Case Report

Successful Outcome of Pregnancy with Addison's Disease & Hypothyroidism

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Abstract

Hypocortisolism or hypoadrenalism is well known as Addison's disease which is a long term endocrine disorder. In pregnancy it requires much awareness and attention of treating physicians. Early diagnosis, adequate supplement of glucocorticoid and mineralocorticoid and fetal surveillance through regular antenatal checkup is essential for pregnant ladies with Addison's disease. Patients should be counselled appropriately regarding medication, life-style and precautions to be taken in case of infection, operational exposure or any other stress.

Key-words: Addison's Disease, Hypothyroidism.

Introduction

Primary adrenal insufficiency is a long term endocrine disorder in which the adrenal glands do not produce enough steroid hormones[1]. Symptoms generally come on slowly and may include abdominal pain, weakness, weight loss and hypotension[2]. Darkening of the skin in certain areas may also occur. Under certain circumstances, an adrenal crisis may occur with low blood pressure, vomiting, lower back pain and loss of consciousness. An adrenal crisis can be triggered by stress, such as from an injury, surgery or even infection. It is a rare and chronic disease of adrenal cortex where insufficient production of glucocorticoid and mineralocorticoid is present.

Addison's disease has harmful and deadly impacts on pregnancy. It may cause abortion, intrauterine growth retardation, intrauterine fetal death and postpartum adrenal crisis. Due to having some common symptoms like fatigue, vomiting, nausea, weakness, hyperpigmentation and hypotension Identification of Addison's Disease in pregnancy requires much awareness and attention of treating physicians.

Early diagnosis, adequate supplement of glucocorticoid and mineralocorticoid[3] and fetal surveillance through regular antenatal checkup is essential for pregnant ladies with Addison's disease. Patients should be counseled appropriately regarding medication, life-style and precautions to be taken in case of infection, operational exposure or any other stress.

Untreated Hypothyroidism may cause problems during pregnancy. Unborn baby has a higher risk of neurod- evelopment problems like lower IQ. Controlled medication under close supervision of treating physician is very much essential to ensure proper health for both mother and child. Few medications like radioactive iodine should be avoided to safeguard unborn baby's Thyroid gland.

Objective of this article is to represent a successful outcome of pregnancy with Addison's Disease through a case report of a patient who has undergone her antenatal period under the supervision of the Department of Obstetrics & Gynaecology, CMH, Dhaka.

Case Report

This article will demonstrate the case of Mrs. "X", patient of Addison's disease and the case will represent the overall patient management process during her third pregnancy. Mrs. "X" with 3rd gravida came for her first antenatal checkup on January 2018 with known case of Addison's disease. According to history of patient, she underwent Caesarian Section at her 1st pregnancy on January 2012. In June 2012 she was diagnosed as a case of Addison's disease. She had a history of spontaneous abortion in 2014 at 7th week of gestation. With this brief, we can conclude that at her 3rd pregnancy she has been identified as a pregnant woman with Addison's disease.

Having being diagnosed as a case of Addison's disease in June 2012 she has been taken care under the treatment of an endocrinologist and has been getting tablet Prednisolone 7.5 mg daily as supplementary drug. From the very beginning of her antenatal checkup treating obstetrician approached a multi disciplinary care covering endocrinologist, neonatologist and obstetrician as well as anesthesiologist. During her first antenatal visit levels of Serum Cortisol was 38.81 nmol/L and Serum ACTH level was 47.00 pg/mL [normal range is 10-60 pg/mL at morning] which is a confirmatory indication of pregnancy with Addison's Disease.

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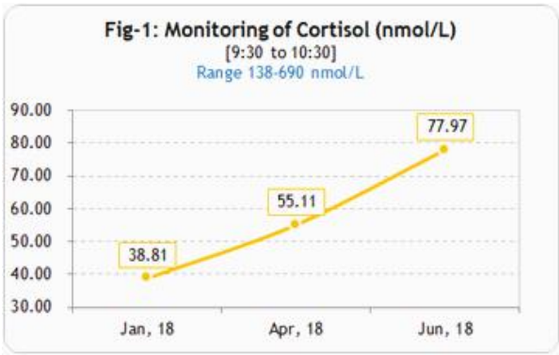
Analyzing history of the patient and her family she had been suggested for monthly antenatal checkup for fetus surveillance, quarterly pathological tests for regular monitoring of Serum Cortisol and ACTH Level and regular medication accordingly. To fight-back against Addison's disease's harmful impacts, her treatment can be summarized as follows-

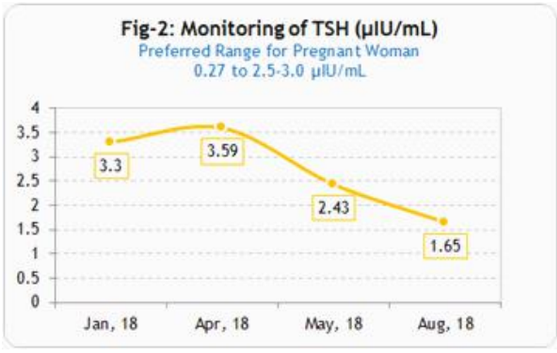
Table-I: Treatment Summary

Antenatal Checkup	Monthly
Endocrinologist Visit	Quarterly
Check Serum Cortisol	Quarterly
Check Serum ATCH	Quarterly
Prednisolone 5 mg	Daily (1 + 0 + ½)

With this management her vitals and physical activities were normal. Following figures will show the development of her Cortisol level during her pregnancy tenure at morning. It has significant development considering a pregnant lady through controlled medication (Fig-1).



During her regular antenatal checkup in April 2018 Hypothyroidism has been identified with abnormal values. Overall patient Management became more challenging as very controlled medication was required to battle the challenge under close supervision. The multidisciplinary medical board decided to start Thyroxin 25 µg on daily (1 + 0 + 0) basis as follows which had a visible outcome (Fig-2).



Throughout the pregnancy period different routine examinations have been done and no other abnormality was observed. Her Serum Sodium level was found 137 nmol/L [normal range is 135 to 145 nmol/L] and Serum Potassium level was found 4.6 nmol/L [normal range is 3.5 to 5 nmol/L]. Ultrasound examinations of whole abdomen revealed no abnormality ever. As a whole, this 360º multidisciplinary approach really worked well and kept patient on her way towards a successful outcome.

As she has a history of previous C/S and an abortion, the medical board didn't take further risk associated with Vaginal Delivery, rather they decided for elective C/S after completion of 37 weeks. As a part of this decision, Mrs. "X" was admitted in CMH, Dhaka on 30 July 2018 as a case of 3rd gravida with 36 weeks pregnancy with Addison's disease and Hypothyroidism and her caesarian section was planned to be performed on 13 August 2018. During this period she was admitted in the Gynae-HDU and guided towards successful outcome by doing all necessaries to ensure fetal surveillance and to avoid antepartum and postpartum complications. Her Caesarian Section was done on 13 August 2018 under spinal anesthesia. A male baby weighing 2.7 kg was delivered. Injection Hydrocortisone 100 mg intravenously 12 hourly was started before induction of anesthesia and maintained for 3 consecutive days. After that, oral Prednisolone 7.5 mg was continued as before. Her wound healing was normal and Puerperium was uneventful. She was able to breastfeed her baby satisfactorily. The patient was discharged from CMH, Dhaka on her 5th postoperative day with advice to review after two weeks with Serum Electrolyte report. She was also advised to maintain the Steroid card. Two weeks follow up report showed normal Serum Electrolytes, good wound healing and successful breastfeeding. The progress of baby was normal on follow up visit and her Serum Electrolyte levels were normal.

Discussion

In this case study we have tried to highlight the patient facts, treatment followed and the outcome. Few discussions will help us to understand the decision making evidences.

Patient's first complain in 2012 was of skin darkening, fatigue, nausea, vomiting and weight loss. She has been getting medication since then. She also has a history of spontaneous abortion in 2014 at 7th week of her 2nd pregnancy. Both this historical facts indicate that she probably was more sensitive to impacts of Addison's disease. As Addison's disease in pregnancy is a rare disorder, opportunity to get experience based decisive leads are also rare. Hence treating physician has to analyze all possibilities and consider all facts.

As clinical features include nonspecific sign and symptoms, high degree of suspicion is essential for proper diagnosis. Low Serum Cortisol and inappropriate diurnal variation, Short Synacthem test ACTH level may confirm or refute the diagnosis of Addison's disease[4]. But the reference ranges for pregnant and non-pregnant woman are not same as the concentration of Corticosteroid Binding Globulin (CBG) and cortisol in serum as well as urinary free cortisol level increases two to three fold during the pregnancy[5]. But the P-ACTH level remains unchanged during pregnancy, and hence diagnosis of Addison's disease during pregnancy should be based on P-ACTH[3]. A raised Plasma ACTH level confirms the diagnosis of Addison's disease. All these facts were discussed among the multidisciplinary medical board and as a previously identified case decisions had become easy to take.

The presence of Adrenal antibodies indicates autoimmune Addison's disease. 21-Hydroxylase antibodies are more sensitive (present in 90% cases) than Adrenal Cortex antibodies. About 30% of them will have antibodies to 17-Hydroxylase and side-chain cleavage enzymes[6]. Though the board didn't find any indication of its presence through pathological tests, but patient's Thyroid gland was also affected along with Adrenal gland. And this indicates Polyendocrinopathy which usually indicates presence of Adrenal antibodies.

Maternal anti-Adrenal auto-antibodies may cross the placenta, but usually does not cause any fetal/neonatal adrenal insufficiency[7]. Poor fetal outcome, even death may occur in case of severe maternal hypernatremia or metabolic acidosis[8]. The risk of miscarriage is raised if other autoimmune conditions such as Anticardiolipin antibodies are associated with Addison's disease[8].

The replacement of glucocorticoid and mineralocorticoid should be continued throughout pregnancy, delivery and lactation. The dose depends on clinical condition and Serum Electrolyte level. The increment of dose is usually required during third trimester. During labor adequate hydration should be maintained through intravenous normal saline (mineralocorticoid) and glucocorticoid (i.e., Hydrocortisone Sodium Succinate) and the multidisciplinary medical board decided to give by intravenous route as a dose of 100 mg 8 hourly 24 hours before delivery. At the time of delivery or if the labor is prolonged dose can be increased as 100 mg 6 hourly or as a continuous infusion. This case was elective Caesarian Section and hence the physicians decided to continue the dose in a tapered form through a maintenance dose of 50 mg 8 hourly for next 48 hours[9]. The blood pressure should be measured hourly as it is at the best guide to dictate the dose of Hydrocortisone. If the blood pressure is low, the dose of Cortisone should be raised. Serum Electrolytes and blood sugar determinants are not of much value as controls. From the third day Puerperium, when the dose of Cortisone was gradually reduced to its previous level, the blood pressure should be measured 4 hourly[10] and for this case patient management was done accordingly.

Postpartum haemorrhage can be prevented by administration of Carbetocin or Prostaglandinin the third stage of labor. Tolerance to analgesic and anesthesia is normal in patients who had received sufficient replacement of Glucocorticoid and Mineralocorticoid. Satisfactory lactation depends on adequate supply of Adrenal Glucocorticoids[10]. Normal and regular breast feeding indicates satisfactory lactation for the case of Mrs. "X".

In this case, the baby was free from any congenital defect and her development was normal at follow up visit. The normal Serum Electrolytes level was found the baby which is a confirmation of having no antenatal over activity of fetal adrenals[10]. The baby was kept in observation for 24 hours, all necessary tests were done and everything found normal.

According to a Cohort Study which was done based upon a Swedish population, patients with diagnosed and undiagnosed autoimmune Addison's disease are at increased risk of preterm delivery, intrauterine growth retardation and other unfavorable pregnancy outcome[11]. A pregnant woman with Addison's Disease is a case of high risk pregnancy and she needs careful monitoring and more frequent follow up to identify signs of fetal growth retardation which may lead to short and long term consequences for the infant.

Addison's disease may be associated with ovarian insufficiency and it may partly explain low parity Addison's disease. Potential risk of development of premature ovarian failure is a real concern, so the patients should be advised to become pregnant as soon as possible, if she desires to be a mother[12].

As shown in Fig-2, patient's TSH level was well controlled during pregnancy through proper medication. She continued the dose as a usual oral dose. In follow up visit, patient's and baby's TCH, F-T4, Serum Electrolytes and other test reports were normal which indicates controlled level of Hypothyroidism during pregnancy period without any unfavorable pregnancy outcome.

Conclusion

Addison's disease in pregnancy is a rare disorder. Hypothyroidism made it more critical. Because of adverse effects of glucocorticoid deficiency on pregnancy, fertility was rare before introduction of synthetic glucocorticoid and mineralocorticoid supplement. Even if conception takes place, the ratio of fetal and maternal complication, fetal growth reduction, perinatal mortality and

maternal morbidity and mortality were very high (25% to 45%) before the era of glucocorticoid and mineralocorticoid supplement with availability of substitution therapy, the prognosis of pregnancy in Addison's Disease in now much better[13]. More patients with Addison's disease are now approaching adulthood and becoming pregnant. Therefore, more awareness regarding this disease is vital for the early diagnosis and appropriate management. Adequate steroid replacement along with regular follow up before and during pregnancy may allow normal fetal growth and prevent complications of pregnancy, labor and Puerperium[14,15].

Women with Addison's disease should have pre-pregnancy counseling as they constitute much higher risk group for fetal and maternal complications. They should continue their steroid supplement and keep their medical alert steroid card. And they should maintain close contact with their health care facility[12]. Close monitoring of these patients allows uneventful pregnancy, labor and Puerperium and assures a healthy normal baby.

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