

SPONTANEOUS OVARIAN HYPERSTIMULATION SYNDROME AT TERM PREGNANCY IN EARLY LABOR

INTRODUCTION

Ovarian hyper stimulation syndrome (OHSS) is a rare, iatrogenic, life-threatening, complication of infertility treatment.

OHSS was first described in 1943.

Rotmensch and Scommegna describe the first case of spontaneous OHSS in 1989 in hypothyroid woman.

In 1996 Olatunbosun et al. first reported case of severe spontaneous OHSS associated with pregnancy and polycystic ovarian disease to result in live birth

Spontaneous ovarian hyper stimulation ((s OHSS)) is extremely rare in naturally conceived pregnancies. Although OHSS is predominantly an iatrogenic condition, there are reports of it occurring in association with: Multiple pregnancies, Hydatiform moles, Hypothyroidism, Polycystic ovary syndrome, and High levels of AMH. S OHSS also observed in non pregnant women with underlying risk factor.

S OHSS is likely to occur at 8-14 weeks of gestation, while iatrogenic OHSS usually occurs earlier at 3-8 weeks of gestation.

OHSS rarely continues beyond the first trimester.

DISCUSSION

Spontaneous ovarian hyperstimulation is a rare entity. In most reports s OHSS was observed early in the first trimester and ovaries regress by the end of first trimester. Late onset in the second trimester is very rare.

s OHSS in a term pregnancy is extremely rare.

In this case OHSS has seen in a singleton spontaneous gestation late at term pregnancy and during labor. There are only one reported case of late onset at term pregnancy.

Although pregnancy outcome were not studied well in patients with this rare syndrome, there are many reports of negative pregnancy outcome like abortion; missed or induced, stillbirth and spontaneous or iatrogenic preterm delivery due to severe maternal complications.

A literature review of s OHSS reports that proceed to term delivery only included in this discussion.

The etiology & pathogenesis of spontaneous OHSS is still not clear. Some authors reports s OHSS with unknown etiology and unexplained pathophysiology in patients proceeds to term delivery despite early onset of a disease. Table (1).

Royal College of Obstetricians and Gynecologists in 2006. Proposed a classification of OHSS as: Mild, Moderate, Severe and Critical. The incidence of Mild, Moderate and Severe varies respectively between 5–10%, 3-6%, 0.2–1.2% of cycles in anovulatory women treated with different preparations for induction of ovulation.

In its most severe form, there is a tremendous increase in ovarian size (greater than 10 cm increase in diameter) with attendant abdominal distention, ascites, pleural effusion, and decreased intravascular volume. Rarely, OHSS may be associated with life threatening complications, including renal failure, acute respiratory distress, hemorrhage from ovarian rupture and thromboembolism. Unfortunately there are reports of 5 fatal cases which lead to death.

Treatment of mild and moderate OHSS is conservative. Treatment of severe form aimed at maintaining intravascular volume and preventing hemoconcentration and hypovolemia and their adverse consequences on coagulation and kidney function.

Tokmak Aytekin et al., 2015; published the first case of spontaneous ovarian hyper stimulation in a term pregnancy. And that was the only one.

My interest is to report a second case of rare spontaneous OHSS at term pregnancy and the first one who present s OHSS in early stage of labor.

The pathophysiology of the syndrome has been not completely elucidated yet.

Certain illnesses like hydatidiform mole, hypothyroidism or multiple pregnancies, which come along with elevated HCG concentrations, can theoretically cause spontaneous OHSS (Guvenal et al., 2006; Ludwig et al., 1998; Taher et al., 2004; Tanaka et al., 2001).

The explanation of the pathophysiology of s OHSS associated with hypothyroidism is given as that elevated levels of Estradiol and TSH play a role in stimulation of the ovaries for OHSS.

Early recognition and stabilization of the thyroid gland in patients hypothyroidism can improve clinical and radiological findings of s OHSS and results in successful pregnancy outcome. Table (2).

Only two cases of polycystic ovary having OHSS, reported to have a term delivery.

Zalel and colleagues described a case of OHSS associated with spontaneous pregnancy in a woman with polycystic ovarian disease.

s OHSS can be associated with hormone-producing tumors or endocrinological dysfunctions. HCG is thought to play a crucial role in the development of the syndrome.

There are many studies explain the relation between elevated levels of BHCG and OHSS Table (3).

CASE REPORT

A 20 year old primi-gravida, at 38 weeks with history of regular menstrual cycle, married for 10 months, has no significant past medical or surgical history.

She conceived spontaneously and denied having ever taken any ovulation induction drugs.

She was observed up until 35 weeks of gestation, and her pregnancy was normal.

She presented to my clinic , on 11th June 2014, during the 38th week of gestation with complaints of abdominal pain, abdominal distention and nausea .

MANAGEMENT

A diagnosis of mild spontaneous s OHSS at term pregnancy in labor was done. The patient referred to maternity hospital for delivery.

Laboratory testing revealed normal CBC values and normal liver and renal functions.

The Patient was managed conservatively and followed for labor progress as usual. At 7am next morning, she has spontaneous normal vaginal delivery, of a healthy male baby weighed 2700 gm.

The patient was discharged the second day post-delivery without problems. The ovaries returned to normal at 4 weeks after delivery.

Smits et al. (2003) and Vasseur et al. (2003) described for the first time a mutation in the FSHR as a cause of spontaneous OHSS.

De Leener et al (2008), classified spontaneous OHSS in to three types based on the clinical presentation and FSH receptor mutation.

*Type I corresponds to the mutated FSHr cases.

* Type II corresponds to the spontaneous OHSS secondary to high levels of hCG. This type is probably the most frequently encountered

* Type III is related to hypothyroidism. In some cases, a combination of supposed risk factors and simultaneous FSHR mutation might have led to s OHSS, (Cardoso et al., 1999; Guvenal et al., 2006; Ludwig et al., 1998; Suzuki, 2004).

There are four different FSHR mutations have been described in relation to s OHSS, Dieterich et al.(2008), De Leener et al. (2006), Montanelli et al. (2004), Vasseur et al. (2003), Smits et al. (2003).

ABDOMINAL EXAMINATION

The abdomen was distended tender and tense. with irregular contour lateral to the uterine fundus, fundal height is 34cm, longitudinal lie and cephalic presentation, contractions 2/10'/20-25" and active fetal heart rates 150/mint.

ULTRASOUND FINDINGS

Single alive fetus
Cephalic presentation
BPD corresponds to 36th weeks

Active FHR=145bpm
Adequate amniotic fluid
Fundal mature placenta
EFW=2750gram

The right ovary measured 8.6 x 8.4 cm, With multiple cysts of variable sizes.

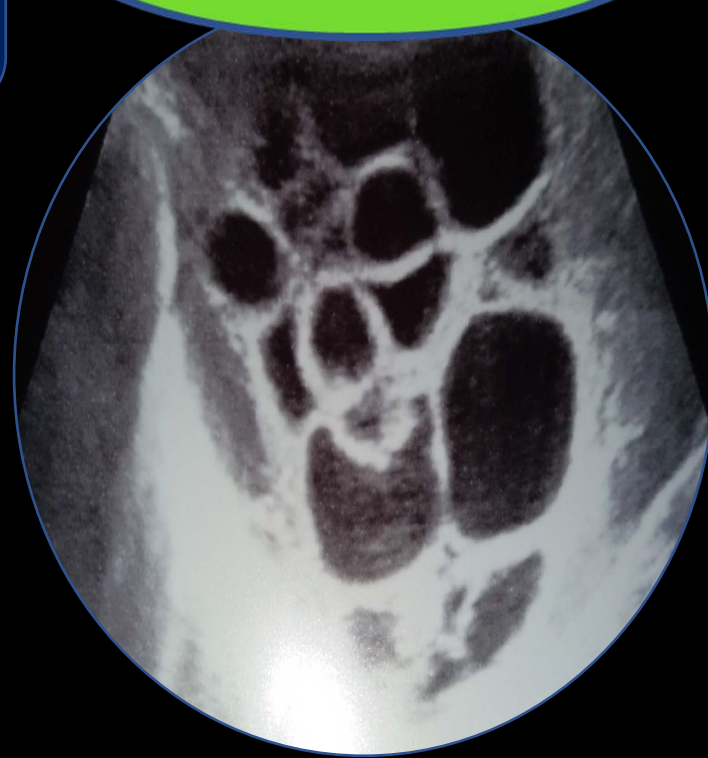
The Left ovary measured 9.0 x 6.1 cm, With multiple cysts of variable sizes.

No ascites were detected.

PELVIC EXAMINATION

Cervix opened 2 ½ cm
Cervix effaced 50%
Membrane intact
Vertex presentation
At zero station

The Right ovary



The Left ovary

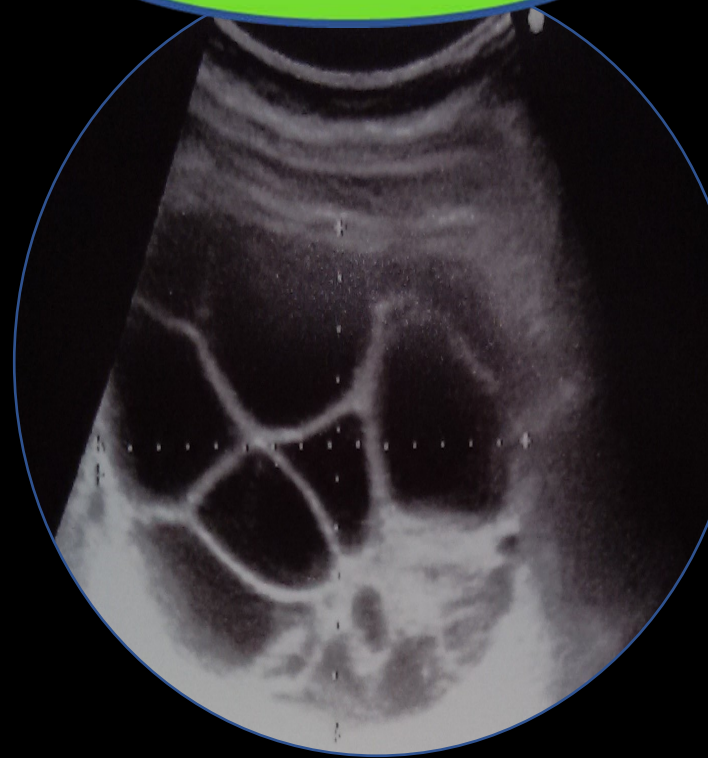


Table (1): Overview of the literatures describing cases of s OHSS with term delivery with unknown etiology & pathogenesis.

Published author	First diagnosis	Severity of OHSS	Management	Regression of Ovaries	Result
Kantarci S. et al. (2021)	10 th week	Moderate	Conservative	At 6 th week post delivery	Delivery by CS at 39 weeks/ PFT
Ainsworth A. et al. (2016).	8 th week	Severe	Conservative, Thoracocentesis	At 11 th week	Induced at 35 , 7 weeks
Same patient	7 th	Severe	Supportive therapy in ICU	At 10 th week	Delivery at 37 weeks
Stolorz k. et al. (2016)	11 th week	Moderate	Conservative	At 14 th week	Delivery at 39 weeks
Osalikhuwomwan et al. (2016)	10 th week	Severe	Symptomatic	At 26 th week	Delivery at 39 weeks
Tokmak A. et al. (2015)	37 th week	Moderate	Conservative Ovaries were drilled during CS	Two weeks after birth	Delivery at 39 weeks
Temur I. et al. (2014)	10 th week	Severe	Conservative respiratory physiotherapy, Thoracocentesis	At 14 th week	Delivery at 37 weeks
Cepni et al. (2006)	11 th week	Severe	Symptomatic	At 23 rd week	Delivery at term
Shergill S. et al. (2005)	12,5 th week	Severe	Supportive therapy	At 20 th week	Delivery at 40 weeks
Chae et al. (2001)	10 th week	Severe	Symptomatic, plasma expanders	Four weeks after delivery	Delivery at 41+4 weeks
Amiri A. et al. (200)	7 th week	Severe	Conservative, paracentesis,	At 20 th week	Delivery at 38 weeks
Ayhan A. et al. (1996)	12 th week	Severe	Laparotomy for Cyst excision and aspiration of ascites,	7 days post-operative	Delivery at term

Table (2): Overview of the literatures describing cases of s OHSS with term delivery having Hypothyroidism / polycystic ovary

Published Author	Etiology & pathogenesis	First diagnosis of OHSS	Severity of OHSS	Management	Regression of Ovaries	Result
Souza Lucas. et al. (2021)	Hypothyroidism	13 th week	Moderate	Levothyroxine	8 months after delivery	Delivery at 37 weeks
Rohatgi B. et al. (2017)	Polycystic ovary syndrome	4 th week	Mild	conservative	-----	Delivery by CS at term /non progress.
Sridev S. et al (2013)	Hypothyroidism	9 th week	Mild	Levothyroxine	At 20 th week	Delivery at 39 weeks
Dieterich M. et al. (2010)	FSH Mutation Epilepsy Hypothyroidism	10 th week	Moderate	Conservative, Levothyroxine , Paracentesis	-----	Delivery at 39 weeks
Akbay E. et al. (2010)	Hypothyroidism	10 th week	Mild	Levothyroxine	3 months postpartum	Delivery at 38 weeks
Same patient		12 th week	Mild	Levothyroxine	At 8 th week postpartum	Delivery at 38 weeks
Borna and Nasery et al. (2007)	Hypothyroidism	20 th week	Mild	Levothyroxine , aspiration of cysts during CS	At 10 th week postpartum	Delivery by CS at 38 th week/ Breech
Guvenal et al. (2006)	Hypothyroidism	-----	-----	Levothyroxine	-----	Delivery at term
Olatunbosun et al. (1996)	Polycystic ovary syndrome	8 th week	Severe	Observation	At 8 weeks postpartum	Delivery at term
1994		14 th week	Mild	Observation	-----	Stillbirth at 41+5 weeks
1989		13 th week	Mild	Observation	Postpartum	Delivery at term
1987						
The same patient with recurrent s OHSS						

Table (3): Overview of the literatures describing cases of s OHSS with term delivery related to HCG.

Published author	Etiopathogenesis	First diagnosis of s OHSS	Severity of OHSS	Management	Regression of Ovaries	Result
Rastin Z. et al.(2019)	HCG=96,100 IU/L	8 th week	Moderate	Conservative	At 18 th week	Delivery at 39 weeks
Gul Juan et al. (2019)	HCG= >200,000 IU/L	12 th +5 weeks	Severe	Conservative , Pleurocentesis	-----	Delivery at 40 weeks
Demirel E. et al. (2016)	HCG=630,631 IU/L	11 th week	Severe	Conservative,	At 17 th +6 week	Delivery at 40 weeks
Oztekin et al. (2006)	HCG=143,393 IU/L	10 th week	Moderate	Symptomatic	At 20 th week	Delivery at 39 weeks
R.Haimov-Kochman et al.(2004)	HCG= 137,100 IU/L	13 th week	Moderate	Expectant	After 2 months	Delivery at term
Suzuki (2004)	HCG=89,000 IU/L	10 th week	Severe	Conservative	At 13 th + 4 week	Delivery at 40 weeks
Same patient		10 th week	Mild	Conservative	-----	Delivery at term
Her sister		11 th week	Moderate	Conservative	-----	Delivery at term
Positive family history						

Table (4): Overview of the literatures describing cases of s OHSS with term delivery and FSHR Mutations.

Published author	Etiopathogenesis	First diagnosis of OHSS	Severity of OHSS	Management	Regression of Ovaries	Result
Yilmaz E. et al. (2018)	FSH Mutation	12 th week	Moderate	Conservative	Postpartum	Delivery at 38 weeks
Another patient		10 th week	Moderate	Conservative	-----	Delivery at 40 weeks
Dieterich M. et al. (2010)	FSH Mutation Epilepsy Hypothyroidism	10 th week	Moderate	Conservative, Levothyroxine , Paracentesis	-----	Delivery at 39 weeks
De Leener et al (2008)	FSH Mutation	12 th week	Severe	Symptomatic	Postpartum	Delivery at term
Ropers et al (2005)	FSH secreting pituitary adenoma	-----	-----	Transphenoidal resection of the adenoma	-----	Delivery at term
Montanelli et al. (2004)	FSH Mutation	10 th week	Mild	Conservative	-----	Delivery at term
Same patient		10 th week	Severe	Conservative	-----	Delivery at 40 weeks
Her sister		11 th week	Severe	Conservative	-----	Delivery at term
Positive family history						
Vasseur et al (2003)	FSH Mutation	8 th week	Severe	Conservative	-----	Delivery at 38 week
Same patient		8 th week	Moderate	Conservative	After delivery	Delivery at term
Positive family history						
Smits et al. (2003)	FSH Mutation	13 th week	Mild	Untreated	8 weeks postpartum	Delivery at term.
Accident in 4 pregnancies of the same patient						
		14 th week	Severe	Untreated	12 weeks postpartum	Intrauterine death at 41+5 week
		8 th week	Severe	Paracentesis	8 weeks postpartum	Delivery at term