AOGD BULLETIN

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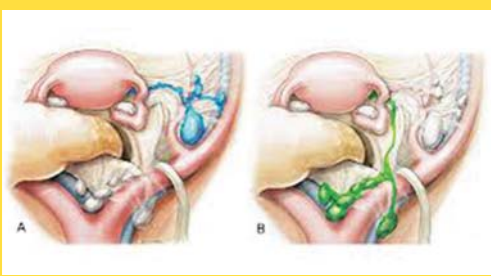
AOGD Theme 2018-19

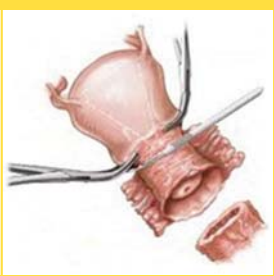
Empowering Providers: Enhancing Women's Health

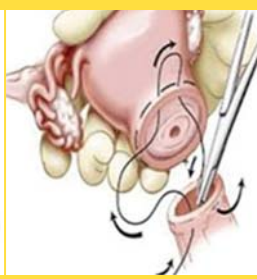
***Issue:* Current Update**

Endocrine Disorders in Pregnancy

Gynecological Oncology







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President's Message

Dear Friends,

Greetings and best wishes in this festive season which included Deepawali. In the celebrations I hope you found time to read the last Bulletin and found it useful. This edition of our Bulletin is devoted to Endocrine Disorders in Pregnancy and Gynecological Oncology.

Thyroid disorders, diabetes and osteoporosis are silently affecting a significant proportion of women. We have tried to address a few key and controversial aspects of thyroid disorders in pregnancy. India is referred as the diabetic capital of the world. Diabetes during pregnancy if not detected and treated timely can affect the maternal and neonatal outcome. Obstetricians are at many times the first health-care providers that these young women visit and should be able to identify and provide treatment for an optimal outcome. A healthy mother is the most important pillar for a family and nation.

Cancer of the female genital tract and breast are leading to many deaths and are common in our country. Cervical cancer cytology screening and HPV testing have a role in prevention and early detection. The importance of early detection of breast cancer by self-examination cannot be overlooked.

I also take this opportunity to invite our esteemed members to the 40th annual conference of AOGD and the preconference workshops. The workshops are being held on 22nd & 23rd November followed by the conference on 24th & 25th November. Young budding obstetricians and gynecologists will get an opportunity to improve their clinical skills at these workshops conducted by experienced faculty. I am sure this conference will be a memorable academic event for all of us.

Happy Reading!!

Dr Abha Singh
President AOGD (2018-19)

Secretary's Message

Greetings from AOGD Secretariat LHMC,

The 40th Annual Conference of AOGD the much awaited event is almost there as this bulletin reaches you all. The organising committee is all geared up to welcome you all at the conference at India Habitat Centre on 24-25th November with preconference workshops on 22nd and 23rd November, 2018. Our young colleagues have submitted number of free papers and posters reflecting their enthusiasm to share their research and interesting cases.

The program has been meticulously crafted for one and all promising to be an academic feast

October had number of activities with second module of PG training in infertility being a runaway success. We really appreciate the work being put up by the subcommittees.

The editorial team has come up with another issue pertaining to Gynecological Oncology and Endocrine disorders of Pregnancy. Both the topics very apt to present scenario of increasing cancers especially breast and endocrine disorders on the rise like thyroid disorders and diabetes in pregnancy.

Latest evidence summarised in the bulletin is worth reading.

Hoping to see you all in big numbers and wishing to greet you all at the Annual Conference.

Thanks

Dr Kiran Aggarwal
Secretary AOGD (2018-19)

Monthly Clinical Meeting

Monthly Clinical Meet will be held at MAMC & LN Hospital, New Delhi
on **Friday, 30th November, 2018 from 04:00pm to 05:00pm**.

Editorial Team's Message

Dr Ratna Biswas
Editor

Dr Pikee Saxena

Dr Sharda Patra

Dr Swati Agrawal

Co-Editors

Hello ! Friends,

Greetings of the festive season!!

We are ready with the November issue of AOGD bulletin with the themes, "Endocrine Disorders in Pregnancy" and "Gynecological Oncology"

The opening chapter is on "Best practices for Optimizing outcome in Pregnancy with Diabetes". This article gives a comprehensive coverage on the antepartum surveillance protocols for pregnancy with diabetes and the management guidelines on diet, exercise and pharmacotherapy.

The recent advances section focuses on the emerging role of "Oral hypoglycemic agents in pregnancy". The evidence on OHA justifies its use in a limited manner.

Controversy on "Whether or not we are over treating subclinical hypothyroidism" is an issue which needs to be clarified. Although adverse outcomes are commoner in this group than the general population yet the treatment of subclinical hypothyroidism (SCH) has not shown significant improvement in outcome parameters. But considering that hypothyroidism may cause neurodevelopment delay in children, the use of thyroxine replacement therapy in SCH may seem justified to prevent this complication.

"Hyperthyroidism in Pregnancy" can cause significant neonatal and maternal morbidity and serious life threatening complications in form of thyroid storm in mother and stillbirths in fetus. It is imperative that we are well versed with the work up and management of hyperthyroidism in pregnancy and hence this topic being addressed in the case approach section.

The motivational article on "Creating an Anger Free Life" re-inforces that anger is a problem much like a disease and should be dealt with appropriately to create a peaceful & healthy life.

The gynecology section begins with "Best Practices: Familial Gynecological Tumors: Risk Assessment & Management". Genetic aberrations result in a cluster of malignancies in predisposed individuals and their families. Pedigree analysis of such families helps to identify the defective gene and initiate preventive strategies. The Hereditary Breast Ovarian Cancer (HBOC) associated with BRCA1 & 2 genes and Lynch Syndrome associated with MLH & MSH genes are the two most important hereditary gynecological cancers. Management options include surveillance for early detection or risk reducing surgeries & chemoprevention.

Recent advances section includes "Frontline Targeted Therapy in Ovarian Cancer". Anti-angiogenesis factors like bevacizumab have been incorporated in primary chemotherapy with paclitaxel and carboplatinum for advanced epithelial tumors. It prolongs the progression free survival. Other agents like PARP inhibitors have shown promising results when combined with frontline chemotherapy in phase III trials.

Controversy about "Routine Lymphadenectomy in Endometrial cancers" has propelled us to review the evidence on routine, selective or sentinel node sampling in endometrial cancer. This article throws light on the best possible course of action with regards to lymphadenectomy. Grade 1 to 2 Endometriod tumors of size <2cm with less than 50% myometrial involvement do not require lymphadenectomy. For others the choice is between routine lymphadenectomy or sentinel lymph node biopsy.

Case approach section deals with management of "Pregnancy with Cervical Cancer". The article has systematically delineated the best management plan based on period of gestation and the stage of the disease. In early pregnancy less than 22 weeks, ESGO recommends lymphadenectomy for Stage 1a2 & B1 tumors. If lymphnode is negative, simple trachelectomy with continuation of pregnancy is recommended whereas for node positive tumors termination of pregnancy followed by definitive management is done. For women diagnosed after 22-24 weeks lymphadenectomy is not recommended.

The maze of knowledge-crossword and the pictorial quiz will keep you interested.

Journal scan has done a review on treatment options in GDM and targeted therapy in epithelial ovarian cancers.

We are immensely grateful to our contributors for the prompt submission of their immaculate articles.

We look forward to any suggestions and comments from our readers

Happy Reading !!!

Editorial Team

BEST PRACTICES

Optimising Outcome in Pregnancy with Diabetes

Rini Pachori[1], Asmita M Rathore[2]

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Dr Asmita M Rathore

Pregnancy is an unrealized window of opportunity for primary prevention of diabetes. The aim of the St Vincent's declaration in 1989 was to achieve pregnancy outcomes in women with diabetes that approximate those of women without diabetes but unfortunately, this goal has not been achieved.[1] Approximately a third of women diagnosed with type 2 diabetes (T2DM) have a history of gestational diabetes mellitus (GDM). Specialist centers worldwide strive to optimize care of women with established diabetes before and during pregnancy to minimize the risk of poor pregnancy outcome. These interventions include: pre-pregnancy care, tight pre- and antenatal glycemic control, management of gestational weight gain and optimal intra and postnatal care. However, these interventions are difficult to achieve in the routine clinical environment for a number of reasons, including socioeconomic status, education, and competing healthcare resource utilization.

Pre-Pregnancy Interventions

Goal is to improve the outcome of pregnancies complicated by pre-existing Type 1 and Type 2 diabetes to equate with that of pregnancies without diabetes. Pre-Pregnancy counseling and planning have been shown to have the following benefits: reduce congenital malformation rate by up to 75%, reduce perinatal mortality by up to 80% and reduce pre-term delivery by up to 50%.[2]

Counseling Points

A. **Pre-existing Diabetes mellitus**

1. **Timing of pregnancy** – Pregnancy should be planned after achieving optimal diabetes control. The American Diabetes Association (ADA) defines an optimal preconceptional control as pre-prandial glucose–70-100 mg/dL, post-prandial–100-129 mg/dL and HbA1c of <7%. The HAPO Study Cooperative Research Group demonstrated that adverse perinatal outcomes were related to hyperglycemia in pregnancy resulting in fetal hyperinsulinemia, macrosomia and birth trauma.[3] Thus achieving euglycemia is the key. Optimising glycemic control includes-
   - Oral hypoglycemic agents(OHA's) – These are simple to administer, convenient, pain free, and cost effective. Glyburide and metformin are classified by the FDA as Category B drugs for use in pregnancy and are the only 2 OHA's which can be safely used in pregnancy after 20 weeks of gestation. Ideally, pregestational diabetics should be switched over to insulin but patients well controlled on these 2 drugs may continue them after counseling. Although Acarbose has also been categorized as FDA category B drug, research is needed before clinical use.
   - Insulin-remains the standard of care for type 1 and 2 diabetics, and uncontrolled GDM during pregnancy. Regular insulin, insulin aspart, insulin lispro, and NPH have the most human pregnancy data. All types of insulin are FDA category B drugs except–Glulisine, Degludec and inhaled human insulin which are category C. There is insufficient human pregnancy data for Glargine.[4]
2. **Prenatal folic acid use** – Peri-conceptional folic acid 5mg is recommended as diabetes increases the risk of neural tube defects by 3 fold.[5]
3. **Weight control**- 'DIABESITY' i.e diabetes plus obesity is a spreading pandemic. American college of obstetricians and gynaecologists(ACOG) 2014 guidelines on Pregnancy and obesity recommends a 5-7% weight loss before conception by modest caloric restriction along with 60 minutes of moderately active or 30 minutes of vigorously active exercises on most days of the week. Obesity also increases the risk of miscarriage, congenital anomalies, preterm delivery, pregnancy induced hypertension, GDM per se, cesarean section, sleep apnea and post-operative complications.[6]
4. **Stabilizing complications**- Discuss the potential effects of pregnancy on diabetes complications. Explain that ongoing complication screening will be needed in pregnancy: eye and renal status at least each trimester, review with renal physician and cardiologist on individual need. Blood pressure will need ongoing monitoring. An end organ workup and electrocardiogram(ECG) to check for cardiac complications are recommended. The following investigations are required pre-conceptionally-
   - *Eyes* – Pregnancy is a risk factor for progression of diabetic retinopathy. The National institute of health and care excellence(NICE) 2008 guidelines recommend fundoscopy–pre-conceptionally, at the 1st ANC visit and then at 28 weeks. The Royal college of obstetricians and gynaecologists(RCOG) 2012 guidelines clearly state that proliferative retinopathy is

not a contraindication to vaginal birth. If it is present requiring laser, treat prior to pregnancy to prevent progressive deterioration

- *Kidneys* - In general, pregnancy does not worsen diabetic nephropathy. Current ADA guidelines recommend any of these 3 tests to measure urinary albumin excretion- 24 hour (<30mg/24 hours), timed(<20mg/minute) and untimed random albumin creatine ratio(<30 mg/mg creatine). A baseline glomerular filtration rate is also recommended patients with type 1 diabetes with duration of 5 years, in all patients with type 2 diabetes with comorbid hypertension. If microalbuminuria is present there is an increased risk of preeclampsia, prematurity and fetal growth restriction. Generally stop ACE inhibitors and A2 receptor antagonists pre-pregnancy, unless risk:benefit ratio indicates otherwise.
- *Neuropathy* – peripheral neuropathy does not appear to be a specific concern in pregnancy, whereas autonomic neuropathy if present, may lead to hyperemesis, inadequate nutrition and significant difficulties with glucose control.

5. **Contraception** - Contraception should be advised in antenatal period to increase the uptake of contraception in postpartum period. In patients with history of GDM, oral contraceptive pills, progesterone only pills, intrauterine copper containing devices (IUCD's), DMPA are all medical eligibility criteria (MEC) 1 and can be safely advised. In patients with diabetes mellitus only copper containing IUCD's are MEC 1, rest all are MEC 2. Similarly in diabetics with microvascular complications, only copper containing IUCD's are MEC1, and rest are MEC 3.[7]
6. **Behavioral modification for improving nutrition and exercise –** Patients need to be counseled about nutrition and exercise at every antenatal care(ANC) visit.
7. **Multi-disciplinary approach**- Involving a physician, dietitian, obstetrician ± renal physician ± cardiologist ± ophthalmologist is important in individualized cases.
8. **Type 1 Diabetes –**They require evaluation for the following associated conditions -
   - Check Thyroid function tests and thyroid antibodies as 10-20% women with Type 1 diabetes also have autoimmune thyroid disease. If they require thyroxine replacement or if thyroid antibodies are positive they will need ongoing TFT monitoring.
   - Screen for coeliac disease – **Prevalence of celiac disease is about 1% in the Indian population but increases in diabetics to about 10%.[8] Screening is by Tissue Transglutaminase Antibodies which** will be positive in about 98% of patients with celiac disease who are on a gluten-containing diet.
9. Relative contraindications to pregnancy include retinopathy requiring laser treatment until treatment is undertaken or eye status is stablized, nephropathy with serum creatinine >200µmol/l or pre-existing cardiac disease, especially previous myocardial infarction.

B. **Patients with history of GDM in a previous pregnancy**- They should try to reach a normal weight and engage in modest exercise. They should be sensitized about the 40% risk of recurrence of GDM in next pregnancy. According the Government of India 2018 guidelines on GDM, fasting levels of < 100mg/dL and 2 hour post prandial levels < 140mg/dL are desired pre-conceptionally.[9]

Antenatal Care

The mother and fetus are at risk due to both hyperglycemia and hypoglycemia and thus the pillar of antenatal care is maintaining a state of euglycemia.

Maternal care – Morbidity and mortality rates are higher among pregnant women with diabetes. Obstetric complications include antepartum (pre-eclampsaia [12.7%], preterm labor [10% in GDM & 25.5% in pre-gestational], PPROM, polyhydroamnios, chorioamniotis and recurrent pregnancy losses)and medical complications(diabetic ketoacidosis, non ketotic hyperosmolar coma, infections, microvascular complications progression or macrovascular complications).[10]

1. **Frequency of visits** - In patients with type 1 and 2 diabetes, prenatal visits begin as soon as pregnancy is recognized and the frequency of visits is determined by degree of glycemic control. For patients with history of GDM, a 75 grams Oral glucose tolerance test(OGTT) at first visit followed by repeat testing at 24-28 weeks with a minimum 4 weeks gap is advised. Cutoff is taken at 140 mg/dL irrespective of fasting status or gestational age.[9] Routine appointments at every 2 weeks, with the frequency increased/decreased as deemed necessary.
2. **Diet** -Generally, 3 meals and 3 snack /day (55% carbohydrates, 25% fats and 20% proteins) are recommended, with emphasis on consistent timing. For women newly diagnosed with GDM, 2 weeks of diabetic diet and exercises for 30 minutes/day are advised before testing for 2 hour post-prandial sugars. Total energy requirement for a sedentary, moderate and heavy worker are 2250, 2580, 3200 kilocalories respectively. For patients with BMI <18.5 kg/m2 – an additional 500 kilocalories a day are recommended and for women with BMI > 25 kg/m2 – 500 kilocalories per day are deducted from the baseline requirement.[9]
3. **Pharmacotherapy–** Amongst the OHA's only Metformin and Glyburide are safe in pregnancy and even glyburide has an inconsistent profile. As metformin crosses the placenta, the potential

effects of metformin on growth of the children were studied in The Offspring Follow-Up(TOFU) study which demonstrated no long term side effects.[11]

4. **Insulin-** Insulin therapy is recommended in diabetics before 20 weeks at blood glucose levels > 120mg/dL or uncontrolled diabetics on OHA's after 20 weeks. In patients diagnosed with GDM, if 2 hour postprandial values > 200 mg/dL – 8 units insulin mixtard is started. If gestation >20 weeks, we can choose between metformin or insulin, for postprandial sugars <120 mg/dL– continue PPBS monitoring. These doses have to be titrated by checking FBS and PPBS every 3rd day.[9] Women and their family members should be cautioned about the dangers of hypoglycemia(blood sugar <70mg/dL) during exercise and at night. Newer insulin delivery methods include- insulin pumps. These are small computerized devices that deliver insulin in two ways: in a continuous dose or as a bolus dose, around mealtime. This delivery system most closely mimics the body's normal release of insulin.[12] Non-injectable insulins include Human insulin inhalation powder and ORMD-0801 which is an oral insulin that has completed its phase I trials, both of which are currently unavailable in India.[13,14]
5. **Monitoring**– Maternal monitoring includes blood sugar testing and close screening for complications.
   - **A.** Blood sugar monitoring – Self blood glucose monitoring using a calibrated glucometer is encouraged. For diabetics controlled on diet or OHA's a 4 point profile once a week(fasting and post meals) whereas for diabetics on insulin, a 7 point profile once a week(fasting, pre and post meals, 2 AM) are recommended. A 2016 Cochrane database review found few differences in outcomes between very tight and tight-moderate glycaemic control targets in pregnant women with pre-existing type 1 diabetes. There was evidence of harm(increased pre-eclampsia, caesareans and birthweights greater than 90th centile) seen for 'loose' control(FBG above 126mg/dL).[15]
   - **B.** Monitoring for complications: HbA_{1c} level should be checked every trimester. BP and urine albumin monitoring is recommended at every visit. Fundoscopy at first antenatal visit and then at 28 weeks is advised for pregestational diabetes. Baseline ECG to rule out any cardiac complications. A multi-disciplinary approach with structured regional diabetes/antenatal clinics with dedicated nurse specialists, obstetricians and physicians along with development of local guidelines are also required.
6. **Patient education-** It is very important to reinforce knowledge at each antenatal visit. Development of patient information booklets and Diabetes-in-pregnancy app for smart phones as well as prerinatal website can all go a long way in patient education.

FETAL MONITORING– Most of the fetal complications are attributed to sub-optimal glycemic control and are thus preventable. The following are the key points in fetal monitoring which if not totally preventable, can at least help in the early detection of any poor fetal outcome-

1. **1st Trimester**-1st Trimester screen to rule out aneuploidies. Most recent studies have shown that median PAPPA levels and ß-hCG levels are decreased in women with pre-gestational diabetes and correction factors must be applied.[16,17]
2. **2nd Trimester**– Maternal serum alpha fetoprotein levels between 16-20 weeks and a targeted level 2 sonogram between 18-20 weeks. Due to the 4 times prevalence of cardiac anomalies in pregestational diabetes, a fetal echo is recommended at 24 weeks. Congenital malformations in infants whose mother's HbA_{1c} had been 8.5 or less at <14 weeks was 3.4%, whereas for HbA1c > 8.5, it was 22.4%.[5] Malformations of major organs are predicted by elevated HbA_{1c} levels at conception and during the first 8 wk of pregnancy as majority of the organogenesis is completed by 6 weeks.
3. **Growth scans-** They are recommended between 28-30 weeks followed by at 34-36 weeks.[9] Hyperglycemia after organogenesis is a risk factor for large-for-gestational-age babies, macrosomic babies(>4,500 g), shoulder dystocia, neonatal hypoglycemia, hyperbilirubinemia, and admission to the neonatal intensive care unit. Antenatal sonographic markers for predicting shoulder dystocia are unreliable but include- Abdominal circumference – Biparietal diameter > 2.6cm , and humeral fat pad thickness. A cheek to cheek diameter > 7.9cm is associated with a 94% risk of cesarean section.[18]
4. **Fetal wellbeing**- Daily fetal movement counts are advised specially nearing term. Antenatal testing with Nonstress tests or Biophysical profiles is usually started from 32 weeks onwards weekly or earlier if indicated.
5. **Timing of delivery**- RCOG recommends induction of labor for uncomplicated GDM on diet at 40 weeks and for GDM on pharmacotherapy or pregestational diabetes at 38 weeks. Government of India 2018 guidelines recommend an elective cesarean section at 39 weeks for macrosomic babies.[9]

Intrapartum Interventions

Intrapartum complications may be maternal (Diabetic ketoacidosis, chorioamnionitis, nonketotic coma, infections, obstructed labor, cesarean delivery) or fetal (fetopelvic disproportion, risk of shoulder dystocia, sudden unexplained stillbirth, fetal heart rate irregularities).

1. **Planned induction of labor-** The woman eats her usual diet the night before and takes her usual insulin/OHA dose. The morning dose of metformin or insulin is omitted, morning fasting glucose and serum electrolytes measured and patient shifted to labor room after consents. Soft oral diet and fluids

are given and 5 U insulin in 500 ml of 5% dextrose started at 100 ml/hour. Thereafter blood sugars and urine ketones checked 4 hourly.

- Target dextrose– 80-140 mg/dL
- Dextrose < 80mg/dL– plain 5% dextrose at 100ml/hour
- Dextrose >140mg/dL– insulin as per sliding scale

2. **Spontaneous labor-** Management is the same, except that if intermediate-acting insulin was taken in the previous 12 hours, the insulin dose is decreased and initially more frequent glucose monitoring required. For women who have fever, infection, or other complications and for obese women who have type 2 and have require >100 units of insulin/day before pregnancy, the insulin dose is increased.
3. **Diabetic ketoacidosis (DKA)**– It is a life threatening complication to both the mother and the fetus. The treatment of DKA includes correction of dehydration(typical water deficits are 5-10 L), hyperglycaemia and electrolyte imbalance(the most dangerous of which is hypokalaemia) combined with treatment of the provocative illness and frequent maternal monitoring.
4. **Chorioamnionitis-** A triple antibiotic regime along with vitals and temperature charting are required. Insulin dose may need to be increased.
5. **Shoulder dystocia**- It occurs in 0.5% to 2% of infants weighing less than 4000 grams but in 5% to 10% in deliveries of infants weighing between 4000 and 4500 g.[19] A cut-off value of abdominal circumference ≥350 mm, in predicting of fetal macrosomia, had a sensitivity and specificity of 78.7% and 76.8% respectively. Immediate neonatal injury was apparent in 47% of infants with shoulder dystocia after prolonged second stage.
6. **Cesarean section** – Absolute indication is only macrosomia > 4.5kg.[9]

POSTNATAL CARE– Immediate postpartum complications include uterine atony causing postpartum hemorrhage, perineal injuries due to instrumental delivery or macrosomic baby or both, wound sepsis and puerperal sepsis.

1. **Glycemic control-** After delivery, loss of the placenta, which synthesizes large amounts of insulin antagonist hormones throughout pregnancy, the insulin requirement decreases immediately. For all diabetics, a day 3 blood sugar fasting and postprandial should guide further treatment. For uncontrolled diabetics and for post-cesarean patients, insulin according to sliding scale can continue for 24 hours post partum. Pregestational diabetics should be discharged on their pre-pregnancy OHA/insulin. In patients with GDM-2 hour oral glucose tolerance test with 75 g of glucose at 6 weeks postpartum is done to determine whether diabetes has resolved. If value is less than 140 mg/dL annual testing with PPBS is recommended.
2. **Breastfeeding-** Caution should be advised regarding maternal hypoglycemia associated with breastfeeding. In the mother, breastfeeding has been suggested to reduce the incidence of type 2 diabetes mellitus, metabolic syndrome and cardiovascular diseases. Breastfeeding also reduces the insulin/OHA requirement or eliminate it altogether.
3. **Postpartum infections**- The most common infection is that of the uterus and surrounding tissues known as puerperal sepsis, postpartum metritis, or postpartum endometritis. Judicious use of antibiotics and maintaining strict asepsis both intra and postpartum are the key to avoiding it.
4. **Contraception –**It should always be offered to the patient. IUCD's, Mirena, progesterone only pills and DMPA injections after 3 weeks-are all Medical eligibility criteria 1 and thus can be recommended. OCP's are MEC 3 and thus should be avoided immediate postpartum in uncontrolled diabetics.
5. **Follow-up–** It ranges from yearly to 2–3 yearly and more frequent follow up in high risk groups. Education and lifestyle modifications must be advised and pre-pregnancy counseling and optimization of sugar levels before the next conception should be told.
6. **Neonatal complications**- Hypoglycemia is the most common neonatal complication that occurs in diabetic pregnancies, defined for a healthy newborn as blood glucose < 45 mg/dL. Also after the section of the umbilical cord, the deprivation of maternal nutrient flow, can lead to hypocalcemia(Ca++ <7 mg/dL) and hypomagnesiemia(Mg++ <1.5 mg/dL).Chronic hyperinsulinemia can lead to hyperbilirubinemia -two-fold more frequently found in newborns of mothers with diabetes. Polycythemia is diagnosed by a venous hematocrit > 65% or hemoglobin > 20 g/dL. This occurs in about 30% of newborns of mothers with diabetes.
7. Long term consequences –
   - Maternal- GDM has a further progression to type 2 Diabetes mellitus in 15.7% cases at 10 year follow up.[20] Sivaraman et al reported that the risk of developing diabetes was 6.9% at five years and 21.1% at ten years following the initial diagnosis of GDM.[21]
   - Neonates - U or J-shaped relationship between birth weight and adult obesity and metabolic disease demonstrating that both a limited or excessive nutritionally intrauterine environment can lead to postnatal obesity and related chronic diseases. This might result in a vicious cycle that could explain the great increase in the rates of obesity, gestational diabetes and type 2 diabetes seen in the last decades.

Going forward, we need to target women before pregnancy in order to optimize BMI and introduce a structured weight management program during pregnancy to avoid excessive gestational weight gain, both of which will be associated with improved outcomes. Finally new technologies, in particular real-time continuous glucose monitoring and insulin pump

therapy, are likely to help a greater number of women achieve optimal glycemic control. Such technologies need to be freely available in clinical practice.

Key Points

1. Women with history of GDM in a previous pregnancy are at increased risk of developing GDM in subsequent pregnancies and of developing T2DM later in life. Interventions include: pre-pregnancy care, pre-pregnancy folic acid, tight pre- and antenatal glycemic control, and management of gestational weight gain.
2. The aim of pre-pregnancy planning is to improve the outcome of pregnancies complicated by pre-existing Type 1 and Type 2 diabetes to equate with that of pregnancies without diabetes. A target glycosylated hemoglobin (HbA1c) of 6.5% before a positive pregnancy test, weight loss if BMI is >25 kg/m^2, and screening for microvascular complications form the tri-core of pre-pregnancy counseling.
3. Antenatal care includes strict glycaemic control using diet, insulin or insulin pumps and OHA's and monitoring for pregnancy induced hypertension or microvascular disease progression. Fetal monitoring must include detailed anomaly scans and growth scans to rule out macrosomia, as well weekly biophysical profile starting from 32 weeks.
4. Intrapartum complications include shoulder dystocia, difficult or instrumental delivery, perineal lacerations or post partum hemorrhage and diabetic ketoacidosis. Cesarean section is advised for obstetric indications or for macrosomic babies weighing > 4.5 kgs.
5. Postpartum care must include adjustment of insulin or OHA dose, caution for hypoglycemia during breastfeeding, contraception advice, and long term follow-up and lifestyle modifications.
6. Finally, a multidiscliplinary approach including an obstetrician, physician, dietician, ophthalmologist, nephrologist and pediatrician must be incorporated at all steps.

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RECENT ADVANCES

Oral Hypoglycemic Agents in Management of Diabetes in Pregnancy – What does evidence say

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Diabetes in pregnancy is on the rise globally and more so in India mainly due to genetic factors and rapidly changing lifestyle issues. The initial management consists of medical nutritional therapy, which has to be supplemented with pharmacological agents in cases where the glucose targets are not met. The gold standard for pharmacological management of diabetes in pregnancy is considered to be insulin. However of late, oral hypoglycemic have established a definite place in the management of diabetes in pregnancy mainly due to its ease of administration, comparable efficacy, lower cost and good patient compliance. This article will review the role of OHA as compared to insulin and also compare the two most commonly used OHA in pregnancy, namely metformin and glyburide.

Traditionally, insulin therapy has always been considered the gold standard for management of women with gestational diabetes because of its efficacy in achieving tight glucose control and high safety profile as it does not cross the placenta. The use of oral hypoglycemic agents was discouraged as a few case reports and small-scale studies found them to increase the risk of fetal anomalies.[1] When in depth study was done it was found that it is the high blood sugars rather than the drug which increases the rate of fetal anomalies.[2]

Presently, oral hypoglycemic agents are gaining recognition as a safe and effective alternative to insulin. Ease of administration (tablet form) increases the compliance and improves patient satisfaction. However in certain conditions as shown in Table 1 the drug of choice remains insulin and OHAs are not considered as primary treatment in these situations.

Table 1: Absolute indications for insulin in pregnancy

High HbA1c
Ketonuria
Significant medical morbidity
Associated renal dysfunction
Associated hepatic dysfunction
Significant obstetric morbidity
Macrosomia
Intrauterine growth retardation
Hydramnios
Expected deterioration of glycemia control
Antenatal corticosteroid therapy

OHA have been classified into eight classes out of which Sulfonylureas and Biguanides have been used in women with gestational diabetes mellitus. Table 2 shows their mechanism of action, adverse effects including that in pregnancy (the FDA has recently withdrawn the drug classification categories-A, B, C, D, X for pregnancy).

Safety of Oral Hypoglycemic agents-In the past decade, studies have suggested there is no association between oral hypoglycemic agents and congenital malformations. The HAPO Study Cooperative Research Group stated that the adverse perinatal outcomes were proportional to hyperglycemia in pregnancy and not as a result of oral hypoglycemics.[3]

Table 2: Classification of OHA

Class	Mechanism of Action	Adverse Effect
Sulfonylureas **First generation** · Acetohexamide · Chloropropamide · Tolbutamide **Second generation** · Glipizide · Glyburide · Glimepride	Stimulate the release of insulin from pancreatic B-cells	Hypoglycemia Prolonged neonatal hypoglycemia if given in 3rd Trimester Human data suggest low risk for fetus
Meglitinides · Repaglinide · Nateglinide	Stimulate the release of insulin from pancreatic B-cells	Hypoglycemia
Biguanide · Metformin	-Decreases hepatic glucose output -Increases insulin sensitivity (muscle, liver) - Decreases amount of free fatty acids (anti-lipolytic effect)	Diarrhea, metallic after taste, nausea Human data suggest low risk for fetus
Thiazolidinediones · Rosiglitazone · Pioglitazone	-Increase insulin sensitivity (muscle and liver) -Decrease glucose production by the liver	Weight gain, fluid retention Pioglitazone: increased risk of bladder cancer Rosiglitazone: increased risk of non-fatal heart attack
Alpha-glucosidase inhibitors · Acarbose · Miglitol	Slows and limits the absorption of glucose. It inhibit GI enzymes, alpha-glucosidases, which convert carbohydrates into monosaccharides.	Bloating and flatulence
Dipeptidyl-peptidase-4 (DPP-4) inhibitors	Intensify the effect of intestinal hormones (incretines) involved in the control of blood sugar	Pharyngitis, headache

Glucagon-like peptide-1 agonist (GLP-1)	Mimic the effect of certain intestinal hormones (incretines) involved in the control of blood sugar	Nausea, diarrhea, vomiting
Sodium glucose cotransporter 2 inhibitors (SGLT2)	Help eliminate glucose in the urine	Genital and urinary infections, frequent urination

Metformin

Metformin is a biguanide antihyperglycemic approved for management of type 2 diabetes mellitus when hyperglycemia cannot be managed by diet and exercise alone. Unlike sulfonylureas, it does not produce hypoglycemia in either normal subjects or patients with type 2 diabetes. Its mechanism of action is shown in Table 2. The starting dose of metformin is 500 mg twice daily; maximum dose recommended is 2500mg. Metformin has been shown to pass freely across the placenta but it is not teratogenic

Efficacy of Metformin as compared to insulin

A number of studies have demonstrated adequate glycemic control on treatment of GDM with metformin and no increased risk of adverse perinatal outcomes.[4-7]

In a recent retrospective case control study, there was no difference in mode of delivery, birth weight or incidence of large- or small-for-gestational-age neonates between the 2 groups treated by metformin and insulin. The incidence of adverse perinatal outcomes was similar between groups. They concluded that metformin is a useful alternative to insulin in the management of GDM.[8]

In another recent meta-analysis of three randomized controlled studies comprising of women with GDM, average fasting and post-prandial glycemic levels were slightly lower in the metformin group than insulin group, but the difference was not statistically significant. There was no significant difference between the two groups in average HbA1c% level at gestational 36-37 week. The same study also concluded that average weight gain and pregnancy-induced hypertension rates in women after enrollment was significantly lower in the metformin group than in insulin group . There was no significant difference in the rate of pre-eclampsia between the two groups. Average gestational ages at delivery was significantly lower in the metformin group. Pre-term birth rate was significantly more in the metformin group. There was no significant difference in the cesarean delivery rate between the two groups[9].

Metformin for prevention of pregnancy complications

Metformin is also used in the treatment of polycystic ovary syndrome (PCOS). When women on metformin become pregnant, the drug can be continued in the first trimester as it is seen that the drug is not teratogenic. Even though some studies have found that the miscarriage rate with metformin is lower, this has not been seen in a meta-analysis of 17 trials[10]. Use of metformin in the preconception period reduced the incidence of gestational diabetes in some observational studies but this was not confirmed in a trial of 273 pregnancies among 257 women with PCOS who were randomly assigned to receive metformin (2000 mg/day) or placebo from the first trimester until delivery. There was no significant difference in prevalence of GDM between groups (metformin 17.6 percent versus placebo 16.9 percent)[11]. However it has been seen in clinical practice that many obstetricians continue metformin in pregnancy for the above mentioned benefits.

Glyburide

Glyburide is a second generation oral sulfonylurea hypoglycemic agent. It acts by enhancing the release of insulin from the pancreatic beta cells, therefore for its action, some degree of pancreatic insulin-releasing function is required. It is well-absorbed following oral administration and is metabolized by the liver. The initial dose of glyburide is 2.5-5.0 mg once or twice a day with a maximum dose of 20 mg/day. The overall incidence of hypoglycemia from glyburide is 1-5%

Placental transfer: glyburide has been demonstrated to have minimal transfer across the human placenta. Glyburide is not present in the milk of lactating mothers when measured in vivo and *in vitro*

A systematic review which included three RCTs (478 participants) on comparison of glyburide with insulin found no differences in glycemic control including fasting blood glucose or 2-hour post-prandial glucose.[12] One RCT found significantly lower fasting blood glucose and 2-hour post-prandial glucose in insulin group as compared to glyburide group[13]. A recent prospective comparative study from India, which compared 32 patients each in glyburide and insulin group has found no significant difference in glycemic control[14].

Metformin vs Glyburide

Studies have shown that both metformin and glyburide are equally effective and have more or less similar maternal and fetal outcomes.

Silva *et al*. evaluated the perinatal impact of metformin and glyburide in the treatment of GDM. Patients were randomized to use metformin (n = 104) or glyburide (n = 96). They found significantly lower weight gain in metformin group. There was no significant difference in the percentage of cesarean deliveries, gestational age at delivery, number of newborns LGA, neonatal hypoglycemia, admission to intensive care unit, and perinatal death between the two groups. There was significant difference in birth weight of neonate (lower in metformin group) and neonatal blood glucose levels at the 1st hour after birth (lower in glyburide group).[15]

Moore *et al*. compared the efficacy of metformin with glyburide for glycemic control in gestational diabetes. Patients with gestational diabetes who did not achieve glycemic control on diet were randomly assigned

to metformin (*n* = 75) or glyburide (*n* = 74) as single agents. In the patients who achieved adequate glycemic control, the mean fasting and 2-hour post-prandial blood glucose levels were not statistically different between the two groups. However, 26 patients in the metformin group (34.7%) and 12 patients in the glyburide group (16.2%) did not achieve adequate glycemic control and required insulin therapy (significant difference). The incidence of maternal hypoglycemia and pre-eclampsia was not different between the two groups. Cesarean deliveries were significantly higher with metformin. The mean birth weight of babies in the metformin group was significantly smaller than the mean birth weight of babies in the glyburide group. Other neonatal outcomes (LGA; neonatal hypoglycemia; NICU admission and shoulder dystocia) did not differ in the two groups.[16]

Acarbose

Dose: Initial acarbose dosing is 25 mg orally three- times daily, increased to a maximum of 100 mg orally three-times daily.

Placental transfer: Acarbose does not cross the placenta.

Glucosidase inhibitors (acarbose) reduce intestinal absorption of carbohydrates. It lowers postprandial glucose values. Less than 2% of a dose is absorbed as active drug in adults. Animal studies have shown that it is not teratogenic in pregnant rats or rabbits. However there is very limited data about its use in pregnancy.

Meglitinides

Meglitinides are insulin secretogogues like sulfonylurea. Their action is similar to sulfonylurea but via different receptor. There is no data regarding the use of nateglinide during pregnancy. Until further data is available, these drugs should not be used in pregnancy. A randomized controlled trial with repaglinide and insulin demonstrated that the pre and postprandial glucose levels were the same in the treatment and the control groups and there was no difference in the fetal and neonatal outcome

Thiazolidinediones

Thiazolidinediones act on the peroxisome proliferator-activated receptor and thus reduces the insulin resistance. The pharmacodynamics follows the same principle as glyburide.

Placental transfer: Rosiglitazone crossed the placenta

Use of thiazolidinediones, glinides and glucagon-like peptide 1 agonists during pregnancy are considered experimental.

Society/National recommendations for OHA use in pregnancy

National Institute for Health and Care Excellence (NICE) guidelines[17]

- Consider metformin and glyburide safe in pregnancy and lactation
- Metformin can be offered to women with gestational diabetes if blood glucose targets are not met with diet and exercise within 1–2 weeks unless contraindicated or unacceptable to the patient
- Glibenclamide can be offered to women with gestational diabetes in whom blood glucose targets are not achieved with metformin but who decline insulin therapy or who cannot tolerate metformin.

American College of Obstetricians and Gynaecologists[18]

- In women who decline insulin therapy or who the obstetrician or other obstetric care providers believe will be unable to safely administer insulin, or for women who cannot afford insulin, metformin is a reasonable alternative choice. (Level B)
- Glyburide treatment should not be recommended as a first-choice pharmacologic treatment because, in most studies, it does not yield equivalent outcomes to insulin or metformin. (Level B)

Endocrine Society Recommendations[19]

- Glyburide (glibenclamide) is a suitable alternative to insulin therapy for glycemic control in women with gestational diabetes who fail to achieve sufficient glycemic control after a 1-week trial of medical nutrition therapy and exercise except for those women with a diagnosis of gestational diabetes before 25 weeks gestation and for those women with fasting plasma glucose levels >110 mg/dL (6.1 mmol/L), in which case insulin therapy is preferred.
- Metformin therapy may be used for glycemic control only for those women with gestational diabetes who do not have satisfactory glycemic control despite medical nutrition therapy and who refuse or cannot use insulin or glyburide and are not in the first trimester.

Government of India Recommendations[20] (Feb 2018)

- Metformin or Insulin therapy is the accepted medical management of pregnant women with GDM not controlled on MNT. Insulin is the first drug of choice and metformin can be considered after 20 weeks of gestation for medical management of GDM. Before 20 weeks insulin is to be started if MNT fails
- Metformin can be started at or beyond 20 weeks of pregnancy, if MNT has failed to control her blood sugar. If the woman's blood sugar is not controlled with the maximum dose of metformin (2 gm/day) and MNT, Insulin is to be added. The dose of metformin is 500 mg twice daily orally up to a maximum of 2 gm/day.

Conclusion

Metformin and glyburide are oral hypoglycemic agents that can be used in pregnancy. Metformin has lately been recommended as an optional first line treatment (along with insulin) in women with gestational diabetes who do not respond to MNT and are more than 20

weeks gestation by the Government of India. The oral hypoglycemic agents are affordable and safe option for women with gestational diabetes mellitus not controlled on medical nutrition therapy or those who refuse to take insulin.

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Forthcoming Events

- 40th Annual Conference of AOGD, on 24th -25th November, 2018 India Habitat Centre.
- Preconference workshops
  22nd November 2018: Fetal Surveillance, Colposcopy (live workshop), Hysteroscopy.
  23rd November 2018: Operative Obstetrics, Ovulation induction and Follicular Tracking, Pelvic Reconstructive Surgery
- Next Monthly Clinical Meeting on 30th November, 2018 at MAMC & LNJP Hospital.
- Regional GCH Asia Pacific International Hysteroscopy Congress IHC 2018 on 1st-2nd December at Crown Plaza Gurgaon. Contact: Dr Rahul Manchanda 9810017651 & Dr Richa Sharma 7011484180
- CME on Recent Updates in Obstetrics & Gynaecology organized by the Multidisciplinary Committee AOGD with ICOG on 9th December, 2018, 10:00am to 5:00pm Contact: Dr A G Radhika 9818065527

CONTROVERSY

Are We Over Treating Subclinical Hypothyroidism in Pregnancy


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Introduction

Pregnancy has a profound effect on thyroid gland function, and thyroid disease is common in pregnancy, with an estimated 300,000 pregnancies affected by thyroid disease in the United States annually. There is insufficient evidence to recommend for or against universal screening for abnormal thyroid-stimulating hormone (TSH) concentrations in early pregnancy or preconception. However, TSH screening is recommended for women planning assisted reproduction or those known to have positive thyroid autoantibodies. [1]

Changes in thyroid physiology during pregnancy result in the normal range of thyroid stimulating hormone (TSH) being lower than among non-pregnant adults. The recommended fixed upper threshold for TSH concentration is 2.5 mIU/L during the first trimester and 3.0 mIU/L during the second and third trimesters.

Subclinical hypothyroidism is defined by an increased TSH but a normal T4. The overt hypothyroidism should be treated; especially when diagnosed during pregnancy in the mother, otherwise there are problems during pregnancy and it interferes with normal development of the baby. A recent meta-analysis of 18 cohort studies found that pregnant women with untreated subclinical hypothyroidism are at higher risk for pregnancy loss, placental abruption, premature rupture of membranes and neonatal death compared with euthyroid women. It is less clear about the benefits of treating subclinical hypothyroidism, just as it is controversial whether there are any problems with the pregnancy if the mother is not treated.[2]

The overt hypothyroidism is diagnosed when the TSH is above 4.5-5.0 mIU/L, and a TSH greater than 2.5 mU/L is diagnostic of subclinical hypothyroidism during the first trimester of pregnancy. Subclinical hypothyroidism is associated with infertility when using a TSH in the range of 2.5-4.0 mIU/L, however, there is fair evidence that TSH levels greater than 4.0 mIU/L is associated with miscarriage. There is also fair evidence that treatment of subclinical hypothyroidism with thyroid hormone replacement when TSH levels are greater than 4.0 mIU/L is associated with improved pregnancy rates and decreased miscarriage rates. But there is limited evidence to support treatment with thyroid hormone when TSH levels prior to pregnancy are only between 2.5 and 4 mIU/L. In this setting, management options include either monitoring levels or treating when exceeds TSH >4 mIU/L, or treating with levothyroxine to maintain TSH <2.5 mIU/L.

American Thyroid Association or by the American Endocrine Society suggested following reference range for TSH: first trimester, 0.1 to 2.5 mU/l; second trimester, 0.2 to 3.0 mU/l; third trimester, 0.3 to 3.0-3.5 mU/l. [2]

Incidence

The subclinical hypothyroidism, defined as an elevated TSH concentration with concurrent normal thyroid hormone concentrations, is estimated to affect up to 15% of pregnancies in the US and 14% in Europe.[3]

It occurs in approximately 2–2.5% of pregnant women, although in China the incidence has been reported to be 4.0%, in Belgium 6.8% and in Northern Spain as high as 13.7%.

Diagnosis of SCH in Pregnancy

SCH can only be diagnosed on the basis of laboratory test results as the symptoms of both SCH and hypothyroidism are non-specific and mimic symptoms that can be associated with variations in lifestyle or those of many other conditions, like pregnancy itself. As the median TSH level is lower in the first trimester of pregnancy when compared with the non-pregnant reference range, the implementation of trimester- specific reference ranges is recommended in order to avoid misclassification of thyroid dysfunction during pregnancy.

These metabolic changes may also influence the T4 concentration that appears to be increased during the first trimester and relatively decreased during the second and the third trimesters. In developing countries the most frequent cause of hypothyroidism is represented by severe iodine deficiency, while in developed countries it is by chronic autoimmune thyroiditis (CAT). Thyroid auto-antibodies are detected in about 50% of pregnant women with SCH and in more than 80% with overt hypothyroidism. Hence in patients with SCH the measurement of thyroid peroxidase antibodies (TPOAb) is recommended to establish if the woman has thyroid autoimmunity.

Recommendations

- Trimester-specific reference ranges for TSH and T4 (total or free) should be established in each antenatal hospital setting. Local variations may occur.
- If TSH trimester-specific reference ranges are not available in that laboratory, the following reference

range upper limits are recommended: first trimester, 2.5 mU/l; second trimester, 3.0 mU/l; third trimester, 3.5 mU/l.

- TT 4 and FT4 assays are both suitable for thyroid function testing in pregnancy.
- TSH should be measured at the beginning of pregnancy if screening is performed. If TSH is elevated, FT4 and TPOAb should be determined. This will enable SCH or overt hypothyroidism to be diagnosed, in addition to identifying patients with isolated hypothyroxinaemia as well as central hypothyroidism.
- In the case of elevated TSH and negative TPOAb, TgAb should be measured. Thyroid ultrasound may be performed to evaluate hypo-echogenicity or an inhomogeneous echo pattern.

The Role of Iodine in SCH

Recommendations

- The daily iodine intake during pregnancy and lactation should be at least 250 µg and should not exceed 500 µg.
- A sufficient iodine intake is usually provided by supplementing euthyroid pregnant and lactating women with formulas containing 150 µg of iodine/day, ideally before conception.
- The effectiveness and side effects of iodine prophylaxis together with or without levothyroxine therapy in subclinically hypothyroid women should be assessed.

Adverse Effects of SCH on Mother and Child

- Current data indicate an increase in pregnancy loss, gestational diabetes, gestational hypertension, pre-eclampsia and preterm delivery in women with SCH in pregnancy.
- The association between SCH in pregnancy and impaired neuropsychological development of the offspring is inconsistent. Maternal hypothyroxinaemia is associated with impaired neuropsychological development of the offspring.

Recommendation

- Further studies are required to determine the precise effects of SCH on obstetric outcome in addition to their effects on childhood neuro-intellectual development.

Effects of Treatment of SCH and IH with Levothyroxine

Recommendations

- SCH arising before conception or during gestation should be treated with levothyroxine.
- To date, no study of intervention is available to demonstrate a benefit from treating hypothyroxinaemic women in terms of obstetric complications.
- However, levothyroxine therapy may be considered in isolated hypothyroxinaemia detected in the first trimester because of its association with neuropsychological impairment in children.

Levothyroxine therapy is not recommended in isolated hypothyroxinaemia detected in the second to third trimester.

Screening for Thyroid Hypofunction in Pregnancy

- Evidence for screening for SCH in pregnancy is equivocal.
- The decision regarding screening for SCH must be reconsidered when new high-quality evidence becomes available.
- There is no evidence that screening specifically for isolated hypothyroxinaemia is indicated.

Recommendations

- Despite the beneficial effects of levothyroxine treatment on obstetric outcome and the fact that the previously recommended targeted approach to screening thyroid function will miss a large percentage of women with thyroid dysfunction, it is not recommended to do universal screening for SCH because of the lack of grade 1 evidence.
- Note: although there are still no well-controlled studies to justify universal screening, the majority of the authors recommend universal screening because of the beneficial effects of levothyroxine treatment on unknown overt hypothyroidism, on obstetric outcome and the fact that the targeted approach will miss a large percentage of women with SCH, especially in mildly iodine-deficient women.

Practical Management of SCH in Pregnancy

Recommendations

- The recommended treatment of maternal hypothyroidism is administration of oral levothyroxine. The use of levothyroxine-T3 combinations or desiccated thyroid is not recommended.
- The goal of levothyroxine treatment is to normalize maternal serum TSH values within the trimester-specific pregnancy reference range.
- In newly diagnosed patients with SCH in pregnancy, a starting dose of 1.20 µg/kg/day is advised.
- Women with SCH and those with overt hypothyroidism desiring pregnancy should take levothyroxine in a dose to ensure a TSH level of <2.5 mU/l.
- In hypothyroid women already treated with levothyroxine before conception, the amount of increase in levothyroxine may vary from 25 to 50%,

depending on the aetiology of hypothyroidism and pre pregnancy TSH level.

- TSH values should be checked every 4–6 weeks during the first trimester and once during the second and third trimesters, and the levothyroxine dose should be adjusted as necessary to reduce TSH to <2.5 mU/l or within the trimester-specific reference range.
- Following delivery the levothyroxine dose should be reduced to the preconception dose. Women diagnosed with SCH during pregnancy with TSH less than 5 mU/l and negative TPOAb could stop levothyroxine after delivery and have thyroid function checked 6 weeks after delivery.
- Women diagnosed with SCH during pregnancy should be re-evaluated 6 months and 1 year after delivery to ascertain the continuing requirement for levothyroxine.

Effect of Treatment on Pregnancy related adverse outcomes

In a study to see the effect of treatment on adverse outcome, pregnancy loss was significantly less common among treated women (n=89; 10.6%) than among untreated women (n=614; 13.5%) (P<0.01), with a median time from TSH measurement to pregnancy loss of 3.3 (IQR 1.6-5.6) weeks. After adjustment for potential confounders of pregnancy loss—specifically age, TSH concentration, ethnicity, income, Charlson index, hypertension, obesity, history of thyroid disease, and history of pregnancy loss—treated women had a 38% lower odds of pregnancy loss compared with untreated women.

In the study by Spyridoula et.al they found that the use of thyroid hormone was associated with decreased risk of pregnancy loss, but it was also associated with increased risk of preterm delivery, gestational diabetes, and pre-eclampsia. Moreover, the benefit of thyroid hormone use on pregnancy loss was observed only among women with pre-treatment TSH concentrations of 4.1-10.0 mIU/L, not those with concentrations of 2.5-4.0 mIU/L, raising questions about the current guideline recommended threshold of 2.5 mIU/L for treating subclinical hypothyroidism when population reference ranges are unavailable.[4]

Although no published randomized clinical trials have evaluated the effect of thyroid hormone use on obstetric outcomes in subclinical hypothyroidism during pregnancy, small observational studies have suggested a potential benefit. A prospective study in China screened women in the first trimester of pregnancy for thyroid dysfunction and found an association between subclinical hypothyroidism and pregnancy loss, but it did not show any benefits of levothyroxine treatment. [5]

Another prospective study in Italy that included pregnant women with serum TSH above 2.5 mIU/L and positive thyroid peroxidase antibody concentrations found that the proportion of women with at least one adverse obstetric or neonatal outcome was significantly higher in the untreated subgroup than in a subgroup of women at similar risk who were treated. This suggested a possible benefit from levothyroxine treatment. These studies were limited by a small sample size and number of events leading to imprecision and failed to adjust for covariates of pregnancy complications.[6]

Policy Implications

Both clinicians and patients with subclinical hypothyroidism in pregnancy still face uncertainty about the effect of thyroid hormone treatment on maternal and neonatal outcomes. On the basis of the findings of Spyridoula et. al, continuing to offer thyroid hormone treatment to decrease the risk of pregnancy loss in pregnant women with TSH concentrations of 4.1-10.0 mIU/L is reasonable. Owing to the smaller magnitude of effect in the group with TSH concentrations of 2.5-4.0 mIU/L, and in light of the possible increased risk of other adverse events, treatment may need to be withheld in this group and guidelines may need to be revised. In fact, in the 2016 draft Guidelines for Subclinical Hypothyroidism in Pregnancy presented at the 2016 Endocrine Society meeting, levothyroxine treatment is recommended for women positive for thyroid peroxidase antibody if TSH is above 4.0 mIU/L (strong recommendation; moderate quality evidence) and may be considered if TSH is above 2.5 mIU/L (weak recommendation; low quality evidence) or for thyroid peroxidase antibody negative women (weak recommendation; low quality evidence).

SCH are associated with neuro-intellectual impairment of the child, but there is no evidence that maternal levothyroxine therapy improves this outcome. Targeted antenatal screening for thyroid function will miss a substantial percentage of women with thyroid dysfunction.[7]

Conclusion

To facilitate the decision making process for pregnant women with subclinical hypothyroidism, clinicians are encouraged to use a shared decision making approach. With this approach, clinicians can discuss with patients the uncertainty behind the treatment recommendations and explore what is important to them when making decisions about their health with the goal of reaching a decision about treatment that best fits their situation. The timing of thyroid hormone initiation is another important area of research. Treatment may be needed only in the first trimester of pregnancy. Finally, if treatment is started, monitoring of thyroid function and adjustment of treatment dose are essential.

Thyroid hormone use is associated with a decreased risk of pregnancy loss , especially those with TSH concentrations of 4.1-10 mIU/L. Further research is needed to understand whether a causal mechanism exists behind this association in SCH. In addition, the

increased risk of other adverse outcomes calls for randomized trials evaluating the safety of thyroid hormone treatment in SCH.

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FOGSI Awards and Prizes 2018

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Best Society Award	AOGD Team, UCMS
Chairperson, Medical Education Committee, FOGSI	Dr Abha Singh, LHMC
C G Sariayya Oration, North Zone, at AICOG 2019	Dr Manju Puri, LHMC
ICOG Usha Sariayya Oration	Dr Shalini Rajaram UCMS, GTB Hospital
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FOGSI Imaging Science Award	Dr Neelanchali Singh, LNJP, MAMC

CASE APPROACH

Pregnancy with Hyperthyroidism

Abha Singh[1], Astha Srivastava[2]

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Dr Abha Singh

Introduction

Thyroid disorders in pregnancy can range from commonly encountered hypothyroidism to hyperthyroidism which is rare. The evaluation and treatment of pregnant women with thyroid disease is similar to that of non pregnant women and men but presents some unique problems due to changes in physiology of thyroid gland in pregnancy. These changes are summarised below.

Thyroid Physiology During Normal Pregnancy

There are certain changes in physiology of thyroid gland to meet the increased metabolic rate during pregnancy. These changes include the following:

- Thyroid hormone-binding globulin (TBG) excess results in high serum total T4 and total T3 concentrations but serum free T4 or free T3 concentrations are not high.
- High serum human chorionic gonadotropin (hCG) concentrations during early pregnancy and in hyperemesis gravidarum or multiple pregnancies may result in transient subclinical or rarely overt hyperthyroidism.

Trimester-specific reference ranges - Guidelines of the American Thyroid Association (ATA) for the Diagnosis and Management of Thyroid Disease during Pregnancy and Postpartum recommend to use population-based, trimester-specific reference ranges for TSH and assay method and trimester-specific reference ranges for serum free T4 [1]. If trimester-specific reference ranges for free T4 are not available and free T4 levels appear discordant with TSH, measurement of total T4 may be done.

In the absence of population and trimester-specific normal ranges, ATA guidelines suggest the following for interpretation of thyroid function tests[1]:

- 7 to 12 weeks – Reduce the lower limit of the reference range of TSH by approximately 0.4 mU/L and the upper limit by 0.5 mU/L(corresponding to a TSH reference range of approximately 0.1 to 4 mU/L).
- Second and third trimester – There should be a gradual return of TSH towards the nonpregnant normal range.
- The upper reference range for total T4 increases by approximately 5 percent per week, starting at 7 weeks. At approximately 16 weeks, total T4 and T3 levels during pregnancy are 1.5-fold higher than in non pregnant women (due to TBG excess).

Hyperthyroidism in Pregnancy

Hyperthyroidism is defined by abnormally high levels of thyroid hormone caused by an increased synthesis and secretion of thyroid hormone from the thyroid gland. Hyperthyroidism can be overt (suppressed TSH and elevated T3 and/or T4) or subclinical (suppressed TSH and normal T3 and T4). Overt hyperthyroidism is relatively uncommon during pregnancy, occurring in 0.1 to 0.4 percent of all pregnancies[2]. Diagnosis of hyperthyroidism presenting for the first time in pregnancy often becomes difficult because the symptoms and signs of hyperthyroidism like excessive sweating, palpitations, nervousness, dyspnoea, extreme fatigue and cardiac systolic murmurs can also be seen in normal pregnancy.

Clinical manifestations - Pregnant women with hyperthyroidism present with symptoms like tachycardia, heat intolerance, palpitation and increased perspiration. Other manifestations are anxiety, hand tremor, and weight loss despite a normal or increased appetite. Specific features such as goiter and ophthalmopathy if present suggest Graves' hyperthyroidism.

Pregnancy Complications

Hyperthyroidism in pregnancy is associated with adverse fetal, maternal and obstetrical outcome.

Overt hyperthyroidism Pregnant women with poorly controlled overt hyperthyroidism, most often due to Graves' disease are at increased risk for spontaneous abortion, premature labor, fetal growth restriction, stillbirth, preeclampsia, thyroid storm and congestive heart failure[3].

- **Subclinical hyperthyroidism** –usually not associated with adverse pregnancy outcomes[4].

DIAGNOSIS — The diagnosis of hyperthyroidism during pregnancy is based upon clinical manifestations and thyroid function tests. Specific findings on physical examination such as goiter and ophthalmopathy suggest Graves' hyperthyroidism.

The diagnosis of overt hyperthyroidism during pregnancy should be based primarily upon a suppressed (<0.1 mU/L) or undetectable (<0.01 mU/L) serum TSH value and a free T4 and/or free T3 (or total T4 and/or total T3) measurement that exceeds the normal range for pregnancy.

ESTABLISHING THE CAUSE - Once the diagnosis of hyperthyroidism is established, the cause of hyperthyroidism should be determined. Graves' disease (occurring in 0.1 to 1 percent of all pregnancies) and human chorionic gonadotropin (hCG)-mediated hyperthyroidism (1 to 3 percent of pregnancies) are the most common causes of hyperthyroidism[5] in pregnancy. Other rare causes of hyperthyroidism include silent or subacute thyroiditis, toxic adenoma, toxic multinodular goiter, and factitious thyrotoxicosis.

The primary objective is to differentiate Graves' disease

from hCG-mediated hyperthyroidism. The two disorders typically can be distinguished based upon clinical findings and laboratory tests. Ultrasound with measurement of thyroidal blood flow can aid in the diagnosis of Graves' disease. The differentiating features between the two is summarised in table 1.

Condition	Clinical feature	Severity	Thyrotropin receptor Antibody (TRAb)	Doppler ultrasound
Graves disease	Presence of goiter or ophthalmopathy	Less severe during later stages of pregnancy due to reduction in TRAb	TRAb positive in 96-97% of cases	High thyroidal blood flow
hCG mediated thyrptoxicosis	Goiter or ophthalmopathy not a classical feature	Occurs transiently in first half Less severe than graves disease	TRAb usually absent	No evidence

Graves' disease - Graves› disease is a syndrome that may consist of hyperthyroidism, goiter, eye disease (orbitopathy), and occasionally a dermopathy referred to as pretibial or localized myxedema. Hyperthyroidism is the most common feature of Graves' disease. It is caused by TRAbs which activate the receptor, thereby stimulating thyroid hormone synthesis and growth of thyroid gland (causing a diffuse goiter). The presence of TRAbs in serum and orbitopathy on clinical examination distinguishes the disorder from other causes of hyperthyroidism.

hCG-mediated hyperthyroidism - During normal pregnancy, serum human chorionic gonadotropin (hCG) concentrations rise soon after fertilization and peak at 10 to 12 weeks gestation, and the levels decline thereafter. There is considerable homology between the beta-subunits of hCG and TSH. hCG has weak thyroid-stimulating activity and may cause hyperthyroidism during pregnancy.

Gestational transient thyrotoxicosis — During the time of peak hCG concentrations (10 to 12 weeks), total serum T4 and T3 concentrations increase and serum TSH concentration is reduced. This phenomenon is called gestational transient thyrotoxicosis (GTT). It occurs near the end of the first trimester, and subsides as hCG production falls (typically 14 to 18 weeks gestation).

Hyperemesis gravidarum — Women who develop hyperemesis gravidarum have higher serum hCG and estradiol concentrations than normal pregnant women. Therefore, their serum TSH concentrations are often lower than those in normal pregnant women. Some of these women have high serum free T4 concentrations and, therefore, have overt hyperthyroidism.

The thyroid hyperfunction in women with hyperemesis gravidarum usually does **not** require treatment, because it is mild and subsides as hCG production falls. If overt hyperthyroidism persists for more than several weeks or beyond the first trimester, it is probably not hCG mediated.

Trophoblastic hyperthyroidism - Hyperthyroidism can also occur with gestational trophoblastic disease due to high serum hCG concentrations and abnormal hCG isoforms.

Treatment

The goal of treatment is to maintain persistent but mild hyperthyroidism in the mother in an attempt to prevent fetal hypothyroidism. Overtreatment of maternal hyperthyroidism with thionamide antithyroid drugs (ATDs) can cause fetal goiter and primary hypothyroidism.

To attain the goal of mild hyperthyroidism, the mother's serum **free** thyroxine (T4) concentration should be maintained at or just above the trimester-specific normal range for pregnancy or the **total** T4 and triiodothyronine (T3) should be maintained at 1.5 times above the nonpregnant reference range. The serum thyroid-stimulating hormone (TSH) concentration should be below the reference range for pregnancy using the lowest possible dose of medication.

Attaining these goals requires four weekly assessment of thyroid function with appropriate adjustment of medication

Indications for treatment — Women with symptomatic, moderate-to-severe, overt hyperthyroidism require treatment.

In women who are being monitored without therapy, TSH, free T4 (if there is a trimester-specific reference range), and/or total T4 or total T3 should be measured every four to six weeks.

Therapeutic options - The therapeutic options for hyperthyroid pregnant women are limited because of the potential adverse fetal effects of the available treatments. Most women are treated with thionamides. Thyroidectomy in the second trimester can be performed in women who are unable to take thionamides because of allergy or agranulocytosis. Plasmapheresis has also been used to rapidly control hyperthyroidism in women with trophoblastic disease and severe hyperthyroidism[6].

- **Thionamides** – Thionamides are the primary mode of treatment of hyperthyroidism during pregnancy. They are actively transported into the thyroid gland, where they inhibit both the organification of iodine to tyrosine residues in thyroglobulin and the coupling of iodotyrosines
- **Beta blockers** – Beta blockers, such as metoprolol or propranolol (but not atenolol), can be used to treat tachycardia and tremor. However, long term treatment – greater than two to six weeks should be avoided because of danger of fetal growth restriction and hypoglycemia, especially with atenolol.

Choice of Thionamide

- **Diagnosed prior to pregnancy** – Women diagnosed with Graves› disease prior to pregnancy who are taking methimazole could[7]:
- Elect to have definitive therapy with surgery or radioiodine prior to pregnancy. Women should be counselled to postpone pregnancy until she becomes euthyroid.
- Switch to PTU before trying to conceive or switch to PTU as soon as the pregnancy test is confirmed.
- Discontinue methimazole with careful monitoring of thyroid function tests weekly throughout the first trimester, then monthly. This option is for women who

have already been treated with methimazole for 12 to 18 months, have a normal TSH level on low-dose therapy, and are thyrotropin receptor antibody (TRAb) negative. If hyperthyroidism recurs after discontinuation, the patient should be treated with PTU.

- **Diagnosed during the first trimester** – Women diagnosed with symptomatic, moderate-to-severe hyperthyroidism during the first trimester of pregnancy should take PTU. Patients may continue PTU for the remainder of pregnancy or switch back to methimazole at 16 weeks.
- **Diagnosed after the first trimester** – Women diagnosed with symptomatic, moderate-to-severe hyperthyroidism after the first trimester should take methimazole.

All three antithyroid drugs (ATDs) have been associated with possible teratogenic effects, but teratogenic effects are more severe with methimazole and carbimazole compared with PTU. There are numerous case series of aplasia cutis, a scalp defect, in newborns exposed to methimazole in utero[8]. More serious congenital malformations, such as tracheoesophageal fistulas, patent vitellointestinal duct, choanal atresia, omphalocele, and omphalomesenteric duct anomaly, have also been observed with maternal use of methimazole and carbimazole but not PTU[8,9]. However, mild birth defects, including preauricular sinuses and cysts and urinary tract abnormalities, have been observed after PTU[9].

Gestational weeks 6 to 10 is the period of highest risk for birth defects from exposure to thionamides. Therefore, PTU is preferred during the first trimester. However, reports of severe PTU-related liver failure have raised concerns about the routine use of PTU, including the use of PTU in pregnancy[10].

Initial dosing — To minimize the risk of hypothyroidism in the fetus, lowest dose of thionamide necessary to control thyroid function should be given:

- PTU 50 mg two to three times daily
- Methimazole 5 to 10 mg daily, or
- Carbimazole 5 to 15 mg daily

Thionamide intolerance — For women with Graves› disease who cannot tolerate thionamides because of allergy or agranulocytosis, thyroidectomy during pregnancy may be advised.

- **Radioiodine** – Radioiodine is contraindicated during pregnancy. Fetal thyroid tissue begins to function by 10 to 12 weeks and therefore can get ablated by radioiodine.

FETAL OR NEONATAL HYPERTHYROIDISM - Approximately 1 to 5 percent of mothers with hyperthyroidism caused by Graves› disease have fetuses or neonates with hyperthyroidism.

High fetal heart rate (>160 beats/minute), fetal goiter, advanced bone age, poor growth, and craniosynostosis are manifestations of fetal hyperthyroidism. Cardiac failure and hydrops may occur with severe disease/

Thyroid Storm

Thyroid storm, also referred to as thyrotoxic crisis, is an acute rare but life-threatening, hypermetabolic state induced by excessive release of thyroid hormones in individuals with thyrotoxicosis which can lead in cardiac arrest and death. A total of 20% to 30% of all cases are fatal. This hypermetabolic emergency state is associated with a high risk of maternal heart failure. Diagnosis is based on a combination of signs and symptoms: fever, tachycardia out of proportion to the fever, altered mental status like nervousness, restlessness, confusion, seizure, vomiting, diarrhea, and cardiac arrhythmia. An inciting event like surgery, infection, labor, delivery may be identified. Untreated thyroid storm can result in shock, stupor, and coma. Serum-free triiodothyronine (FT_3), FT_4, and TSH levels help confirm the diagnosis, but treatment should not be delayed for test results.

A standard series of drugs may be used to treat thyroid storm: propylthiouracil or methimazole; saturated solution of potassium iodide or sodium iodide (alternatives: Lugol's solution, lithium); dexamethasone (with a history of severe bronchospasm: reserpine, guanethidine, diltiazem); and phenobarbital. General supportive measures, as antipyretics, oxygen, and appropriate monitoring are important. The perceived underlying cause of thyroid storm should be treated.

Depending on gestational age the fetal status should be evaluated with ultrasound examination, nonstress testing and biophysical profile. Unless deemed necessary, delivery during thyroid storm should be avoided.

Postpartum Issues

Breastfeeding—Methimazole is preferred during lactation because of the concerns about propylthiouracil (PTU)-associated hepatotoxicity. Methimazole should be administered following a feed in divided doses. When the maternal dose of methimazole is >20 mg daily, infants should have thyroid function tests assessed after one and three months.

Relapse - Postpartum hyperthyroidism may be due to a relapse of Graves' disease or to postpartum thyroiditis. Women with Graves' disease who have been treated during pregnancy need careful monitoring during the postpartum period as they may experience an exacerbation.

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DISTRESS TO DE-STRESS

Creating an Anger Free Life

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Dr Mohit D Gupta

We will not be punished for our anger, we are punished by our Anger!

Our world is in the midst of an emotional meltdown. People and nations are anxious, restless, volatile and our tempers either blowing or about to blow. A recent Magazine had a cover story, "Rage Goes Viral". It describes how from east to west and north to south, a wave of rage is rocking the world and creating negativity. When we pause and ponder: what is the origin of this wave; it is clear that the nations fight, when the states, families and people are restless and have instability in mind. When our life is in turbulence and we have lost control over ourselves, then there is no smooth sailing. So, it is quite evident that anger is also prevalent in our everyday lives: There's constant anger and restlessness in our own thoughts, that trickles down in our relations and families, which further goes down to our professional and social life and to the environment

Have we ever wondered why anger is so rampant? This is because we fail to understand a simple equation of life: Which is more powerful? Situations or Our Mind.

Situations are never more powerful than our mind. The power of our mind is often unexplored, and unharnessed. Situations in our life are like waves in a sea. The waves have the power to sink the sailing ship only when they get in.

Let us today explore some simple tips to deal with a common wave that keeps coming in different intensity every day in our life. This is the wave of anger. How can we create an anger free zone and hence an anger free life?

1. **Understand that Anger is a Problem:** We have trained our mind to understand that anger is a natural emotion. It is essential. Some of us even categorize anger as good or bad anger. **Anger is a problem first and foremost because it is an ineffective way of operating in the (social) world, can occasionally backfire, and ultimately ruin relationships. S**urveys tell us that approximately 80% of day-to-day anger actually occurs with family and loved ones whom you care about. Almost every bit of research suggests that having warm (non-angry) relationships is the key to human happiness and emotional wellbeing. So, let us today understand that **Anger is Unnatural, Love is natural.**
2. **Monitor your anger:** Experts today strongly suggest that we should try to keep an anger log over at least two or three weeks. You may be surprised at what it reveals. Monitor any and every episode of anger, from fleeting moments of frustration or impatience, to extreme rage. Such a checking will automatically help us gain a little perspective and govern our responses.
3. **Think before you speak:** Our commonest outbursts happen when people are expressing anger. In the heat of the moment, it's easy to say something and then we commonly regret it later. Take a few moments to inspect your thoughts before saying anything. Such an exercise of checking our thoughts helps us to keep the anger at bay and not allow it to influence our self.
4. **Create Acceptance and let go of expectation:** Let us pause and remember one small reason why I got angry last time on others. One of the major reasons for us getting irritated and angry is people not fulfilling what we expect from them or behaving they way we want them. Expectation are always associated with pain. Change of consciousness to accepting everyone as they are, brings peace and joy in our life.
5. **Don't hold grudges:** Holding grudges is like holding rotten food in our kitchen and expecting it not to smell. It is not possible. Quite commonly, we do the same in our mind. Small little negative feelings crowd out positive feelings and we find ourselves swallowed up by our own bitterness or sense of injustice. Forgiveness is a powerful tool. But if you can forgive someone who angered you, you might both learn from the situation and strengthen your relationship.
6. **Practice Silence and Meditation:** Few minutes of silent meditation everyday empowers our mind and enables its decisive power. Practicing 10 minutes of meditation in morning and evening charges our mind for creating positive, powerful and purposeful thoughts.

Creating an Anger Free Zone:

Let us choose to create an anger free zone in our home and work place. Creating such zones will constantly remind us not to lose our inner peace and calm. This automatically will create harmony in ourselves and our relations.

Wishing you all an anger free life: today and always !!

Obituary

Dr Manjit Kochhar

Dr. Manjit Kochhar, M.B.B.S, M.D, an excellent and dynamic Gynaecologist and Obstetrician, passed away on 11th July, 2018 in New Delhi. She was born on 21st October, 1952 at Delhi. She completed her MBBS in 1974 and later specialised for MD in 1980 in Obstetrics & Gynaecology at Maulana Azad Medical College, New Delhi.

Dr Kochhar had her private practice and was affiliated with Indraprastha Apollo Hospital earlier and later was a consultant and Director of Obstetrics & Gynaecology at Fortis La Femme. Her field of interest was mainly high risk pregnancy.

She was a strong and hard working lady and was working till the last week of her life. She was widely respected and deeply loved by her patients and colleagues.

The AOGD fraternity mourns the departure of Dr. Manjit Kochhar, a clinician-par-excellence. May her soul rest in peace.

Obituary

Dr Kailash Madan

Dr. (Mrs.) Kailash Madan, M.B.B.S, M.D, veteran Gynaecologist and Obstetrician with more than 50 years of dedicated service to the profession and multitudes of patients, passed away on 31st October, 2018 in New Delhi. She completed her MBBS in 1960 from Lady Hardinge Medical College and later specialised for MD in 1970 in Obstetrics & Gynaecology at Maulana Azad Medical College, New Delhi.

Dr Madan worked at Kasturba Hospital for 12 years as a specialist before shifting to Dr Ram Manohar Lohia (RML) Hospital from 1980 till her retirement in 1995 as Consultant and Head of the Department of Obstetrics & Gynaecology. Dr Madan served as Honorary Surgeon to the President of India for three terms, from 1982-1995. After her retirement, Dr Madan was visiting consultant with several hospitals including Sukhda, Fortis La Femme and Apollo Cradle Royal in south Delhi. She specialised in Gynaecological, Laparoscopic and Hysteroscopic surgeries, management of infertility and high-risk pregnancies.

Her life's priority was always her patients, above all else.

The AOGD fraternity stand by the family of Dr. Kailash Madan in this hour of grief. May the departed soul rest in peace.

Association of Obstetricians & Gynaecologists of Delhi

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40th Annual Conference of Association of Obstetricians and Gynecologists of Delhi

Organised by

Department of Obstetrics and Gynecology

Lady Hardinge Medical College and Smt Sucheta Kriplani Hospital, New Delhi

Date: **24th, 25th November, 2018**

Venue: **India Habitat Centre, Lodhi Road, New Delhi**

Invitation

Dear Friends,

It is our proud privilege to invite you to the 40th Annual Conference of AOGD. The most sought after event by all, the Annual conference is scheduled on 24-25th November 2018 at India Habitat Center, New Delhi.

The era has come to hone up our skills periodically so as to provide the best health care to our patients. Keeping this in mind the theme of the conference has aptly been chosen as "Updating Knowledge Enhancing Competencies".

The academic program has been meticulously crafted with orations and keynote addresses by the very experienced faculty. Panel discussions bringing out solutions to clinical dilemnas, videos to enhance your skills, razor sharp debates on every day issues and updates on recent advances and innovations are all there in the academic deliberations.

Delegates keen on presenting free papers, competiton papers, posters, slogans are most welcome. Young gynaecologists are invited to participate in the Quiz which is going to be one of the most exciting events of the conference.

The annual conference is also an event to meet old friends and learn and socialise in a relaxed atmosphere. We request you all to register for the conference and participate in large numbers.

Hoping to interact with all of you at the Annual Conference.

Dr Abha Singh
AOGD President,
Organising Chairperson

Dr Manju Puri
Vice President,
Co-Organising Chairperson

Dr Reena Yadav
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Dr Anuradha Singh
Joint Secretary

Dr Nishtha Jaiswal
Joint Secretary

40th Annual Conf

Venue: **India Habita**

Scientific P

24 November, 2018

07:30 am onwards Registration

08:00 am - 05:00 pm	Free Papers/ Posters/ Quiz Theory	Hall - C

Hall - A

Session: 1	Abnormal Uterine Bleeding		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
09:00 am - 09:15 am	Fertility sparing surgeries in Adenomyosis	Dr Neema Sharma	Dr Malavika Sabharwal Dr Anita Rajoria Dr Jyoti Aggarwal
09:15 am - 09:30 am	Asymptomatic Fibroids; When to treat	Dr Mala Srivastava	
Panel 09:30 am - 10:15 am	AUB- Management update: Current Evidence	Dr Sunita Malik Dr Manju Khemani Dr Renuka Malik Dr Devender Dr Chandra Mansukhani	Dr Reena Yadav
10:15 am - 10:30 am	**Tea & Exhibition**		
Session: 2	**Let's Improve Care**		
Time	**Topic**	**Speakers**	**Chairpersons**
10:30 am - 10:45 am	Maternal Mortality: Lessons learnt from models of low resource countries	Dr Taru Gupta	Dr Maya Sood Dr S N Basu Dr Jharna Behura
10:45 am - 11:00 am	Respectful Maternity Care	Dr Shalini Singh	
11:00 am - 11:15 am	Laqshya: Quality Assurance: A GOI Initiative	Dr Dinesh Baswal	
11:15 am - 11:30 am	Rationale use of Antibiotics in Ob/Gyn practice	Dr Amita Suneja	

Hall - B

Session: 1	What's New in Labor		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
09:00 am - 09:15 am	Unyielding Cervix	Dr Ratna Biswas	Dr Sunita Yadav Dr Poonam Khera Dr Latika Sahu
09:15 am - 09:30 am	Partogram in Transition	Dr Kiran Gulleria	
Panel 09:30 am - 10:15 am	Induction of Labor in Challenging Situations	Dr Sangeeta Gupta (ESI) Dr Poonam Yadav Dr Ashok Kumar Dr Y M Mala Dr Rinku Sen Gupta Dr Harsha Gaikwad	Dr Reva Tripathi Dr Arpita De
10:15 am - 10:30 am	**Tea & Exhibition**		
Session: 2	**Medical Disorders in Pregnancy**		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
10:30 am - 10:45 am	Immunisation in pregnancy: An update	Dr Pikee Saxena	Dr Nirmala Agarwal Dr Puneeta Mahajan Dr Nivedita Sarda
10:45 am - 11:00 am	Management of Hepatitis B positive pregnant Woman	Dr S K Sarin	
Panel 11:00 am - 11:45 am	Preconceptional Counselling: Optimising Fetomaternal outcome	Dr Harsha Khullar Dr Anjali Tempe Dr Rashmi Vyas Dr Jyotsna Suri Dr Swati Sinha	Dr Asmita Rathore

Session: 3	Plenary Session : Hall A	
Time	**Topic**	**Chairpersons**
11:45 am - 12:15 pm	AOGD President's Oration: Dr Shalini Rajaram "Evolution of Screening Tests for Cervical Cancer: Entering an Era of Biomarkers and Genomics"	Dr S N Mukherji, Dr S B Khanna, Dr S S Trivedi, Dr Abha Singh
12:15 pm - 12:40 pm	Brigadier Khanna Oration: Dr J B Sharma "Current thinking in diagnosis and management of Female Genital Tuberculosis"	Dr Urmil Sharma, Dr N B Vaid, Dr Chitra R, Dr Kiran Aggarwal
12:45 pm - 01:15 pm	**Inauguration**	
01:15 pm - 02:00 pm	**Lunch**	

Session: 4	Contraception		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
02:00 pm - 02:15 pm	Post Abortal Contraception	Dr Jyoti Sachdeva	Dr Archana Verma Dr Suman Mendiratta Dr Aastha Srivastava
02:15 pm - 02:30 pm	Newer initiatives in Family Planning Programme	Dr S K Sikdar	
Panel 02:30 pm - 03:15pm	Contraception in Women "At Medical Risk"	Dr Sangita Ajmani Dr Abha Sharma Dr Sushma Sinha Dr Jigyasa Govil Dr Krishna Aggarwal	Dr Achla Batra
Session: 5	**Difficult Situations: Addressing Medico Legal issues**		
Time	**Topic**	**Speakers**	**Chairpersons**
03:15 pm - 03:30 pm	Intrapartum Maternal death	Dr Geetendra Sharma	Dr Sharda Jain Dr Vijay Kadam Dr Tapas Koley
03:30 pm - 03:45 pm	Sudden Fetal Demise	Dr Uma Singh	
03:45 pm - 04:00 pm	Reversed End Diastolic Flows in Early Preterm Pregnancy	Dr K Aparna	
04:00 pm - 04:15 pm	Congenitally Malformed Fetus after 20 weeks of Gestation	Dr Manisha Kumar	
Session: 6	**Let's Debate**		
Time	**Topic**	**Speakers For / Against**	**Chairpersons**
04:15 pm - 04:40 pm	Endometriomas should be treated surgically in Infertile Women	Dr Kanika Jain / Dr Surveen Ghumman	Dr Aruna Batra Dr Rekha Jain Dr Poonam Laul
04:40 pm - 05:05 pm	Laparoscopy is the standard of care for ovarian tumors	Dr Seema Singhal / Dr Meenakshi Singh	
05:05 pm - 05:30 pm	All Women with Unexplained Infertility should be offered IVF	Dr Ruma Satwik / Dr Isha Khurana	

Session: 4	Persistent Problems:Is there a solution		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
02:00 pm - 02:15 pm	Recurrent Pruritis Vulvae	Dr Vibhu Mendiratta	Dr Renuka Sinha Dr Geeta Chadha Dr S L Kabra
02:15 pm - 02:30 pm	Chronic Pelvic Pain	Dr Prabha Lal	
Panel 02:30 pm - 03:15 pm	Recurrent Endometriosis	Dr Sudha Prasad Dr Gita Radhakrishnan Dr Sanjeevani Khanna Dr Chitra Setya Dr Angela Sehra	Dr Renu Misra
Session: 5	**Gynecological Surgery: Enhancing Skills**		
Time	**Topic**	**Speakers**	**Chairpersons**
03:15 pm - 03:30 pm	Caesarean Scar Ectopic Pregnancy: Management Pearls	Dr Alka Kriplani	Dr Punita Bhardwaj Dr Rahul Manchanda Dr Garima Kachwaha
03:30 pm - 03:45 pm	Facilitating Dissection in Vaginal Surgeries	Dr M Puri	
03:45 pm - 04:00 pm	Sacrohysteropexy	Dr Dinesh Kansal	
04:00 pm - 04:15 pm	Operative Hysteroscopy: Addressing Challenges	Dr K K Roy	
Session: 6	**UROGYNECOLOGY: Enhancing Competency**		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
04:15 pm - 04:30 pm	Overactive Bladder: Unaddressed issue	Dr Nita Thakre	Dr Shakuntala Kumar Dr Mamta Dagar Dr Monika Madan
04:30 pm - 04:45 pm	Obstertric Anal Sphincteric injuries fresh and old	Dr A G Radhika	
Panel 04:45 pm - 05:30pm	Tailoring the Surgical Approach to Uterovaginal Prolapse	Dr Nita Thakre Dr Uma Rani Swain Dr Indu Chugh Dr Amita Jain Dr Manisha Sharma	Dr Geeta Mendiratta

ference of AOGD

t Centre New Delhi

Programme

25 November, 2018

07:30 am onwards Registration

08:00 am - 04:00 pm	Free Papers/ Posters	Hall - C

Hall - A

Session: 1	Fetal Medicine		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
09:00 am - 09:15 am	Dilemmas in management of FGR	Dr Sangeeta Gupta (MAMC)	Dr Vandana Chadha Dr Seema Thakur Dr Sumita Aggarwal
09:15 am - 09:30 am	Vaginal Microbiome and Fetal Protection	Dr Mala Arora	
Panel 09:30 am - 10:15 am	Multiple Pregnancy: Optimising care	Dr Anita Kaul Dr Reema Bhatt Dr Madhavi Gupta Dr Sushma Nangia Dr Kuldeep Singh	Dr Vatsala Dadhwal
10:15 am - 10:30 am	**Tea & Exhibition**		
Session: 2	**Contemporary Obstertrics**		
Time	**Topic**	**Speakers**	**Chairpersons**
10:45 am - 11:00 am	Recognition & Response to "Red Flag": Clinical Features in Pregnancy & Puerperium	Dr Pratima Mitttal	Dr Neera Aggarwal Dr S S Trivedi Dr Uma Rai
11:00 am - 11:15 am	What tests when for Prenatal Diagnosis	Dr Narendra Malhotra	
11:15 am - 11:30 am	Challenges of Obesity in Obstetrics	Dr Kiran Aggarwal	
11:30 am - 11:45 am	Advanced age: Impact on Reproductive Outcome	Dr M Gouri Devi	

Hall - B

Session: 1	Menopause: Age Gracefully		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
09:00 am - 09:15 am	Strengthening life beyond Menopause	Dr Ragini Aggarwal	Dr Shashi Prateek Dr Susheela Gupta Dr Aishwarya Kapoor
09:15 am - 09:30 am	Perimenopausal Turbulence: Management Strategies	Dr Anjila Aneja	
Panel 09:30 am - 10:15 am	Premature Ovarian Insufficiency	Dr Nalini Mahajan Dr Sonia Malik Dr Sohani Verma Dr Pankaj Talwar Dr Neeta Singh	Dr Deepti Goswami
10:15 am - 10:30 am	**Tea & Exhibition**		
Session: 2	**Evolution of management of Gynaecological Cancers**		
Time	**Topic**	**Speakers/ Panelists**	**Chairpersons/ Moderators**
10:45 am - 11:00 am	Changes in Radicality of surgery in Cervical and Endometrial Cancers	Dr Kavita Singh	Dr Neerja Goel Dr Gauri Gandhi Dr Mitra Saxena
11:00 am - 11:15 am	Fertility preservation in Gynecological Cancers	Dr H D Pai	
Panel 11:15 am - 12:00 pm	HRT in Cancer Survivors	Dr Vijay Zutshi Dr H D Pai Dr Kavita Singh Dr Sonal Bhatla Dr Shyam Aggarwal Dr Maninder Ahuja Dr Rajesh Khadgawat	Dr Neerja Bhatla/ Dr Seema Singhal

Session: 3	Plenary Session : Hall A	
Time	**Topic**	**Chairpersons**
12:00 pm - 12:25 pm	Fogsi President's Oration: Dr Jaideep Malhotra "Adbhut Matrutva"	Dr Kamal Buckshee, Dr Swaraj Batra, Dr Abha Singh
12:25 pm - 12:50 pm	Key Note Lecture: Dr Shantha Kumari "Viable issue in Periviable Gestations"	Dr V L Bhargava, Dr Suneeta Mittal, Dr Narendra Malhotra Dr Reena Yadav
12:50 pm - 01:15pm	Key Note Lecture, "Uterine Transplant": Dr Shailesh Puntambekar	Dr Jaideep Malhotra, Dr Amita Suneja, Dr Manju Puri
01:15 pm - 02:00 pm	**Lunch & Exibition**	

Session: 4	Oncology Update: Learn from the Experts		
Time	**Topic**	**Speakers**	**Chairpersons**
02:00 pm - 02:15 pm	Minimal Energy in Minimally Invasive Surgery	Dr Vivek Marwah	Dr U P Jha Dr Yuvakshi Juneja Dr Debasis Dutta
02:15 pm - 02:30 pm	Laparoscopic Radical Hysterectomy	Dr Rupinder Sekhon	
02:30 pm - 02:45 pm	Pelvic and Para Aortic Lymph Node Dissection	Dr Amish Chaudhary	
02:45 pm - 03:00pm	Radical Vulvectomy	Dr Sunesh Kumar	

Session: 4	Competion Papers	
Time		**Chairpersons**
02:00 pm - 03:30 pm	Competion Papers	Dr Reena Yadav Dr Ratna Biswas

Session: 5	Hall A		
Time	**Topic**	**Speaker**	**Chairpersons**
03:00 pm - 03:30 pm	HIFU: High intensity focussed ultrasound Treatment- minimise harm to patients	Dr Huang-Pin-Shen	Dr Sunesh Kumar, Dr Ashok Kumar, Dr Sharda Patra

Session: 6	Obstetric Videos: All about Cesarean		
Time	**Topic**	**Speakers**	**Chairpersons**
03:30 pm - 03:45 pm	Evidence based Technique of Cesarean Section	Dr Swati Aggarwal	Dr Sadhna Gupta Dr Sumedha Sharma Dr Amrita Singh
03:45 pm - 04:00 pm	Adherent Bladder in Cesareans	Dr Aruna Nigam	
04:00 pm - 04:15 pm	Deeply Impacted Head/Free Floating Head	Dr Sharda Patra	
04:15 pm - 04:30 pm	Morbidly Adherent placenta; decisions and skills	Dr Abha Singh	

Session: 6	Debate: Obstetric		
Time	**Topic**	**Speakers For / Against**	**Chairpersons**
03:30 pm - 03:50 pm	Destructive Operations have a Place in Modern Obstetrics	Dr Vidhi Chaudhary / Dr Sandhya Jain	Dr Kishore Rajurkar Dr Rachna Aggarwal Dr Ritu Sharma
03:50 pm - 04:10 pm	Instrumental Vaginal Delivery: A must know Obstetric Skill	Dr Nishtha Jaiswal / Dr Jayshree Sundar	
04:10 pm - 04:30 pm	Primary Caesarean is Safer in IVF Pregnancies than Normal Vaginal Deliveries	Dr Anuradha Singh / Dr Shilpi Nain	

Session: 7	Main Hall	
Time	**Quiz**	**Quiz Masters**
04:30 pm - 05:30 pm	Surgical Procedures in Gynaecology: Optimising Patient Outcome (Oral Round)	Dr Ratna Biswas, Dr Manisha Kumar, Dr Swati Aggarwal
05:30 pm	**Slogan Competition & Valedictory**	

Events Held

- CME on "Endometriosis Update" on 5th October, 2018 at Moolchand Hospital, New Delhi



- PG Training Program on Infertility: 2nd Module 7th October 2018, at SJ Auditorium, Lady Hardinge Medical College, New Delhi



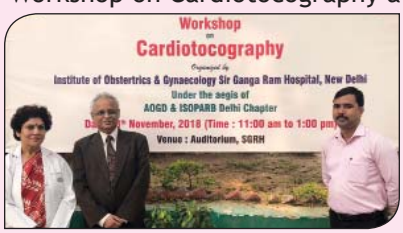
- Monthly Clinical Meeting on 26th October, 2018 at ESI Hospital, New Delhi


- CME under the aegis of DGF-North and Adolescent committee AOGD on 1st November, 2018 at Fortis Hospital, New Delhi



- CME on "Diabetes in Pregnancy" on 1st November, 2018 at SJ Auditorium, LHMC, New Delhi


- Workshop on Cardiotocography at Institute of Obstertics & Gynaecology, SGRH, New Delhi




40th Annual Conference of Association of Obstetricians and Gynecologists of Delhi

24th - 25th November, 2018

Venue: **India Habitat Centre, Lodhi Road, New Delhi**

REGISTRATION FORM

Full Name ..... Qualification ..... Institution .....

Speciality .....

Category: (Tick any) Delegate ( ) PG Student ( ) Faculty ( )

Department ..... Designation .....

Address .....City ..... Pin Code.....

Mobile No. .....Landline No. ..... E-Mail .....

AOGD Membership No.....

ACCOMPANYING PERSON'S Details

Name ..... Age .....

THEME TOPICS FOR ABSTRACT SUBMISSION

1. Critically ill mother ( )
2. Adolescent gynaecology ( )
3. Gynaecological cancers ( )
4. Endoscopy ( )
5. Contraception ( )
6. Miscellaneous ( )

Guidelines for abstract submission on aogd.org

Last date for Abstract Submission for Free Communication and Poster: 15th September 2018

Preconference workshops (Tick any)

22nd November 2018

1. Fetal Surveillance ( )
2. Colposcopy (live workshop) ( )
3. Hysteroscopy ( )

23rd November 2018

4. Operative obstetrics ( )
5. Ovulation induction and follicular tracking ( )
6. Pelvic Reconstructive surgery ( )

Registration Fees: (inclusive of 18% GST)

	Conference			Workshop		
Registration Category	**Upto 30th Sept. '18**	**Upto 30th Oct '18**	**Spot Registration**	**Upto to 30th Sept. '18**	**Upto 30th Oct '18**	**Spot Registration**
AOGD Member	Rs. 5300	Rs. 5700	Rs. 5900	Rs. 2400	Rs. 2600	Rs. 3000
PG Student	Rs. 4700	Rs. 5000	Rs. 5300	Rs. 1800	Rs. 2100	Rs. 2400
Non- AOGD Member	Rs. 5900	Rs. 6500	Rs. 7100	Rs. 2400	Rs. 3000	Rs. 3200
Accompanying Person	Rs. 5100	Rs. 5300	Rs. 5700			

All DD/Cheque payable at New Delhi & should be made in favour of **"Association of Obstetricians and Gynecologists of Delhi"**

- ❖ Write your Name and Contact No. at the back of DD/Cheque
- ❖ Registration for the conference is mandatory in order to register for the pre conference workshops.

AOGDIANS above the age of 70 years are exempted from registration fees. Kindly submit copy of your Aadhar Card.

PAYMENT DETAILS

Please find enclosed herewith DD/Cheque No. ..... Dated .....

Drawn on (Name of the Bank)..... Branch .....

For Rs. ..... (In words) .....

FOR ONLINE TRANSFER THROUGH NEFT/RTGS

NAME OF BANK: CENTRAL BANK OF INDIA BRANCH: LADY HARDINGE MEDICAL COLLEGE BRANCH

NAME OF ACCOUNT: ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS OF DELHI

ACCOUNT NUMBER: 3674596638 IFSSC CODE: CBIN0283462 MICR CODE 110016067

REGISTRATION GUIDELINES

1. Conference registration is mandatory for registration for the pre conference workshops.
2. AOGDIANS above the age of 70 years are exempted from registration fees, please submit copy of your Aadhar card as age proof along with the duly filled registration form.
3. Post Graduates to attach a certificate from HOD and also should be an annual member of the AOGD in order to attend and present a paper.
4. Conference registration includes delegate kit, lunch & tea on 24th - 25th November 2018, participation in scientific session & exhibitions. No gurantee of delegate kit for spot registration.

CANCELLATION & REFUND POLICY

1. All cancellation should be made in writing and sent to AOGD secretariat.
2. All cancellation received before 15th Oct 2018 will be entitled for 75% refund of the amount paid.
3. All cancellation received between 15th Oct 2018 to 1st Nov 2018 will be entitled for only 25% refund of the amount paid.
4. No refund for cancellation made after 1st Nov 2018.
5. The refund process will begin only 30 days after the completion of the conference.

Secretariat
Department of Obstetrics and Gynaecology
Lady Hardinge Medical College and Smt Sucheta Kriplani Hospital, New Delhi-110001
Contact Tele 011-23408297, Mr Arun 9045820602; Email: secretarylhaogd2018@gmail.com

Pre Conference Workshops

Fetal Surveillance in Pregnancy

Date: Friday, 22nd November 2018
Venue: Auditorium, Max Hospital West, Wing Saket

Convenor: Dr Manju Khemani
Co-Convenors: Dr Poonam Tara, Dr Rinku Sen Gupta

08:20 am - 08:30 am	Registration	
09:00 am - 09:15 am	Overview of Fetal Surveillance	Dr Poonam Tara
09:20 am - 09:35 am	CTG Interpretation and Guidelines	Dr Rinku Sengupta
09:40 am - 09:55 am	Clinical Application of Doppler	Dr Manju Khemani
09:55 am - 10:10 am	Fetal Growth Restriction - Newer Concepts	Dr Sangeeta Gupta
10:10 am - 10:30 am	**Breakfast**	
10:30 am - 11:00 am	**Inauguration**	

Stations (11:00am - 03:00 pm) 30 mins each

1. **CTG scenarios:** Dr Bela Makhija, Dr Arpana Haritwal, Dr Ruchi Bhandari, Dr Bithika
2. **Abnormal CTG interesting case studies:** Dr Rinku, Dr Neeru Jain, Dr Priya Sindhwani
3. **Diagnosis of FGR – case scenarios:** Dr Alka Gujral, Dr Poonam Tara, Dr Payal Singhal
4. **Dopplers – Role of Umbilical artery, DV:** Dr Manju Khemani, Dr Manisha Kumar, Dr Kiranjeet
5. **Dopplers – Role of MCA:** Dr Anuradha Kapur, Dr Chanchal Singh, Dr Usha M Kumar
6. **Role of BPP, Liquor abnormalities – case scenarios:** Dr Sangeeta Gupta, Dr Madhu Goel, Dr Anita Sharma
7. **Surveillance of Twin pregnancies:** Dr Vatsala Dadhwal, Dr Reema Kumar, Dr Suneeta Gupta

03:00 pm - onwards **Lunch & Certificate Distribution**

For more information contact: Dr Manju Khemani (9810611598), **Dr Poonam Tara** (9717077700)

Workshop on Colposcopy

Date: Friday, 22nd November 2018
Venue: UCMS & GTB Hospital, Dilshad Garden, Delhi

Convenors: Dr Amita Suneja, Dr Shalini Rajaram
Co-Convenors: Dr Rashmi Malik, Dr Bindiya Gupta

08:30 am - 09:00 am	Registration	
	Chairpersons: Dr NB Vaid, Dr Vijay Zutshi, Dr Kanika Gupta	
09:00 am - 09:15 am	Instrumentation & Technique of Colposcopy	Dr Saritha Shamsunder
09:20 am - 09:35 am	Tissue Basis of Colposcopy	Dr Sumita Mehta
09:40 am - 09:55 am	Interpretation of Colposcopic findings and IFCPC Terminology	Dr Shalini Rajaram
10:00 am - 10:30 am	Lamp lighting & Tea	
	Chairpersons: Dr Anjali Tempe, Dr Nirmala Agarwal, Dr Rupinder Sekhon, Dr Maninder Ahuja	
10:30 am - 10:45 am	Management of CIN	Dr Gauri Gandhi
10:50 am - 11:05 am	Looking Beyond the Cervix	Dr Amita Suneja
11:10 am - 11:25 am	Case Based Management of Screen Positives	Dr Neerja Bhatla
11:30 am - 04:00 pm	**Colposcopy Live workshop (OT)**	
01:30 pm - 02:00 pm	**Lunch**	
	Demonstration of mobile ODT for cervical cancer screening Colposcopy of cervical lesions: normal and abnormal	
	Demonstration of thermocoagulation	Dr Roopa Hariprasad Organizing faculty
	Cryotherapy for low grade disease	
	LEEP technique in high grade disease	
	Hands on LEEP training	
04:00 pm - 04:15 pm	**Valedictory and distribution of certificates**	

Workshop on Hysteroscopy

Date: Friday, 22nd November 2018,
Venue: CMET, AIIMS, New Delhi

Organized by: Department of Obstetrics & Gynecology, All India Institute of Medical Sciences, New Delhi

Convenor: Prof. K K Roy
Co-Convenors: Dr Garima Kachhawa, Dr Vidushi Kulshrestha

08:30 am - 09:00 am	**Registration**
09:00 am - 09:15 am	**Welcome Address & Brief Introduction to the Conference** Dr Sunesh Kumar
Session I	**Chairperson:** Dr J B Sharma, Dr Dinesh Kansal, Dr Nema Sharma, Rajesh Kumari
09:15 am - 09:45 am	**Relay of Live Hysteroscopic surgeries: 1st Case**
09:45 am - 10:00 am	Pre-Test Questionnaire
10:00 am - 10:45 am	**Relay of Live Hysteroscopic surgeries: 2nd Case**
10:45 am - 11:00 am	Discussion & Audience Interaction
Session II	**Chairperson:** Dr Renu Misra, Dr Anupam Kapoor, Dr Reeta Mahey, Dr Jyoti Meena
11:00 am - 11:45 am	**Relay of Live Hysteroscopic surgeries: 3rd Case**
11:45 am - 12:00 pm	**Recent Guidelines on hysteroscopy (part-I)**
12:00 pm - 12:45 pm	**Relay of Live Hysteroscopic surgeries: 4th Case**
12:45 pm - 01:00 pm	**Recent Guidelines on hysteroscopy (part-II)**
01:00 pm - 01:45 pm	**Relay of Live Hysteroscopic surgeries: 5th Case**
01:45 pm - 02:00 pm	Discussion & Audience Interaction
02:00 pm - 02:45 pm	**Lunch**
02:45 pm - 03:45 pm	**Panel on Preventing Complications of Hysteroscopy** **Moderators:** Dr K K Roy, Dr Vidushi Kulshrestha **Panelists:** Dr Manju Purie, Dr Nutan Agarwal, Dr Sangeeta Gupta, Dr Anupam Kapoor, Dr Bijoy Nayak, Dr Garima Kachhawa
03:45 pm - 04:00 pm	Post-Test Discussion: Dr Vidushi Kulshrestha

Live relay of operative hysteroscopy including hysteroscopic adhesiolysis, septal resection, hysteroscopic cannulation, myomectomy, polypectomy, Removal of displaced IUCD; subjected to the availability of cases.

Operative Obstetrics

Date: Saturday, 23rd November 2018
Venue: Auditorium, Sir Gangaram Hospital, New Delhi

Convenor: Dr Mala Shrivastava
Co-Convenors: Dr Kanika Jain, Dr Mamta Dagar

Time	Topic
Session 1	**Chairpersons:** Dr S K Bhandari, Dr Abha Mazumdar, Dr Neeti Tiwari
08:00 am - 09:00 am	**Registration**
09:00 am - 09:20 am	Making An episiotomy- What does the evidence says **Speakers:** Dr Aruna Nigam
09:20 am - 09:40 am	What went wrong in episiotomy-CPT **Speakers:** Dr Geeta Mediratta
Session 2	**Lost art of delivery** **Chairpersons:** Dr B G Kotwani, Dr Debasis Dutta, Dr Vidushi Kulshrestra, Dr Shweta Mittal
09:40 am - 10:00 am	External cephalic Version- Role in Modern Obstetrics **Speakers:** Dr Achla Batra
10:00 am - 10:20 am	Assisted Breech Delivery, **Speakers:** Dr Sunita Malik
10:20 am - 10:40 am	Shoulder Dystocia, **Speakers:** Dr Sumita Mehta
Session 3	**Instrumental Deliveries- Where do we stand?** **Chairpersons:** Dr P Chaddha, Dr Punita Bhardwaj, Dr Ruma Satwik
11:20 am - 11:40 am	Forceps Delivery, **Speakers:** Dr Sohani Verma
11:40 am - 12:00 noon	Vaccum Delivery, **Speakers:** Dr Pratima Mittal
Session 4	**Caesarean Sections** **Chairpersons:** Dr M Kochhar, Dr Kanika Jain, Dr Mala Srivastava
12:00 noon - 12:20 pm	Audit of Caesarean Section (Ten Group Caesarean Section) **Speakers:** Dr Renu Mishra
12:20 pm - 12:40 pm	Basics of Caesarean Delivery- Evidence Based Techniques **Speakers:** Dr Sharda Patra
12:40 pm - 01:00 pm	Caesarean Myomectomy, **Speakers:** Dr Harsha Khullar

Session 5	**Panel Discussion**
01:40 pm - 02:40 pm	**Panel on -Menance of Morbidly Adherent Placenta** **Moderator:** Dr Kanwal Gujral **Panelist:** Dr Chandra Mansukhani, Dr Sangeeta Gupta, Dr Garima Kucchawa, Dr Sunita Lamba, Dr Rekha Bharti, Dr Kuldeep Singh, Dr Ambrish Satwik, Dr Anjeelina
Session 6	
02:40 pm - 04:00 pm	**Hands on training on CPT** Dr Geeta Mediratta, Dr Chandra Mansukhani, Dr Mala Srivastava, Dr Mamta Dagar, Dr Sharmistha Garg, Dr Tarun K Das, Dr Pallavi Sharma

Ovulation Induction and Follicular Tracking

Date: Saturday, 23rd November 2018

Venue: MEC Hall, S J Auditorium, LHMC, New Delhi

Convenor: Dr Manju Puri
Co-Convenor: Dr Pikee Saxena

Time	Topic	Speakers
	Session I - Ovulation Induction	
	Chairpersons: Dr Anjali Tempe, Dr Kiran Aggarwal	
09.00am - 09.15am	Principles of Ovulation Induction	Dr Ratna Biswas
09.15am - 09.35am	OI with Oral Ovulogens	Dr Renu Mishra
09.35am - 10.00am	OI with Gonadotropins- which, when, how?	Dr Surveen Ghumman
10.00am - 10.15am	Discussion	
	Session II - Panel Discussion	
	Moderator: Dr Manju Puri **Panelist:** Dr Gauri Devi, Dr Neeti, Dr Shivani, Dr Anuradha, Dr Jyoti Bali	
10.15am - 11.00am	Tailoring Ovulation Induction Protocols: Case based discussion	
11.00am - 11.15am	**Tea**	
	Session III - Intrauterine Insemination	
	Chairpersons: Dr Abha Singh, Dr Prabha Lal	
11.15am-11.30am	Indications and Work Up for IUI	Dr Reena Yadav
11.30am-11.45am	Setting Up of IUI Lab	Mr R K Sehgal
11.45am-12.00noon	Live Demonstration of Semen Analysis and Semen preparation for IUI	
12.00noon - 12.15pm	**Discussion**	
	Session IV - Panel Discussion	
	Moderator: Dr Pikee Saxena **Panelists:** Dr Leena Wadhwa, Dr Bindu, Dr Puneet Kochar, Dr Shweta Gupta, Dr Pinkee Saxena	
12.15pm - 01.00pm	IUI: Optimizing Results, Minimizing Complications	
01.00pm - 02.00pm	**Lunch**	
	Live Workshop	
02.00pm - 03.15pm	Live Ultrasound for Follicular Tracking	Dr Kuldeep Singh (Sonologist) Dr Sonia Malik (Gynecologist)
03.15pm - 04.30pm	Hands on Semen Preparation for IUI	Mr Sehgal & Team
04.30pm - 05.00pm	Practice IUI Technique on Dummy	Dr Manju Puri Dr Pikee Saxena

Who should attend?

• Practicing gynecologists, interested in infertility • Residents • Specialists

Salient Features

• USG for follicular tracking- Live demo • Step by step ovulation induction and COS
• Hands on semen preparation for IUI
• Practice IUI technique on dummy • Interactive sessions with experts

Pelvic Reconstructive Surgeries

Date: Saturday, 23rd November 2018

Venue: Auditorium, Second Floor, Medanta The Medicity Hospital, Gurugram

Convenor: Dr Amita Jain
Co-Convenor: Dr Rajesh Ahlawat

08:20 am - 08:30 am	Welcome Address	Dr Rajesh Ahlawat, Medanta-The Medicity, Gurugram
Session I: Lectures		
08:30 am - 08:45 am	**Pelvic Floor Imaging**: Rationale and Clinical Application	Dr Kulbir Ahlawat, Medanta–The Medicity, Gurugram
08:45 am - 09:00 am	Role of **Urodynamics** inpelvic reconstructive surgeries	Dr Aparna Hegde, Delhi
09:00am - 09:10am	Discussion	
Session II: Management of Stress Urinary Incontinence (SUI)		
09:10 am - 09:25 am	Selection of patient and Rationale of various Reconstructive Procedures for SUI	Dr Sanjay Sinha, Apollo, Hyderabad
09:25 am - 09:40 am	**Applied Anatomy** in reference to various reconstructive procedures for SUI	Dr Surbhi Wadhwa, AIIMS, Delhi
09:40 am - 09:50 am	Discussion	
Midurethral Sling Trans-obturator Tape: Inside out approach / Outside in approach		
09:50 am - 09:55 am	Technique (Videodemonstration)	Dr JB Sharma, AIIMS, Delhi
09:55 am - 10:05 am	Complications and Management	Dr Pawan Vasudeva, Safdarjang, Delhi Dr Amita Jain, Medanta–The Medicity, Gurugram
10:05 am - 10:10 am	Discussion	
Retropubic sling: Downup approach / Up down approach		
10:10 am - 10:15 am	Technique (Video demonstration)	Dr JB Sharma
10:15 am - 10:25 am	Complications and Management	Dr Pawan Vasudeva / Dr Amita Jain
10:25 am - 10:30 am	Discussion	
10:30 am - 11:00 am	Tea Break	
Minisling		
11:00 am - 11:05 am	Technique (Video demonstration)	Dr Amita Jain
11:05 am - 11:10 am	Complications and Management	Dr Amita Jain
11:10 am - 11:15 am	Discussion	
Autologus facial sling		
11:15 am - 11:30 am	Technique (Video demonstration)	Dr Pawan Vasudeva Dr Nikhil Khattar, Medanta–The Medicity, Gurugram
11:30 am - 11:40 am	Complications and Management	Dr Pawan Vasudeva
11:40 am - 11:45 am	Discussion	
Burch Colposuspension		
11:45 am - 11:50 am	Technique (Videodemonstration)	Dr Amita Tandon, Agra
11:50 am - 11:55 am	Complications and Management	Dr Rishi Nayyar/ Dr Karishma, AIIMS, Delhi
11:55 am - 12:00 am	Discussion	
SessionIII: Complex Pelvic Surgeries		
12:00 am - 12:15 pm	**Vaginoplasty**	Dr Vineet Mishra, IKDRC, Ahmedabad
12:15 pm - 12:20 pm	Discussion	
12:20 pm - 12:40 pm	**Vesicovaginal Fistula Repair**	Dr Uma Rani Swain, Delhi Dr Amita Jain
12:40 pm - 12:45 pm	Discussion	
12:45 pm - 12:55 pm	**Complete PerinealT ear**	Dr Sandhya Jain, UCMS, Delhi
12:55 pm - 01:00 pm	Discussion	
01:00 pm - 02:00 pm	Lunch Break	
02:00 pm - 02:10 pm	**Uterovesical / Urethrovaginal fistula**	Dr Rishi Nayyar
02:10 pm - 02:15 pm	Discussion	
Session IV: Panel Discussion		
02:15 pm - 03:00 pm	**Urinary Tract Infection**–How to treat and when not to treat!!	Moderator: Dr Amita Jain
Panelists: Dr Vineet Mishra, Dr Sanjay Sinha, Dr Pawan Kesarwani (Max, Delhi), Dr Dinesh Kansal (BLK, Delhi), Dr Manvita Mahajan (Artemis, Gurugram), Dr Amit Tandon		
Session V: Lectures		
03:00 pm - 03:15 pm	**Cystoscopy**: instruments, techniques and indications in pelvic reconstructive surgeries	Dr Pawan Vasudeva
03:15 pm - 03:20 pm	Discussion	
03:20 pm - 03:35 pm	**Female Urethroplasty** – Indications & techniques	Dr Nikhil Khattar
03:35 pm - 03:40 pm	Discussion	
03:40 pm - 03:55 pm	**Vaginal Laser Therapy**–current concept and evidence	Dr Ragini Agarwal, Gurugram
03:55 pm - 04:00 pm	Discussion	
04:00 pm - 04:10 pm	Vote of thanks	Dr Amita Jain
04:10 pm - 5:00 pm*	Tea–opportunity to interact with all faculty	

*Utilize this free time for hands on experience on simulators

BEST PRACTICES

Familial Gynaecological Cancer - Risk assessment and management


Dr Seema Singhal

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Introduction

Familial gynaecological cancers are inherited cancers of the female genital tract that occur more frequently in a genetically predisposed population than would be expected by chance. This occurs as a result of one or more gene mutations present in parental germ-line cells. They usually occur at an early age than sporadic cancers and may have a defined inheritance pattern, usually autosomal dominant[(1)]. Most of the gynaecological cancers are sporadic in nature. Historically, it was thought that approximately 5% of endometrial carcinomas and 20% of epithelial ovarian carcinomas are hereditary[(2)]. More recent data indicate that at least 25% of newly diagnosed cases are due to a hereditary mutation in a single gene[(3)]. Identifying a woman with gynaecological cancer as having hereditary cancer syndrome has tremendous implications for both patient as well as her family.

Although individuals with hereditary cancer syndromes inherit one defective allele from their father or mother, they have a second, functional allele. If the second allele becomes nonfunctional, cancer can develop[(4)]. Women with hereditary cancer syndromes have inherited one of the defective allele from either parent, and a copy of this defect is present in all of their cells. For cancer to develop in these individuals only the second working copy of relevant gene needs to be lost. If this second copy is not lost, the individual will not develop cancer despite 50% risk of inheriting the cancer predisposition.

Hereditary cancer syndromes with gynaecologic manifestations

The most common hereditary syndromes with gynaecological manifestations are depicted in Table 1[(5)]. HBOC syndrome (caused by germ line mutations in BRCA 1, 2) and Lynch syndrome (caused by germline mutations in MLH1, MLH2, MSH6 or PMS2) are the most common hereditary syndromes that include gynaecological cancers as part of their spectrum. These two syndromes account for at least 20% of ovarian cancers[(3)]. BRCA1 and BRCA2, account for the approximately 85% of all cases of hereditary breast and epithelial ovarian cancer (EOC). Lynch syndrome may contribute for 5-10% of all hereditary ovarian cancers[(6)].

Table 1: Hereditary cancer syndromes and associated malignancies[(5)]:

Syndrome	Affected gene	Predominant cancers
HBOC (Hereditary breast ovarian cancer)	BRCA1, BRCA2	Breast, ovary, other organs (fallopian tube, prostate, male breast, pancreas)
Lynch Syndrome	MLH1, MSH2, MSH6, PMS2	Colon, endometrium, ovary, urinary tract, gastric cancer
Cowden syndrome	PTEN	Breast, thyroid, endometrium
Li Fraumeni syndrome	TP 53	Breast, sarcoma, leukemias, brain
Peutz-Jeghers syndrome	STK11	Colon, breast, gastric, ovarian sex cord stromal tumors with annular tubule

Clinical Characteristics of Patients with BRCA Mutations:

The risk of developing cancer among BRCA mutation carriers by age of 70 years is shown in Table 2 (7):

Table 2: Risk of developing breast and ovarian cancer among BRCA mutation carriers:

Mutation	Breast cancer	Contralateral breast cancer	Ovarian cancer
BRCA 1	60% (44-75%)	83% (69-94%)	59% (43-76%)
BRCA 2	55% (41-70%)	62% (44-79.5%)	16.5% (7.5-34%)

Women with BRCA mutation are more likely to harbor high grade serous or less commonly endometrioid epithelial ovarian cancer. Borderline, non-epithelial and mucinous ovarian tumors are less likely to be associated with a genetic mutation[(8)].

Women with a germline BRCA1 mutation were more likely to have triple-negative breast cancer than those with a BRCA2 mutation or those who were BRCA mutation negative (61 versus 10 and 18 percent, respectively). Overall survival (OS) in women with triple-negative breast cancer and a germline BRCA mutation was slightly better than those without a BRCA mutation at two years, but there was no difference at 5 or 10 years. This could be partly because of better response to chemotherapeutic agents including platinum compounds and PARP inhibitors[(9)].

Pretest Counselling

Genetic testing for cancer predisposition requires informed consent that should include pre-test education and counselling concerning the risks, benefits and limitations of testing, including the implications of both positive and negative genetic test results. Individuals

considering genetic testing should be aware that the potential risks of genetic testing include psychological stress and changes to family dynamics. The patient should be provided general information about the gene, technical aspects and accuracy of the test, economic considerations, psychosocial aspects such as anticipated reaction to results and coping strategies, timing and readiness for testing, family issues and preparing for result disclosure. The components of pre-test counselling include pedigree evaluation and risk assessment stratification[10].

Identification of High Risk Families

The American Society of Clinical Oncology (ASCO)[11] has recommended that hereditary cancer predisposition should be offered only when:

A) The individual has a strong family history of cancer or very early age of onset of disease

B) Correct interpretation of the result is possible

C) The test results will influence medical management.

A family history of early onset breast cancer is more likely to indicate hereditary risk than breast cancer at a later age. Paternal inheritance is equally important as that of maternal side. Ovarian carcinoma especially high grade serous variant in a woman's personal or family history is a significant indicator of the presence of a mutation in *BRCA1or BRCA 2*[8].

Several risk assessment tools namely BOADICEA, BRCAPRO, Manchester system, etc., are available to stratify an individual's life time risk of breast and ovarian cancer risk depending predominantly on ethnicity, family history and personal health history. Women with greater than a 30% lifetime risk of breast cancer from age 20 years are considered to be high risk and should be managed by a multidisciplinary tertiary team and decisions regarding surveillance and risk reducing surgery are then made accordingly[1]. However, none of these models are validated for use in Indian population.

Indications for Genetic Testing[8]:

Patients with:

1. Female breast cancer diagnosed ≤50 years
2. Triple-negative breast cancer (TNBC) diagnosed ≤60 years
3. Two or more primary breast cancers
4. Invasive ovarian or fallopian tube cancer, or primary peritoneal cancer
5. Male breast cancer
6. Any HBOC-associated cancers, regardless of age at diagnosis,
7. Ashkenazi (central or eastern European) Jewish ancestry
8. Family members with known mutation

Type of Testing[12]:

The type of mutation analysis required depends upon the family history.

Comprehensive testing is performed when the mutation in the family has not been identified. If possible, this testing should be done on an individual in the family who has had breast or ovarian cancer. The testing involves both sequencing and deletion/duplication studies. It is the most sensitive, costly, and time-consuming test, and it is likely to identify variants of uncertain significance also.

Multisite testing looks for the presence of the three founder mutations that are common in those with Ashkenazi Jewish ancestry. For those with this ancestry, this is where genetic testing would typically start.

Single-site testing is done when the mutation in the family has been identified; this test looks only for the presence of that specific mutation. Targeted testing can save money and time.

Post Test Counselling[10]:

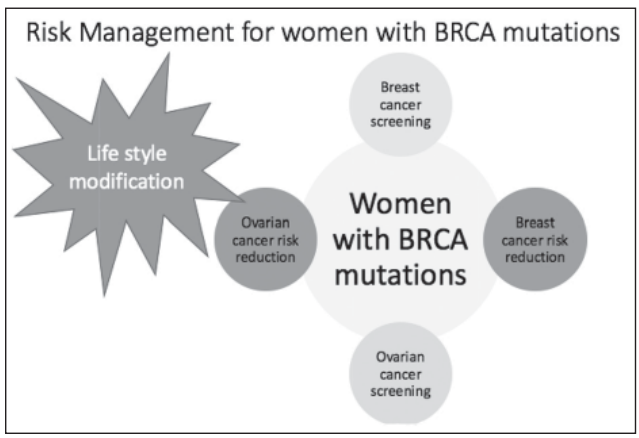
Once identified with known genetic syndrome detailed counselling explaining implications and risk management should be done. However, not everyone who undergoes genetic testing receives a definitive result indicating the presence or absence of a deleterious mutation. Of those undergoing testing for BRCA1/2 mutations, approximately 7% are found to have a variant of uncertain significance (VUS). VUS are usually mis sense or potential splice site changes that have not, as yet, been shown to be definitively associated with adverse clinical outcomes. In such situations, counsellors must use their skills to provide a clear and measured overview of the meaning and implication of the test, and provide emotional support for a patient who may be distraught because of the inability to obtain a definitive assessment of her risk for developing cancer.

Risk management of women with HBOC (Fig 1):

The components of risk management include:

- Surveillance
- Chemo prevention
- Risk reducing surgery

Figure 1: Risk management for women with BRCA mutations:



Ovarian Cancer Risk Reduction in BRCA Mutation Carriers:

1. **Screening for ovarian cancer**
   Annual surveillance in general population with TVS and CA 125 has not been useful and it has been shown that there was no change in the stage of cancer at the time of detection in the screened population or a decrease in the cancer specific or overall mortality[13,14,]. On the other hand there was higher incidence of false positive laparotomies and surgical complications. In the genetically predisposed high risk population TVUS and serial serum CA-125 (ROCA) may be considered at the clinician discretion starting at 30-35 years or five to 10 years earlier than the earliest age of first diagnosis of ovarian cancer in the patient's family[8]. However, limited efficacy of this strategy should be explained to the patient.

2. **Chemoprevention**
   There is some evidence to suggest the role of combined oral contraceptive pills to reduce the risk of ovarian cancer by 40-60% in the high risk population but the role is not established and there is conflicting data on increased risk of breast cancer in these individuals.[1,8]

3. **Risk reducing surgery**
   The only proven risk reducing strategy in BRCA carriers is risk reducing salpingo-oophorectomy. Risk reducing salpingo oophorectomy (RRSO) reduces the risk of ovarian malignancy by 85% compared with observation alone. A survey of 5783 women who were BRCA mutation carriers demonstrated that RRSO was associated with an 80% reduction in the risk of ovarian, fallopian tube, or peritoneal cancer (hazard ratio [HR] 0.20, 95% CI 0.13-0.30, p <0.001) and a 77% reduction in all-cause mortality to age 70 years (HR 0.23, 95% CI 0.13-0.39, p <0.001) [15]. RRSO also reduces the risk for breast cancer approximately by 50%. Few studies have reported 1-4% risk for primary peritoneal carcinoma even 20 years after RRSO[1]. In BRCA 1 mutation carriers RRSO is recommended between age 35 and 40 and upon completion of child bearing and in BRCA2 mutation carriers RRSO should be carried out between 40-45 years of age[16]. The usual recommended approach for RRSO is laparoscopic approach with detailed survey of upper abdomen, bowel surface, omentum, appendix and pelvic organs. Pelvic washings should be sent for cytology. Tube should be resected at the level of cornua and all surrounding peritoneum with areas of adhesion and 2 cm of infundibulo-pelvic ligament should be removed [8].

   If RRBSO is undertaken in premenopausal age group, *BRCA1* and *BRCA2* mutation carriers who do not have a personal history of breast cancer should be offered hormone replacement therapy (HRT) at least until the age of natural menopause, around 50 years, in order to avoid the cardiovascular and bone complications[11]. For women with a history of breast cancer, the use of HRT is not usually recommended. No guideline recommends prophylactic hysterectomy in BRCA mutation carriers.

Breast Cancer Risk Reduction in BRCA Mutation Carriers:

1. **Surveillance:**
   Breast self examination should begin at 18 years of age so that the woman is aware of changes in her breast. Clinical breast examination should be started from 25 years of age, every 6-12 months. Annual MRI should start after 25 years till 30 years. After 30 years of age, yearly mammogram and yearly MRI can be scheduled alternately, every 6 months.

   The sensitivity of mammography in BRCA mutation carriers is lower because women are younger with higher breast density and also due to increased risk of developing interval malignancy.

2. **Chemo prevention:**
   Tamoxifen has been found to be effective in reducing the risk of breast cancer especially in women with BRCA 2 mutation carriers. Tamoxifen reduced breast cancer risk by 62% in BRCA2 carriers (relative risk [RR] 0.38, 95% CI 0.06-1.56), but not in BRCA1 carriers (RR 1.67, 95% CI 0.32-10.07) (16,17). However, this analysis is limited by the small number of mutation carriers. Tamoxifen might be expected to have an impact only against ER-positive tumours, and BRCA2-associated tumours have a greater likelihood than BRCA1-associated tumours of being ER-positive.

3. **Prophylactic mastectomy:**
   While prophylactic surgery is effective in cancer risk reduction, women should be counselled preoperatively about the potential morbidity of such procedures, and the possibility that surgery may affect libido, sexual functioning, and body image.

   NCCN recommends that BRCA carriers be offered prophylactic bilateral mastectomy after genetic risk assessment , as it reduces the risk for developing breast cancer by 90% in eligible cases [8]. However, given the availability of highly effective screening strategy (unlike ovarian cancer screening), the decision is based on personal choice after informed counselling and risk assessment.

Lynch Syndrome:

Lynch syndrome has autosomal dominant predisposition accounts for 2% to 4% of all colorectal cancer cases and approximately 2.5% of endometrial cancer cases. The mean age at diagnosis of colorectal cancer (CRC) in affected patients is 44 to 61 years, while for endometrial cancer mean age at diagnosis is 48 to 62 years [18]. The DNA mismatch repair genes in which mutations lead to LS are *MLH1* and *MSH2*, *MSH6* and *PMS2*.

Amsterdam II Criteria [8]:

For a diagnosis of LS the Amsterdam II Criteria require

at least three relatives with an LS-associated cancer (CRC and cancers of the endometrium, stomach, ovary, ureter or renal pelvis, brain, small bowel, hepatobiliary tract and skin (sebaceous tumours)):

1. One is a first-degree relative of the other two
2. At least two successive generations are affected
3. At least one of the LS-associated cancers should be diagnosed at <50 years of age
4. Familial adenomatous polyposis should be excluded in any colorectal cancer case
5. Tumours should be verified by pathology whenever possible

Risk Reducing Management

Colonoscopy, is initiated at age 18 and repeated biennially through age 40 and then annually thereafter[8]. For the screening of endometrial cancer annual endometrial sampling may be considered with limited efficacy. TVUS and CA 125 is not endorsed as they have not been shown to be sufficiently sensitive or specific[8].

Option for prophylactic hysterectomy and bilateral salpingo-oophorectomy is performed at age 35 (or when pregnancy is no longer an option) in germ line MMR gene mutation carriers.[8] Owing to evidence of increased synchronous and metachronous CRCs in LS, Church and Lynch suggested a role for prophylactic colectomy in LS patients.[19]

Cowden Syndrome:

Cowden syndrome results from germ line mutations in PTEN and causes hemartomatous neoplasms of the skin and mucosa, GI tract, bones, CNS, eyes, and genitourinary tract. Skin is involved in 90-100% of cases, and the thyroid is involved in 66% of cases [20]. Genetic testing for Cowden syndrome is offered to individuals from a family with a known PTEN mutation, a personal history of Bannayan-Riley-Ruvalcaba syndrome, adult Lhermitte-Duclos disease (cerebellar tumours) or family history of breast, endometrial, follicular thyroid cancer, colon cancer, renal cell carcinoma or autism spectrum disorders.

Risk reducing management[8]: Increased surveillance for breast cancer and endometrial cancer as discussed above is recommended. Trans vaginal ultrasound to screen for endometrial cancer in postmenopausal women may be considered at the clinician's discretion in the postmenopausal age group. Option of hysterectomy may be given upon completion of childbearing. Oophorectomy is not indicated in cases of Cowden's syndrome.

LI -Fraumeni Syndrome:

Li-Fraumeni syndrome is characterized by the wide variety of rare cancers seen in affected individuals, a young age at onset of malignancies, and the potential for multiple primary sites of cancer including soft tissue sarcoma, osteosarcoma, pre-menopausal breast cancer, brain tumors, adreno-cortical carcinoma (ACC), and leukemias during the lifetime of affected individuals[21]. The risk of cancer is estimated at 50% by age 30 years and 90% by age 60 years.

Risk reducing management[8]: consist of surveillance and risk reducing surgery options for breast cancer. Comprehensive physical exam including neurologic examination with high index of suspicion for rare cancers and second malignancies in cancer survivors is done every 6–12 months. Colonoscopy and upper endoscopy is done every 2–5 years, starting at age of 25 or 5 years before the earliest known colon cancer in the family. Annual dermatologic examination should be done as patient reaches 18 years. Annual whole body MRI may be advised. For patients of reproductive age, options for prenatal diagnosis and assisted reproduction including pre-implantation genetic diagnosis should be advised.

Conclusion

In recent times the demand for genetic counselling and testing is rising, necessitating the need for increased genetic counselling and risk reduction. In order to timely diagnose and treat hereditary cancer syndromes, it is important to work toward increasing awareness among patients, healthcare providers, and society.

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LIST OF PRIZES – AOGD CONFERENCE 2018	
1. Dr S N Mukherjee-Rotating Trophy	Best AOGD Monthly Clinical Meeting
2. Research Paper-Best Competition Paper	Gold, Silver, Bronze
3. Dr Batra's Medal-Winning Team of AOGD Quiz	Gold Medal
4. Dr Neera Agarwal's Medal-Best Paper on theme topic of Obstetrics (Maternal Health)	Gold Medal
5. Dr Neelam Bala Vaid's Medal-Best Paper on theme topic of Gynecology (Adolescent Health)	Gold, Silver
6. Dr Suneeta Mittal's Medal-Population Stabilization	Gold Medal
7. Dr U P Jha & Dewan Balakram's Medal (Best Presentation in Gynae Oncology)	Gold Medal
8. Dr U P Jha & Raj Soni's Medal (Best Oral/Video/Paper Presentation in Endoscopy)	Gold Medal
9. Mr. S Bhattacharya & Dr Ganguly's Medal-Free Paper competition Miscellaneous Category	Gold, Silver
10. Poster Presentation	Gold, Silver
11. Slogan Competition	First Prize, Second Prize

RECENT ADVANCE

Frontline Targeted Therapy in Ovarian Cancer

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Dr K Chitrathara

Introduction

Prevention strategies of ovarian cancer based on germline genetic testing known as "Angelina Jolie Effect" sends immense hope to people across the world. The enigma surrounding spontaneous mutation, its causes, detection and clinical implications are unclear.

In the absence of cost effective highly efficacious screening tool 70-80% of ovarian cancer are still diagnosed in advanced stages. 90% initial clinical, radiological and tumor marker remission is achieved with optimal surgery and chemotherapy. However the relapse rate is about 70% in 2 years[1] and with repeated chemotherapy protocols the 5 year survival achieved is a dismal 30%. Researches are on the search of treatment protocols which can give cure or at least prolongation of remission thus increasing the duration of disease free survival. The new promising approaches in this direction are the addition frontline targeted therapy and maintenance therapy after initial chemotherapy.

Tumor angiogenesis has a pivotal role and is an integral part of ovarian carcinogenesis. It is assumed that downregulation of angiogenesis can inhibit cancer growth. The potential therapeutic anti angiogenic molecules identified are anti-VEGF/VEGFR inhibitors and non-VEGF inhibitors.

Anti-VEGF/VEGFR angiogenic inhibitors

Inhibition of the legand (VEGF) with antibodies or soluble receptors and inhibition of the receptor with tyrosine kinase inhibitors are the two primary strategies that have been used to inhibit VEGFR signaling pathway. Bevacizumab, a recombinant monoclonal anti-VEGF antibody is the most thoroughly investigated antiangiogenic drug in ovarian cancer. The two major phase 3 randomized trials in the frontline adjuvant setting are GOG 218 and ICON-7. GOG 218[2] was a three arm placebo controlled study. 1. standard treatment arm: patients were given carboplatin and paclitaxel every 3weeks for 6 cycles. 2. Bevacizumab through out arm : Bevacizumab was given with for 2-6 cycles and continued every 3 weeks for 22cycles. 3. Bevacizumab initiation arm: Bevacizumab was given for 2-6cycles and then continued with placebo for 7-22 cycles. Bevacizumab Dose used in this trial was (15mg/kg) was double the dose given in ICON 7[3]. Median Overall survival in chemotherapy arm was 38.6months and chemo+ bevacizumab arm was 42.1 month which did not attain statistical significance. However there was significant improvement in median progression free survival.

ICON -7 enrolled 1528 patients with stage 111c and 1V ovarian cancer. The median overall survival in the chemotherapy arm was 44.7months and for chemo-Bevacizumab arm was 45.5 months. High risk subgroup comprising of inoperable or suboptimally cytoreduced patients was the group most benefitted with an increase in overall survival (34.5 versus 39.3 months). Addition of Bevacizumab was well tolerated in both the trials. Grade > 2 hypertension was observed in 16.5 and 22.6 % in the two Bevacizumab arms compared with 7.2% in the control arm. The other adverse effects like gastrointestinal bleeding, proteinuria, fatigue were infrequent. Caution must be exerted to tackle the increased rate of myelosuppression with the combination regimens

Non-VEGF Angiogenic Inhibitors

Alternate strategy of antiangiogenesis is by targeting the angiopoetin axis with non-VEGF inhibitors. Trebananib, a peptide-Fc fusion protein (peptibody) inhibiting the interaction of angiopoietin-1 and -2 to the Tie2 receptor, has been evaluated in recurrent ovarian cancer in a phase 111 trial with promising results[4]. Participants were treated with paclitaxel alone or paclitaxel and trebananib[5]. Notably, PFS was significantly longer in the combination therapy group at 7.2 months compared with 5.4 months for those treated with paclitaxel alone. It has not been tried in a frontline setting.

PARP Inhibitors

PARP inhibitors target and block repair of DNA single-strand and double- strand breaks. These drugs exert action through the inhibition of base excision repair pathway and homologous recombination (HR) repair pathway. Numerous research have been done to pinpoint the role of PARP inhibitors in the management of malignant ovarian tumors. PARP inhibitors have demonstrated maximal effect in germline *BRCA*-associated tumors and sporadic cases deficient in repair of DNA damage.

With the growing availability and scope of multiplex-gene testing and massive parallel sequencing, patients with mutations in HR-related genes are being identified and may be suitable PARP inhibitor candidates. PARP inhibitors that have demonstrated promising activity in EOC treatment include Olaparib, Niraparib, Velaparib, Rucaparib, and Talazoparib.

Recent data demonstrated potency in trapping PARP differs markedly among niraparib, olaparib and

velaparib, and patterns of trapping were not correlated with the catalytic inhibitory properties for each drug[6] .

PARP inhibitors are approved in the United State and Europe for the treatment of platinum sensitive recurrent ovarian cancer regardless of BRCA mutation and BRCA mutated patients regardless of platinum sensitivity. Its role in frontline setting lacks appropriate and conclusive data. Olaparib has been tried in the phase 111 SOLO1 trial as frontline maintenance therapy for newly diagnosed ovarian cancer patients with BRCA1/2 mutation. The median time to the first subsequent therapy or death was 51. 8 months in Olaparib group and 15.1months in the placebo group. Olaparib reduces the risk of progression or death by 70% when compared to placebo[7]. Many studies suggest that this efficacy of Olaparib seen in patients with germline mutation could be applicable to patients with a somatic BRCA1/2 mutation.

The major adverse effects were nausea, vomiting, fatigue and anemia. Anemia was the most common serious side effect occurred in 7% of patients in the Olaparib group and none in the placebo arm. The incidence of acute myeloid leukemia was 1% in treatment group.

Immune Check Point Inhibitors

A small trial of 10 patients who received first line PD-1 inhibitor Pembrolizumab (Keytruda) and chemotherapy followed by Pembrolizumab maintenance was presented at the 2018 Society of Gynecologic Oncology Annual meeting. The trial showed that the administration of Pembrolizumab combined with chemotherapy is safe and feasible in advanced ovarian cancer. One has to wait for enough data to recommend it as an initial therapy choice[8].

Conclusion

Bevacizumab is all ready with Data to enter into the arena of frontline drug therapy of advanced epithelial ovarian cancer. Numerous data ha proved its efficacy in suboptimally debulked disease. PARP inhibitors as maintenance therapy after first line chemotherapy has shown improved progression free survival, awaits conclusive data to compete for first place in the treatment landscape of advanced ovarian carcinoma. Many molecular targets are in line including immune check point inhibitors, EGFR inhibitors, folate receptor inhibitors etc. We may have to wait indefinitely and patiently to see that O'vary' is no more an O'worry'.

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Calendar of Monthly Clinical Meetings 2018-19

Months	Name of the Institute
November, 2018	MAMC & LN Hospital
December, 2018	Sir Ganga Ram Hospital
January, 2019	Dr RML Hospital
February, 2019	UCMS & GTB Hospital
March, 2019	LHMC
April, 2019	Apollo Hospital

CONTROVERSY

Lymphadenectomy in Endometrial Cancer

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Endometrial cancer is the most common gynecologic cancer in developed countries and worldwide there are approximately 3,82,000 cases diagnosed annually.[1] The disease occurs predominantly in postmenopausal women with more than 90% of cases being reported in women over 50 years old, average age of diagnosis being 63 years.[2] Diagnosis in young females is rare, indeed less than 5 % patients are less than 40 years of age.[3] Fortunately majority of cases are diagnosed in early stages and are amenable to surgery.

Standard approach for management of endometrial cancer is total hysterectomy with bilateral salpingo-oophorectomy with evaluation of pelvic and para-aortic lymph nodes. Peritoneal washings are collected for cytology which have a prognostic significance. Pelvic lymphadenectomy has been defined as removal of the nodal tissue from the distal half of the common iliac arteries, the anterior and medial aspect of the proximal half of the external iliac artery and vein, and the distal half of the obturator fat pad anterior to the obturator nerve. Para-aortic lymph node dissection includes removal of nodal tissue over the distal inferior vena cava from the level of renal vein to the common iliac.[4]

Federation of International Gynecology and Obstetrics (FIGO) adopted the surgico-pathological staging in 1988 after the results of GOG 33 study.[5] This study prospectively evaluated 621 patients with clinical stage I endometrial cancer. All patients underwent a standard comprehensive staging procedure, including hysterectomy, bilateral salpingo-oophorectomy, collection of pelvic washings, and selected pelvic and para-aortic lymph node dissection. Based on multivariant analysis, three risk categories were defined. Patients with low-risk disease, defined as grade 1 tumor with endometrial involvement only and no intraperitoneal disease, had no pelvic or para-aortic lymph node metastasis. Those with moderate-risk disease, defined as, 50% myometrial invasion and no intraperitoneal disease, had a 3% to 6% incidence of pelvic lymph node metastasis, and a 2% incidence of para-aortic lymph node involvement. High-risk disease was defined by two criteria: deep myometrial invasion and/or intraperitoneal disease. Those with deep myometrial invasion had 15 to 18 % incidence of pelvic and para-aortic lymph node metastasis, respectively. Patients with intraperitoneal disease with only 50% myometrial involvement had a 33% risk of pelvic lymph node metastasis and 8% risk of positive para-aortic lymph nodes. Patients with both high-risk criteria were at the highest risk with 61% pelvic lymph node metastasis and 30% para-aortic lymph node involvement. This study shifted the paradigm of endometrial cancer staging from clinical to surgical. Since then information about primary tumor and lymph node status has helped in guiding prognosis and adjuvant therapies.

However, surgical staging has always been mired in controversies due to the risks associated with it. Comprehensive lymph node dissection not only increases the surgical time but can also lead to complications like vessel or nerve injury, post op lymphedema or lymphocysts formation. Whether lymphadenectomy should be done in all cases or not, does it have any survival or prognostic advantage and what should be the extent of lymph node dissection, have been the main dilemmas.

Lymphadenectomy as a part of comprehensive surgical staging helps in appropriate triage of patients to radiation therapy and prognostication of the patient. As per GOG 33, 9% of clinically stage I patients had pelvic nodal metastases and 6% had para-aortic metastases at the time of surgery.[5] Patients with more advanced stage disease have poorer prognosis, which may go unrecognized without complete lymph node dissection. In addition to accurate stage, GOG 33 presented evidence that clinical stage I disease may pathologically include risk factors warranting adjuvant radiation therapy in 15% to 25% of patients with early stage disease. Furthermore, those patients without high risk factors can also be identified, avoiding overtreatment with adjuvant radiation therapy. Many retrospective studies have also shown survival advantage with lymphadenectomy. An observational study examined recurrence pattern for patients with intermediate or high-risk factors who underwent surgery with pelvic lymphadenectomy with or without para-aortic lymph node dissection. There was a survival benefit for those who had a paraaortic lymphadenectomy compared with those who did not, but this effect was not seen in patients with low-risk cancers.[6] In 2012 SEER database reported survival data of more than 56,000 patients that showed a definite survival advantage in the patients who had lymphadenectomy as a part of surgical staging.[7]

However, these results were not identified when analyzed in prospective randomized trials. Benedetti Panici et al. randomized 514 women with clinical stage I endometrial cancer to either systematic pelvic lymphadenectomy or no lymph node dissection. Though there was 10 % increase in nodal metastasis detection rate, no advantage in disease free or overall survival was seen. On the contrary, documented rate of lymphedema was much higher in lymphadenectomy arm.[8] These observations were consistent with the results of the ASTEC trial, which included 1408 patients with stage I endometrial

cancer randomized to receive surgical staging with or without pelvic lymphadenectomy. This trial also failed to show a beneficial effect of lymphadenectomy and an increase in lymphedema.[9] These trials were criticized as no standard lymphadenectomy protocol or standard adjuvant therapy was used in them. Nevertheless, these trials did raise the question of routine lymphadenectomy in all endometrial cancer patients.

Based on histologic criteria from GOG 33 as well as their own patients Mariani et al defined a low risk population in whom lymphadenectomy could be safely avoided.[10] Criteria's for low risk were defined as grade 1 or 2 disease, <50% myometrial invasion, and tumor diameter < 2 cm. These were then analyzed prospectively by Mayo Clinic. It was an observational study and the diagnosis was dependent on intra-operative frozen section. They found that patients who met the above criteria had <1% risk of positive lymph node metastasis and lymphadenectomy could be safely avoided in them.[11] This group of patients had a 99% 5-year survival rate and none of them had a nodal recurrence at the median follow-up of 5 years. But the caveat is that these results were obtained in high volume center with a dedicated gynecologic onco-pathologist and reliability on frozen section. Also, of patients who underwent lymphadenectomy, 22% of patients with high-risk disease had lymph node metastases, 51%had both positive pelvic and para-aortic nodes, 33% had positive pelvic lymph nodes only, and 16% had isolated para-aortic lymphadenopathy. As the majority (77%) of patients with para-aortic lymph node involvement had metastases above the inferior mesenteric artery, para-aortic lymphadenectomy up to the renal vessels was recommended.[11]

The consensus guidelines from Europe and US state that lymphadenectomy is a staging procedure and allows tailoring of adjuvant therapy. Patients with low-risk endometrioid carcinoma (grade 1 or 2 and superficial myometrial invasion <50%) have a low risk of lymph node involvement, so lymphadenectomy is not recommended for these patients. For patients with intermediate risk (deep myometrial invasion >50% or grade 3 superficial myometrial invasion < 50%), data have not shown a survival benefit. Lymphadenectomy can be considered for staging purposes in these patients. For patients with high risk (grade 3 with deep myometrial invasion >50%), lymphadenectomy should be recommended. If lymphadenectomy is performed, systematic removal of pelvic and para-aortic nodes up to the level of the renal veins should be considered. Lymphadenectomy to complete staging could be considered in previously incompletely operated high-risk patients to tailor adjuvant therapy.[12, 13]

Until the controversies regarding lymphadenectomy are resolved, a more balanced approach targeting alternative to complete pelvic and para-aortic lymphadenectomy has been suggested known as Sentinel lymph node dissection (SLND). It represents a compromise between no dissection (leaving a small proportion of node positive patients) and full dissection (adding a useless procedure for most node-negative patients). It aims at providing secure complete information about lymph node status for treatment planning while avoiding the collateral damage.

SLND can be done using colorimetric methods which uses Isosulfan blue or methylene blue. Typically, 3– 5 cm^3 of a 1% solution of isosulfan blue is injected into the cervix, after which there is immediate uptake of the dye into lymphatic channels and accumulation in the SLNs within 10–20 min. Disadvantages of isosulfan blue include its expense, limited availability, and the risk (1.1%) of allergic reaction (anaphylaxis).[14] Methylene blue is a less expensive alternative to isosulfan blue. This is an off-label use of the dye, however, though there is evidence that suggests equivalency for SLN mapping in other cancers.[15] The injection of radiolabeled colloid technetium 99 (Tc99) and detection with nuclear imaging and/or intraoperative gamma counters is one of the original techniques of SLN mapping and is often used in synergy with a blue dye (or indocyanine green [ICG]) to optimize detection rates.[16]A gamma-detecting probe identifies areas of "hot" tracer signal intraoperatively. After discriminating the general area of increased uptake, the surgeon employs dissection to visually identify blue (or green) dyes in the area of increased gamma signal. The gamma-detecting probe is then used to quantify the signal strength of the resected SLNs. ICG is a water soluble tricarbocyanine dye that emits a fluorescent signal in the near-infrared (NIR) light range. The ICG signal not only penetrates tissues, but also allows for real-time visualization during dissection, combining the assets of colorimetric and radio nuclear techniques. ICG has been shown superior to blue dyes for detection, particularly in obese patients.[17,18]

Majority of the large series use cervix as the site of injection. The reproducibility of the cervical injection technique, high success rate, and low-risk for isolated aortic metastasis has led most investigators to use cervical injections of tracers.[19]The question of alternative injection sites in the endometrium or uterine fundus, which are anatomically more logical, is still a topic for investigation. Injection under hysteroscopic, ultrasound, laparoscopic or open guidance in patients with endometrial cancer has been addressed, without evidence of benefit of the more demanding and less practical modalities.

With the initial studies of SLN mapping by Abu-Rustum et al., a low false-negative rate was demonstrated.[20] The same investigators described a learning curve with an increase in SLN detection from 77% to 94% (p=0.03) following a 30-case experience.[21] A meta-analysis by Kang et al which included more than 100 patients of early endometrial cancer who underwent SLN mapping showed a 78% detection rate for sentinel nodes and 93% sensitivity.[22] The 2014 NCCN guidelines adopted SLN mapping in the surgical management of endometrial cancer provided the algorithm by Barlin et al. is adhered to.[23] In their multicentric prospective cohort study Rossi et al compared sensitivity and negative predictive

value of sentinel-lymph-node mapping to complete lymphadenectomy in detecting metastatic disease for endometrial cancer (FIRES study). 385 patients and 18 surgeons from ten centers of USA participated. Nodal metastases were identified in the sentinel lymph nodes of 97% patients, yielding a sensitivity to detect node-positive disease of 97·2% (95% CI 85·0–100), and a negative predictive value of 99·6% (97·9–100). They concluded that sentinel lymph nodes identified with indocyanine green have a high degree of diagnostic accuracy in detecting endometrial cancer metastases and can safely replace lymphadenectomy in the staging of endometrial cancer. Sentinel lymph node biopsy will not identify metastases in 3% of patients with node-positive disease but has the potential to expose fewer patients to the morbidity of a complete lymphadenectomy.[24]

Though large series suggest the feasibility of sentinel lymph node dissection, it is still considered experimental in majority of the consensus guidelines. It does increase the detection of lymph nodes with small metastases and isolated tumor cells, the importance of these findings is unclear. Sentinel lymph node is the way forward.

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CASE APPROACH

Pregnancy with Early Invasive Cancer Cervix (Stage IA2 to IB1)


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Cervical cancer is the most common gynecologic cancer diagnosed during pregnancy. The reported incidence is 0.8 to 1.5 cases per 10,000 births[1]. Among the patients with cervical cancer, 1 to 3% are pregnant or in the postpartum at the time of the diagnosis[2]. Over 70% of cervical cancers in pregnancy present in stage I and have excellent survival rates.

Women with cervical cancer in pregnancy may present with abnormal bleeding, vaginal discharge and abdomino-pelvic pain[3]. This may be mistaken for threatened abortion in early pregnancy and placenta praevia/ abruptio placenta in late pregnancy. Thus, it is imperative to do a speculum examination to visualize and identify any abnormalities in cervix in a woman presenting with bleeding during pregnancy. Cervical intraepithelial neoplasia diagnosed by colposcopy and biopsies in pregnancy, should be followed by colposcopy at least once in every trimester to assess lesion size and progress of disease. Definitive management is offered 6-8 weeks after delivery for high grade lesions. The management of pregnant women with cervical cancer is however more complex. The treatment of cervical cancer during pregnancy depends on the period of gestation at the time of diagnosis, stage of the disease, size of the tumor, lymph node involvement, and the decision of the pregnant woman to continue her pregnancy or not. Hence treatment for this disease in pregnancy is individualized. Immediate, definitive treatment regardless of age is generally appropriate with documented lymph node metastases, progression of disease in pregnancy and the patients desire to terminate the pregnancy[4].

Stage IA1 tumors without lymphovascular space invasion are sufficiently treated by conization and is best done between 12-20 weeks of gestation[5]. The term 'coin biopsy' is sometimes used in pregnancy to highlight the fact that the cone should not be deep enough to damage the fetal membranes. Best performed in the theatre with adequate anesthesia. Prophylactic cerclage may be an option both for the prevention of premature labor and the management of operative bleeding[4].

In patients with early stage cervical cancer (IA2 or IB1) who are diagnosed in late pregnancy (third trimester), definitive treatment may be delayed until after fetal maturity. These patients are delivered by cesarean section and a classical uterine incision is used to avoid encroaching into the lower uterine segment or cervix; preventing hemorrhage and avoiding dissemination of disease. Definitive surgery including radical hysterectomy is done for early-stage disease after the cesarean section. For advanced cancer, chemoradiation is started after the cesarean section, generally within 3 weeks of involution of uterus.

Treatment strategies for stage IA2 or IB1 tumors are different if diagnosis is before or after 22 to 25 weeks of gestation. According to International Gynecologic Cancer Society (IGCS) and European Society of Gynecologic Oncology (ESGO) guidelines, women who are diagnosed before 22–25 weeks, should undergo pelvic lymphadenectomy in the second trimester[5]. If the lymph nodes are found to be positive, termination of pregnancy should be offered followed by definitive chemoradiation. Lymphadenectomy can be done by laparotomy, laparoscopically or by robotic approach. Laparoscopic lymphadenectomy is best performed before 20 weeks of gestation[4]. During laparoscopy in pregnancy, the prerequisites to be followed are; maximal laparoscopic procedure time of 90 minutes, a maximal intraabdominal pressure of 10 to 13mmHg with pneumoperitoneum, open entry of trocars and an experienced surgeon. These conditions minimize the potential risks to the fetus during laparoscopic surgery.

For tumors < 2 cm with negative nodes on pelvic lymphadenectomy, simple trachelectomy or conization is recommended, followed by close surveillance with cesarean delivery after fetal maturity. In stage IB1 tumors smaller than 2 cm and negative pelvic lymph nodes, the risk of parametrial involvement is reported to be less than 1%[6]. Parametrectomy can be omitted in these cases and simple trachelectomy is sufficient, feasible and associated with low complication rates during pregnancy[7,8]. Simple trachelectomy is a less complicated procedure and is defined as excision of cervix 1 cm above tumor border[9]. Radical vaginal or abdominal trachelectomy, on the other hand is associated with high rate of obstetric and surgical complications including pregnancy loss and significant blood loss. Thus, radical trachelectomy is not recommended during pregnancy[5].

The management for patients with stage IB1 tumors > 2 cm and negative nodes after pelvic lymphadenectomy, is neoadjuvant chemotherapy (NACT) until fetal maturity[5]. Close observation and delay of treatment is also feasible in cases of negative nodes. A review of 76 patients with stage IB1 cervical cancer diagnosed during pregnancy reported a 95% survival rate of women who were kept on surveillance till fetal maturity without

definitive treatment. The median treatment delay was 16 weeks and a mean follow up period of 37.5 months did not report any recurrences[10].

In women where cervical cancer is diagnosed after 22 to 25 weeks of gestation, lymphadenectomy is not recommended. This is because after the 22nd week of pregnancy, a complete pelvic and/or paraaortic lymphadenectomy is difficult to perform due to the size of the uterus and there is a significant decrease in the number of harvested lymph nodes which does not ensure oncological safety. Thus, after the 22nd week of pregnancy when lymphadenectomy is not feasible, neoadjuvant chemotherapy can be given or a close follow-up of patients followed. In stage IA2 and IB1 tumors smaller than 2 cm, treatment is delayed until fetal maturity with delivery after discussion with a neonatologist. If disease progression is found on surveillance, early delivery or neoadjuvant chemotherapy (NACT) is advocated. For women with stage IB1 tumors > 2cm, NACT is advocated, although patients have been managed with close monitoring and delayed treatment with cesarean delivery at fetal maturity. For stages IB2 and higher, the only means of preserving pregnancy without unduly compromising patient outcome, is the administration of neoadjuvant chemotherapy.

The most commonly used neoadjuvant chemotherapy drugs are platinum agents in combination with other compounds (paclitaxel, vincristine, 5-fluorouracil, cyclophosphamide or bleomycin), given at 3-weekly intervals. Currently, the recommended regimen for NACT is cisplatin (75 mg/m2) with paclitaxel (175 mg/m2) at a 3-week interval. Carboplatin has been used as an alternative to cisplatin due to its better maternal toxicity profile. The use of NACT in stage IB1 tumors during pregnancy has allowed the pregnancy to continue until an average of 33.2 weeks, with 6.25% patients showing a complete response, 62.5% a partial response, 28.1% disease stabilization, and disease progression in 3.1% of patients. Overall survival rate was 94% in stage IB1 patients at a median follow-up of 12 months[11]. There is an increased risk of premature rupture of membranes, intrauterine growth restriction and preterm labour. Therefore, fetal monitoring during each chemotherapy cycle throughout the pregnancy is recommended. According to the available data, there have not been any significant long-term complications in fetuses exposed to chemotherapy during the second and third trimesters of pregnancy.

The ESGO guidelines from an International Consensus Meeting on Gynecological Cancers in Pregnancy[5] have recommended NACT under the following circumstances:

- In stage 1B1 cervical cancer with tumor size greater than 2 cm, NACT treatment can be given either to node-negative patients or primarily before nodal assessment by lymphadenectomy, to preserve pregnancy until maturity and delivery.
- In stage 1B2 or higher, NACT is the only way to preserve pregnancy until maturity and delivery.

The European Society for Medical Oncology consensus on cancer, pregnancy, and fertility[12] laid forth the following clinical practice guidelines:

- Pregnancies where the fetus has been exposed to chemotherapy starting in the second trimester should be regarded as high risk, and regular fetal monitoring during gestation should be considered.
- Full-term delivery (≥ 37 weeks) should be targeted whenever possible.
- Dose calculation should follow the standard recommendations in the non-pregnant settings, acknowledging that the pharmacokinetics of some cytotoxic drugs might be altered during pregnancy.
- There should be a 3-week period between the last chemotherapy dose and the expected date of delivery, to reduce the risk of bleeding, infection and anemia for both mother and child.
- Radical surgery can be offered concomitantly with cesarean delivery in qualified centers.

Described below are two case discussions of women diagnosed with early cervical cancer during pregnancy. Figure 1 describes the algorithm for management of women with early cervical cancer diagnosed before 22 to 25 weeks gestation.

Case 1

A 32 year-old lady, G3P2L2, presented at 16 weeks gestation with stage IB1 squamous cervical cancer. Pelvic exam showed a 2 cm cervical lesion with no extension to vagina or parametrium. MRI showed no evidence of lymph node involvement or metastatic disease. The patient underwent a laparoscopic bilateral pelvic lymphadenectomy and simple vaginal trachelectomy at 18 weeks gestation. Histopathology showed squamous cell carcinoma of cervix, T size 2 x 2 cm, grade II, with < 50% cervical stromal invasion and no LVSI. All margins were negative and 18 lymph nodes removed were negative for metastases. Patient was followed up with clinical examination as well as fetal monitoring with USG and Doppler. She delivered a healthy baby via cesarean section at 38 weeks gestation weighing 3100 gm with an Apgar score of 8. The patient underwent a radical hysterectomy at the time of cesarean section. Final specimen did not show any tumor. The patient was disease-free, and the child alive and healthy, 42 months after her definitive surgery.

Case 2

A 28 year-old lady, G2P1L1 was referred at 10 weeks gestation with a 4 X 3 cm exophytic growth on cervix. Cervical biopsy revealed squamous cell carcinoma and her stage was IB1. MRI showed a 4 X 3.5 cm mass in the cervix involving the posterior cervical lip with no pelvic or retroperitoneal lymphadenopathy. At 14 weeks gestation, the patient underwent a bilateral laparoscopic pelvic lymphadenectomy and a simple trachelectomy. Histopathology revealed a 4 x 3.5 cm grade III squamous

cell carcinoma, with deep cervical stromal invasion and positive LVSI. One pelvic lymph node out of total 19 lymph nodes was positive for metastasis.

The patient was counseled for termination of pregnancy and to undergo chemo radiation. However the patient refused termination and decided to continue her pregnancy with chemotherapy. She was begun on neo-adjuvant chemotherapy – three weekly carboplatin and paclitaxel starting at 17 weeks gestation. She had preterm labour at 34 weeks and a cesarean section was done. The baby weight was 2550 gm and the Apgar score was 7. Chemoradiation was started 4 weeks after cesarean section. On follow up, 18 months after the completion of chemoradiation (including 3 cycles of brachytherapy), patient has no evidence of disease and the baby is alive and healthy.

In conclusion, as advised by The European Society of Gynaecological Oncology[13], the following guidelines should be followed for women diagnosed with cervical cancer during pregnancy:

- These women must be counseled by a multidisciplinary team consisting of experts in the fields of gynecologic oncology, neonatology, obstetrics, anesthesiology, radiation oncology, medical oncology, psychooncology, and, if requested, theology or ethics.
- An individualized consensual treatment plan should be formulated according to patient's intention to continue pregnancy or not, tumor stage and the gestational age of pregnancy at the time of cancer diagnosis. Primary aims of recommended treatment plan are oncological safety of the pregnant woman, as well as survival without additional morbidity of the fetus.
- Treatment of pregnant women with cervical cancer should be done exclusively in gynecologic oncology centers associated with a highest level perinatal center with expertise in all aspects of oncologic therapy in pregnancy and intensive medical care of premature neonates.
- Besides clinical examination and histologic verification of cervical cancer, preferred imaging modalities for staging in these women include MRI or expert ultrasound. Because of limited experience and inherent radioactivity, PET-CT or PET-MRI should be indicated only under select circumstances (grade D).
- Tumor involvement of suspicious nodes should be verified histologically up to 24th week of gestation, preferably by minimally invasive approach because of its prognostic significance and impact on further management.
- Depending up on the tumor stage and the gestational week of pregnancy, the following treatment options have to be discussed with the patient including risks and benefits of individual approaches (grade D):
  a. Surgery including conization, trachelectomy and lymph node staging according to the stage of the disease with the intent to preserve the pregnancy.
  b. Radical surgery or definitive chemoradiation, as appropriate for the stage of the disease without preservation of the pregnancy.
  c. Delay of oncological treatment until fetal maturity (if possible > 32 weeks of gestation) and beginning of cancer-specific treatment immediately after delivery by cesarean section.
  d. Chemotherapy until fetal maturity and beginning of cancer-specific treatment immediately after delivery by cesarean section.

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Journal Scan

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Insulin for the Treatment of Women with Gestational Diabetes

Brown J, Grzeskowiak L, Williamson K, Downie MR, Crowther CA

Background

Gestational diabetes mellitus (GDM) is associated with short- and long-term complications for the mother and her infant. Women who are unable to maintain their blood glucose concentration within pre-specified treatment targets with diet and lifestyle interventions will require anti-diabetic pharmacological therapies. This review explores the safety and effectiveness of insulin compared with oral anti-diabetic pharmacological therapies, non-pharmacological interventions and insulin regimens.

Objectives

To evaluate the effects of insulin in treating women with gestational diabetes.

Search Methods

We searched Pregnancy and Childbirth's Trials Register (1 May 2017), ClinicalTrials.gov, WHO International Clinical Trials Registry Platform (ICTRP) (1 May 2017) and reference lists of retrieved studies.

Selection Criteria

We included randomized controlled trials (including those published in abstract form) comparing: a) insulin with an oral anti-diabetic pharmacological therapy; b) with a non-pharmacological intervention; c) different insulin analogues; d) different insulin regimens for treating women with diagnosed with GDM. We excluded quasi-randomized and trials including women with pre-existing type 1 or type 2 diabetes. Cross-over trials were not eligible for inclusion.

Data Collection and Analysis

Two review authors independently assessed study eligibility, risk of bias, and extracted data. Data were checked for accuracy.

Main Results

We included 53 relevant studies (103 publications), reporting data for 7381 women. Forty-six of these studies reported data for 6435 infants but our analyses were based on fewer number of studies/participants. Overall, the risk of bias was unclear; 40 of the 53 included trials were not blinded. Overall, the quality of the evidence ranged from moderate to very low quality. The primary reasons for downgrading evidence were imprecision, risk of bias and inconsistency. We report the results for our maternal and infant GRADE outcomes for the main comparison. Insulin versus oral anti-diabetic pharmacological therapy .For the mother, insulin was associated with an increased risk for hypertensive disorders of pregnancy (not defined) compared to oral anti-diabetic pharmacological therapy (risk ratio (RR) 1.89, 95% confidence interval (CI) 1.14 to 3.12; four studies, 1214 women; moderate-quality evidence). There was no clear evidence of a difference between those who had been treated with insulin and those who had been treated with an oral anti-diabetic pharmacological therapy for the risk of pre-eclampsia (RR 1.14, 95% CI 0.86 to 1.52; 10 studies, 2060 women; moderate-quality evidence); the risk of birth by caesarean section (RR 1.03, 95% CI 0.93 to 1.14; 17 studies, 1988 women; moderate-quality evidence); or the risk of developing type 2 diabetes (metformin only) (RR 1.39, 95% CI 0.80 to 2.44; two studies, 754 women; moderate-quality evidence). The risk of undergoing induction of labour for those treated with insulin compared with oral anti-diabetic pharmacological therapy may possibly be increased, although the evidence was not clear (average RR 1.30, 95% CI 0.96 to 1.75; three studies, 348 women; I^2 = 32%; moderate-quality of evidence). There was no clear evidence of difference in postnatal weight retention between women treated with insulin and those treated with oral anti-diabetic pharmacological therapy (metformin) at six to eight weeks postpartum (MD -1.60 kg, 95% CI -6.34 to 3.14; one study, 167 women; low-quality evidence) or one year postpartum (MD -3.70, 95% CI -8.50 to 1.10; one study, 176 women; low-quality evidence). The outcomes of perineal trauma/tearing or postnatal depression were not reported in the included studies.For the infant, there was no evidence of a clear difference between those whose mothers had been treated with insulin and those treated with oral anti-diabetic pharmacological therapies for the risk of being born large-for-gestational age (average RR 1.01, 95% CI 0.76 to 1.35; 13 studies, 2352 infants; moderate-quality evidence); the risk of perinatal (fetal and neonatal death) mortality (RR 0.85; 95% CI 0.29 to 2.49; 10 studies, 1463 infants; low-quality evidence);, for the risk of death or serious morbidity composite (RR 1.03, 95% CI 0.84 to 1.26; two studies, 760 infants; moderate-quality evidence); the risk of neonatal hypoglycaemia (average RR 1.14, 95% CI 0.85 to 1.52; 24 studies, 3892 infants; low-quality

evidence); neonatal adiposity at birth (% fat mass) (mean difference (MD) 1.6%, 95% CI -3.77 to 0.57; one study, 82 infants; moderate-quality evidence); neonatal adiposity at birth (skinfold sum/mm) (MD 0.8 mm, 95% CI -2.33 to 0.73; random-effects; one study, 82 infants; very low-quality evidence); or childhood adiposity (total percentage fat mass) (MD 0.5%; 95% CI -0.49 to 1.49; one study, 318 children; low-quality evidence). Low-quality evidence also found no clear differences between groups for rates of neurosensory disabilities in later childhood: hearing impairment (RR 0.31, 95% CI 0.01 to 7.49; one study, 93 children), visual impairment (RR 0.31, 95% CI 0.03 to 2.90; one study, 93 children), or any mild developmental delay (RR 1.07, 95% CI 0.33 to 3.44; one study, 93 children). Later infant mortality, and childhood diabetes were not reported as outcomes in the included studies. We also looked at comparisons for regular human insulin versus other insulin analogues, insulin versus diet/standard care, insulin versus exercise and comparisons of insulin regimens, however there was insufficient evidence to determine any differences for many of the key health outcomes. Please refer to the main results for more information about these comparisons.

Authors' Conclusions

The main comparison in this review is insulin versus oral anti-diabetic pharmacological therapies. Insulin and oral anti-diabetic pharmacological therapies have similar effects on key health outcomes. The quality of the evidence ranged from very low to moderate, with downgrading decisions due to imprecision, risk of bias and inconsistency. For the other comparisons of this review (insulin compared with non-pharmacological interventions, different insulin analogies or different insulin regimens), there is insufficient volume of high-quality evidence to determine differences for key health outcomes. Long-term maternal and neonatal outcomes were poorly reported for all comparisons. The evidence suggests that there are minimal harms associated with the effects of treatment with either insulin or oral anti-diabetic pharmacological therapies. The choice to use one or the other may be down to physician or maternal preference, availability or severity of GDM. Further research is needed to explore optimal insulin regimens. Further research could aim to report data for standardised GDM outcomes.

Editor's Comment

Insulin is the mainstay of pharmacotherapy in GDM. However oral hypoglycemic agents metformin has been accepted for use after 20 weeks of gestation. Although it crosses placenta it is not teratogenic and does not cause hypoglycemia. Therefore for women who are unwilling to take injection Insulin metformin is a viable alternative because of its ease of administration (oral route) and because of low risk for adverse outcome.

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Front-line Therapy of Advanced Epithelial Ovarian Cancer: Standard treatment

C Marth D Reimer A G Zeimet

Paclitaxel and carboplatin combination chemotherapy has remained the standard of care in the front-line therapy of advanced epithelial ovarian cancer during the last decade. Maintenance chemotherapy has not been proven to impact on overall survival. Acceptable alternatives include weekly paclitaxel plus 3-weekly carboplatin, the addition of bevacizumab to 3-weekly carboplatin and paclitaxel, and intraperitoneal chemotherapy. In particular, anti-angiogenic therapy has been identified as the most promising targeted therapy, and the addition of bevacizumab to first-line chemotherapy followed by a maintenance period of bevacizumab in monotherapy has shown to prolong progression-free survival. This was considered the proof of concept of the value of anti-angiogenic therapy in the front-line of ovarian cancer, and the results of two additional clinical trials with anti-angiogenic tyrosine kinase inhibitors have shown results in the same direction.

The GOG-218 trial was a double-blind, randomized clinical trial that included patients with ovarian cancer, fallopian tube cancer or primary peritoneal carcinomatosis with suboptimal or optimal cytoreduction (<1 cm) but with residual macroscopic tumor after front-line debulking surgery [9]. A total of 1873 patients were included. All patients received standard chemotherapy with intravenous paclitaxel 175 mg/m^2 and carboplatin AUC 6 administered every 3 weeks for six cycles, and were randomized to one of the following three arms: the control arm consisted of the administration of intravenous placebo in cycles 2 through 22; the second group, also called the 'bevacizumab initiation group', consisted of the administration of bevacizumab 15 mg/kg every 3 weeks in cycles 2 through 6 concurrently with chemotherapy followed by placebo from cycles 7 to 22; and the bevacizumab-throughout group was chemotherapy with bevacizumab 15 mg/kg added in cycles 2 through 6 followed by a period of maintenance from cycles 7 to 22 (▫15 months in total). The main end point of the GOG trial was progression-free survival (PFS) determined by CA-125 GCIG progression criteria or radiological progression according to RECIST criteria. The bevacizumab initiation group did not obtain any significant benefit in outcome over the control group. However, the bevacizumab-throughout group had a significantly longer PFS than the control group (14.1 versus 10.3 months; HR 0.71; 95% CI 0.625–0.824; $P < 0.001$). The maximal separation of the PFS

curves for the bevacizumab-throughout group and the control group occurred at 15 months, with convergence ▫9 months later.

In the ICON7 trial, a total of 1528 patients with EOC, fallopian tube cancer or primary peritoneal carcinomatosis with FIGO (International Federation of Gynecology and Obstetrics) high-risk stage I (defined as grade 3 or clear cell histology) to stage IV were randomized to one of the following arms: the standard arm was intravenous paclitaxel 175 mg/m^2 and carboplatin AUC 6 every 3 weeks, and the experimental arm was the same chemotherapy regimen with bevacizumab 7.5 mg/kg every 3 weeks added from cycles 1 to 18 (a total of 12 months) . Patients were stratified according to the extension of the disease and debulking (stage I–III with optimal debulking <1 cm versus stage I–III with suboptimal debulking >1 cm versus inoperable stage III and IV), timing of treatment initiation (<4 weeks versus >4 weeks) and GCIG group. The primary end point in this trial was also the PFS, but in this case progression was defined by RECIST criteria only. The median PFS was 17.3 months in the standard therapy group and 19.0 months in the bevacizumab group. A comparison of Kaplan–Meier curves for PFS showed a significant difference between the two groups (estimated HR for progression or death in the bevacizumab group, 0.81; 95% CI 0.70–0.94; *P* = 0.004). The effect of bevacizumab was maximal at 12 months, with an improvement in PFS at this time of 15.1% compared with the standard arm. No significant differences in OS have been found in GOG-218 or ICON7.

In the multinational prospective single-arm ROSIA study, eligible patients had FIGO stage IIB to IV or grade 3 stage I to IIA EOC without clinical signs or symptoms of gastrointestinal obstruction or history of abdominal fistula, GIP, or intra-abdominal abscess within the preceding 6 months. Prior neoadjuvant chemotherapy was permitted. After debulking surgery, patients received bevacizumab 15 (or 7.5) mg/kg every 3 weeks (q3w) with 4–8 cycles of paclitaxel (investigator's choice of 175 mg/m^{2}q3w or 80 mg/m^2 weekly) plus carboplatin AUC 5–6 q3w. Single-agent bevacizumab was continued until progression or up to 24 months. A total of 1021 patients were enrolled and treated for more than 15 months in 53%. Median PFS was 25.5 months (95% CI 23.7–27.6 months), which is the longest PFS reported for front-line bevacizumab-containing therapy. This single arm study suggested that extended bevacizumab may improve PFS without substantially compromising safety. This important hypothesis has to be demonstrated by a clinical trial which has already closed enrolment: the BOOST trial.

Trebananib (AMG-386; Amgen, Thousand Oaks, CA) is a first-in-class investigational peptide-Fc fusion protein peptibody that neutralizes the interaction between the Tie2 receptor and angiopoietin-1 (Ang-1) and angiopoietin-2 (Ang-2). The angiopoietin axis promotes vascularization in ovarian cancer by a different pathway than the VEGF–VEGFR interaction. Trebananib has entered an extensive program for clinical development, known as TRINOVA, which includes three different studies. However, inclusion of trebananib into the upfront therapy (ENGOT-ov6/TRINOVA-3) failed to meet the primary end point of improved PFS [12].

Pazopanib (Votrient™; GlaxoSmithKline, London, UK) is an oral small-molecule angiogenesis inhibitor targeting VEGF receptors (VEGFR-1, -2, and -3), PDGF receptors (PDGFR-α and ß), FGF receptors (FGFR-1 and -3), and c-Kit. Based on the antitumor activity shown in patients with recurrent and small-volume disease, pazopanib was investigated as maintenance therapy in front-line therapy in an international cooperative AGO-OVAR-16 trial led by the AGO group (Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovar). In this study, patients without progression after first-line therapy based on platinum/taxanes and a tumor of less than 2 cm in baseline evaluation were randomized to maintenance with placebo or pazopanib. Results demonstrated that pazopanib as maintenance therapy had a statistically significant PFS benefit (HR 0.766; 95% CI 0.64–0.91; *P* = 0.0021; median 17.9 versus 12.3 months, respectively), but no effect on OS [13].

Nintedanib (BIBF 1120; Boehringer Ingelheim, Ingelheim, Germany), a 6-methoxycarbonyl-substituted indolinone, is a potent inhibitor of VEGFR-1, -2, and -3, as well as PDGF receptors (PDGFR-α and -ß) and FGF receptors (FGFR-1, -2, and -3). Additionally, it inhibits Src and fms-like tyrosine kinase 3 (FLT-3). Nintedanib was studied in the international cooperative phase III trial AGO-OVAR 12/LUME-OVAR-1. This trial included patients with an initial diagnosis of ovarian, primary peritoneal or fallopian tube cancer stage IIB–IV after initial debulking surgery, or with only biopsy for patients with stage IV in whom surgery was not considered an option. A total of 1366 patients were randomized to paclitaxel/carboplatin every 3 weeks with placebo or nintedanib for 6 cycles followed by maintenance therapy with placebo or nintedanib for 120 weeks (including the period of concurrence with chemotherapy) if no progression or intolerance was detected. Nintedanib added to paclitaxel and carboplatin chemotherapy significantly increased PFS from 16.6 to 17.2 months (HR 0.84; 95% CI 0.72–0.98; *P* = 0.0239). OS data have not been reported yet.

Conclusion

Front-line chemotherapy for EOC has not changed in the last decade and the combination of paclitaxel and carboplatin administered every 3 weeks has remained the standard of care. Alternative schedules, such as, for instance, intraperitoneal administration of chemotherapy or dose-dense regimen, are still controversial and have not been adopted widely in clinical practice. This scenario has recently changed due to the introduction of targeted agents, especially antiangiogenic agents. Data from two large, randomized clinical trials have shown that adding bevacizumab to the chemotherapy regimen followed by a maintenance period of bevacizumab

prolongs the PFS, mainly in patients considered at high risk of relapse. The results of the clinical trials with bevacizumab have been considered the proof of concept of the value of antiangiogenic therapy in the front-line therapy of ovarian cancer. The addition of bevacizumab to paclitaxel and carboplatin can be considered as standard of care at least in patients with FIGO stage IIIb or higher. However, several questions have risen about the optimal setting, dose and duration of bevacizumab. Additionally, we already have positive results of other phase III trials with antiangiogenic agents, in front-line (pazopanib and nintedanib) therapy. The great challenge for the near future will be the selection of patients with advanced ovarian cancer obtaining more benefit from these different options in front-line therapy and in recurrent disease. More recently in recurrent ovarian cancer immune checkpoint inhibitors and PARP inhibitors have demonstrated interesting results with long-term responses. The inclusion of these new agents in the chemotherapy backbone is therefore highly interesting and is currently under investigation in large phase III trials.

Editor's comment

Chemotherapy in advanced epithelial ovarian cancers may have a survival benefit by addition of antiangiogenesis factor Bevacizumab to the primary chemotherapy regime consisting of Paclitaxel and Carboplatinum. Similarly addition of antiangiogenic agents factor pazopanib and nintedanib in frontline therapy and as maintenance therapy has shown superior progression free survival rates.

Clinical Proceedings of AOGD Clinical Meeting held at PGIMSR & ESI Hospital Basaidarapur, New Delhi on 26th October, 2018

Unusual Presentation of Degenerative Fibroid Postpartum: A case report

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INTRODUCTION: Leiomyoma or fibroid is the most common benign pelvic tumour of uterus. Its presentation during pregnancy and postpartum period may vary. In our case, a 32 year old P2L2, day 43 postpartum normal vaginal delivery presented to Gynae casualty in lactational amenorrhea with high grade fever, foul smelling discharge, pain lower abdomen, and history of receiving inj DMPA on day 37 postnatally and a fleshy, dark brown, fungating, friable mass of 8 cm coming out per vaginum. On examination, mass was adherent to the uterus. An initial diagnosis of degenerated fibroid, retained products and chronic inversion was made. Under antibiotic cover, the patient was taken up for exploration followed by emergency obstetrical hysterectomy. The post-operative period was uneventful and the histopathology report confirmed the diagnosis of degenerative and necrotic fibroid.

CONCLUSION: Usually leiomyomas regress spontaneously, but a differential diagnosis of degenerative fibroid should be considered with the aforesaid clinical picture. Patient with fibroid uterus in antenatal period should be kept in regular follow up in post natal period and progesterone containing contraceptive should be avoided or used with caution.

Angiomyxoma: A rare diagnosis of a recurrent labial cyst

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Labial cysts have been a paradox for clinicians; often misdiagnosed and mismanaged. With only 250 cases reported worldwide till date, angiomyxoma remains a very rare mesenchymal tumour of vulva. We present a case of a 22 year old unmarried female with chief complaints of a slow growing, painless, non tender vulval swelling of 4x5cm on left labia majora for 6 months. An initial diagnosis of labial cyst, inclusion cyst and lipoma was made. Cyst excision was done under local anesthesia; but the histopathology report showed features of angiomyxoma. The patient presented with similar complaints 3 months later; after confirming the extent of the tumour on MRI, wide excision with negative margins was done, and the patient has been under regular follow up and is asymptomatic.

Thus, a differential diagnosis of angiomyxoma should also be considered for recurrent or locally invasive vulval cysts.

Key words: angiomyxoma, vulva, labial cyst

A Rare Case of Hemolytic Uremic Syndrome

Amrita Tiwari[1], Aanchal Sablok[2], Taru Gupta[3], Sangeeta Gupta[4]
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Case: Mrs X, 26 year old female,presented to the emergency department with the diagnosis of G2 P1L1with 39 weeks pregnancy with previous LSCS in labor. She underwent LSCS in view of previous LSCS not willing for TOLAC on 22/07/2018. Her immediate post partum period was uneventful. However,after 20 hours, her urine output started to decrease. She received fluid challenge test but her output did not improve and the patient became anuric. On investigating the patient it was found that her Hemoglobin has dropped from 11.1gm% to 6.7gm%. There was a mild increase in TLC but her platelet count had decreased significantly from 1.6 lakh/mm to 34000/mm. KFT had grossly deranged but LFT was mildly abnormal. Serum electrolytes were normal. LDH was markedly elevated. Peripheral smear examination revealed schistocytes. In view of anuria and grossly deranged KFT nephrologist opinion was taken and USG KUB was done which revealed normal size kidney with enhanced cortical echogenicity. There was no relevant present and past history suggestive of any medical, surgical illness. Immunology was also advised which showed decreased complement protein C3 levels. In view of Acute kidney injury, hemolytic anemia and thrombocytopenia with decreased complement protein C3 level,with normal size kidney in ultrasonography, the diagnosis of Hemolytic uremic syndrome was made. There was also a strong suspicion of thrombotic thrombocytopenic purpura but as there was no fever,no neurological involvement the diagnosis was lesslikely.

Patient received supportive measures and four sessions of plasmapheresis. Gradually her urine output,KFT and platelet count started improving and she was discharged on day 19 with near normal KFT,normal Hb and platelet count.

Hemolytic uremic syndrome is a rare and severe form of thrombotic microangiopathy characterized by hemolytic anemia, thrombocytopenia and kidney failure. Atypical hemolytic uremic syndrome is a rare life threatening disease that is not related to E-coli infection and constitutes 5-10% of HUS cases.[1] Pregnancy is known to be a stressful condition and if HUS occurs in pregnancy, it is called as pregnancy associated atypical HUS. The prevalence is 1 out of 25 000 pregnancies[1] and usually occurs after anuneventful pregnancy one day to several months after delivery.[2] Pregnancy associated atypical HUS occurs due to aberrant activation of complement system leading to endothelial injury and hence leading to the clinical picture of hemolytic anemia, thrombocytopenia and renal failure. If left untreated the prognosis remains poor with a 50-60% mortality rate[3] and 60-70%patients may develop end stage renal disease.[1,4] The treatment includes multidisciplinary team involvement and plasma exchange therapy. Recently Eculizumab has been introduced which is a recombinant monoclonal antibody inhibiting the terminal pathway of complement system activation.[3,5] It has been approved by the FDA in USA[1,4] but is available with great difficulty in India and is not available in the government practice.

Conclusion

- Early diagnosis of atypical haemolytic uremic syndrome is challenging often mimicking other diseases that occur during pregnancy.
- Correct diagnosis and timely management are crucial to improve outcomes.
- Management involves a multidisciplinary team, prompt PE, and Eculizumab.
- Maternal Mortality may be reduced to as much as 90%.

Answer to Quiz: October Issue

Answers of Crossword - October Issue

Down: 1. Geriatrician, 3. Roux-en-Y, 4. Bariatric surgery, 6. Transverse

Across: 2. DEXA, 5. Oligoovulation, 7. Micronutrients, 8. Colpocleisis, 9. Paroxetine 10. Cardiogeriatrics

Answer of Pictorial Quiz - October Issue

Figure 1: Ans 1. Sleeve gastrectomy
Ans 2. 12-18 months

Figure 2: Ans 1. Vaginal dryness, preoperative preparation of vagina in cases with atrophic vaginitis.
Ans 2. 2-4 grams of cream daily for 2 weeks followed by application on alternate days for 10 weeks.

* * * * *

Congratulations to Dr Anita Rajohria for successfully answering the quiz and crossword of October issue correctly!!

CROSSWORD

The Maze of Knowledge

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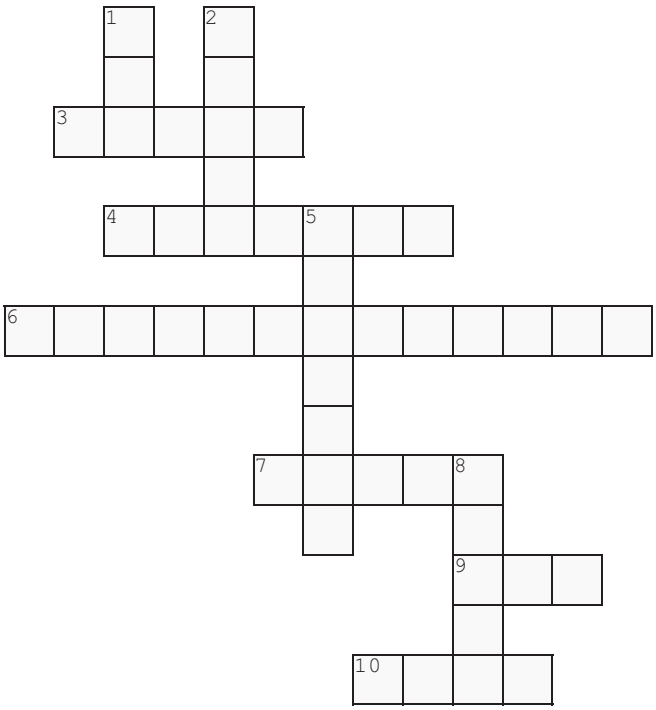
Dr Swati Agrawal



Down

1. Scoring system for ovarian tumours
2. A colposcopic scoring system
5. Method for assessment of insulin resistance
8. Criteria developed for detection of GDM in India

Across

3. Heated chemo therapy treatment for ovarian cancer
4. Syndromeres ulting due to pituitary necrosis secondary to ischemia within hours of delivery
6. Life threatening complication of hypothyroidism
7. Mammography score for prediction of breast cancer
9. Drug of choice for hyperthyroidism in pregnancy
10. Type of radical hysterectomy

PICTORIAL QUIZ

A Picture is Worth a Thousand Words

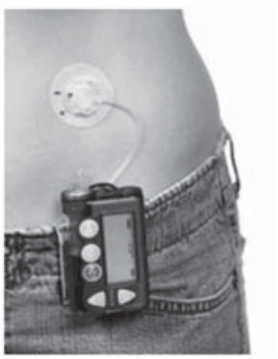


Figure 1:

Q1. Identify the equipment?

Q2. Name one advantage and one disadvantage

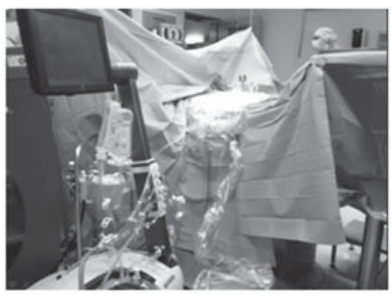


Figure 2:

Q1. Identify the procedure being done

Q2. In which gynaecological malignancy is it usually performed?

Refer page 53 for previous answer key.

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