Case Report

Triplet Pregnancy Outcome Experience Following Ovulation Induction Treatment of A Hypogonadotropin Hypogonadism Patient

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Abstract
Hypogonadotropic hypogonadism (HH) is the situation of lack of the Gonadotropin Releasing Hormone (GnRH) release from hypothalamus or the inadequate response of the hypophysis gland to the GnRH stimulation. Congenital HH is a rare clinical situation which exhibits itself with low sex hormone levels. Patients mostly present with amenorrhea, delayed puberty, infertility. Pregnancy can be achieved by ensuring ovulation with GnRH or gonadotropin replacement. The multiple pregnancy rates following ovulation have been reported between 20% and 50%. Diabetes, anemia, amniotic fluid abnormalities, pregnancy-related hypertension, eclampsia, cervical insufficiency, placenta previa, the use of tocolysis, twin to twin transfusion, preterm and cesarean delivery rates are increased among high order pregnancies.

Key Words:
Hypogonadotropic hypogonadism; triplet pregnancy; intrauterine insemination; multiple pregnancies

Introduction
Hypogonadotropic hypogonadism (HH) is rare etiologic form of female infertility. In these patients prediction of the ovarian reserve is not always possible before the treatment. After the implementation of ovulation induction by using gonadotropins, higher order pregnancies can be observed due to multifolliculary development with a reported incidence of 20-50% [1]. Utilization of assisted reproductive techniques for women with HH has the advantage of lower multiple pregnancy rates due to the restriction of transferred embryo numbers. In triplet pregnancies, the risk of maternal and neonatal complications is higher than twin pregnancies. Monitoring and appropriate management of these high risk pregnancies is mandatory in order to prevent the incidence of these complications. In this case report, we aimed to show the maternal and fetal outcomes of a triplet pregnancy of a woman with HH who has conceived with induction of ovulation by using gonadotropins.

Case Presentation
A 32-years-old patient with a diagnosis of HH has presented to our antenatal unit with a diagnosis of triplet pregnancy who has conceived with ovulation induction by using gonadotropins and utilization of intrauterine insemination in another fertility clinic. The patient was applied to our hospital at 12th gestational week. Upon evaluation of the patient’s history, she was diagnosed with idiopathic HH during investigation of primary amenorrhea when she was 18-years-old. Physical and ultrasonographic examination of the patient revealed tanner stage 1 telarche and tanner stage 2 pubarche regarding her sexual development level and her uterus was hypoplastic concomitant with atrophic ovaries. Her hormonal profile has been evaluated and FSH,
LH, estradiol, prolactin and TSH levels were 2.13 mIU/ml, 0.63 mIU/ml, 10 pg/ml, 9.04 ng/ml and 2.39 uIU/ml respectively. The caryotype analysis of the patient has been detected as 46,XX and she was diagnosed with HH based on her laboratory and clinical results. Historically, she has not presented with any visual symptoms or headache regarding an intracranial space occupying lesion and a cranial imaging study has been deferred. She was currently using daily 4000 IU/0.4 ml low molecular weight heparin because of the existing thrombophilic status with Factor V Leiden homozygous and prothrombin gene homozygous mutations. Ultrasonographic examination revealed a triamniotic trichorionic pregnancy of 12 weeks of gestation. Any gross fetal abnormality has not been detected and the nuchal translucency (NT) and nasal bone measurements of each fetus have been determined within normal scale regarding gestational week of pregnancy. Second trimester anomaly scan of the patient at 16th and 20th week of pregnancy has not revealed any abnormal findings. Her cervical length has been determined as of 38 mm. After this stage, the patient had received antenatal care for every two weeks. Finally, at 28th weeks of gestation, the patient was hospitalized with the diagnosis of preterm labor. In addition to intravenous fluid therapy two doses of 6 mg betamethasone was administered 24 hours apart. Following treatment, her preterm labor symptoms have resolved and she was discharged from the hospital with precautions regarding close follow-up until delivery. During follow-up, a 2 weeks size discordance has been detected between a fetus and other two foetuses. However, the pregnancy has been followed up until 34th weeks of gestation by reassurance of biophysical profile scores of 8 for all fetuses. Due to the decrease in the amniotic fluid volume, loss of diastolic flow in the evaluation of umbilical artery, and observing late deceleration seen in the non-stress test (NST) of the small for gestational age fetus, the pregnancy was terminated by caesarean section in emergency condition. Antenatal corticosteroid therapy to accelerate the fetal lung maturation decreases the incidence of RDS, the risk of intraventricular hemorrhage (IVH), the length of stay in the neonatal intensive care. Based on these clinical positive effects, corticosteroid administration has been shown to increase fetal survival rates [4]. The clinical usefulness of second-trimester screening tests is low in multiple pregnancies and Down syndrome detection rate is reduced to about 47% for multiple pregnancies [5]. This is attributed to the fact that abnormal fetal markers are shadowed by the normal fetus. Clinical utility of screening tests made in multiple pregnancies are limited and many centers don’t offer this test to women that have multiple pregnancy. Although preterm birth is the most common complication in the triplet pregnancies, route of birth is also a determining factor for perinatal mortality and morbidity. Although the situation is controversial in terms of mode of delivery, many writers support caesarean delivery for triplet pregnancies. In the same study they also reported that Apgar scores are

**Discussion**

Due to the increase in availability of assisted reproduction techniques worldwide, the incidence of multiple pregnancies has increased significantly in recent years. Multiple pregnancies pose increased risks of worse fetal and maternal outcome measures so multiple pregnancy is an unwanted obstetric entity and also considered to be a complication in the infertility treatment [2]. When the number of fetuses increase in the multiple pregnancies, length of the pregnancy and birthweight of the newborn decreases also. The average length of pregnancy is considered between 33rd and 34th weeks of gestation in triplet pregnancies. Average birth weight is 2500 grams in twins and 1800 grams in triplets [3]. The most common complication of higher order pregnancies is preterm labor and serial cervical length measurement, prophylactic cerclage application and progesterone treatment have not been shown to prevent early birth. RDS (respiratory distress syndrome) is a major complication of preterm birth and 40-50% of preterm infants struggle with this clinical situation. Antenatal corticosteroid therapy to accelerate the fetal lung maturation decreases the incidence of RDS, the risk of intraventricular hemorrhage (IVH), the length of stay in the neonatal intensive care. Based on these clinical positive effects, corticosteroid administration has been shown to increase fetal survival rates [4]. The clinical usefulness of second-trimester screening tests is low in multiple pregnancies and Down syndrome detection rate is reduced to about 47% for multiple pregnancies [5]. This is attributed to the fact that abnormal fetal markers are shadowed by the normal fetus. Clinical utility of screening tests made in multiple pregnancies are limited and many centers don’t offer this test to women that have multiple pregnancy. Although preterm birth is the most common complication in the triplet pregnancies, route of birth is also a determining factor for perinatal mortality and morbidity. Although the situation is controversial in terms of mode of delivery, many writers support caesarean delivery for triplet pregnancies [6]. In a study conducted by Weismann et al., mortality rate has been determined as doubled in the vaginal delivery against to cesarean section in triplet pregnancy. In the same study they also reported that Apgar scores are
higher in triplets babies delivered by cesarean section [7]. Postpartum haemorrhage is the most common cause of maternal mortality among triplet pregnancies with an incidence of 10-35%. Risk of uterine atony is higher in the cases of overstretched uterus as in the multiple pregnancies. Improvement of anemia or hypovolemia and preparation of blood components, planned delivery is helpful for preventing postpartum bleeding [8]. In conclusion, triplet pregnancies include high risks for increased maternal and neonatal morbidity rates. Rates of diabetes, anemia, amniotic fluid abnormalities, pregnancy-related hypertension, eclampsia, cervical insufficiency, placenta previa, need for tocolysis, syndrome of twin to twin transfusion, preterm birth and caesarean section have increased among triplet pregnancies. Avoiding multiple follicular development and cancellation of treatment by withholding intrauterine insemination when more than 3 mature follicles have been encountered during ovulation induction will decrease the probability of higher order pregnancies for infertile couples.

Acknowledgement
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Declaration of Interest
None

References