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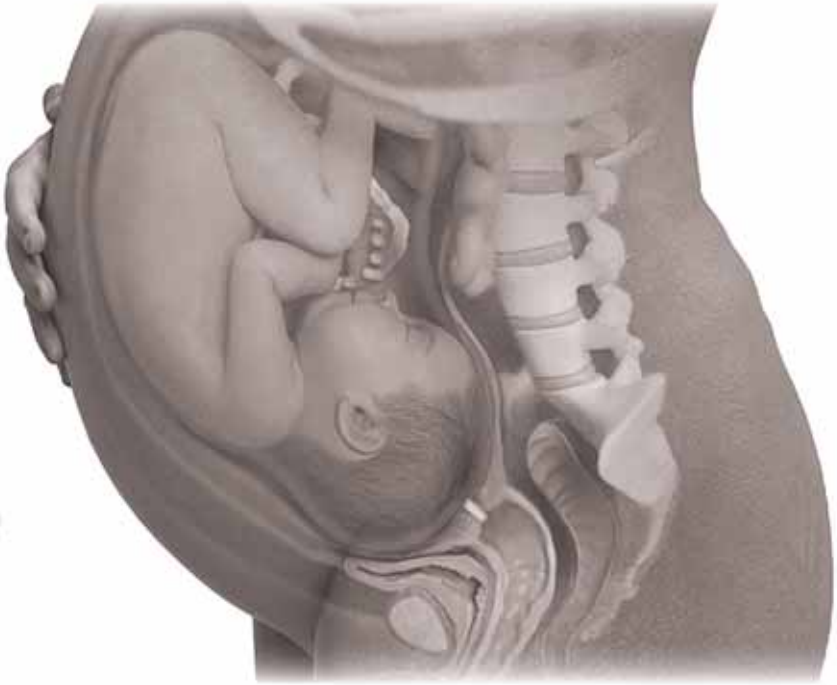
FOGSI's POSTGRADUATE OBSTETRICS

A TEXTBOOK

Volume 1



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Contents

Volume 1

PART 1: Obstetrics and Perinatology

Section 1: Introduction to Obstetrics

1.1. **A Brief History of Women's Health** 3
Parikshit Tank

1.2. **Communication and Counseling** 10
Tripti Nagaria

1.3. **Evidence-Based Medicine and Medical Informatics** 22
Anahita Chauhan, Madhva Prasad S

1.4. **Good Clinical Practice and Research Methodology for Obstetricians** 31
Ramalingappa C Antaratani, Sanjana K

1.5. **Pelvic Anatomy for the Obstetrician and Gynaecologist** 37
Bhavik Doshi, Ashvin Vachhani

1.6. **Violence against Healthcare Professionals** 46
MC Patel, Dilip Walke

Section 2: Normal Pregnancy

2.1. **Fertilization, Implantation, and Placental Development** 53
Milind R Shah, Rajesh V Darade

2.2. **Fetal Physiology: Growth and Development** 61
Halvi Ediger Ramaraju, Surya Malik

2.3. **Clinically Relevant Embryology for Obstetricians** ... 65
Madhuri Arvind Patel, Hemraj R Narkhede, Navin Srinivasan

2.4. **Maternal Adaptations in Normal Pregnancy** 80
Sadhana Gupta, Hema J Shobhane

2.5. **Preconception and Routine Antenatal Care** 88
Vanita Suri, Bharti Sharma

2.6. **Minor Ailments in Pregnancy and Care** 98
Aswath Kumar

2.7. **Normal Laboratory Values in Pregnancy** 104
Sumitra Yadav, Shraddha Paliwal

Section 3: Fetal Evaluation

3.1. **Genetics and Genomics for the Obstetrician** 113
Pragya Mishra Choudhary, Manisha Madhai Beck

3.2. **Fetal Abnormalities: Definitions, Etiology, and Pathophysiology** 122
Mandakini Pradhan

3.3. **Ultrasound in First Trimester: Milestones and Pathology** 126
PK Shah, Pooja Lodha

3.4. **Biochemical Test for Fetal Screening** 133
Vinita Das, Smriti Agrawal

3.5. **Second-trimester Anatomy Scan** 138
Narendra Malhotra, Neharika Malhotra, Jaideep Malhotra, Rahul Gupta, Nitin Agrawal

3.6. **Invasive Tests for Fetal Diagnosis** 149
Purnima Satoskar, Shilpa Agrawal

3.7. **Antepartum Fetal Surveillance Tests in Third Trimester** 157
Shailesh Kore, Mansi Medhekar

3.8. **Color Doppler in Obstetrics** 165
Chinmayee Ratha

3.9. **Fetal Echocardiography** 174
Jayprakash Shah, Parth Shah

3.10. **Noninvasive Prenatal Test** 186
Hemant Deshpande, Monika Maan Sharma

Section 4: Early Pregnancy Complications

4.1. **Abortion** 193
Ranjana Desai

4.2. **Ectopic Pregnancy** 202
K Aparna Sharma, Archana Kumari

4.3. **Gestational Trophoblastic Disease** 210
VP Radhadevi, PK Sekharan

4.4. **Pregnancy after Previous Fetal Loss** 227
Sudha Gandhi, Savitri Verma

Section 5: Pregnancy with Pre-existing Morbidities

5.1. **Chronic Hypertension in Pregnancy** 233
Ragini Verma, Vijeta Jagtap

5.2. **Heart Disease in Pregnancy** 243
Vanita Raut, Shruti Panchbudhe, Anahita Chauhan

5.3. **Diabetes Mellitus** 258
Sujata Misra

5.4. **Thyroid Disorders in Pregnancy** 266
Kanan Yelikar, Sonali Deshpande, Ashwini Kale

5.5. **Anemia** 273
Hema Divakar, Arulmozhi Ramarajan

JAYPEE BROTHERS

5.6. Other Anemias in Pregnancy....279
Jyothika Desai, Megha Chauhan

5.7. Renal Disease and Pregnancy....291
Pralhad Kushtagi

5.8. Liver and Gastrointestinal Disease: Abnormal Pregnancy with Pre-existing Conditions....301
Sujata A Dalvi

5.9. Autoimmune Disorders of Pregnancy....308
Vinita Salvi, Ami Surti

5.10. Respiratory Conditions, the Lung and Pregnancy....318
Ravindra Rupwate, Sonal Kumta

5.11. Neurological Conditions....327
Jyoti Bindal

5.12. Dermatological Disorders in Pregnancy....335
Bharathi KR, Pooja Bhat

5.13. Mental Health Issues and Substance Use in Pregnancy and Puerperium....340
Parul P Tank

5.14. Obesity....347
Ashis Kumar Mukhopadhyay, Maya Mukhopadhyay

5.15. Cancer in Pregnancy....356
Amita Maheshwari, Vikash K Chatrani, Sudeep Gupta

5.16. HIV/AIDS and Other Sexually Transmitted Infections....367
Archana Kumari, Monika Anant

5.17. Infections in Pregnancy....378
Prakash K Mehta, Aparna Setia

5.18. COVID–19 in Pregnancy....393
Ajith S, Kasturi Donimath, Sabnam Nambiar

Section 6: Maternal Complications Arising in Pregnancy

6.1. Hypertensive Disorders in Pregnancy (Gestosis)....398
Sanjay Gupte, Arati Shah

6.2. Liver Diseases in Pregnancy: (HELLP, IHCP, AFLP, HELLP and Infective Hepatitis)....408
Suyajna Joshi D, Manjula Patil

6.3. Gestational Diabetes....420
Girija Wagh

6.4. The Surgical Abdomen in Pregnancy....428
Shashank Parulekar

6.5. Trauma in Pregnancy....434
Alok Sharma, Aanya Sharma

6.6. Poisoning in Pregnancy....442
Sujata Sharma, Amarjeet Kaur

Section 7: Fetal Complications

7.1. Fetal Infections....450
Geetha Balsarkar

7.2. Multiple Pregnancy....457
Sanjay Singh, Parag Biniwale

7.3. Abnormalities of Amniotic Fluid Volume....470
Sasikala Kola, Vidya M Ranga Rao

7.4. Abnormalities of the Placenta and Cord....478
Tamkin Khan, Ayesha Ahmad

7.5. Fetal Growth Restriction....485
Pratik Tambe, Sarita Bhalerao, Usha Krishna

7.6. Fetal Hydrops....495
Muralidhar V Pai, Krishnendu Gupta

Section 8: Late Pregnancy Complications

8.1. Antenatal Care: Malpresentations....499
N Palaniappan

8.2. Preterm Labor....503
MB Bellad, Bhawna Garg

8.3. Preterm Premature Rupture of Membranes....512
Shyam V Desai, Gaurav S Desai

8.4. Antepartum Hemorrhage....518
Madhuri Chandra

8.5. Placenta Accreta Spectrum Disorders....528
Shrinivas N Gadappa, Ankita Rajesh Shah

8.6. Post-term Pregnancy....535
Mala Srivastava, Ankita Srivastava

8.7. Intrauterine Fetal Demise....539
Vandana Bansal, Kaizad R Damania

Section 9: Labor

9.1. Mechanism of Labor....550
Shirish N Daftary, Gaurav S Desai

9.2. Labor in Malposition and Malpresentations....555
Sareena Gilvaz

9.3. Routine Intrapartum Care and Intrapartum Tests..567
Ganpat Sawant, Sachin Ajmera

9.4. Induction of Labor....577
Uday Thanawala, Manasi Venkatraman, Saloni Suchak, Nanak Bhagat

9.5. Labor in Special Situations (Previous Cesarean Birth, Poor Progress in Labor, Fetal Compromise in Labor, Meconium Stained Amniotic Fluid)....585
BS Jodha, Sudhakshi Kinger

9.6. Instrumental Vaginal Delivery....595
Haresh Doshi

9.7. Shoulder Dystocia....604
Abha Rani Sinha, Bhawana Tiwary

9.8. Cesarean Section....609
Suchitra N Pandit, Rakhee R Sahu

9.9. Rupture Uterus....616
Vidya Thobbi, Priyanka S Deshpande

9.10. Obstetric Analgesia and Anesthesia....621
Siddesh Iyer, Shanthakumari S, M Krishna Kumari

JAYPEE BROTHERS

Section 10: Postpartum Issues: Maternal and Neonatal

10.1. Normal Puerperium....628
Indrani Roy

10.2. Episiotomy and Perineal Trauma....635
Picklu Chaudhuri, Arindam Halder, Hiralal Konar

10.3. Postpartum Hemorrhage and its Management....641
Parul J Kotdawala, Sapana Shah, Sunil Shah

10.4. Obstetric Hysterectomy....652
Ajit C Rawal, Janki Pandya

10.5. Postpartum Pyrexia....663
Indranil Dutta, Dilip Kumar Dutta

10.6. Problems with Breastfeeding....670
Sarita Agrawal, Rajeshwari G

10.7. Neonatal Adaption to Extrauterine Life....682
Ruchi Nimish Nanavati, Suman Rao PN

10.8. Neonatal Resuscitation....688
Sonali Tank

10.9. Perinatal Asphyxia....696
Ashish Mehta

10.10. Birth Injuries....704
Upendra Kinjawadekar, Anjali Otiv

10.11. Common Neonatal Problems....710
Bakul Jayant Parekh

Section 11: Social Obstetrics

11.1. Perinatal Mortality, Surveillance and Response....720
Manju Puri, Kanika Chopra

11.2. Safe Motherhood Initiative....725
Alka Pandey

11.3. Maternal Death: Surveillance and Response....733
Jayam Kannan

11.4. Role of Midwifery in Obstetrics....736
Evita Fernandez

Section 12: Critical Care in Obstetrics

12.1. Role of HDU/ICU in Obstetrics....743
Pratima Mittal, Rekha Bharti

12.2. Monitoring in Obstetric HDU and ICU....749
Nuzhat Aziz, Siri Yerubandi, Ananth K

12.3. Fluid and Blood Therapy in Obstetric Shock....762
Jyotsna Suri, Divya Pandey

12.4. Sudden Obstetric Collapse....770
Alpesh Gandhi, Amita Gandhi

Index....783

Volume 2

PART 1: Contraception and Termination of Pregnancy

Section 1: General

1.1. Population Dynamics: The Indian Perspective....3
Anita Soni, Seeru Garg, Ruchi Shah

1.2. Government Policies and Population Stabilization....7
Mandakini Megh, Bhumika Kotecha Mundhe

1.3. Legal Aspects in Medical Termination of Pregnancy and Contraception....12
Nikhil Datar, Meghana Shedge

Section 2: Contraception: Spacing Methods

2.1. Natural and Behavioral Methods of Contraception....16
Vijyalakshmi Pillai

2.2. Male Barrier Methods....22
Rujuta Fuke

2.3. Female Barrier Methods....27
Shobha Gudi

2.4. Vaginal Spermicides....31
Gorakh Mandrupkar

2.5. Combined Oral Contraceptive Pills....33
Poonam Varma Shivkumar, Darshana Legha

2.6. Progesterone-only Pills....38
Nalini Anand

2.7. Injectable Contraceptives....41
Mukta Jain

2.8. Newer Routes for Contraceptions: Implants, Rings and Patches....47
Ashwini Bhalerao-Gandhi, Sanket Pisat, Minal Dhanvij

2.9. Intrauterine Contraception (Including PPIUCD): Copper Devices....54
Pushpa Junghare, Sayali Jahagirdar

2.10. Levonorgestrel Intrauterine System....60
Priya Ballal K, Nikhil Shetty

2.11. Emergency Contraception....68
Lila Vyas, Preeti Sharma

JAYPEE BROTHERS

Section 3: Termination of Pregnancy

3.1. Termination of Pregnancy: Counseling and Evaluation 75
Chandravati, Priti Kumar, Bhawna Khera

3.2. Choices and Methods of Procedures in Pregnancy Termination in First and Second Trimesters 81
Suma Natarajan, Gayathri V, Jayashree Natarajan

3.3. Difficult Situations in Pregnancy Termination 90
Jaydeep Tank, Kunal Doshi

3.4. Complications of Termination of Pregnancy 96
Bharti Maheshwari

3.5. Counseling after Pregnancy Termination 104
Basab Mukherjee

3.6. Access to Safe Pregnancy Termination 107
Atul Ganatra, Freni Shah

Section 4: Permanent Contraception

4.1. Male Sterlization including Nonscalpel Vasectomy: Methods and Strategies to Improve Acceptance 112
Phiroze Soonawala

4.2. Female Sterilization: Standards, Surgical Approaches, and Techniques 116
Madhuri Mehendale, Shraddha Mevada

4.3. Sterilization Failure 121
Kiran Pandey, Pavika Lal

4.4. Reversal of Sterilization 126
Abha Singh, Prabha Lal

Section 5: Contraception and Pregnancy Termination for Special Groups

5.1. Contraception in Adolescents 136
Sucheta Kinjawadekar, Unmesh Santpur

5.2. Perimenopausal Women 143
Nisha Rani, Shikha Sachan

5.3. Contraception and Pregnancy Termination for Women with Medical Disorders 150
Ashok Kumar, Sai Charisma

5.4. Contraception and Pregnancy Termination in the Postabortal Period 157
Trupti Nadkarni

5.5. Contraception in Postdelivery and Lactation 161
Kavita Singh, Deepti Gupta

PART 2: Gynaecology

Section 6: Reproductive Physiology and Basic Sciences

6.1. Embryonic Development and Sexual Differentiation 171
Madhu Nagpal, Manjitkaur Mohi

6.2. Neuroendocrinology and Reproductive Cycle 193
Kamini A Rao, Vyshnavi A Rao

6.3. Normal Menstrual Cycle: Physiology and Care 213
Ameya Purandare, Ritu Hinduja

6.4. Normal Puberty and Adolescence: Physiology and Care 221
Maya Padhi, Lucy Das

Section 7: Basic Aspects of Gynaecological Care

7.1. Eliciting History and Examining Gynaecological Patients 229
S Sampathkumari

7.2. Cytology: Cervicovaginal Smear and Endometrial Biopsy 236
Anita Singh, Richa Jha

7.3. Ultrasound in Gynaecology: Uterine Disease 251
Sonal Panchal, Chaitanya Nagori

7.4. Ultrasound in Gynaecology: Adnexal Disease 267
Archana Baser, Anshu Baser

7.5. CT and MRI in Gynaecology 276
Jyoti Jaiswal, Anand Kumar Jaiswal

7.6. Hormone Assays: Indications, Techniques, and Interpretation 295
Anuradha Ridhorkar

7.7. Preoperative Care and Preparation 304
Gokul Das, Shehla Jamal

7.8. Postoperative Care in Obstetrics and Gynaecology 311
Kavita V Kapadia, Vaibhav V Kapadia

Section 8: Puberty and Adolescence

8.1. Amenorrhea: Evaluation and Management 320
Rajrani Sharma, Ameya Purandare, Parikshit Tank

8.2. PCOS in Adolescence 329
Ameet Patki, Mrinmayi Dharmadhikari

8.3. Developmental Abnormalities of Genital Tract 337
Ragini Agrawal, KV Divya

8.4. Disorder of Sex Development in an Adolescent Girl 342
Kunal Thakkar, Vijaya Sarthi, Nalini Shah

8.5. Body Issue Images in Adolescents 351
Reeti Dutta Mehra

8.6. Eating Disorders in Adolescence 357
Nirmala Sharma, Anand Sharma, Neha Seehara

8.7. Precocious Puberty 364
Surveen Ghumman, Rajal Thaker

Section 9: General Gynaecology

9.1. Premenstrual Syndrome 371
Abha Singh

JAYPEE BROTHERS

9.2. Dysmenorrhea....377
PB Hiremath

9.3. Chronic Pelvic Pain....380
Anupam Gupta, Shikha Singh

9.4. Heavy Menstrual Bleeding: Approach to Evaluation and Treatment....387
Amala Khopkar Nazareth, Gillian Ryan, Alka Kriplani, CN Purandare

9.5. Heavy Menstrual Bleeding: Uterine Conservative Surgery....404
Anuradha Khanna, Shikha Sachan

9.6. Fibroid Uterus....413
PC Mahapatra, Nitin Raithatha

9.7. Adenomyosis....427
N Sanjeeva Reddy, Radha Vembu

9.8. Endometriosis....437
Kanthi Bansal, Anu Agarwal, Shweta Shah

9.9. Hysterectomy: Choice of Surgical Approach....450
Shirish S Sheth, Kurush P Paghdiwalla

9.10. Technical Aspects of Abdominal and Vaginal Hysterectomy....457
VP Paily, Raji Raj

9.11. Technical Aspects of Laparoscopic Hysterectomy....465
PG Paul, George Paul, Sanghamitra Thakur

Section 10: Benign Gynaecological Conditions

10.1. Vaginal Discharge....473
Sheela Mane

10.2. Sexually Transmitted Infections and HIV in Women....489
Atul Munshi, Munjal Pandya

10.3. Pelvic Inflammatory Disease....497
Kusum Lata Singhal, Uma Jain

10.4. Female Genital Tuberculosis....510
Jai Bhagwan Sharma, Eshani Sharma, Sona Dharmendra

10.5. Benign Diseases of Ovary and Fallopian Tube....516
Shobhana Mohandas, Haritha C

10.6. Benign Lesions of Vulva and Vagina....525
Rajashree Dayanand Katke, Deepti Prasad

10.7. Genital Tract Trauma and Sexual Assault....529
Saroj Singh, Neha Agarwal

10.8. Dyspareunia and Vaginismus....537
Shantanu Abhyankar

10.9. Premature Ovarian Insufficiency....545
Duru Shah, Vishesha Yadav

10.10. Menopause: Physiology and Adaptations....554
Sheela HS, Ashwini Neelakanthi

10.11. Implications of Menopause on Cardiovascular and Bone Health....561
Revathy Janakiram, Krithika Meenakshi

10.12. Hormone Therapy in Menopause....568
Suvarna Khadilkar, Madhva Prasad S

10.13. Non-hormonal Therapy at Menopause....576
Meeta, Akanshi Madan, Tanvir

Section 11: Endoscopy

11.1. Laparoscopy: Safe Entry Technique and Instrumentation....584
Rajendra Sankpal, Damodar Rao

11.2. Hysteroscopy: Instrumentation and Distension Media....592
Subash Mallya

11.3. Robotic Surgery in Gynaecology....596
Seema Singhal, Alka Kriplani

11.4. Complications of Gynaecological Laparoscopy....603
Sunita Tandulwadkar, Abhishek Chandavarkar, Rohan Krishnakumar

11.5. Surgical Training in Gynaecological Endoscopic Surgery....613
Pragnesh Shah, Foram Vora

11.6. Energy Sources in Endoscopic Surgery....623
Prakash Trivedi, Soumil Trivedi

Section 12: Reproductive Endocrinology and Infertility

12.1. Infertility: Etiology and Clinical Evaluation....631
Charmila Ayyavoo, Sunil Shah

12.2. Investigations for the Male Partner....638
Fessy Louis T, Parvathy T

12.3. Investigations for the Female Partner....645
Rishma Dhillon Pai, Meenu Handa

12.4. Male Infertility: Etiology and Management....652
Ajay S Shetty, Rupin Shah

12.5. Anovulation: Etiology and Management....662
Manish Banker, Jwal Banker

12.6. Hormonal Issues and Infertility: Thyroid, Prolactin and Androgens....669
Krishnendu Gupta, Muralidhar V Pai

12.7. Tubal Factor Infertility: Etiology and Management....672
Pratap Kumar, Aswathy Kumaran

12.8. Uterine Factor in Infertility: Etiology and Management....682
Laxmi Shrikhande

12.9. Unexplained Infertility: Treatment Approach....690
Rohan Palshetkar, Nandita Palshetkar

12.10. Intrauterine Insemination....693
Sudha Prasad, Aswathy Kumaran, Saumya Prasad

JAYPEE BROTHERS

12.11. Assisted Reproductive Technology 699
Jaideep Malhotra, Shally Gupta, Neharika Malhotra, Neerja Sachdev, Narendra Malhotra, Keshav Malhotra

12.12. Assisted Reproductive Technologies: New Techniques and Research....712
Hrishikesh Pai, Sunita Arora, Nandan Roongta, Rishma Dhillon Pai, Nandita Palshetkar

12.13. Recurrent Pregnancy Loss....721
Mala Arora

12.14. Third Party Reproduction....727
Nayana Patel, Molina Patel, Niket Patel, Yuvraj Jadeja, Harmi Thakkar

12.15. Adoption 735
T Ramani Devi, D Gayathri

PART 3: Urogynaecology and Gynaecological Oncology

Section 13: Urogynaecology

13.1. Assessment of Lower Urinary Tract Complaints and Function....743
Achla Batra, Karishma Thariani

13.2. Nonsurgical and Surgical Treatment of Stress Urinary Incontinence....747
N Rajamaheswari, Vaishnavy

13.3. Overactive Bladder....755
Subhash Ch Biswas, Ramprasad Dey

13.4. Urinary Tract infections 760
Susheela Rani BS

13.5. Urogenital Prolapse: Assessment and Treatment Approaches....767
RM Saraogi, Chirag Patel

13.6. Posthysterectomy Vaginal Vault Prolapse....780
L Krishna, N Shailaja

13.7. Anal Incontinence....785
Pranav Mandovra, Roy Patankar

13.8. Fistulas in Obstetrics and Gynaecology 791
Manu Sobti

Section 14: Gynaecological Oncology

14.1. Neoplastic Diseases of Vulva 796
Niranjan Chavan, Dinesh Wade, Prathamesh Kane, Richa Deshmukh

14.2. Vulval Carcinoma 799
SP Somashekhar

14.3. Intraepithelial Disease of the Cervix....810
Nikhil Parwate, Sabina Hasan Ali Moman

14.4. Malignant Diseases of Vagina 829
Shalini Rajaram, Bindiya Gupta

14.5. Malignant Disease of Vagina 834
Saritha Shamsunder

14.6. Premalignant and Malignant Diseases of the Uterus 844
SK Giri, BL Nayak

14.7. Benign Ovarian Neoplasia 861
Neerja Bhatla, Anju Singh, Seema Singhal

14.8. Malignant Ovarian Neoplasia....872
Harshad Parasnis, Suchita Dabhadkar

14.9. Neoplastic Diseases of Fallopian Tube....883
Uma Singh, Manjulata Verma

14.10. Principles of Radiation Therapy 889
Umesh Mahantshetty, Gargee Mulye, Lavanya Gurram

14.11. Principles of Chemotherapy 902
Anant Ramaswamy, Sudeep Gupta

14.12. Palliative Care in Gynaecologic Oncology 909
Jayaraman Nambiar M, Thiencherry Rema

14.13. Screening for Ovarian Cancer Current Perspective....914
Usha B Saraiya, Nidhi Shah Gandhi

Index *921*

JAYPEE BROTHERS

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LONG AND SHORT QUESTIONS

1. Discuss the causes of recurrent pregnancy loss. How will you manage a patient who is 30 years old with history of four consecutive abortions in first trimester of pregnancy?
2. Define abortion. Discuss the types and management of various types of abortion.

MULTIPLE CHOICE QUESTIONS

1. The most common viral infection which has been linked with fetal death is:
   a. Zika virus b. Herpes simplex virus
   c. Cytomegalovirus d. Parvovirus B19
2. Which statement is not true for type II unexplained recurrent miscarriage:
   a. There is an underlying pathology which is not diagnosed by routine investigation
   b. Usually seen in younger women (<30 years of age)
   c. The products of conception of recurrent miscarriage shows aneuploidy
   d. All losses have been occurred after fetal heart rate has been visualized
3. The incidence of late pregnancy loss (after 12 weeks) after antiretroviral therapy (ART) is:
   a. 1% b. 2–4%
   c. 4–6% d. 5%
4. Which investigation is not needed in recurrent spontaneous abortion?
   a. Test for antiphospholipid antibodies
   b. Glucose challenge test
   c. Thyroid function test
   d. TORCH test
5. McDonald's stitch is applied in all, except:
   a. Incompetent os b. Placenta previa
   c. Septate uterus d. Recurrent preterm labor

Answers

1. d 2. c 3. b 4. d 5. b

4.2 ECTOPIC PREGNANCY

K Aparna Sharma, Archana Kumari

INTRODUCTION

Ectopic pregnancy occurs when the blastocyst gets implants in tissue other than the endometrium. Although, the ampullary region of the fallopian tube is the most common site for ectopic implantation (70%), it may occur in other sites **(Fig. 1)**.

INCIDENCE

Ectopic pregnancy has been reported to occur in around 20 cases per 1,000 population and contributes significantly to the maternal mortality in first trimester.[1] In various reports from India, its contribution to maternal deaths has been 3.5–7.1% with an incidence of 0.91% without any maternal mortality.[2]

RISK FACTORS

Globally, the rising incidence of ectopic pregnancy can be attributed to increased incidence of salpingitis due to sexually transmitted infections, ovulation induction, surgeries on tubes as well as earlier detection through imaging. The various risk factors for ectopic gestations have been summarized in **Table 1**.

EVOLUTION AND POTENTIAL OUTCOMES OF ECTOPIC PREGNANCY

An ectopic implantation can evolve in various ways and have different outcomes. *Tubal rupture* can occur if the fertilized

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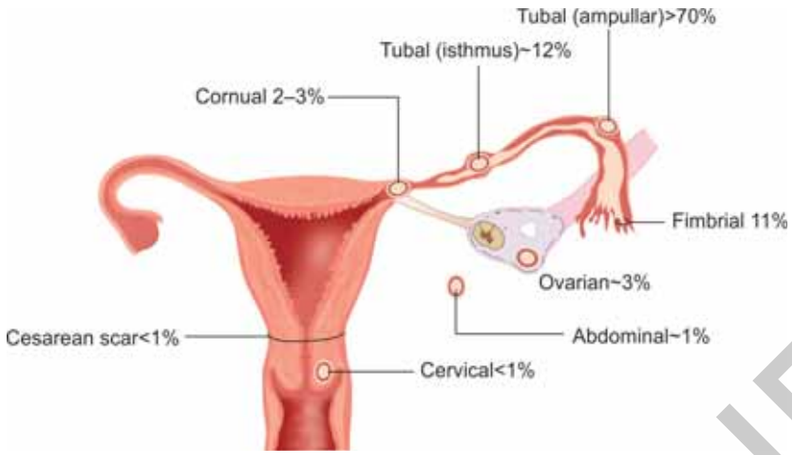

Fig. 1: Site of ectopic implantation.

TABLE 1: Risk factors for ectopic pregnancy.

	Risk factors	***Remarks***
1.	Previous ectopic pregnancy	*Increase in risk after:* • *After one:* 10–15% • *After two:* 30%
2.	*Pelvic infection:* • Chlamydia • Gonorrhea • Nonspecific salpingitis	*Increase in risk after:* • After one episode: 13% • After two episodes: 35% • After three episodes: 75%
3.	*Tubal surgery:* • Tubal reconstructive surgery • Tubal sterilization	7.3 per 1,000 sterilization procedures (10-year cumulative incidence)
4.	Infertility	4–40 times increase (depending on the etiology of infertility)
5.	*ART can cause atypical implantations:* • Cornual • Abdominal • Cervical • Ovarian • Heterotopic	1.6%
6.	*IUD:* • LNG IUD • Copper IUD	>50% of pregnancies with an IUD in situ are ectopic
7.	*Tubal pathology:* • Developmental anomalies • Salpingitis isthmica nodosa	
8.	Cigarette smoking	Dose-dependent manner

(ART: assisted reproductive technology; IUD: intrauterine device; LNG: levonorgestrel)

ovum comes to lie near or close to the muscularis after burrowing through the epithelium due to the invasion by the proliferating trophoblast. This happens because fallopian tube lacks submucosal layer. When the zygote gets extruded into the abdomen through the tubal ostium, it is termed as *tubal abortion*. In this, the bleeding may stop and symptoms may disappear. Bleeding may persist as long as products remain in tube leading to hemoperitoneum. If however, the fimbriated end of the tube is closed, hematosalpinx may form. In very rare conditions, aborted fetus can implant on any peritoneal surface leading to abdominal pregnancy. Sometimes, after spontaneous failure to thrive, *complete resorption* may occur. *Chronic ectopic* pregnancy may occur when abnormal trophoblast dies early. Beta-human chorionic gonadotropin (β-hCG) gradually becomes negative or static. It commonly forms complex pelvic mass which may later rupture.

CLINICAL FEATURES

History

The classic presentation of amenorrhea followed by pain and vaginal bleeding occurs in only 50% of patients, typically in those with ruptured ectopic pregnancy. Most common symptom presenting symptom of an ectopic gestation is abdominal pain. It may be continuous or intermittent, dull or sharp. Commonly, the presentation can be of two types depending on the hemodynamic stability as in **Table 2**.

Physical Examination

Mostly, prior to rupture, the diagnosis is made incidentally during an early dating scan. The patient is stable with normal vitals with nontender or mildly tender abdomen. The uterus may be just bulky. Cervical motion tenderness and adnexal mass may be present. But the mass may vary markedly in size, consistency, and tenderness.

When the ectopic pregnancy ruptures, hemoperitoneum occurs leading to features of hypovolemic shock such as tachycardia and hypotension. There is marked abdominal tenderness and rebound tenderness. Bowel sounds are decreased or absent. Cervical motion tenderness is present. A conclusive diagnosis may not be reached based on history and physical examination, requiring additional tests for differentiation between early viable intrauterine pregnancy, abnormal intrauterine pregnancy, and suspected ectopic pregnancy **(Flowchart 1)**.

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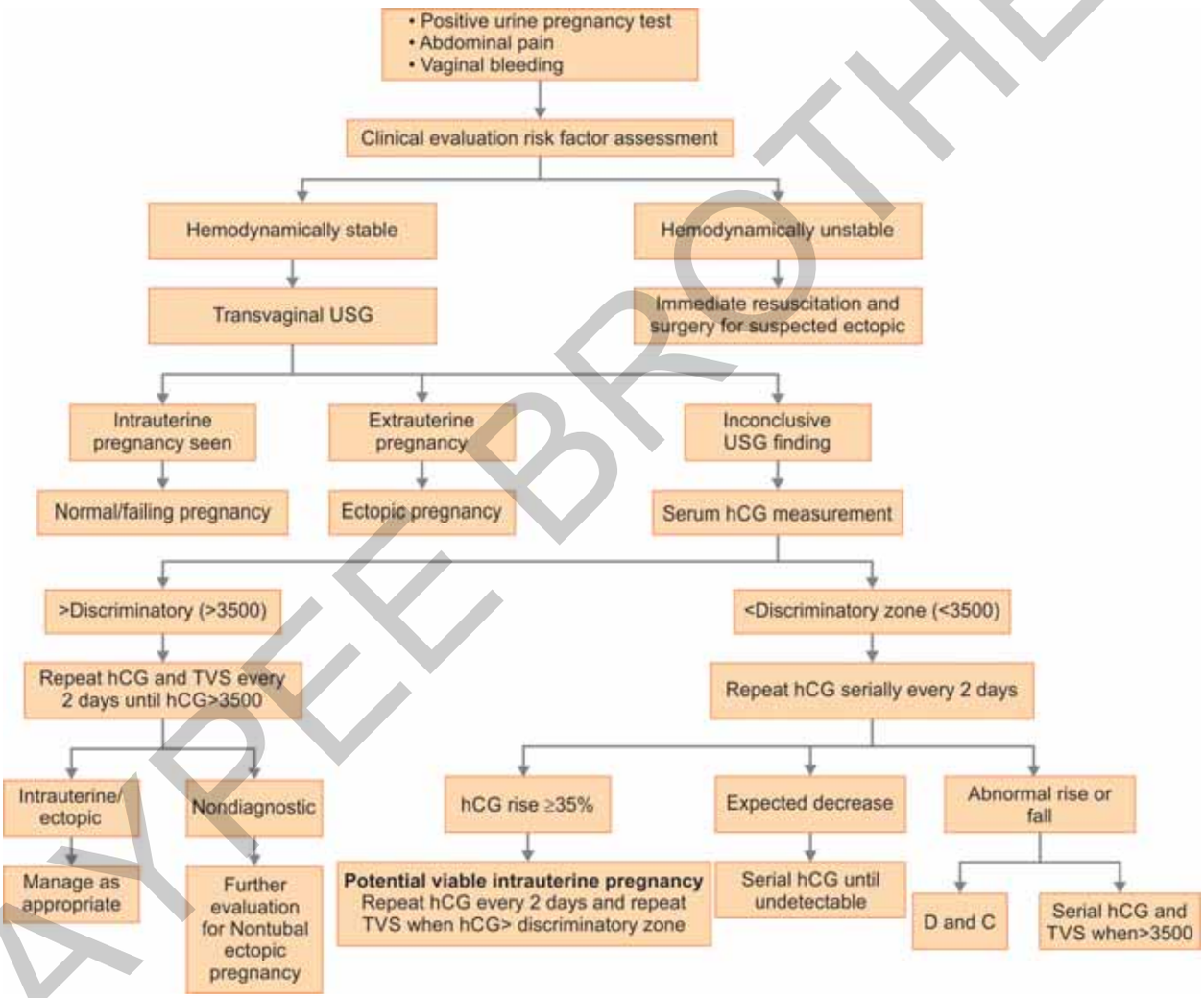
TABLE 2: Clinical presentation based on hemodynamic status.

		Unstable hemodynamic status	***Stable hemodynamic status***
1.	History	Shoulder pain (due to hemoperitoneum irritating inferior surface of diaphragm)	
2.	Vital signs	• Signs of hypovolemic shock • Tachycardia • Hypotension	Normal
3.	Per abdomen	Signs of peritonism-guarding, rigidity, rebound tenderness, shifting dullness	Generalized abdominal tenderness
4.	Per vaginal	Palpable adnexal mass	Cervical motion tenderness may or may not be present

Flowchart 1: Diagnostic algorithm.



(D and C: dilation and curettage; hCG: human chorionic gonadotropin; TVS: transvaginal scan; USG: ultrasonography)

DIAGNOSIS

Transvaginal Ultrasonography

Diagnosis of ectopic pregnancy is made when the uterine cavity is empty and there is a visualization of a gestational sac in the adnexa **(Table 3)**. In most cases, however, there is an ill-defined mass which is seen in the adnexa in cases of early unruptured tubal ectopics with ovaries being visualized separately **(Fig. 2)**.[3,4]

Serum Beta-Human Chorionic Gonadotropin Measurement

Until the location of the pregnancy is confirmed, the diagnosis remains a pregnancy of unknown location (PUL).

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TABLE 3: Ultrasound features of ectopic pregnancy.

USG finding	*Typical appearance*	*Approximate proportion*
Blob sign	An inhomogeneous mass separate from ovary	60%
Bagel sign	A hypoechoic gestation sac within a mass	20%
Extrauterine gestational sac	Gestational sac with developing yolk sac or fetal pole with or without cardiac activity	20%
Free fluid in POD	Not seen until volume reaches 400–700 mL	
Intrauterine pseudo-gestational sac	Anechoic fluid collection in uterine cavity that conforms to shape of uterine cavity and is central in location	

(POD: pouch of Douglas; USG: ultrasonography)



Fig. 2: Ultrasonography (USG) image of ectopic mass with ring of fire pattern in adnexa.

The intrauterine location of gestational sac with a yolk sac rules out ectopic pregnancy.[5,6]

However, quantitative serum β-hCG level can be used for diagnosis in the absence of such definitive finding. If the initial serum β-hCG level exceeds the set discriminatory level (level above which failure to visualize a uterine pregnancy indicates a failing pregnancy or an ectopic), diagnosis narrows to a failing intrauterine pregnancy, a recent complete abortion or an ectopic pregnancy or an early multifetal gestation.

However, recently[7] a case series reported intrauterine gestational sac on follow-up scan despite β-hCG level above the discriminatory level at initial scan, this raises a question on the utility of the discriminatory level.[8-10] Hence, the hCG discriminatory value should be kept high at 3,500 mIU/mL to avoid any misdiagnosis. [7,10]

Serial Serum Beta-Human Chorionic Gonadotropin Measurement

Because of the inability of a single β-hCG to confidently rule out ectopic pregnancy, serial hCG measurement can be employed.

The rise of serum β-hCG occurs in a curvilinear fashion until a plateau at 100,000 mIU/mL is reached by 10 weeks of gestation. Recently, it has been found that the minimum increase in hCG for a potentially viable intrauterine pregnancy occurs at a slower rate[11,12] and is dependent on the initial value.[13]

The rise on β-hCG may vary from 33% to up to 50% depending on the initial values and a rise below a minimal threshold raises the suspicion of an abnormal pregnancy either ectopic or an early pregnancy loss. However, even β-hCG patterns consistent with a growing or resolving gestation do not rule out an ectopic pregnancy.[14]

A failing pregnancy is suggested by decreasing β-hCG value. It should be monitored till spontaneous resolution to nonpregnant levels because rupture of an ectopic pregnancy can occur even while levels are decreasing or are very low.

Dilation and Curettage

Uterine curettage is performed for either a confirmed nonviable pregnancy or an undesirable pregnancy with unknown location.

Culdocentesis

Culdocentesis is now rarely used for diagnosis of ectopic pregnancy.

Laparoscopy

With the advances in ultrasound technology, more ectopic pregnancies are being diagnosed earlier allowing for medical interventions and reducing the need for surgical management. Hence, laparoscopy is no longer considered the gold standard for diagnosis.

DIFFERENTIAL DIAGNOSIS

Pregnancy should be ruled out in any sexually active woman of reproductive age who presents with abdominal pain or vaginal bleeding regardless of current history of contraceptive usage.[15,16]

Because of varied presentation ranging from asymptomatic to acute abdomen and shock, clinicians must have a high degree of suspicion in order to any delay in diagnosis. History, physical examination along with serum β-hCG estimation, and ultrasonography aid in making the final diagnosis of ectopic pregnancy and differentiating it from other causes of acute abdomen **(Table 4)**. Until the location of the pregnancy is confirmed, the diagnosis remains a pregnancy of unknown location.

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MANAGEMENT OF ECTOPIC PREGNANCY

Depending on the hemodynamic status and clinical scenario, expectant, medical, or surgical management can be used for management of ectopic pregnancy **(Flowchart 2)**.

Both laparoscopic surgery and medical management have equivalent safety and effectiveness for an unruptured ectopic pregnancy in clinically stable women. The decision should be made by the patient after discussion of benefits and risks of each approach in different clinical settings.

TABLE 4: Differential diagnosis of acute abdomen in early pregnancy.

S. No.	*Diagnosis*	*Features*
	Gynecologic conditions	
1.	Pelvic inflammatory disease	Urine pregnancy test is negative
2.	Threatened/incomplete miscarriage	Bleeding per vagina is usually heavier, no adnexal mass
3.	Ovarian torsion	Urine pregnancy test is negative, pain is intermittent initially and progresses to constant excruciating or dull pain, USG Doppler is helpful
4.	Ruptured ovarian cyst (corpus luteum or endometrioma)	Difficult diagnosis if pregnant
5	Degenerating or enlarging myoma	• USG localization of a myoma • Adnexa will be normal
	Nongynecologic condition	
6	Appendicitis/ gastroenteritis/diverticulitis	Negative UPT with normal vaginal examination findings
7.	Urinary tract infection	
8.	Renal/ureteric calculus	

(UPT: urine pregnancy test; USG: ultrasonography)

Medical Management

Methotrexate (Mtx) is the first-line drug for medical management for ectopic pregnancy. Other drugs which can also be used are potassium chloride, prostaglandin (PGF2α), hyperosmolar glucose, and actinomycin. It is imperative to rule out all contraindications (listed in **Table 5**) before initiating Mtx therapy. The reported success rates with systemic Mtx are approximately 70–95%.[17,18] The protocol of single dose versus multiple dose is based on the initial levels of β-hCG with higher levels requiring multiple dose protocols **(Table 6)**.

The patient should be counseled thoroughly regarding the following:

- Effects and side effects of Mtx
- Need for follow-up
- Need to report urgently—if severe abdominal pain and fainting attack
- Avoiding excessive sun-exposure, alcohol, vitamins, aspirin, and nonsteroidal anti-inflammatory drugs (NSAIDs).

Surgical Management

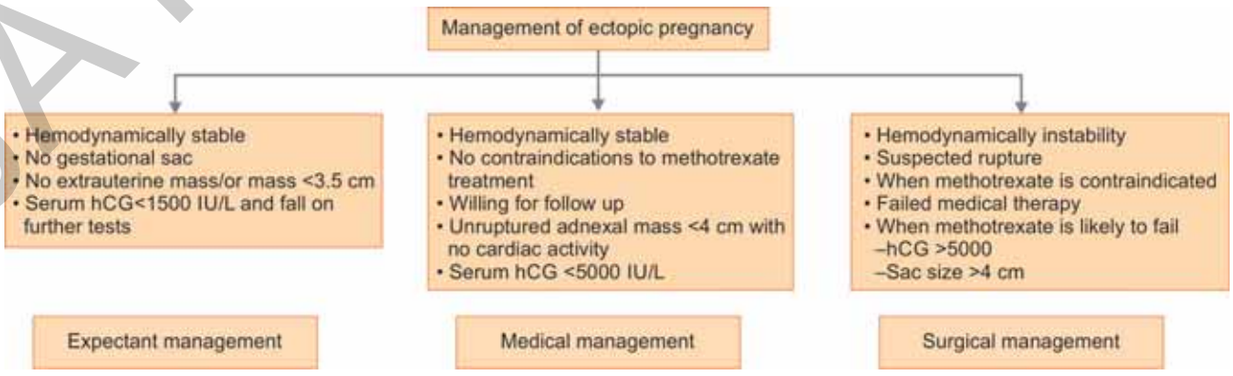
Laparoscopy is the preferred surgical treatment for ectopic pregnancy **(Figs. 3 and 4)** unless a woman is hemodynamically unstable. The choice between laparoscopic salpingectomy (when a part or whole of the tube is removed) and laparoscopic salpingostomy (when only the ectopic gestation is removed leaving the tube in situ) depends upon the future fertility desires of the patient and extent of fallopian tube damage. Following salpingostomy, a follow-up is required to ensure complete resolution of the ectopic mass, while this is not required following salpingectomy.[19]

Laparotomy is preferred in unstable patients, with massive hemoperitoneum **(Figs. 5 and 6)** or in patients in whom visualization is expected to be poor or compromised at laparoscopy.

NONTUBAL ECTOPIC PREGNANCY

Although they represent a minority of ectopic pregnancies, they pose significant diagnostic challenge and disproportionate

Flowchart 2: Prerequisites for various treatment options for ectopic pregnancy.



(hCG: human chorionic gonadotropin)

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TABLE 5: Methotrexate therapy: Contraindications.

Absolute contraindications	• Confirmed intrauterine pregnancy • Ruptured ectopic pregnancy • Known sensitivity to methotrexate • Immunodeficiency • Hematological disorders such as severe anemia, thrombocytopenia, or leukopenia • Active peptic ulcer disease • Hepatic/renal dysfunction • Active pulmonary disease • Breastfeeding mother • Unwilling for follow-up
Relative contraindications	• Presence of cardiac activity on transvaginal ultrasonography • Very high hCG concentration • Gestational sac more than 4 cm in size • Refusal to accept blood transfusion

(hCG: chorionic gonadotropin)

TABLE 6: Regimens for methotrexate treatment for ectopic pregnancy.

	Single dose	***Multiple dose***
Dosing	One dose	Four doses
Schedule	50 mg/m^2 BSA D1	1 mg/kg (D1, 3, 5, 7) 0.1 mg (D2, 4, 6, 8)
Serum β-hCG	D1, 4, 7	D1, 3, 5, 7
Indication for additional dose	If fall in β-hCG is not 15% between D4 and D7	If fall in β-hCG is not 15%
Surveillance	Weekly	Weekly

(β-hCG: beta-human chorionic gonadotropin)

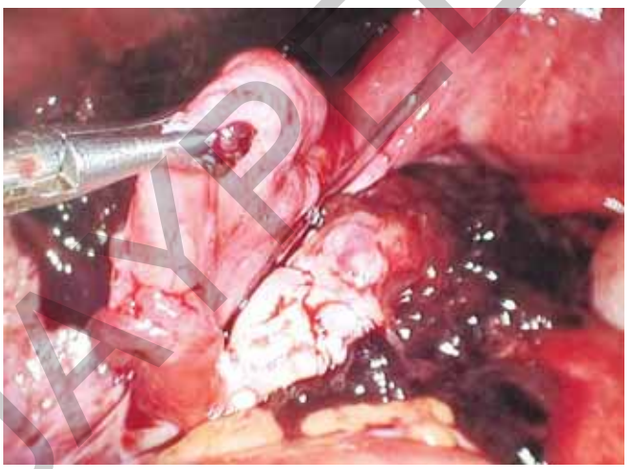

Fig. 3: Ruptured left tubal ectopic pregnancy with hemoperitoneum—laparoscopic view.

level of morbidity. These include interstitial, cesarean scar **(Fig. 7)**, cervical, heterotopic, and cornual and abdominal ectopic pregnancy. All these are discussed briefly in **Table 7**.



Fig. 4: Unruptured Left tubal ectopic pregnancy (black arrow) laparoscopic view.

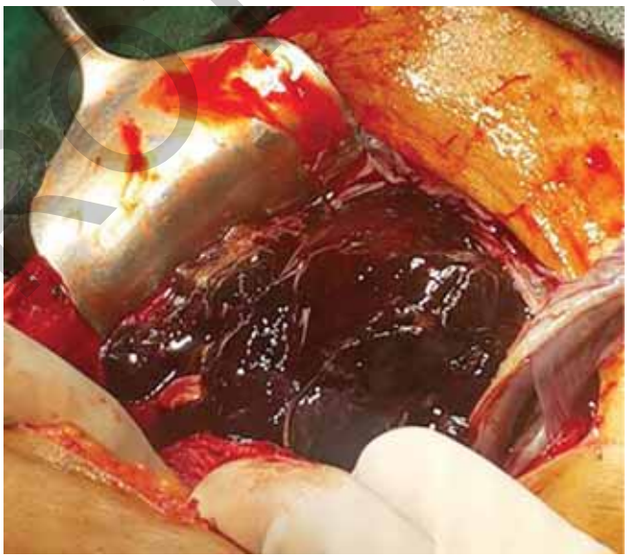

Fig. 5: Massive hemoperitoneum in a ruptured ectopic pregnancy.



Fig. 6: Specimen of fallopian tube (salpingectomy) performed for ruptured ectopic pregnancy.

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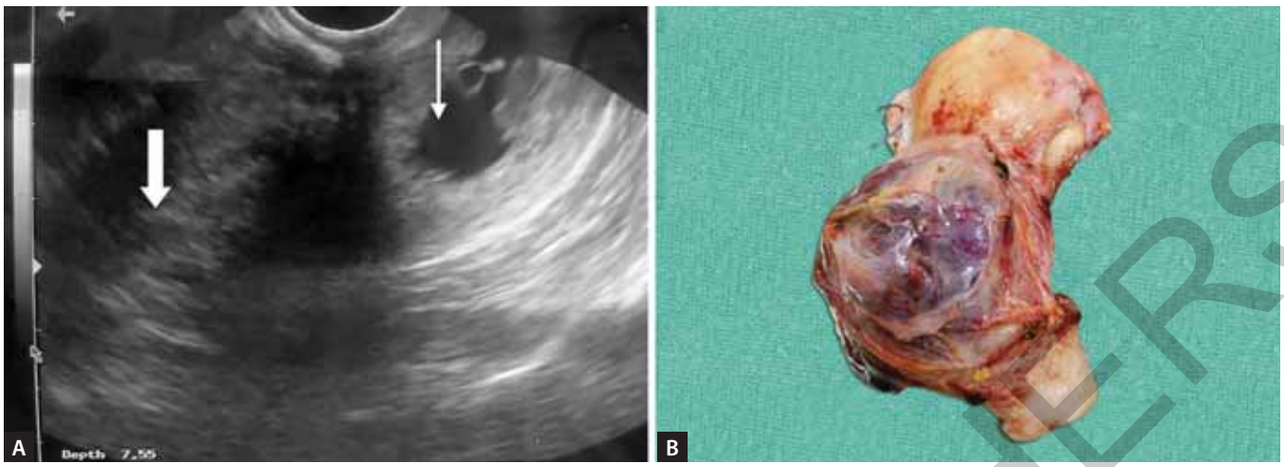

Figs. 7A and B: Scar ectopic pregnancy. (A) Ultrasound showing an empty endometrial cavity (white block arrow) and pregnancy (white plain arrow) in lower segment or scar; (B) Surgical specimen of hysterectomy performed for scar ectopic pregnancy of the same woman.

TABLE 7: Nontubal ectopic pregnancy.

Type of pregnancy	*Incidence*	*USG features*	*Management*
Cervical pregnancy	0.15%	• Empty uterus with gestational sac below the level of the internal cervical os • Barrel-shaped cervix • Absent "sliding sign" • Vascularity around the gestational sac in cervix	• Medical management with methotrexate • Chemoembolization • Intracardiac KCL injection
Interstitial pregnancy	1–6%	• Uterine cavity is empty • Gestational sac in the interstitial portion of tube surrounded by <5 mm of myometrium • The thin echogenic central uterine cavity echo can be seen extending to the edge of the interstitial sac and is referred to as the "interstitial line sign" (sensitivity 80%, specificity 98%)[20]	• Laparoscopic or open cornual excision • Local or systemic methotrexate • Hysteroscopic resection under laparoscopic or USG guidance
Cesarean scar pregnancy	1 in 2,000 pregnancies	• Uterus and cervix are empty • Gestational sac embedded into the scar site • Myometrium between the gestational sac and the bladder is thin or absent • Vascularity around the gestational sac[21-23]	• Local injection of methotrexate into the gestational sac under ultrasound guidance or systemic[24] • Suction evacuation or hysteroscopic resection or excision[25-29]
Abdominal pregnancy		• Uterus and adnexa are normal • Bowel loops seen surrounding the gestational sac, separated from them by peritoneum • Mobility noted toward the posterior cul-de-sac on pressure with transvaginal probe[30]	• Laparoscopic removal or systemic methotrexate with USG-guided feticide • Laparotomy for advanced pregnancy
Ovarian pregnancy		No specific criteria	Removal of POC by enucleation or wedge resection by laparoscopy or laparotomy
Heterotopic pregnancy		Co-existent gestational sac in uterine cavity along with an ectopic pregnancy	• The contents of the sac are aspirated • Local injection of KCL or hyperosmolar glucose given • Methotrexate to be given only if nonviable or undesirable pregnancy • Surgical management if vitals unstable

(KCL: potassium chloride; POC: products of conception; USG: ultrasonography)

KEY MESSAGES

- Diagnosis of ectopic pregnancy can be established by a comprehensive approach of history, examination, and use of transvaginal ultrasound.
- Serial serum β-hCG values may be needed to be performed and correlated with the clinical presentation and ultrasound findings for diagnosis of ectopic pregnancy.

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- Medical or laparoscopic management can be offered if the woman has an unruptured ectopic and is hemodynamically stable. Single-dose Mtx is preferred if medical therapy is indicated and selected.
- The risk of subsequent ectopic pregnancy following an ectopic is approximately 15%.
- Surgical management and medical therapy have similar future reproductive outcome.

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LONG QUESTION

1. What is ectopic pregnancy? How will you manage a case of 24-year-old G2A1 female with 6-week pregnancy with pain in lower abdomen and slight vaginal bleeding?

SHORT QUESTIONS

1. Medical management of ectopic pregnancy
2. Diagnosis and management of cesarean scar pregnancy
3. Role of ultrasound for diagnosis of ectopic pregnancy
4. Surgical management of ectopic pregnancy

MULTIPLE CHOICE QUESTIONS

1. Which of the following is not a risk factor for an ectopic pregnancy?
   a. Prior tubal pregnancy
   b. Smoking
   c. A history of pelvic inflammatory disease
   d. In-vitro fertilization
   e. A prior ovarian pregnancy
2. The classic signs and symptoms of an ectopic pregnancy include all of the following, except:
   a. Vaginal bleeding
   b. Syncope
   c. Adnexal tenderness
   d. Adnexal mass
3. The discriminatory zone beyond which a gestational sac will be visualized in the uterus in 95% of cases is:
   a. 500 mIU/mL
   b. 1,000 mIU/mL
   c. 1,500 mIU/mL
   d. 3,000 mIU/mL
   e. 6,000 mIU/mL
4. Which of the following sonographic signs associated with an ectopic pregnancy is the most common?
   a. A pseudogestational sac
   b. An extrauterine gestation with cardiac activity
   c. An "echogenic ring"
   d. Debris-filled cul-de-sac fluid
   e. A complex adnexal mass
5. Which of the following ectopics will grow to the largest size before becoming symptomatic?
   a. Isthmus
   b. Fimbrial
   c. Cervical
   d. Cornual
   e. Ovarian
6. The medical management of an ectopic pregnancy requires that the β-hCG level drops by what percent between day 4 and 7 after therapy?
   a. 10%
   b. 15%
   c. 20%
   d. 25%
   e. 30%
7. The prevalence of a persistent ectopic pregnancy after linear salpingostomy at laparotomy is?
   a. 1%
   b. 2–5%
   c. 6–10%
   d. 11–15%
   e. 15%
8. In a case of ectopic pregnancy, medical treatment is contraindicated, if:
   a. Sac size is 3.0 cm
   b. Blood in pelvis is 70 mL
   c. Presence of fetal heart activity
   d. Previous ectopic pregnancy
9. Which of the following is not a radiological sign of cesarean scar pregnancy?
   a. Empty uterine cavity
   b. Empty cervical canal
   c. Thick myometrium between bladder and gestational sac
   d. Intrauterine mass seen in anterior part of the uterine isthmus
10. Which of the following is incorrect regarding management of cervical pregnancy?
    a. Chemoembolization has been tried with success
    b. Intracardiac injection of KCL can be done
    c. Intramuscular injection of methotrexate is best treatment modality
    d. Conservative management is feasible for many women

Answers

1.	e	2.	b	3.	d	4.	a	5.	d	6.	b
7.	b	8.	c	9.	c	10.	c				

4.3 GESTATIONAL TROPHOBLASTIC DISEASE

VP Radhadevi, PK Sekharan

INTRODUCTION

Gestational trophoblastic disease (GTD) is a group of premalignant and malignant conditions resulting from abnormal trophoblastic proliferations. The benign lesions are complete and partial hydatidiform moles, resulting from abnormal fertilization of a defective ovum, and in both the conditions, there is an excess of paternal genome. The malignant lesions are gestational choriocarcinoma (CC), invasive mole (IM), placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT)—together grouped as gestational trophoblastic neoplasia (GTN). The atypical placental site nodule (APSN) is also added to the GTD spectrum

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5.18 COVID–19 IN PREGNANCY

Ajith S, Kasturi Donimath, Sabnam Nambiar

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) strain of corona virus and first reported from Wuhan City, China toward the end of 2019, was declared a pandemic by World Health Organization (WHO) on March 11th, 2020. The common cold, Middle East respiratory syndrome (MERS) and SARS are the other known common corona virus infections. This rapidly evolving virus has shown numerous mutations with development of various new strains, four of which – alpha, beta, gamma, and delta variants are increasingly of concern. The delta variant has been found to have a significantly higher transmission rate and resulted in a more severe disease.

The viral transmission occurs through close contact with infected person and rarely from contaminated surfaces.

Pregnancy seldom increases the chances of infection with the COVID-19 virus. In fact, various studies have shown that the affected pregnant women are rarely symptomatic and those symptomatic presenting only with mild or moderate cold/flu-like symptoms. The chief symptoms are cough, fever, sore throat, dyspnea, loss of sense of taste, anosmia, and diarrhea.[1] The impact of pregnancy, on development of prolonged symptoms or signs after acute COVID-19 infection ("long COVID" or post COVID), is rather indistinct at present.

CLINICAL STAGES OF SEVERITY

- *Mild:* No breathlessness or hypoxia, respiratory rate <24/minute, SpO_2 >94 on room air and otherwise asymptomatic
- *Moderate:* Dyspnea and/hypoxia, respiratory rate 24–29/minute, SpO_2 90–94 on room air or fever and cough
- *Severe:* Dyspnea and/hypoxia, respiratory rate > 30/minute, SpO_2 <90 on room air, pulse rate >125 with or without pneumonia
- *Critical:* Acute respiratory distress syndrome (ARDS), sepsis, or complications such as pulmonary embolism, acute coronary syndrome.

Although generally asymptomatic, the pregnant women have an increased risk of developing severe illness when compared with non-pregnant women, especially in the third trimester. The pregnant women who develop severe disease have been found to require higher rates of intensive care unit (ICU) admissions and need for ventilation.[1]

Additional risk factors for severe infection:[2]

1. *Obesity:* Body mass index (BMI) > 30 kg/m^2
2. *Pre-pregnancy comorbidity:* Diabetes, hypertension
3. Maternal age > 35 years
4. Living in areas or households of increased socioeconomic deprivation.

EFFECT OF COVID-19 ON PREGNANCY

There is no evidence of increased miscarriage rate or congenital anomalies after COVID-19 infection. There may be a 2–3 times increase in preterm deliveries in symptomatic women. According to the PregCOV-19 Living Systematic Review, risk of preterm birth is approximately 17%, most of these being iatrogenic (94%).[1] The COVID-19 infection is associated with approximately double the risk of stillbirth and a predisposition for increased incidence of small for gestational age babies.[2] The risk of vertical transmission is low, most babies tested positive are asymptomatic.

There are reports of higher rates of perinatal mental health disorders such as anxiety and depression during the pandemic. The COVID-19 infection is also associated with an increased rate of cesarean birth. The UKOSS data shows a cesarean section rate of 49% in symptomatic women compared to 29% in a historical control group in 2018.[2]

Antenatal Care during COVID Pandemic

The antenatal care is an essential service. The pregnant women should be advised to continue their antenatal visits and care although some modification of services could be advised to enable social distancing and good ventilation to reduce the risk of transmission of virus. Consideration should be given to pregnant women with comorbidities which make them susceptible to severe COVID-19. Shared waiting areas should be avoided as far as possible. There should be an area segregated to see suspected or confirmed cases.

The option of remote consultation such as video conferencing or teleconferencing should be considered if there is local lockdown. However, lack of mobile devices/computer and internet access could pose severe limitations. Lack of privacy could prevent women from disclosing personal and sensitive issues. The pandemic has caused higher levels of anxiety and other mental health problems in pregnant women than others, hence mental health should be assessed at each visit and support provided to those in need of the same.

Care of Suspected Cases

Women with symptoms suggestive of COVID-19 should undergo appropriate testing **(Fig. 1)**. They should be self-isolated and admitted to hospital if symptoms are severe, associated comorbidities are present or if near term.

Antenatal Management of Confirmed Cases

This can be divided into those of management of asymptomatic women without any comorbidities, symptomatic women, or women with comorbidities and of women with severe infection.

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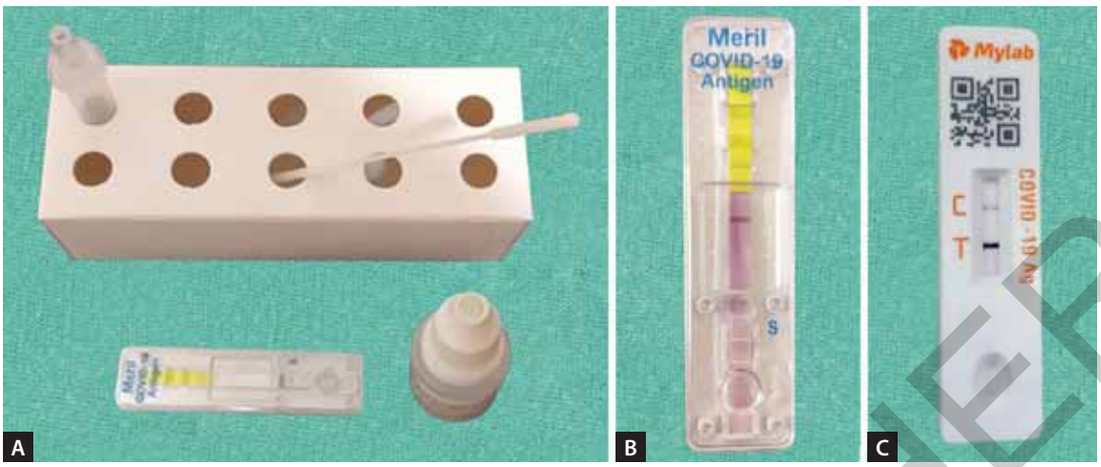

Figs. 1A to C: Rapid antigen testing for COVID-19. (A) Test set up; (B) Negative test; (C) Positive test.

Management of Asymptomatic Women without Comorbidities

They may be advised care at home especially if < 34 weeks, with advice on self isolation. They should continue iron, calcium and vitamin D supplementation and they should be advised against complete bed rest and dehydration to try and prevent venous thromboembolism. They should be informed about red flag symptoms such as breathlessness, chest pain, drowsiness, hemoptysis, cyanosis, and hypotension and should contact medical facility immediately if they are present. Severe fatigue, malaise, and persistent fever are indicative of active disease and medical advice should be taken. It is preferable to procure a pulse oximeter for personal use. They must report to the medical facility if symptomatic or if SpO_2 falls below 94%. They must be taught 6-minute walk test – where they walk for 6 minutes or take 40 steps and are told to measure the SpO_2 before and after – a fall of more than 3% from baseline is significant and they must promptly seek medical advice. Women more than 34 weeks should be assessed in a medical facility and if stable allowed home care.[3]

Management of Symptomatic Women and those with Comorbidities

They require hospital admission, investigations, and symptomatic treatment **(Table 1)**. Laboratory investigations such as complete blood count, blood sugar, liver function tests, renal function test, C–reactive protein and serum electrolytes should be sent **(Table 2)**. ECG is advised for patients with tachycardia or other heart rate abnormalities. Chest X-ray with shielding of abdomen is advised in those with persistent cough or fall in SpO_2. Additional markers such as D-dimer, serum ferritin, LDH and CPK are sent if persistent symptoms. Symptomatic treatment includes paracetamol and antitussives. Oseltamivir 75 mg twice daily for 5 days may be started if suspicion of H1N1.

TABLE 1: Laboratory investigations for hospital admitted patients.[3]

At admission	CBC, RFT, LFT, CRP, RBS, serum electrolytes, ECG, pulse oximetry
If clinically Indicated	Portable CXR, D-Dimer, ferritin, LDH, CPK, procalcitonin, blood culture, troponin T, HRCT thorax (only in case of worsening)
To repeat every 48 hours if clinically deteriorating	CBC, creatinine, AST/ALT, CRP, LDH, CPK, ferritin, D-Dimer
For immunocompromised patients, e.g., transplant recipients, HIV	Tests to rule out opportunistic infections such as *Mycobacterium tuberculosis, Pneumocystis jiroveci*, etc.

TABLE 2: Risk markers in COVID-19.

Marker	***Normal value***	***High risk***
CRP	<5	CRP >100 mg /L
D-dimer	*1st trimester:*169–1,202 µg/L *2nd trimester:* 393–3,258 µg/L *3rd trimester:* 551–3,333 µg/L	
Ferritin	<60	Ferritin >300 µg/L
LDH	<400	LDH >400 U/L
		NLR >3.13, ALC <0.8

(ALC: absolute lymphocyte count; NLR: neutrophil lymphocyte ratio)

Steroids

Steroids are generally started only after 5 days of disease onset. The appropriate dose of steroid in the right patient at the correct time can prove lifesaving. Budesonide 800 µg MDI/DPI twice a day is started when cough is persists beyond 5 days of onset of disease.

Indications of Parenteral or Oral Steroids[3]

1. Moderate to severe rise in respiratory rate or fall in SpO_2
2. 3% fall in SpO_2 with 6-minute walk test

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3. Bronchopneumonia
4. Marked rise in proinflammatory markers.

Involvement of multidisciplinary team is of prime importance. The usual regime is to start with Injection dexamethasone 6 mg intramuscular 12 hourly × 4 doses, followed by Injection methylprednisolone 0.5–1 mg/kg body weight or 40 mg once daily or oral prednisolone 40 mg once daily for 10 days or until discharge whichever is earlier. Higher dose of steroids may be needed in severe cases and can be decided by the multidisciplinary team. Injection Dexamethasone can be skipped if lung maturity is not an issue. Prolonged use of dexamethasone is not recommended in pregnancy as it crosses the placenta. Methylprednisolone does not cross placenta; hence, it cannot be a substitute for dexamethasone to enhance lung maturity. Blood sugar should be monitored in patients on steroids.

Anticoagulants

Pregnancy is a hypercoagulable state. Evolving evidence suggest that patients admitted to hospital with moderate or severe COVID-19 infection are also hypercoagulable.

Women who are advised self-isolation at home should be advised regarding adequate hydration and to stay ambulant. Venous thromboembolism (VTE) risk assessment should be assessed, and appropriate anticoagulant should be advised. All pregnant admitted should be offered prophylactic low-molecular-weight heparin (LMWH), unless birth is expected within 12 hours or there is significant risk of hemorrhage. Prophylactic dose of enoxaparin is 1 mg/kg body weight, higher dose of enoxaparin may be needed in severely ill patients or those with higher D-dimer values (1 mg/kg twice daily). The LMWH should be stopped 12 hours prior to delivery or cesarean section (24 hours if taking higher dose). Thromboprophylaxis should be continued for duration of hospital stay and 10 days following hospital discharge. A longer duration thromboprophylaxis should be considered in patients with persistent morbidity. Thrombocytopenia may be associated with severe COVID-19 infection, LMWH and aspirin should be stopped if platelet count is less than 50,000.

If the woman is admitted within 6 weeks postpartum, they should be offered thromboprophylaxis during the entire period of hospital stay and for at-least 10 days following discharge. The duration may be extended to 6 weeks for those with significant ongoing morbidity.

Remdesivir

Remdesivir should only be considered in those who are not improving or who are deteriorating.[2] Though its safety in pregnancy is not established it may be offered on a compassionate basis after taking consent. It needs to be started within 10 days of onset of symptoms. The recommended dose is 200 mg IV on day 1, followed by 100 mg IV daily × 4 days. The RFT and LFT must be normal.

Tocilizumab

Tocilizumab (interleukin-6 receptor antagonist) improve outcomes, including survival, in hospitalized patients with hypoxia and evidence of systemic inflammation (CRP above 75 mg/L)[2]. The data on use of tocilizumab in pregnancy is limited, but there is no report of teratogenicity. The decision to start tocilizumab should be taken by a multidisciplinary team.

Monoclonal Antibodies

Monoclonal antibodies (casirivimab and imdevimab) may be considered in pregnant and postpartum high risk patients with COVID-19 and who are vulnerable to severe infection before progressing to hypoxia.[2]

CLINICAL DETERIORATION

The signs of decompensation are:[2]

1. Increasing oxygen requirements or FiO_2 above 35%
2. Increasing respiratory rate above 25 breaths/minute
3. Reduction in urine output/acute kidney injury
4. Drowsiness

Chest imaging: X-ray chest/HRCT Thorax should be performed when indicated and not to be delayed for concerns regarding radiation exposure.

A multidisciplinary team should assess the woman and a decision taken regarding need for delivery/cesarean section of a pregnant woman in third trimester to facilitate resuscitation. Oxygen should be given to maintain SpO_2 of 94–98% using nasal cannula, face mask, venturi mask, non-breather mask, noninvasive continuous positive airway pressure (CPAP), intubation and positive pressure ventilation (IPPV) and extracorporeal membrane oxygenation (ECMO) as appropriate. Care should be taken regarding fluid management, hourly input/output chart should be recorded in patients with moderate/severe symptoms and aim to maintain a neutral fluid balance. There should be suspicion of bacterial infection if white cell count is raised (lymphocytes are usually low with COVID-19) and antibiotics should be started. In patients with chest pain, worsening hypoxia or in those whose breathlessness persists or worsens after expected recovery from COVID-19, a differential diagnosis of pulmonary embolism or heart failure should be considered and additional tests such as ECG, echocardiogram, CT pulmonary angiogram and ventilation perfusion lung scan may be done.

When to Deliver?

The decision regarding timing and mode of delivery is mostly made on obstetric grounds. Sometimes decision has to be taken considering the maternal resuscitative purpose or because of concern regarding the fetal health. The decision must be taken by multidisciplinary team. It must be decided on individual basis beyond 26–28 weeks if the patient is deteriorating and not responding to noninvasive ventilation

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and if invasive ventilation is needed. The mode of delivery depends on the emergent nature and gestational age and will usually be through cesarean section. The mode of anesthesia also depends on general condition of patient. When iatrogenic preterm delivery is required, consider giving antepartum steroids for lung maturity and $MgSO_4$ for neuroprotection.

Intrapartum Care

Labor should be conducted in a dedicated labor room. There are reports of increased risk of fetal compromise in active labor and cesarean section in symptomatic women, hence continuous electronic fetal monitoring should be offered to symptomatic women. The number of staff members entering the room should be minimized. The hospital should have a local policy regarding companion during labor. In addition to routine parameters monitored in labor, SpO_2 also should be monitored carefully. The time taken for shifting the patient to COVID operation theater and for donning of PPE should be considered while taking decision for emergency cesarean. The option of epidural analgesia should be discussed. The Entonox (50% nitrous oxide and 50% oxygen) with single-patient microbiological filter is also safe. The delayed cord clamping and early skin to skin contact with baby in line with usual practice can be advised. The healthcare professionals should wear appropriate PPE while giving care to the woman.

Postpartum Care

The woman should be supported to take an informed decision regarding breastfeeding. The breastfeeding and rooming-in can be permitted, the risk of newborn getting infection from the mother being low especially if appropriate precautions such as wearing a mask and practicing hand hygiene are followed meticulously.[4]

Breast milk provides protection against many illnesses and is the best source of nutrition for babies. The rooming-in has the added benefit of facilitating breastfeeding and maternal-newborn bonding. The precautions recommended are washing hand with soap and water for at least 20 seconds before holding or caring the baby, keeping the baby more than 6 feet from the mother, and wearing a mask. When women are expressing breast milk in hospital a dedicated breast pump should be used and adhere to recommendations for pump cleaning after each use. The baby should be separated only if maternal critical care or additional neonatal care required.[5]

Thromboprophylaxis should be offered for at least 10 days following discharge. Proper contraception advice should be given. The family members should be given proper advice regarding self-isolation, identifying illness in newborns, and worsening of woman's symptoms and appropriate contact details if they have concerns. The institution should have proper discharge guidelines.

Follow-up of Affected Pregnancies

There should not be any change in the standard antenatal care. Those affected in first trimester or early second trimester should be offered a detailed anomaly scan. Those affected in late second trimester or in third trimester should be offered a growth scan after 2 weeks.

Vaccination

Vaccination against COVID-19 is strongly recommended in pregnancy.[2] It can be given at any time in pregnancy. The rare syndrome of vaccine-induced thrombosis and thrombocytopenia (VITT) has been reported after viral vector vaccine such as Covishield, Astra Zeneca vaccine, Johnson and Johnson vaccine, etc. It is an idiosyncratic reaction and not associated with any of the usual venous thromboembolism risk factors. The usual presentation is 5–28 days after first dose. The risk is extremely low (1:100,000). There is no evidence that pregnant and postpartum women are at higher risk of VITT. There is no known risk of VITT with Pfizer-BioNTech and Moderna vaccines. Breastfeeding is not a contraindication for COVID-19 vaccination. It does not affect fertility and vaccine can be given to those planning pregnancy and those getting fertility treatment.

CONCLUSION

COVID-19 is an emerging and evolving threat, more so in pregnancy. Hence, we have to prepare accordingly and adopt practical and pragmatic approaches toward containing the spread of the disease along with taking headlong the challenge of treatment and care of all those affected especially the pregnant women. The situation may continue perceptibly for some time to come, hence there has to be constant vigilance and it is not time to let down our guard, yet!

KEY MESSAGES

- Pregnancy seldom increase the chance of getting COVID-19 infection, most patients are asymptomatic or with mild symptoms.
- Those admitted with severe symptoms, there is more need for ICU admission and ventilatory support.
- Anticoagulant has an important role in management as both pregnancy and COVID-19 infection are hypercoagulable state.
- The right dose of right steroid in right time is life saving.
- Monoclonal antibodies may be considered in high-risk pregnant women before developing hypoxia.
- Tocilizumab may be lifesaving in patients with hypoxia.
- Delivery or cesarean section may be needed in clinically deteriorating women in third trimester to facilitate resuscitation.
- Vaccination is strongly recommended in pregnancy.

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LONG QUESTION

1. Discuss the clinical presentation and management of COVID-19 infected pregnancies.

SHORT QUESTIONS

1. How does COVID-19 infection affect pregnancy?
2. How do you manage clinically deteriorating pregnant COVID-19 infected patients?
3. Discuss labor management of Covid-19 infected patients.
4. Discuss the post-partum management of COVID positive patients.
5. Discuss the importance of COVID vaccination in pregnancy.

MULTIPLE CHOICE QUESTIONS

1. Which COVID vaccine is associated with VITT?
   a. Covishield b. Moderna
   c. Pfizer-BioNTech d. All the above
2. Which one is true regarding postpartum care?
   a. Thromboprophylaxis is important
   b. Absolute bed rest needs to be advised
   c. Breastfeeding is contraindicated
   d. Rooming-in is not advised
3. Risk factors for severe COVID-19 infection in pregnancy are all, except:
   a. Obesity
   b. Preexisting diabetes
   c. Age >35 years
   d. Placenta previa
4. Which of the following is true?
   a. Remdesivir should be started in all symptomatic COVID positive pregnant ladies
   b. Tocilizumab is safe in pregnancy
   c. Monoclonal antibodies are option in vulnerable pregnancies before development of hypoxia
   d. Methyl prednisolone is useful in enhancing fetal lung maturity
5. Which of the following is false?
   a. Delivery should be considered in pregnant Covid positive ladies in third trimester needing intubation to help resuscitation
   b. Epidural analgesia may be used for labor analgesia
   c. Entonox is contraindicated as labor analgesia in Covid positive patients
   d. Prophylactic LMWH should be stopped 12 hours before delivery/cesarean
6. Which of the following is sign of decompensation?
   a. Acute kidney injury
   b. Drowsiness
   c. Increasing oxygen requirement FiO_2 >35
   d. All the above
7. Which of the following is true regarding management of labor in symptomatic COVID positive patients?
   a. Continuous electronic fetal monitoring is recommended
   b. Cesarean section is the best mode of delivery
   c. Early cord clamping is recommended
   d. Skin to skin contact with baby should be avoided
8. Vaccine-induced thrombosis and thrombocytopenia is:
   a. Idiosyncratic reaction
   b. More common in pregnancies compared to age matched controls
   c. More common hypertensive patients
   d. More common in patients with past history of venous thromboembolism
9. Regarding vertical transmission of COVID-19:
   a. Cesarean section is protective
   b. Vertical transmission rate low
   c. Use of antiviral medication reduce risk
   d. Early cord clamping reduce the risk
10. Upper limit of normal D-dimer value in third trimester pregnancy:
    a. 1111 b. 2222
    c. 3333 d. 4444

Answers

1.	a	2.	a	3.	d	4.	c	5.	c	6.	d
7.	a	8.	a	9.	b	10.	c				

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- Chapters are compiled into two volumes for quick reference
- Contributing authors are experts in their fields and represent a broad geographic distribution as well as representing the public and private healthcare settings
- Key messages, diagrams, photographs and tables have been provided to adequately illustrate the subject matter
- Multiple choice questions, short and long questions with every chapter to facilitate self-assessment and preparation for examinations.

Hope that the book is useful for every trainee and practitioner in their endeavor to lay a foundation, and constantly endeavor to evolve to a higher clinical standard of care.



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