

Impending Thyroid Storm in Pregnancy with Pre-eclampsia with Severe Feature and Gestational Diabetes Mellitus in Limited Resources Facilities (a Case Report)

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Abstract:

Objective: To describe the case of impending thyroid storm in pregnancy with pre-eclampsia with severe feature and gestational diabetes mellitus (GDM) as the complication in limited resources facilities.

Introduction: In pregnant women, mortality rate for patients with unrecognized and untreated thyroid storm ranges from 10-30%. When there is a history of previous thyroid dysfunction on pregnant women are said to be associated with an increased risk of pre-eclampsia and GDM, although more research were required.

Case Presentation: This case report was taken from Natuna General Hospital which is an area with limited resources facilities. A 41 year old multigravida woman with 36 weeks of gestational age. The woman experienced impending thyroid storm, pre-eclampsia with severe feature and GDM, then delivered a healthy baby girl by emergency caesarean section. The patient was hospitalized for 5 days and her condition was improved, the patient was already discharged.

Conclusion: Thyroid storm on pregnancy has high mortality rate, therefore an early diagnosis and treatment are needed for these patients. Thyroid disorder associated with the incidences of pre-eclampsia and GDM.

Keywords: impending thyroid storm, pre-eclampsia with severe feature, gestational diabetes mellitus

1. INTRODUCTION

Pregnancy with impending thyroid storm, pre-eclampsia with severe feature and gestational diabetes mellitus could lead into condition with possibilities of adverse maternal-fetal outcome and complications. This case report was taken from Natuna General Hospital which is an area with limited resources facilities. In limitation resources facilities, this condition issued several problematic considerations, either in diagnostic or management, complications and maternal-fetal survival affected by this condition. Thyrotoxicosis is a term to describe a set of

symptoms of excess thyroid hormone. While hyperthyroid is a condition of thyrotoxicosis due to overactive thyroid gland produces hormones, with 85% of these cases resulting from graves disease.^{1,2} The incidence of graves disease in the United Kingdom ranged 1-2 per 1000 pregnancies.³ Indonesia Basic Health Research 2013 based on *Riset Kesehatan Dasar* (Riskesdas) shows a population of ≥ 15 years diagnosed with hyperthyroid approximately 700,000 people, with the percentage of 0.4% of the total number 176.689.336.⁴ Untreated thyrotoxicosis in women will increase the risk for severe complications of thyroid storm and pre-eclampsia as high as 21% and 14-22% respectively.⁵ Thyroid storm based on score Burch and Wartofsky is distinguished as early stage (the impending storm) and thyroid crisis (thyroid storm), a fairly high mortality figures up to 10-30% if unknown and handled improperly.^{1,6} The prevalence of pre-eclampsia is 2-8% from all pregnancies with mortality rate as high as 76.000 death annually in the world.⁷ In Indonesia, the prevalence of pre-eclampsia is 3-10%.¹ Therefore it is necessary to diagnose and treat the thyrotoxicosis as early as possible in pregnancy, although the symptoms can sometimes overlapped. However, the symptoms and signs which should be more aware of is an abnormal weight gain beside of normal appetite, tremors and signs of grave ophthalmopathy (the exophthalmos).^{3,5}

Gestational Diabetes Mellitus (GDM) is the presence of glucose intolerance onset occurred or is first detected during pregnancy.^{8,9} Prevalence in Asian countries varies, ranged of 1-20% based on case screening and diagnosis criteria.^{8,9} Research has been done in a decade trying to describe the relationship of GDM, thyroid dysfunction and pre-eclampsia. The results were vary and the underlying mechanisms of it still need further research.

The case that will be reported is the case of the impending storm in pregnancy thyroid suspect of graves disease with pre-eclampsia with severe feature and GDM as the complication in limited resources facilities.

2. CASE REPORT

A 41 yearold woman G3P2 at 36 weeks of gestational age was examined at emergency room of Natuna General Hospital. She complaint palpitation, headache, whole body trembling, and sweaty. The vital signs examination showed a composmentis state, blood pressure 170/110mmHg, heart rate 150 bpm, respiratory rate 28 bpm, body temperature 37,6°C, and peripheral SpO₂ 99% with 2 litre oxygen using nasal canule. The patient has confirmed that she had the history of uncontrolled high blood pressure on the previous pregnancy. The last baby was delivered by caesarean section due to uncontrolled blood pressure. The physical examination showed exophthalmos, diffuse enlargement of thyroid gland, and fine tremors on both hands were found. The past illness history was thyrotoxicosis suspect of grave disease that has known since 2009 which was also poorly controlled. The only laboratory examination that has been conducted were fT4 2,7 ng/dL and TSH < 0,02 µIU/mL on 2015. The patient was also diagnosed with GDM based on the laboratory findings of fasting oral glucose tolerance test (OGTT) was 111mg/dl, 1 hour post prandial OGTT was 198 mg/dl and 2 hour post prandial OGTT was 210 mg/dl. There was no signs of delivery and cardiocography was also normal. Random blood sugar test was 106 mg/dL. The complete blood count, liver function, renal function, and coagulation function test was normal and no proteinuria was found. Complete urine test has discovered urinary tract infection. The patient was diagnosed with impending thyroid storm (Burch and Wartofsky score of 30), pre-eclampsia with severe feature, GDM, emergency caesarean section was choosed for delivering the baby. Pre-operation therapy for patient, nifedipin, PTU, propranolol, lugol were given orally, 40% MgSO₄ and dexametasone were given intravenously, with pre-operation target for the blood pressure was less than 140/90mmHg, heart rate less than 80 bpm, and the random blood glucose in the range of 140-180 mg/dL. Preoperative targets were reached within 3 hours. Termination was conducted and then there was born 2910 grams baby girl with APGAR score 9/10. The mother was hemodinamically stable and transferred to ICU for further post operative observation, 200 mg PTU was given orally 6 times a day, 40 mg propranolol was given orally 4 times a day, 8 drops of lugol was given orally 4 times a day, and 2 mg intravenously of dexametasone every 6 hours. The patient transferred to the ward after 1 day intensive observation in the ICU with TSH result 0,05 and then discharged home 5 days later with propranolol 4x20 mg po, PTU 4x200 mg po and methyl dopa 3x500 mg po.

3. DISCUSSION

Thyrotoxicosis in pregnancy defined by the over activity of thyroid hormone because the increase of its level in the bloodstream marked by the decrease of TSH level. The most common cause of thyrotoxicosis in pregnancy is Gestational Transient Thyrotoxicosis (GTT) that physiologically occurs because of similarity of the molecular structure between β-HCG with TSH, and we know that β-HCG increases with a peak at 8-12 weeks gestation and then continued to fall and reach its nadir point until birth. β-HCG also stimulates the thyroid gland to produce triiodothyronine/fT3. Gestational Transient Thyrotoxicosis (GTT) may be experienced by approximately 1-5% of pregnant women in the early trimester and its effect on thyroid function usually meaningless.^{2,3,10-12} Other changes that elevated levels of Thyroxine Binding Globulin (TBG) as a result of estrogen stimulation so that the levels of T3 and T4 increased, although fT3 and fT4 remained normal. This is a basic statement that the examination of thyroid function during pregnancy is better to use fT4 as the parameter.^{3,5}

Beside of that physiological process, thyrotoxicosis can also occur pathologically, caused by some conditions which already existed before pregnancy, such as the existence of such antibodies that stimulate the TSH (graves disease), adenoma toxic, or goiter.^{12,13} Neither GTT nor graves disease complained of symptoms such as palpitations, anxiety, tremors, and temperature intolerance. The difference is graves disease has diffuse toxic goiter and ophtalmopathy on both eyes, and already diagnosed as hyperthyroidism.^{11,13,14} In this case, the patient was diagnosed with thyrotoxicosis suspected for graves disease which present before pregnancy. The diagnosis can be confirmed with the examination of TSH receptor stimulating antibody, TRAb. Suspicion above is also supported by data that showed that, 85% of cases of hyperthyroidism that occurs during pregnancy and in women of young age is caused by graves disease.^{9,15} The patient's medical history for hyperthyroid treatment using PTU is also showed poor compliance and the patient never conduct any laboratory examination for thyroid function if the medications are given to see the response of the treatment. Therefore can be concluded that this patient was having an uncontrolled thyrotoxicosis. If the patient was having grave disease before the pregnancy, based on *Korevar et al* study, there was a high possibility that this patient was showing pre-eclampsia because of the pathological thyrotoxicosis condition before the pregnancy, which is suspect of grave disease.¹

Pre-eclampsia is defined as hypertension that occurs on 20 weeks of gestational age or more and proteinuria was no longer needed to enforce the diagnosis. In this

case, the diagnosis of pre-eclampsia with severe feature has enforced based on the blood pressure of 170/110 mmHg. Pre-eclampsia with severe feature was one of the classification for hypertension in pregnancy, which the diagnosis can be enforced when one or more of these condition was found, blood pressure $\geq 160/110$ mmHg, serum creatinin >1.1 mg/dl, elevated liver function test for two folds or more, thrombocytopenia <100.000 /microlitre, lung edema, other clinical features such as headache, vision problem, and or epigastric pain.^{15,16} Mechanism of pre-eclampsia has not known yet, but it is suggested that the pathological process was disturbance of implantation and invasion of the trophoblast to endometrium, followed by spiral artery remodeling and inflammatory, metabolic, and thrombotic responses in the end. Thyroid hormone also has an important role for the development of placenta and as an important regulator for metabolic and inflammatory processes that occurred.^{10,12,15} Study by Korevaar found an association between ft_4 and hCG levels with the incidence of pre-eclampsia, but there was a difference in women with low and high levels of hCG. When stratification was done based on the level of hCG, it was found that women with low levels of hCG and a high ft_4 had 4.6 times higher probability to develop pre-eclampsia compared with other groups. The incidence of pre-eclampsia also 4.3 times higher in the group of women with low levels of hCG and fully suppressed TSH (TSH <0.10 mU / L) compared with the other group.¹² Women with a high BMI (> 25 kg / m²) also increases the risk of pre-eclampsia 2.9 times higher and increased to 7.7 to 8.3 times higher when associated with low hCG levels and high FT_4 . High BMI is also associated with lower levels of hCG, some reason that causes increased incidence of pre-eclampsia in women with a high BMI.¹² Study conducted by Männistö *T et al* showed that hyperthyroid women have a higher possibility for pre-eclampsia (OR 1.78), hypertension superimposed pre-eclampsia (OR 3.64), prematurity (OR 1.81), and almost 4 times higher to stay on ICU (OR 3,70).¹⁷

In the emergency room, the patient complaint for headache, whole body trembling, sweaty, and palpitation. From the physical examination, hypertension, tachycardia, and tachypneu with normal peripheral oxygen saturation were found. Thyroid storm is a rare complication of hyperthyroidism but the mortality rate was 10-30% if undiagnosed and untreated properly. This condition can be divided to 2 stage, the early stage (impending thyroid storm) and actual thyroid crisis (thyroid storm). Burch and Wartofsky score still used to classify the stage of thyroid storm.^{1,6,18,19} The patient was assessed with impending thyroid storm based on 30 points of Burch and Wartofsky score (the temperature for 5 points, and tachycardia ≥ 140 bpm for 25 points. This condition

must be recognized as fast as possible to prevent the actual thyroid crisis. This condition can occur for many reasons, which is surgery procedure, labor process, infection, pre-eclampsia, induction process, diabetic ketoacidosis, and the others stress conditions.^{1,7,18} For this patient, pre-eclampsia with severe feature and urinary tract infection can be suggested as the reason for impending thyroid storm to occur.

It's said that, when exophthalmos, thyroid gland enlargement, tachycardia or bradycardia were found, and the TSH testing can be precisely taken for pre-surgery evaluation. Some β -blocker like atenolol is more chosen for several cases. Metoprolol, atenolol are selective beta-1 blocker that can be well tolerated for reactive respiratory tract disease. Longer half life time is also easier for the patient for a single dose daily. Propranolol is a non-selective beta blocker agent and the shorter half life time make the patient must take more dose daily, it has some other benefit, propranolol can inhibit the activity of type 1 monodeiodinase enzyme that convert T₄ to T₃ which is biologically more active. The dosage of propranolol is 10-40 mg every 4-6 hour per orally and also can be given intravenously to control the blood pressure and heart rate below 80 bpm, even to lower the temperature if fever was occurred.^{14,20-22} Other sources said that propranolol use are more recommended because the other beta blocker such as atenolol was associated with low birth weight delivery. As a note, beta blockers are contraindicated for patient with severe heart failure or cardiogenic shock.¹¹

All the patient with thyroid storm should be hospitalized in intensive care unit (ICU). The management that should be done such as: thionamide must be given (load 1000 mg of PTU continued with 200 mg of PTU every 6 hours), propranolol can be given 10-40 mg every 4-6 hours to control the heart rate, 1-2 hours after that, 500-1000 mg of sodium iodide can be given every 8 hours, or 5 drops of potassium iodide every 8 hours per orally, or 8 drops of Lugol every 6 hours per orally, or 300 mg of lithium carbonate every 6 hours if there was history of iodide allergy.¹⁰ Steroid considered to be given within 24 hours (2 mg of dexamethasone intravenously every 6 hours or 100 mg of hydrocortisone every 8 hours).¹¹ The patient was also given $MgSO_4$ and nifedipine for pre-eclampsia. Intravenous $MgSO_4$ can be given for severe pre-eclamptic patient using the procedures 4 - 6 grams of magnesium sulphate can be given in 100 cc of infusion fluid within 15-20 minutes, continued with 1 - 2 grams/ hour in 100 cc of maintenance fluid. Magnesium sulphate must be stopped in 24 hours after delivery.^{10,15}

Severe pre-eclampsia, infection, or anemia condition must be treated before delivery was considered.¹⁰ In the other word, caesarian section is not a must for patient

with thyroid storm. The caesarean section was considered to be done because the impending thyroid storm was accompanied with pre-eclampsia with severe feature.

Gestational diabetes mellitus (GDM) defined as glucose intolerance that detected first time in pregnancy.^{9,23}The inflammation process was suggested as the pathological process that relate the autoimmune condition and insulin resistance that occur on GDM.³Oral Glucose Tolerance Test (OGTT) can be conducted to screen or diagnose GDM. For screening, this test must be conducted on 24-28 weeks of gestational age for all pregnant women that don't have any history or unknown history of diabetes melitus. For diagnosis, there are 2 ways, which are: one and two step procedure. One test procedure: 75 g of OGTT's glucose is given to the patient and the blood glucose level will be measured within 8 hours of fasting, and then 1 and two hours after initial measurement. The diagnosis can be enforced if the fasting blood glucose level ≥ 92 mg/dL, 1 hour blood glucose level ≥ 180 mg/dL, and 2 hours blood glucose level ≥ 153 g/dL. On two step procedure, 50 g of OGTT's glucose will be given without fasting, then blood glucose measurement will be conducted 1 hour after that, if the result shows ≥ 140 g/dL, the patient will drink 100 g of OGTT's glucose and then fasting. The diagnosis can be enforced if 2 or more of these criterias are met: fasting blood glucose ≥ 95 g/dL or 1 hour blood glucose ≥ 180 g/dL or 2 hours blood glucose ≥ 155 g/dL.²⁴

The meta-analysis study conducted by *Ying Yang et al* it is known that GDM occur because of insulin resistance process and is not the decrease of insulin secretion. The autoimmunity process on thyroid function was suggested to stimulate the increase of the number and the activity of pro-inflammation cytokine that give raise to insuline resistance to occur. From this study showed that the risk of GDM will increase if the patient was also had thyroid dysfunction condition with positive result of thyroid antibody (RR 1,35, 95% dan CI 1.06-1.71).⁷Contradictive result was shown from the study that conducted by *Gong et al*, it is showed that severe hypothyroid condition was associated with GDM (OR 1,892, 95% dan CI 1,679-2,132). Lower thyroid hormone level suggested to increase the risk of insulin resistance which make the GDM occur.²³

Gestational diabetes mellitus (GDM) was also related to the possibility of pre-eclampsia occurrence. The study conducted by *Lee et al* showed that previous pregnancy history of pre-eclampsia can increase the risk of GDM in the next pregnancy. Endothelial dysfunction and vascular damage in pre-eclampsia were suggested that stimulate GDM to occur. The actual process of the occurrence of GDM still need further clarification.²⁵The study conducted by *Yogev et al* showed that as high as 10% of the patients that diagnosed with GDM was also

having pre-eclampsia and also having another pathological conditions such as obesity, overt increase of body weight on pregnancy, and quicker labor rate.²⁶

4. CONCLUSION

Despite we found in low resources facilities, with appropriate management has led to better results and outcome in this patient. Thyroid storm on pregnancy has high mortality rate, therefore an early diagnosis and treatment are needed for these patients. Clinical conditions based on Burch and Wartofsky score are enough to enforce the diagnosis of thyroid storm or impending thyroid storm without any laboratory findings. The patient's history of antenatal care visits are also in a good criteria, but it will be better if pre-pregnancy counsellings are also conducted to control all others pathological conditions for better pregnancy condition. Thyroid disorders are associated with incidences of pre-eclampsia and GDM, pre-eclampsia is also associated with incidences of GDM, therefore a comprehensive and hollistic treatments are needed for these conditions.

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