

**Ovarian Hyper Stimulation Syndrome OHSS: About a Case Report**N Gribi<sup>\*</sup>, H Zniber, R Bzikha, A Grine, B Elbekkali, A Lakhdar, A Baidada, A Kharbach

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**Abstract:** Ovarian hyper stimulation syndrome is a complication of stimulating ovulation treatments in the context of assisted procreation. The manifestations of this syndrome are then classified in 5 states with possible severe complications: hypovolumic shock, acute renal failure, respiratory distress, disruption of liver functions, venous or venous thromboembolic events, exceptionally until death we report a case of a patient with ovarian hyper stimulation syndrome in a setting of assisted medical procreation. A 31years old woman who received ovarian stimulation, 12 days after the IVF, she was admitted in Emergency Department with severe abdominal pain, ascite, pleural effusion and dyspnea. Beside the medical treatment, the patient had a puncture of ascites and a pleural puncture showing a fluid exudative type whose cytology is benign. Ovarian hyper stimulation syndrome is a serious complication in the context of assisted medical procreation. Manifestations of OHSS may be local or general and may even be life-threatening. Hence the interest of the good recognition of risk factors for OHSS with monitoring of ovarian stimulation in the context of IVF with doses adapted to the patients, the prevention and the monitoring and the therapeutic management well adapted to each stage of OHSS disease.

**Keywords:** Ovarian hyper stimulation syndrome(OHSS), renal failure, abdominal pain, ascite, pleural effusion.

**INTRODUCTION**

Ovarian hyper stimulation syndrome is a complication of stimulating ovulation treatments in the context of assisted procreation. This is a totally iatrogenic complication, sometimes unpredictable or unavoidable. Although this syndrome is only rarely seen in clomiphene citrate therapy, its presence has been reported even after spontaneous ovulation[1].

The manifestations of hyper stimulation may be local (strong increase in ovarian volume, torsion, ovarian rupture) or general. They are then classified in 5 states with possible severe complications: hypovolumic shock, acute renal failure, respiratory distress, disruption of liver functions, venous or venous thromboembolic events, exceptionally until death [2]. With an estimated mortality rate between 1/45000 and 1/500 000 [3].

In our work we report the observation of a patient who presented with ovarian hyperstimulation syndrome after in vitro fertilization and review of literature, detailing pathophysiology, risk factors, classification, prevention and treatment of OHSS.

**CASE REPORT**

The patient, 31years old, married for 13 years, G0P0 with a regular cycle. She underwent ovarian stimulation with decapeptyl 0.1 mg subcutaneously for 14 days and then an injection of FSH at a dose of 150

IU per day for 12 days subcutaneously. Ovulation was triggered by Ovitrelle single dose 500ug subcutaneously.

12 days after the IVF, she was admitted in Emergency Department with severe abdominal pain with vomiting, diarrhea, abdominal distension and dyspnea IV according NYHA. It is a conscious patient, tachypneic, PULSE 118bat/min, temperature at 37°C, BP is 130 / 90mmhg and BMI 87,64.

The physical examination revealed a severely distended abdomen with evidence of ascites but without any palpable mass in the abdomen. Pulmonary auscultation revealed an abolition of vesicular murmur in the left hemi pulmonary field. Absence of edema in the lower limbs nor jugular turgidity.

Laboratory tests revealed hemoglobin at 14.5 g / dl, a hematocrit at 44.2%, serum LDH at 152 IU / L, a hypo proteinemia at 53 g / l with a hypo albuminemia at 26 g / l. CRP, normal liver function. HCG at 271UI/l.

Thoraco-abdominopelvic ultrasonography is performed and found a normal-sized uterus with a 25mm thickened and hyper-echogenic endometrium Ovaries greatly increased in size, normal blood flow to the color Doppler measuring 10X8cm the right and 7X8cm the left, they are the seat of multiple follicular cysts of variable sizes from 40mm to 52mm some are

hemorrhagic (Fig 1,2). Ascites of great abundance, left

pleural effusion of average abundance (Fig 3, 4).



**Fig-1: Left ovary large follicles 3 to 5cm long axis**



**Fig-2: Right ovary with several follicles taking a cystic appearance of 3 to 4 cm long axis**



**Fig-3: Effusion in the inter-hepatorenal space**



**Fig-4: Intraperitoneal peritoneal fluid effusion peri splenic.**

The patient had a puncture of ascites and a pleural puncture showing a fluid exudative type whose cytology is benign. The patient was put on analgesic treatment with paracetamol 1G / 8h and omeprasole 40mg lovenox 0.4 / d subcutaneously.

The patient improved with disappearance of abdominal pain and dyspnea after 24 hours. The etiology retained is the ovarian hyperstimulation syndrome. Laboratory parameters normalized and pleural effusion resolved and she was discharged after 24 days of hospital stay, in stable condition and still pregnant.

## DISCUSSION

Most cases of OHSS are mild with little clinical expression. However, when the OHSS is severe, it is occasionally associated with serious morbidity; cases of death have been reported [4,5].

It is a severe complication of the means of in vitro fertilization. The reported incidence of moderate OHSS is between 3% and 6%, while the incidence of severe OHSS is between 0.1% and 2% [7,8]. The mild form of OHSS, which is of little clinical importance, occurs in approximately 20% to 33% of IVF cycles [7,8].

This is why there is a need to know the women exposed to this risk, to implement preventive strategies and to ensure active care for women who are at risk of experiencing a more serious form of OHSS.

## PHYSIOPATHOLOGY OF OHSS

OHSS is a systemic disease caused by the release of vasoactive peptides by granulosa cells in hyper-stimulated ovaries. This leads to an increase in the vascular permeability responsible for the water exchanges between the intravascular space and third sectors [9,10]. Ovarian secretion of the most important mediator in this process is vascular endothelial growth factor (VEGF)[11]. A correlation between hCG administration and VEGF messenger RNA expression is incidentally reported [12]. By promoting endothelial cell mitosis, VEGF increases vascular permeability, promotes the passage of macromolecules and thus allows inducing serous exudate [13], so its serum level correlates with the severity of OHSS [14, 15].

Other mediators such as and interleukin 6, 2, 8,10 angiotensin II that are found in follicular fluid and in the ascites fluid of OHSS are involved in the inflammatory process during follicular maturation were involved [16].

In the case of the patient described above, the patient had a high abundance ascites with moderate left pleural effusion. The mild pleural effusions that accompany ascites in the context of ovarian hyperstimulation are not uncommon (21% of cases) [17]. On the other hand, unilateral pleural effusion without ascites in a significant amount is a rare manifestation of this syndrome. Only isolated cases have been described [18, 19]. Several physiopathological hypotheses have been advanced to understand ascites with or without unilateral effusion [20]:

- A release of vasoactive factors in the pleural space;
- Drainage of the abdominal fluid to the pleural space by the lymphatic system;
- The passage of ascites by tendinous diaphragmatic breaches.

## RISK FACTORS

According to Delvigne *et al.* [21], different risk factors favor the development of this syndrome. The young age of the patients, a low body mass index, a history of hyperstimulation of the ovaries or pregnancy. Atopic patients, patients with micropolycystic ovaries are at risk. Among the different protocols, stimulation according to an agonist protocol seems more at risk than the antagonist protocol. The agonist protocol consists of preventing ovulation and resting the ovaries with a GnRH agonist on the first day of menses and then stimulating the ovaries 14 days later with an FSH analogue [22]. In the antagonist protocol, the ovaries are stimulated by an analogue of FSH and, 6-8 days later, ovulation is inhibited by a GnRH antagonist [23]. When high doses of exogenous hCG are used to trigger ovulation, the frequency of ovarian hyperstimulation syndromes is increased. The high baseline state of blood estradiol and a late peak after stimulation are also correlated with the occurrence of this syndrome.

Al. and Dulitsky [24] reported a significantly higher rate of thrombophilia in patients with severe OHSS. Two studies are contradictory: one finds a very large proportion of markers of congenital thrombophilia in women who have made a severe hyperstimulation [25] while the other does not find any difference with the general population [26].

## THE DIAGNOSIS

When suspecting an OHSS it is important to look for a recent history of ovarian stimulation followed by ovulation or HCG administration.

**Table-1: The OHSS classifications are based on severity [27] and are summarized in**

OHSS	Forme légère	Forme modérée	Forme sévère
Douleur abdominale	Faible ou gêne	Modérées	Le plus souvent intenses
Nausées vomissements	±	±	±
Diarrhées	±	±	±
Ascite sous tension	Absence cliniquement	Non	Oui
Oligoanurie	Non	Non	Oui
Dyspnée	Non	±	Oui
Hyperleucocytose/mm <sup>3</sup>	Inférieure à 15 000	Entre 15 et 25 000	Supérieure à 25 000
Hématocrite	< 45 %	45—55 %	> 55 %
Cytolyse hépatique	Non	±	Oui
Hyponatrémie	Non	Non	Oui
Hyperkaliémie	Non	Non	> 5 mmol/l
Ascite à l'échographie	Limitée au cul de sac de douglas	Dépasse l'utérus	Présente dans la loge de Morrison
Taille des ovaires	9—12 cm	> 12 cm	> 12 cm
Épanchement pleural	Non	Non	Oui

Table 1: Ovarian hyperstimulation syndrome classification among Humaidan *et al.* and the ‘‘Practice Committee of the American Society for Reproductive Medicine’’.

OHSS mild is in the form of feeling of pelvic discomfort or abdominal pain associated with vomiting, diarrhea. Increased ovarian volume (<5 cm), Excessive steroid production greater than 150ug / 24h with hematocrit remaining normal at this stage.

Moderate OHSS is in the form of abdominal distension and abdominal pain associated with vomiting and diarrhea. An ovarian volume increase of 5-12 cm with serous effusions. A hematocrit between 40% and 55%.

In addition, the severe OHSS presents: an increase in ovarian volume greater than 12 cm with ascites with or without pleural effusion, renal failure and coagulation disorder with a very high risk of thromboembolic events.

Biologically; hematocrit greater than 55%, leukocytosis greater than 25000/mm<sup>3</sup>, hepatic cytolysis, hyponatremia less than 135mmol/L, hyperkalemia. High hematocrit should be considered as a marker of severity [28,29] because there is a correlation with the level of vascular substances dependent on plasma volume.

Hepatic cytolysis is found in 30% of severe OHSS [30] it corrects itself spontaneously with the improvement of the painting. CRP could be a pathology marker and / or a gravity marker [31].

#### MANAGEMENT OF OHSS

The treatment will depend on the severity of the OHSS and the occurrence of complications, the treatment is mainly symptomatic and preventive. There

is no need to discontinue luteal phase replacement therapy because low-dose aspirin and progesterone may have a protective effect on SHO [32-34]. It should not be overlooked that an OHSS can get worse quickly, so surveillance should be part of the management. Women who have the severe form of OHSS and the moderate form with difficulty in overcoming the discomfort of abdominal distension using oral analgesia should be managed in hospital.

Symptomatic relief of abdominal pain can be achieved with acetaminophen and, if necessary, opioids administered orally or parenterally. Nonsteroidal anti-inflammatory drugs with antiplatelet properties should not be used, as they may interfere with implantation and compromise renal function in patients with severe OHSS [35].

To reduce nausea and / or vomiting; antiemetic drugs should be used and should be considered safe at the beginning of pregnancy.

Hospitalized patients should be considered at risk for thrombosis due to haemoconcentration and immobilization. Daily prophylactic doses of low-molecular-weight heparin (dalteparin sodium 5000 IU / day) and anti-embolic stocking should be considered at the time of admission and continued until getting discharge from the hospital. In addition, several cases of thromboembolism have been reported in women with OHSS treated with thromboprophylaxis[36-38].

Intravenous hydration with a crystalloid solute (100-150 ml / h) should be used until diuresis is reached. When clinical and laboratory results indicate persistent intravenous volume depletion despite intravenous aggressive hydration, intravenous albumin administration (15 to 20 ml / h 25% albumin for 4 hours) should be implemented and repeated until the water status is improved [39]. Diuretics should be

avoided since they can further deplete intravascular volume.

The indication of ascites fluid evacuation puncture is an issue still raised in the management of patients with OHSS. Indeed, significant ascites creates a certain discomfort for the patient who will present a feeling of heaviness, bloating, nausea and vomiting. A single evacuation puncture will help relieve these symptoms. Other common indications for ascites drainage are respiratory deterioration (74%), oliguria (11%), hemodynamic instability (2%) or a combination of several factors (13%) (28).

External management is usually possible for women with mild to moderate OHSS [35]. External management may be considered in women who have a severe form of the disease when they are able to comply with treatment and clinical guidelines. Abdominal discomfort can be treated with acetaminophen, with or without a narcotic agent. Nonsteroidal anti-inflammatory drugs with antiplatelet properties should not be used as they may interfere with implantation and compromise renal function in patients with severe OHSS. To prevent additional hemoconcentration, women should be encouraged to drink two to three liters of fluid a day. Women should not practice vigorous exercise or have sex because of the possibility of rupture or twisting hypertrophied and hyper-stimulated ovaries. Paracentesis guided by transvaginal ultrasonography can be performed in an outpatient clinic [40].

### **SURGERY**

The place of surgery is very limited in this syndrome. Only the rare cases of ovarian torsion or rupture of the ovarian hemorrhagic cyst revealing surgical management[41].

Management of complications renal failure, thromboembolism, pericardial effusion and adult respiratory distress syndrome are potentially life-threatening complications of OHSS. These pathologies should be diagnosed early and managed by a multidisciplinary team within an intensive care unit, as far as possible.

### **EVOLUTION**

In the majority of cases, patients improve with the decline in HCG and leave the hospital for the seventh to eighth day in the absence of complications. Severe cases can last up to 4 weeks especially in case of multiple pregnancy.

### **CONCLUSION**

Ovarian hyper stimulation syndrome is a serious, iatrogenic and sometimes unpredictable complication in the context of assisted medical

procreation. Manifestations of OHSS may be local or general and may even be life-threatening.

Hence the interest of the good recognition of risk factors for OHSS with monitoring of ovarian stimulation in the context of IVF with doses adapted to the patients, the prevention and the monitoring and the therapeutic management well adapted to each stage of OHSS disease.

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