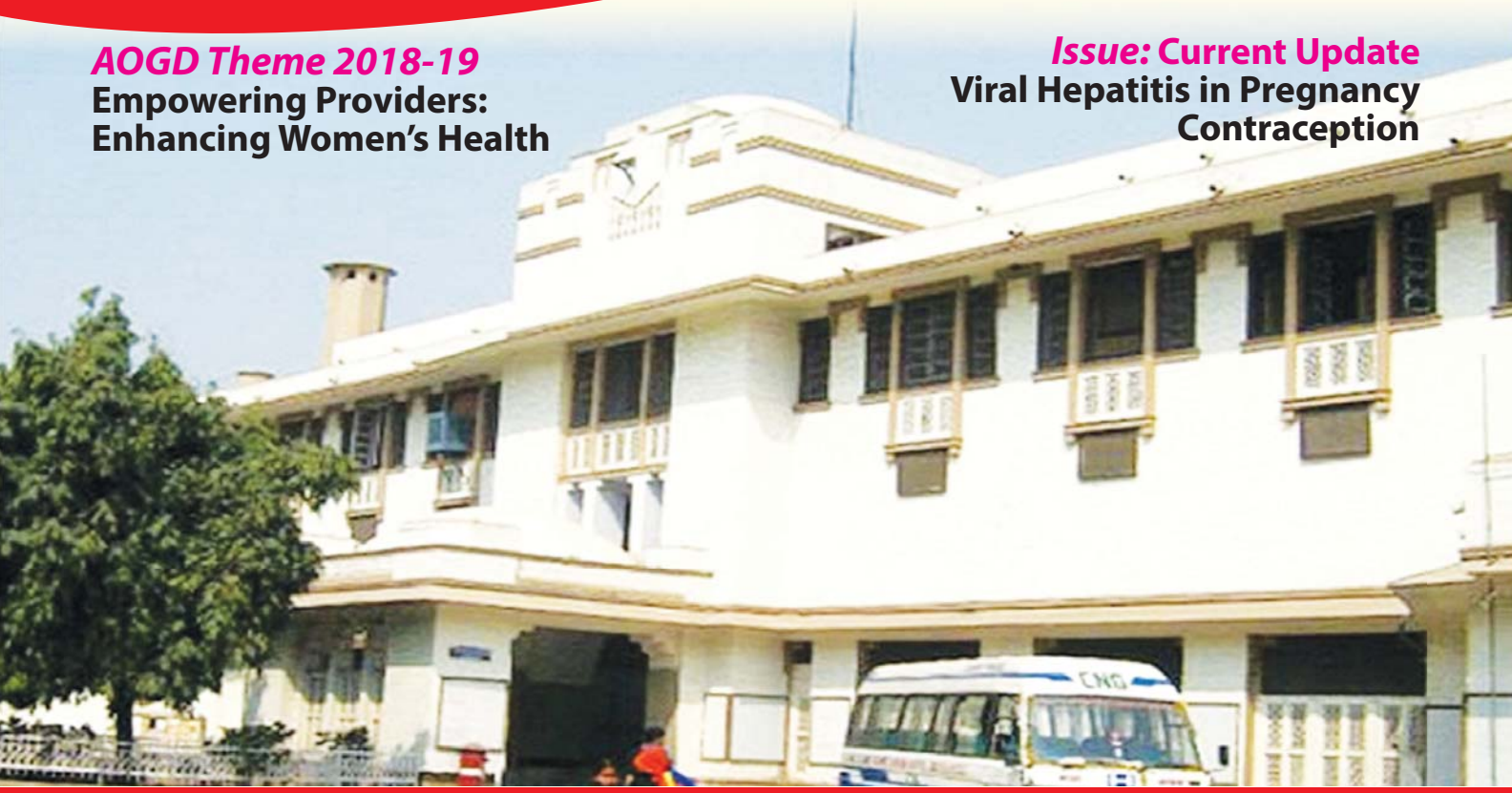
AOGD BULLETIN

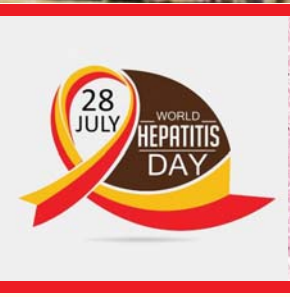
Volume 18; Issue No.3; July 2018

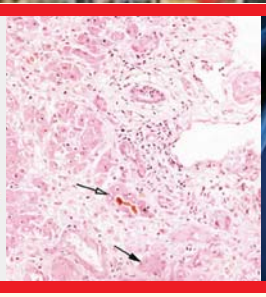
Price: ₹ 30 only

AOGD Theme 2018-19
Empowering Providers: Enhancing Women's Health

***Issue:* Current Update**
Viral Hepatitis in Pregnancy
Contraception







AOGD SECRETARIAT
Department of Obstetrics and Gynecology
Lady Hardinge Medical College & Smt. Sucheta Kriplani Hospital, New Delhi-110001
secretarylhaogd2018@gmail.com
www.aogd.org

AOGD Office-Bearers 2018-19

Dr Abha Singh
President

Dr Manju Puri
Vice President

Dr Reena Yadav
Scientific Advisor

Dr Kiran Aggarwal
Hon. Secretary

Dr Anuradha Singh

Dr Nishtha Jaiswal

Joint Secretaries

Dr Prabha Lal
Treasurer

Dr Shilpi Nain
Co Treasurer

Editorial Board

Dr Ratna Biswas
Editor

Dr Manisha Kumar
Web Editor

Dr Pikee Saxena

Dr Sharda Patra

Dr Swati Agrawal

Co-Editors

Dr Vidhi Chaudhary
Co-Web Editor

Dr Meenakshi Singh
Clinical Secretary

Dr Muntaha

Dr Amrita

Dr Aastha Shrivastava

Dr Deepika Meena

Dr Aishwarya Kapur

Public Relations & Hospitality

AOGD Secretariat
Department of Obstetrics and Gynecology
Lady Hardinge Medical College & Smt. Sucheta Kriplani Hospital, New Delhi 110001
Tel No: 011-23408297; Email: secretarylhaogd2018@gmail.com
www.aogd.org

AOGD BULLETIN
Vol. 18, No.3; July, 2018

Contents

BEST CLINICAL PRACTICE - Standards of Care: Hepatitis B in Pregnancy 7
Ankur Jindal

RECENT ADVANCES - Hepatitis E Vaccination in Pregnancy 14
Swati Sinha, Manoj Kumar

CONTROVERSY - Management of Fulminant Hepatic Failure due to Hepatitis E in Pregnancy 18
Sharda Patra

CASE APPROACH - Liver Transplantation in Acute Hepatitis E Induced Fulminant Hepatic Failure in Pregnancy- A way forward 22
Piyush Kumar Sinha

DISTRESS TO DE-STRESS - What are You Cooking ..... Inside? 26
Mohit D Gupta

CROSSWORD - The Maze of Knowledge and Pictorial Quiz 28
Swati Agrawal

BEST CLINICAL PRACTICE - Standard of Care for Post Abortion and Post Partum Contraception 35
Prabha Lal

RECENT ADVANCES - Male Contraception 37
R.C.M. Kaza

CONTROVERSY - Contraception in Adolescent 47
Shakuntla Kumar

CASE APPROACH - Contraception in Obese 54
Swati Agrawal, Nihita Pandey

JOURNAL SCAN 58
Ratna Biswas

Proceedings of AOGD Monthly Clinical Meeting 61

Publisher/Printer/Editor
Dr Ratna Biswas on behalf of Association of Obstetricians & Gynecologists of Delhi.

Printed at
Process & Spot C-112/3, Naraina Industrial Area, Phase-1, New Delhi 110 028

Published from
Department of Obstetrics and Gynecology
Lady Hardinge Medical College & Smt. Sucheta Kriplani Hospital, New Delhi - 110001

Editor
Dr Ratna Biswas
Ph. No. 011-23408297; Email: secretarylhaogd2018@gmail.com

Total number of pages = 64

President's Message

Dear Friends,

Monsoon Greetings!

It is indeed my privilege to be able to reach out to all AOGD members each month through the AOGD bulletin. Last month marked the celebration of the International Yoga Day on 21st June 2018. The AOGD members actively participated in the International Yoga Day organised at Rajpath. Public awareness forum was conducted for antenatal women on 20th June to emphasize the importance of yoga for the pregnant mother and her developing fetus. Trained Ayush instructors demonstrated asanas suitable for pregnant women in the antenatal OPD of Smt Sucheta Kriplani Hospital.

Another important occasion was "Doctors Day" on 1st of July. The event was marked by planting of trees at Panchsheel Park by more than 100 enthusiastic members of FOGSI and AOGD. The slogan given by President FOGSI for the year was "Plant a tree." The Clinical meeting was also organised by R&R Hospital on 29th June.

We are committed to the theme of AOGD, "To empower providers to enhance women's health". Empowerment of Health care professionals requires sustained efforts from all of us. I hope you have found the contents of the journal informative. CME are also organized in this regard from time to time.

World Population Day falls on 11th July so, this month's issue of the AOGD Bulletin deals with "Contraception". Another important day this month is the World Hepatitis Day on 28th July so this issue will also cover "Viral Hepatitis in Pregnancy". I urge the members to organize contraception awareness programs for public and doctors.

The Annual Conference is slated for 24th & 25th November with preconference workshops and we assure you a great scientific bonanza with wide coverage of all key areas in Obstetrics and Gynecology. Please block the dates for this most important event of the year. We hope the AOGD members will attend and participate in the Annual Conference in large numbers and also encourage their fellow colleagues and friends to become AOGD members to strengthen this organization.

I would like you to encourage your PGs and friends to become member of this association. We have an active website www.aogd.org where you can find all new announcements and glimpse of the past activities. We welcome any suggestions and comments which you may mail us at secretarylhaogd2018@gmail.com

Best wishes and happy reading.

Dr Abha Singh
President AOGD (2018-19)

Secretary's Message

Greetings from AOGD office,

The weather was hot and humid in the preceding month but the spirits were soaring and we had a lot of activity going on at our end. The AOGD members were also active and did various projects.

Endometriosis committee of AOGD had a successful CME on 10th July with a Sunday houseful of delegates and faculty. Breast and cervical screening camps were also organised.

A very successful public forum titled "Importance of Yoga" was held in Smt Sucheta Kriplani hospital. It was heartening to note the zeal with which the pregnant women wanted to learn about simple yoga exercises to improve the pregnancy outcome. It was indeed a magnificent experience to celebrate the "International day of Yoga" with thousands at Rajpath.

Doctor's day celebrations were done along with the clinical meeting at Army hospital R-R and also with tree plantation by enthusiastic members of FOGSI &AOGD.

The Editorial team has brought out a comprehensive and well planned bulletin. It is indeed encouraging to receive request from number of members who want to participate in academic activities and we will try to involve as many members as we can in the forthcoming events.

Save your dates for the Annual conference on 24-25th November 2018 at India Habitat Centre.

We are trying to reach you and inform you about all the events through website aogd.org, emails and sms's. If the information is not reaching you please communicate on the following mail secretarylhagod2018@gmail.com.

Enjoy the monsoon

Dr Kiran Aggarwal
Secretary AOGD (2018-19)

Monthly Clinical Meeting

Monthly Clinical Meet will be held at All India Institute of Medical Science, New Delhi on **Friday, 27th July, 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

Dear Friends,

This month we celebrate the World Population Day on 11th July and World Hepatitis Day on 28th July, hence this month's Update is on Contraception and Viral Hepatitis in Pregnancy.

Best practices in the management of Hepatitis B in pregnancy is our opening article of this issue with special emphasis on prevention of mother to child transmission of infection. Indications and recommendations for anti - retroviral drugs in chronic hepatitis B infection have been discussed in depth.

Viral Hepatitis in pregnancy is a significant cause of morbidity and mortality especially Hepatitis E which is endemic in India. What has been observed in many centres in Delhi like our hospital is that Hepatitis E is contributing to a major chunk of maternal mortality and has surpassed many other causes of maternal death. It is transmitted by feco-oral route and the major source of infection is contaminated water or food. Therefore clean water and sanitation is crucial for prevention of this infection. Another key factor in prevention is Hepatitis E vaccination which has been dealt in detail in this issue. This vaccine has being manufactured in China but has not been approved by WHO for use in pregnancy as of now. Once a mother contacts the infection it can lead to *fulminant hepatic failure* which has a dismal prognosis but newer horizons have opened up with *liver transplant* which can be a life saver. This issue addresses both these topics in depth and throws light on the best possible course of action in treating fulminant hepatic failure.

Our thoughts govern our action. This month's motivational article is all about directing our thought process towards positivity.

Contraception is a right of all eligible couples. Standards of care in post-abortal and postpartum contraception is our first article in this section. The Directorate of Family Welfare is promoting 100% contraceptive coverage in post-abortal period. Though it is a sensitive issue to talk about contraception in women who have had abortions but still they must be counselled and given some form of contraception till they recover their health and are prepared for the next conception. Our article on male contraception covers all aspects of male sterilization and other forms of male contraception and the postgraduates will not get a better review on it than this. New guidelines have been released on adolescent contraception and changing practices in contraception in the young has been elaborated in this issue. Also all major myths and facts have been addressed. Obesity is a growing problem and a good contraceptive cover in this population would avert unwanted pregnancy. Pregnancy in obese is associated with a high morbidity. A well planned pregnancy will lead to better outcome hence the contraceptive choices are discoursed.

The maze of knowledge-crossword and the pictorial quiz is interesting as usual.

Journal scan section has reviewed some important aspects of Hepatitis E infection and Contraception in recipients of organ transplant.

We have tried our best to bring forth an issue worthy enough for our learned and esteemed members. Hope it lives up to your expectations. Happy reading!!!

Editorial Team

BEST CLINICAL PRACTICE

Standards of Care: Hepatitis B in Pregnancy

Ankur Jindal
Associate Professor of Hepatology, Institute of Liver and Biliary Sciences


Dr Ankur Jindal

Hepatitis B virus (HBV) infection during pregnancy presents with unique management issues for both the mother and the fetus. These include the effects of HBV on maternal and fetal health, the effects of pregnancy on the course of HBV infection, treatment of HBV during pregnancy, and prevention of mother-to-child transmission.

Prevention of mother-to-child transmission is an important component of global efforts to reduce the burden of chronic HBV since vertical transmission is responsible for approximately one-half of chronic infections worldwide. The risk of developing chronic HBV infection is inversely proportional to the age at time of exposure. The risk is as high as 90 percent in those exposed at birth without vaccination, while the risk is much lower (about 20 to 30 percent) in those exposed during childhood. Maternal screening programs and universal vaccination of infants have significantly reduced transmission rates.

Acute Hepatitis B Virus Infection

Acute viral hepatitis is the most common cause of jaundice in pregnancy[1]. Other causes include liver diseases associated with pregnancy, such as acute fatty liver of pregnancy, HELLP syndrome, and intrahepatic cholestasis of pregnancy. Acute hepatitis B virus (HBV) infection during pregnancy is usually mild and not associated with increased mortality or teratogenicity[1,2]. Thus, infection during gestation should not prompt consideration of termination of the pregnancy. However, there have been reports of an increased incidence of low birth weight and prematurity in infants born to mothers with acute HBV infection[2,3].

Acute HBV occurring early in the pregnancy has been associated with a 10 percent perinatal transmission rate[3]. Transmission rates significantly increase if acute infection occurs at or near the time of delivery, with rates as high as 60 percent reported[1]. Thus, serial monitoring should be performed throughout pregnancy, and if the mother remains hepatitis B surface antigen (HBsAg) positive or has detectable serum HBV DNA, the infant should receive hepatitis B immune globulin in addition to the first dose of the hepatitis B vaccine at birth. Antiviral therapy to reduce maternal viral load should also be considered if the mother has high serum HBV DNA levels near the time of delivery.

Treatment of acute infection is mainly supportive. Liver biochemical tests and prothrombin time should be monitored. Antiviral therapy is usually unnecessary, except in women who have acute liver failure or protracted severe hepatitis[4]. For those with acute HBV infection who require antiviral therapy, the choice of which agent to use should be based upon the predicted duration of treatment, and the accessibility and cost for the patient. Tenofovir disoproxil fumarate (TDF) (300 mg daily) or lamivudine (100 mg daily) are both suitable options in this setting because both have been safely used during pregnancy, and the risk of developing resistance is low since the duration of treatment is expected to be short[5]. However, we prefer TDF as there is less risk of resistance. A more detailed discussion of the safety of antiviral agents for the treatment of HBV during pregnancy is found below.

Chronic Hepatitis B Virus Infection

Impact of pregnancy on the natural history of chronic HBV — Pregnancy is generally well tolerated in women with chronic hepatitis B virus (HBV) infection who do not have advanced liver disease. However, pregnancy is considered to be an immune tolerant state and is associated with high levels of adrenal corticosteroids that may modulate immune response. Thus, the following clinical manifestations may be seen in pregnant women with chronic HBV:

- **Hepatic flares –** The immunological changes during pregnancy and the postpartum period have been associated with hepatitis flares (including hepatic decompensation). A flare of HBV infection is typically defined as a greater than two- to threefold rise in the alanine aminotransferase (ALT) that is at least three to five times above the reference range. However, flares with serious clinical sequelae appear to be uncommon[6,7]. In a prospective study that followed 126 women during pregnancy and the postpartum period, 2 patients developed a flare during pregnancy whereas 27 (25 percent) developed a flare in the postpartum period[7]. During the postpartum period, flares may be related to immune reconstitution, a situation immunologically analogous to flares that have been described following the withdrawal of corticosteroids in nonpregnant patients with chronic HBV[8-10]. Predictors of HBV flares during pregnancy have not been established. However, flares appear to be more common in women who are hepatitis B e antigen (HBeAg) positive[7]. In addition, flares have been associated with HBeAg seroconversion in approximately 12 to 17 percent of patients[8], a rate similar to what has been described in patients who are not pregnant.

- **Progression of liver disease –** The immunologic, metabolic, and hemodynamic changes that occur during pregnancy have the potential to worsen or unmask underlying liver disease. Although progression to cirrhosis is not expected within such a short time for most patients, decompensation can occur in the setting of a severe flare. However, it can be difficult to assess the progression of liver disease during pregnancy because of normal physiologic changes that can mimic clinical features of chronic liver disease. Similarly, physical examination may reveal findings suggestive of stigmata of chronic liver disease such as palmar erythema, lower extremity edema, and spider angiomas.
- **HBV DNA –** The immunologic changes associated with pregnancy also have the potential to increase HBV viremia; however, most studies have found that HBV DNA levels remain stable during pregnancy.

  Effect of chronic HBV on pregnancy outcomes — For mothers with chronic HBV, the impact of HBV infection on newborns is not well defined and data are conflicting. Studies have found possible associations between chronic HBV and gestational diabetes mellitus[14,15,19], increased risk of prematurity[20], lower birth weight[21], and antepartum hemorrhage[19].

  Women with cirrhosis are at significant risk for perinatal complications and poor maternal and fetal outcomes, including intrauterine growth restriction, intrauterine infection, premature delivery, and intrauterine fetal demise. Many reports have described an increased risk of variceal bleeding, particularly during the third trimester and during labor because of increased intra-abdominal pressure and plasma volume expansion.

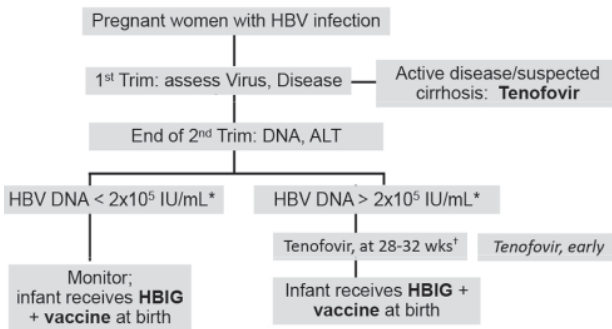
  Management considerations — Various factors need to be assessed when determining the management of pregnant women with chronic HBV during pregnancy, including the indications for treatment, the anticipated duration of therapy, the potential adverse effects to the fetus, the risk of developing drug resistance, and the accessibility and cost of the antiviral agents. The health of the mother and fetus must be considered independently when deciding on treatment. Pregnant women with chronic HBV should be managed in conjunction with a hepatologist.

  Women who are pregnant — Some women with chronic HBV require antiviral therapy to prevent progression of liver disease (e.g., those with immune-active hepatitis), while others can be observed.
- **Patients who become pregnant while receiving antiviral therapy –** Women should inform their clinician immediately if they become pregnant while receiving antiviral therapy, and the risks and benefits of continuing treatment should be discussed. Continuing treatment may pose a risk to the fetus while discontinuing treatment may pose a risk of hepatitis flare for the mother.

  Discontinuing treatment can be considered in women without cirrhosis if the patient has achieved a therapeutic endpoint. Otherwise, women receiving entecavir, adefovir, interferon, or tenofovir alafenamide can continue treatment by switching to an alternative agent, such as tenofovir disoproxil fumarate (TDF), which has more safety data available, and appears to be safe for use in pregnancy. These women should be monitored closely during the transition period to ensure viral suppression.
- **Monitoring women without indications for antiviral therapy –** Women who are not on antiviral therapy during pregnancy should be monitored closely to evaluate for a flare. Liver biochemical tests should be done every three months during pregnancy and for up to six months postpartum. HBV DNA should be tested concurrently or when there is ALT elevation. In addition, the HBV DNA should be measured at 26 to 28 weeks to determine if antiviral therapy should be offered to reduce the risk of mother-to-child transmission. Thereafter, monitoring will be the same as for other hepatitis B patients not requiring antiviral therapy, generally every six months for HBeAg-positive patients in the immune tolerant phase and every 6 to 12 months for those who are confirmed to be in the inactive carrier phase.
- **Indications for antiviral therapy**

  The indications for antiviral therapy in pregnant women are generally the same as those for patients who are not pregnant. Antiviral therapy is recommended for patients with a persistently elevated ALT >2 times the upper limit of normal and an elevated HBV DNA (HBV DNA >20,000 international units/mL in HBeAg-positive patients or HBV DNA ≥2000 international units/mL in HBeAg-negative patients) (table 1). However, in pregnant women without cirrhosis, some scenarios may differ. For example:
- A woman may choose to defer therapy until after delivery if she has evidence of mild disease activity, such as aminotransferase levels just above the treatment threshold.
- By contrast, a woman with a viral load >2 x 105 international units/mL should initiate therapy in the third trimester even if the aminotransferase levels are normal. In this setting, the goal of therapy is to prevent transmission to the child.

  TDF is preferred if antiviral therapy is contemplated in pregnant women because of its potency, safety profile, and low risk of resistance.



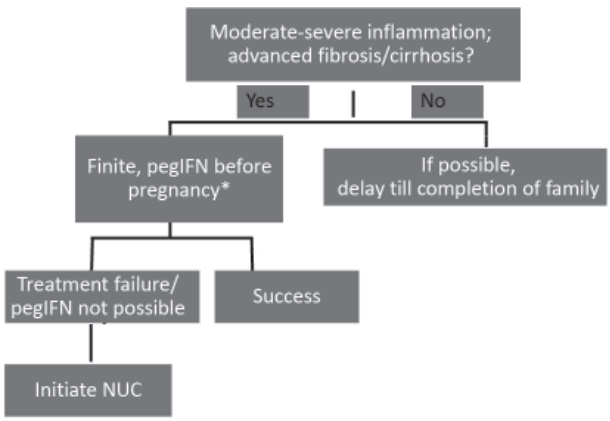
*The cut-off level of maternal HBV DNA level for initiation of therapy is unclear, and HBV DNA from 6-8 $\log_{10}$ IU/mL can be considered for therapy based on physician and patient preference.

†Tenofovir is preferred if treatment is expected to be > 12 weeks or if treatment is expected to continue while breastfeeding.

Fig 1: Algorithm for HBV Management in Women During Pregnancy

- **Women with cirrhosis –** The management of cirrhosis in a pregnant woman does not differ from that of non-pregnant patients. Variceal screening with endoscopy is still recommended and is safe during pregnancy. Active variceal bleeding should be managed the same way with banding. Indications for use of beta blockade for prophylactic or post-variceal bleeding management is the same as in nonpregnant individuals, but the use of beta blockers is associated with a small increase in risk of intrauterine growth restriction, fetal/neonatal bradycardia, neonatal hypoglycemia, and/or neonatal respiratory depression. Octreotide should not be given during management of acute variceal bleeding because of the risk of uterine ischemia. A more detailed discussion of the management of pregnant women with cirrhosis is found elsewhere.

Women with childbearing potential — Indications for antiviral therapy are the same as those for patients who do not have childbearing potential. They are determined by the HBeAg status, the HBV DNA level, and the activity or stage of liver disease. Those with mild liver disease who are planning to conceive in the near future may choose to defer treatment and be observed until they have completed childbearing. Those who elect to undergo treatment before attempting pregnancy may opt for pegylated interferon because of its finite duration (48 weeks), provided they use contraception during treatment. However, if the patient chooses treatment with a nucleos(t)ide analogue, TDF is preferred; limited experience supports its safety in pregnancy, and the risk of drug resistance is low. Patients who become pregnant while on therapy should contact their provider immediately.



**Effective contraception indicated.*

Fig 2: Algorithm of first time detected HBsAg +ve in reproductive age group female

Breastfeeding — Infants who received HBIG and the first dose of hepatitis B vaccine at birth can be breastfed[24,25]. However, it is important that the infant completes the hepatitis B vaccine series. Mothers with chronic hepatitis B who are breastfeeding should also exercise care to prevent bleeding from cracked nipples. Carrier mothers should not participate in donating breast milk. For women with chronic HBV who continue antiviral treatment after delivery, the safety data on the use of HBV antiviral therapy during breastfeeding is unclear. Thus, the benefits of breastfeeding should be discussed with women who require postpartum antiviral therapy. The decision to breastfeed should be based upon patient preference. Data from HIV-infected women also support the safety of antiviral therapy during breastfeeding.

Mother-to-Child Transmission

Risk of transmission — The risk of mother-to-child transmission of hepatitis B virus (HBV) from hepatitis B surface antigen (HBsAg)-positive mothers to their infants has been reported to be as high as 90 percent without the use of active and passive immunization[35]. Transmission can occur in utero, at birth, or after birth. However, the risk of HBV transmission has been significantly reduced with the introduction of universal maternal HBV screening, hepatitis B vaccination of all newborns, and the use of prophylactic (HBIG) for infants of HBsAg-positive mothers. The high protective efficacy of neonatal vaccination suggests that most infections occur at birth when maternal secretions and blood in the birth canal come into contact with the infant's mucosal membranes.

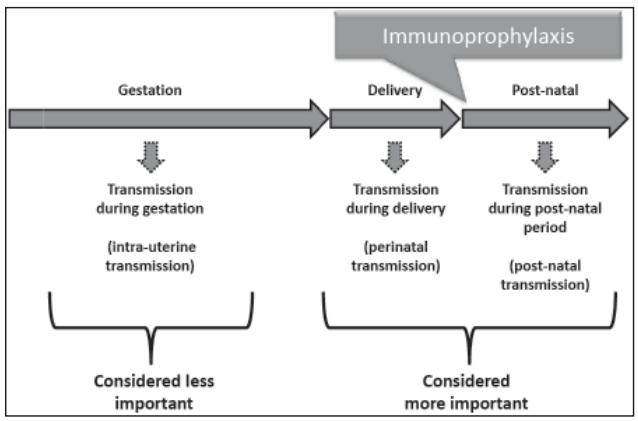


Fig 3: Timing of Mother to child HBV Transmission

Risk factors for transmission — The most important risk factors for mother-to-child transmission, despite proper administration of prophylaxis (HBIG and first dose of hepatitis B vaccine given within 12 hours of birth, and completion of hepatitis B vaccine series), appear to be a positive HBeAg and/or a high HBV DNA level in the mother.

Transplacental transmission and transmission due to obstetrical procedures are infrequent causes, and breastfeeding does not appear to pose a substantial risk. In addition, the benefit of cesarean delivery in protecting against transmission has not been clearly established.

HBV DNA level — Maternal serum HBV DNA levels correlate with the risk of transmission. Vertical transmission of hepatitis B occurs in 9 to 39 percent of infants of highly viremic mothers despite postnatal vaccination[40-43]. The

risk of HBV transmission is rare when maternal HBV DNA is <105 to 106 international units/mL.

Transplacental transmission - Transplacental transmission appears to cause only a minority of infections. It can occur due to leakage, such as during a threatened abortion[49,50]. HBV has been found in the villous capillary endothelial cells and the trophoblasts of the placenta[37,51]. This supports the hypothesis that breach of the placental barrier is a possible mechanism for intra-uterine infection. As a result, in preterm labor or threatened abortion there may be mixing of maternal and fetal blood, which may result in HBV transmission[49]. One study found that HBV is able to translocate through the placenta from the mother to the fetal trophoblast[52]. The causes of transplacental infection are unclear. High maternal viral load and preterm labor have been described as risk factors, but the strength of these associations is uncertain.[37,45].

Amniocentesis and other procedures — Diagnostic amniocentesis, if clinically indicated, should not be withheld. Transmission following amniocentesis has been described, but the risk appears to be low[53], particularly if the mother is HBeAg negative with a low HBV viral load, and the procedure is done using a 22-gauge needle under continuous guidance[54,55].

Preterm premature rupture of membranes — There are limited data that have examined preterm premature rupture of membranes as a risk factor for HBV transmission, and the available data are conflicting[57,58]. As a result, management of such patients should not differ from that of women with chronic HBV without preterm premature rupture of membranes.

Cesarean delivery — The benefit of cesarean delivery in protecting against HBV transmission has not been clearly established in well-conducted controlled trials[59-61]. Thus, cesarean delivery should not be routinely recommended for carrier mothers for the purpose of reducing HBV transmission[24,62].

Breastfeeding and transmission — Transmission of HBV through breastfeeding is unlikely, particularly in infants who received HBIG and hepatitis B vaccine at birth. Although HBV DNA has been detected in the colostrum of HBsAg-positive mothers, a study of 147 infants born to carrier mothers revealed no evidence for a relationship between breastfeeding and the subsequent development of chronic HBV infection in the babies[63]. In another study involving 369 neonates born to mothers with chronic HBV infection, of whom all received and completed the HBV immunoprophylaxis program, none of the 101 breastfed infants and 9 formula-fed infants were positive for HBsAg[64].

Prevention of mother-to-child transmission — Preventing mother-to-child transmission involves screening pregnant women, providing antiviral therapy to women with high HBV DNA levels, and administering passive-active immunization to newborns of mothers who are HBsAg positive.

Maternal screening — Testing for HBsAg should be performed on all women at the first prenatal visit. This blood test will determine whether a woman has current HBV infection and is at risk of transmitting HBV to her infant.

- Women who are HBsAg positive should have further testing to measure baseline HBeAg, hepatitis B e antibody (anti-HBe), HBV DNA, and aminotransferase levels. Women who have a high HBV DNA (ie, >2 x 105 international units/mL or >106 copies/mL), elevated aminotransferase levels, and/or a positive HBeAg should be referred to a hepatologist to see if early initiation of antiviral medications is needed. In addition, the HBV status of any older children should be evaluated.

  Women with low HBV DNA levels in the first trimester should have repeat HBV viral load testing around weeks 26 to 28. If the levels have increased, antiviral therapy should be considered.

- Women who are HBsAg negative and are at high risk for HBV infection (eg, injection drug use, having a sexual partner or household contact with chronic HBV, having had more than one sex partner in the previous six months, having been evaluated or treated for a STI) should be tested for hepatitis B surface antibody (anti-HBs) and hepatitis B core antibody (anti-HBc).

  Mothers without evidence of prior HBV infection or exposure (negative for anti-HBs and anti-HBc) should be vaccinated[23]. In addition, such women should have HBsAg repeated late in pregnancy (approximately 28 weeks). A booster dose of vaccine is also reasonable for patients who are isolated anti-HBc positive to see if anti-HBs titers can increase to >10 milli-international units/mL. However, the clinical importance of this is unclear.

  Women who are not tested prenatally should be tested at the time of admission for delivery[65].

Maternal antiviral therapy to prevent transmission — We suggest antiviral therapy for HBsAg-positive mothers with HBV DNA levels >2 x 105 international units/mL or >106 copies/mL, in addition to standard passive-active immunization of the infant, to further reduce the risk of mother-to-child transmission. HBV DNA level should be repeated at 26 to 28 weeks for those not already on treatment and initiate therapy thereafter (ie, 28 to 30 weeks) if HBV DNA levels are >2 x 105 IU /mL (>106copies/mL). Treatment should be started at the beginning of the third trimester so there is sufficient time for the HBV viral load to decrease, even if the patient delivers early. For those who require treatment, prefer TDF rather than other antiviral agents since resistance to TDF is rare. This is important since many of these young mothers may require antiviral treatment for their liver disease in the future. In addition, this agent appears to be safe for use in pregnancy, and has been evaluated in several prospective clinical trials[67-69]. A newer formulation of tenofovir, tenofovir alafenamide is available. Although there is less bone and kidney

toxicity with this agent compared with TDF, at this time we do not use tenofovir alafenamide during pregnancy given the lack of sufficient safety data.

Although other agents (eg. Lamivudine, Telbivudine) also reduce mother-to-child transmission and appear to be safe when administered during pregnancy[67,70-73], they are associated with high rates of antiviral resistance. Lamivudine may be a reasonable alternative if cost is a barrier to obtaining antiviral therapy and treatment is going to be administered for a short duration (ie, ≤3 months). However, it is important that patients have not received lamivudine in the past, since such patients are at risk of having lamivudine resistant virus. Women who start antiviral therapy during pregnancy for the sole purpose of preventing mother-to-child transmission may stop antiviral therapy immediately after delivery, especially if they want to breastfeed. Some experts prefer to continue treatment for 4 to 12 weeks after delivery, in part to reduce the risk of a flare postpartum[74].

Regardless of when antiviral therapy is discontinued, women should be monitored for a flare of their HBV disease by measuring the ALT level every three months for six months after therapy has been stopped.

Newborn immunization — Newborns of mothers who test positive for HBsAg should receive passive-active immunization, with the first dose of the hepatitis B vaccine series and one dose of HBIG administered within 12 hours of delivery at different sites. Infants should then complete the hepatitis B vaccine series.

References

1. Sookoian S. Liver disease during pregnancy: acute viral hepatitis. Ann Hepatol 2006; 5:231.
2. Hieber JP, Dalton D, Shorey J, Combes B. Hepatitis and pregnancy. J Pediatr 1977; 91:545.
3. Jonas MM. Hepatitis B and pregnancy: an underestimated issue. Liver Int 2009; 29 Suppl 1:133.
4. Degertekin B, Lok AS. Indications for therapy in hepatitis B. Hepatology 2009; 49:S129.
5. Potthoff A, Rifai K, Wedemeyer H, et al. Successful treatment of fulminant hepatitis B during pregnancy. Z Gastroenterol 2009; 47:667.
6. Rawal BK, Parida S, Watkins RP, et al. Symptomatic reactivation of hepatitis B in pregnancy. Lancet 1991; 337:364.
7. Giles M, Visvanathan K, Lewin S, et al. Clinical and virological predictors of hepatic flares in pregnant women with chronic hepatitis B. Gut 2015; 64:1810.
8. Lin HH, Wu WY, Kao JH, Chen DS. Hepatitis B post-partum e antigen clearance in hepatitis B carrier mothers: Correlation with viral characteristics. J Gastroenterol Hepatol 2006; 21:605.
9. ter Borg MJ, Leemans WF, de Man RA, Janssen HL. Exacerbation of chronic hepatitis B infection after delivery. J Viral Hepat 2008; 15:37.
10. Yang YB, Li XM, Shi ZJ, Ma L. Pregnant woman with fulminant hepatic failure caused by hepatitis B virus infection: a case report. World J Gastroenterol 2004; 10:2305.
11. Nguyen G, Garcia RT, Nguyen N, et al. Clinical course of hepatitis B virus infection during pregnancy. Aliment Pharmacol Ther 2009; 29:755.
12. Tan HH, Lui HF, Chow WC. Chronic hepatitis B virus (HBV) infection in pregnancy. Hepatol Int 2008; 2:370.
13. Söderström A, Norkrans G, Lindh M. Hepatitis B virus DNA during pregnancy and post partum: aspects on vertical transmission. Scand J Infect Dis 2003; 35:814.
14. Lao TT, Chan BC, Leung WC, et al. Maternal hepatitis B infection and gestational diabetes mellitus. J Hepatol 2007; 47:46.
15. Lao TT, Tse KY, Chan LY, et al. HBsAg carrier status and the association between gestational diabetes with increased serum ferritin concentration in Chinese women. Diabetes Care 2003; 26:3011.
16. Lobstein S, Faber R, Tillmann HL. Prevalence of hepatitis B among pregnant women and its impact on pregnancy and newborn complications at a tertiary hospital in the eastern part of Germany. Digestion 2011; 83:76.
17. Connell LE, Salihu HM, Salemi JL, et al. Maternal hepatitis B and hepatitis C carrier status and perinatal outcomes. Liver Int 2011; 31:1163.
18. Wong S, Chan LY, Yu V, Ho L. Hepatitis B carrier and perinatal outcome in singleton pregnancy. Am J Perinatol 1999; 16:485.
19. Tse KY, Ho LF, Lao T. The impact of maternal HBsAg carrier status on pregnancy outcomes: a case-control study. J Hepatol 2005; 43:771.
20. Reddick KL, Jhaveri R, Gandhi M, et al. Pregnancy outcomes associated with viral hepatitis. J Viral Hepat 2011; 18:e394.
21. Safir A, Levy A, Sikuler E, Sheiner E. Maternal hepatitis B virus or hepatitis C virus carrier status as an independent risk factor for adverse perinatal outcome. Liver Int 2010; 30:765.
22. Shaheen AA, Myers RP. The outcomes of pregnancy in patients with cirrhosis: a population-based study. Liver Int 2010; 30:275.
23. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology 2018; 67:1560.
24. Society for Maternal-Fetal Medicine (SMFM), Dionne-Odom J, Tita AT, Silverman NS. #38: Hepatitis B in pregnancy screening, treatment, and prevention of vertical transmission. Am J Obstet Gynecol 2016; 214:6.
25. American Academy of Pediatrics. Hepatitis B. In: Red Book: 2015 Report of the Committee on Infectious Diseases, 30th ed, Kimberlin DW, Brady MT, Jackson MA, Long SS (Eds), American Academy of Pediatrics, Elk Grove Village, IL 2015. p.400.
26. Cundy KC, Sueoka C, Lynch GR, et al. Pharmacokinetics and bioavailability of the anti-human immunodeficiency virus nucleotide analog 9-[(R)-2-(phosphonomethoxy)propyl] adenine (PMPA) in dogs. Antimicrob Agents Chemother 1998; 42:687.
27. Van Rompay KK, Hamilton M, Kearney B, Bischofberger N. Pharmacokinetics of tenofovir in breast milk of lactating rhesus macaques. Antimicrob Agents Chemother 2005; 49:2093.
28. Benaboud S, Pruvost A, Coffie PA, et al. Concentrations of tenofovir and emtricitabine in breast milk of HIV-1-infected women in Abidjan, Cote d'Ivoire, in the ANRS

12109 TEmAA Study, Step 2. Antimicrob Agents Chemother 2011; 55:1315.
29. Ehrhardt S, Xie C, Guo N, et al. Breastfeeding while taking lamivudine or tenofovir disoproxil fumarate: a review of the evidence. Clin Infect Dis 2015; 60:275.
30. Waitt C, Olagunju A, Nakalema S, et al. Plasma and breast milk pharmacokinetics of emtricitabine, tenofovir and lamivudine using dried blood and breast milk spots in nursing African mother-infant pairs. J Antimicrob Chemother 2018; 73:1013.
31. Gouraud A, Millaret A, Bernard N, et al. Tenofovir exposure through breast feeding: Serum concentrations in neonates and clinical follow-up. Fundam Clin Pharmacol. 2012;26 (Suppl 1):9
32. Pan CQ, Mi LJ, Bunchorntavakul C, et al. Tenofovir disoproxil fumarate for prevention of vertical transmission of hepatitis B virus infection by highly viremic pregnant women: a case series. Dig Dis Sci 2012; 57:2423.
33. Ganne-Carrie N, Causse X, Zarski JP et al. Efficacy and safety results of tenofovir DF (TDF) treatment from the first trimester in HBV pregnant women in real-life clinical practice. Hepatology. 2013;58 (Suppl 1):664A-5A
34. Lactmed. Tenofovir. http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~SOkg2H:1.
35. Stevens CE, Beasley RP, Tsui J, Lee WC. Vertical transmission of hepatitis B antigen in Taiwan. N Engl J Med 1975; 292:771.
36. Schillie S, Walker T, Veselsky S, et al. Outcomes of infants born to women infected with hepatitis B. Pediatrics 2015; 135:e1141.
37. Xu DZ, Yan YP, Choi BC, et al. Risk factors and mechanism of transplacental transmission of hepatitis B virus: a case-control study. J Med Virol 2002; 67:20.
38. Stevens CE, Toy PT, Tong MJ, et al. Perinatal hepatitis B virus transmission in the United States. Prevention by passive-active immunization. JAMA 1985; 253:1740.
39. Chen HL, Lin LH, Hu FC, et al. Effects of maternal screening and universal immunization to prevent mother-to-infant transmission of HBV. Gastroenterology 2012; 142:773.
40. Thompson ND, Perz JF, Moorman AC, Holmberg SD. Nonhospital health care-associated hepatitis B and C virus transmission: United States, 1998-2008. Ann Intern Med 2009; 150:33.
41. Guidelines for Perinatal Care. In: American Academy of Pediatrics and American College of Obstetricians and Gynecologists, 4th ed, Washington, DC 1997. p.286.
42. Soldan K, Ramsay M, Collins M. Acute hepatitis B infection associated with blood transfusion in England and Wales, 1991-7: review of database. BMJ 1999; 318:95.
43. Zou H, Chen Y, Duan Z, et al. Virologic factors associated with failure to passive-active immunoprophylaxis in infants born to HBsAg-positive mothers. J Viral Hepat 2012; 19:e18.
44. Burk RD, Hwang LY, Ho GY, et al. Outcome of perinatal hepatitis B virus exposure is dependent on maternal virus load. J Infect Dis 1994; 170:1418.
45. Li XM, Shi MF, Yang YB, et al. Effect of hepatitis B immunoglobulin on interruption of HBV intrauterine infection. World J Gastroenterol 2004; 10:3215.
46. Wiseman E, Fraser MA, Holden S, et al. Perinatal transmission of hepatitis B virus: an Australian experience. Med J Aust 2009; 190:489.
47. Wen WH, Chang MH, Zhao LL, et al. Mother-to-infant transmission of hepatitis B virus infection: significance of maternal viral load and strategies for intervention. J Hepatol 2013; 59:24.
48. Kubo A, Shlager L, Marks AR, et al. Prevention of vertical transmission of hepatitis B: an observational study. Ann Intern Med 2014; 160:828.
49. Lin HH, Lee TY, Chen DS, et al. Transplacental leakage of HBeAg-positive maternal blood as the most likely route in causing intrauterine infection with hepatitis B virus. J Pediatr 1987; 111:877.
50. Ohto H, Lin HH, Kawana T, et al. Intrauterine transmission of hepatitis B virus is closely related to placental leakage. J Med Virol 1987; 21:1.
51. Bai H, Zhang L, Ma L, et al. Relationship of hepatitis B virus infection of placental barrier and hepatitis B virus intra-uterine transmission mechanism. World J Gastroenterol 2007; 13:3625.
52. Zhang SL, Yue YF, Bai GQ, et al. Mechanism of intrauterine infection of hepatitis B virus. World J Gastroenterol 2004; 10:437.
53. López M, Coll O. Chronic viral infections and invasive procedures: risk of vertical transmission and current recommendations. Fetal Diagn Ther 2010; 28:1.
54. Towers CV, Asrat T, Rumney P. The presence of hepatitis B surface antigen and deoxyribonucleic acid in amniotic fluid and cord blood. Am J Obstet Gynecol 2001; 184:1514.
55. Yi W, Pan CQ, Hao J, et al. Risk of vertical transmission of hepatitis B after amniocentesis in HBs antigen-positive mothers. J Hepatol 2014; 60:523.
56. Ko TM, Tseng LH, Chang MH, et al. Amniocentesis in mothers who are hepatitis B virus carriers does not expose the infant to an increased risk of hepatitis B virus infection. Arch Gynecol Obstet 1994; 255:25.
57. Chen LZ, Zhou WQ, Zhao SS, et al. A nested case-control study of maternal-neonatal transmission of hepatitis B virus in a Chinese population. World J Gastroenterol 2011; 17:3640.
58. Song YM, Sung J, Yang S, et al. Factors associated with immunoprophylaxis failure against vertical transmission of hepatitis B virus. Eur J Pediatr 2007; 166:813.
59. Wang J, Zhu Q, Zhang X. Effect of delivery mode on maternal-infant transmission of hepatitis B virus by immunoprophylaxis. Chin Med J (Engl) 2002; 115:1510.
60. Yang J, Zeng XM, Men YL, Zhao LS. Elective caesarean section versus vaginal delivery for preventing mother to child transmission of hepatitis B virus--a systematic review. Virol J 2008; 5:100.
61. Chang MS, Gavini S, Andrade PC, McNabb-Baltar J. Caesarean section to prevent transmission of hepatitis B: a meta-analysis. Can J Gastroenterol Hepatol 2014; 28:439.
62. Tran TT. Hepatitis B in Pregnancy. Clin Infect Dis 2016; 62 Suppl 4:S314.
63. Beasley RP, Stevens CE, Shiao IS, Meng HC. Evidence against breast-feeding as a mechanism for vertical transmission of hepatitis B. Lancet 1975; 2:740.
64. Hill JB, Sheffield JS, Kim MJ, et al. Risk of hepatitis B transmission in breast-fed infants of chronic hepatitis B carriers. Obstet Gynecol 2002; 99:1049.
65. Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2018; 67:1.
66. National Academies of Sciences, Engineering, and Medicine.

A national strategy for the elimination of hepatitis B and C. Washington, DC. The National Academies Press, 2017.

67. Chen HL, Lee CN, Chang CH, et al. Efficacy of maternal tenofovir disoproxil fumarate in interrupting mother-to-infant transmission of hepatitis B virus. Hepatology 2015; 62:375.
68. Brown RS Jr, McMahon BJ, Lok AS, et al. Antiviral therapy in chronic hepatitis B viral infection during pregnancy: A systematic review and meta-analysis. Hepatology 2016; 63:319.
69. Pan CQ, Duan Z, Dai E, et al. Tenofovir to Prevent Hepatitis B Transmission in Mothers with High Viral Load. N Engl J Med 2016; 374:2324.
70. Han GR, Cao MK, Zhao W, et al. A prospective and open-label study for the efficacy and safety of telbivudine in pregnancy for the prevention of perinatal transmission of hepatitis B virus infection. J Hepatol 2011; 55:1215.
71. Pan CQ, Han GR, Jiang HX, et al. Telbivudine prevents vertical transmission from HBeAg-positive women with chronic hepatitis B. Clin Gastroenterol Hepatol 2012; 10:520.
72. Shi Z, Yang Y, Ma L, et al. Lamivudine in late pregnancy to interrupt in utero transmission of hepatitis B virus: a systematic review and meta-analysis. Obstet Gynecol 2010; 116:147.
73. Xu WM, Cui YT, Wang L, et al. Lamivudine in late pregnancy to prevent perinatal transmission of hepatitis B virus infection: a multicentre, randomized, double-blind, placebo-controlled study. J Viral Hepat 2009; 16:94.
74. Visvanathan K, Dusheiko G, Giles M, et al. Managing HBV in pregnancy. Prevention, prophylaxis, treatment and follow-up: position paper produced by Australian, UK and New Zealand key opinion leaders. Gut 2016; 65:340.
75. Nguyen V, Tan PK, Greenup AJ, et al. Anti-viral therapy for prevention of perinatal HBV transmission: extending therapy beyond birth does not protect against post-partum flare. Aliment Pharmacol Ther 2014; 39:1225.
76. Jourdain G, Ngo-Giang-Huong N, Harrison L, et al. Tenofovir versus Placebo to Prevent Perinatal Transmission of Hepatitis B. N Engl J Med 2018; 378:911.
77. World Health Organization. Immunization, Vaccines and Biologicals: Data, statistics and graphics. http://www.who.int/immunization/monitoring_surveillance/data/en/ (Accessed on March 19, 2018).
78. Hill HA, Elam-Evans LD, Yankey D, et al. Vaccination Coverage Among Children Aged 19-35 Months - United States, 2016. MMWR Morb Mortal Wkly Rep 2017; 66:1171.
79. Intron-A [package insert]. Kenilworth, NJ. Schering Corporation; 1994.
80. Pan CQ, Duan ZP, Dai E, et al. Tenofovir disoproxil fumarate (TDF) reduces perinatal transmission of hepatitis B virus in highly viremic mothers: A multi-center, prospective, randomized and controlled study. Presented at the AASLD Liver Meeting 2015. San Francisco, 2015.
81. Hoyert DL, Mathews TJ, Menacker F, et al. Annual summary of vital statistics: 2004. Pediatrics 2006; 117:168.
82. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry Interim Report for 1 January 1989 through 31 July 2017. Wilmington, NC: Registry Coordinating Center; 2017. Available from URL: www.APRegistry.com. (Accessed on February 07, 2018).
83. Van Rompay KK, Durand-Gasselin L, Brignolo LL, et al. Chronic administration of tenofovir to rhesus macaques from infancy through adulthood and pregnancy: summary of pharmacokinetics and biological and virological effects. Antimicrob Agents Chemother 2008; 52:3144.
84. Gill US, et al. Factors determining bone mineral density loss in chronic hepatitis B patients: is tenofovir disoproxil fumarate the main culprit? Gut 2011; 60:A230.
85. Gibb DM, Kizito H, Russell EC, et al. Pregnancy and infant outcomes among HIV-infected women taking long-term ART with and without tenofovir in the DART trial. PLoS Med 2012; 9:e1001217.
86. Wang L, Kourtis AP, Ellington S, et al. Safety of tenofovir during pregnancy for the mother and fetus: a systematic review. Clin Infect Dis 2013; 57:1773.
87. Siberry GK, Jacobson DL, Kalkwarf HJ, et al. Lower Newborn Bone Mineral Content Associated With Maternal Use of Tenofovir Disoproxil Fumarate During Pregnancy. Clin Infect Dis 2015; 61:996.
88. Viganò A, Mora S, Giacomet V, et al. In utero exposure to tenofovir disoproxil fumarate does not impair growth and bone health in HIV-uninfected children born to HIV-infected mothers. Antivir Ther 2011; 16:1259.
89. Siberry GK, Williams PL, Mendez H, et al. Safety of tenofovir use during pregnancy: early growth outcomes in HIV-exposed uninfected infants. AIDS 2012; 26:1151.
90. Jao J, Abrams EJ, Phillips T, et al. In Utero Tenofovir Exposure Is not Associated With Fetal Long Bone Growth. Clin Infect Dis 2016; 62:1604.
91. Trotter JF, Zygmunt AJ. Conception and pregnancy during interferon-alpha therapy for chronic hepatitis C. J Clin Gastroenterol 2001; 32:76.

RECENT ADVANCES

Hepatitis E Vaccination in Pregnancy

Swati Sinha[1], Manoj Kumar[2]

[1]Department of Obstetrics and Gynecology, Sita Ram Bhartia Institute of Science and Research,
[2]Department of Hepatology and Liver Transplantation, Institute of Liver and Biliary Sciences

Dr Manoj Kumar

Introduction

Hepatitis E virus (HEV) is a small, nonenveloped virus in the Hepeviridae Family, which is divided into two genera: *Orthohepevirus* with four species (A–D) and *Piscihepevirus* with one species (A). *Orthohepevirus A* species include almost all mammalian HEV variants; it is divided into seven genotypes, of which at least five of them are of interest in human public health. Genotypes 1 and 2 infect only humans and are responsible for sporadic cases and large waterborne outbreaks in endemic areas. Genotypes 3 and 4 are able to infect humans and animals and are enzootic in pigs, which are considered their main reservoir in the environment. Until now, only one report of human HEV infection with genotype 7 has been documented.[1]

Epidemiological patterns of HEV infection

Two distinct epidemiological patterns of HEV infection have been observed in different regions of the globe. These patterns seem to be correlated with the distribution of HEV genotypes, transmission routes, source of virus infection, disease prevalence, and, in some cases, clinical characteristics of the disease. [Table 1]. HEV genotypes 1 and 2 are highly endemic in tropical and subtropical areas where hepatitis E occurs as outbreaks and sporadic cases transmitted by a fecal-oral route through contaminated water caused by genotypes 1 or 2. Regions with adequate sanitary conditions and well controlled water supplies are considered low endemic areas for hepatitis E. In these regions, the disease is less frequent and occurs as sporadic cases. Autochthonous cases of HEV infection in these areas appear to be associated with occasional zoonotic transmission by genotypes 3 and 4 from domestic animals (most often from pigs to humans). This transmission can occur through the ingestion of raw or undercooked food containing the virus, especially swine products.[2]

Hepatitis E virus (HEV) infection is hyperendemic in India. The transmission is primarily through fecal contamination of water supplies. Outbreaks of acute hepatitis E are common. In addition, HEV infection accounts for 30-50% of sporadic acute hepatitis. Only genotype 1 HEV has been reported from human cases in India; genotype 4 has been isolated from pigs, but not from humans, suggesting zoonotic transmission to be rare.

HEV infection and pregnancy

During epidemics of HEV infection in endemic areas, pregnant females have been documented to be more prone to contract the infection, and more often develop severe liver disease with accompanying increased mortality rate. Even in the sporadic setup in these regions similar observations have been reported. Various reports evaluating etiological spectrum in individuals with acute hepatitis during both epidemic and sporadic settings indicate the following observations in India[3]:

1) The frequency of HEV as the cause of acute viral hepatitis (AVH) is significantly higher among pregnant females (82-85.5%) than in non-pregnant females (41.5-49%) and males (40-50%).
2) Further, certain studies have also documented that susceptibility to contract HEV infection during pregnancy increases in a linear fashion with increasing trimester of pregnancy. During epidemics, pregnant women in their second and third trimesters get infected more frequently (12–20%) than men and non-pregnant women (2–4%).

Table 1: Characteristics of two distinct epidemiological patterns of hepatitis E infection

Characteristics	Low endemic	Highly endemic
Global Distribution	Areas with safe drinking water supplies North America, South America, Europe, Australia, South Africa, East Asia	Resource-poor areas with frequent water contamination Central America, Africa, South and Central Asia
Transmission	Normally transmitted through animal sources and blood transfusion	Transmission mainly through contaminated water sources
Clinical features	Occasional cases, asymptomatic and symptomatic acute hepatitis,chronic hepatitis in immunocompromised individuals	Frequent outbreaks, asymptomatic and symptomatic acute hepatitis, acute liver failure
Morbidity and mortality	Low mortality and morbidity	High/intermediate mortality and morbidity
Genotypes	3 and 4	1 and 2

3) The frequency of ALF is significantly higher in pregnant females (10-22%) than in non-pregnant females and males (1-2%) with HEV infection. Once acute liver failure develops it has a poor prognosis.

4) Transmission of HEV can also occur from mother to unborn child. Both maternal and fetal complications may occur, including abortion, fetal demise, preterm labor and maternal or neonatal death.

Also IgG anti-HEV a neutralizing antibody wanes over time after initial exposure and therefore repeated HEV infection is possible in an individual and cohort.

HEV Vaccine

Although 5 HEV human genotypes and significant geographic genome variability have been described, all HEV subtypes share major cross-reactive epitopes, prompting the development of a recombinant HEV vaccine based on the capsid protein. The HEV genome contains 3 open reading frames (ORFs). The ORF1 encodes nonstructural protein(s) and, therefore, ORF1 protein(s) would not be a target for humoral immunity. ORF3 overlaps with ORFs 1 and 2 and encodes a small protein of unknown function but significant antigenicity. However, antibodies to ORF3 do not neutralize virus in vitro assays, whereas antibody to ORF2 does. ORF2 encodes the capsid protein and, because the ORF2 protein is the major protein in the virion, it has been the focus of vaccine development.

The various options for a vaccine include attenuated or killed virus vaccine, recombinant protein-based vaccine and nucleic acid-based vaccines. The development of an attenuated or killed virus vaccine is not currently feasible, because an efficient cell culture system for HEV does not exist. Therefore, either a recombinant protein-based or nucleic acid-based vaccine is needed. Most work has focused on recombinant vaccines.

Several recombinant ORF2 antigens of different lengths have been expressed using a variety of expression systems (*Escherichia coli*, insect cells, yeasts, and transgenic plants) and have been shown to induce anti-ORF2 antibody responses.

Only one candidate vaccine has been approved for HEV till date. This vaccine has been manufactured using a bacterial expression system (HEV 239 vaccine). The safety and efficacy of HEV 239 vaccine was evaluated in a randomized, double blind, placebo-controlled, single-center phase III clinical trial conducted in a known endemic location,

Dongtai, Jiangsu Province, China from August 2007 to May 2009 among a general population of healthy men and women (aged 16–65 years). Participants were randomly assigned to vaccine (n= 56,302) or placebo (n= 56,302). The 48,693 participants in the vaccine group and 48,663 participants in the placebo group received 3 vaccine doses and were included in the primary efficacy analysis. During the 12 months after 30 days from receipt of the third dose, 15 per-protocol participants in the placebo group developed overt hepatitis E compared with none in the vaccine group. Vaccine efficacy against clinically apparent hepatitis E disease according to the protocol case definition (ALT >2.5 times upper limit of normal) was 100% and protection extended to all participants throughout the 12 months. Five participants developed hepatitis E during the 14 days after the second dose and before the third dose; all were in the placebo group. Vaccine efficacy after 2 doses was 100%. Vaccine efficacy for participants who received ≥1 dose was 95.5%.[4]

In the extension of the phase III clinical trial, the blind was maintained and all subjects were followed out for 4.5 years (55 months) using the same surveillance system. The efficacy of HEV 239 vaccine against clinically apparent hepatitis E disease according to the protocol case definition (ALT >2.5 times upper limit of normal) was 93.3% (95% CI, 78.6–97.9) in a per-protocol analysis and 85.1% (95% CI, 67.1–93.3) in an intention-to-treat analysis. As was expected in the geographic area of the clinical trial, 26 of 29 HEV isolates obtained from subjects were genotype 4; the others were genotype 1. The high efficacy afforded by the genotype 1 HEV 239 vaccine against disease caused by genotype 4 HEV supports the concept that the diverse HEV genotypes form a single serotype and HEV 239 vaccine can protect against all genotypes. Over the extended 4.5-year follow-up period, a similar number of participants reported serious adverse events in the vaccine and placebo groups. None of the serious adverse events were attributed to the investigational vaccine.[5] Overall, HEV 239 was considered to have an acceptable safety profile. An analysis of follow-up at 7 years post vaccination is ongoing.

Data from the phase III trial were submitted to the Chinese State Food and Drug Administration in late 2009 by the manufacturer Xiamen Innovax Biotech in Xiamen, China. The HEV 239 vaccine, named Hecolin (Hepatitis E vaccine, E. coli), was approved for use in persons 16 years of age and older in December 2011. The resulting vaccine efficacy estimates reported in the approved product insert are 65% (95% CI, 26–84) for the per-protocol analysis and 67% (95% CI, 38–82) for an intention-to-treat analysis.

From isolation of the parent genotype 1 virus from a patient to registration of the recombinant vaccine, the development of Hecolin took 14 years. Following the product launch in 2012, the vaccine is available in the private market in China, but Innovax is seeking approval of the HEV 239 in Pakistan, Nepal, India, and Thailand.[6]

Safety of HEV 239 vaccine in pregnancy

Although pregnancy was an exclusion criterion for enrollment, there were 37 women in the vaccine group and 31 in the control group who were inadvertently administered vaccine during pregnancy. The rates of adverse events were similar between the women in the HEV 239 group and the control vaccine recipients, as

were the anthropometrics and gestational ages of the infants.[7] A study to determine the effectiveness of HEV 239 vaccine in preventing hepatitis E disease among women of childbearing age is ongoing in Bangladesh (NCT02759991).

Cost effective strategies for use of HEV vaccine to prevent HEV related maternal mortality

Currently, only inactivated influenza and tetanus, diphtheria, and pertussis (Tdap) vaccines are approved for use in pregnant women during their second or third trimesters, and other vaccines available to pregnant women should be used with caution.

One strategy could be to use HEV vaccine before planning pregnancy. One Chinese study assessed the economics of pregnant women who had vaccinated before conception by using a decision tree model to evaluate the cost-effectiveness of hepatitis E vaccination among pregnant women living in epidemic regions in order to determine if hepatitis E vaccination should be considered a useful strategy. Screening for IgG HEV antibodies and vaccination if negative for HEV antibodies was found to be the most economical strategy for pregnant women in epidemic region.[8]

Cost effectiveness analysis and the best strategy for use of HEV vaccine in India has not been done.

Recommendations from the World Health Organization (WHO)

In May 2015, the WHO published a hepatitis E vaccine position paper. In that paper, the WHO Scientific Advisory Group of Experts (SAGE) acknowledged the significant public health problem posed by hepatitis E, particularly among special populations, pregnant women being one of them. Although Hecolin was considered to be a promising vaccine, the WHO SAGE concluded that there were insufficient data to justify a recommendation for routine use. It was acknowledged that national authorities may decide to use the vaccine based on their local epidemiology, and certain high-risk situations, such as outbreaks, warranted consideration for vaccine use. The WHO SAGE suggested specific areas of additional study for Hecolin, which included high risk group of pregnant women. WHO SAGE also noted that vaccine efficacy had only been shown against disease caused by genotype 4.[9]

Since vaccine registration in China in 2011, there has been no use of Hecolin outside of China other than the ongoing effectiveness study in Bangladesh.

Hepatitis E vaccine is approved in China, but there is no recommendation for its use in China's national immunization program as a result of the low incidence of hepatitis E (2.1 cases per 10,000 person-years in the phase III control group.[5]

Also HEV vaccine is not yet prequalified by the World Health Organization, a necessary step for introduction into those low- and middle-income countries where the disease burden is highest.

Summary

Hepatitis E virus (HEV) is transmitted predominantly through the fecal contamination of water and food. It is the most common cause of acute hepatitis and liver failure in endemic areas including India. Pregnant women from the Indian subcontinent and Africa are at increased risk of contracting acute HEV infection as well as developing severe complications including acute liver failure. Although several potential candidate vaccines against HEV have been studied for their immunogenicity and efficacy, only HEV 239 vaccine which is developed by Xiamen Innovax Biotech Co., Ltd. and approved by China Food and Drug Administration in 2012, is the licensed HEV vaccine in the world so far. Extensive studies on safety, immunogenicity and efficacy in phase III clinical trials in non-pregnant population have shown that HEV 239 vaccine is a promising vaccine for HEV prevention and control. But, it is not yet prequalified by the World Health Organization, a necessary step for introduction into those low- and middle-income countries where the disease burden is highest. Hepatitis E vaccine can save lives, among women of reproductive age living where hepatitis E is endemic like India. The HEV vaccine is expected to be cost-effective also. However, sanitary and environmental improvements would still be the most important strategy against HEV infection.

Conclusions

Hepatitis E vaccine can save lives, particularly among women of reproductive age living where hepatitis E is endemic. HEV vaccine is not yet prequalified by the World Health Organization, nevertheless, the stage is set for the final act in the hepatitis E vaccine story—policymaking, advocacy, and pilot introduction of vaccine in at-risk populations, in which it is expected to be cost-effective.[6]

Sanitary and environmental improvements would still be the most important strategy against HEV infection. Effective prevention relies primarily on maintaining a clean drinking water supply and paying strict attention to sewage disposal. Vaccines should never be considered a substitute for, or reason to delay, basic improvements in overall sanitation.

References

1. Melgaço JG, Gardinali NR, de Mello VDM, Leal M, Lewis-Ximenez LL, Pinto MA. Hepatitis E: Update on Prevention and Control. Biomed Res Int.; 2018:5769201
2. Sarin SK, Kumar M. A vaccine for hepatitis E: has it finally arrived? Gastroenterology. 2011 ;140:1349-52
3. Shalimar, Acharya SK. Hepatitis E and acute liver failure in

pregnancy. J Clin Exp Hepatol. 2013;3:213-24

4. Zhu FC, Zhang J, Zhang XF, Zhou C, Wang ZZ, Huang SJ, Wang H, Yang CL, Jiang HM, Cai JP, et al. Efficacy and safety of a recombinant hepatitis E vaccine in healthy adults: A large-scale, randomised, double-blind placebo controlled, phase 3 trial. Lancet 2010; 376: 895–902
5. Zhang J, Zhang XF, Huang SJ, Wu T, Hu YM, Wang ZZ, Wang H, Jiang HM, Wang YJ, Yan Q, et al. Long term efficacy of a hepatitis E vaccine. N Engl J Med 2015; 372: 914–922
6. Innis BL, Lynch JA. Immunization against Hepatitis E. Cold Spring Harb Perspect Med. 2018 Mar 12. pii: a032573. doi: 10.1101/cshperspect.a032573. [Epub ahead of print]
7. Wu T, Zhu FC, Huang SJ, Zhang XF,Wang ZZ, Zhang J, Xia NS. 2012. Safety of the hepatitis E vaccine for pregnant women: A preliminary analysis. Hepatology 55: 2038
8. Zhao Y, Zhang X, Zhu F, Jin H, Wang B. A preliminary cost-effectiveness analysis of hepatitis E vaccination among pregnant women in epidemic regions. Hum Vaccin Immunother. 2016;12:2003-2009
9. World Health Organization. 2015. Hepatitis E vaccine: WHO position paper, May 2015. Wkly Epidemiol Rec 90: 185–20

Forthcoming Events

- Public Forum on "Awareness of Contraceptive Methods" on occasion of World Population Day on 17th -18th July 2018, Gyne OPD, and Maternity wards. Smt S K Hospital New Delhi.
- CME and hands on workshop on "Contraception" on occasion of World Population Day, 20th July, 2018, ME hall, SJ Auditorium, LHMC.
- CME on "Liver disease in Pregnancy", 28th July, 2018, SJ Auditorium, LHMC.
- Next Monthly Clinical Meeting at All India Institute of Medical Science, 27th July 2018.
- UCMS & GTB Hospital in association with AOGD, RCOG North Zone will be holding "Simms Black Fellowship" Lecture on 1st August, 2018 at UCMS LT-4. Talk by Professor Pat O'Brien
- Vaginal birth after Cesarean section (VBAC) – Thrashing out the controversies, CME at Sitaram Bharatiya Institiute of Science and Research, Auditorium, 24th August, 2018. Contact DR RinkuSen Gupta
- Quarterly meet of the Society of Fetal Medicine with aegis of AOGD 29th August, 2018 at UCMS, GTB Hospital Delhi.
- 21st Practical Course and CME at Maulana Azad Medical College Auditorium from 7th - 9th September 2018.
- 40th Annual Conference of AOGD, 24-25th November, 2018 Preconference Workshops on 22nd and 23rd November 2018.

CONTROVERSY

Management of Fulminant Hepatic Failure due to Hepatitis E in Pregnancy


Dr Sharda Patra

Sharda Patra
Professor, Dept of Obstetrics & Gynecology, Lady Hardinge Medical College, New Delhi

It is a matter of irony that liver disease in pregnancy clinically presents as a spectrum ranging from mild asymptomatic transaminitis to fatal and irreversible deterioration in liver functions leading to mortality. Of the various causes of liver disease in pregnancy viral hepatitis is the commonest variant. Viral hepatitis in pregnancy has been a subject of continuing interest and controversy. Incidence of hepatitis in developed countries is around 0.1% where as in developing countries it is 3-20% or even higher. Hepatitis E is the commonest cause of Hepatitis in pregnancy as hepatitis E virus (HEV) is an endemic infection in India. It is alleged that pregnant women are more susceptible to it. The clinical course of Hepatitis in pregnancy is unpredictable. HEV causes fulminant hepatic failure (FHF) in pregnant women leading to high maternal mortality (up to 20-40%). This rate increases further with increasing gestation period. HEV also causes abortions, stillbirths and neonatal deaths leading to very high perinatal mortality rate. Vertical and trans-placental transmission of the virus has also been implicated by some studies. The reasons for increased maternal and perinatal mortality and morbidity in pregnant women with Hepatitis are not clear.

Management of a case of Hepatitis E in pregnancy

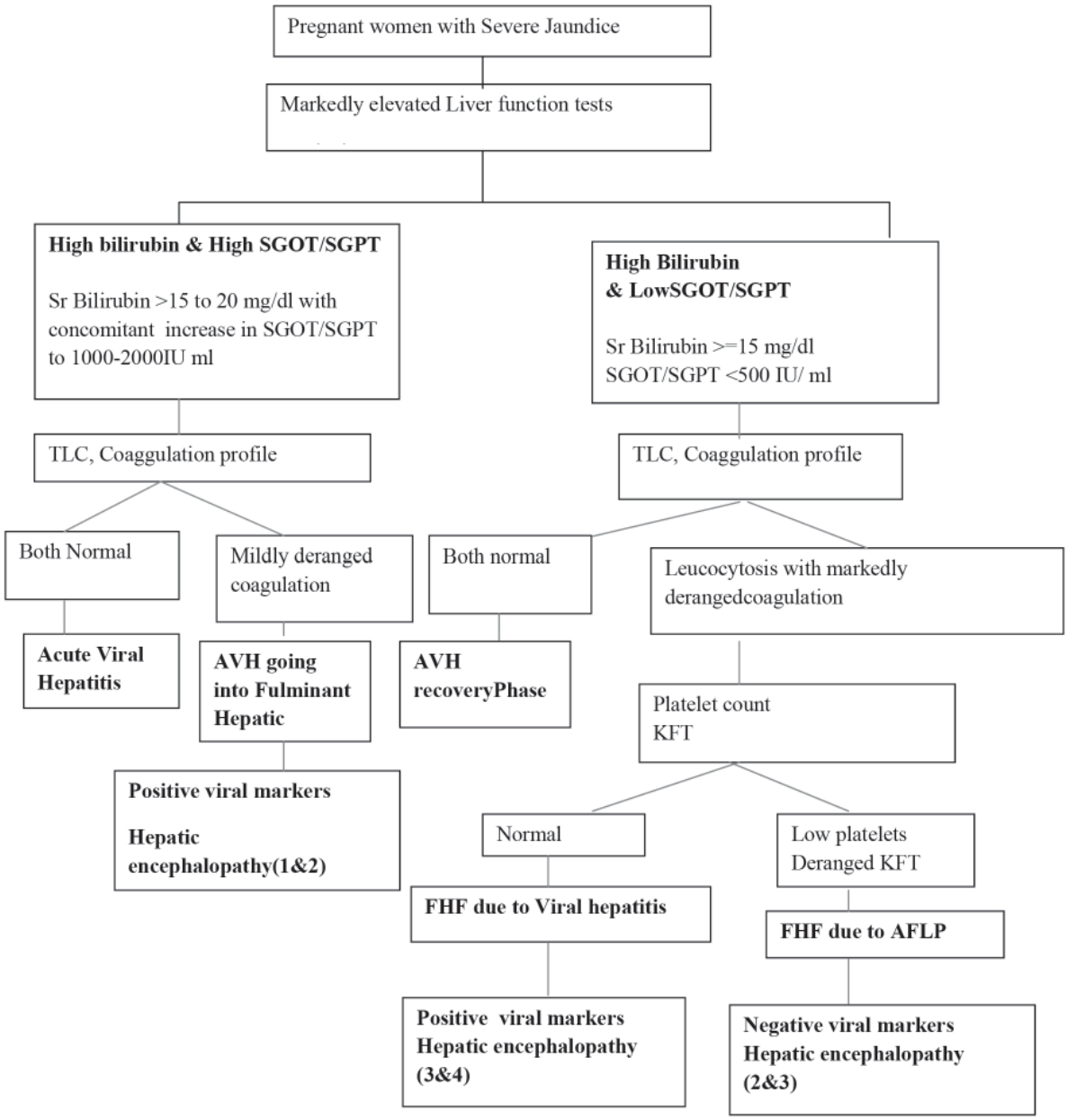
Pregnant women presenting with fulminant hepatic failure often poses a diagnostic dilemma. It is very important to recognize the cause of hepatic failure whether due to Hepatitis E or AFLP(Acute fatty liver of pregnancy) as the management are different for these two conditions. Pregnant women may present in different stage of the liver failure from mild to severe. Recognition of certain clinical and biochemical factors help in diagnosing the stage of the disease as well as the cause, thus helping in planning the management. An algorithmic work up of women with FHF based on clinical and lab investigation is given in Fig 1.

The mechanism of liver injury in hepatitis E is not clear and all the hypotheses put forth has not yet been conclusively proven. In this situation of uncertainty, the management of HEV infection induced liver failure assumes more importance than ever before. All studies have shown that pregnant women have differential immune response to infection and in some it triggers fulminant liver failure. So the logical treatment should be to deliver the fetus as soon as possible. Unfortunately, very few such studies have been undertaken in this field. Therapeutic termination of pregnancy, which has been proved to be beneficial in pregnancy specific disorders like HELLP syndrome and acute fatty liver of pregnancy, have not been fully, explored in hepatitis E infection. However in a retrospective study from India, Banait *et al*, studied 42 patients with HEV induced liver failure, there was no difference in maternal mortality in pregnant women who delivered and those who did not questioning the role of therapeutic termination. The literature at present is not supportive of the fact that delivery of the baby may decrease the maternal mortality. However this was a small retrospective study and must not discourage physicians from pursuing that option considering that HEV infection produces immunological changes in the fetus too.

The clinical presentation of HEV in pregnancy varies from mild acute hepatitis to fulminant hepatic failure. The outcome in women with acute hepatitis is favourable compared to those with fulminant liver failure. A spontaneous recovery is seen in majority of cases as in non pregnant state. However, those progressing to a fulminate course mostly do not survive. A study by **Patra et al in 2007** on 220 pregnant women with acute viral hepatitis (AVH) in a 3 yr period has shown that HEV was the commonest etiological agent in 58% of women. Of these, 45% of the women had a non fulminant course who following supportive management recovered completely with a favourable maternal-perinatal outcome e. Amongst the women with fulminant hepatic failure (55%), 75% died and 25% survived. None of the women with FHF were induced in this study. Almost 85% of these went into spontaneous labor and 15% died undelivered. The median interval between admission and delivery was 24 hours (range, 1 to 312 hours). The median duration from onset to development of FHF was 108 hours. Hence, the role of termination of pregnancy on disease severity is still not clear.

The scenario today is changing with availability of liver transplant facility, being the only option to save mothers from dying due to this deadly condition. The role of pregnancy termination in women for liver transplantation has been emphasized in some of the case reports. Data in this regard is still grim. Nevertheless a major obstetrical dilemma is optimal timing of delivery and the route of delivery. A deterrent to termination of pregnancy amongst the obstetrician is fear of postpartum hemorrhage due to presence of deranged coagulation. Coagulopathy remains an important complication associated with viral hepatitis E infection. Pregnant women with Hepatitis E virus (HEV) infection and deranged coagulation profile pose a real obstetric challenge. Hence there is reluctance and delay in decisions for termination of pregnancy even for obstetric indications.

Algorithm of work up of a pregnant women presenting with severe jaundice



A study by **Puri et al in** 2011 on factors influencing the occurrence of postpartum hemorrhage in pregnant women with hepatitis E infection with coagulopathy have shown that in 13 out of 38 women with Hepatitis E and deranged coagulation profile had PPH and the various factors which predicted PPH was a low ALT (p= 0.016), high INR (>6, p=0.003), high levels of D-dimer (p=0.008), presence of hepatic encephalopathy (p=0.028), intrauterine fetal death (p= 0.001) and gastrointestinal bleeding (p=0.004). The only independent variable that predicted PPH was the presence GI bleed (OR-11.363, 95% CI: 1.003, 125, p=0.050). Thus women with severe deranged coagulation (INR>6) with GI bleed had eleven times higher risk of PPH than those without GI bleed. Thus the authors concluded that early recognition of factors which predict the risk of PPH and timely intervention with judicious use of blood and blood components in the peripartum period pregnancy can be terminated only in cases of long standing IUD or women who require liver transplant.

Regarding the route of delivery, vaginal delivery is preferable. However, operative delivery should be undertaken for obstetric indications like non progress of labor due to CPD.

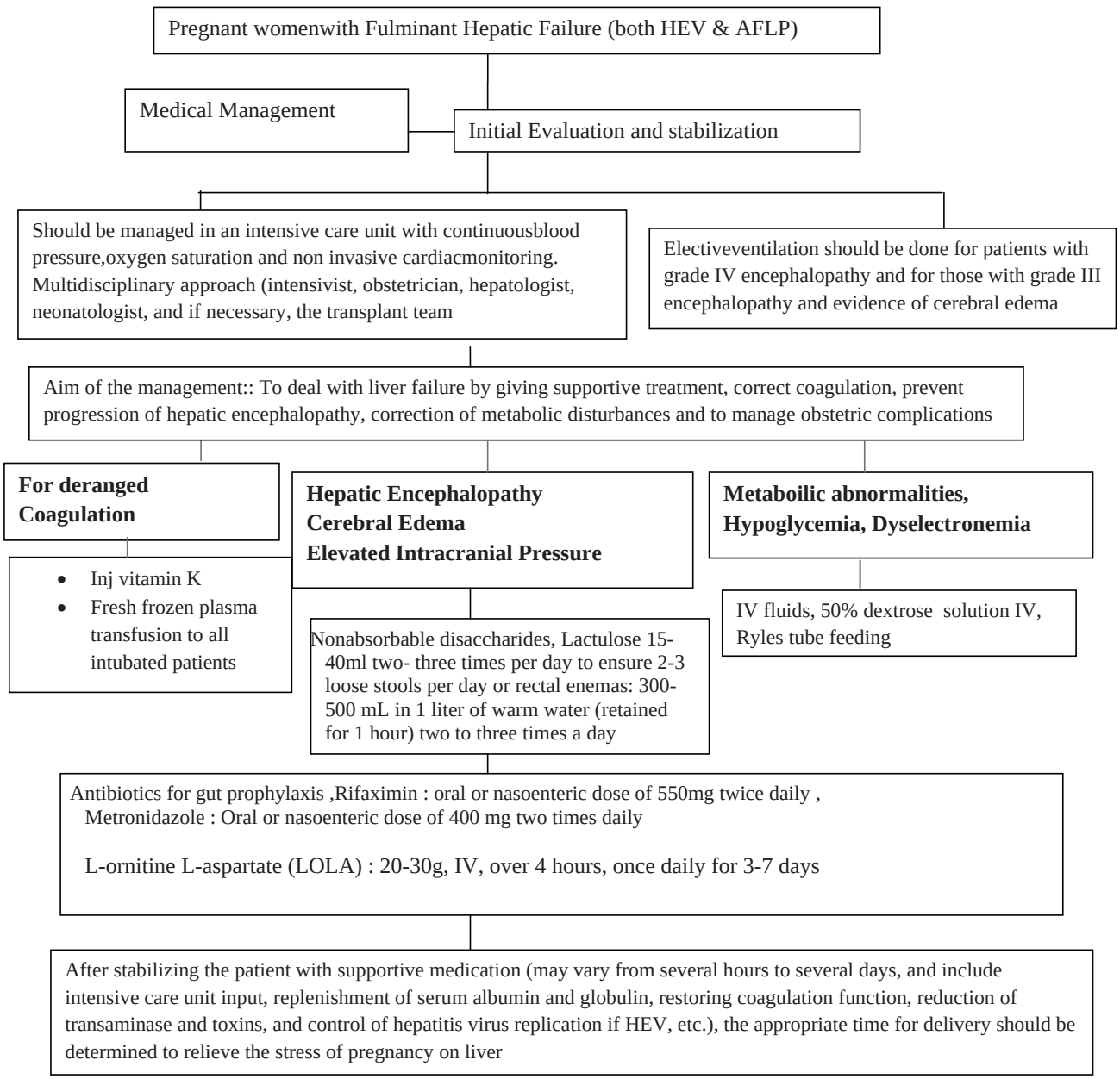
Recently, due to improved techniques in anesthesia, blood transfusion, anti-infective management and enhanced caesarean section skills among obstetricians complications in caesarean section deliveries have been reduced. In cases with intractable PPH, one should directly resort to peripartum hysterectomy rather than venturing with conservative management.

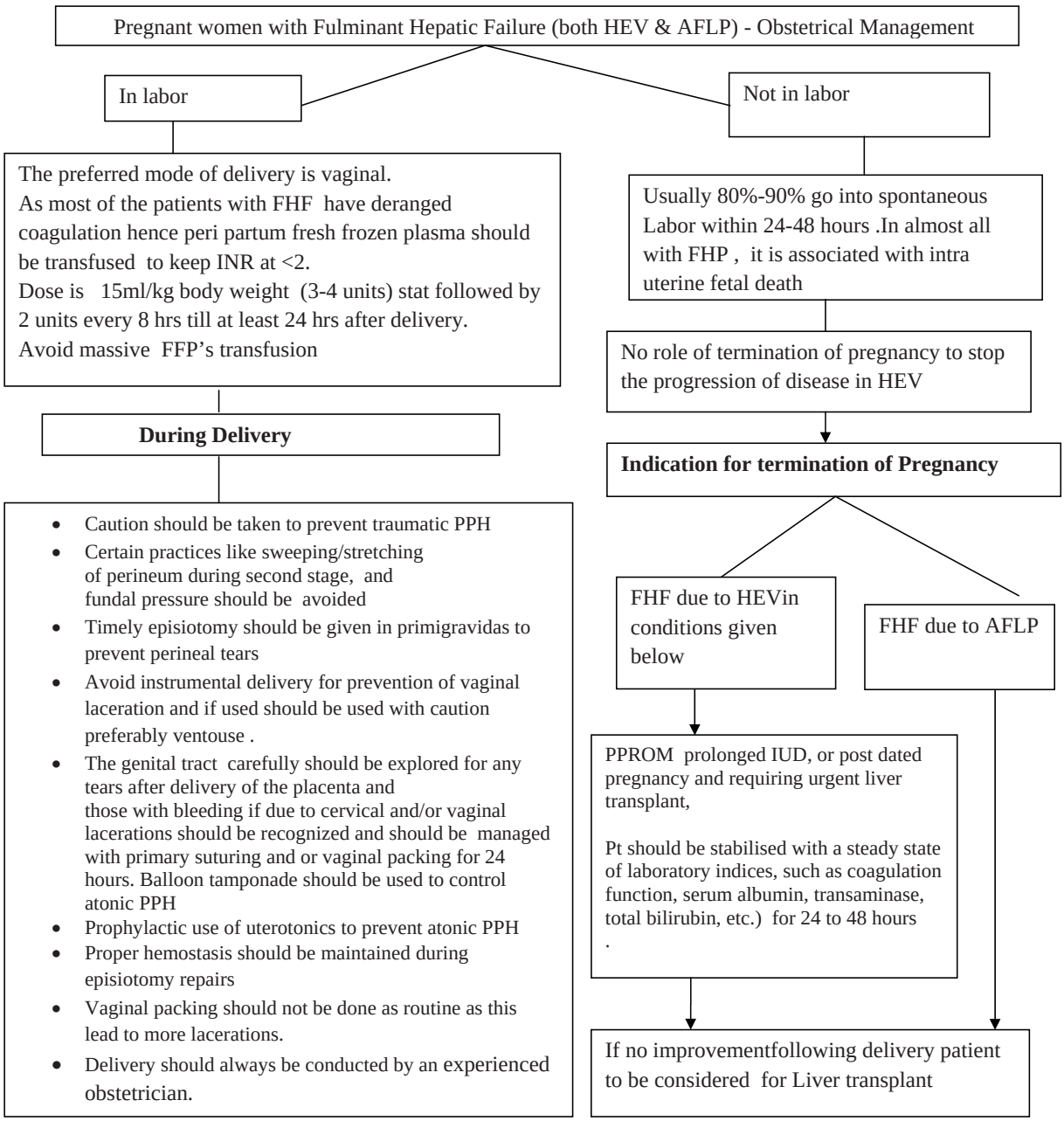
A proposed medical & obstetrical treatment algorithm is given in Fig 2.

A pregnant women with FHF with altered sensorium and liver failure due to HEV will require a combined and coordinated effort by the intensivist, obstetrician, hepatologist, neonatologist, and if necessary, the transplant team. Aim would be to stabilize the patient, maintain optimum haemodynamics, treat cerebral oedema/intra-cranial hypertension, evaluate and treat any infections, correct coagulopathy, hypoglycaemia, dyselectrolytaemia, maintain nutrition, give volume replacement and vasopressor support if needed and ensure adequate renal perfusion. Safety of both the mother and the foetus needs to be ensured. However, maternal outcome takes precedence over fetal wellbeing in life-threatening situations. The management comprises of supportive therapy with anti-coma regime correction of coagulation defect and a caution during delivery to prevent traumatic PPH.

Intensive care management of such a patient should be focused on cardiovascular, hemodynamic and respiratory support. Such patients need multidisciplinary approach in tertiary care centre with intensive monitoring and frequent reviews of maternal- fetal status by experts to decide on the best course of action and may even require liver transplantation mandating delivery.

Algorithm of management of a pregnant women presenting with Fulminant Hepatic Failure-Medical management





Suggested Reading

1. Fagan EA. Disorders of the liver, biliary system and pancreas. In: de Swiet M, (ed). Medical Disorders in Obstetric Practice. 4th ed. Oxford: Blackwell Science, 2002: 282-345
2. Patra S, Kumar A, Trivedi SS, Puri M, Sarin SK (2007) Maternal and fetal outcomes in pregnant women with acute hepatitis E virus infection. Ann Intern Med.2007. 147: 28-33
3. Banait VS, Sandur V, Parikh F, Murugesh M, Ranka P, Ramesh VS. Outcome of acute liver failure due to acute hepatitis E in pregnant women. Indian J Gastroenterol. 2007 Jan-Feb; 26(1):6-10
4. Manju Puri Sharda Patra, Preeti Singh, Nidhi Malhotra, Shubha Sagar Trivedi, Shiv Kumar Sarin. Factors influencing occurrence of postpartum haemorrhage in pregnant women with hepatitis E infection and deranged coagulation profile. Obstetric Medicine 2011; 4: 108–112
5. Shi Z, Li X, Yang Y, Ma L, Schreiber A. Obstetrical Management of Fulminant Viral Hepatitis in Late Pregnancy. Reproductive Sys Sexual Disord. 2012;1:102.
6. Acute Liver Failure in an Obstetric Patient: Challenge of Critical Care for 1 Patient Crit Care Nurse 2013;33:48-56
7. Shalimar, Subrat K. Acharya. Hepatitis E and Acute Liver Failure in Pregnancy.Journal of Clinical and Experimental Hepatology, September 2013;Vol.3, No.3:213–224
8. Valentina Rosa Bertuzzo. Pregnant woman saved with liver transplantation from acute liver failure due to hepatitis E virus.. ESOT 27 (2014) e87–e89
9. Bittencourt PL, Terra C, Parise ER, Farias AQ; Intensive care management of patients with liver disease: Arq Gastroenterol. 2015; 1:55-72
10. Tram T. Tran, Joseph Ahn, Nancy S. Reau, AGA ACG Clinical Guideline: Liver Disease and Pregnancy Am J Gastroenterol. 2016: 1-19

CASE APPROACH

Liver Transplantation in Acute Hepatitis E Induced Fulminant Hepatic Failure in Pregnancy- A way forward


Dr Piyush Kumar Sinha

Piyush Kumar Sinha
Assistant Professor, Liver Transplant Surgery, ILBS

Hepatitis E related acute liver failure in pregnancy, occurs predominantly in developing countries, has a more severe course compared to nonpregnant population and has a very high mortality. In self limiting cases it resolves without much sequel but in severe cases liver transplant is the only option. Situation becomes even more difficult when there is scarcity of deceased donor organs and live donation is the only way out. This article is a case based approach towards liver transplantation in acute hepatitis E related acute liver failure.

Magnitude of problem

India is considered as an endemic area for hepatitis E (HEV) with high seroprevalence. Pregnancy is known to aggravate the course of hepatitis E. With lack of awareness and medical facility the mortality is very high as shown in the table.

	No of pregnant females/total population	HEV as cause of AVH/ ALF	Outcome (maternal deaths) HEV
Beniwal, 2003, New Delhi	97	AVH: 25/69 (36%) ALF: 21/28 (75%)	HEV group: 18/46 (39.1%) expired 18/21 (85.7%) of HEV-ALF died
Jaiswal, 2001, Indore	P: 127 NP: 146 (controls)	P (AVH): 40/83 (48%) P (ALF): 33/44 (75%)	P (AVH) 1/40 (2.5%) P (ALF): 15/33 (45.4%)
Patra, 2007 New Delhi	220 consecutive P females (2nd and 3rd trimester	AVH: 59/129 (46%) ALF: 73/91 (80%)	HEV group: 54/132 (41%)
Bhatia, 2007, New Delhi	1015 ALF P: 249 NP: 341 M: 425	HEV-ALF: 342/1015 (34.4%) P (ALF): 145/249 (59.4%) NP (ALF): 100/341 (30.4%)	HEV: P: 74/145 (51%) NP: 46/100 (46%) M: 36/97 (37%) Non-E: P: 52/95 (55%) NP: 132/214 (62%) M: 184/293 (63%) NS
Khuroo, 2003, Kashmir	P: 76 NP: 337	P: 65/76 P (ALF): 45/47 (96%) NP: 140/337 NP (ALF): 14/34 (41.2%)	ALF: HEV: 30/59 Non-HEV: 20/22

P: pregnant; NP: non-pregnant; M: men; AVH: acute viral hepatitis; ALF: acute liver failureHEV Hepatitis E virus

As can be seen a significant proportion of acute viral hepatitis during pregnancy is caused by hepatitis E and is responsible for majority of acute liver failures. The most important observation is high mortality associated with acute liver failure which ranges from 40 to 80%.

History and clinical examination

Classically there are prodromal symptoms which include fatigue, nausea, vomiting, fever, dark urine, anorexia, and rash followed by development of jaundice. These symptoms are generally attributed to upper respiratory tract infection or gastrointestinal disturbances. The acute liver failure is recognized by the occurrence of encephalopathy and coagulopathy without history of previous underlying pre-existing liver disease. The interval between jaundice and encephalopathy is variable and has prognostic implications. In the largest study from India the mean jaundice to encephalopathy interval was 5.2 days. Clinical examination reveals jaundice, altered sensorium and there can be hepatomegaly or shrunken liver. Later in the course patients may develop seizures, gastrointestinal bleeding, sepsis and renal failure.

Laboratory parameters

The liver biochemistry generally shows hyperbilirubinemia in the range of 10-15 mg/dl, and transaminases in thousands. INR is generally high and has a direct prognostic importance. Ultrasonography shows hepatomegaly or shrunken liver with pericholecystic edema and mild ascites. Other investigations show features of sepsis and renal failure as the disease progresses. Viral markers show HEV IgM positivity.

Management

At the onset the patient should be managed at a center which has both obstetrics and liver transplant facility. The referral should not be delayed as transportation in advance cerebral edema may prove fatal if precautions are not taken.

Diagnosis

The first step of diagnosis is to rule out chronic liver disease

Ultrasonography can be useful but sometimes in subacute presentation the features if liver may mimic chronic liver disease. Transjugular liver biopsy can be done to rule out chronic liver disease if there is diagnostic dilemma.

The second step is etiological work up

Although hepatitis E related acute liver failure is

common other etiologies should be ruled out. This is important because some of the etiologies have very different management strategy and prognosis.

The common causes of acute liver failure and investigations

Etiology	Investigation
Drug related	History of drug intake (ATT or CAM are common)
Acute viral hepatitis	anti HAV IgM anti-HEV IgM If above mentioned are negative go for anti-HSV IgM, anti VZV IgM, CMV, HSV, EBV, parvovirus and VZV PCR
Budd-Chiari syndrome	Doppler will show absent hepatic venous outflow
Autoimmune	ANA, ASMA, anti-soluble liver antigen, globulin profile, ANCA.IgG
HBV reactivation	HBsAg, anti-HBc IgM (HBV DNA)
Fulminant presentation of Wilson disease	Coombs negative hemolytic anemia, and high bilirubin to alkaline phosphatase ratio. In 50% of cases, Kayser-Fleischer rings are present. Serum and urinary copper are markedly increased

Liver disease in pregnancy which may require liver transplant

HELLP syndrome

The diagnosis of HELLP is most often made through recognition of typical laboratory results. Signs of hemolysis with elevated liver enzymes and thrombocytopenia. Right upper quadrant and epigastric pain, nausea, vomiting, malaise, headache, edema, and weight gain are common complaints. Hypertension and proteinuria should be expected, occurring in up to 80% of cases. Jaundice is rare, occurring in only 5% of patients. Hepatic consequences include hepatic infarction, subscapular hematomas, and intraparenchymal hemorrhage. When the ALT or AST is >1,000 U/l or abdominal pain radiates into the right shoulder, cross-sectional imaging can assist in excluding hepatic complications.

Acute fatty liver disease of pregnancy (AFLP)

AFLP is a rare, life-threatening condition characterized by microvesicular fatty infiltration of the liver leading to hepatic failure. The median gestation age at the time of identification is 36 weeks. Risk factors include twin pregnancies and low body mass index .Presenting symptoms are non-specific: nausea, vomiting, and abdominal pain. Concomitant preeclampsia is present in roughly one half of the affected women. Striking aminotransferase elevations and hyperbilirubinemia are typical. Hepatic failure can manifest with signs of hepatic dysfunction such as encephalopathy, coagulopathy, and hypoglycemia. Renal dysfunction and pancreatitis are common.

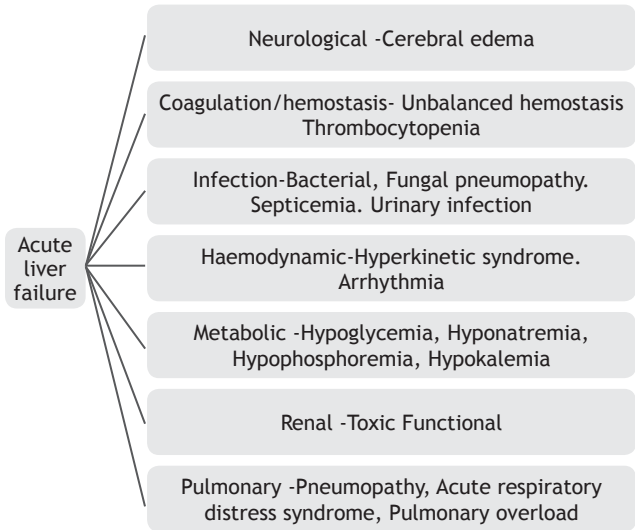
Clinical management of acute liver failure

Acute liver failure affects other organ systems and aim of management is supportive with continuous measurement of prognostic variables for liver transplant

Initial management

Routine monitoring	1. Oxygen saturation, blood pressure, heart rate, respiratory rate 2. Hourly urine output 3. Clinical neurological status
Standard care	1. Glucose infusions (10–20%): glycemic target ± 140 mg/dl 2. Na 135–145 mmol/L 3. Stress ulcer prophylaxis 4. Restrict clotting factors unless active bleeding 5. N-acetylcysteine
In case of hepatic encephalopathy:	1. Quiet surrounding, head of bed >30, head in neutral position 2. Intubate, ventilate and sedate if progresses to >3 coma. 3. Low threshold for empirical start of antibiotics 4. normalize biochemical variables (Na, Mg, PO4, K) 5. Euvolemia

The complications should be expected and managed accordingly. As shown in the figure ALF is associated with multiorgan involvement.



At present, the most frequent causes of death in patients with ALF are MOF and severe sepsis. Therefore, the general supportive management of patients with ALF should focus on the prevention and prompt treatment of infections. Careful monitoring of organ function and appropriate management of dysfunction as early as possible should be carried out. The progression risk of

HE must be recognized and emphasized, and appropriate nursing observations undertaken. The development of cerebral irritation or change in level of consciousness should be assumed to be HE.

Pregnancy related complications in HEV

Maternal Complications

Severe complications may occur in patients with acute liver failure in pregnancy. The complications are reported to be more in the second and the third trimester. The maternal complications include preterm labour and spontaneous abortions. A study from North India, involving 132 pregnant women with HEV infection, reported obstetric complications in the form of antepartum hemorrhage (23%), postpartum hemorrhage(14%) and premature rupture of membranes (9%). Coagulopathy is responsible for the increased risk of bleeding seen in these patients.

Fetal Complications and Outcomes

The clinical presentation in the neonate may be as hypothermia, jaundice, anicteric hepatitis, acute liver failure, recurrent diarrhoea, fever or stillbirth. Hypoglycaemia may occur. The liver function test abnormalities include elevated bilirubin alone, elevated aminotransferases or a combination of both. The diagnosis is made by the presence of IgM HEV antibody and/or HEV RNA positivity. In a sporadic setting, among all pregnant women infected with HEV, still births have been reported in 54% and neonatal deaths in 17% whereas in an epidemic, fetal deaths including intrauterine and neonatal deaths were reported to be 12.4% in HEV related AVH and 75% in HEV ALF patients.The principles of management of abortions, preterm labor, premature rupture of membranes and still birth are same as for a normal pregnancy. There is an increased risk of bleeding due to associated coagulopathy.

Course and prognostication models

HEV infection is usually self limiting and, in the absence of complications, does not require therapeutic intervention. In cases of uncomplicated viral hepatitis symptomatic treatment leads to improvement.

The most important part of management is prognostication of patient using clinical and lab parameters so that they can be referred for liver transplantation. Although several variables have been described in literature none is 100 percent accurate and none have been proposed specifically for this patient population. Another important point is these parameters are not developed in live donor liver transplant scenario where their is risk to donor and the risk should be balanced with the risk to recipient commonly called the principle of double equipoise in live donor liver transplant and the graft is patients' personal gift so there are no competitors for the graft as is the case in deceased donor liver transplant.

King's college criteria has been the most validated and most commonly used criteria worldwide. It was developed in western setting where the etiology is different from our country. The indication of liver transplant was according to KCH criteria in non-paracetamol poisoning group are, single criteria INR >6.5 or meeting three out of five poor prognostic factor (age<10 or >40, jaundice to encephalopathy duration > 7 days, total bilirubin value > 17.5 gm/dl and Non A, Non B etiology). We at our center use this criteria for liver transplant for acute liver failure.

Multiple prognostic models have been proposed for ALF in India but they lack validation. In a large Indian study, the following variables present at admission have been identified as independent risk factors for patient outcomes: (i) age >40 years (ii)bilirubin > 15 mg/dL; (iii) prothrombin time prolongation>25 s (iv) clinical features of cerebral edema. With an increasing number of risk factors, mortality increases; with three or more factors it is 93%. In another study from India, clinical prognostic indicators reported include age>50 years, Jaundice encephalopathy interval >7 days, grade 3 or 4 encephalopathy, presence

of cerebral edema, prothrombin time > 35 and creatinine >1.5 mg/dL. Presence of any 3 of 6 was superior to MELD or KCH in identifying survivors and non-survivors. Pregnancy per se or its duration of gestation does not affect the prognosis and HEV is associated with a better prognosis than other causes of ALF.ALF is a dynamic process in which variables determining prognosis at admission change over time, and thus the clinical course varies accordingly. A new prognostic model from India, ALF early dynamic (ALFED) model is based on four variables: arterial ammonia, serum bilirubin, international normalized ratio and hepaticencephalopathy > grade II. This model takes into account the values of these variables over 3 days. The performance of the ALFED model has been reported to be superior to the King's College Hospital criteria and the Model for End stage Liver Disease score.

Although several criteria has been proposed one has to go by clinical course and lab results. There is a window period when transplant should be done. If done too early there will be a significant proportion of patients who would have recovered without transplant. If done too late in the course the mortality is too high after liver transplant. The foetus should be delivered before transplant.

Live donor liver transplant

Once indication is clear, family is counseled about critical nature of illness and need of emergency liver transplantation as lifesaving procedure. As deceased donation is sparse in our part of country so family is counseled about need of voluntary healthy donor in family if available. After informed detailed discussion with the prospective donor and their family members on the risks and benefits of the operation, donor workup is initiated. Voluntary healthy group compatible donors, between 18 and 50 years of age, with a body mass

index between 18 and 28 kg/m2, free of medical and psychiatric illness are considered for donor evaluation. They are evaluated or liver function and anatomy followed by general fitness for surgery. Detailed evaluation protocol is out of scope of this review.

The Contraindication in recipients includes patients with uncontrolled sepsis, rapidly escalating need of Vasopressor; evidence of compromised brain stem function especially fixed and dilated pupils, invasive fungal infection, and severe irreversible cardiopulmonary disease.

Detailed description of surgery is out of scope of this review, in short donors undergoes right or left hepatectomy. The graft is taken out and perfused with preservative solution. Meanwhile the recipient total hepatectomy is performed. In implantation hepatic vein anastomoses followed by portal vein anastomoses is done followed by artery and bile duct. The recipient is shifted to transplant ICU and their course is determined by graft function, resolution of cerebral edema and infections.

Deceased donor liver transplant

On this scenario once the patient meets predefined criteria they are listed for transplant. Status 1 is given to these patients and any organ which becomes available in the region is offered to this patient. In our country the organ donation rate is too low to wait for organ in acute liver failure setting although there is provision of status one once the patient meets king's college criteria.

Result of liver transplant for ALF

Result of liver transplant for acute liver failure ranges from 60% to 90%. The variability is explained by selection criteria, type of graft DDLT vs LDLT and era of reporting. At our center we have performed 61 live donor liver transplants for acute liver failure (unpublished data). The median jaundice to encephalopathy time was 15(9-29) days, majority (66%) were in grade ¾ encephalopathy at presentation and 70% on ventilator preoperatively. Preoperative culture was positive in 47%. Recipient outcome has been good with1 year survival of 65% keeping view of sicker cohort of patients as they were referred late or transplant was delayed due to logistic regions. There was no donor mortality with major complication in only one donor in the form of wound infection requiring secondary suturing.

Conclusion

HEV related ALF in pregnancy is associated with very high mortality and morbidity. Once patient meets criteria for LT the chances of spontaneous survival is hardly 10 percent. With timely referral and good operation the survival after liver transplant can be excellent. So it is actually a way forward in this cohort of patients. Having said that the most important part is prevention which can easily be done. Simple awareness that of the fact that these viruses can be eradicated by boiling water at 100^0C or by appropriate chlorination can be very effective.

Suggested reading

1. Wendon J, Cordoba J, Dhawan A, Larsen F, Manns M, Nevens F et al. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. Journal of Hepatology. 2017;66(5):1047-1081.
2. Shalimar, Acharya S. Hepatitis E and Acute Liver Failure in Pregnancy. Journal of Clinical and Experimental Hepatology. 2013;3(3):213-224.
3. Bernal W, Hyyrylainen A, Gera Aetal.Lessons from look-back in acute liver failure? A single centre experience of 3300 patients. J Hepatol. 2013; 59:74-80.
4. Bhatia V., Singhal A., Panda S.K., Acharya S.K. A 20-year single-center experience with acute liver failure during pregnancy: is the prognosis really worse? Hepatology. 2008;48:1577–1585.
5. Pamecha V, Mahansaria S, Bharathy K, Kumar S, Sasturkar S, Sinha P et al. Selection and outcome of the potential live liver donor. Hepatology International. 2016;10(4):657-664.

Calendar of Monthly Clinical Meetings 2018-19

Months	Name of the Institute
July, 2018	AIIMS
August, 2018	VMMC & Safdarjung Hospital
September, 2018	Deen Dayal Upadhyay Hospital
October, 2018	ESI Hospital
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

DISTRESS TO DE-STRESS

What are You Cooking ..... Inside?

Mohit D Gupta
Professor of Cardiology, GB Pant Hospital, New Delhi
Author is associated with Brahma Kumaris World Spiritual University


Dr Mohit D Gupta

There is nothing in this world that can trouble you as much as your own thoughts!!

At an initial thought, overthinking doesn't sound so bad: Actually, thinking is good…. Then what is the problem?

Situation: Just create a situation when you are sitting comfortably at home waiting for someone near who comes by 5 PM. The clock ticks 6 PM, you try mobile and it says switched off or not reachable. The clock advances further and its 7PM. There is no message. Now, what kind of thoughts come to your mind? Let us check.

Is it ……worry, stress and anticipating the worst. We create thoughts and hence an experience that never existed. This is the art of overthinking that has become synonymous with present day living. Why does this happen?

Let us analyze this phenomenon. Overthinking is an art of creating problems that never existed.

Overthinking and Worrying involves negative predictions about the future: Simple thoughts like I will never get promoted, I will never be able to achieve this and so on can really generate fear and uncertainty in our mind that can take away the pleasure of present.

We can have the best of the utensils to cook, but the quality of food is dependent on the quality of ingredients. Isnt it? Similarly, the direction of flow of our thoughts and the outcome in a particular situation is dependent on quality of our thinking that we are doing throughout the day. Endlessly spinning our mental wheel and exhausting our mind power seems to be a common phenomenon. We often experience similar situations like above for which we end up initiating series of thoughts. Such uncontrolled thinking ends up depleting the power of our mind and makes it think negative naturally in every situation.

Why does this happen? Just as our physical health depends on the quality of food, mind power is also dependent on the quality of thoughts that we are giving it every day. If we allow our mind to get influenced and absorb everything that is happening outside, then it loses its capability to think logically, rationally and positively.

Let us practice these simple arts to overcome overthinking.

1. **Notice When You're Thinking Too Much:** Awareness is the first step in putting an end to overthinking. Start paying attention to the way you think. When we notice yourself replaying events in your mind over and over, or worrying about things you can't control, acknowledge that your thoughts aren't productive and it's time to put change.
2. **Cultivate Positive emotions:** Just as overthinking and negative emotions are hard to neutralize; positive emotions also initiate powerful chain reaction to spread comfort and warmth. Thinking positive is a habit. It needs to be cultivated by daily practice. Let us see positive in situations, people, relations, behaviors and everything. This brings a shift in focus and we naturally create positive and powerful thoughts.
3. **Practice forgiveness:** It is common for us carry in our mind hatred, anger, irritation and negative emotions for many people (who have misbehaved with us). Carrying these feelings is like cooking food with rotten vegetables. They keep hurting us and then they naturally influence our thinking patterns throughout the day. Let us practice forgiveness for our peace and wellbeing. This cleans our mind and makes it light.
4. **Busy or Be-Easy:** Most common phrase used by us is "I am busy". Busy is an energy deplete and decreases our efficiency. One task at a time and that's it. This is the rule to remain light and easy. Let us choose to mindfully complete simple tasks and the most complex ones will automatically fall in place.
5. **Focus on creating a solution rather than rethinking about the problem:** Dwelling on problems isn't helpful, but looking for solutions is. Ask yourself what steps we can take to learn from a mistake or avoid a future problem.
6. **Practice mindfulness/meditation:** Meditation is a mirror to look into our own thoughts and renew, recharge and replenish our mind. Let us try to take out 2 minutes frequently throughout the day and reconnect ourselves with supreme consciousness.

Let us make a healthy choice today to feed our mind with good thoughts and make it naturally think positive.

Wishing you a happy, peaceful and rightful thinking.

Association of Obstetricians & Gynaecologists of Delhi

MEMBERSHIP FORM

Name:.....

Surname: .....

Qualification: .....

Postal Address: .....

City:..... State: ..... Pin code: .....

Place of Working: .....

Residence Ph. No..... Clinical / Hospital Ph. No. .....

Mobile No:..... Email: .....

Gender: Male: ..... Female: .....

Date of Birth: Date ..... Month ..... Year.....

Member of Any Society:.....

Proposed by.....

Cheque/DD / No: .....

Enclosed: Cheque/Demand Draft should be drawn in favour of:

For Life Membership : Rs. 11,000 + Rs. 1,980 (18% GST applicable) = Rs. 12,980

For New Annual Membership* : Rs. 2,000 + Rs. 360 (18% GST applicable) = Rs. 2,360

For Old Renewal Membership+ : Rs. 1,200 + Rs. 216 (18% GST applicable) = Rs. 1,416

Encl.: Attach Two Photocopies of All Degrees, DMC Certificate and Two Photographs

***-Annual Membership is for the calendar year January to December.**

+ - In case of renewal, mention old membership number.

Note: 18% GST will be applicable as FOGSI requires it.

Send Complete Membership Form Along With Cheque / DD and Photocopy of required documents.

AOGD Secretariat

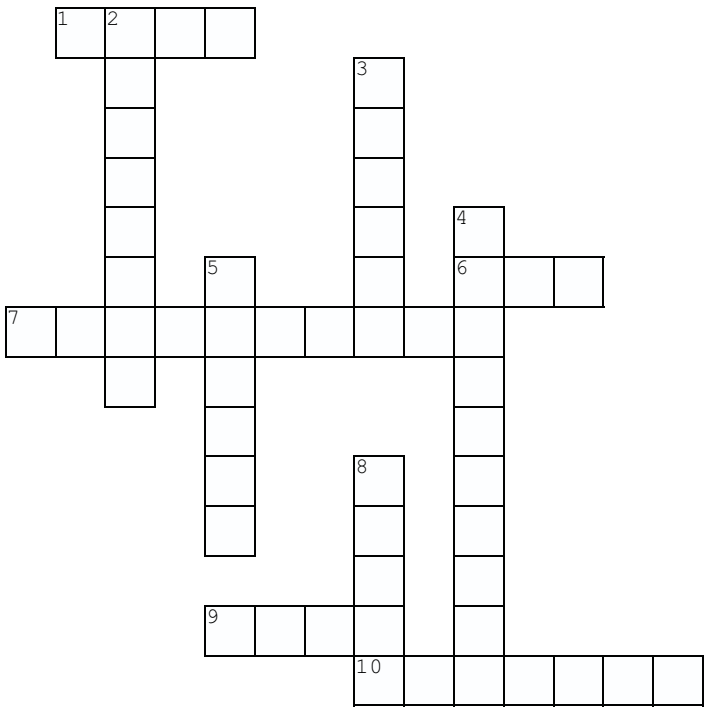
Department of Obstetrics and Gynecology,
Lady Hardinge Medical College & SSK Hospital, New Delhi 110001
Ms. Shefali 9205292980
www.aogd.org. Email: secretarylhaogd2018@gmail.com, info@aogd.org

CROSSWORD

The Maze of Knowledge

Swati Agrawal
Associate Professor, Department of Obs & Gynae, LHMC & SSK Hospital, New Delhi


Dr Swati Agrawal



Down

2. Most common route of transmission of hepatitis in pregnancy
3. Non- steroidal once a week contraceptive included in GOI contraceptive basket
4. FDA approved drug for the treatment of hepatitis B in pregnancy
5. Device for hysteroscopic females terilisation
8. Serum test which indicates the risk of perinatal transmission in hepatitis B

Across

1. Diagnos is of exclusion in jaundice in pregnancy
6. Method of ligation & excision of vas deference without use of a knife
7. Treatment option for fulminant hepatic failure in pregnancy
9. Contraceptive associated with bone loss
10. The frameless copper IUD

PICTORIAL QUIZ

A Picture is Worth a Thousand Words

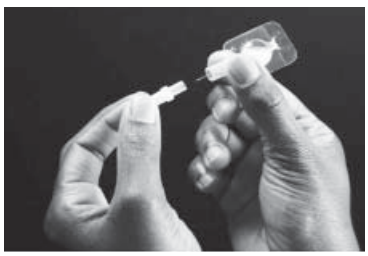


Figure 1:

Q1. What does the given picture show?
Q2. What is the dose of the drug shown in the picture?
Q3. What is the advantage over conventional method of administration?

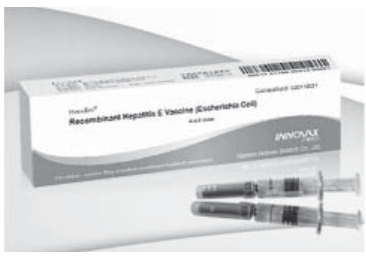


Figure 2:

Q1. In which country is the above vaccine manufactured and registered for use?
Q2. What is the dosage schedule of the above vaccine?
Q3. What is the age group in which it is recommended?

Refer page 62 for Previous answer key.

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: (Fees plus 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 **"Associations 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 Cash/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, Shefali 9205292980, Email: secretarylhaogd2018@gmail.com

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

Events Held

- Textbook of Gynecology authored by Dr J B Sharma being released by Sh. J P Naddaji Hon'ble Union Health Minister

- CME on Endometriosis organized by AOGD Endometriosis Sub-Committee on 10th June 2018 at India International Centre

- Cervical and Breast Cancer Screening Camp organized by Department of Obstetrics & Gynecology and Department of Preventive and Social Medicine, UCMS and GTB Hospital on 11th June 2018 at Ghazipur Urban Health Centre

- CME on "Breast and Cervical Cancer Awareness organized by Screening Sub-committee" on 19th June 2018 at Hotel City Park, Pitampura

- Adolescent Health Awareness Program organized by Rural Health Committee on 19th June 2018 at CR Das Kanya Vidyalaya, Village-Seelampur, Delhi

- Public Forum on 'Importance of Yoga in Pregnancy" on International Day of Yoga organized by Department of Obstetrics and Gynecology LHMC and SSK Hospital on 20th June 2018 at Gynae OPD, SSKH

- AOGD members participating in International Yoga Day celebrations on 21st June 2018 at Rajpath


- AOGD Monthly Clinical Meeting on 29th June 2018 at Army Hospital Research & Referral, New Delhi



- Doctor's Day celebration marked by planting tree on 1st July 2018 at Panchsheel Park



- Gurukul Classes organised by Institute of Obstetric & Gynecology, from 30th June to 1st July 2018 at Sir Ganga Ram Hospital, New Delhi


- Project: Cervical Cancer Awareness, Screening & Vaccination. This Project was a joint effort of Okti Foundation and ONGC, Delhi initiated and implemented by Dr Priti Arora Dhamija, Dr Sonal Bathla & Dr Nirmala Agarwal. This was supported by FOGSI, AOGIN INDIA, AOGD, IMS, RCOG NZ India, ISCCP, Friends of SPH, Inner Wheel & Rotary Club Gurgaon


DGES-ESGE 2018

Delhi Gynaecological Endoscopists Society – Annual
European Society of Gynaecological Endoscopy – Regional

Date: **17th, 18th, 19th August, 2018**
Venue: **Hotel Le Meridien, New Delhi**

CME Credit Point Applied For

Making a Difference with Endoscopy
in
Gynae Surgeries, Urogynaecology, Oncosurgery, Infertility

International Operating Faculty

Prof. Dr Dr Rudy Leon De Wilde
Oldenburg, Germany

Dr Hugo. C Verhoeven
Düsseldorf, Germany

Dr Rajesh Devassy
Oldenburg, Germany

Prof. Dr Sven Becker
Frankfurt, Germany

National Operating Faculty

Dr Alka Kriplani
Dr Amit Tandon
Dr B Ramesh
Dr Dinesh Kansal
Dr Dipak Limbachiya
Dr Hafeez Rahman
Dr Hara Pattanaik
Dr Jyoti Mishra
Dr Kiran Coelho
Dr Malvika Sabharwal
Dr Nutan Jain
Dr Prakash Trivedi
Dr Prashant Mangeshikar
Dr Punita Bhardwaj
Dr Rajendra Sankpal
Dr Rajesh Modi
Dr Rekha Kurien
Dr Sanjay Patel
Dr Shailesh Putambekar
Dr Shivani Sabharwal
Dr S Krishna Kumar
Dr Sunita Tandulwadkar
Dr Vidya V Bhat
Dr Vineet Mishra
Dr Vivek Marwah

Highlights

- Understanding Pelvic Anatomy
- TLH made easy - with different vessel sealers
  Large Uterus/ Scarred Abdomen/ Endometriosis
- Changing Trends in Laparoscopic Onco Surgeries
- Advancement in Urogynaecology
- Aesthetic Gynaecology - Emerging Trends
- Fertility Enhancing Surgeries
- Setting benchmarks in Infertility
- Transumblical Laparoscopy
- Non descent Vaginal Hysterectomy
- Transvaginal Laparoscopy
- Sentinel Lymphadenectomy
  with ICG Flurescence Mapping

Special Offer for PG
Rate per day 2000 INR

2 Days Live Operative Workshop

Call For Abstracts/Posters Last 15th July 2018

Exciting Prizes Quiz

Cases Subject to Availability

Dates	DGES Members	Non Members	Foreign Delegate
Upto 1st July 2018 (early bird)	9000 INR + GST = 10620	9900 INR + GST= 11682 INR	300 USD
2nd July-1st Aug 2018	9500 INR + GST = 11210	10400 INR + GST= 12272 INR	400 USD
Late & Spot	10500 INR + GST = 12390 INR	11400 INR + GST= 13452 INR	500 USD

Includes Three Lunches + Conference kit + Live Surgical Workshop on 17th & 18th Aug. 2018 + Scientific Session on 19th Aug. 2018

Banquet on 18th August at Hotel Le Meridien, 2500 INR + 18% GST for Indian Delegate and 65 USD for Foreign Delegate

Organising Chair

Dr Malvika Sabharwal
President, Delhi Gynaecological Endoscopists Society

Prof. Dr Dr Rudy Leon De Wilde
Director of the ESGE (European Society for Gynaecological Endoscopy)

Dr Shivani Sabharwal
Secretary, Delhi Gynaecological Endoscopists Society

Office Secretariat:
Jeewan Mala Hospital
67/1 New Rohtak Road, New Delhi-110005
(M): 8744063330, 9212150571, 9811557511
E-mail: dgesjmh@gmail.com, Website: www.dges.in

BEST CLINICAL PRACTICE

Standard of Care for Post Abortion and Post Partum Contraception


Dr Prabha Lal

Prabha Lal
Professor, Dept of Obstetrics & Gynecology, Lady Hardinge Medical College, New Delhi

India was the first country in the world to have launched a National Programme for Family Planning in 1952. Post abortion and post partum family planning can avert unintended pregnancies and abortion associated problems. Counselling has a critical role in providing post-abortion and post partum family planning services and involves communication between a service provider/ counsellor and a client.

In India unmet need for family planning in 1st year post-partum period is 65%[1]. Only 26% of women are using any method of family planning during the first year postpartum. Contraception plans should be discussed during the prenatal and postpartum course and plans should be documented in notes.

Post partum post abortal contraception

Postpartum family planning is the initiation and use of family planning methods in the first six weeks following delivery up to 12 months. The aim is to prevent unintended pregnancy, particularly soon after childbirth.

Post-abortion family planning is the initiation and use of family planning methods immediately after and within 48 hours of an abortion, before fertility returns occur. WHO recommends spacing of at least 6 months between abortion and next conception.

Fertility returns within four to six weeks for women who are not exclusively breastfeeding, up to 6 months in exclusively breast feeding and as early as 10-14 days after an abortion.

Choice of different contraceptive methods are:

Post-partum breast feeding women-

- Non hormonal contraceptive are > Lactation menorrhea method (LAM), Diaphragm, Male and female condoms, Spermicides, IUCD, Male and female sterilisation, Natural Family Planning (NFP).
- Hormonal contraceptive> Progestin-only pills, Injectables (DMPA, NET-EN), Implants (Jadelle, Implanon). Less preferable are Combined oral contraceptive pills (COCs), Monthly injectable (Mesigyna, Cyclofem).
- In postpartum women non breast feeding women best choice is non-hormonal method followed by Progestin-only methods and combined oral contraceptives are the last choice.

Post-abortion women

- Condoms (which also prevent STIs and HIV), Oral contraceptives, IUCDs, Injectables, Implants, Spermicides, male and female sterilization.

Intrauterine contraceptive device

The following standards of care must be maintained [2]:

1. Woman must be counselled regarding advantages, limitations, effectiveness, side effects and problems related to IUCD.

   Women should be ideally counselled in the antenatal period for immediate PPIUCD insertion. If a woman presents in early labour, she can be counselled for an immediate PPIUCD and prior to planned caesarean section. Post insertion counselling regarding follow ups and warning signs.

Counselling should be done before abortion procedure and will help in adopting various contraceptive methods.

2. The provider must explain the procedure for insertion and/or removal of the immediate PPIUCD.
3. Woman must be screened for clinical situations as per WHO Medical Eligibility Criteria (MEC). Screening should take place in the antenatal period, as well as immediately prior to insertion, immediate postpartum.
4. The woman must be counselled and offered another suitable postpartum family planning method if her clinical situation does not allow for insertion of the immediate PPIUCD.
5. The provider must insert the IUCD by following all recommended clinical and infection prevention measures for successful insertion.
6. Insertion must be done using a long instrument, such as a placental forceps, to ensure that the IUCD is placed at the fundus.
7. The provider must maintain records regarding PPIUCD insertions and services as per protocol.
8. Woman must be followed up by a provider oriented to PPIUCD services.

The usual timings are: Immediate Postpartum (Post placental Insertion within 10 minutes after expulsion of the placenta), Intra caesarean, Within 48 hours after delivery, Post abortion, Extended Postpartum / Interval (after 6 weeks postpartum).

Family planning method	Exclusively Breast feeding	Non breast feeding	Post abortion	JUSTIFICATION
Lactational amenorrhea	Immediately up to 6 months	Not applicable	Not applicable	
Cu T IUCD	Up to 48 hours postpartum, after 4 weeks MEC Cat 1, 48 hours to 4 weeks cat 3		Immediately after surgical evacuation and after 15 day of medical abortion	• more cost effective than shorter-acting methods due to very low failure rates • very minimal action by the user, apart from undergoing the initial insertion procedure.[6]
Female sterilization	After 24 hours to 7 days of delivery or after 6 weeks		Immediately surgical abortion or within 7 days and after next mentruation in medical abortion.	
Male and female condoms	Immediately when sex is resumed			
Progesterone only methods (tablets /injectables)	POP < 6 weeks cat 2 DMPA < 6 weeks cat 3	POP and DMPA<3 weeks postpartum cat 1	Surgical abortion immediately. Medical abortion on day 3[3].	• Direct evidence demonstrates no harmful effect of POC on breastfeeding performance • no harmful effects on infant growth, health or development.[7]
Combined OCP	< 6 weeks cat 4 6 weeks to 6 months cat3	<6 weeks cat 3 >6 weeks cat 1	Surgical abortion immediately. Medical abortion on day 3	• While Breast Feeding o One systematic review reports that the impact of COC on breastfeeding duration and success is inconsistent. o Results are conflicting on whether early initiation of COC affects infant outcomes, but generally find no negative impact on infant outcomes with later initiation of COC.[5] • Non Breast Feeding o VTE risk is elevated during pregnancy and the postpartum period; o risk is most pronounced in the first 3 weeks after delivery, declining to near baseline levels by 42 days postpartum.4–8 o Risk of pregnancy during the first 21 days postpartum is very low, but increases after that as ovulation before first menses is common.[4]

Follow up should be done after 3-6 weeks of insertion and should co-inside with PNC visits.

References

1. Frontiers in Reproductive Health. "Population Council Enhancing Quality for Clients: The Balanced Counselling Strategy". Programme Brief No. 3: July 2003.
2. PPIUCD reference manual 2010 nrhm.
3. Post abortion family planning update 2016 MOHFW.
4. Faculty of Sexual and Reproductive Healthcare. Barrier Methods for Contraception and STI Prevention. 2012.
5. Stephen G, Brechin S, Glasier A. Using formal consensus methods to adapt World Health Organization Medical Eligibility Criteria for Contraceptive Use. Contraception 2008; 78: 300–308.
6. Sonalkar S, Kapp N. Intrauterine device insertion in the postpartum period: a systematic review. Eur J Contracept Reprod Health Care 2015; 20: 4–18.
7. Elsedeek MS. Puerperal and menstrual bleeding patterns with different types of contraceptive device fitted during elective cesarean delivery. Int J Gynaecol Obstet 2012: 116: 31–34.

RECENT ADVANCES

Male Contraception

R.C.M. Kaza
National Trainer NSV & Micro Surgery Recanalization, Govt. of India
Senior Consultant & Academic Head, Dept. of General & Laparoscopic Surgery,
Max Super Specialist Hospital, Vaishali


Dr R.C.M. Kaza

The scenario for contraception in men has not changed much over the years. Men have only two contraceptive methods. One is condom, which is temporary and the other; Vasectomy, which is permanent.

The developments in condom are more at a research stage. The technique of vasectomy has been refined at various levels by the development of Jet injector and fine needle technique in anesthesia and addition of fascial interposition between the two cut ends of vas that prevent failure of vasectomy. The other developments like the use of thermal cautery for occlusion of vas has also become standardized. The research work in condoms mostly involves development of materials that do not hinder sensation and thereby increase acceptance of condoms among men.

Male sterilization forms 1.1% of all sterilizations in the country. Global scenario is also roughly the same with male sterilization accounting for nearly 2.5% of all sterilizations. Clearly a major effort has to be made to rope in men.

No Scalpel Vasectomy:

No Scalpel vasectomy (NSV) is the gold standard of the male sterilizations. It is a refined method of vasectomy, first developed by Dr. Li Shun Qiang of China in 1974. It is a minimally invasive approach to vas, done under local anesthesia, without any formal incision or a stitch. NSV has replaced tubectomy in some districts of China. More than 10 million men have accepted NSV in china.

NSV was introduced in India in 1992. It was formally made into a national programme in 1997. A massive training campaign was coupled with the launch of NSV. Author has personally trained over 4000 surgeons in NSV. There is a formal system of training for trainers and service providers.

NSV with fascial interposition is National standard for male sterilization. There is no formal incision and stitches in NSV and this allays the fears of men about wound related complications and leads to greater acceptance of the procedure; while, fascial interposition prevents spontaneous recanalization and failure. It is also logistically simple with only two instruments and 2'0' silk for vasal occlusion.

There are many recent developments in NSV both in techniques of anesthesia and occlusion. Use of jet injector for administration of local anesthesia, is almost painless but the injector is expensive. If cost comes in the way use of fine needle technique with 30G needles to administer anesthesia is equally effective and almost as painless as jet injector. Methods of occlusion of vas have also evolved. Increasingly thermal cautery and titanium clips are replacing traditional silk suture for occlusion. Excision of a segment of vas deferens that has been the hall mark of all forms of vasectomy has also been questioned in a new procedure, the In line vasectomy. Studies indicate that use of thermal cautery to cauterize a split open segment of vas without excising the segment is equally effective in producing azoospermia.

Approaches to vasectomy

There are two methods of approaching vas. The Incisional/Conventional vasectomy and Nonscalpel vasectomy.

Regardless of the method of scrotal entry, the first step in the vasectomy is to identify and immobilize the vas through the skin of the scrotum and make it subcutaneous. The second step is to exteriorize the vas by either an incision or by the No Scalpel approach.

Conventional vasectomy

This procedure should no longer be practiced. However in the absence of a trained surgeon in NSV this is still an option and accepted as adequate by the government of India. There are no recent developments here. But some of the developments mentioned with NSV can be practiced here such as the anesthetic and occlusion techniques.

In the conventional vasectomy, bilateral or single midline incision is made with a scalpel in the scrotal skin, each usually 1-2 cm long and overlying the vas deferens. Jhaver (1958) developed a single midline incision, single stitch method of performing conventional vasectomy thereby proving that bilateral vasectomy can be performed through one incision. The incision is closed with sutures after the vasectomy has been completed. In general, with conventional vasectomy, only the area around the skin entry site is anesthetized and vasal block, if attempted, is a blind injection at the root of scrotum into the cord.

No-scalpel vasectomy

NSV utilizes two specialized instruments - a ringed

clamp and a dissecting forceps (a sharp, curved modified hemostat). The dissecting forceps is used to make a small skin puncture to access and exteriorize the vas. Scrotal skin puncture made with the dissecting forceps is so small that scrotal skin closure with a stitch is not required.

No-scalpel vasectomy offers several advantages over conventional vasectomy: fewer complications, less pain during the procedure and leaves a smaller wound than conventional techniques, and earlier resumption of sexual activity after surgery. Because it requires no scrotal incision and eliminates the scalpel, no scalpel vasectomy is believed to decrease men's fears about vasectomy. Neither conventional nor no-scalpel vasectomy is time-consuming, but it has been reported that the vasectomy procedure time is shorter when skilled providers use the no-scalpel approach. On the other hand, others believe that NSV does not reduce the risk of surgical complications over the standard incisional approach to expose the vas. The point was however settled by an RCT done at Kings Birthday vasectomy festival in Thailand in 1982 where two teams of expert surgeons performed both conventional vasectomy and NSV. It was proved that NSV takes less time and has fewer complications.

Anesthesia in vasectomy

Technique of anesthesia in vasectomy is critical to its acceptance. Almost all vasectomies are performed under local anesthesia. General anesthesia may be used because of the fear of pain on the part of client. Many vasectomists use multiple blind injections with local anesthetic into the spermatic cord. This may result in hematomas and injury to the testicular vessels. A study in animals suggested that such blind injections may result in injury to the testicular artery with subsequent testicular atrophy in up to 5% of the cases, despite the use of a fine-gauge needle.

Spermatic cord block at the level of pubic tubercle has previously been proposed for scrotal surgery. However, it is difficult to isolate the vas deferens from internal spermatic vessels in the region of pubic tubercle.

External spermatic sheath injection for vasal nerve block has been used in over 10 million vasectomies in China. The vas deferens is surrounded by three layers. The external and internal spermatic fascial layer with an intervening cremasteric layer which is also called cremasteric fascia. This layer has bundles of cremasteric muscle separated by loose areolar tissue and is an ideal layer to infiltrate the local anesthetic.

The technique involves a deep injection alongside the vas and creates a vasal block. Conventional techniques anesthetize only the area around the skin-entry site. Injection of the anesthetic away from the vasectomy site in the direction of the inguinal ring helps painless handling of vas. Care is taken when injecting the lignocaine to keep the needle away from the internal spermatic fascia that encloses the testicular artery and veins. Because the surgeon makes only a single needle puncture and one smooth injection for each vas, the risk of bleeding and cord hematoma is reduced. In a randomized trial comparing no-scalpel vasectomy to the conventional technique, men undergoing no-scalpel vasectomy with vasal block anesthesia reported experiencing less operative pain than did men undergoing conventional vasectomy (Sokal et al., 1999). Philip Li et al described the technique of injecting into the external spermatic sheath for vasal nerve block in over 500 patients in United States in 1992. They did not detect any complication attributable to this technique. External spermatic sheath injection for vasal nerve block into the cord is now the most common method used for local anesthesia in NSV.

Jet injector is a nearly painless, rapid, needle-free method for administration of drug. It has previously been used to administer vaccination to more than a billion people worldwide. Jet injector has evolved as an instrument that could allow needle free, virtually painless anesthesia for most primary care procedures. The physiological advantages of the jet injection is that it can provide effective anesthesia using small volume of local anesthetic of at least 2% concentration, with minimal patient discomfort compared to conventional needle and when used the patient is totally unaware of the either the injection or the procedure that follows. Another advantage of jet injection technique is that a very small amount by volume (0.1 cc of 2% anesthetic) provides unusually high levels of tissue anesthesia.

Another Recent development is Mini needle Anesthesia where a 30G needle is used to administer anesthetic directly into the vas of both sides. This is claimed to be as painless and equally effective as Jet injector. It is also much cheaper and avoids expensive equipment.

Occlusion Techniques

Once the vas has been brought into the open, it is then occluded using a variety of methods. The same techniques are used to occlude the vas in both conventional and no-scalpel vasectomy. Although there are few complications associated with vasectomies, sometimes problems arise and the method of vas occlusion is sometimes the cause. At least 28 occlusive methods have been described over the years.

Different techniques for occlusion are:

1. Ligation & excision
2. Ligation & excision with fascial interposition
3. Electro-cautery
4. Thermal cautery
5. Clips
6. Combination of different methods
7. Open ended vasectomy
8. Inline vas occlusion

Simple ligation and excision: It is the most common method being used in developing countries including India. This is very simple, most practical and inexpensive method of occlusion. It involves tying the vas deferens with suture material, cutting it, and in many cases, removing a section of the vas.

Fascial Interposition: In this technique fascia is interposed between two cut ends of vas. This is done by tying (or securing with clip) the thin layer of tissue that surrounds the vas (internal spermatic fascia) over one end of vas.

Electro-cautery: In this method using minimum of electric power the two cut ends of vas are sealed with the help of electro-cautery. This method has limitations in that when the more common monopolar electrosurgical unit is used for fulguration, tissue destruction may be inadequate; on the contrary, it may be so extensive that the end of vas sloughs, thus allowing leakage of sperms and formation of granuloma. Unfortunately, bipolar needle which precisely regulates the amount of current is not commonly available.

Thermal cautery: Thermal cautery is a highly effective and safe method to occlude the vas for vasectomy. With this method, only the inner layer of the vas is sealed closed; the muscle wall of the vas remains intact. A segment of the vas is removed as well.

Metal clips: Clips are also being used by some vasectomists, which are applied to open end of vasal stump. Questions have been raised about the use of clips concerning the practicality and cost of procedure in less developed countries.

Open ended vasectomy: In this method testicular end of vas is not ligated. Although it has been tried, it is not commonly used. Data have shown that this technique causes less pressure-induced damage to the epididymis and reduces incidence of granuloma formation in epididymis. Thus, it is possible that vasectomy reversal will be more successful following an open-ended vasectomy. However, no studies on open-ended vasectomy and the success of reversal efforts have been reported in the literature. Overall results from available studies suggest that the open ended, technique is not associated with increase in vasectomy failure risk when the prostatic end is adequately closed by means of fascial Interposition and cautery.

INLINE METHOD OF VAS OCCLUSION: In this method neither any scalpel, nor any suture is used. Furthermore. mesentery of vas is not touched and no portion of vas is removed. This method is rapid and can be performed with NSV instruments but in addition requires a fine skin hook, a short bladed fine scissors and a hand held thermal cautery. It utilizes luminal cautery, detubularization of vas and fascial disruption. Vas lumen is opened on abdominal and testicular side to a distance of one centimeter, cauterized on both abdominal and testicular sides. Intervening portion of vas is detubularized and edges are trimmed to prevent re-tubularization. This method seems to produce less incidence of hematoma, granuloma and failures.

The various steps of NSV are being illustrated in the accompanying diagrams.

Efficacy

Vasectomy is one of the safest and most effective methods of permanent contraception. But it has the disadvantage that it is not immediately effective because viable sperms have to be cleared from the vas distal to vas occlusion.

The success of the procedure is confirmed by absence of sperms in the semen sample obtained after vasectomy. Thus, the vasectomy user and his spouse must practice alternative methods of contraception for some time after the procedure. Only 75% men are azoospermic after 3 months. Early and late failures are occasionally observed. Nature of vas occlusion techniques also impacts on early azoospermia as well as failures. Ligation and excision has the highest failures rates. Addition of Fascial Interposition (FI) not only reduces failures but results in early azoospermia. Thermal cautery occlusion has the lowest failure rates.

A number of reports have shown that men with low numbers of non-motile sperm remaining after vasectomy are at low risk of causing pregnancy. Some have suggested that these men can rely on their vasectomy for contraception even before reaching azoospermia. However, endpoint of vasectomy other than azoospermia, have not been widely accepted. According to the standards for Male& Female Sterilization set by Ministry of Health and Family Welfare, Government of India the client should undergo semen analysis after three months. However, in the best of situations and after good counseling, men do not return for follow up even in USA and Europe. Best follow up rates are not more than 45%.

No-scalpel Vasectomy Procedure

No-scalpel vasectomy procedure has been described in detail under the following steps:

Step 1: Ringed clamp is also known as extracutaneous vas fixation clamp (Figure 1). This fully explains its function of fixing the vas over the skin to make it subcutaneous. The inside of the blades are smooth to make it atraumatic. This instrument comes in three ring sizes: 3.0 mm, 3.5 mm, and 4.0 mm.

Step 2: Vas-dissection forcep is a modified curved artery forceps with the tip sharpened and set to 35°. It puncture dissects vas and acts hemostat (Figure 2).

Step 3: The penis is kept away from the field of surgery by rubber band placed at corona glandis and clipped to client's shirt (Figure 3).

Step 4: Cross-sectional anatomy of spermatic cord is showing the vas with its vessels and nerves at a distance from vascular structures. Anesthesia is administered in

the cremasteric plane outside internal spermatic fascia and under external spermatic fascia as shown in figure 4.

Step 5: Vas is isolated and stabilized by three-finger technique. Middle finger and thumb fix vas, while index finger stretches the skin over the scrotal raphe (Figure 5).

Step 6: Two percent lidocaine is first administered, as a 1 cm skin wheal at the junction of upper one-third and lower two-thirds of anterior scrotal raphe (Figure 6).

Step 7: The local needle is then advanced in strictly perivasal plane toward the ipsilateral external inguinal ring, 2 mL of local anesthetic is deposited here. Second side is similarly anesthetized (Figure 7).

Step 8: The vas is then fixed at the anesthetized site with vas fixation forceps. The fixation is perpendicular to the axis of the vas and in line with its axis (Figure 8).

Step 9: The handles of the fixation forceps are depressed, and the vas is rendered prominent in the subcutaneous plane (Figure 9).

Step 10: Next the blades of the vas dissection forceps are opened, and one of the blades (blade closer to surgeon's body) is pushed through skin and all layers above the vas into the lumen of the vas. This is felt as a sudden give (Figure 10).

Step 11: Next both the blades of the dissecting forceps are pushed into the lumen of the vas to the same depth and in the same direction. Care is taken not to go past the posterior wall of the vas (Figure 11).

Step 12: The blades are now opened and all layers above the vas are gently separated. The bare vas is now seen lying at the bottom of the wound (Figure 12).

Step 13: The vas is now elevated by a supination maneuver out of the wound, while simultaneously releasing the ring clamp. The clamp is now used to grasp the elevated vas (Figure 13).

Step 14: The vascular structures in the loop of vas are stripped away (Figure 14).

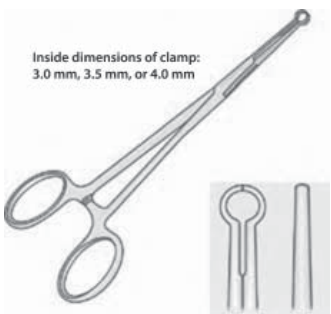
Step 15: A one centimetre segment of vas is excised after ligating both the ends of the vas (Figure 15).

Step 16: Recently thermal cautery ablation of the mucosa of vas has been found to be more effective in preventing failure. The cauterized mucosa becomes a firm fibrotic plug (Figure 16).

Step 17: The second side of vas is also brought out through the same aperture and treated in a similar manner (Figure 17).

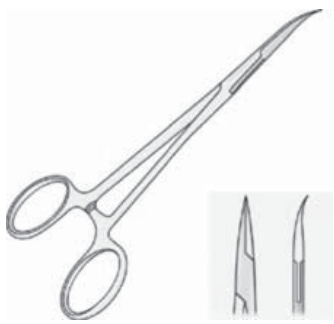
Step 18: After completion of the procedure and ensuring hemostasis, a small bandge is applied over the puncture site. Scrotal support is also given (Figure 18).

Step 19: It has now been proved that fascial interposition is mandatory after ligation and excision of vas. This results in early azoospermia and prevents spontaneous recanalization. After ligation the suture on the abdominal end of vas is kept long. Once vas segment is removed, cut ends of the vas are allowed to go back into scrotum. Next, the abdominal end is pulled up into wound where it emerges covered by a layer of thin fascia. This is grasped and tied with the cut vasal end as shown in figure 19. This results in fascial interposition between two cut ends.



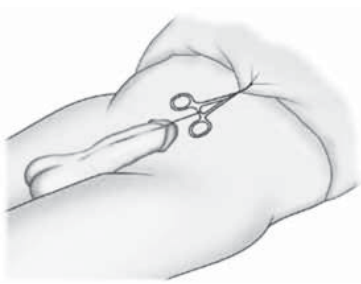
Ringed clamp is also known as extracutaneous vas fixation clamp (Figure 1). This fully explains its function of fixing the vas over the skin to make it subcutaneous. The inside of the blades are smooth to make it atraumatic. This instrument comes in three ring sizes: 3.0 mm, 3.5 mm, and 4.0 mm

Figure 1: Ringed clamp.



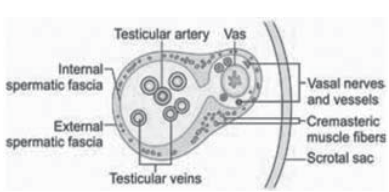
Vas-dissection forcep is a modified curved artery forceps with the tip sharpened and set to 35°. It puncture dissects vas and acts hemostat (Figure 2).

Figure 2: Dissecting forceps..



The penis is kept away from the field of surgery by rubber band placed at corona glandis and clipped to client's shirt (Figure 3).

Figure 3: Securing the penis.



Cross-sectional anatomy of spermatic cord is showing the vas with its vessels and nerves at a distance from vascular structures. Anesthesia is administered in the cremasteric plane outside internal spermatic fascia and under external spermatic fascia as shown in figure 4.

Figure 4: Cross-section of the spermatic cord.

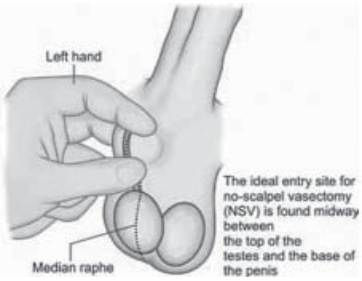
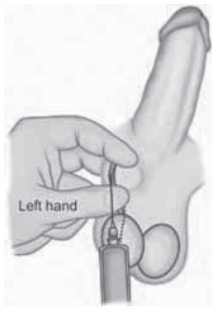


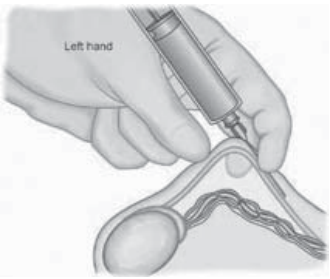
Figure 5: Determining the entry site.

Vas is isolated and stabilized by three-finger technique. Middle finger and thumb fix vas, while index finger stretches the skin over the scrotal raphe (Figure 5).



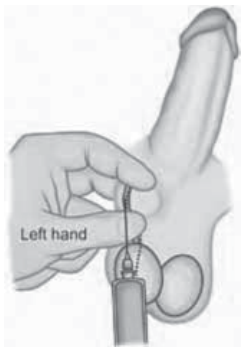
Two percent lidocaine is first administered, as a 1 cm skin wheal at the junction of upper one-third and lower two-thirds of anterior scrotal raphe (Figure 6).

Figure 6: Raiding the skin wheel.



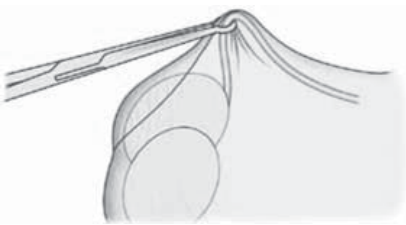
The local needle is then advanced in strictly perivasal plane toward the ipsilateral external inguinal ring, 2 mL of local anesthetic is deposited here. Second side is similarly anesthetized (Figure 7).

Figure 7: Advancing the needle parallel to the vas within the external spermatic fascial sheath toward the inguinal ring.



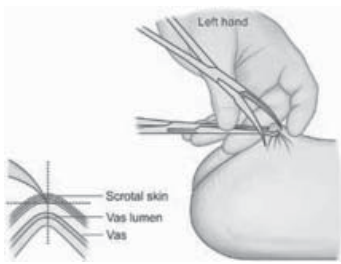
The vas is then fixed at the anesthetized site with vas fixation forceps. The fixation is perpendicular to the axis of the vas and in line with its axis (Figure 8).

Figure 8: Pressing the tips of the ringed clamp onto the scrotal skin overlying the right vas.



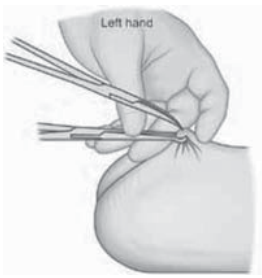
The handles of the fixation forceps are depressed, and the vas is rendered prominent in the subcutaneous plane (Figure 9).

Figure 9: Lowering the handles of the ringed clamp to elevate the vas.



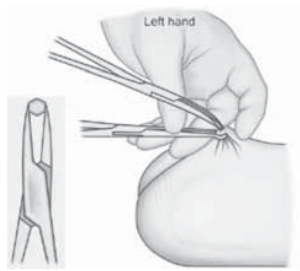
Next the blades of the vas dissection forceps are opened, and one of the blades (blade closer to surgeon's body) is pushed through skin and all layers above the vas into the lumen of the vas. This is felt as a sudden give (Figure 10).

Figure 10: Piercing the skin with the medial blade of the dissecting forceps.



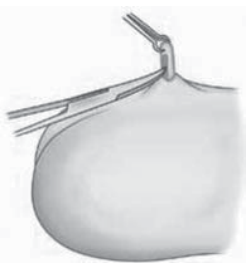
Next both the blades of the dissecting forceps are pushed into the lumen of the vas to the same depth and in the same direction. Care is taken not to go past the posterior wall of the vas (Figure 11).

Figure 11: Inserting both tips of the dissecting forceps into the puncture site.



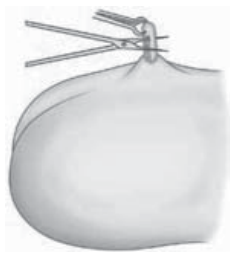
The blades are now opened and all layers above the vas are gently separated. The bare vas is now seen lying at the bottom of the wound (Figure 12).

Figure 12: Spreading the tissue to make a skin opening twice the diameter of the vas.



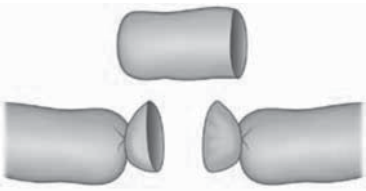
The vas is now elevated by a supination maneuver out of the wound, while simultaneously releasing the ring clamp. The clamp is now used to grasp the elevated vas (Figure 13).

Figure 13: Grasping a partial thickness of the elevated vas.



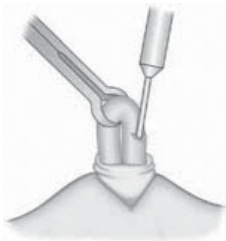
The vascular structures in the loop of vas are stripped away (Figure 14).

Figure 14: Opening the dissecting forceps to strip the sheath.



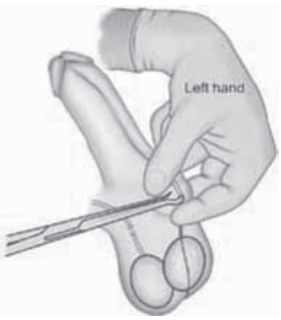
A one centimetre segment of vas is excised after ligating both the ends of the vas (Figure 15).

Figure 15: Ligation of both ends.



Recently thermal cautery ablation of the mucosa of vas has been found to be more effective in preventing failure. The cauterized mucosa becomes a firm fibrotic plug (Figure 16).

Figure 16: Cautery with a blunt wire inserted into the hemitransected vas (done in each direction).



The second side of vas is also brought out through the same aperture and treated in a similar manner (Figure 17).

Figure 17: Isolating the left vas before occlusion.

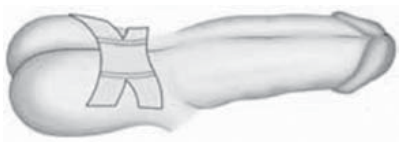


Figure 18: Dressing the wound.

After completion of the procedure and ensuring hemostasis, a small bandge is applied over the puncture site. Scrotal support is also given (Figure 18).

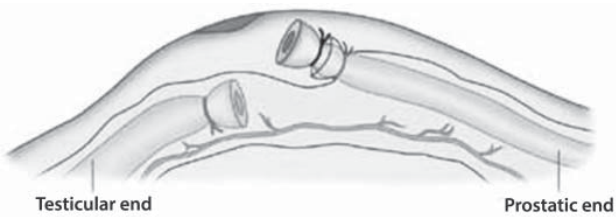


Figure 19: A layer of thin fascia grasped and tied with the cut vasal end.

It has now been proved that fascial interposition is mandatory after ligation and excision of vas. This results in early azoospermia and prevents spontaneous recanalization. After ligation the suture on the abdominal end of vas is kept long. Once vas segment is removed, cut ends of the vas are allowed to go back into scrotum. Next, the abdominal end is pulled up into wound where it emerges covered by a layer of thin fascia. This is grasped and tied with the cut vasal end as shown in figure 19. This results in fascial interposition between two cut ends.

R. C. M. Kaza, "No scalpel vasectomy—an overview," *Journal of the Indian Medical Association*, vol. 104, no. 3, pp. 129–141, 2006.

Complications

Intraoperative complications of vasectomy, such as vasovagal reaction, lidocaine toxicity, and excessive bleeding, are unusual. Explaining the procedure to the client in advance, ensuring an effective anesthetic block, using gentle surgical technique, and reassuring the client during the procedure can prevent vasovagal reaction. Lidocaine toxicity and excessive bleeding can be prevented if providers follow appropriate vasectomy guidelines for administration of local anesthesia and surgical techniques.

Most postoperative vasectomy complications are minor, subsiding within 1-2 weeks. Common complaints after surgery are swelling of the scrotum, bruising, and pain. Minor bleeding under the skin is common. Some men experience tenderness or a dragging sensation in the scrotum for up to a week after vasectomy. A scrotal support, mild pain medication, and local application of ice are usually sufficient treatment.

More significant complications such as heavy bleeding, hematoma (a collection of blood underneath the skin) or infection are generally quite rare. The incidence of hematoma is related to the provider's experience with vasectomy: Physicians who perform larger numbers of vasectomies have lower hematoma rates than those who perform fewer procedures.

Importantly, rates of heavy bleeding, hematoma, and infection vary depending on the approach taken to the vas. Numerous studies have demonstrated that the no-scalpel approach consistently results in lower rates of hematoma and infection than does conventional vasectomy.

In most cases, using good surgical technique to minimize tissue trauma and limit bleeding, practicing aseptic technique, and giving clients good postoperative instructions can prevent bleeding, hematoma, and infection. Because the loose scrotal tissue allows injured blood vessels to continue bleeding, it is important to maintain good homeostasis during the procedure if hematoma formation is to be prevented. Many Hematomas can be prevented if men avoid physical activity for a few days after the procedure; clients should be carefully instructed in this regard.

Table - 1: Comparison of complications in different types of vasectomies

Study	No. of Vasectomies	% With infections	% With hematoma/ bleeding
Incisional vasectomy			
Philp, Guillebaud, & Budd, 1984	534	1.3	4.5
Kendrick et al, 1987[31]	65.155	3.5	2.0
Nirapathpongorn, Huber, & Krieger, 1990[19]	523	1.3	1.7
Alderman, 1991[25]	1,224	4.0	0.3
Sokal et al, 1999[18]	627	1.3	10.7
No-scalpel vasectomy			
Nirapathpongporn, Huber, & Krieger, 1990[19]	680	0.2	0.3
Li et al, 1991[15]	179,741	0.9	0.1
Li et al, 1991[15]	238	0.0	0.0
Sokal et al, 2003[28] (In both the groups, Fascial interposition and non interposition)	841	1.4	0.48
Sokal et al, 1999[18]	606	0.2	1.7
Arellano et al, 1997[94]	1,000	0.0	2.1

Sperm granuloma can occur either at the site of vas occlusion or in the epididymis. These small nodules form when sperm leak out of the vas or the epididymis, inducing an inflammatory reaction. While the true incidence of sperm granuloma following vasectomy is not known, they are seen in 15-40% of men having vasectomy reversal. This provides a reasonable estimate for incidence in men following vasectomy as the rates of granuloma formation are likely to be similar in men having a reversal and in the general population of vasectomized men.

The majority of sperm granuloma is asymptomatic. Only 2-3% of vasectomized men have sperm granuloma that is painful or in some way symptomatic; most of these occur in the second or third week after the procedure. The factors that lead to the formation of sperm granuloma are not well understood; thus, there are no measures known to prevent or decrease their occurrence.

Long- Term effects

Potential physiological effects and long-term sequelae of vasectomy have been the subject of extensive research over the past two decades. This research provides reassurance that vasectomy does not have any significant long-term negative physical or mental health effects. Results of large-scale, well-designed epidemiological studies in men have consistently shown no adverse effects of vasectomy in terms of heart disease, testicular or prostate cancer, immune complex disorders, and a host of other conditions. Vasectomy appears to be a largely safe and highly effective method of contraception, certainly with risks no greater than those for any of the contraceptive methods used by women.

Comprehensive studies of disease Incidence

There are five large-scale retrospective cohort studies that have examined the incidence of a number of diseases in thousands of vasectomized and non-vasectomized men. For the disease categories or organ systems studied, vasectomized men were no more likely to be hospitalized or to develop a disease than were controls. In these studies, there were large number of cases of disease among both vasectomized and non-vasectomized men in all categories. Thus, taken together, the studies are reassuring that vasectomy does not increase the risk of adverse physical or mental health outcomes.

Antisperm Antibodies

The number of circulating antisperm antibodies increases after vasectomy: Antisperm antibodies are found in 50-80% of vasectomized men but in only 8-21% of men in the general population. The theoretical concern that these antibodies may have adverse health consequences has led to numerous studies, the results of which have shown no evidence of any immunological or other diseases related to the formation of antisperm antibodies after vasectomy. However, antisperm antibodies may play a role in decreased fertility after vasectomy reversal.

Prostate cancer

Since the mid-1980s, more than a dozen epidemiological studies of the risk of prostate cancer after vasectomy have been reported in the literature. Results have been difficult to interpret because of conflicting study findings, lack of a convincing biological mechanism for an association between vasectomy and prostate cancer, and generally weak associations when they have been found. Also, the potential for bias in some studies was high and likely led to an overestimation of any effect.

Based on the results of the research published to date, there is little evidence for a causal association between vasectomy and prostate cancer. A panel of experts gathered by the U.S. National Institutes of Health in 1993 concluded that no change in the current practice of vasectomy was necessary nor should vasectomy reversal be done as a measure to prevent prostate cancer.[48] Studies published after the expert panel report also support this conclusion.

Postvasectomy pain syndrome

A small percentage of vasectomized men have reported chronic pain in the testis following vasectomy. While up to one-third of men have reported occasional testicular discomfort following vasectomy, only around 2% of all

vasectomized men said that the pain had negatively affected their life or that they regretted having had the vasectomy because of chronic pain.[51-52] Conservative therapy such as nonsteroidal anti-inflammatory drugs, sitz baths, antibiotics, or spermatic cord blocks is sufficient treatment in most cases. When this fails, there is some evidence that vasectomy reversal or denervation of the spermatic cord may be helpful.

Mortality

Mortality following vasectomy has generally been very low. The few reports from the literature have demonstrated minimal mortality associated with vasectomy. The most comprehensive study, based on data from more than 400,000 vasectomies worldwide, reported a mortality rate of 0.5 deaths per 100,000 vasectomized men.

Vasectomy regret and reversal

Regret

Regret following a vasectomy is more common among men who at the time of the vasectomy were in an unstable marriage, were younger than 31, or had no children or had very young children, or among men who made the decision to have a vasectomy during a time of financial crisis or for reasons related to a pregnancy. Providers should use risk factors for regret to identify men who may need more in-depth counseling to ensure that vasectomy is right for them at the time, but not to deny vasectomy to men who want it. In addition, the fact that regret is often seen when vasectomy users have an adverse health effect that is either caused by the procedure or perceived to be caused by it emphasizes the importance of good counseling prior to the procedure

Reversal

The most common reasons for reversal requests are remarriage after divorce or after the death of a partner, the death of one or more children, a desire for more children, or problems of either a physiological or psychological nature that the vasectomized man or his provider believe will be alleviated by vasectomy reversal.

Vasovasostomy (reattaching the cut ends of the vas) is the most common procedure for reversing a vasectomy. In some situations, it may be necessary to attach the vas directly to the epididymis; this procedure is known as vasoepididymostomy. Both procedures are complex, technically demanding, and expensive; most importantly, there is no guarantee that fertility can be restored. This highlights the importance of carefully screening, counseling, and selecting vasectomy users.

Both macroscopic and microsurgical techniques for vasovasostomy and vasoepididymostomy have been used for vasectomy reversal; the current consensus is that microsurgical techniques are more successful. Reported rates of patency (evaluated by the presence of sperm in the ejaculate) following vasovasostomy range from 74% to 92% for macroscopic reversal and from 75% to 100% for microsurgical reversal. Reported pregnancy rates are lower, however, ranging from 35% to 57% for macroscopic and from 38% to 82% for microsurgical vasovasostomy approaches.[61,62,66,68,69] Vasoepididymostomy is generally less successful than vasovasostomy and while pregnancy rates as high as 42-55% have been reported, most are lower, ranging from 10% to 30%.

Several factors affect the success of vasectomy reversal: the technical demands of the surgery itself; the type of vasectomy procedure performed; the length of time between the vasectomy and the reversal procedure; the levels of antisperm antibodies that may have developed after the vasectomy or the reversal; and changes in the epididymis or partial obstruction of the vas after reversal that prevent sperm from moving through the vas.

The time that has elapsed between vasectomy and reversal is a major factor in the success of reversal: The longer the interval between vasectomy and reversal, the less likely the man is to be fertile after reversal. Reversal is usually more successful when it is done within 10 years of the vasectomy; pregnancy rates drop to less than 50% when vasectomy reversal is performed more than 9-10 years later.

Reports of the effect of antisperm antibodies on fertility following vasectomy reversal vary; some studies have shown decreased pregnancy rates due to antisperm antibodies, while others have not. The consensus is that fertility following vasectomy reversal is inhibited only by high levels of antisperm antibodies.

Partial obstruction of the vas after vasectomy reversal (e.g., because of a sperm granuloma or adhesions from the surgery) has been shown to affect the success of reversal. In these cases, semen quality may be poor in terms of sperm numbers, sperm motility, or both. When partial obstruction is the cause for failure of reversal, repeat vasectomy reversal has produced good pregnancy results.

Assisted reproduction technologies have been successful in vasectomized men who want children but who either do not want to attempt a vasectomy reversal or have had one or more unsuccessful reversal surgeries. Sperm can be retrieved from the epididymis or testis and then used in a procedure known as intracytoplasmic sperm injection (ICSI), in which sperm are injected directly into the ova in a laboratory. Pregnancy rates following ICSI with epididymal sperm are reported to be between 25% and 36%. Pregnancy rates ranging from 17% to 36% have been reported when testicular-sperm are used.

Research continues on methods of vasectomy reversal that produce better success rates. Additionally, new assisted reproduction techniques are also being explored that might be applied in the cases of vasectomized men who are interested in having children. However, there is no guarantee that pregnancy will occur following

vasectomy reversal or use of assisted reproduction techniques, and these procedures are expensive and not widely available-especially in low-resource settings. Thus, vasectomy should be considered a permanent contraceptive method.

Innovations

New methods of vas occlusion are unlikely to become available in the near future, but investigators have explored several alternatives to surgical sterilization in men. Experimental methods of occluding the vas include injecting chemicals into the vas percutaneously (through the skin), to scar the vas closed or physically block the passage of sperm through the vas.

Studies on occluding the vas for contraceptive purposes by injecting chemicals percutaneously began in the 1970s in China. This technique was easily performed and led to high rates of azoospermia and low pregnancy rates, although reversal was no easier than for vasectomy because the occluded portion of the vas needed to be excised and reanastamosis of the vas performed.

Formed-in-place plugs use a liquid material that is injected into the vas and forms a solid plug to block the vas lumen; such plugs have been examined as a method of vas occlusion. A formed-in-place polyurethane plug had low rates of complications, was highly effective, and was easily reversible. However, uncertainty regarding the safety of the polyurethane product led to an investigation of medical-grade silicone plugs. Variable rates of success have been reported for a formed-in-place silicone plug known as Vasoc. Vasoc vas occlusion does not appear to be suitable for use as a male contraceptive at this time. Researchers have also attempted to develop devices that can be placed in the vas to obstruct sperm but then later can be removed or opened to allow sperm to pass. Such devices have had several problems, however; for example, the surgery has been difficult and the devices have not consistently stayed in place within the muscular vas.

In India Phase 3 trials are on using Styrene Malleic Anhydride. This chemical is injected into vas percutaneously or by NSV technique. This is not a plug but stays within the Vas and renders the sperms incapable of fertilization by changing the charge on acrosomal cap. Results are still awaited.

Condoms

"Condoms can be ribbed, flavored, and even glow-in-the-dark, but generally speaking, they're all pretty much the same. Despite the different new materials and available bells and whistles, condoms, which date back to 11,000 BC, haven't evolved much in the last several hundred years." (as quoted from "one medical")

Materials of condoms are likely to undergo a major change particularly with the developments of hydrogel. Galactic cap is another innovation where a cap sticks only to the glans. These may replace the existing condoms in near future.

Hormonal Methods

Research in this area is far ahead and nearly complete at various levels. However, Lack of market support from producing companies and financial support for research are holding this method back.

Hormonal male contraception clinical trials began in the 1970s. The method is based on the use of exogenous testosterone alone or in combination with a progestin to suppress the endogenous production of testosterone and spermatogenesis. Studies using testosterone alone showed that the method was very effective with few adverse effects. Addition of a progestin increases the rate and extent of suppression of spermatogenesis. Common adverse effects include acne, injection site pain, mood change including depression, and changes in libido that are usually mild and rarely lead to discontinuation. Current development includes long-acting injectables and transdermal gels and novel androgens that may have both androgenic and progestational activities. Surveys showed that over 50 % of men will accept a new male method and female partners will trust their partner to take oral "male pills." Partnership between government, nongovernment agencies, academia, and industry may generate adequate interest and collaboration to develop and market the first male hormonal contraception. (Wang et al)

References

1. Li, S.Q.: Vasal sterilization techniques: Teaching material for the National standard Workshop, Chongqing, People's Republic of China: Scientific and technical literature press, p.176, 1988.
2. Li SQ, et al. The no-scalpel vasectomy. Journal of Urology 1991; 145(2): 341-344.
3. AVSC International. 1997. No-scalpel vasectomy: An illustrated guide for surgeons. 2nd edition. New York
4. Sokal DC, et al. A comparative study of the no scalpel and standard incision approaches to vasectomy in 5 countries. The Male Sterilization Investigator Team. Journal of Urology 1999; 162(5): 1621-1625.
5. Nirapathpongpom A, Huber DH, Krieger JN. No-scalpel vasectomy at the King's Birthday vasectomy festival. Lancet 1990; 335(8694): 894-895.
6. Li,P.S., Li,S.Q., Schlegel, P.N. and Goldstein, M.: External spermatic sheath injection for vasal nerve block. Urology, 39: 173,1992
7. Labrecque M, Dufresne C, Barone MA, St-Hilaire K.: Vasectomy surgical techniques: a systematic review. BMC Med. 2004 May 24;2:21
8. Joel LM, Stuart K, Victor H H. A minimal invasive vasectomy with no suture, inline method of vas occlusion. In j Fertil 2001; 46:257-64.
9. Dr. R.C.M. Kaza, "No scalpel vasectomy—an overview," *Journal of the Indian Medical Association*, vol. 104, no. 3, pp. 129–141, 2006.

10. Sokal D, et al. (2001) Vasectomy with fascial interposition vs. ligation and excision alone: A randomized controlled trial. Presentation at the annual meeting of the Association of Reproductive Health Professionals, December 12-15, Washington, DC.
11. Kendrick JS, et al. Complications of vasectomies in the United States. Journal of Family Practice 1987; 25(3): 245-248.
12. Healy B. From the National Institutes of Health: Does vasectomy cause prostatecancer? Journal of the American Medical Association 1993; 269(20): 2620
13. Belker AM. Evaluation of partial anastomotic obstruction after vasovasostomy and predictors of success after vasoepididymostomy. Journal of Urology 1998; 159(3): 835-836.
14. Silber SJ. Results of microsurgical vasoepididymostomy: Role of epididymis in spermmaturation. Human Reproduction 1989; 4(3): 298-303.
15. Dohle GR, et al. Surgical sperm retrieval and intracytoplasmic sperm injection as treatment of obstructive azoospermia. Human Reproduction 1998; 13(3): 620-623.
16. Abuzeid ML, Sasy MA, Salem H. Testicular sperm extraction and intracytoplasmic sperm injection: A simplified method for treatment of obstructive azoospermia. Fertility and Sterility 1997; 68(2): 328-333.
17. Zhao SC. Vas deferens occlusion by percutaneous injection of polyurethane elastomer plugs: Clinical experience and reversibility. Contraception 1990; 41(5): 453--459.
18. Soebadi DM, Gardjito W, Meurik HJ. Intravasal injection of formed-in-place medical grade silicone rubber for vas occlusion. International Journal of Andrology 1995; 18 (Suppl. 1): 45-52.
19. Herrel L, Hsiao W, Microsurgical vasovasostomy, Asian Journal of Andrology 15 (1)44-8 2013
20. Grace shih, Merlin Njoya, Marylene Lessard, Michel Labrecque, Minimizing Pain During Vasectomy: The Mini-Needle Anesthetic Technique J.urol183, 1959-1963, 2010.
21. Christina Wang, Mario P.R. Festn etal. Male Contraception Where are we now. Curr obstet Gynecol Rep 2016;5:38-47

CONTROVERSY

Contraception in Adolescent

Shakuntla Kumar
Sr. Consultant & MD, Nulife Hospital and Fortis Hospital


Dr Shakuntla Kumar

WHO defines 'Adolescents' as individuals in the 10-19 years age group and 'Youth' as the 15-24 year age group. While 'Young People' covers the age range 10-24 years. This is the time when young people start experiencing sexual feelings and many start developing sexual relationships also. About 30% of India's population is in the age group of 10-19 years. NFHS-3 data shows that over 19.7 million Indians aged 15–19 are currently sexually active – they are either unmarried, married or living together.

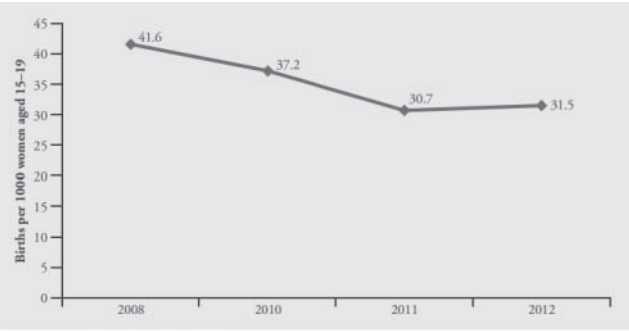


Figure: Trends in adolescent fertility rate, 2008-2012

Adolescents are likely to face a range of health and social challenges. For instance, initiation of sexual activity while they lack adequate knowledge and skills for protection places adolescents at a higher risk of unwanted pregnancy, unsafe abortion and sexually transmitted infections including HIV/AIDS. High prevalence of early marriage and childbearing in some states, is associated with higher maternal mortality and morbidity as well as neonatal and infant mortality in adolescents. Pregnancy during adolescence is associated with higher risk of health problems like anemia, sexually transmitted infections, unsafe abortion, postpartum haemorrhage, and mental disorders (like depression). Pregnant adolescents also bear negative social consequences and often have to leave school reducing their employability leading to long-term economic implications.

Unmet needs for family planning especially for spacing are high among adolescents. There are 39 000 child marriages every day. More than 140 million girls will marry between 2011 and 2020. About 1 million girls under 15 give birth every year—most in low- and middle-income countries. Every year, some 3 million girls aged 15 to 19 undergo unsafe abortions.

For many adolescents who need sexual and reproductive health services, such as appropriate information, contraception and treatment for sexually transmitted infections, these are either not available or are provided in a way that makes adolescents feel unwelcome and embarrassed. Hence, there is a need for Adolescent Friendly Health Services to address these issues and make it easier for adolescents to obtain the required services. There is an urgent need to implement programmes that both meet the contraceptive needs of adolescents and remove barriers to services.

With only 7 per cent of 15-19-yearolds using contraceptives as per the NFHS 3, the unmet need for family planning is higher among them at 27% compared to 13% unmet need across all age groups. With increasing awareness, contraceptive use has increased in adolescents, especially in western world, but they rarely use the most effective methods. Adolescents mostly use contraceptive methods with high typical use failure rate like condoms, withdrawal or oral pills.

Table 1: Lifetime Use (Ever-Use) of Contraception Among Sexually Experienced Women Aged 15 to 19 Years: United States, 2006 to 2010

Method	% Distribution
Any method	98.9
Injectable	20.3
Pill	55.6
Contraception patch	10.3
Contraception ring	5.2
Emergency contraception	13.7
Condom	95.8
Female condom	1.5
Periodic abstinence-calender	15.0
Withdrawal	57.3
Other methods	7.1
Long-acting reversible contraceptives (IUDs and implants)	4.5

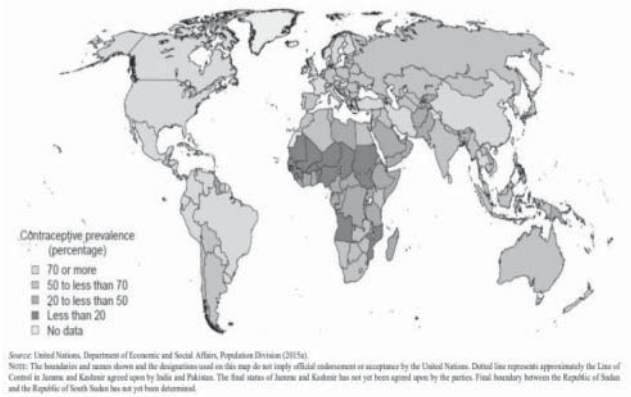


Figure: Percentage of women using any method of contraception among those aged 15 ti 49 who are married or in a union, 2015

Counselling Adolescents for contraception

The American College of Obstetricians and Gynecologists (ACOG) makes the following recommendations and conclusions:

- Regardless of a patient's age or previous sexual activity, the obstetrician–gynecologist routinely should address her contraceptive needs, expectations, and concerns.
- Statutes on the rights of minors to consent to health care services vary by state, and obstetrician–gynaecologists should be familiar with the regulations that apply to their practice.
- Emergency contraception routinely should be included in discussions about contraception, including access issues. The American College of Obstetricians and Gynecologists recommends that obstetrician–gynaecologists write advance prescriptions for oral emergency contraception for their patients.
- Long-acting reversible contraceptive (LARC) methods have higher efficacy, higher continuation rates, and higher satisfaction rates compared with short-acting contraceptives. Because LARC methods are safe, they are excellent contraceptive choices for adolescents.
- Discussions about contraception should begin with information on the most effective methods first.
- Obstetrician–gynaecologists should be aware of and be prepared to address the most common misperceptions about contraceptive methods in a way that is age appropriate and compatible with the patient's health literacy.
- The initial encounter and follow-up visits should include continual reassessment of sexual concerns, behaviour, relationships, prevention strategies, and testing and treatment for sexually transmitted infections (STIs) per the Centres for Disease Control and Prevention's (CDC) guidelines.

Methods of Contraception

Adolescents are eligible to use all the same methods of contraception as adults, and must have access to a variety of contraceptive choices. Age alone does not constitute a medical reason for denying any method to adolescents. While some concerns have been expressed about the use of certain contraceptive methods by adolescents (e.g. the use of progestogen-only injectables by those below 18 years), these concerns must be balanced against the advantages of preventing unintended pregnancy. It is clear that many of the same eligibility criteria that apply to older clients also apply to young people.

Social and behavioural issues should be key considerations in the choice of contraceptive methods by adolescents. For example, in some settings, adolescents are also at increased risk for STIs, including HIV. While adolescents may choose to use any one of the contraceptive methods available in their communities, in some cases, using methods that do not require a daily regimen may be more convenient.

Whether married or unmarried, all adolescents have also been shown to be less tolerant of side-effects and therefore have high discontinuation rates. Method choice may also be influenced by factors such as sporadic patterns of intercourse and the need to conceal sexual activity and contraceptive use. For instance, sexually active adolescents who are unmarried have very different needs from those who are married and want to postpone, space or limit pregnancy. Expanding the number of method choices offered can lead to improved satisfaction, increased acceptance and increased prevalence of contraceptive use. Proper education and counselling – both before and at the time of method selection – can help adolescents address their particular needs and make informed and voluntary decisions. Every effort should be made to prevent the costs of services and/or methods from limiting the options available.

Importance of Confidentiality and Consent

Careful attention to minor consent and confidentiality are important, because confidentiality is a major concern of adolescents and a reason for foregoing contraceptive care.

Contraceptive Methods for Adolescents

Long-acting reversible contraception (LARC)

Long-acting reversible contraceptives (LARC) provide effective contraception for an extended period without requiring user action. They include intrauterine devices (IUDs) and subdermal contraceptive implants. Intrauterine devices are safe for adolescents, with very low rates of complications such as pelvic inflammatory disease (PID) or uterine perforation. LARC is the most effective type of reversible birth control (Failure rates < 1% in first year). LARC is safe, not user dependent, does not impact future fertility, does not require frequent use and depending on the method, can be used to prevent pregnancy for three to 10 years. American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Paediatrics (AAP), have endorsed LARC as a first-line contraceptive choice for teens. When proactively counselled, adolescents are more likely to choose IUD or implant as their method of contraception. It is especially useful immediate post-partum and post abortion and has a high continuation rate.

Most common side effect with LARC usage is irregular bleeding. All LARC methods may affect menstrual patterns in different ways. Clinical trials involving the copper IUD indicate that abnormal heavy bleeding may occur in 10% of cases which may decrease to 5% after 8 months or more of use. Clinical trials involving

the 5-year 52-mg LNG-IUS indicate that bleeding decreases over time, with as many as 70% of users developing amenorrhea or oligomenorrhea. Despite side effects, continuation for LARC methods is high. In the Contraceptive CHOICE study, the continuation at 24 months for the 52-mg LNG-IUD, the CuT380A, and the ENG implant specifically in adolescents 14 to 19 years of age, was 67% compared with 37% for non-LARC methods.

Summary of Recommendations based on levels of evidence:

Level A recommendations:

Insertion of IUD immediately after first trimester uterine aspiration is safe and effective option and should be offered routinely to patients.

Similarly, patient can be safely offered contraceptive implant on the same day as first-trimester or second-trimester induced or spontaneous abortion.

Routine antibiotic prophylaxis is not advised before IUD insertion.

Level B recommendations:

IUDs and contraceptive implants are not contraindicated in nulliparous women and adolescents, and carry the same safety and efficacy as in multiparous women. US MEC Category 2, (advantages outweigh the risks).

Level C recommendations

LARCs are suitable, safe and effective, have few contraindications and should be routinely recommended to most women.

The copper containing IUD is the preferred choice for emergency contraception in women who are eligible for IUD insertion.

All patients receiving LARC should undergo adequate counselling and reassurance about irregular bleeding pattern and be assured that it is harmless.

Endometrial biopsy, endocervical sampling, colposcopy, and cervical ablation or excision may all be performed with an IUD in place.

In case of accidental pregnancy with the device in place, it can be safely removed if the strings are visible.

If a woman attains menopause while IUD or implant in place, it is not necessary to remove it before its expiration date.

Actinomyces detected on cell cytology is an incidental finding, and does not warrant the removal of IUD or antimicrobial treatment in absence of symptoms

Myths and facts about LARC

MYTH: Adolescents and nulliparous women are not appropriate candidates for IUDs.

FACT: Adolescents and nulliparous women can be offered LARC methods, including IUDs. The U.S. Medical Eligibility Criteria for Contraceptive Use, classifies both women who haven't had children and adolescents as Category 2, finding the advantages generally outweigh the risks. IUDs and implants have the highest efficacy, continuation rates, and user satisfaction of all reversible methods.

MYTH: IUDs cause infertility.

FACT: IUDs do NOT cause infertility or make it harder to conceive in the future. Infertility is no more likely after discontinuation of IUD use than after discontinuation of other reversible methods of contraception. Ample research shows that today's IUDs do not increase STI infection rates or lead to infertility. STI testing should be performed at the time of IUD insertion, if indicated. However, all women, including those using IUDs, should see a health care provider if they have new or unusual vaginal discharge or pelvic pain.

MYTH: IUDs cause ectopic pregnancy.

FACT: The IUD does not cause ectopic pregnancy. Since the chance of becoming pregnant while using an IUD is so low, the overall risk of having an ectopic pregnancy is greatly reduced while using an IUD as compared to not using any contraceptive method.

MYTH: If a woman using an IUD develops an STI or pelvic inflammatory disease (PID), the IUD should be removed immediately.

FACT: If a woman using an IUD develops an STI or PID she should be treated with antibiotics right away and can keep the device in place if her symptoms improve within 72 hours (3 days). If the symptoms do not improve within that time, the device should be removed.

MYTH: IUD insertion may be technically more difficult in adolescents and nulliparous women

FACT: Little evidence is available regarding technical difficulty and moderate to severe pain with insertion can be managed by proper counselling and analgesia.

MYTH: IUD expulsion is less common in adolescents

FACTS: Limited data available suggests that expulsion, which occurs in fewer than 5% of women using IUDs, may occur more frequently in younger women (5-22%). Prior expulsion is not considered a contraindication for another IUD insertion.

Implant

Etonogestrel Implant (Implanon) is approved by US FDA and is effective for 3 years. Pregnancy must be excluded before insertion. Most common side effects are irregular bleeding and weight gain. In clinical trials, 12% of women reported weight gain and 2.3% discontinued for this reason. However, in an analysis from CHOICE project, although mean weight gain in the first year was 2 kg, when controlling for potential confounders, this gain was not statistically significant compared with

the copper IUD. Contraindications for ENG implant are based on the hormonal content and include diseases uncommon in the adolescent population, such as breast or endometrial cancer and severe liver cirrhosis.

Intermediate acting

Depo-Provera

Depo-Provera, or 150 mg of depot medroxyprogesterone acetate (DMPA) administered intramuscularly, is becoming increasingly popular in the adolescent population. Advantages include lack of a need for daily compliance and privacy. However, it is still user-dependent in that it requires the patient to return to a health care professional's clinic for repeat injections every 12 weeks to ensure contraceptive efficacy. Although recommended dosing is every 3 months, its mechanism of action is suppression of ovulation, which does not occur for at least 14 weeks after the standard 150-mg injection.

Menstrual cycle irregularities provoke the most concern and may be the most common reason for premature discontinuation of DMPA. Irregular bleeding and/or spotting occurs in as many as 25% to 50% of users in the first 6 to 12 months after initiation. Over time, however, this excessive vaginal bleeding may be circumvented by the administration of the usual 150-mg dose on a monthly basis during the first 3 months after initiation; by decreasing menstrual blood loss, compliance is increased. Alternatively, when persistent bleeding or spotting threatens to cause discontinuation, estrogen supplementation (*e.g.* 1.25 mg conjugated estrogen daily or its equivalent) usually reduces or eliminates any bleeding.

Most DMPA users become amenorrheic. Most teenagers find this to be a positive aspect of the drug, and the sooner oligomenorrhea or amenorrhea can be achieved, continuation rates improve by more than 50%. In patients with amenorrhea who present for reinjection more than 14 weeks after their previous dose, pregnancy should be excluded before the next dose is administered.

DMPA offers a unique advantage in certain handicapped adolescent patients, particularly those with seizure disorders. In addition to the advantages of oligomenorrhea or amenorrhea injectable medroxyprogesterone acetate has been shown to result in an increase in seizure threshold, thus resulting in a lowered seizure frequency. DMPA also provides improved contraceptive efficacy compared with estrogen-containing oral contraceptives in patients also taking antiseizure medications that induce hepatic enzymes, notably phenobarbital, phenytoin, and carbamazepine. Increased hepatic metabolism of the estrogen in oral contraceptives in these cases can lead to an increased failure rate. Reliable contraception is also particularly important in sociologically disadvantaged patients such as these, who may be partially or wholly institutionalized and hence at risk for sexual assault (molestation). Thus, the use of a method such as DMPA in these patients may have multiple benefits.

Misconceptions with DMPA usage:

a) **Risk of decrease bone mineral density**. Most studies have found that women lose bone mineral density (BMD) during DMPA use, but recover BMD after discontinuation. There is a concern whether adolescents can reach peak bone mass after discontinuation of DMPA. The relationship between these changes in BMD during the reproductive years and future fracture risk is unknown. The ACOG Committee on Adolescent Health and Association of Reproductive Health Professionals state that concerns about bone loss should not limit the use of DMPA in adolescents. They should follow age-appropriate recommendations for calcium and vitamin D supplementation. Estrogen supplementation, dual-energy x-ray absorptiometry scans should only be advised in girls who have osteopenia or are at increased risk of osteoporosis, and discontinuation at 2 years is not required.

b) **Weight gain**: All contraceptive options are considered safe in overweight and obese adolescents (category 1 or 2). Depot medroxyprogesterone acetate is a WHO MEC category 2 in obese adolescents. Although obesity does not seem to affect efficacy, further weight gain is a concern. Adolescents interested in DMPA should be counselled about possible weight gain. Studies in both adolescents and adults suggest that weight gain status at 6 months is a strong predictor of future excessive weight gain with ongoing DMPA use

Short-acting hormonal methods

Combined hormonal contraceptives contain both estrogen and a progestin and include 1) COCs (various formulations), 2) a transdermal contraceptive patch Ortho Evra (which releases 150 μg of norelgestromin and 20 μg ethinyl estradiol daily), 3) a vaginal contraceptive ring Nuva Ring (which releases 120 μg etonogestrel and 15 μg ethinyl estradiol daily) and 4) progestogen only pills. These methods are reversible and can be used by women of all ages. Combined hormonal contraceptives are generally used for 21–24 consecutive days, followed by 4–7 hormone-free days (either no use or placebo pills). These methods are sometimes used for an extended period with infrequent or no hormone-free days. Combined hormonal contraceptives do not protect against STDs.

Combined OCPs The combined pill is the most commonly used method in this group with the usage rate reaching up to 50% because it is safe, predictable, ensures regular and pain free menses, convenient, and privacy can be maintained. A wide range of options are available and all the brands are almost equally effective and any one can be used conveniently.

Types of pills

Standard pills with etinylestradiol (30 microgram) and levonorgestrel given for 21 days in a 28 days cycle is most commonly used. Pills with newer progestogens like desogestrel and cyproterone acetate can be given in polycystic ovarian disease and hirsutism.

Extended cycle pills given for 84 days are useful in adolescents with anemia, endometriosis and abnormal uterine bleeding. There are many advantages of combined hormonal methods including improved acne, regulation of menstrual blood flow and cyclicity, treatment of dysmenorrhea, improved premenstrual symptoms, reduced risk for ectopic pregnancy and pelvic inflammatory disease, as well as reduced risk for ovarian and endometrial cancer, benign breast disease and iron deficiency anemia. Unfortunately, despite the wide use of OCPs, adolescents have failure rates as high as 15% in the first year of use because of missed pill. Such cases may need more motivation and can be advised quick start method i.e. initiation of the contraceptive method at any day of cycle with a backup of 7 days when desired.

Nuva Ring

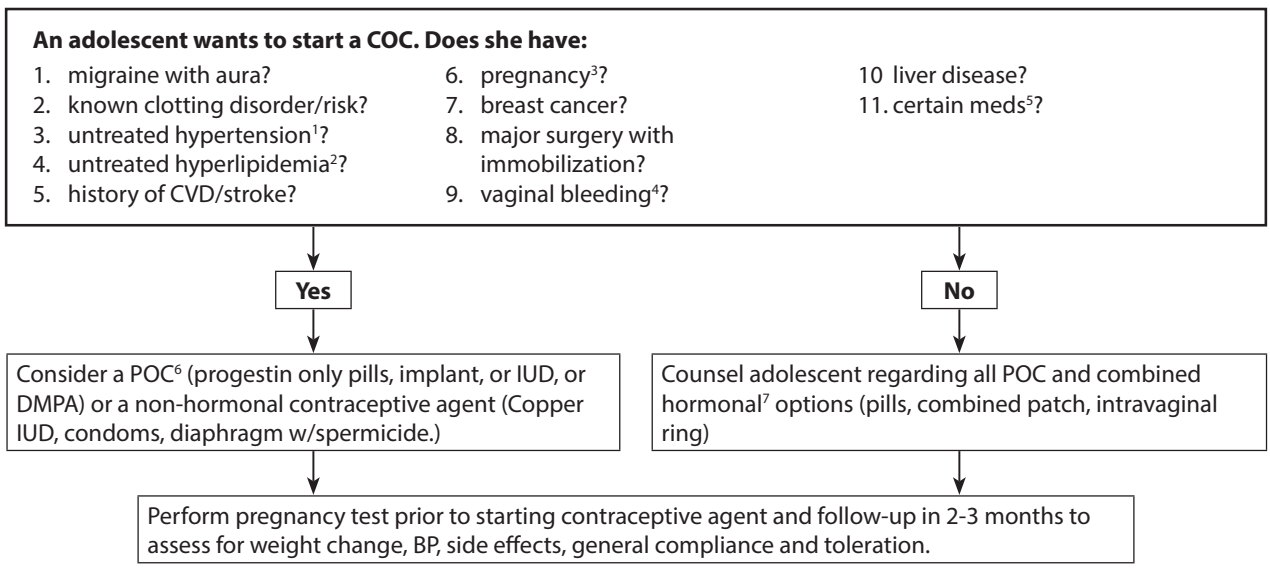
It is a contraceptive ring containing ethinyl estradiol and etonorgestrel. Failure rate is <1% as there is high compliance with minimal side effects like discharge, discomfort or device related problems.

Ortho Evra patch

It is a weekly patch containing etinylestradiol and norelgestromin, with less side effects. The compliance is also high because of easy and less frequent administration and less side effects.

Progestin-only pills

Progestin-only pills, work primarily by thickening cervical mucus, and the newer progestogen desogestrel also inhibits ovulation. The advantage is it avoids estrogen related side effects and especially useful in conditions where estrogens are contraindicated. Disadvantages include a higher failure rate as stringent adherence to timing of dose is necessary. If pill intake is delayed



[1]Consider combined hormonal agent use in adolescents with well controlled hypertension, but cely with close monitoring of BP, POCs preferred.
[2]Consider combined hormonal agent use in adolescents with well controlled hyperlipidemia, but only with close monitoring of lipids POCs preferred.
[3]Clearly if the patient is pregnant, cely borrier methods are recommended to prevent the acquisition of sexually transmitted infections.
[4]Abnormal vaginal bleeding should be evaluated before starting a combined hormonal agent or POC.
[5]Combined hormonal agent efficacy may be reduced with certain HIV medication,
[6]Side effects for POCs vary depending on agent, but irregular bleeding is common. DMPA has been associated with weight gain, acne, hair lose, mood changes and bone loss during use
[7]Side effects from combined hormonal agents include nausen, appetite change, headache, mood change, breast tenderness, irregular bleeding.

From: Approach to the Adolescent Requesting Contraception
J Clin Endocrinol Metab. 2012; 97(1):9-15. doi:10.1210/jc.2011-1780

by more than 12 hours, this increases failure rate and requires back up method. Breakthrough bleeding is a common problem that can lead to non - compliance. Therefore POPs are not considered good choice for adolescent girls.

Some practical issues regarding hormonal contraception are discussed below:

a) Is it necessary to do a speculum or bimanual examination before initiating oral contraceptive pill?

Bimanual examination with cervical inspection is not needed before initiation of COCs or the contraceptive patch or the vaginal ring. ACOG recommends that sexually active adolescents have their first Papanicolaou test at the age of 21 years. Before that examination, STI testing, if needed, can be done by urine testing or vaginal swab without a speculum examination. Further examinations are necessary only if the adolescent has a specific complaint or concern.

b) Should adolescents who smoke be prescribed combined hormonal methods? Although all adolescents who smoke should be encouraged to quit, smoking does not impact their contraception choices. The WHO MEC gives a category of 2 for all combined hormonal use with any quantity of smoking younger than 35 years.

c) Should COC be prescribed in adolescent with migraine/headache ?

If a diagnosis of migraine with aura is established, the adolescent is not a candidate for estrogen containing birth control methods (MEC category 4). If a woman younger than 35 years has migraine without aura, initiation of estrogen-containing methods is MEC category 2.

d) Should COC be prescribed to adolescents with history of DVT?

Adolescent females with a personal history of deep vein thrombosis (DVT) or pulmonary embolism (PE) are not candidates for estrogen-containing methods (MEC category 3 or 4 depending on risk for recurrence), nor are women with a known thrombogenic mutation (MEC category 4). For these women, it is essential to get a detailed history of the event or even medical records because many adolescents may not be sure of the diagnosis. Low dose (less than 50 mcg of ethinyl estradiol) oral contraceptives pose less risk than older, higher dose formulations. Cigarette smoking increases the risk of DVT in women using combination contraceptives, particularly who smoke more than 15 cigarettes per day.

e) Do hormonal contraceptives increase risk of fractures in adolescents?

Evidence about whether CHC use affects fracture risk is inconsistent, although recent studies show no effect. CHC use may decrease bone mineral density (BMD) in adolescents, especially in those choosing very low dose formulations.

f) Do hormonal contraceptives in adolescents increase risk of breast cancer later in life?

A 1996 analysis of epidemiologic data from more than 50 studies worldwide by the Collaborative Group on Hormonal Factors in Breast Cancer found that women who were current or recent users of birth control pills had a slightly higher risk of developing breast cancer than women who had never used the pill. The risk was highest for women who started using oral contraceptives as teenagers. However, 10 or more years after women stopped using oral contraceptives, their risk of developing breast cancer had returned to the same level as non-users, regardless of family history of breast cancer, reproductive history, geographic area of residence, ethnic background, differences in study design, dose and type of hormone(s) used, or duration of use. In addition, breast cancers diagnosed in women who had stopped using oral contraceptives for 10 or more years were less advanced than breast cancers diagnosed in women who had never used oral contraceptives. Recent study suggested that use of combined oral contraceptives is associated with an increased breast cancer risk, which may vary by formulation. Estrogen is the driver in breast cancer pathogenesis and estradiol is the most likely estrogen implicated. Role of progesterone is uncertain, mitotic activity in breast tissue does increase in luteal phase and progesterone may be responsible. The risk is maximum before a full-term delivery as estrogens act more on less differentiated tissue.

g) Do oral contraceptives increase cervical cancer risk?

Report by the International Agency for Research on Cancer found threefold increase in cervical cancer risk among human papillomavirus infected women who had used oral contraceptives for 5 to 9 years compared with non-users. Oral contraceptives used for 10 years or longer increased risk to four times. Virtually all cervical cancers are caused by persistent infection with oncogenic HPV, and the association of cervical cancer with oral contraceptive use is likely to be indirect.

h) Do oral contraceptives increase liver cancer risk?

Oral contraceptive use is associated with an increase in the risk of benign liver tumors, such as hepatocellular adenomas. However, association with malignant hepatocellular carcinoma is less clear with studies reporting contradictory findings.

i) Do oral contraceptives increase risk of all genital malignancies?

Oral contraceptive use has consistently been found to be associated with a reduced risk of ovarian cancer and endometrial cancer. The risk reduction is higher with longer duration of use and protection continues even after stopping the pills. The risk decreases by 10 to 12 percent after 1 year of use and by approximately 50 percent after 5 years of use. The Cancer and Steroid Hormone (CASH) study has indicated that oral contraceptive formulations with

high levels of progestin were associated with a lower risk of ovarian cancer than formulations with low progestin levels. Steroid Hormones and Reproduction (SHARE) Study found no difference in ovarian cancer risk between androgenic and nonandrogenic pills.

Barrier methods

Male condom

This is the most common contraceptive method used by adolescents with advantage of being easily available, male involvement and protection from various sexually transmitted diseases. But with the typical use failure rate is 18% for all users and still higher among adolescents, this is not an ideal method for contraception. This is the best method for protection against STI's.

Female Condom

The female condom is the only women-controlled device that protects against both unintended pregnancy and STDs, including HIV. It is a polyurethane sheath that is inserted into the vagina, with a flexible internal plastic ring that holds the top of the sheath near the apex of the vaginal vault. The sheath extends to partially cover the external genitalia. Effectiveness rates approach 97%. Disadvantages include its somewhat unusual appearance and the slight crackling sounds heard during coitus when used without a lubricant (now included in the packaging), both of which may be more discouraging to the adolescent than to the older patient. However, to highly motivate female adolescents, particularly those with a latex allergy or a less-than-fully-cooperative partner, it remains a viable alternative.

Emergency Contraception

Emergency contraception consists of methods that can be used by women after sexual intercourse to prevent pregnancy. Emergency contraception methods have vary in their ranges of effecacy depending on the method and timing of administration. Four options are available: the Cu-IUD and three types of ECPs.

Types of Emergency Contraception

Intrauterine Device

- Cu-IUD

ECPs

- Ulipristal Acetate in a single dose (30 mg)
- Levonorgestrel in a single dose (1.5 mg) or as a split dose (1 dose of 0.75 mg of levonorgestrel followed by a second dose of 0.75 mg of levonorgestrel 12 hours later)
- Combined estrogen and progestin in 2 doses (Yuzpe regimen: 1 dose of 100 μg of ethinyl estradiol plus 0.50 mg of levonorgestrel followed by a second dose of 100 μg of ethinyl estradiol plus 0.50 mg of levonorgestrel 12 hours later).

Cu-IUDs are highly effective as emergency contraception and can be continued as regular contraception. UPA and levonorgestrel ECPs have similar effectiveness when taken within 3 days after unprotected sexual intercourse; however, UPA has been shown to be more effective than the levonorgestrel formulation 3–5 days after unprotected sexual intercourse. The combined estrogen and progestin regimen is less effective than UPA or levonorgestrel and also is associated with more frequent occurrence of side effects (nausea and vomiting). The levonorgestrel formulation might be less effective than UPA among obese women.

Two studies of UPA use found consistent decreases in pregnancy rates when administered within 120 hours of unprotected sexual intercourse. Five studies found that the levonorgestrel and combined regimens decreased risk for pregnancy through the fifth day after unprotected sexual intercourse; however, rates of pregnancy were slightly higher when ECPs were taken after 3 days. A meta-analysis of levonorgestrel ECPs found that pregnancy rates were low when administered within 4 days after unprotected sexual intercourse but increased at 4–5 days (Level of evidence: I to II-2, good to poor, direct).

Conclusions

LARC methods are now considered as first choice for adolescent contraception. Dual protection i.e. use of barrier contraception along with some other form like hormonal method or intrauterine device is ideal as it also provides protection against STI's. However, it is utmost important to counsel the adolescents regarding contraception and encourage sexual abstinence.

Suggested Reading

1. Census of India 2011
2. American Academy of Pediatrics. POLICY STATEMENT: Contraception for Adolescents, Pediatrics 2014. Available at: www.pediatrics.org/cgi/doi/10.1542/peds.2014-2299. Acessed on 5th April 2017.
3. World health Organization. Medical eligibility criteria for contraceptive use 5th Edition, 2015. Available at www.who.org. Accessed on 9th April 2017.
4. American College of Obstetricians and Gynecologists Committee Opinion number 710, August 2017.
5. Trends in contraceptive use worldwide, 2015
6. Ob/Gyn Updated: ACOG updates its guidelines on LARC https://obgynupdated.blogspot.com/**2017**/10/acog-updates-its...
7. Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected Practice Recommendations for Contraceptive Use, 2016. MMWR Recomm Rep 2016; 65(No. RR-4):1–66.
8. Approach to the Adolescent Requesting Contraception J Clin Endocrinol Metab. 2012; 97(1):9-15. doi:10.1210/jc.2011-1780
9. Slupik, R, *Glob. libr. women's med., (ISSN: 1756-2228)* 2008; DOI 10.3843/GLOWM.10377

CASE APPROACH

Contraception in Obese

Swati Agrawal[1], Nihita Pandey[2]

[1]Associate Professor, [2]Senior Resident, Department of Obstetrics & Gynaecology, LHMC & SSK Hospital, New Delhi

Dr Swati Agrawal

Background

Obesity is quickly turning into a modern epidemic affecting over 300 million obese women worldwide.[1]

It has been proven that obese women are less likely to use contraception than women with normal BMI.[2] One of the main reasons may be the fear of hormones contributing to weight gain. However, evidence suggests that weight gain associated with most of the contraceptives is age-related and not attributable to contraceptive usage. A Cochrane review showed that there is no effect of combined hormonal contraception on weight gain.[3] Another Cochrane review has found small changes in weight associated with progestin-only methods such as Depot- Medroxyprogesterone (DMPA), Norplant and the levonorgestrel intrauterine device (LNG-IUD).[4]

Unintended pregnancies in obese women are a matter of great concern as they are associated with increased risk of fetomaternal complications.[5] The incidence of gestational hypertension, preeclampsia, gestational diabetes and cesarean section is increased in these patients. The fetus is at a higher risk of developing congenital malformations, macrosomia and stillbirths in addition to long term sequelae of childhood obesity and type 2 diabetes.

Thus, it is imperative for clinicians to effectively counsel and advise these patients regarding contraceptive methods to reduce future obstetrical complications.

Contraceptive options in obese

Obese women are prone to co-morbidities like hypertension, hypercholesterolemia and diabetes which makes them vulnerable to side effects and complications of contraceptives such as venous thromboembolism (VTE). It is unfortunate that most of the research regarding contraceptive efficacy has excluded women above 130% of ideal body weight, making it difficult to make any definitive conclusions in these women. The various contraceptive options with their pros and cons are discussed below:

Oral contraceptives (OCs)

Several studies have shown oral contraceptives to be less effective in obese women as compared to normal weight women because of dilution of the drug in larger blood volume and fat mass and inadequate suppression of the hypothalamic pituitary axis.[6] The altered clearance of hormones in OCs results in higher levels of FSH & LH in these patients which can allow ovulation to occur with low dose combined oral contraceptives (COCs) or missed pills. The window of contraceptive safety is even narrower with progestin only pills (POPs) as compared to COCs and they have slightly lower efficacy than the COCs even with perfect use.

The results of a recent Cochrane review suggest that women with a BMI > 25 Kg/m^2 are significantly more likely to conceive on oral contraceptives.[7] However, some studies have concluded that there is no overall difference in failure rates according to BMI and body weight.[8] This conflicting data calls for more prospective clinical trials to establish the contraceptive efficacy of OCs in obese women.

The propensity of estrogen-containing contraceptives to increase the incidence of deep venous thrombosis (DVT) is well established and obesity significantly increases this risk.[9] However, the absolute risk of venous thromboembolism with COCs is quite small and the additional risk of obesity is still less than the risk of VTE that pregnancy and postpartum period poses in an obese woman.[10] POPs may be a safer alternative for obese women at risk for thromboembolism and cardiovascular disease.

Considering the doubtful suboptimal efficacy and increased risk of VTE, the authors conclude that OCs should be offered to obese women only when other contraceptive options are either unavailable or unacceptable.

Contraceptive Vaginal Ring

The contraceptive vaginal ring (CVR) contains 15 mcg EE and 120 mcg etonogestrel . The CVR is inserted into the vagina by the user and remains in place for 21 days; it is then removed for 7 days to allow for withdrawal bleeding. Women who use the CVR are exposed to lower doses of EE, but the exposure is more stable and precise. A prospective clinical trial compared 31 overweight or obese women who used COC to 34 similar women who used the CVR. The study concluded that the COC group had greater insulin resistance than the CVR group.[11] The efficacy of the CVR was found to be similar to the COC; its failure rate is 0.3% with perfect use and 9% with typical use.[12] The CVR may thus be used as a preferred method for obese women since it exposes them to lower doses of EE, has fewer side effects related to insulin sensitivity and thrombosis, and is not affected by body weight. However, the CVR may be more difficult for obese women to insert and remove correctly.

Transdermal patch

The transdermal patch contains 0.75mg EE and 6 mg norelgestromin over a contact surface of 20cm^2. One fresh patch is placed by the user weekly for 3 weeks anywhere on the body except the breasts, followed by 1-week patch-free period to allow for withdrawal bleeding.

Obesity has been shown to reduce the effectiveness of the patch especially in women weighing more than 90Kg.[13] Also a systematic review revealed that the patch produces more side effects than the COC or CVR.[14] The risk of DVT and pulmonary embolism (PE) is also increased significantly in patch users as compared to COC users. Thus transdermal patch does not seem to be a good contraceptive option for obese women.

Depot-medroxyprogesterone acetate(DMPA) injection

DMPA comes in intramuscular injection (IM) and subcutaneous (SQ) forms. Injectable MPA intramuscular preparation has been recently added to the contraceptive basket by the Government of India under the "Antara" program. The dose for injectable DMPA is 150 mg/1 mL IM every 3 months and that for SQ DMPA is 104/0.65 mL, also given every 3 months. Both are thought to be as effective in obese women as in normal weight women.[15]

However, the use of DMPA is associated with side effects such as bone loss and weight gain. Several systematic reviews have suggested that bone loss is associated with IM DMPA but is reversible once women no longer receive it.[16] Adequate intake of calcium and vitamin D is therefore recommended for women receiving DMPA. Studies have also shown that DMPA users gain on an average 4.4 kg in 2 years and 5.1 kg in 3 years.[17] This can be a significant deterrent for girls or women already overweight or obese. In addition, DMPA users also have an increase in visceral fat, which is most metabolically active in promoting dyslipidemia. These findings suggest that DMPA recipients should be monitored for BMI after 6 month and regularly thereafter and should receive appropriate health counselling related to exercise and nutrition.

Implant

The commercially available implant contains a single-rod device containing 68 mg of etonogestrel which is effective for 3 years. Studies have found the plasma levels of etonogestrel to be lower in obese women than in normal weight women but this was not shown to affect the contraceptive efficacy as the serum levels were maintained above the minimum amount needed to prevent ovulation.[18]

Intrauterine device(IUD)

IUDs have not been found to alter weight in women hence, they can be a good contraceptive choice for obese women, especially those who wish to avoid estrogen-related side effects. The LNG-releasing IUD is especially a good option as the progestin prevents endometrium hyperplasia which may result from long-term exposure to excess estrogen related to obesity. The only concern in obese women is the difficulty of insertion of IUD. Obesity can make the determination of the size and direction of the uterus and complete visualization of the cervix more difficult in these women. Modifications such as the use of ultrasound, longer instruments and insertion by a skilled practitioner are proven to be helpful.[19]

Centchroman

Centchroman (INN: Ormeloxifene) synthesized at the Central Drug Research Institute, Lucknow, is a nonsteroidal once-a-week oral contraceptive. It is being marketed in India since 1992 as "Saheli" and has been included in the contraceptive basket by the Government of India in 2017 under the name "Chhaya". It has an excellent therapeutic index and is considered safe for chronic administration.[20] It has an added benefit of being effective in certain hormone-related disorders (such as Abnormal Uterine Bleeding). Hence it is safe to infer that it can be used effectively in obese women without much concern about the side effects. Prospective control trials which study the efficacy of this drug in the subset of obese women need to be undertaken before any definitive conclusions.

Emergency Contraception

Ulipristal acetate(UPA) has been found to be superior to Levonorgestrel (LNG) in providing emergency contraception to women with a BMI > 25 Kg/m^2.[21] However, insertion of IUD still remains the most effective mean of emergency contraception in normal and overweight women alike.

Sterilization

An increased complication rate, both surgical and anaesthetic, was found in obese women with interval laparoscopic tubal ligation in a Cochrane review.[22] Sterilization of male partners should be offered to all obese women who have completed their families as it is a highly effective method with negligible complication rate.

Contraception after Bariatric Surgery

It is estimated that approximately 50% of all bariatric surgeries are done in women of reproductive age group. The American College of Obstetricians and Gynaecologists (ACOG) recommends postponing pregnancy for at least 12-18 months to avoid the risk of malnourishment to the fetus due to sudden weight loss following bariatric surgery.[23]

There may be an increase in fertility post-surgery due to restoration of ovulatory function secondary to weight loss. The above fact coupled with the change in body image may lead to increased rates of unintended

pregnancies, making contraceptive counseling a must for these women.

The use of oral contraceptives is not recommended in women who have undergone malabsorptive bariatric surgery procedures such as the Rouex-Y gastric bypass or the jejunoileal bypass as there may be decreased contraceptive efficacy due to impaired absorption of the OCs. The above recommendation has been endorsed by the United States Medical Eligibility Criteria for Contracetive use (USMEC). [24] Use of non-oral contraception is an acceptable option in such patients.

All contraceptives methods can be used in patients undergoing restrictive bariatric surgery such as lap band and gastric sleeves according to the USMEC.[24]

Patients taking anti obesity drugs such as phentermine/ topiramate should to be counselled regarding the high teratogenic potential of these drugs and the need for highly effective contraception.[25]

Clinical Approach for contraception counseling in an obese patient

Before the clinician decides on the best contraceptive option for an obese woman, a detailed history to document the risk factors should be elicited. The clinician should document the age, history of smoking, diabetes, hypertension, dyslipidemia, migraine, thrombophilia and a personal or family history of a venous thromboembolic event. The examination should include a documentation of the weight and blood pressure. A clinical breast examination is desirable in all women. Clinical inspection of the cervix and bimanual palpation may be done in all women especially those opting for IUD insertion. Laboratory tests which may be offered include blood sugar- fasting and post-prandial, lipid profile, thrombophilia screen and PAP smear. The authors wish to emphasise that apart from a detailed history and basic examination, the tests do not contribute substantially to safe and effective use of a contraceptive method and are optional.

An obese woman should be encouraged to make an informed decision about contraception based on her needs, after the risks and benefits of all the methods have been explained to her.

Conclusion

The authors conclude that contraceptive counseling is mandatory in all sexually active obese women given the high rate of unintended pregnancies and consequent obstetrical complications in them. Progestin only contraceptives and IUDs have minimal to no metabolic side effects and are therefore the preferred choices. Combined contraceptive vaginal ring is another viable option as it provides effective contraception with an acceptable safety profile. More research is needed regarding the safety profile and efficacy of Centchroman in obese women before any definite conclusions can be made. Male partners should be encouraged for vasectomy if a permanent method is desired.

References

1. WHO. [Accessed 29 March 2013]; Obesity and overweight fact sheet. 2013
2. Vahratian A, Barber JS, Lawrence JM, Kim C. Family planning practices among women with diabetes and overweight and obese women in the 2002 National Survey For Family Growth. Diabetes care. 2009; 32(6):1026–1031. [PubMed: 19279299]
3. Gallo MF, Lopez LM, Grimes DA, Carayon F, Schulz KF, Helmerhost FM. Combination contraceptives: effects on weight. Cochrane Database of Systematic Reviews. 1:CD003987– CD003987.
4. Lopez LM, Edelman A, Chen M, Otterness C, Trussell J, Helmerhost FM. Progestin-only contraceptives: effects on weight. Cochrane Database of Systematic Reviews. 7:CD008815– CD008815.
5. Heslehurst N, Simpson H, Ells LJ, Rankin J, Wilkinson J, Lang R, Brown TJ, Summerbell CD. The impact of maternal BMI status on pregnancy outcomes with immediate short-term obstetric resource implications: a meta-analysis. Obes Rev. 2008; 9:635–683. [PubMed: 18673307]
6. Edelman AB, Carlson NE, Cherala G, Munar MR, Stouffer RL, Cameron JL, Stanszyk FZ, Jensen JT. Impact of obesity on oral contraceptive pharmacokinetics and hypothalamic-pituitary-ovarian activity. Contraception. 2009; 80:119-127. [PubMed: 19631786]
7. Lopez LM, Grimes DA, Chen M, Otterness C, Westhoff C, Edelman A, Helmerhorst FM. Hormonal contraceptives for contraception in overweight or obese women. Cochrane Database of Systematic Reviews. 2013; 4:CD008452–CD008452. [PubMed: 23633356]
8. McNicholas C, Zhao Q, Secura G, Allsworth JE, Madden T, Peipert JF. Contraceptive failures in overweight and obese combined hormonal contraceptive users. Obstet. Gynecol. 2013; 121:585– 592. [PubMed: 23635622]
9. Abdollahi M, Cushman M, Rosendaal F. Obesity: risk of venous thrombosis and the interaction with coagulation factor levels and oral contraceptive use. Thrombosis & Haemostasis 2003;89:493–8
10. Trussell J, Guthrie K, Schwarz E. Much ado about little: obesity, combined hormonal contraceptive use and venous thrombosis. Contraception 2008;77:143–6
11. Elkind-Hirsch KE, Darensbourg C, Ogden B, Ogden LF, Hindelang P. Contraceptive vaginal ring use for women has less adverse metabolic effects than an oral contraceptive. Contraception. 2007 Nov; 76(5):348-56.
12. Trussell J. Contraceptive failure in the United States. Contraception. 2011 May; 83(5):397-404
13. Zieman M, Guillebaud J, Weisberg E, Shangold GA, Fisher AC, Creasy GW. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. Fertil Steril. 2002; 77:S13–S18. [PubMed: 11849631]
14. Lopez LM, Grimes DA, Gallo MF, Schultz KF. Skin patch and vaginal ring versus combined oral contraceptives for contraception. Cochrane Database of Systematic Reviews.

2008; (Issue 1) Art. No.: CD003552. doi: 10.1002/14651858.CD003552.pub2.

15. Pfizer Full prescribing information: DEPO-PROVERA CI. 2010. Retrieved from http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/020246-s036lbl.pdf.
16. Viola AS, Castro S, Bahamondes MV, Fernandes A, Viola CF, Bahamondes L. A cross-sectional study of the forearm bone mineral density in long-term current users of the injectable contraceptive depot medroxyprogesterone acetate. Contraception. 2011 Nov; 84(5):e31-7.
17. Berenson AB, Rahman M. Changes in weight, total fat, percent body fat, and central-to-peripheral fat ratio associated with injectable and oral contraceptive use. Am J Obstet Gynecol. 2009 Mar; 200(3):329.e1-8
18. Mornar S, Chan LN, Mistretta S, Neustadt A, Martins S, Gilliam M. Pharmacokinetics of the etonogestrel contraceptive implant in obese women. Am J Obstet Gynecol. 2012 Aug; 207(2):110.e1-6.
19. Weisberg E.Contraceptive options for women in selected circumstances. Best Pract Res Clin Obstet Gynaecol. 2010 Oct; 24(5):593-604.
20. Singh MM. Centchroman, a selective estrogen receptor modulator, as a contraceptive and for the management of hormone-related clinical disorders. Med Res Rev. 2001 Jul;21(4):302-47.
21. Glasier A, Cameron ST, Blithe D, Scherrer B, Mathe H, Levy D, Gainer E, Ulmann A. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. Contraception. 2011; 84(4):363–367. [PubMed: 21920190]
22. Jamieson D, Hillis S, Duerr A, Marchbanks P, Costello C, Peterson H. Complications of interval laparoscopic tubal sterilization: findings from the United States Collaborative Review of Sterilization. Obstet Gynecol 2000;96:997–1002
23. American College of Obstetricians and Gynecologists Committee Opinion No. 315, September 2005. Obesity in pregnancy. Obstet Gynecol. 2005; 106:671–675. [PubMed: 16135613]
24. CDC. U.S. medical eligibility criteria for contraceptive use, 2010. MMWR. 2010; 59(No.RR-4)
25. Sheila K Mody, Michelle Han.OBESITY AND CONTRACEPTION. Clin Obstet Gynecol. 2014 September ; 57(3): 501–507. doi:10.1097/GRF.0000000000000047.

KAMINI RAO ORATION (2019)

FOGSI invites applications for **FOGSI Dr. Kamini A. Rao Orators** from all 4 zones for the year 2019. Application form is annexed herewith.

The members of FOGSI are requested to send the filled application form directly to FOGSI Office.

Eligibility criteria for the **Yuva FOGSI Dr. Kamini A. Rao Orators.**

1. Candidate should be at or below the age of 40 years during 2019, the year of the oration. (Born during or after 1980)
2. Should have contributed to Obstetrics and Gynecology in the form of papers and publications.
3. Should have made a contribution towards FOGSI as an organization and its activities.

May we request all the members to fill the form completely and send it along with a biodata to FOGSI Office not later than August 16, 2018

Application form for FOGSI Dr. Kamini A. Rao Orator

1) Name of the Candidate:
2) Date of Birth:
3) Complete postal address with pincode:
4) Name of the Obstetric and Gynaecological Society:
5) Academic Achievements:
6) Contribution to Local Society:

Journal Scan

Ratna Biswas
Director Professor, Obstetrics & Gynecology, Lady Hardinge Medical College & SSK Hospital, New Delhi


Dr Ratna Biswas

J Virol. 2018 May 14;92(11). pii: e01999-17. doi: 10.1128/JVI.01999-17. Print 2018 Jun 1.

Positive Regulation of Hepatitis E Virus Replication by MicroRNA-122

Haldipur B[1], Bhukya PL[1], Arankalle V1, Lole K[2]

Abstract

The molecular mechanisms of liver pathology and clinical disease in hepatitis E virus (HEV) infection remain unclear. MicroRNAs (miRNAs) are known to modulate viral pathogenesis either by directly altering viral gene expression or by enhancing cellular antiviral responses. Given the importance of microRNA-122 (miR-122) in liver pathobiology, we investigated possible role of miR-122 in HEV infection. *In silico* predictions using HEV genotype 1 (HEV-1), HEV-2, HEV-3, and HEV-4 sequences showed that the majority of genomes (203/222) harbor at least one miR-122/microRNA-122-3p (miR-122*) target site. Interestingly, HEV-1 genomes showed a highly (97%) conserved miR-122 target site in the RNA-dependent RNA polymerase (RdRp) region ($RdRp_c$). We analyzed the significance of miR-122 target sites in HEV-1/HEV-3 (HEV-1/3) genomes by using a replicon-based cell culture system. HEV infection did not change the basal levels of miR-122 in hepatoma cells. However, transfection of these cells with miR-122 mimics enhanced HEV-1/3 replication and depletion of miR-122 with inhibitors led to suppression of HEV-1/3 replication. Mutant HEV-1 replicons with an altered target $RdRp_c$ sequence (CACTCC) showed a drastic decrease in virus replication, whereas introduction of alternative miR-122 target sites in mutant replicons rescued viral replication. There was enrichment of HEV-1 RNA and miR-122 molecules in RNA-induced silencing complexes in HEV-infected cells. Furthermore, pulldown of miR-122 molecules from HEV-infected cells resulted in pulldown of HEV genomic RNA along with miR-122 molecules. These observations indicate that miR-122 facilitates HEV-1 replication, probably via direct interaction with a target site in the viral genome. The positive role of miR-122 in viral replication presents novel opportunities for antiviral therapy and management of hepatitis E.

Importance

Hepatitis E is a problem in both developing and developed countries. HEV infection in most patients follows a self-limited course; however, 20% to 30% mortality is seen in infected pregnant women. HEV superinfections in patients with chronic hepatitis B or hepatitis C virus infections are associated with adverse clinical outcomes, and both conditions warrant therapy. Chronic HEV infections in immunocompromised transplant recipients are known to rapidly progress into cirrhosis. Currently, off-label use of ribavirin (RBV) and polyethylene glycol-interferon (PEG-IFN) as antiviral therapy has shown promising results in both acute and chronic hepatitis E patients; however, the teratogenicity of RBV limits its use during pregnancy, while alpha IFN (IFN-α) increases the risk of transplant rejections. Experimental data determined with genotype 1 virus in the current study show that miR-122 facilitates HEV replication. These observations present novel opportunities for antiviral therapy and management of hepatitis E.

Editor's Comments

Hepatitis E infection in pregnancy is associated with high incidence of fulminant hepatic failure.Ribavirin therapy for 3 wk in patients with severe hepatitis E causes rapid improvement of liver enzymes and functions in liver transplant recepients. Thus despite the fact that ribavirin is a teratogenic drug, the dangers of untreated HEV to the mother and embryo are high, and trials of drug therapy may be advantageous in such patients.

American J Transplant 2018 May: 189(5): 1068-1076

Reproductive Health in Women following Abdominal Organ Transplant

Monika Sarkar, Kate Bramham ,Michael J. Moritz,,Lisa Coscia

Fertility in the Pre- and Post Transplant Setting

End-stage renal disease and end-stage liver disease are associated with impaired fertility in women. Nearly three quarters of women listed for liver transplant (LT) have secondary amenorrhea, with cessation of menstrual cycles in the setting of progressive liver disease. Similar patterns have long been noted in women with end-stage renal disease, with more than 90% of women on dialysis having irregular or absent menstrual cycles. Impaired fertility is largely due to dysregulation in the hypothalamic–pituitary–ovarian axis, which resolves following transplant. The majority of women resume regular menstrual cycles within 1 year posttransplant, though ovulation may resume as early

as within the first postoperative months, highlighting the importance of reproductive counseling in the initial posttransplant period.

Contraception in Transplant Recipients

As the majority of women awaiting transplant are amenorrheic, pregnancy concerns and restoration of fertility may not come to mind. In a US study of reproductive-aged LT and kidney transplant (KT) recipients, only half of women used any form of contraception, and 44% were unaware that pregnancy was possible after transplant. In another study of KT/LT recipients, nearly half were using no contraception, and ≈40% of women were relying upon high failure methods such as condoms, rhythm, or withdrawal.[4] Among women who conceived posttransplant, more than one third had unplanned pregnancies. Prior US data have shown that women desire more information from their transplant providers on use of effective contraceptive options.[5] To best support women's reproductive intentions and ensure they are appropriately informed about anticipated changes in fertility, it is important that transplant providers assess reproductive intentions and provide contraceptive or preconception counseling as appropriate, particularly in the perioperative period when patients may not access reproductive health services elsewhere.

The Centers for Disease Control and Prevention (CDC) has issued formal recommendations to guide contraceptive use in the Medical Eligibility Criteria Guidelines, including recommendations for solid organ transplant recipients.[6] These recommendations are categorized as 1 = No restriction, 2 = Benefits outweigh theoretical or proven risks, 3 = Risks may outweigh benefits, but is safer than pregnancy and may be used if other agents are unavailable or unacceptable to the patient, and 4 = Unacceptable risk (Figure 1). These recommendations are separately provided for stable and for complicated graft function (the latter defined as acute or chronic graft failure, or rejection). All hormonal methods are considered safe in women with stable, uncomplicated graft function. Only progestin-only agents have a favorable safety grade 2 for complicated graft function, although these recommendations did not incorporate additional larger studies also demonstrating favorable safety data of intrauterine devices (IUDs).

	Copper IUD	Hormonal IUD	CHC	POP	DMPA	Implant
Graft Condition						
Uncomplicated	2	2	2	2	2	2
Complicated*	3	3	4	2	2	2

*Defined by the Centers for Disease Control as acute or chronic rejection or graft failure

1 = No restriction 2 = Benefits outweigh theoretical/proven risks
3 = Risks may outweigh benefits 4 = Unacceptable risk

Figure 1: Centers for Disease Control recommendations for contraception use after solid organ transplant.[6]CHC, combined hormonal contraception; DMPA, depot medroxyprogesterone acetate; IUD, intrauterine device; POP, progestin-only pill.

Of note, the CDC does not provide a specific threshold of liver or kidney impairment when classifying graft function as "complicated." However, the primary contraceptive option that is affected by severity of graft dysfunction is combined hormonal contraception (CHC). These estrogen-containing agents may worsen hypertension and predispose to thrombosis, and therefore have a safety grade 4, or unacceptable risk, in women with complicated graft function. For women who prefer use of CHCs, these are a reasonable choice if kidney function is stable with glomerular filtration rate of at least 90 mL/min per 1.73 m^2, blood pressure is well controlled at <130/80 mm Hg, and there is absence of decompensated cirrhosis. In general, we favor the use of hormonal IUDs in transplant recipients, which may also be safely left in place (safety grade 2) in the event of future graft impairment. For women who have complicated graft function and who want to avoid an IUD, progestin-only agents have a favorable safety grade (Figure 1),[6]though some challenges to using these agents are discussed below.

2.1 Intrauterine devices (IUDs)

IUDs, including the nonhormonal copper or hormonal IUD with levonorgestrel, are among the most effective contraceptive methods. Failure rates in the general population are <1% (0.8% for copper IUDs and 0.2% for hormonal), which contrasts with high failure rates of nonhormonal methods such as condoms (≈18%), rhythm methods (≈20%), or withdrawal (≈22%). Copper IUDs may be used for up to 10 years, and women maintain regular menstrual cycles with this agent. Menstrual bleeding in women with copper IUDs is often heavier, which is less ideal for women with existing posttransplant anemia and those with coagulopathy and increased bleeding risk. Levonorgestrel IUDs are effective for 3–5 years, depending on the specific brand, and result in lighter menses, or amenorrhea.

Concerns surrounding the use of IUDs in transplant recipients stemmed from an early report of 2 adolescent KT recipients who became pregnant while using the copper IUD. It was postulated that immunosuppression (IMS) lowers the inflammatory response needed for IUD efficacy. However, the local inflammatory response induced by IUDs is a macrophage-driven process and not affected by transplant IMS. The largest study in the transplant population included 647 KT recipients, 178 of whom were using IUDs. While 15% of the cohort had an unwanted pregnancy, no pregnancies occurred in the IUD group. Similar results were reported in KT and LT recipients using hormonal IUDs, with no pregnancies in 3 years of follow-up. Current data also indicate that immunosuppressed women have no increased risk of pelvic inflammatory disease compared to the general population of non-IUD users. There have been no published cases of pelvic inflammatory disease among >200 KT and LT recipients to date.

2.2 Combined hormonal contraception (CHC)

CHC contains estrogen and progestin, and works primarily by impairing ovulation. Delivery methods include oral contraceptive pills, the transdermal patch, and vaginal ring, all with failure rates of ≈9%. Safety concerns in the general population include risk of venous thromboembolism, stroke, and elevated blood pressure. These agents are metabolized by cytochrome P450; therefore, medications that induce P450 may reduce their efficacy. Older formulations were commonly associated with liver enzyme elevation, though current agents carry only rare risk of cholestatic liver injury.[17] There are no controlled studies evaluating side effects in transplant patients. In an uncontrolled study of 36 KT recipients using oral contraceptive pills or the patch, approximately one third required increased blood pressure medication, 1 developed thrombophlebitis, and another had graft failure 10 years posttransplant.[18] In a 1-year follow-up of 16 LT recipients, no embolic events or elevated blood pressure were noted.[19]

2.3 Progestin-only agents

Progestin-only pills are not associated with increased risk of thrombosis or hypertension. Failure rate is also ≈9% but requires stricter adherence such that women take the pill at the same time each day. Menstrual cycles are also less regular due to the lack of an estrogen component. Depot medroxyprogesterone acetate (DMPA) is an intramuscular injection given every 12 weeks, with a slightly lower failure rate of ≈6%. DMPA is associated with a delayed return to fertility of up to 18 months. Unfortunately, a black box warning was issued by the US Food and Drug Administration (FDA) in 2004, warning of associated decline in bone mineral density. Although bone density normalizes with cessation of DMPA use,[20] there are lingering concerns for transplant patients in view of baseline osteomalacia in the setting of renal disease, and the additional risk of osteopenia related to posttransplant steroid use. The subcutaneous implant is not associated with bone loss, though no studies have evaluated its use in transplant patients. The implant is highly effective, may be used for 3 years, and carries the lowest failure rate of all hormonal agents (0.05%). The implant is associated with irregular bleeding.

Summary & Conclusion

The majority of reproductive-aged women will have restoration of fertility following KT and LT, which may occur within weeks to months of their surgery. Ideally, family planning should be discussed at several time points, including pretransplant, prior to postoperative discharge, with continued discussion in the outpatient setting.

Editor's Comments

There is growing population of women post renal or liver transplant who are at risk of unintended pregnancy. An effective contraceptive with least side effects would be the contraceptive of choice in such women. Uncomplicated recipients may use any of the hormonal contraceptives or IUCD because of low risk of adverse events but complicated renal transplant recipients are at risk of thromboembolic episodes, hypertension or graft failure with CHC therefore progestin only agents are the preferred methods in them. Although there exists a risk of osteomalacia with DMPA injections this has not been observed with subcutaneous implants which may be the method of choice. As regards IUCD there is a theoretical risk of PID and failure due to the immunosuppressant drugs but this has not been observed in current studies and therefore more RCT's are needed to collaborate this observation.

Clinical Proceedings of AOGD Clinical Meeting held at Army Hospital Research & Referral, Delhi on 29th June, 2018

Case 1: Post Partum Headache: A case series

Lt Col Gargi Sharma, Maj Rohin Kumar, Dr LB Singh

We present a case series of Post partum headache with varied diagnosis and how they were managed at our hospital.

Our first case was a 36 yrs old primipara who underwent emergency LSCS at POG 36 weeks 06 days on 01May,18 for Post IVF ET twin pregnancy with first breech in labour with pre-eclampsia. She was readmitted on 23 May,18 with left sided headache associated with blurring of vision left side. CT scan revealed an acute on chronic SDH left fronto-temporo parietal region with midline shift of 7mm. Initially managed conservatively with Inj Mannitol, Analgesics and serial neurological imaging. Later, underwent craniotomy and drainage of hematoma for deteriorating neurological status on 01 Jun,18. She had uneventful post op recovery and discharged on 05 Jun,18.

Our Second case was a 30 yrs old primipara with uneventful antenatal period who underwent normal delivery on 05 May 18 with epidural analgesia. She was readmitted on 09 May 18 with complaints of severe headache. Initially managed conservatively with no improvement of symptoms. NCCT done was normal. CSF for culture sensitivity grew Streptococcus Pneumoniae sensitive to Vancomycin. Patient was started on Vancomycin with complete recovery after 02 days. Patient was discharged on 20 May 18.

Our third case was 33 yrs old Primipara, Post IVF-ET twin pregnancy with uneventful antenatal period who had normal delivery on 23 May, 17. She was readmitted on 03 Jun,17 with complaints of excruciating headache for 02 days. An NCCT followed by MR venogram was done which revealed left transverse venous sinus thrombosis. Managed conservatively with Inj Mannitol, Acetaminophen, Tab Sodium Valproate 500 mg BD and Inj LMWH in therapeutic doses. Patient had complete resolution of symptoms by 08 Jun, 17 and was discharged on 11 Jun, 17.

Our fourth patient was 35 years, primipara who underwent LSCS for failed induction on 30th jan,18. She was readmitted with complaints of acute onset holocranial headache, vomiting and generalised tonic clonic seizure on 3rd Feb,18. She underwent an MRI which revealed Posterior Reversible Encephalopathy Syndrome. She was managed with Inj Sodium Valproate, Mannitol and multiple antihypertensives. She responded well with treatment and was discharged on 12 Feb 18.

Discussion

Post Partum Headache is described as a complaint of headache, neck or shoulder pain in the first few weeks after delivery. It is one of the most common symptoms with up to 40% women reporting it in the first week postpartum. The causes can be varied- 47% - primary causes and 53% - secondary causes. 95% are due to benign and 5% can be life threatening. A thorough history and clinical examination followed by timely neurological imaging can be life saving in the cases with life threatening postpartum headache.

Case 2: OHSS

Lt Col Satyabroto Chatterjee

Case History

A 31 year old lean lady, case of primary infertility with PCOS and prior history of pulmonary Kochs underwent COH with Letrozole and inj HMG followed by IUI on day 16 of her cycle. On day 19 she developed mild GI upset. She was put on observation. Thereafter she progressively developed bilateral pleural effusion and mild ascitis with massive enlargement of her ovaries. By day 21 she had developed respiratory distress and pigtail catheter placement under ultrasound guidance was carried out. By day 27, her serum beta-HCG started rising, with no visible intrauterine gestational sac and a tubal ectopic by day 35(serum beta-HCG of 973). She was treated with inj Methotrxate and her symptoms and signs alongwith haematological & biochemical parameters started improving. Resolution of ascitis & pleural effusion and regression of ovarian enlargement was also seen and patient discharged thereafter.

Discussion

OHSS is a possible life threatening complication of ovulation induction which can present as primary or secondary OHSS. The pathogenesis is VEGF mediated and various strategies can reduce the incidence of OHSS.

Case 3: Medical Management of Large Ovarian CYST in a Young Girl

Lt Col Suneeta Singh, Sqn Ldr Shushil Guard

Case History

An eleven year old girl was referred with insidious onset progressively increasing size of her abdomen. On evaluation, she was intelligent, well oriented, with coarse thick skin with delayed bone age on X-ray. Ultrasound revealed bilateral polycystic thin walled ovarian masses without any solid areas. Her TSH was more than 400 microIU/ml. She was managed with thyroxine supplements. Three months after initiation of treatment, her ovarian cysts had regressed and she had a normal TSH.

Discussion

In 1960, Van Ely and Grumbach found association between long standing primary hypothyroidism, isosexual precocious puberty and multicystic enlarged ovaries. Thyroid replacement resolves the symptoms of hypothyroidism and also symptoms of ovarian enlargement.

Case 4: Increased Nuchal Translucency: What can it mimic?

Lt Col Gargi Sharma, Sqn Ldr Chetan Yadav

30 yrs, Primi, Post IVF – ET pregnancy, Twins (DCDA). Reported at 13 wks POG with increased NT in both twins. Karyotype was normal for both twins on amniocentesis done at POG -16 wk. Anomaly scan done at POG – 19 wk showed increased MCA: PSV for both twins suggestive of fetal anemia in both twins. 2D – ECHO done at POG – 19 wk was normal for both twins. Patient was investigated for causes of fetal anemia. Patient blood group was O positive. Minor blood groups – Negative. Maternal blood sample was sent for infectious screen in which Parvovirus IgM detected to be positive. Parvovirus B19 DNA detection by PCR on maternal blood sample came out to be positive confirming fetal anemia due to Parvovirus infection. Patient was councelled regarding prognosis of pregnancy. Patient chose to continue the pregnancy. Pregnancy was intensively followed up with weekly USG to look for MCA: PSV, features of hydrops and other stigmata of infection. At 34 wk POG, MCA: PSV of Twin I was detected to be more than 1.5 MoM. Intra-uterine transfusion of 80 ml blood was given to Twin I. At 35 wk POG, patient went into preterm labour and because twin 1 was in breech presentation, emergency LSCS was done. Twin 1 had subnormal APGAR, was given resuscitation and shifted to NICU. Twin 2 had normal APGAR, was shifted to NICU for observation. Presently, both twins are doing well and are on follow up in paediatric OPD.

Answer to Quiz: June Issue

Congratulations to Dr. Anita Rajohria, Dr. Anu Handa & Dr. Sonali Jain for successfully answering the quiz and crossword correctly!!

Answer Key for Crossword June issue

Down: 1. TRAP, 2. fetuspapyraceous, 4. lambda, 7. KCl, 9. hasson

Across: 3. palmer, 5. barbed, 6. mangeshikar, 8. thunderbeat, 10. quintero

Answer Key for pictorial quiz June issue

Figure 1: Conjoint twin 2. 1 in 49,000 births to 1 in 189,000 births, 3. Termination of pregnancy

Figure 2: 1. Single incision laparoscopic surgery port (SILS Port), 2. Lack of maneuverability, 3. Robotic-assisted natural orifice transumbilical endoscopic surgery

40th Annual Conference AOGD

Date: 24th -25th November 2018, Venue: India Habitat Centre

Pre- conference workshops: 22nd - 23rd November 2018

Theme: Updating knowledge Enhancing Competencies

Pre–Conference Workshops

22nd November 2018

Fetal Surveillance

Colposcopy (live workshop)

Hysteroscopy

23rd November 2018

Operative obstetrics

Ovulation induction and follicular tracking

Pelvic Reconstructive surgery

Theme topics for Invited abstracts

Critically ill mother

Adolescent gynaecology

Gynaecological cancers

Endoscopy

Contraception

Miscellaneous

Registration open

Last date for abstract submission 15th September 2018.

Details on website: aogd.org

Postal Registration No. DL(ND)-11/6186/2018-20
RNI No. DELENG/2001/04547
Posted on July 14 - 15 from New Delhi GPO
Date of Publication July 7 - 8, 64 pages with cover