Dr. Abha Majumdar did her graduation and post graduation in Obstetrics and Gynecology from Agra Medical College, India and was awarded the Presidents Medal for being the Best Medical Graduate for 1975.

She was awarded Fellowship of International College of Surgeons in 1994. She is attached to Sir Ganga Ram Hospital, New Delhi since 1987. At present she is a Senior Consultant and heads the unit of IVF and Reproductive Medicine of Sir Ganga Ram Hospital. This hospital provides comprehensive infertility services and is the largest infertility center of Northern India.

She was felicitated by Dr. B.C Roy's prestigious award in 1999, for her outstanding contribution towards medicine and her field of specialty. In the year 2002 she was awarded Bharat Vikas Ratan Award by nations Economic Development and Growth Society.

Her field of interest is in management of all cases related to infertility with special focus on reproductive endocrinology

Management of OHSS

Dr. Abha Majumdar
Senior Consultant & Head
Center of IVF & Human Reproduction
Sir Ganga Ram Hospital
New Delhi

This management protocol has been laid down from RCOG guidelines 2005 which aim to offer evidence based support for physicians involved in the management of patients with OHSS.

For writing these guidelines original articles were obtained from following sources:

- **□**Computer search
 - Medline 1966-March 2005
 - Embase 1980-March 2005
- ☐ Hand search from original references and reviews

Classification of evidence levels

- 1(a &b): Evidence from randomized controlled trials.
- 2(a &b):
 Evidence from at least one well designed controlled study without randomization or quasi experimental study.
- 3: Evidence from well designed, non experimental descriptive studies, such as comparative, correlation and case studies.
- 4: Evidence from expert committee reports or opinions / clinical experience of respected authorities

Diagnosis of OHSS

H/o ovarian-stimulation followed by symptoms of abdominal distension, abdominal pain, nausea and vomiting.

Differential diagnosis

- Ovarian cyst torsion, rupture or haemorrhage
- Septicemia / Pelvic infection
- Acute appendicitis
- Ectopic pregnancy

Staging of OHSS for management purpose

Schenker & Weinstein (1978), modified by Golan et al(1989), Navot et al (1992) & Mathur et al(2005).

Mild OHSS: abdominal distension with mild abdominal pain with ovarian size <8cm

Moderate OHSS: Moderate abdominal pain, ultrasound evidence of ascitis with ovarian size 8-12cm.

Severe OHSS: clinical ascitis (occasionally hydrothorax), oliguria, hemo-concentration with PCV>45%, hypoproteinaemia & ovarian size usually> 12cm.

Critical OHSS: Tense ascitis or large hydrothorax, hematocrit >55% WBC>25000/ml, oligo/anuria, thrombo-embolism with ARDS.

Ovarian size may be variable due to aspiration of follicles

Management depends on

Severity of presentation

- Mild to moderate stage as: Out-patient
- Severe and critical stage as: in-patient or in ICU.

Onset

- Early presentation: more severe in course
- Late presentation: less severe in course

Pregnancy

- Presence of pregnancy: more severe & lasts longer.
- Absence of pregnancy:self limiting

Staging of disease for management purpose

- □ Clinical examination
- □Pelvic ultrasound
- □Lab investigation such as
 - > Hemoglobin, hematocrit, WBC
 - S. creatinine and electrolytes
 - >LFTs.
 - Thrombophilia profile if past personal or family history.

Out patient management

- ✓ Analgesia: paracetamol, codiene & derivatives, NSAID's NO! – may compromise renal function
- ✓ Avoid strenuous exercise and sexual intercourse Fear of torsion or injury to enlarged ovaries.
- Light physical activity but strict bed rest avoided to prevent thrombo-embolic phenomenon.
- ✓ Drink to thirst. Minimize "free water", intake but encourage "sports drink".

When to admit

- **□**Severe and critical OHSS
- Moderate OHSS with poor pain control
- ■Nausea vomiting not allowing oral treatment
- Difficulty in ensuring ongoing monitoring
- Moderate OHSS with worsening staging (increasing distension, shortness of breath, Impression of reduced urine output).

In patient care

Multi disciplinary care with expertise in managing renal failure, ARDS, thrombo-embolism.

Intensive care in patients with critical OHSS

Counseling to allay anxiety

Assess daily or more if critical OHSS

Level 3 evidence

In patient monitoring Examination

- Assessment of Pain
- Weight gain
- Hydration / Fluid balance
- Breathlessness/ respiratory parameters
- Cardiovascular:

heart rate, rhythm

Abdominal:

girth, distension, ovaries, ascites, bowel sounds

In patient monitoring Investigation

Laboratory tests

- Full blood count: Hemoglobin, hematocrit, WBC
- S. creatinine, Urea and electrolytes
- Liver function tests
- Clotting factors

Imaging

- Pelvic ultrasound for ascitis & ovarian size
- Chest x-Ray or ultra sound
- Echocardiogram if suspected pericardial effusion

Management

- Analgesia:
 - paracetamol, opiates (avoid constipation)
- *Anti- emetics:
 - Prochlorperazine, metoclopramide & cyclizine
- Fluid balance
 - Allow patient to drink to thirst. Evidence Level 3
 - I/V saline 2 to 3 liters in 24 hours if oral intake cannot be maintained.
 - Hemoconcentration: Hbg >14 gm/dl, PCV>45%: Intensive initial rehydration (I Litre NaCl over I hour)

Resistant hemo-concentration with urine output <0.5ml/kg/hr benefit from colloids: albumin, HES, dextran, mannitol, haemaccel

Human Albumin

- Half life of 10-15 days
- Mol.wt. 69 kD
- Expensive
- Biological in origin
- Hypoproteinemia Rxed
- No effect on coagulation profile

Hydroxy ethyl starch

- Half life of 10 –12 hour
- Mol.wt. 200-1000 kD
- 10 times less costly
- Non-biological in origin
- Hypo-proteinemia not Rxed
- Derange coagulation

Persistant hemoconcentration & oliguria despite initial rehydration

Colloids: HES 500 ml 1 hour (higher mean urinary output, fewer paracentesis, and shorter hospital stay than human albumin)

Consider Paracentesis for persistent oliguria.

Evidence GPP

<u>Diuretics avoided</u> or used very judiciously with multi-disciplinary involvement & CVP monitoring <u>Evidence level 3</u>

Management of ascitis

➤ Paracentesis if distress due to abd. distension or persistent oliguria despite volume replacement.

Evidence level 2b

- Controlled rate of ascitic fluid drainage with I/V colloids and BP/ pulse monitoring. Evidence level 3
- ➤Ultrasound guided to prevent injury to ovaries

 Evidence level 3
- >Trans abdominal better tolerated by patients.
- Avoid repeated paracentesis by pigtail catheter.

Hydrothorax

Drainage of ascitis alone may suffice to resolve hydrothorax also, but symptomatic hydrothorax that persists despite abdominal para-centesis or unilateral or bilateral hydrothorax presenting exclusively may be drained directly

Thrombo-prophylaxis

- •Incidence of thrombosis in OHSS -- 0.7-10%
- Preponderance— upper body sites
- Affected Vasculature Arterial system
- Mechanism of thrombosis—
 - Hemoconcentration
 - Altered coagulation system
 - Reduced venous return
 - increased intra abdominal pressure
 - immobilisation

Thrombo-prophylaxis

Thrombo-prophylaxis to all patients admitted with OHSS, continue till discharge or longer depending on risk factors.

evidence level 3

Routine screening for thrombophilia for all ART patients not warranted, although testing is helpful if personal or family H/O thrombosis.

evidence level 2b

Unusual neurological symptoms following ovarian stimulation should raise the possibility of a thrombotic episode evidence level 3

Management Thrombo-prophylaxis

- Life threatening complication: prophylactic heparin to all patients 2500 units S/C BD.
- Pts confined to bed: full length venous support stockings with intermittent pneumatic compression.
- Stop heparin on resolution of OHSS if no pregnancy.
- Continue till end of first trimester if pregnant.
- Thrombosis: therapeutic anti coagulation.

Surgery

OHSS with pregnancy: risk factor for ovarian torsion

- **□**Suspect
- Further ovarian enlargement, worsened unilateral pain, leukocytosis & anaemia
- DiagnosisColor doppler of ovarian blood flow
- Surgery

Only in adenexal torsion & by experienced operator Laparoscopy or laparotomy: detort and watch.

Evidence level 4

Complications

Morbidity

- •Pulmonary edema, pleurisy, complicated pnemonia, hydrothorax, ARD's .
- •Thrombo-embolism: cerebral stroke, ICH heart attack, paralysis or amputation of forearm,
- •Irreversible hepato-renal failure

Kaaja et al; Lancet 1989, Rizk et al, Hum Reprod 1990, Fournet et al; Fertil Steril 1991, Waterstone et al; BJOG 1992, Abramov et al; Fertil Steril 1999, Semba et al Pathol Int 2000, Cluroe et al, Pathol 1995, Balasch et al; Hum. Reprod 1990

Complications

Mortality

ARD's (2 cases), Cerebral Infarction (2 cases), Hepato-renal failure (1 case pre-existing Hepatitis C)

Kaaja et al; Lancet 1989, Rizk et al, Hum Reprod 1990, Fournet et al; Fertil Steril 1991, Waterstone et al; BJOG 1992, Cluroe et el, Pathol 1995 Abramov et al; Fertil Steril 1999, Semba et al Pathol Int 2000, Cluroe et al, Pathol 1995, Balasch et al; Hum. Reprod 1990

One must be reassured that pregnancy continues normally despite OHSS

Prevention of full blown OHSS is better than its consequences even at the cost of failure of ART cycle



No evidence of an increased risk of congenital anomalies

