Recurrent pregnancy loss (RPL) is really a depressing problem. Random chromosomal alterations numerically like trisomy, monosomy, as well as polyploidy are the commonest reasons of miscarriage during the 1st 10 weeks of gestation age (GA), that literally are responsible for 50% of cases [1]. Following exclusion of these explained miscarriages, RPL correlates with endocrinopathies, immunological, anatomical as well as inherited genetic causes [2].

Normal thyroid function is significant for reproduction. About a quarter of overt thyroid women present with menstrual abnormalities [3]. Maternal thyroid function is further known as significant for normal embryonic as well as fetal formation, especially neurodevelopment [4]. Hence it is important that thyroid abnormality might correlate with pregnancy loss.

Stagno-Green., et al [5], documented a correlation among thyroid autoimmunity, (by definition positive titres of thyroid peroxidase antibodies (TPOAb) as well as/or thyroglobulin antibodies) as well as miscarriage. Lot of observational studies associated both overt hypothyroidism-that by definition is an escalation of TSH along with low free thyroxine- as well as subclinical hypothyroidism, whose definition is an escalation of TSH along with normal free thyroxine to pregnancy loss [6]. Yet what is the exact definition of enhanced TSH amounts, remains contradictory at present, with new guidelines pointing that an upper limit of 4.0 miu/L should be thought to be diagnostic as compared to earlier guidelines of 2.5 miu/L [7].

American Society of Reproductive Medicine (ASRM) defines RPL as 2 or clinical pregnancy losses [8]. Whereas European Society of Human Reproduction and Embryology (ESHRE) defines it as 2 or clinical pregnancy losses at any GA, excluding ectopic as well as molar pregnancy [9]. Recurrent Miscarriage (RM) by Royal College of Obstetricians and Gynaecologist (RCOG) definition is 3 or pregnancy losses prior to 24 weeks of GA [10]. Thus RM is a more strictly defined of a subset of RPL. Presently ASRM [2012] recommends-examine TSH although thyroid Ab’s not mentioned [8]. ESHRE [2018] recommends examine TSH along with thyroid Ab’s [9]. RCOG [2011] recommends examine for RPL but does not take thyroid screening in account [10].

The meta-analysis of Dong., et al [11] evaluates delivery of levothyroxine to women with subclinical hypothyroidism along with association with pregnancy results as well as correlation among thyroid autoimmunity as well as RPL. These topics are of interest in our patients although create confusion amidst treating physicians.

Levothyroxine delivery is recommended for treatment in Thyroid Hormone (TH) deficiency which might/might not be of autoimmune origin for normalizing thyroid function. As per American Thyroid Association Guidelines for diagnosis as well as management of Thyroid disease in pregnancy as well as 2017 [7,12], there is no need for treating healthy pregnancy women with normal Thyroid function using levothyroxine, independent of their Thyroid antibodies status.

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A recent Randomized study [13], points levothyroxine does not help euthyroid women with Thyroid autoimmunity. This studies design is dependent on an unusual posit: reducing the miscarriage rate using levothyroxine in euthyroid patients.

It has been tacitly agreed that overt hypothyroidism needs treatment, since maternal function is very significant for normal embryonic as well as fetal formation, particularly neurodevelopment. However, the correlation among thyroid autoimmunity as well as RPL remains contradictory.

Dong’s [11] study concluded that thyroid autoimmunity does correlate with RPL. Meta-Analysis of studies gave a correlation among TPOAb with an escalated chance of miscarriage as well as preterm birth despite normal thyroid function. That patients with positive TPOAb have an escalated risk of miscarriage is well accepted.

The maternal immune system is one of the major players on the maternal-immune interface. Its impairment as lack of activation or over-reactivity appears to affect placentation as well as pregnancy results.

Lot of studies have suggested an association among antiphospholipid syndrome (APL/APS) as well as thyroid autoimmunity [11]; some of them pointing common pathophysiologic events as well as genetic background. A literature review [14,15] was done on this present data on APL/APS as well as thyroid autoimmune disorders, giving special emphasis to the probable part in obstetric complications.

Prevalence of antiphospholipid Abs or lupus anticoagulant was marked greater in women without thyroid autoimmunity (TAI). APS represents an acquired autoimmune thrombophilic problem that causes pregnancy complications that can be explained by placental insufficiency, that include RPL, intrauterine growth restriction (IUGR), oligohydramnios preeclampsia as well as placental abruption. Patients with APS don’t have an infertility rate as compared to general population. But they have bad reproductive results with a chance of pregnancy complications.

Immune impairments especially those stimulated via APS Ab’s are known to stimulate miscarriage. Their management that is widely accepted does not include levothyroxine or intravenous immunoglobulin. This is why studies on the basis of treating euthyroid women with RPL as well as thyroid autoimmunity with levothyroxine did not show any positive influence on pregnancy results.

This current Meta-Analysis [11] corroborates a correlation among RPL as well as thyroid autoimmunity. The examination of women with RPL needs to include APL Ab’s screen along with present guidelines, giving emphasis to Thyroid autoimmunity as well as euploid embryo losses.

Greater studies that have a proper selection of pts, euploid ET’s, as well as autoimmune TPOAb as well as APL Ab’s, molecular as well as transcriptomic signatures of molecules implicated in placentation are required to be isolated to see if the influence of thyroid autoimmunity is a marker of immune imbalance which could impact maternal-fetal tolerance as well as escalate the chances of RPL. Currently the total immune modes of RPL in euthyroid TPO-positive women have not been totally clarified, although there seems to be a correlation [16].

This was further corroborated by the study of Biddal, et al. [17] in 2019 where they posited that thyroid autoimmunity is a marker of the breach of immunotolerance in women with recurrent pregnancy loss. This study investigated thyroid peroxidase antibody (TPOAb) status as a predictor of live birth in women with unexplained recurrent pregnancy loss. They conducted a cohort study of 825 consecutive women with recurrent pregnancy loss followed at the tertiary referral center for Recurrent Pregnancy Loss, Copenhagen University Hospital (Rigshospitalet), from 2011 to 2017. Recurrent pregnancy loss was defined as ≥ 3 consecutive losses, and as unexplained by absence of antiphospholipid syndrome, parental chromosome abnormality, or uterus malformation. Upon first visit, all women were screened for thyrotropin (TSH) and TPOAbs (TPOAb positivity: ≥ 60 kIU/L). Adjusted logistic regression analyses included as covariates the following: maternal age, TSH, previous number of losses, body mass index, smoking, pregnancy achieved by assisted reproductive technology, and
thyroxine replacement (T4) treatment. Of the Women included 825, having a total of 3246 previous losses, of whom 139 (16.8%) were TPOAb positive. TPOAb positivity was not associated with the previous number of losses (p = 0.41). Women with unexplained recurrent pregnancy loss had a live birth rate in the first pregnancy after referral of 62.8% (285 of 454). TPOAb positivity was found in 78 of 454 (17.2%) women and was associated with a reduced live birth rate (51.3% vs. 65.2%, p = 0.02, adjusted odds ratio [aOR] 0.2 [0.1 - 0.6] p = 0.001). Treatment with T4 increased live birth rate significantly (aOR 3.7 [1.4 - 9.8], p = 0.007), and TPOAb-positive women receiving T4 had a live birth rate similar to that of TPOAb-negative women not receiving T4 (p = 0.70). Only 30% of TPOAb-positive women and 39% of women treated with T4 during pregnancy had known thyroid disease at referral. Hence concluding that in a large cohort of women with unexplained recurrent pregnancy loss, TPOAb positivity was predictive of a reduced live birth rate. However, T4 treatment improved odds of live birth. The study supports screening for TPOAbs as a risk factor in women with unexplained recurrent pregnancy loss. The beneficial effect of T4 treatment in this high-risk group needs confirmation by randomized controlled trials. Close collaboration between fertility experts and endocrinologists is of paramount significance [17]. However, Amrane S and McConnel R did not find any association of endocrine causes with RPL [18] just like when we reviewed that role of TPOAb was controversial [19], thus again warranting deeper studies.

Bibliography


Significance of Thyroid Peroxidase Antibodies in Cases of Recurrent Pregnancy Loss in Patients who are Euthyroid-A Short Communication


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