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Review Article

Navigating the complexities of pregnancy with ovarian hyperstimulation syndrome: an in-depth narrative exploration

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ABSTRACT

Ovarian hyperstimulation syndrome (OHSS) is a potentially severe complication of assisted reproductive technology (ART) procedures, particularly *in vitro* fertilization (IVF) treatments. While OHSS typically occurs during the stimulation phase of ART, it can also manifest during pregnancy, posing significant challenges to maternal and fetal health. This comprehensive narrative review tries to provide a detailed description of pregnancy with OHSS, encompassing its epidemiology, pathophysiology, clinical manifestations, risk factors, diagnosis, management strategies, and pregnancy outcomes. Relevant literature was identified through a systematic search of electronic databases, with more focus on recent studies and guidelines. Insights from clinical experience and expert opinions are also integrated into the discussion. This review highlights the importance of early recognition, risk stratification, and multidisciplinary management in optimizing outcomes for women with pregnancy-associated OHSS. Areas requiring further research and strategies for prevention and management are also discussed.

Keywords: Ovarian hyperstimulation syndrome, Assisted reproductive technology, Vascular endothelial growth factor, Human chorionic gonadotropin, Pleural effusion, Ascitis

INTRODUCTION

Ovarian hyperstimulation syndrome (OHSS) is a potentially serious complication that can occur as a result of ovarian stimulation during fertility treatments, particularly IVF or ovulation induction. It is characterized by an exaggerated response of the ovaries to hormonal stimulation, leading to the development of multiple ovarian follicles and the release of excessive amounts of vascular endothelial growth factor (VEGF) and other similar substances.[1] This can result in the accumulation of fluid as ascites or pleural effusion, electrolyte imbalances, and potentially life-threatening complications such as blood clots and kidney failure.

OHSS typically occurs within a week following the administration of human chorionic gonadotropin (hCG) to trigger ovulation, or in early pregnancy when endogenous hCG levels rise. The severity of OHSS can vary from mild cases, characterized by abdominal discomfort and bloating, to severe cases requiring hospitalization and intensive medical intervention.

Central to many ART protocols is ovarian stimulation, a process aimed at inducing the development of multiple follicles within the ovaries to increase the chances of successful fertilization and embryo implantation. Ovarian stimulation involves the administration of exogenous gonadotropins, such as follicle-stimulating hormone (FSH) and luteinizing hormone (LH), to promote follicular growth and maturation.[2] However, ovarian stimulation can sometimes lead to an exaggerated response, resulting in OHSS. OHSS represents one of the most serious complications of ART, potentially jeopardizing both the safety of the patient and the success of the treatment cycle.

Risk factors for OHSS include young age, low body weight, polycystic ovary syndrome (PCOS), high ovarian

reserve, and the use of certain fertility medications.[3] Strategies to prevent OHSS include individualizing ovarian stimulation protocols, using antagonist medications to prevent premature ovulation, and triggering ovulation with a GnRH agonist instead of hCG in high-risk patients.

Management of OHSS focuses on supportive care to alleviate symptoms and prevent complications. Mild cases may be managed on an outpatient basis with close monitoring of fluid intake and electrolyte levels, while severe cases may require hospitalization for intravenous fluids, electrolyte replacement, and drainage of fluid accumulation. In extreme cases, where there is a risk of severe complications, cycle cancellation may be necessary to prevent OHSS from progressing further.

Despite its potential risks, OHSS remains a relatively rare complication of fertility treatments, occurring in approximately 1-5% of IVF cycles.[4] Advances in ovarian stimulation protocols and improved patient monitoring have helped to reduce the incidence and severity of OHSS in recent years. However, one has to be vigilant for identifying and managing OHSS promptly to minimize its impact on patients' health and fertility treatment outcomes.

EPIDEMIOLOGY OF PREGNANCY-ASSOCIATED OHSS

The incidence of moderate-to-severe OHSS is approximately 2-3%, and milder forms may develop in up to 20- 30% of all IVF patients.[5] The variability in incidence may be attributed to differences in patient populations, ART protocols, and diagnostic criteria used to define OHSS. Despite its relatively low incidence compared to OHSS during ovarian stimulation, pregnancy-associated OHSS remains a clinically significant concern due to its potential impact on maternal and fetal health. Risk factors for developing OHSS during pregnancy include a history of OHSS with prior ART cycles, high serum estradiol levels, young age, polycystic ovarian syndrome, low body mass index, presence of multiple gestations and the use of gonadotropin-releasing hormone agonists for pituitary suppression. Women with PCOS are also at increased risk of developing OHSS during pregnancy due to their inherent predisposition to hyperstimulation.[6] While OHSS most commonly occurs during the ovarian stimulation phase of ART, it can also manifest during early pregnancy, presenting unique challenges for patients and clinicians.

While the overall incidence of OHSS during pregnancy may have remained relatively stable over time, advancements in ART protocols and clinical management have contributed to a reduction in the severity and complications associated with pregnancy-associated OHSS. Strategies aimed at minimizing the risk of OHSS, such as individualizing ovarian stimulation protocols, using antagonist medications to prevent premature ovulation, and elective freeze-all cycles, have helped to mitigate the incidence and impact of OHSS in pregnant women undergoing ART.

PATHOPHYSIOLOGY OF OHSS

OHSS is characterized by enlarged ovaries and fluid accumulation in the abdominal cavity and/or thorax, leading to a range of symptoms from mild discomfort to severe complications such as thromboembolism and renal failure. The hallmark of OHSS is increased vascular permeability, which results in fluid shifting from the intravascular space into the third space, including the peritoneal and pleural cavities.[7] This phenomenon is mediated by various factors, including VEGF, which is significantly elevated in OHSS. VEGF, produced by granulosa cells in the ovaries, promotes angiogenesis and vascular permeability, contributing to the accumulation of ascites and pleural effusions seen in severe cases of OHSS. VEGF has been found to be expressed in human ovaries and it has been observed that VEGF mRNA levels increase after hCG administration in granulosa cells and the elevated levels of serum proteins have been detected in serum, plasma, and peritoneal fluids in women at risk or with OHSS.[8]

Dysregulation of hormonal factors also plays a central role in the pathophysiology of OHSS. hCG, which is commonly administered to trigger final oocyte maturation and ovulation, has been implicated in the development of OHSS. In susceptible individuals, high levels of hCG can overstimulate the ovaries, leading to the production of excessive amounts of VEGF and other vasoactive substances.[9] Additionally, the presence of high levels of estradiol, a result of multiple developing follicles, further contributes to the vascular permeability and fluid retention characteristic of OHSS.

Inflammation plays a significant role in the pathogenesis of OHSS. Pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), are elevated in the serum and follicular fluid of women with OHSS.[10] These cytokines contribute to the increased vascular permeability and capillary leakage observed in OHSS by disrupting the endothelial cell junctions and promoting the extravasation of fluid into the third space.

The renin-angiotensin-aldosterone system is activated in OHSS, leading to sodium and water retention.[11] This activation is mediated by factors such as VEGF, which not only increases vascular permeability but also stimulates the release of renin from the kidneys. The subsequent increase in angiotensin II levels promotes aldosterone secretion from the adrenal glands, enhancing renal sodium reabsorption and contributing to fluid retention and electrolyte imbalances in OHSS.

Severe OHSS can be associated with a hypercoagulable state, predisposing affected individuals to thromboembolic events such as deep vein thrombosis (DVT) and pulmonary embolism (PE).[12] The combination of

hemoconcentration, increased blood viscosity, and endothelial dysfunction contributes to the prothrombotic milieu seen in OHSS. Additionally, the release of pro-inflammatory cytokines further exacerbates endothelial activation and promotes thrombus formation.

CLINICAL MANIFESTATIONS

The clinical manifestations of OHSS can vary widely in severity, ranging from mild symptoms such as abdominal discomfort to severe complications including ascites, pleural effusion, renal failure, and thromboembolic events.

Mild OHSS

In its milder forms, OHSS may present with symptoms like abdominal bloating. Patients may experience a sensation of fullness in the abdominal region due to the enlargement of the ovaries and accumulation of fluid within the peritoneal cavity. Patients may experience mild abdominal discomfort. This can range from a dull ache to intermittent sharp pain and is often attributed to ovarian enlargement and stretching of the ovarian capsule.

Some women with mild OHSS may experience nausea, although vomiting is less common in this stage. Mild OHSS is also associated with mild gastrointestinal disturbances, including loose stools or diarrhea, which can occur due to the effects of ovarian hormones and fluid shifts on the digestive tract.

Moderate OHSS

As OHSS progresses, symptoms become more pronounced and may lead to progressive abdominal distension: The abdomen may become visibly distended as a result of fluid accumulation in the peritoneal cavity. This can lead to discomfort and difficulty with breathing or movement.

Pelvic examination may reveal enlarged ovaries, which may be tender or cystic on palpation due to the presence of multiple follicles. Patients may notice a rapid increase in weight due to fluid retention, which can exacerbate abdominal discomfort and bloating. Difficulty breathing or shortness of breath may occur as a result of ascites compressing the diaphragm or pleural effusion causing lung restriction.

Severe OHSS

In its most severe form, OHSS can lead to life-threatening complications and may present with severe abdominal pain: Patients may experience intense abdominal pain, which can be diffuse or localized and may mimic symptoms of acute abdomen. This pain is often accompanied by significant abdominal distension and tenderness. Increase in pleural effusion, characterized by the exaggerated accumulation of fluid in the pleural space surrounding the lungs, can cause severe dyspnoea, tachypnea, and decreased oxygen saturation. Patients may require supplemental oxygen or mechanical ventilation also.

Renal complications such as acute kidney injury (AKI) may manifest as decreased urine output, oliguria, or anuria.[13] This is typically a result of intravascular volume depletion secondary to third-spacing of fluid and electrolyte imbalances.

OHSS is associated with a hypercoagulable state, increasing the risk of thromboembolic complications such as DVT and PE.[14] Patients may present with symptoms such as leg swelling, pain, or dyspnoea.

In severe cases, profound intravascular volume depletion due to fluid extravasation into the third space can lead to hypovolemic shock, characterized by hypotension, tachycardia, and altered mental status. Untreated severe OHSS can result in multi-organ dysfunction syndrome (MODS), characterized by dysfunction of multiple organ systems including the kidneys, lungs, liver, and cardiovascular system. This can manifest as a constellation of symptoms such as hypotension, coagulopathy, hepatic dysfunction, and metabolic disturbances.

The clinical presentation of OHSS can vary greatly among individuals, and not all patients will experience the same symptoms or severity of illness. The onset and progression of OHSS can be rapid, particularly following hCG administration for ovulation induction. Therefore, close monitoring of patients undergoing ovarian stimulation is essential to promptly recognize and manage OHSS, thereby reducing the risk of complications and optimizing patient outcomes.

DIAGNOSIS

Diagnosis of OHSS during pregnancy can be challenging due to overlapping symptoms with normal pregnancy discomforts and other obstetric complications. Diagnosing OHSS requires a comprehensive evaluation of clinical symptoms, physical examination findings, and laboratory parameters. As OHSS can vary in severity from mild to severe, timely and accurate diagnosis is crucial to initiate appropriate management and prevent potential complications. The diagnosis of OHSS involves considering the patient's medical history, conducting a thorough physical examination, and performing relevant laboratory and imaging studies.

Patients undergoing ovarian stimulation treatments should be monitored closely for symptoms of OHSS. These symptoms may include abdominal distension, bloating, nausea, vomiting, diarrhea, and abdominal pain. Additionally, patients with severe OHSS may present with respiratory distress, decreased urine output, and signs of hypovolemic shock.

Symptoms typically develop within week following administration of hCG for ovulation induction and may worsen over subsequent days. However, in some cases, symptoms may present earlier/later depending on individual factors such as type and dose of gonadotropins used.

A thorough abdominal examination should be performed to assess for signs of ovarian enlargement, ascites, and peritoneal irritation. Enlarged ovaries may be palpable on pelvic examination and are often described as tender or cystic. Abdominal distension due to ascites may also be evident, along with shifting dullness on percussion.

In cases of severe OHSS, respiratory examination is essential to evaluate for signs of pleural effusion and respiratory distress. Auscultation of the lungs may reveal decreased breath sounds, dullness to percussion, or signs of pleural rub.

Measurement of serum estradiol and hCG levels can aid in the diagnosis and monitoring of OHSS. Elevated levels of estradiol are commonly observed in patients undergoing ovarian stimulation, particularly in those with a high number of developing follicles. Additionally, a significant rise in hCG levels following ovulation trigger may predispose individuals to OHSS.

Hemoconcentration, characterized by an elevated hematocrit and haemoglobin concentration, is a common finding in OHSS due to intravascular volume depletion secondary to 3rd spacing of fluid.[15] Serial measurements of hematocrit and haemoglobin levels can help assess for the degree of hemoconcentration and guide fluid management.

Electrolyte imbalances, particularly hyponatremia and hyperkalemia, may occur in severe cases of OHSS due to renal dysfunction and impaired fluid balance. Measurement of serum electrolytes, blood urea nitrogen (BUN), and creatinine can provide valuable information regarding renal function and electrolyte status. Liver function tests, including serum transaminases (AST, ALT), bilirubin, and albumin, should be obtained to assess for hepatic dysfunction, which may occur as a result of hypovolemia, hypoperfusion, or thrombotic complications associated with OHSS.

Transvaginal ultrasound is a valuable diagnostic tool for assessing ovarian morphology and detecting the presence of ovarian enlargement and multiple follicular cysts characteristic of OHSS. The ovaries may appear enlarged with multiple cystic spaces, and the presence of ascites may also be visualized. In cases of severe OHSS with respiratory compromise, chest X-ray or thoracic ultrasound may be indicated to evaluate for the presence of pleural effusion and assess lung parenchyma. Pleural effusion is characterized by blunting of costophrenic angles on X-ray and fluid accumulation in the pleural space on ultrasound.[16] Abdominal ultrasound or computed tomography (CT) may be performed to assess for presence of ascites, evaluate ovarian morphology, and exclude other potential causes of abdominal distension and pain.

RISK FACTORS FOR PREGNANCY-ASSOCIATED OHSS

Pregnancy-associated OHSS is a rare but potentially serious complication that can occur during early pregnancy, typically in the first trimester. Although OHSS is more commonly associated with ovarian stimulation treatments for infertility, such as IVF, it can also occur spontaneously in the absence of exogenous gonadotropin administration. Patient-related factors:

Younger women, particularly those under the age of 30, are at increased risk of developing OHSS during pregnancy.[17] This may be attributed to higher ovarian reserve and responsiveness to endogenous gonadotropins, predisposing them to excessive follicular development and ovarian hyperstimulation. PCOS is a common endocrine disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries. Women with PCOS have an inherent predisposition to ovarian hyperstimulation due to alterations in gonadotropin secretion, increased follicular recruitment, and enhanced ovarian sensitivity to gonadotropins.

Women, who have previously experienced OHSS, whether spontaneously or following ovarian stimulation treatments, are at higher risk of developing recurrence during subsequent pregnancies. The presence of underlying predisposing factors like PCOS or high ovarian response leads to further increase in OHSS recurrence.

Low BMI (<18.5 kg/m²) has been identified as a risk factor for pregnancy-associated OHSS.[17] Women with low body weight may have higher ovarian sensitivity to endogenous gonadotropins, leading to excessive follicular development and increased risk of OHSS.

Some genetic factors may also contribute to the development of OHSS, although the specific genes involved have not been fully elucidated. Variations in genes related to ovarian function, gonadotropin receptor sensitivity, and VEGF signalling pathways may influence individual susceptibility to OHSS.

Elevated levels of endogenous gonadotropins, particularly FSH and LH, during early pregnancy can predispose women to OHSS. These hormones stimulate follicular development and ovarian steroidogenesis, leading to increased ovarian vascularity and vascular permeability.

Pregnancies with multiple gestations, such as twins or higher-order multiples, are associated with a higher risk of OHSS.[18] This is attributed to the increased production of hCG by multiple gestational sacs, resulting in higher circulating levels of hCG and exaggerated ovarian response. Gestational trophoblastic diseases, including complete and partial hydatidiform moles, are characterized

by abnormal trophoblastic proliferation and elevated hCG levels. Molar pregnancies can lead to excessive ovarian stimulation and the development of OHSS, particularly in cases of complete hydatidiform mole with markedly elevated hCG levels.[19] OHSS can occur during molar pregnancy, and can be exacerbated after D and E.

Although rare, spontaneous pregnancies can also be associated with OHSS.[20] This may occur in setting of ovarian hyper reactivity to endogenous gonadotropins or in association with conditions such as ovarian hyper thecosis or functional ovarian tumors.

Women with a high ovarian response to gonadotropin stimulation, characterized by the development of numerous follicles and high serum estradiol levels, are at increased risk of OHSS during pregnancy. This heightened ovarian sensitivity may be influenced by genetic factors, underlying ovarian pathology, or exogenous gonadotropin administration in previous fertility treatments.

The use of exogenous progesterone for luteal phase support in assisted reproductive treatments may contribute to the development of OHSS, particularly when administered in conjunction with hCG. Progesterone can enhance ovarian steroidogenesis and promote the secretion of VEGF, thereby exacerbating the risk of OHSS in susceptible individuals.[21]

MANAGEMENT STRATEGIES FOR PREGNANCY-ASSOCIATED OHSS

The management of pregnancy-associated OHSS requires a multi-faceted approach aimed at alleviating symptoms, preventing complications, and optimizing maternal and fetal outcomes. While mild cases of pregnancy-associated OHSS may resolve spontaneously with supportive measures, severe cases require close monitoring and aggressive interventions to mitigate potential risks. Management strategies for pregnancy-associated OHSS include supportive care, pharmacological interventions, and in severe cases, hospitalization and specialized medical management.

Adequate hydration is essential in managing OHSS to maintain IV volume and prevent dehydration.[22] Encouraging oral fluid intake and administering intravenous fluids, such as isotonic saline/balanced crystalloids, can help restore fluid balance and alleviate symptoms of dehydration. Electrolyte imbalances, particularly hyponatremia and hyper kalemia, may occur in OHSS due to renal dysfunction and fluid shifts.[23] Monitoring electrolyte levels, correcting imbalances with appropriate supplementation, such as oral/IV electrolyte solutions is essential in preventing complications.

Analgesic medications, such as acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs), can provide relief from abdominal discomfort and pain associated with OHSS. Opioid analgesics may be required for severe pain, although caution should be exercised to minimize respiratory depression and other adverse effects. Advising patients to rest and avoid strenuous physical activity can help alleviate symptoms and prevent exacerbation of OHSS-related complications. Bed rest may be recommended in severe cases to reduce the risk of ovarian torsion and thromboembolic events.

Cabergoline, a dopamine agonist is the first drug of choice in OHSS. Dopamine agonists prevent the phosphorylation of VEGFR2 and reduce the *in vitro* and *in vivo* release of vasoactive angiogenic agents. As a result, vascular permeability is also reduced.[24] Dopamine agonist, cabergoline, reduces the incidence of OHSS when used by women who are at high risk and can be used for prophylactic prevention of OHSS. Calcium gluconate infusion or albumin are also considered an equally effective for preventing OHSS.[25]

In cases of severe OHSS, the administration of gonadotropin-releasing hormone (GnRH) agonists, such as leuprolide or buserelin, can suppress endogenous gonadotropin secretion and mitigate ovarian hyperstimulation. GnRH agonists induce a temporary pituitary desensitization, reducing the production of FSH and LH and thereby attenuating ovarian stimulation.

Loop diuretics, such as furosemide, may be used to promote diuresis and reduce fluid accumulation in cases of severe ascites and pleural effusion.[26] Diuretics should be used judiciously and monitored closely for electrolyte abnormalities, particularly hypokalemia and dehydration. Anticoagulant therapy with low molecular weight heparin (LMWH) or unfractionated heparin (UFH) may be indicated in patients with severe OHSS who are at high risk of thromboembolic events.[27] Thromboprophylaxis should be individualized based on the patient's risk factors, coagulation profile, and overall clinical status.

Antiemetic medications, such as ondansetron or metoclopramide, can help alleviate nausea and vomiting associated with OHSS and improve oral intake. Intravenous administration may be necessary in cases of severe nausea and vomiting refractory to oral therapy.

HOSPITALIZATION AND SPECIALIZED MANAGEMENT

Patients with severe OHSS may require hospitalization for intensive monitoring and management of complications. Close monitoring of vital signs, fluid balance, electrolytes, renal function, and hematologic parameters is essential to identify and promptly address any deterioration in clinical status.

Therapeutic paracentesis may be performed to alleviate symptoms of abdominal distension and respiratory compromise associated with severe ascites.[26]Paracentesis can provide rapid relief by draining excess fluid from the

peritoneal cavity, although the procedure carries risks of infection, bleeding, and fluid-electrolyte imbalances.

Patients with severe pleural effusion and respiratory distress may require supplemental oxygen therapy or mechanical ventilation to maintain adequate oxygenation and ventilation. Non-invasive positive pressure ventilation (NIPPV) may be used as a temporizing measure to improve respiratory mechanics and avoid intubation in selected cases. Collaboration between obstetricians/ gynaecologists, reproductive endocrinologists, and other healthcare providers is crucial in providing comprehensive care for women with pregnancy-associated OHSS.

PREGNANCY OUTCOMES AND MATERNAL-FETAL CONSIDERATIONS

Pregnancy complicated by OHSS may be associated with adverse obstetric outcomes, including an increased risk of preterm birth, gestational diabetes, and preeclampsia.[28] The presence of OHSS during pregnancy requires close monitoring and multidisciplinary management to optimize maternal and fetal outcomes. Additionally, the presence of OHSS during pregnancy may necessitate modifications to prenatal care, such as more frequent antenatal visits and additional surveillance for complications.

MATERNAL CONSIDERATIONS

Pregnant women with a history of OHSS, particularly those with severe or recurrent cases, may be at increased risk of certain complications during pregnancy. These complications may include thromboembolic events, ovarian torsion, renal dysfunction, electrolyte imbalances, and respiratory compromise due to pleural effusion.

Close monitoring of maternal health status is essential throughout pregnancy, especially in women with a history of OHSS. Regular antenatal visits with obstetricians/ gynecologists allow for assessment of maternal symptoms, fluid balance, electrolyte levels, renal function, and other relevant parameters. Early detection and prompt management of complications are paramount to ensuring optimal maternal outcomes. Maintaining adequate hydration and electrolyte balance is critical in pregnant women with a history of OHSS, particularly those at risk of developing complications such as renal dysfunction or electrolyte imbalances. Fluid management strategies should be individualized based on maternal hydration status, renal function, and presence of ascites/pleural effusion.

Women with a history of severe OHSS or other risk factors for thromboembolic events may require thromboprophylaxis during pregnancy. Anticoagulant therapy with LMWH or UFH may be indicated to reduce the risk of venous thromboembolism, particularly in women with additional risk factors such as multiple gestation or prolonged bed rest.

FETAL CONSIDERATIONS

Maternal complications associated with OHSS, such as dehydration, electrolyte imbalances, and hypovolemia, can potentially affect fetal well-being. Fetal growth and development may be compromised in cases of severe maternal illness, highlighting the importance of early recognition and management of maternal complications to optimize fetal outcomes.

Certain medications used in the management of OHSS, such as diuretics or anticoagulants, may have fetal implications and should be used judiciously. Close monitoring of fetal growth, development, and well-being is warranted when pharmacological interventions are necessary during pregnancy.

In cases of severe OHSS or maternal complications that pose a significant risk to maternal or fetal health, the timing and mode of delivery may need to be carefully considered. Preterm delivery or caesarean section may be indicated in selected cases to mitigate risks and ensure the best possible outcomes for both the mother and the fetus.

While the majority of pregnancies associated with OHSS result in favourable outcomes, the long-term effects of OHSS on maternal and fetal health are not well-understood. Further research is needed to elucidate the potential impact of OHSS on offspring health, including risks of metabolic disorders, cardiovascular disease, and reproductive health later in life.

PREVENTION OF OHSS IN ART AND PREGNANCY

Prevention of OHSS in assisted reproductive technology ART and pregnancy involves careful patient selection, optimization of ovarian stimulation protocols, and close monitoring throughout the treatment process. By employing preventive strategies, healthcare providers can minimize the risk of OHSS while maximizing the chances of successful pregnancy outcomes.

Prior to initiating ovarian stimulation, each patient's individual risk factors for OHSS have to be assessed. This includes evaluating factors such as age, BMI, ovarian reserve, and previous history of OHSS. Women with a high ovarian response to gonadotropins, such as those with PCOS, are at increased risk of developing OHSS and may require tailored treatment approaches.

Patients should receive thorough counselling regarding potential risks and benefits of ovarian stimulation treatments, including risk of OHSS. Informed consent should include discussion of alternative treatment options, potential complications, and strategies for minimizing risk of OHSS.

Tailoring gonadotropin dosing based on individual patient characteristics can help minimize the risk of excessive

ovarian response and OHSS.[29] Starting with lower doses of gonadotropins and using a step-down or antagonist protocol may reduce the risk of ovarian hyperstimulation while still achieving adequate follicular development.

Choice of trigger for final oocyte maturation can impact risk of OHSS. GnRH agonists, which induce a temporary pituitary desensitization, can be used as an alternative to hCG trigger in high-risk patients to reduce the risk of OHSS.[30] Dual trigger with both GnRH agonist and low-dose hCG may also be considered in certain cases to optimize oocyte maturation while minimizing OHSS risk.

Coasting, or the temporary cessation of gonadotropin administration, may be employed in high-risk patients to prevent the development of OHSS.[31] By withholding gonadotropins when follicular development is nearing completion and serum estradiol levels are high, coasting allows for a reduction in ovarian stimulation intensity and mitigates the risk of OHSS.

Close monitoring of ovarian response and serum hormone levels throughout the ovarian stimulation cycle is essential in detecting early signs of excessive response and OHSS risk. Serial transvaginal ultrasound and measurement of serum estradiol levels allow for assessment of follicular growth and adjustment of gonadotropin dosing as needed.

Timing the trigger for final oocyte maturation is critical in minimizing the risk of OHSS. Triggering when the leading follicles are of optimal size and serum estradiol levels are within a safe range can help reduce the likelihood of OHSS while still achieving a sufficient number of mature oocytes for retrieval.[15]

Individualizing monitoring and treatment protocols based on patient characteristics and response to ovarian stimulation is key in preventing OHSS.

FUTURE RESEARCH

Future directions and research need in the management of OHSS in pregnancy are essential to improve patient outcomes and minimize risks. Developing accurate predictive models to identify women at highest risk of developing OHSS during pregnancy, based on factors such as ovarian reserve, hormonal profiles, and previous response to ovarian stimulation. Investigating novel preventive strategies to reduce the incidence and severity of OHSS in pregnant women undergoing assisted reproductive technologies (ART), including optimization of ovarian stimulation protocols, trigger strategies, and pharmacological interventions. Long-term follow-up studies are needed to assess the impact of OHSS on maternal and fetal health outcomes, including risks of metabolic disorders, cardiovascular disease, and reproductive health in offspring.

Continued research efforts in these areas will contribute to a better understanding of OHSS in pregnancy and facilitate the development of more effective prevention and management strategies.

CONCLUSION

Pregnancy with OHSS poses unique challenges for clinicians involved in the care of women undergoing ART procedures. Early recognition, risk stratification, and multidisciplinary management are crucial to mitigate the adverse effects of OHSS on maternal and fetal health. Further research is needed to elucidate the long-term implications of pregnancy-associated OHSS and to refine strategies for its prevention and management.

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