1. Introduction and Who Guideline applies to

This guideline is intended for the use of all medical, nursing and other hospital staff involved in the management of patients with Ovarian Hyperstimulation Syndrome.

Background:

OHSS is an iatrogenic and potentially life-threatening complication of fertility treatment whereby ovarian stimulation is induced pharmacologically to increase the number of oocytes obtained for assisted conception treatment. In cycles of conventional in vitro fertilisation (IVF), 'mild' OHSS can affect one-third of cycles, while the incidence of moderate and/or severe OHSS varies from 3.1% to 8% [1].Predisposing risk factors for development of OHSS include women with a previous history of OHSS, polycystic ovary syndrome, increased antral follicle count (AFC) or high levels of anti-Müllerian hormone (AMH).

2. Guideline Standards and Procedures

Recommendation One:

All patients undergoing treatment with gonadotrophins whether for ovulation induction (OI) and intrauterine insemination (IUI) or for IVF should receive verbal and written information regarding the potential risk of OHSS.

- All patients should have been provided with a patient information leaflet detailing risks, symptoms, and 24 hr. contact numbers in the event of developing OHSS.

Recommendation Two:

Within clinic hours, women undergoing treatment at UHL Leicester Fertility Centre (Assisted Conception Unit (ACU)) are to be reviewed by the Specialist nurses between 9 -5 Monday to Friday in the ACU.

- Women undergoing treatment elsewhere should be advised to contact the Gynaecology Assessment Unit (GAU) at the Leicester Royal Infirmary.

Recommendation Three:

Outside of clinic hours, if an ACU patient contacts GAU complaining of symptoms of OHSS, the ward MUST contact a member of the ACU team within clinic hours.

- Symptoms include: abdominal pain, abdominal distension, nausea, vomiting or diarrhoea, breathlessness, or having passed urine less than 3 times in 24 hours,
- Telephone numbers of the team are held on GAU as well as through switchboard.

Table 1. Assessment of a woman with suspected OHSS (RCOG GTG No.5, 2016)

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
Number of embryos replaced if embryo transfer went ahead
Diagnosis of Polycystic Ovaries
Symptoms
Abdominal bloating
Abdominal discomfort/pain, need for analgesia
Nausea and vomiting
Breathlessness, inability to lay flat, talk in full sentences
Reduced urine output
Leg swelling
Vulval swelling
Comorbidities and thrombotic risk factors
Examination
General: obvious discomfort, dehydration, oedema (pedal, vulval and sacral); measure heart rate, respiratory rate, blood pressure, body weight
Abdominal: measure abdominal girth, check for ascites, palpable mass, peritonism
Respiratory: assess for pleural effusion, pneumonia, pulmonary oedema
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
Other tests that may be indicated
Blood gases
D-dimers
Electrocardiogram (ECG)/Echocardiogram
Chest X-ray
Computerised tomography pulmonary angiogram (CTPA) or ventilation/perfusion (V/Q) scan

Recommendation Four:

A GP may contact the ward requesting the admission of a patient with one or more of the above symptoms who has had assisted conception treatment at another unit outside Leicester. Such a patient **MUST** be admitted urgently.

The on call doctors must NOT refuse admission to any ACU patient referred because of possible OHSS.

Recommendation Five:

OHSS severity should be classified as per the RCOG Guidance.

Table 2: Classification of OHSS (RCOG Green Top Guideline No 5, 2016)

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

*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.

Recommendation Six:

Women with **mild OHSS** or **moderate OHSS** may be managed as outpatients, and in selected cases, those with severe OHSS.

- Advise about plenty of fluid intake and output monitoring, mobilisation and simple analgesia (paracetamol/codeine).
- Avoid NSAIDS.
- Advise to avoid strenuous exercise and sexual intercourse due to risk of injury or torsion.
- Women with severe OHSS being managed on an outpatient basis should receive thromboprophylaxis with LMWH. The duration of treatment should be individualised, taking into account risk factors and whether or not conception occurs
- If symptoms worsen, woman needs to contact ACU/GAU urgently.
- Reassure patients that pregnancy may continue normally despite OHSS.
- ACU should be informed to arrange follow up (usually in 2-3 days).

Severe OHSS:

Recommendation Seven:

Hospital admission on GAU should be considered for women who:

- Are unable to achieve pain control
- Unable to maintain fluid intake due to nausea

- Have symptoms/signs of: vomiting/ diarrhoea; shortness of breath; oliguria (less than 1000 mL/24 hr or positive fluid balance of >1000 mL/24 hr.)/anuria; severe abdominal pain
- Signs of worsening OHSS despite outpatient intervention
- Unable to attend for regular outpatient follow-up
- Have critical OHSS

Recommendation Eight:

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

Multidisciplinary assistance should be sought for the care of women with critical OHSS and severe OHSS who have persistent haemoconcentration and dehydration.

A clinician experienced in the management of OHSS should remain overall in charge for the care.

Recommendation Nine:

Nursing staff should carry out the following once the woman is admitted:

- Daily weight
- Daily abdominal girth measurement
- TED stockings
- Fluid input/ output chart
- Oxygen saturation
- Early Warning Score

Recommendation Ten:

Medical/ Nursing staff to review and carry out the investigations and blood tests (Table 1) Blood tests are to be repeated daily or more frequently in women with critical OHSS or when clinically indicated.

Recommendation Eleven:

Initial management should be commenced on admission.

- Manage fluid balance
- Encourage oral fluid intake
- Administer IV fluids if vomiting or decreased urine output. Crystalloid (normal saline one litre 8hrly), urinary catheterisation if oligo/anuric.
- If the urine output falls below 30ml per hour then it may be decided to give IV human albumin solution (HAS) 25% in dose of 50 -100g, infused over 4 hours and repeated 4-12 hourly. The administration of HAS is a consultant decision.
- Avoid diuretics in patients with decreased blood volume and decreased renal perfusion as they deplete intravascular volume. They may have a role in multidisciplinary setting if oliguria persists despite fluid replacement and drainage of ascites.
- Prochlorperazine (PR/IM) can be prescribed for nausea and/or vomiting.
- Provide analgesia: paracetamol/opiates, care should be taken to avoid constipation.

- Inform ACU consultant of all patients admitted with OHSS. They may also be contacted for advice.

Recommendation Twelve:

Abdominal paracentesis should be carried out:

- In presence of severe abdominal distension and pain secondary to ascites
- Shortness of breath and respiratory compromise secondary to ascites and increased intra-abdominal pressure
- Oliguria despite adequate fluid replacement, secondary to increased intra-abdominal pressure causing reduced renal perfusion

Paracentesis should be carried out under ultrasound control (abdominally or transvaginally); fluid should be drained slowly- 500mL over 6 hours with intravenous colloid replacement.

Recommendation Thirteen:

Anticoagulants - Enoxaparin SC OD should be commenced for those admitted with severe or critical OHSS.

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

- Women with moderate OHSS should be evaluated for predisposing risk factors for thrombosis and prescribed either anti-embolism stockings or LMWH if indicated.

- In addition to the usual symptoms and signs of venous thromboembolism (VTE), thromboembolism should be suspected in women with OHSS who present with unusual neurological symptoms, even if they present several weeks after apparent improvement in OHSS.

Recommendation Fourteen:

All women with the criteria for severe OHSS should be commenced on an early warning score chart and referred to critical care outreach when appropriate.

- Women meeting the criteria for severe OHSS or whose early warning score indicates so, should be reviewed by the critical care outreach team - who will assess the patient, discuss management with one of the ACU consultant and arrange either for urgent admission to ITU level 2 or for regular follow up of the patient by the Outreach Team on GAU.

- All contact numbers and bleeps available via switchboard

Critical OHSS:

Recommendation Fifteen:

Women meeting the criteria for critical OHSS are to be managed on ITU - consultant to consultant referral.

- Early involvement of renal physician may be required in addition to Gynaecology/ ITU anaesthetists.
- Level of monitoring on ITU level 2-continuous oxygen saturation, ECG, non-invasive BP, strict fluid balance, long line. Direct intra-arterial pressure monitoring to facilitate frequent blood tests and blood gas analysis.
- Critical OHSS patients may require level 3 ITU care.
- Administration of NSAIDS to be avoided in severe and critical OHSS patients.

Recommendation Sixteen:

Surgery is only indicated in patients with OHSS if there is coincident problem such as adnexal torsion, ovarian rupture or ectopic pregnancy and should be performed by an experienced surgeon.

Recommendation Seventeen:

Patients can only be discharged home after discussion with the ACU/ fertility consultant staff. Follow-up will be arranged on the ACU or at the treating unit.

Recommendation Eighteen:

A datix form on UHL intranet should be filled in once a patient with severe OHSS is admitted on GAU.

Staff on GAU should inform the licensed centre where the fertility treatment was carried out to promote clinical continuity and to allow the licensed centre to meet its legal obligations.

Licensed centres should comply with Human Fertilisation and Embryology Authority (HFEA) regulations in reporting cases of OHSS among their patients.

Recommendation Nineteen:

Clinicians should be aware and women informed that pregnancies complicated by OHSS may be at an increased risk of pre-eclampsia and preterm delivery.

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements

5. Supporting References (maximum of 3)

1. Delvigne A, Rozenberg S. Epidemiology and prevention of ovarian hyperstimulation syndrome (OHSS): a review. *Hum Reprod Update* 2002;8:559–77.

2. The Management of ovarian hyperstimulation syndrome RCOG GreenTop Guideline no 5 2016.

3. NICE Guidance CG156. Fertility Problems: assessment and treatment

6. Key Words

OHSS, Ovarian Hyperstimulation Syndrome, Ovarian,

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) N Potdar – Consultant Gynaecologist	**Executive Lead** A Furlong
Details of Changes made during review: Passed at Gynaecology governance August 2020 Minimal changes. Recommendation 3 amended – ward to contact ACU within clinical hours.	