors: family and/or personal history of thyroid disease (including presence of goitre and signs and symptoms suggestive for thyroid dysfunction), family and/or personal history for autoimmune disease, history of neck irradiation, previous miscarriages and preterm deliveries). After exclusion of transient gestational hyperthyroidism, only 74/159 (47 %) women were classified as high-risk for thyroid disease according to their history. There were no significant clinical and laboratory differences between the high- vs. low-risk women, except for higher proportion of FT4 < 75th percentile and a larger thyroid volume in the high-risk group. These finding were consistent with the results of Horacek et al. (Horacek 2010) who found that case-finding screening strategy would miss one half of the high-risk women.
4. Postpartum follow-up of positively screened women

Between 2009 and 2010, we invited all 822 positively screened women from the first cohort of 5520 pregnant women screened (the cohort of Springer et al.) for follow-up (Potlukova et al. 2011, manuscript in preparation). In order to gain as complete a picture of their clinical state and history as possible, we asked them to fill in a detailed internet-based questionnaire concerning their personal, family and gynaecological history. Furthermore, we invited them for a blood test including analysis of TSH, FT4 and TPOAb. The two main aims of the study were: a) to assess the prevalence of high risk-profile women in this group; b) to evaluate the postpartum thyroid function in this group with regard to the adequacy of treatment.

Of the 822 women invited, 237 (28.8%) joined the study. This group of positively screened women differed from the one analysed in our other two recent studies (Jiskra 2011a, b). The median age of participating women was 31 years at the time of screening in pregnancy. The median interval between delivery and follow-up reached 21 months. The analysis of questionnaires brought a major finding: the use of the new guidelines of American Thyroid Association (Stagnaro-Green 2011) for identification of high-risk women substantially increased the proportion of high-risk women among the positively screened. The “old” risk factors could identify only two thirds of the positively screened women: personal and family history of thyroid disease (only first-degree relatives), diabetes mellitus type 1, other autoimmune diseases in personal history, infertility and history of spontaneous abortion. However, if the “new” risk factor, age>30 years (in our analysis, 31 years and more), was added to the classical ones, 85% of the women could be classified as “high-risk” (Fig. 2). This is a surprisingly high number, especially in the view of previous studies (Jiskra 2011b, Horacek 2010, Vaidya 2002). However, this effect of age could be partially due to selection bias, as the majority of women who answered the questionnaire had good education and therefore they tended to later pregnancies. We also tried to identify the most important risk factors in order to simplify the decision process which women should be screened. We found that four risk factor could identify 82% of the high-risk women: age 31 and more, personal and family history of thyroid disease and the presence of goitre (Fig. 2).

In our follow-up study, we further found that one third of initially euthyroid TPOAb+ pregnant women had TSH outside of normal range at follow-up. In comparison to pregnancy, median TSH (as well as FT4) significantly increased at follow-up (Fig. 3). Thirty-eight (33.6%) of 113 initially euthyroid TPOAb+ women had TSH outside of normal range at follow-up (median 17 months after delivery): 13 (11.5%) had TSH<0.37 mU/l; 18 (15.9%) had TSH >4.0 and <10.0 mU/l (all had normal FT4). Seven (6.2%) had TSH>10.0 mU/l with three having a hypothyroxinemia. It is important to note that many of these women were inadequately treated: all of the women with TSH suppression at follow-up were simply overdosed by LT4; and half of those with TSH elevation at follow-up were treated by too low doses of LT4. Thus, TPOAb positivity even with normal thyroid function in pregnancy carries a high risk of hypothyroidism one and half years postpartum. This is in line with results of Stagnaro-Green, who found that 50% of women with PPT were hypothyroid one year after delivery (Stagnaro-Green 2011). Our results also show that monitoring and treatment of women with AITD in the peripartal period is commonly inadequate.
Fig. 2. Proportion of positively screened pregnant women with at least one risk factor for hypothyroidism. Old: risk factors according to Guidelines of ATA 2007; New: risk factor according to Guidelines of ATA 2011; Four selected: age, personal and family history of thyroid disease and the presence of goitre.

Fig. 3. Postpartum development of the thyroid function in initially euthyroid TPOAb+ pregnant women. A: Thyroid Stimulating Hormone (TSH); B: Free Thyroxine (FT4). Median time between delivery and follow-up was 17 months. Median values of TSH and FT4 are marked in grey. Reference intervals for non-pregnant women are marked by dotted lines.

5. Financial analysis

Two studies have dealt with the cost-effectiveness of universal screening for thyroid disorders in pregnancy and both found it cost-effective under condition that subclinical hypothyroidism decreases IQ of the offspring (Dosiou 2008, Thung 2009). In order to roughly assess the financial aspects of the universal screening in the Czech conditions, we performed a simple statistical analysis of the financial costs of the Pilot Project (Telicka
2010). The goal of this study was to find out the overall costs of the Pilot Project as compared to positively-screened tests and simulate the costs in the current situation when the screening is not paid by the insurance companies. Total costs of both TSH and TPOAb screening included in the Pilot Project were 1 373 218 CZK (15 280 €) for 2 651 tested women. The cost of one positive result in any tested parameter (TSH/TPOAb) amounted 2 243 CZK (91€) and the costs of one positive result for hypothyroidism was 1380 CZK (56€).

6. Conclusions

We have shown that the prevalence of thyroid disorders is relatively high among the Czech pregnant women in comparison with other developed iodine-sufficient countries. About one tenth of pregnant women are TPOAb+ and more than 4% have subclinical or overt hypothyroidism in the first trimester of pregnancy. We have also shown that one third of initially euthyroid TPOAb+ pregnant women have TSH outside of normal range one and half years after delivery. This was due to postpartum thyroiditis and in many cases inadequate treatment. Thus, TPOAb positivity may endanger not only the current, but also the next pregnancies.

Based on the ultrasound findings in the positively screened women, we can furthermore conclude that pregnant TPOAb positive women have less pronounced TUS changes than non-pregnant controls. Thus, sonography may only be a part of a more complex diagnostic procedure in the screening for thyroid disorders in pregnancy. However, it seems that pregnant women with autoimmune pattern in thyroid ultrasound have an increased risk of preterm delivery.

Moreover, in our studies we confirmed that targeted case-finding screening programme based on the “old” risk factors (Abalovich 2007) would miss one-half of pregnant women with thyroid disease. Also, high- and low-risk pregnant women have similar clinical and laboratory characteristics. However, these findings change if “new” risk factors including age over 30 years (Stagnaro-Green 2011) are used for identification of high-risk women. Age over 30 years increases the proportion of positively screened pregnant women with at least one risk factor to 85%; however, this may be an effect of selection bias.

Finally, the financial analysis showed that the costs of the screening for thyroid dysfunction in pregnancy are not high enough to rend the financial issue a main obstacle in an implementation of universal screening. Both TSH and TPOAb should be included in any screening programme.

The awareness on the thyroid problematics in pregnancy has improved in the general population thanks to the activities of the Czech Society of Endocrinology in the recent; however, some health care professionals dealing with pregnant women show lack of interest in this topic. In conclusion, our data provide a contribution to the published guidelines for management of thyroid disease in pregnancy and present a basis for a world-wide discussion.

7. Acknowledgements

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Hypothyroidism is the most common thyroid disorder. It can cause a variety of changes in women's menstrual periods, reduce their chances of becoming pregnant, as well as affect both the course of pregnancy and the neuropsychological development of babies. During pregnancy there is a substantially increased need for thyroid hormones and a substantial risk that a previously unnoticed, subclinical or latent hypothyroidism will turn into overt hypothyroidism. The thyroid inflammation caused by the patient's own immune system may form autoimmune thyroiditis (Hashimoto's thyroiditis). Congenital hypothyroidism (CH) occurs in approximately 1:2,000 to 1:4,000 newborns. Nearly all of the developed world countries currently practice newborn screening to detect and treat congenital hypothyroidism in the first weeks of life. "A New Look at Hypothyroidism" contains many important specifications and innovations for endocrine practice.

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