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MANAGEMENT OF THYROTOXICOSIS IN PREGNANCY

By

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ABSTRACT

Background: Autoimmune GD (Graves' Disease) is the most common cause of hyperthyroidism in women of childbearing age. To prevent maternal and fetal complications, thyrotoxicosis during pregnancy should be adequately managed and controlled. The physiological adaptations associated with pregnancy challenge the assessment of thyroid function in pregnant women, and the treatment with antithyroid drugs (ATD) raises concerns for the pregnant woman and the fetus. Our aim of this study was to discuss the effect of hyperthyroidism on pregnancy, different methods of diagnosis of hyperthyroidism and treatment of hyperthyroidism during pregnancy for a favorable maternal health and fetal outcome.

Objective: To discuss thyrotoxicosis this affects the pregnant woman and the effect of hyperthyroidism on pregnancy. It is to discuss different methods of diagnosis of hyperthyroidism during pregnancy. Also it is to study the treatment of hyperthyroidism and thyrotoxicosis during pregnancy for a favorable maternal health and fetal outcome.

Patients and Methods: A prospective randomized clinical study that was conducted on 20 pregnant female patients with thyrotoxicosis in different stages of pregnancy attending Bab-El Shaaria and El-Hussein University Hospitals through the period from April (2020) to December (2020). The selected patients received one of the two main medications which are propyl-thiouracil (PTU) and methimazole (MMI). Propylthiouracil was given in the 1st trimester and Methimazole was given in 2nd and 3rd trimester.

Results: There was statistically significant difference found between pretreatment and post treatment groups regarding Heat Intolerance, Palpitations, Tremors, and Irritability, while there was no statistically significant difference found between Pretreatment and Post treatment regarding Exophthalmos. Methimazole (MMI) is preferred to propyl-thiouracil (PTU) after the first trimester because PTU has an association with hepatotoxicity. However, PTU is recommended for the first trimester of pregnancy because its teratogenic effects are considered less severe than those of MMI.

Conclusion: Management of hyperthyroidism during pregnancy and lactation requires special considerations and should be meticulously implemented to provide best care to pregnant woman and prevent any adverse effects. Thyrotoxicosis of pregnancy can present unique diagnostic challenges and, if untreated, is associated with increased risks of adverse maternal, fetal, and neonatal complications. The clinical presentation, serum thyroid function test results, and serum TRAb titers can help differentiate the etiology of thyrotoxicosis. However, assessment and monitoring with serum thyroid function tests can be difficult, as there is significant overlap between test results arising from normal pregnancy physiology and intrinsic hyperthyroidism.

Keywords: Graves' Disease, Antithyroid drugs, Thyrotoxicosis.

INTRODUCTION

Thyrotoxicosis is the clinical syndrome of hyper metabolism and hyperactivity that results when a person is exposed to supra physiological amounts of thyroid hormones. The most common cause of thyrotoxicosis is hyper function of the thyroid gland (hyperthyroidism), and the most common cause of hyperthyroidism in women of childbearing age is autoimmune Graves' Disease (GD) occurring before pregnancy in 0.4% – 1.0 % of women and in approximately 0.2% during pregnancy *(Bahn et al., 2011).*

Less common non-autoimmune causes of hyperthyroidism in pregnancy include toxic multinodular goiter and toxic adenoma. Sub-acute painful or painless thyroiditis with passive release of thyroid hormones from a damaged thyroid gland are less common causes of thyrotoxicosis in pregnancy, and a number of other conditions such as a thyroid stimulating hormone (TSH)-secreting pituitary adenoma, strum a ovarii, functional thyroid cancer metastases, or germ line TSH receptor mutations are very rare. A special cause of thyrotoxicosis is overtreatment with or factitious intake of thyroid hormone *(Korelitz et al., 2013).*

The appropriate initial evaluation of a suppressed serum TSH concentration during the first trimester of pregnancy is very important because Serum TSH may decrease in the first trimester of normal pregnancy as a physiological response to the stimulating effect of human chorionic gonadotropin (hCG) upon the TSH receptor. A peak hCG level typically occurs between 7 and 11 weeks gestation *(Devereaux and Tewelde, 2014).*

In particular, a serum TSH below 0.1 mU/L (in some cases even undetectable) may be present in approximately 5% of women by week 11 of pregnancy. Any subnormal serum TSH value should be evaluated in conjunction with serum TT4 (or FT4) and T3 values. The biochemical diagnosis of overt hyperthyroidism is confirmed in the presence of a suppressed or undetectable serum TSH and inappropriately elevated serum TT4/FT4, or T3 *(Lambert-Messerlian et al., 2012).*

The management of patients with Graves' hyperthyroidism during pregnancy discussed by Several studies showing that the obstetric and medical Complications are directly related to control of maternal hyperthyroidism, and the duration of the euthyroid state throughout pregnancy. Poor control of thyrotoxicosis is associated with pregnancy loss, pregnancy-induced hypertension, prematurity, low birth weight, intrauterine growth restriction, stillbirth, thyroid storm, and maternal congestive heart failure. Moreover, some studies suggest fetal exposure to excessive levels of maternal thyroid hormone may program the offspring to develop diseases such as seizure disorders and neurobehavioral disorders win later life *(Alexander et al., 2017).*

Thionamide ATDs (anti thyroid drugs): Methimazole [MMI], carbimazole [CM], and Propylthiouracil [PTU] are the mainstays of treatment for hyperthyroidism during pregnancy. They reduce iodine organification and coupling of monoiodotyrosine and diiodotyrosine, therefore inhibiting thyroid hormone synthesis. Because the block is not absolute and the thyroid contains a depot

of thyroid hormone bound to Tg, the normalization of thyroid function tests takes place gradually over weeks *(Alexander et al., 2017).*

Thyroidectomy should be considered in cases of allergies/contraindications to both ATDs, in the patient who is not compliant with drug therapy, and in women in whom euthyroidism cannot be achieved even on large doses of ATDs. If surgery is indicated, the second trimester is the optimal time. Thyroidectomy is often followed by a gradual, but not immediate disappearance of TRAb, and withdrawal of ATD in the mother after thyroidectomy may lead to isolated fetal hyperthyroidism *(Laurberg et al., 2011).*

The aim of the study is to discuss thyrotoxicosis which affects the pregnant woman and the effect of hyperthyroidism on pregnancy. It is to discuss different methods of diagnosis of hyperthyroidism during pregnancy. Also it is to study the treatment of hyperthyroidism and thyrotoxicosis during pregnancy for a favorable maternal health and fetal outcome.

PATIENTS AND METHODS

This was a prospective randomized clinical study that was conducted on 20 pregnant female patients with thyrotoxicosis in different stages of pregnancy attending Bab-El Shaaria, El-Hussein University Hospitals & National Institute Of Diabetes And Endocrinology through the period from April (2020) to December (2020).

Before the start of the study, all the steps were explained to the participants and every participant have the right to leave at any time without explanation. Also, oral and written consent were taken from the participants before the start of the study.

Ethical principles: This Clinical Trial was conducted in accordance with the principles laid down by the 18th World Medical Association (Helsinki, 1964) and all applicable am-endments laid down by the World Medical Association and ICH guidelines for Good Clinical Practice.

Laws and regulations: This Clinical Trial will be conducted in compliance with all international laws and regulations, and national laws and regulations of Egypt in which the Clinical Trial is performed, as well as any applicable guidelines.

Inclusion criteria: Pregnant females with hyperthyroidism, age: 22 - 35 years old, history of hyperthyroidism prior pregnancy not an exclusion criterion, and body mass index less than 30 kg/m2.

Exclusion criteria: Pregnant with hypothyroidism, pregnant receiving drugs affecting thyroid hormone levels, pregnant with other comorbidities, morbid obesity, patients with age below 22 or above 35 years old, and patients with cancer thyroid.

Patients Evaluation: Clinical evaluation by taking complete medical history and physical examination (general and local), monitoring for maternal wellbeing: Pulse rate, blood pressure, temperature, any other maternal complaint i.e. nausea, vomiting, palpitation, headache was noticed, and investigations.

Laboratory investigations: Serum TSH and Free T3 & T4. TSH-receptor antibodies. Complete blood picture, serum urea & creatnine, liver enzymes (SGOT & SGPT), Na, K, Ca.

Radiological investigations: Thyroid Doppler U/S.

Methods:

In our study there were 10 patients in the 1st trimester and 10 patients were in the 2nd and 3rd trimester while initiation of the study. We started with patients in the clinic by collecting data and taking full history, vital signs and clinical examination of thyroid gland and general condition, taking into consideration the pregnancy condition. Labarotary tests were done (TSH, FT3, FT4) with other clinical signs to diagnose hyperthyroidism and the cases showed low TSH levels and high FT3 & FT4 levels, thyroid stimulating immunoglobulins (TSI) was positive in cases with history of Graves' disease. After doing laboratory tests and diagnosis of hyperthyroidism, the patients received one of the 2 main medications which are propyl-thiouracil (PTU) and methimazole (MMI) as their function is to block thyroid hormone biosynthesis. We informed the patients that discontinuing the treatment would lead to a higher risk of mortality and morbidity to both the mother and her fetus. Propylthiouracil was given in the 1st trimester and Methimazole was given in 2nd and 3rd trimester as recommended by American thyroid association (Andersen and Andersen, 2020). Doses of 5 – 30 mg/d of methimazole or 100 - 600 mg/d of PTU in divided doses 3 times daily were given to the patients according to their body weight and follow up of thyroid hormones.

Patients were followed up and examined in the clinic every 3 weeks to do serum TSH, monitoring blood pressure, pulse, assessment of symptoms and signs of hyperthyroidism beside the regular follow up of pregnancy done by the obstetrician. Once serum thyroid hormone levels return to normal (upper limit of normal levels to avoid fetal hypothyroidism), we reduced the anti-thyroid drugs to the lowest dose sufficient to keep them euthyroid. Other drugs were considered during pregnancy, among them beta-adrenergic blockers as they have an important role in management of sympathetic manifestations in thyrotoxicosis as palpitation and tremors, to be used for the shortest period and discontinued gradually once symptoms have been improved. 2 cases needed to take Propranolol 40mg 3 times/day for 2 weeks to release of sympathetic manifestations then it was gradually stopped. In our study, 15 cases (75%) of patients have been improved, 5 cases (25%) have not improved after 6 weeks of initiating medical treatment and only 2 cases (20%) needed B.blocker as an adjuvant therapy and improved. There were 10 cases given PTU as they were in the 1st trimester (80%) of them improved, while 10 cases were given Methimazole as they were in the 2nd & 3rd trimester (70%) of them improved.

The non-improved cases needed dose modification and longer duration.

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when their distribution found parametric and median with inter-quartile range (IQR) when their distribution found non parametric. Also qualitative variables were presented as number and

percentages. The comparison between groups regarding qualitative data was done by using Chi-square test. The comparison between two paired groups with quantitative data and parametric distribution were done by using Paired t-test. While the comparison between two paired groups with quantitative data and non-parametric distributions were done by using Wilcoxon Rank test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value > 0.05: Non significant (NS). P-value < 0.05: Significant (S). P-value < 0.01: Highly significant (HS).

RESULTS

Demographic data included 20 pregnant females with thyrotoxicosis, the mean of age was (29.30 ± 4.45) years with the range between (22 - 35) years and the mean of their BMI was (19.53 – 29.39) Kg/m2 **(Table 1)**.

Table (1): Distribution of the studied cases according to demographic data

		No. = 20
Age	Mean ± SD Range	29.30 ± 4.45 22 – 35
Weight	Mean ± SD Range	76.90 ± 13.70 50 – 90
Height	Mean ± SD Range	1.71 ± 0.10 1.6 – 1.85
BMI	Mean ± SD Range	26.06 ± 3.05 19.53 – 29.39

There was statistically significant difference found between pretreatment and post treatment regarding heat intolerance, palpitations, tremors, and irritability. While, there was no statistically significant difference found between pretreatment and post treatment regarding exophthalmos.

There were statistically significant differences found between two groups regarding SBP, DBP, pulse, Hb and blood urea. While, there was non-statistically significant difference found between two groups regarding WBC, Plt ×1000 and Cr. There were statistically significant difference found between two groups regarding TSH, FT3, FT4 and Na. While, there was non-statistically significant difference found between two groups regarding K, Ca, Ph, serum Alb, urinary PCR and protein in urine **(Table 2)**.

Table (2): Comparison between pretreatment and posttreatment regarding heat intolerance, palpitations, tremors, irritability, exophthalmos, SBP, DBP, pulse, WBC, Hb, Plt ×1000, Cr, blood urea, TSH, FT3, FT4, Na, K, Ca, Ph, Sgpt and Sgot.

		Pretreatment No. = 20		Posttreatment No. = 20		P-value
		No.	%	No.	%	
Heat Intolerance	No	3	15.0%	20	100.0%	0.000
	Yes	17	85.0%	0	0.0%	
Palpitations	No	0	0.0%	17	85.0%	0.000
	Yes	20	100.0%	3	15.0%	
Tremors	No	3	15.0%	18	90.0%	0.000
	Yes	17	85.0%	2	10.0%	
Irritability	No	0	0.0%	18	90.0%	0.000
	Yes	20	100.0%	2	10.0%	
Exophthalmos	No	18	90.0%	20	100.0%	0.147
	Yes	2	10.0%	0	0.0%	
SBP	Mean ± SD	135.50 ± 12.66		123.00 ± 10.31		0.000
	Range	115 – 160		110 – 140		
DBP	Mean ± SD	84.00 ± 6.81		76.00 ± 5.03		0.000
	Range	70 – 90		70 – 80		
Pulse	Mean ± SD	113.95 ± 5.08		92.40 ± 4.13		0.000
	Range	108 – 120		86 – 100		
WBC	Mean ± SD	7.20 ± 1.05		6.91 ± 0.61		0.344
	Range	5.6 – 8.6		6 – 7.9		
Hb (g/dl)	Mean ± SD	10.50 ± 0.69		10.96 ± 0.58		0.000
	Range	9.9 – 12		10.2 – 12		
Plt ×1000	Mean ± SD	255.95 ± 63.34		264.65 ± 60.28		0.515
	Range	169 – 326		174 – 343		
Cr (mg/dl)	Mean ± SD	1.05 ± 0.13		1.03 ± 0.11		0.535
	Range	0.86 – 1.3		0.86 – 1.2		
Blood urea (mg/dl)	Mean ± SD	65.10 ± 30.86		78.75 ± 34.51		0.000
	Range	36 – 122		40 – 149		
TSH (mIU/L) Normal (0.4 - 4)	Mean ± SD	0.21 ± 0.11		1.46 ± 1.16		0.001
	Range	0.06 – 0.4		0.04 – 3.9		
FT3 (Pg/dL) Normal (2.4-4.2)	Mean ± SD	5.83 ± 0.48		3.68 ± 1.59		0.000
	Range	4.9 – 6.4		2.5 – 6.7		
FT4 (ng/dL) Normal (0.8-1.8)	Mean ± SD	4.62 ± 1.41		2.60 ± 2.43		0.002
	Range	3.2 – 7.1		0.9 – 7.2		
Na (mEq/L)	Mean ± SD	133.30 ± 7.57		137.85 ± 3.72		0.000
	Range	123 – 144		130 – 143		
K (mEq/L)	Mean ± SD	4.28 ± 0.59		4.12 ± 0.48		0.141
	Range	3.5 – 5.36		3.3 – 4.8		
Ca (mg/dl)	Mean ± SD	8.03 ± 0.35		8.00 ± 0.34		0.757
	Range	7.5 – 8.6		7.5 – 8.5		
Sgpt (U/I)	Mean ± SD	16.19 ± 0.79		16.35 ± 0.75		0.109
	Range	10 – 41		10 – 41		
Sgot (U/I)	Mean ± SD	15.42 ± 0.28		15.40 ± 0.19		0.796
	Range	10 – 40		10 – 40		

Ten cases were given PTU as they were in the 1st trimester 80% of them improved, while 10 cases were given Methimazole as they were in the 2nd & 3rd trimester 70% of them improved ,2 cases needed B.blocker as an adjuvant therapy and improved **(Table 3)**.

Table (3): Distribution of the studied cases according to Medical Treatment

	No.	Improved		Non Improved	
		No.	%	No.	%
PTU	10	8	80.0%	2	20.0%
Methimazole	10	7	70.0%	3	30.0%
Total	**20**	**15**	75.0%	**5**	25.0%
B. blocker	2	2	100.0%	0	0.0%

DISCUSSION

Our study included twenty pregnant females with thyrotoxicosis, the mean of age was (29.30 ± 4.45) years with the range between (22 - 35) years and the mean of their BMI was (19.53 – 29.39) Kg/m2.

Thioamide drug therapy (propyl thiouracil, methimazole, carbimazole) is the first line therapy, indicated for moderate or severe hyperthyroidism. The drug of choice in the first trimester is propylthiouracil, given in a dose of 100 – 150 mg three times daily until the patient becomes euthyroid (with normal thyroid function tests) at which time the dose should be reduced to the lowest amount to maintain the euthyroid state. Although there have been no prospective clinical trials, multiple case reports have associated methimazole with two types of fetal abnormalities: choanal or esophageal atresia and aplasia cutis *(DeGroot, 2016)*.

Also, Beta-blockers are relatively contraindicated, but not absolutely, so that propranolol can be used until T4 levels normalized. The complications of the drugs include:-Lower Apgar scores-Intrauterine growth retardation-Postnatal bradycardia, hypothermia and hypoglycemia-Neonatal respiratory distress *(Ji et al., 2017)*.

There are two concerns about anti-thyroid drugs for thyrotoxicosis: that the drugs cause hypothyroidism in the fetus and that they have teratogenic effects. These drugs cross the placenta and can sometimes cause fetal hypothyroidism and goitre *(Taylor and Vaidya, 2012)*.

In two studies in which antithyroid therapy was used in moderate doses maternal and fetal outcomes were satisfactory *(Momotani et al., 2010* and *Wing et al., 2010)*. Close monitoring of thyroid function, roughly once a month, is important because the need for antithyroid treatment often declines through pregnancy, and in the mid-trimester it may occasionally be discontinued.

Recent studies have not suggested that antithyroid treatment has adverse consequences on thyroid size or function or subsequent physical or intellectual development, as occurs in congenital hypothyroidism. There is equivocal evidence suggesting that placental transfer of propylthiouracil may be less than that of carbimazole or methimazole, so this drug may be the least likely to damage the fetal thyroid *(Taylor and Vaidya, 2012)*.

Our study showed highly statistically significant difference found between pretreatment and post treatment groups regarding Heat Intolerance, Palpitations, Tremors, and Irritability, while there was no statistically significant difference found between Pretreatment and Post treatment regarding Exophthalmos.

A retrospective multicenter study by *Tagami et al. (2012),* reported that the signs and symptoms of patients with hyperthyroidism showed a significant improvement after just 4weeks of taking beta-adrenergic blocking agents.

Through our study, we found that 75% of the patients improved and 25% didn't improve, with the improved patients the drug reduced to the lowest amount to maintain the euthyroid state and the non-improved patients continued with the adjusted dose. Only 10% of those thyrotoxic pregnant needed to take B2 blocker.

Close monitoring of thyroid function, roughly once a month, is important because the need for antithyroid treatment often declines through pregnancy, and in the mid-trimester it may occasionally be discontinued.

Current guidelines by the American Thyroid Association, the American Association of Clinical Endocrinologists, and the Endocrine Society recommend the use of propylthiouracil (PTU) in the first trimester of pregnancy, and consideration to switch to methimazole after the first trimester *(Labadzhyan et al., 2014)*. These recommendations are based on concerns of rare congenital abnormalities associated with methimazole use during embryogenesis.

In a retrospective study by *Yoshihara et al. (2012),* comparing treatment of pre-existing Graves' disease in the first trimester with PTU, methimazole, and no treatment, the relative risk of major congenital malformations was significantly higher in the methimazole group.

Propylthiouracil prescriptions should be limited to the amount required for the time until the next scheduled visit. For about one third of patients, PTU can be discontinued in the second half of the pregnancy *(Ross et al., 2016)*.

Thyroidectomy as a definitive treatment option for maternal hyperthyroidism during pregnancy is recommended for patients who are unable to tolerate anti-thyroid medications, require large doses of these medications, or are non-adherent and have severe, uncontrolled hyperthyroidism. Thyroid surgery during the second trimester is thought to be the safest option, although thyroid surgery during any time in pregnancy may confer an increased risk of maternal complications, including higher rate of hypoparathyroidism, recurrent laryngeal nerve injury, and general surgical complications *(Smithson et al., 2019)*.

Methimazole (MMI) is generally preferred to propylthiouracil (PTU) after the first trimester because PTU has an association with hepatotoxicity. However, PTU is recommended for the first trimester of pregnancy because its teratogenic effects are considered less severe than those of MMI. Switching from MMI to PTU in anticipation of conception should be considered. Alternatively,

women may switch to PTU once pregnant *(Nguyen et al., 2018).*

CONCLUSION

Propylthiouracil is the preferred thionamide for treatment of hyperthyroidism in the first trimester. Radioiodine is contraindicated, and surgery, if indicated, should be performed during the second trimester. Appropriate treatment of maternal hyperthyroidism during pregnancy and close monitoring of mother and fetus are essential for optimizing outcomes. Treatment should be targeted to achieve serum TSH concentrations within established pregnancy-specific reference ranges.

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مناجزة التسمم الدرقي أثناء الحمل

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خلفيـــة البحـــث: يُعـد مـرض الـدُراق الجُحـوظي المنـاعي مـن أكثـر أمـراض فـرط نشـاط الغـدة الدرقيـة شـيوعا لـدى السـيدات فـي سـن الإنجـاب. فيجـب وضـع خطـة عـلاج ومراقبـة التسـمم الـدرقي أثنـاء الحمـل بشـكل كـافي، لمنـع حـدوث مضـاعفات لـلأم والجنـين أثنـاء الحمـل. تمثـل التكيفـات الفسـيولوجية المرتبطـة بالحمـل تحـديا صـعبا فـي تقيـيم و وظيفـة الغـدة الدرقيـة عنـد النسـاء الحوامـل، ويثيـر العـلاج بأدويـة مضـادات الغدة الدرقية قلقا للأم والجنين.

الهـدف مـن البحـث: إن هـدفنا مـن هـذه الدراسـة هـو مناقشـة تـأثير فـرط نشـاط الغـدة الدرقيـة علـى الحمـل، والطـرق المختلفـة لتشخيصـه وعلاجـه أثنـاء الحمـل مـن أجـل صحة الأم والجنين.

المريضـــات وطـــرق البحـــث: أجريـت دراسـة سـريرية عشـوائية علـى 20 مريضـة حامـل مصـابة بالتسـمم الـدرقي فـي مراحـل مختلفـة مـن الحمـل بمستشـفى بـاب الشـعرية (سـيد جـلال) و مستشـفي الحسـين الجـامعي، خـلال الفتـرة مـن أبريـل (2020) إلـى ديسـمبر (2020). وتلقـي المرضـى المنتقـاه واحـدا مـن الأدويـة الرئيسـية وهمـا بروبيـل ثيوراسـيل (PTU) وميثيمـازول (MMI)، و إعطـاء بروبرانولـول (B-blocker) كـدواء إضـافي لـبعض الحـالات التـي إحتاجـت لـذلك. وقـد تـم إعطـاء بروبيـل ثيوراسـيل فـي فتـرة الثلـث الأول مـن الحمـل، وأُعطـى الميثيمـازول فـي الثلـث الثـاني والثالـث مـن الحمـل بجرعـه مناسـبه ثـلاث مـرات يوميـا مـع متابعـه تحاليـل وظائف الغده الدرقيه و الأعراض.

نتـائج البحـث: وجـدنا فروقـات ذي دلالـة واضـحة بـين مجمـوعتي مـا قبـل ومـا بعـد العـلاج، فيمـا يتعلـق بعـدم تحمـل الحـرارة والخفقـان والرعشـة والتهـيج، بينمـا لـم يكـن هنـاك فرقـا ذو دلالـة واضـحة بـين مـا قبـل ومـا بعـد العـلاج، فيمـا يتعلـق بجحـوظ العـين.

وكانت نسبه المرضي اللاتي تحسن حوالي 75% و إحتاج حوالي 20% من المرضي إلي إضافه دواء بروبرانولول. و يجب تناول بروبيل ثيوراسيل (PTU) في أشهر الحمل الثلاثة الأولى و ذلك لقلة حدة تأثيره على تشوهات الجنين بينما يفضل الميثيمازول (MMI) على البروبيل ثيوراسيل بعد اشهر الحمل الثلاثة الأولى لإرتباط البروبيل ثيوراسيل بسمية الكبد.

الاستنتاج: تتطلب خطة علاج فرط نشاط الغدة الدرقية اعتبارات خاصة أثناء الحمل والرضاعة، ويجب تنفيذها بدقة لتزويد السيدات الحوامل بأفضل رعاية وتجنب أى آثار ضارة.

الكلمات الدالة: مرض جريفز، أدوية ضد الغدة الدرقية، التسمم الدرقي.