Management of Ovarian Hyperstimulation Syndrome (OHSS)

Document Control:

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Previous Titles for this Document:

Previous Title/Amalgamated Titles	Date Revised
None	Not applicable

Distribution Control

Printed copies of this document should be considered out of date. The most up to date version is available from the Trust Intranet.

Consultation

The following were consulted during the development of this document:
Gynaecology guidelines committee

Monitoring and Review of Procedural Document

The document owner is responsible for monitoring and reviewing the effectiveness of this Procedural Document. This review is continuous however as a minimum will be achieved at the point this procedural document requires a review e.g. changes in legislation, findings from incidents or document expiry.

Relationship of this document to other procedural documents

This document is a clinical guideline applicable to Norfolk and Norwich University Hospital; please refer to local Trust's procedural documents for further guidance.

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1. Introduction

1.1. Rationale

Ovarian hyperstimulation syndrome (OHSS) is a serious and potentially life-threatening complication of induction of ovulation or superovulation. The syndrome is characterised.

by ovarian enlargement and a shift of fluid from the intravascular to the extravascular space due to increased capillary permeability. The pathophysiology of the syndrome is unclear. It has been suggested that exposure of hyperstimulated ovaries to hCG leads to the production of proinflammatory mediators such as VEGF (vascular endothelial growth factor) and cytokines. The proinflammatory mediators increase vascular permeability leading to accumulation of fluid in the peritoneal, pleural and rarely pericardial cavities, thus resulting in intravascular fluid depletion and haemoconcentration.

Clinicians must remain alert to the possibility of OHSS in all women undergoing fertility treatment and women should be counselled accordingly.

Mild forms of OHSS affect up to 33% of IVF cycles. Moderate to severe OHSS has been reported in 3-8 % of IVF cycles. Women at higher risk of developing OHSS include
women with polycystic ovaries, women with a previous history of OHSS, use of GnRH agonists, development of multiple follicles during treatment and induction cycles where conception occurs, particularly multiple pregnancies. Complications are more frequent when conception occurs and a protracted course may evolve.

At Norfolk and Norwich University Hospital NHS Foundation Trust we adhere to the RCOG Green-top Guideline No. 5 entitled The Management of Ovarian Hyperstimulation Syndrome; published February 2016.

1.2. Objective

The objective of the guideline is to:

- Provide evidence-based guidance for gynaecology staff on the assessment and management of women with ovarian hyperstimulation syndrome
- To optimise and standardise our care of this patient group at the Norfolk and Norwich University Hospital

1.3. Scope

This document will only cover suspected and confirmed cases of Ovarian hyperstimulation syndrome presenting to the Norfolk and Norwich University Hospital. It will not cover other gynaecological conditions or complications of early pregnancy.

1.4. Glossary

The following terms and abbreviations have been used within this document:

Term	Definition
OHSS	Ovarian Hyperstimulation Syndrome
hCG	Human chorionic gonadotrophin
VEGF	Vascular Endothelial Growth Factor
IVF	In Vitro Fertilisation
GnRH	Gonadotrophin Releasing Hormone
ECG	Electrocardiogram
CTPA	Computerised Tomography Pulmonary Angiogram
V/Q	Ventilation/Perfusion
CVP	Central Venous Pressure
HDU/ITU	High Dependency Unit / Intensive Treatment Unit
TED	Thromboembolic Deterrent
LMWH	Low Molecular Weight Heparin
VTE	Venous Thromboembolism

2. Responsibilities

All medical staff in gynaecology including junior doctors, consultants, nursing staff have a responsibility to adhere to this document and national guidance.

3. Processes to be followed

3.1. Diagnosis and Assessment of OHSS

Clinicians need to be aware of the symptoms and signs of OHSS, as the diagnosis is based on clinical criteria.

In women presenting with severe abdominal pain or pyrexia, extra care should be taken to rule out other causes of the patient's symptoms.

3.1.1. History

- Time of onset of symptoms relative to trigger
- Medication used for trigger (hCG or GnRH agonist)
- Number of follicles on final monitoring scan
- Number of eggs collected
- Were embryos replaced and how many?
- Polycystic ovary syndrome diagnosis?

3.1.2. Symptoms

- Abdominal bloating
- Abdominal discomfort/pain, need for analgesia
- Nausea and vomiting
- Breathlessness, inability to lie flat or talk in full sentences

- Reduced urine output
- Leg swelling
- Vulval swelling
- Associated comorbidities such as thrombosis

3.1.3. Examination

- **General:** assess for dehydration, oedema (pedal, vulval and sacral); record heart rate, respiratory rate, blood pressure, body weight
- **Abdominal:** assess for ascites, palpable mass, peritonism; measure girth
- **Respiratory:** assess for pleural effusion, pneumonia, pulmonary oedema

3.1.4. Investigations

- Full blood count
- Haematocrit (haemoconcentration)
- C-reactive protein (severity)
- Urea and electrolytes (hyponatraemia and hyperkalaemia)
- Serum osmolality (hypo-osmolality)
- Liver function tests (elevated enzymes and reduced albumin)
- Coagulation profile (elevated fibrinogen and reduced antithrombin)
- hCG (to determine outcome of treatment cycle) if appropriate
- Ultrasound scan: ovarian size, pelvic and abdominal free fluid. Consider ovarian Doppler if torsion suspected

3.1.5. Other tests that may be indicated

- Arterial blood gases
- D-dimers
- Electrocardiogram (ECG)/echocardiogram
- Chest X-ray
- Computerised tomography pulmonary angiogram (CTPA) or ventilation/perfusion (V/Q) scan

3.2. Classification of severity of OHSS

Category	Features
Mild OHSS	Abdominal bloating Mild abdominal pain Ovarian size usually < 8 cm
Moderate OHSS	Moderate abdominal pain Nausea ± vomiting Ultrasound evidence of ascites Ovarian size usually 8–12 cm

Severe OHSS	Clinical ascites (± hydrothorax) Oliguria (< 300 mL/day or < 30 mL/hour) Haematocrit > 0.45 Hyponatraemia (sodium < 135 mmol/l) Hypo-osmolality (osmolality < 282 mOsm/kg) Hyperkalaemia (potassium > 5 mmol/l) Hypoproteinaemia (serum albumin < 35 g/l) Ovarian size usually > 12 cm
Critical OHSS	Tense ascites/large hydrothorax Haematocrit > 0.55 White cell count > 25 000/mL Oliguria/anuria Thromboembolism Acute respiratory distress syndrome

NOTE - Ovarian size may not correlate with severity of OHSS in cases of assisted reproduction because of the effect of follicular aspiration. Women demonstrating any feature of severe or critical OHSS should be classified in that category.

3.3. Management

Women presenting with symptoms suggestive of OHSS should be assessed face-to-face by a clinician if there is any doubt about the diagnosis or if the severity is likely to be greater than mild.

3.3.1. Outpatient management

Patients with **mild and moderate OHSS** are usually managed on an outpatient basis.

Management includes:

a) Analgesia – paracetamol and/or codeine. NSAIDs should not be used as they may compromise renal function.

b) Fluid management – Encourage to drink to thirst, rather than to excess (fluid intake of ≥ 1 litre/day should be advised). Fluid intake and output monitoring.

c) Avoid strenuous exercise and sexual intercourse.

d) Luteal support – continue progesterone luteal support (Cyclogest 400 mg BD).

However, hCG luteal support should be stopped.

The patient should monitor their weight daily.

They should be seen on Cley Ward every 2-3 days with regular bloods until symptoms resolve.

They should have open access and should be told to attend if they have:

- Pain not controlled with simple analgesia and increasing abdominal distension
- Vomiting not controlled with oral antiemetics

- Increasing shortness of breath
- Poor urine output (<1000 mL/24 hours or positive fluid balance of >1000 mL/24 hours)
- Calf pain

3.3.2. Inpatient management

Women with **severe or critical OHSS** and some women with moderate OHSS require hospital admission.

Hospital admission should be considered for women who:

- are unable to achieve satisfactory pain control
- are unable to maintain adequate fluid intake due to nausea
- show signs of worsening OHSS despite outpatient intervention
- are unable to attend for regular outpatient follow-up

The aim of treatment is supportive whilst waiting for the condition to resolve spontaneously:

a) provide reassurance and symptomatic relief

b) avoid haemoconcentration

c) prevent thromboembolism

d) maintain cardiorespiratory and renal function

Women admitted with OHSS should be assessed at least once daily. More frequent assessment is appropriate for women with critical OHSS and those with complications.

Examination

a) General state of hydration

b) Chest: pleural or pericardial effusion

c) Abdomen: degree of distension, ascites

d) Evidence of thrombosis

Investigations

Daily bloods which include full blood count, haematocrit, serum electrolytes, osmolality and liver function tests.

Depending on the clinical features, arterial blood gases, ECG, chest X-ray and other imaging may be required.

Nursing observations

a) BP, pulse and temperature 4-hourly

b) Weight and abdominal girth (measured at the umbilicus) daily

c) Strict fluid input/output chart

d) Consider urinary catheterisation

e) Pulse oximeter if dyspnoeic

Treatment

a) Rehydration The aim is to replace fluids in the vascular compartment to allow resumption of normal urine output (>30mL/hour). Encourage oral fluids if not vomiting.

Where oral intake cannot be maintained crystalloids (e.g. 0.9% normal saline) are recommended for the initial correction of dehydration (up to 2-3 litres/24 hrs). Effective analgesia and anti-emetics may be required to achieve this.

Women with persistent haemoconcentration or urine output <0.5mL/kg/hr despite adequate volume replacement may benefit from colloid in the form of 20% human albumin. Human albumin solution 20% may be used as a plasma volume expander in doses of 40–100 g, infused over 4 hours and repeated 4- to 12-hourly. Human albumin 20% is available in 100 mL bottle i.e. 20 g per bottle.

Diuretics should be avoided as they remove fluid from the vascular compartment only.
Women with persistent haemoconcentration despite volume replacement with intravenous colloids may need invasive monitoring with CVP measurement and urinary catheterisation. This should be managed with anaesthetic input.
Referral to HDU/ITU should be considered

b) Analgesia : as above. In addition other oral or parenteral opiates can be used (eg. Oramorph)

c) Antiemetics as required: metoclopramide, cyclizine or stemetil.

d) Thromboprophylaxis: TED stockings and prophylactic subcutaneous low molecular weight heparin (LMWH) to reduce the risk of venous thrombosis.

The duration of LMWH should be individualised according to patient risk factors and outcome of treatment.

In addition to the usual symptoms and signs of VTE, thromboembolism should be suspected in women with OHSS who present with unusual neurological symptoms even after recovery from OHSS.
Therapeutic anticoagulation is necessary if there is evidence of thromboembolism.

e) Luteal support: as in outpatient management.

f) Abdominal paracentesis: Drainage of ascites is indicated if there is:

- Severe abdominal distension and abdominal pain secondary to ascites

- Shortness of breath and respiratory compromise secondary to ascites and increased intra-abdominal pressure
- Oliguria despite adequate volume replacement, secondary to increased abdominal pressure causing reduced renal perfusion

This should only be done under ultrasound guidance in order to avoid damage to bowel or ovaries. A continuous drainage tube can be left in situ.

Careful attention must be paid to management of fluid replacement. Intravenous colloid therapy should be considered for women who have large volumes of fluid removed by paracentesis. Drainage of pleural effusions is less commonly indicated.

g) Surgical management: Surgery is only indicated in patients with OHSS if there's suspected adnexal torsion, ovarian rupture or ectopic pregnancy.

Patients with critical OHSS or severe OHSS with persistent haemoconcentration and dehydration should be cared for by a multidisciplinary team of Consultant Gynaecologist, Consultant Anaesthetist and senior nursing staff.

They should liaise closely with the renal and ITU physicians as appropriate.

Transfer to ITU should be considered if:

- Poor urine output persists despite rehydration
- Poor oxygen saturation
- Severe ascites/pleural effusions

A copy of the discharge letter should be sent to the fertility centre caring for this patient to inform about the management in the hospital.

4. References

- RCOG Green top guideline no.5. (2016)The Management of Ovarian Hyperstimulation Syndrome. February 2016.
- NICE clinical guideline No. 156 (2017) Fertility problems: assessment and treatment

5. Monitoring Compliance

Compliance with the process will be monitored through the following:

Key elements	Process for Monitoring	By Whom (Individual / group /committee)	Responsible Governance Committee /dept	Frequency of monitoring
Acute unit to inform licensed centre regarding all patients seen with a suspected	Audit	Gynaecology services health care professionals	Gynaecology governance	Annual

diagnosis of OHSS (100%)				
Effectiveness of outpatient management of severe OHSS against locally agreed standard	Audit	Gynaecology services health care professionals	Gynaecology governance	Annual
Women admitted to hospital should have daily clinical review with weight and abdominal girth measurements and monitoring of intake and output of fluid (100%)_	Audit	Gynaecology services health care professionals	Gynaecology governance	Annual
All women with severe or critical OHSS should be prescribed LMWH, unless there is a contraindication, whether admitted to hospital or not (100%)	Audit	Gynaecology services health care professionals	Gynaecology governance	Annual

The audit results are to be discussed at gynaecology governance meetings to review the results and recommendations for further action. The gynaecology governance committee will ensure that the actions and recommendations are suitable and sufficient.

6. Appendices

There are no appendices for this document.

7. Equality Impact Assessment (EIA)

Type of function or policy	Existing

Division	Women and Children	**Department**	Gynaecology
Name of person completing form	Margaret Pilling	**Date**	16.10.23

Equality Area	Potential Negative Impact	Impact Positive Impact	Which groups are affected	Full Impact Assessment Required YES/NO
Race	No	No	No	No
Pregnancy & Maternity	No	No	No	No
Disability	No	No	No	No
Religion and beliefs	No	No	No	No
Sex	No	No	No	No
Gender reassignment	No	No	No	No
Sexual Orientation	No	No	No	No
Age	No	No	No	No
Marriage & Civil Partnership	No	No	No	No
EDS2 – How does this change impact the Equality and Diversity Strategic plan (contact HR or see EDS2 plan)?				

- **A full assessment will only be required if: The impact is potentially discriminatory under the general equality duty**
- **Any groups of patients/staff/visitors or communities could be potentially disadvantaged by the policy or function/service**
- **The policy or function/service is assessed to be of high significance**

IF IN DOUBT A FULL IMPACT ASSESSMENT FORM IS REQUIRED

The review of the existing policy re-affirms the rights of all groups and clarifies the individual, managerial and organisational responsibilities in line with statutory and best practice guidance.