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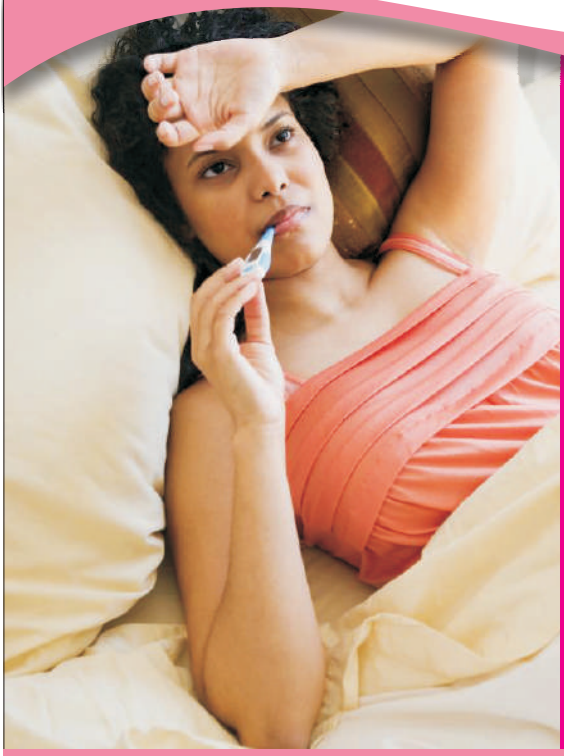

Fever in Pregnancy

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From the PRESIDENT'S DESK...

Dr. ALPESH GANDHI
President FOGSI 2020

A warm wishes to all!

I am very happy that ICOG is bringing out an Ecampus Newsletter on 'Fever in Pregnancy' at the most appropriate time and I must congratulate Dr. Mandakini Megh, ICOG Chairperson and Dr. S. Sampathkumari for their important and valuable effort in preparing this booklet. The topics are well chosen and the contributors have given their best.

Corona, Quarantine, Lockdown have all affected our many plans. Yet, we are happy that we could reach out to our beloved members through electronic means. Let us save all our energies and once the norms are eased we shall work vigorously and enthusiastically to mark a difference as FOGSIans.

With regards to all!

Dr. ALPESH GANDHI
President FOGSI 2020

From the CHAIRPERSON'S DESK...

Dr. MANDAKINI MEGH
Chairperson, ICOG

Greetings from ICOG, the academic wing of FOGSI!

Team ICOG 2020 has another proud occasion. It has been running many courses digitally, yet this year it added one more course in 'Adolescent Gynaecology', run on 6 sessions spread over 3 Saturdays. The tremendous response it received and the encouraging words from many stalwarts of FOGSI are sure to take this course through many editions in the coming months. I congratulate the team behind this massive effort and fervently believe the incoming teams will take this course to higher levels.

I am also happy that ICOG with Dr. S. Sampathkumari as the Editor has come up with another E Campus book, a compendium of sorts on 'Fever in Pregnancy' during this trying time of Corona pandemic. The topics are well researched and put together neatly to serve as a ready reckoner for all practicing OGcians.

As the Chairman of ICOG, I appreciate the efforts taken by Dr. S. Sampathkumari, Editor, Dr. T. Ramani Devi, co-editor and all the ICOG members, who have toiled their best in writing the various chapters of this book.

Long live FOGSI – ICOG!

Dr. Mandakini Megh
Chairperson, ICOG

From the PRESIDENT ELECT'S DESK...

Dr. S. SANTHAKUMARI
President-Elect: FOGSI

Warm wishes to all!

It is nice to know that ICOG is coming out with a newsletter dedicated to Fever in Pregnancy and I congratulate ICOG and the Editor Dr. S. Sampathkumari for the effort. I also congratulate the ICOG Chairperson Dr. Mandakini Megh, Dr. Parag, ICOG Secretary, Dr. Ramanidevi, Vice President, FOGSI and the co editor of this newsletter along with all the contributors for their exemplary contributions.

'Fever in Pregnancy' newsletter is coming at the right time when the whole world is fighting with the pandemic and the medical world is working overtime to find a cure, a vaccine to combat with Corona or Covid19. Mankind had won over pandemics like 'Black Death', Influenza, Plague and Spanish Flu in the past. Similarly we will definitely overcome this disease too. Let us all support the preventive measures, the frontline workers in this hour crisis.

Dr. S. SANTHAKUMARI
President-Elect: FOGSI

From the SECRETARY'S DESK...

Dr. PARAG BINIWALE
Secretary, ICOG

Greetings from ICOG!

Fever in pregnancy is a challenge for us obstetricians as rise in body temperature has an impact not only on mother but foetus also. The result can be preterm birth, foetal distress or even foetal demise.

In difficult covid times, whenever we encounter a pregnant woman with fever; the first thing that comes to our mind is covid19. However, there is a spectrum of infections from bacterial, viral to parasitic. These are responsible for morbidity IN the mother for last so many years. The newest infection is covid19 which has posed a lot of challenges to the women and the health care provider.

My heartfelt thanks to Dr Sampathkumari, Governing Council member of ICOG for taking up this task of putting together the latest information about fever in pregnancy. She has also chosen authors very wisely & all of them have done full justice to this challenging situation.

I am sure this publication will be a ready reckoner for all clinicians and in turn help them to manage women with fever efficiently.

Happy reading

Dr. Parag Biniwale

Secretary, ICOG

From the EDITOR'S DESK...

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The days of celebration - partying, happy congregations, be it for a wedding in the family or in the near and dear ones, scholar assemblies or for that matter party meetings have all come to a standstill!. Wasting of food and splurging of money in unwanted events are in check today, thanks to the novel virus called COVID19!

And as always the world will find means to circumvent such difficulties as it had in the past. Yet, the history will mark this period as the darkest for the reason despite mammoth scientific advancements the world was reeling under a microbe – a virus or a bacteria or a rascal protein molecule. Notwithstanding the historic feats the world is yet to come to grip with this deadly virus and its devastating consequences economically and socially.

While the debate is raging whether it is a man made virus or something that evolved naturally, it has completely crippled life on planet earth. Melting glaciers on one side, rising temperatures, burning forests and shrinking agriculture will all add to the bleak future that our children and their children are going to inherit.

Humanity revered doctors and deified them till now. But now the scenario has changed. Doctors are accountable and are answerable to many government legislations and the junta is ready to pounce on the doctors at the slightest provocation by the vested interests. Amidst these circumstances comes Corona to highlight to the world the selfless services of the medical fraternity – doctors, nursing staff and diagnostic support staff. Many of our brethren have laid down their precious lives in their fight against the virus.

ICOG wanted to seize this opportunity to educate and empower its members. Thus was born this e campus newsletter, which is a compendium of sorts on fevers that could impact the pregnancies across board. The readers will find it handy and useful in their service to mankind.

Our sincere thanks to Dr. Mandakini Megh, ICOG Chairperson, Dr. Parag Biniwale, Secretary ICOG and above all our FOGSI President Dr. Alpesh Gandhi who is ever ready to hold hands whenever such efforts are taken up, and Dr. Jaydeep Tank is another man, our FOGSI Secretary General, who remains as a backbone always – A sincere and heartfelt thank to all these veterans for their consent and support right through.

Thanks to all the contributors for their valuable time and effort. A bouquet to Mr. H. R. Balaji, Vice President, M/s. Shield Health Care for his help and support through his esteemed organisation.

What was meant to be a preface to this issue has turned out to be commentary on today's life. Nevertheless if this small write up churns the heart of a few among its readers we will be happy that we have attempted our mite in this gigantic social cause. Thank you one and all. Have a feast of scientific information.

Au revoire until we meet next!

Editor - **Prof. Dr. S. Sampath Kumari**

Co - Editor - **Dr. T. Ramani Devi**

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UTI IN PREGNANCY

Urinary tract infection (UTI) is the most common bacterial infection and second most common medical disorder after anaemia affecting pregnancy. Overall prevalence of UTI in pregnancy approximately 10%-15%.UTI in pregnancy adversely affects maternal and fetal outcome and there is increased risk of ascending infection . It can be asymptomatic, as well as symptomatic, posing great diagnostic challenge. Therefore, UTI in pregnancy is considered a complicated infection and requires a special diagnostic approach and management.

Definition - Normal urine is sterile: voided urine becomes contaminated in the nonsterile distal urethra. Urinary tract infection is diagnosed when bacterial monoculture in quantity >105 CFU per ml in 2 consecutive midstream, clean catch urine specimen is found. Midstream samples of urine (MSSUs) after careful decontamination of the urethral meatus is taken.

For practical purpose one positive urine culture is accepted. Diagnosis for Quantitative urine culture is, therefore, a necessity for diagnosis.

The criterion of105 bacteria/ml concentrations represent chance of contamination of <1%. With use of the lower concentration of e.g.104 CFU/ml bacteria chances of false positive is high as it may be due to bacterial contamination rather than true infection.

Urine is bacteriostatic to most local commensal bacteria and this is thought to result from its relatively acidic pH, high osmolality, high urea concentration and by free antegrade flow through the ureteral and urethral valves. In pregnancy, significant physiological changes occur in the urogenital tract, increasing the potential for pathogenic colonization. Bladder volume increases and detrusor tone decreases. Additionally, 90% of pregnant women develop ureteric dilatation as the result of a combination of progestogenic relaxation of ureteric smooth muscle and pressure from the expanding uterus. There is relative sparing of the left ureter because of protection from the sigmoid colon and upper rectum. The net effect, however, is increased urinary stasis, compromised ureteric valves and vesicoureteric reflux, which facilitates bacterial colonization and ascending infection.

Seventy percent of pregnant women develop glycosuria and this , in combination with physiological aminoaciduria of pregnancy and a fall in urine osmolality, favours bacterial proliferation urethral instrumentation and catheterisation predispose to ascending bacteriuria

Microbiology:

Escherichia coli (MC)-63%-85%
Staphylococcus saprophyticus (second most common) -15%
Klebsiella pneumoniae- 8%
Staphylococcus aureus-8%
Group B streptococci- 2-7%

Classification of UTI in pregnancy:

In pregnant women UTIs are classified either as asymptomatic bacteriuria (ASB), when the infection is limited to bacterial growth in urine, symptomatic infections (acute cystitis, acute pyelonephritis), when bacteria invade urinary tract tissues, inducing an inflammatory response.

ASYMTOMATIC BACTERIURIA-

Asymptomatic bacteriuria is defined as the presence of a positive urine culture in an asymptomatic woman. It occurs in 2 to 7-10% (1,2,3,4) percent of all pregnancies.

Screening for asymptomatic bacteriuria should be performed ideally at first prenatal visit or at 12 to 16 weeks gestation on all women. Urine microscopy and culture remain the gold standard in detection of asymptomatic bacteriuria. ASB is diagnosed when in asymptomatic gravid woman urine culture is positive. Urine dipstick test and urine analysis alone is not recommended for diagnosis of ASB in pregnancy.

Risk factor:

Lower SES,
DM
H/O UTI
Multiparity

Anatomical or functional abnormality of urinary tract
Sickle cell trait

Asymptomatic bacteriuria is associated with an increased risk of adverse fetal outcomes, like preterm birth, low birth weight infant, PIH, ascending urinary tract infection. 30-50% of women will develop symptomatic UTI if not treated. If untreated serious maternal complication- acute pyelonephritis develops in 30-40% of patients of ASB (VS 3-4% in treated pt.) (5)

Maternal GBS bacteriuria in pregnancy indicates genital colonization of women with this bacteria and is a significant risk factor for PPROM, PTL and early onset severe neonatal infection.

Antibiotic treatment for asymptomatic bacteriuria is indicated to reduce the risk of acute cystitis, pyelonephritis, LBW neonates and Preterm birth.(6)

Treatment -

Co-amoxiclav 625mg TDS for 5 days or 7 days
Cefuroxime axetil 250mg BD OR 500mg BD for 5 days
Cefaclor 500mg for 5-7 days for women with mild penicillin hypersensitivity
Fosfomycin 3g stat dose
Nitrofurantoin 100mg BD PO for 7 days

UTI or GBS significant ASB should be treated.All of them (regardless of level of CFU/ml), at the time of labor or rupture of membranes, should receive appropriate intravenous antibiotics for the prevention of early-onset neonatal GBS disease, and do not need rescreening by genital or urinary tract culture in the third trimester, as they are presumed to be GBS colonized.

Follow -up

Upto 1/3 rd patients of ASB develops recurrent infection, so periodic screening is important. Repeat culture should be obtained 1-2 weeks after treatment, then monthly till delivery. Daily suppressive therapy is given if infection persists after 2 courses.

Management of persistant recurrent bactriuria

Nitrofurantoin 50-100 mg OD at bed time till delivery.

RECURRENCE IN LOW COUNT BACTERIUREA OR NEGATIVE CULTURE;

Uropathogenic E. coli (UPEC) like E.coli CFT073, UTI89, and 536 invades urothelial cells lining the urinary bladder which forms intracellular bacterial communities (IBCs) or BIOFILM. This infection remain undetected in normal urine culture and causes recurrence. It may presents as unexplained dysuria, urgency and known as INTERSTITIAL CYSTITIS OR BLADDER PAIN SYNDROME. For patients with recurrence associated with sexual activity, postcoital prophylaxis may be given — Nitrofurantoin 50-100 mg po or Cephalexin 250-500 mg PO.

Acute cystitis in Pregnanacy-Incidence-1%-4%

It should be suspected in pregnant women with complain of dysuria. It is diagnosed when symptoms such as dysuria, urgency, frequency, nocturia, haematuria and supra pubic discomfort are present in afebrile women with no evidence of systemic illness. + positive urine culture and sensitivity .

Treatment of acute cystitis in pregnancy should be initiated immediately to prevent spread of infection to kidney. Patients are advised for enhanced fluid intake, Tab. paracetamol for pain. Antibiotics should be started empirically after sending urine for culture and sensitivity)and adjusted later on according to urine culture sensitivity report.

Antibiotics-

Nitrofurantoin 50 mg 4 times /day or 100 mg modified release twice daily for 7 days
Cefalexin - 500 mg bd for 7 days.
Amoxicillin 500 mg thrice daily for 7 days.

If C/S report shows organism resistant to empirically started therapy in clinically improving pts.-

a. Change antibiotics according to c/s report
b. Repeat C/S of urine -if urine is sterile continue with same antibiotic, if bacteriuria persists change the antibiotic according to C/S report.

Follow up-

Post treatment urine culture should be offered to confirm eradication of bacteriuria and resolution of infection.

ACUTE PYELONEPHRITIS – It is usually a consequence of undiagnosed or inappropriately treated lower UTI, or a complication of 30–40% of cases of untreated ASB . The overall incidence of pyelonephritis reaches up to 2% of all pregnancies (vs. < 1% in the general population)

Diagnosis- Low threshold for suspicion is needed for diagnosis when a pregnant patient complains of symptoms of Fever > 38°C, lumbar pain, skeletal and joint pains, nausea/vomiting with or without accompanying dysuria, polyuria, costovertebral angle tenderness, in association with positive urine culture.

Treatment-All suspected cases of pyelonephritis should be hospitalized at least for the initial 48 h of treatment.

Investigation:

Complete blood counts,
Electrolytes, creatinine,
Liver parameters,
Coagulation profile

Ultrasound scan - Dilation of pyelocalyceal systems and allows exclusion of other causes of the symptoms (e.g. renal abscess, ureter obstruction, other abdominal infections).

Hydration of the patient is a very important. In all patients, antibiotics should be given parenterally, for at least the first 48 h (until the resolution of fever).Treatment is initiated empirically and verified after obtaining the microbial sensitivity test results. Forty-eight hours after resolution of symptoms,

administration may be switched to the oral route. In case of fever persisting for more than 48 h, blood and urine cultures should be repeated, and any possible causes of treatment failure (perirenal abscess, lithiasis, congenital or acquired structural changes within the urinary tract) have to be carefully considered. Antibiotic therapy is usually continued for 10–14 days.

Ceftriaxone 1 g every 24 h
Cefepime 1 g every 24 h
Amoxicillin with clavulanic acid 1.2 g every 12 h
Aztreonam 1 g every 8–12 h

Treatment of Severe acute pyelonephritis--

Ticarcillin with clavulanic acid 3.1 g every 6 h
Piperacillin with tazobactam 3.375 g every 6 h
Meropenem 0.5 g every 8 h
Ertapenem 1 g every 24 h
Doripenem 1 g every 8 h

COMPLICATION - acute kidney injury, Anaemia, Hypertension, PIH, Sepsis and Septic shock, ARDS. Complications are due to release of endotoxin and systemic inflammatory response with endothelial injury.

Risk of PTL is high

Suppressive therapy is recommended for rest of pregnancy to prevent recurrence.

Obstetric Management - Pyelonephritis is not a indication for delivery .If induction of labor or LSCS is planned then it is ideal to wait till the patient is afebrile.

Safety of Drug -

Amoxicillin, Cephalosporin, Piperacillin, Tazobactam, Daptomycin, Azithromycin, Erythromycin, Morepenem, Clindamycin, Nitrofurantoin – class B

Trimethoprim and Sulfmethexazole - class C drug.

Nitrofurantoin and trimethoprim / sulfamethoxazole are to be avoided during the first trimester. In the second and third trimester, trimethoprim / sulfamethoxazole and nitrofurantoin are well tolerated and may be considered first line agents, except in the last week before delivery, when they may increase neonatal jaundice and predispose to kernicterus. Nitrofurantoin is theoretically associated with a risk of fetal or neonatal hemolytic anemia if the mother has glucose-6-phosphate deficiency,

1) When selecting an antibiotic for a true infection during the first trimester of pregnancy (that is, during organogenesis), one should consider and discuss with patients the benefits as well as the potential unknown risks of teratogenesis and maternal adverse reactions.
2) “Prescribing sulfonamides or nitrofurantoin in the first trimester is still considered appropriate when no other suitable alternative antibiotics are available”;
3) Pregnant women should not be denied appropriate treatment for infections because untreated infections can commonly lead to serious maternal and fetal complications

CONCLUSION:

UTI in pregnancy is common and a serious cause of maternal and perinatal morbidity and mortality. Clinical presentations include asymptomatic bacteriuria,acute cystitis and pyelonephritis. Pregnant women should be screened for asymptomatic bacteriuria by urine culture and treated with appropriate antimicrobials at first antenatal visit or at 12 week . Acute cystitis and pyelonephritis demand full assessment and treatment,with early involvement of other specialists in severe or systemic infection. All women should be reviewed to confirm post-treatment urine sterility.

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ANTIBIOTIC STEWARDSHIP IN OBSTETRICS

Antibiotic usage has remarkably increased in the last few decades. Injudicious use of antibiotics can lead to antibiotic resistance[1]and alteration of neonatal microbiome with short and long term effects. Antibiotic stewardship promotes optimal prescription of antibiotics and promotes safe and appropriate use of antibiotics. The 2019 WHO AWaRe classification classifies antibiotics into Access, Watch and Reserve groups to emphasise on their optimal usage and to make clinicians aware of antimicrobial resistance.

Antibiotics usage in Obstetrics:

In Obstetrics, antibiotics are often a part of prescription. Inappropriate usage of these drugs may give rise to resistance and shrink the spectrum of effective antibiotics. For rational use of antibiotics, spectrum of microorganisms associated with the diseased conditions should be known. Community and Institute specific sensitivities of common nosocomial pathogens should be considered while deciding empirical therapies.[2]

Broadly, the antibiotic usage in obstetrics is divided into Prophylactic and Therapeutic.

Prophylactic usage of Antibiotics in Obstetrics

Aseptic precautions and antibiotic prophylaxis are very essential in annulling the risk of infection post surgery. Hence the antibiotic chosen for prophylaxis should target organisms that are most commonly responsible for post operative infection. The common endogenous organisms are Staphylococcus aureus, Streptococcus, Peptostreptococcus, Propionobacterium on the Skin and Group B streptococcus, anaerobic streptococcus, alpha hemolytic streptococcus, Gardenella vaginalis and Clostridia in Vagina.[1]

Time of administration: Ideally, Prophylactic antibiotic should be given in operating patients just prior to the start of surgery to cover the time during which microbialinoculation may occur.[2]

An ideal prophylactic antibiotic should be safe, effective and should reach a dose in therapeutic range.

Cesarean section	Inj Cefazolin 1-2 g IV within 30 minutes of Skin incision. Additional dose if blood loss is more than 1500ml or surgery is more than 4 hours In BMI>35; double the dose If allergic to cefazolin, Inj Clindamycin 600mg IV or Inj Erythromycin 500mg IV	Ist generation cephalosporin with Gram positive and modest gram negative coverage. Side effects: Local phlebitis, pruritis, nausea, vomiting, leukopenia, thrombocytopenia
III or IV degree perineal tear	Inj Cefoxitin or Inj Cefotetan 1 gm IV	III rd generation cephalosporin. More active against anaerobes (mixed aerobic and anaerobic infections) Side effect: most commonly diarrhoea
Vaginal delivery, Operative vaginal delivery, Manual removal of placenta Term rupture of membranes, Meconium stained liquor, Postpartum Dilatation and evacuation Cerclage	No antibiotic recommended	

Therapeutic usage of antibiotics in Obstetrics:

Antepartum period:

Antibiotics are preferably avoided during pregnancy. It is important to choose an antibiotic that is FDA approved safe in pregnancy with no toxic effects on the fetus. The conditions where antibiotics are used are:

Urinary tract infections

Urinary tract infections may present as Asymptomatic bacteruria, acute cystitis or pyelonephritis.

Antibiotics used in these infections should target- E-coli, Gram positive organisms, Klebsiella and Proteus.

ACOG [2] recommends urine culture and sensitivity in first prenatal visit and a repeat urine culture sensitivity in third trimester.Mid-stream urine sample (MSSU) for culture and sensitivity should be preferred.

Urine alkalinising agents should be avoided as their

benefits have not been proved and there is a risk of hypernatremia and sodium retention in pregnancy.[3]

Days of therapy (DOT) could range from a single day course, three day course or 7 day course. The treatment rate in all of them is about 70% and there is always a chance of recurrence. Cochrane review[4] recommends that treatment schedules are directed by urine culture and sensitivity testing and that appropriate antibiotics are continued for at least 7 days. Several studies have tested shorter treatment courses and even single-dose schedules.[5]The rationale is to improve patient compliance and reduce side-effects but a Cochrane systematic review of short courses found insufficient evidence to confirm treatment efficacy.

Pyelonephritis: Most of the patients require admission. A full maternal clinical history and examination is mandatory to rule out any obstructive uropathy especially in the cases which do not respond after 24 hours of treatment. After sending MSSU culture and sensitivity, empirical treatment with a broad spectrum antibiotic is started. It is important to re-evaluate the treatment once culture reports are obtained after 48 hours. Treatment is usually continued for 10 days. Urinary sterility should be achieved at the end of treatment and throughout pregnancy.[6]

For Recurrent infections treatment has to be continued for longer duration (21 days or throughout pregnancy)

The drugs that are recommended are:[6]

Asymptomatic bacteruria - **Single dose**- Fosfomycin 3 g satchet single dose**3 day course**- Tab Amoxycillin 500mg 8 th hourly for 3 daysTab Cephelexin 500mg 6th hourly for 3 days**7 day course**- Tab Nitrofurantoin 100mg twice daily for 7 days
Acute Pyelonephritis- Inj Ceftriaxone 1 gm IV 12 – 24 hours followed by oral therapy for 1-2 weeksInj Ampicillin 1-2 gm 6 th hourly with Inj Gentamycin 1.5 mg/kg 8 th hourly/ extended spectrum antibiotic
Recurrent bacteruria- Tab Nitrofurantoin 100mg daily at bed time for 21 days or throughout pregnancy

Preterm premature rupture of membranes

Amniotic fluid is normally sterile but infections may ascend from vagina if membranes rupture and may lead to Chorioamnionitis (Suspected Triple I disease or Confirmed triple I disease).In suspected cases, antibiotics are continued to prevent postpartum endometritis.[7,8,9]

Preterm Premature rupture of membranes-[9] Inj Ampicillin 2 grams IV every 6 hours and erythromycin 250 mg IV every 6 hours x 48 hours followed by amoxicillin 250 mg PO every 8 hours for 5 days and erythromycin 333 mg PO every 8 hours for 5 days. If penicillin allergy, low risk (e.g., isolated maculopapular rash without urticaria or pruritis): cefazolin 1 gram IV every 8 hours x 48 hours and erythromycin 250 mg IV every 6 hours x 48 hours followed by cephalexin 500 mg PO every 6 hours x 5 days and erythromycin 333 mg PO every 8 hours x 5 days.If penicillin allergy, high risk (e.g., anaphylaxis, angioedema, respiratory distress, urticaria): vancomycin 1 gram IV every 12 hours x 48 hours and erythromycin 250 mg IV every 6 hours x 48 hours followed by clindamycin 300 mg PO every 8 hours x 5 days and erythromycin base 333 mg PO every 8 hours x 5 days
PPROM with Chorioamnionitis / Suspected Triple I disease/ Confirmed triple I disease[10.11]1- Inj Ampicillin 1-2 gm 6 th hourly with Inj Gentamycin 1.5 mg/kg 8 th hourly with Inj Metronidazole 500 mg IV 8th hourlyIf allergic to Penicillin- Inj Ceftriaxone 1-2 g IV / IM 8 th hourlyInj Cefotaxime 1-2 gm IV 8th hourlyInj Cefuroxime 1.5 gm IV/ IM 8 hourly With Inj Metronidazole 500 mg IV 8 th hourlyIf no response add InjPiperacillin and TazobactumIf MRSA Vancomycin / Teicoplanin/ Linezolid.

Intrapartum

No antibiotic usage is recommended in vaginal delivery, Operative vaginal delivery, Term rupture of membranes, meconium stained liquor or manual removal of placenta or Postpartumdilatation and evacuation. Prophylactic drugs-II generation Cephalosporins are used in III / IV perineal tear as discussed earlier.[12]

Postpartum

Bacterial infection of genital tract after child birth may lead to **Puerperal Sepsis.**

In maternal sepsis, *Escherichia coli* and group B streptococcus are the most common bacterial pathogens, but the most severe outcomes are associated with *E. coli* and group A streptococcus.[13] Therefore, the choice of antibiotic is guided by clinical assessment and the presumed site of infection. Hence, after sending blood and vaginal swab for culture sensitivity, empirical antibiotics are started to cover Gram-positive, Gram-negative and anaerobic organisms, as per community microbial susceptibility patterns. Based on the results of culture sensitivity, if needed, de-escalation is done. De-escalation of antibiotics could be considered if sterile site cultures are negative at 48 hours and the patient is clinically well[14]. The recommended antibiotics for puerperal sepsis are as follows[15.16]

Postpartum endometritis: Inj Clindamycin 600mg IV every 6 to 8 hours with Inj Gentamycin 1.5 mg/kg body weight 6-8 hourly should be continued for 24-48 hours till resolution of symptoms.If no response, Inj Ampicillin 1gm X 6thhourly to be added as enterococcus is suspected

Key points:

1) Judicious use of Antibiotics to prevent antibiotic resistance is the need of the hour in current obstetric practice
2) Routine antibiotics are not recommended for vaginal delivery, operative vaginal delivery, term rupture of membranes or meconium stained liquor
3) For Cesarean sections, Ist generation cephalosporins to be used as prophylactic drugs 30 minutes prior to incision
4) Nitrofurantoin is drug of choice for Asymptomatic bacteruria and Recurrent cystitis in pregnancy
5) Acute Pyelonephritis is to be treated with Intravenous antibiotic with Gram negative coverage-III generation Cephalosporin
6) PPROM with Triple I disease - Ampicillin and Aminoglycoside is the Ist line of treatment
7) Postpartum endometritis to be treated by injectable Clindamycin and Aminoglycoside. De-escalation can be considered based on culture reports.

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CONNECTIVE TISSUE DISORDERS: RHEUMATIC FEVER, RHEUMATOID ARTHRITIS, SYSTEMIC LUPUS ERYTHEMATOSUS

Pregnancy is a state of immune adaptations and immune tolerance to allow the "fetal allograft" to survive and grow in the mother's womb. Rheumatic diseases are associated with various aberrations in immune response. Patients with autoimmune disorders are prone to aggravations (flares) or amelioration of their disease in pregnancy, due to the complex immunological and physiological adaptations in pregnancy and postpartum.

Rheumatic fever

Acute rheumatic fever (ARF)is an autoimmune response/complication of pharyngeal infection with group A Streptococcus (GAS).ARF develops two to three weeks following pharyngitis and presents with polyarthritis, carditis, chorea, subcutaneous nodules, and erythema marginatum. Cardiac involvement is the dreaded complication of GAS and rheumatic fever, as cardiac valve damage, disability and death may occur years after initial rheumatic fever.

Primary infection with GAS and pharyngitis occurs in young children and adolescents, in whom incidence of an acute rheumatic episode following streptococcal pharyngitis is 0.5-3%.ARF is common in impoverished, overcrowded population in developing countries. Acute rheumatic fever is rarely seen in pregnant women but recurrent episodes can occur in women with rheumatic heart disease and these women require prophylaxis against GAS to prevent progression of cardiac disease.

Clinical presentation: ARF develops 2-3 weeks after an episode of GAS pharyngitis. The first manifestation of ARF is a painful polyarthritis, involving the large joints such as knees, ankles, elbows, or shoulders, along with fever and malaise. Arthritis occurs in 80% of patients. Suspicious signs for cardiac involvement include new or changing valvular murmurs, cardiomegaly, congestive heart failure, and/or pericarditis. Nearly 60% of patients with myocarditis develop mitral valve involvement or combined mitral and aortic valve involvement. Sydenham chorea, erythema marginatum and subcutaneous nodules are seen in very few patients. Acute attacks usually resolve in 12 weeks.

Diagnosis: Jones criteria for the diagnosis of initial ARF are the presence of two major manifestations or one major and two minor manifestations. For recurrent ARF, the criteria are two major manifestations, one major and two minor manifestations, or three minor manifestations.

Major manifestations comprise the following:

- Myocarditis
- Arthritis/ polyarthritis
- Chorea
- Erythema marginatum
- Subcutaneous nodules

Minor manifestations comprise the following:

- Polyarthralgia
- Fever ≥38.5°C
- Acute phase reactions: ESR ≥ 60 mm FHR and/or C-reactiveprotein ≥3.0 mg/dL
- Prolonged PR interval

Laboratory:

- Elevated or rising streptococcal antibody titer. Antistreptococcal antibodies usually reach a peak titer at the time of onset of ARF and are useful for diagnosis. Antistreptolysin O (ASO) are found in 80% of patients with ARF.
- A positive throat culture for group A ß-hemolytic streptococci can be found in 20-30% patients. Low sensitivity test.
- A positive rapid group A streptococcal carbohydrate antigen test. 90-100% specificity

Echocardiography is the gold standard for diagnosis and assessment of severity of rheumatic heart disease (RHD) andto identify candidates for secondary prophylaxis to prevent ARF recurrences.

Treatment: consists of anti-inflammatory therapy, antibiotic therapy and management of heart failure. Antibiotic mainstay is parenteral Benzathinebenzyl penicillin or in case of allergy oral cephalosporins. Antimicrobial therapy does not alter the course, frequency, or severity of cardiac involvement. Polyarthritis responds to high doses of salicylates and naproxen. Corticosteroids should be reserved for the treatment of severe myocarditis and arthritis.

Risk factors for recurrent ARF:

- Poor adherence to secondary prophylaxis.
- A greater number of previous attacks.
- A shorter time interval since the last attack.
- A higher likelihood of ongoing exposure to streptococcal infections
- Young age
- Presence of cardiac involvement (rheumatic myocarditis) likely to sustain increasingly severe cardiac involvement with each recurrence.

Prophylaxis of recurrent disease (GAS pharyngitis): The American Heart Association (AHA) Committee on Acute Rheumatic Fever recommends a regimenconsisting of benzathinebenzyl penicillin at 1.2 million units intramuscularly every 3 - 4 weeks. The more frequent dose in patients withheart disease who are at risk of repetitive exposure. Oral prophylaxis, which is less reliable, consists of penicillin V or sulfadiazine. If penicillin allergy is suspected, oral cephalosporin should be used.

AHA recommends that prophylaxis be continued for at least 10 years after the last episode of rheumatic fever oruntil patient is well into adulthood. Prophylaxis must continue indefinitely in patients with established heart disease or in those frequently exposed to streptococci.

Given the risks of ARF/RHD in pregnancy and labor, every female of childbearing age receiving secondary prophylaxis should be given detailed contraceptive advice, and asked to limit family size.

Rheumatoid arthritis

Rheumatoid arthritis is a chronic inflammatory autoimmune disease that affects women, often in their childbearing years. The incidence increases with age and is more frequent in females as compared to males. It's a debilitating disorder (deformities of multiple joints, interstitial lung fibrosis) and drugs available for pain and amelioration may be contraindicated in pregnancy.

Careful pregnancy planning is required to ensure that disease is in remission before conception, and to avoid medication that are contraindicated in pregnancy, before patient contemplates a pregnancy. Though disease remission or low disease activity is seen in pregnancy, there is postpartum flare which impairs the women's capability to take care of herself and infant.

Effect of RA on pregnancy: Most women with RA who desire pregnancy, have difficulty in getting pregnant. This is related to their age, nulliparous status, and preconception use of NSAIDs and prednisone. Disease activity as measured by Disease Activity Score in 28 joints (DAS28) is higher among women with fertility issues. There is increased chance of pre-eclampsia, preterm births, cesarean delivery and low birth weight. Though congenital malformations are not increased, there is 3 fold increase in risk of RA in children born to mothers with RA.

Effect of pregnancy on RA: Diseaseremission with lower disability measures and less pain are seen in third trimester of pregnancy, with deterioration in postpartum period. Remission of disease activity during pregnancy ismore likely in women who are RF negative.

Medication used for RA and effect on pregnancy

Medicine	Category	Indication	Comment
NSAIDS	B,	for symptom control	Interfere with blastocyst implantation, ↑risk of spontaneous abortion, PDA if used in 3/4 trimester of pregnancy
Prednisone	B,	for symptom control	Preterm birth, IUGR, cleft lip & cleft palate. Use lowest dose possible.
Hydroxychloroquine	C,	DMARDS	Preterm birth, IUGR
Sulfasalazine	B,	DMARDS	?hemolytic anemia in newborn
TNFα Inhibitor	B,	DMARDS	Preterm birth, neonatal infection, VACTERL defects
Azathioprine	D,	DMARDS	Though category D, reassuring data in pregnancy
Methotrexate	X	DMARDS	Spontaneous abortion, teratogenic, discontinue 3 months, prior to planning pregnancy.
Leflunomide	X	DMARDS	Birth defects, avoid use for 2 years, before planning pregnancy.
Tocilizumab	C	DMARDS	No sufficient data
Rituximab	C	DMARDS	Hematological abnormality in offspring, stop 1 year before planning pregnancy
Anakinra	B	DMARDS	Limited evidence on use in pregnancy
Abatacept	C	DMARDS	Avoid in pregnancy
JAK inhibitor		DMARDS	Avoid in pregnancy

DMARDS – Disease modifying anti-rheumatic drug

TNFα inhibitors - etanercept, adalimumab, infliximab, golimumab, certolizumab

Janus kinase (JAK) inhibitors - baricitinib, tofacitinib, upadacitinib

RA patients who desire pregnancy should be advised to try for conception when RA disease is in remission. In pregnancy NSAIDS and paracetamol can be safely used for pain relief, with addition of prednisone in low dose (10mg) if pain not controlled. In women with recurrent first trimester abortions, avoid NSAIDS.As regards DMARDS, hydroxychloroquine is drug of choice in pregnancy and lactation. Sulfasalazine, TNF α inhibitor and azathioprine may also be used. Folic acid supplementation must begin preconception.

The disease activity worsen in first-time breast feeding women, probably due to high prolactin levels. For management of an acute flare of RA in a lactatingmother, prednisone is advised. NSAIDs (ibuprofen, diclofenac and naproxen) are also an alternative for pain management. As regards DMARDS, HCQ is a safe option.

Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorders that affects women during their childbearing years. The incidence of SLE in pregnancy is 1/1250, more in African American women. Its etiology is complex with genetic and environmental factors. Pregnancy in SLE patients is associated with high maternal and fetal morbidity and mortality.

Effect of SLE on pregnancy: SLE increases the risk of spontaneous abortion, IUGR, IUFD, GDM, preeclampsia, UTI, premature rupture of membranes and preterm birth. The risk of preeclampsia is higher in patients with antiphospholipid antibodies, renal disease, hypertension or diabetes. Patients with SLE are at risk of cesarean delivery, postpartum hemorrhage and venous thromboembolism. If SSA and SSB antibodies are present, fetus is at risk of heart block and neonatal lupus. In women with SLE, major risk factors for adverse maternal and fetal outcomes include active/flaring SLE, especially active nephritis, history of lupus nephritis and presence of antiphospholipid syndrome.

Effect of pregnancy on SLE: pregnancy does not alter the long term prognosis of SLE. About one third of patients will have a flare in pregnancy or postpartum. Flares present with arthritis, rash and fatigue and are more likely in primigravidas, those with active disease at conception, patients with lupus nephritis and those who have discontinued HCQ. Pregnancy in women with lupus nephritis is associated with an increased risk of fetal loss and with worsening of the renal and extra renal manifestations. Women with lupus nephritis should be encouraged to delay pregnancy until the disease can be rendered inactive for at least 6 months.

Clinical picture: Signs & symptoms of SLE include fatigue, fever, arthritis, photosensitive rash, serositis, Raynaud phenomenon, glomerulonephritis, vasculitis and hematologic abnormalities.

Laboratory tests: positive antinuclear antibody titer, ↑ anti SS-A (Ro) and ↑ anti SS-B (La) titers, ↓ C3 and C4 complement levels, positive lupus anticoagulant test and ↑ anticardiolipin antibodies and anti β2 glycoprotiens.

Management in pregnancy: patients must be managed by obstetrician in consultation with rheumatologist. She must be advised to consider pregnancy when SLE has been quiescent for at least 6 months. Preconception review of her drugs and shift to safer options must be advised. Folic acid supplementation is began 3 months prior to planned conception.

At first antenatal visither complete blood picture (CBC), renal function test, lupus anticoagulant, anticardiolipin antibodies, anti SS-A (Ro) and anti SS-B (La) titers, and C3 and C4 complement levels must be assessed. Along with other routine antenatal lab tests. CBC with platelet count has to be repeated monthly while other tests are repeated in each trimester.

Women with SLE should take hydroxychloroquine (HCQ) starting preconception and continuing throughout pregnancy. In patients with elevated anti SS-A (Ro) and anti SS-B (La) titers, HCQ additionally reduces risk of fetal CHB.All patients with SLE are at risk of preeclampsia and must be given prophylactic low dose aspirin from 12-16 weeks of gestation.

Along with the fetal anomaly scan, a fetal echocardiography is advised from 16-24 week of gestation. The American College of Rheumatology advises women with anti SSA(Ro) and/or anti SSB(La) antibodies and fetal first- or second-degree heartblock shown on echocardiography, be treated with oral dexamethasone 4 mg daily. However if CHB is present, the ACRrecommends against treating with dexamethasone. Neonatal lupus (rash, hematologic and hepatic abnormality, heart block) is rare, occurs in 1-2%, SLE patients with anti SSA (Ro) and/or anti SSB (La) antibodies. The cutaneous manifestations resolve by 8th month but cardiac damage is permanent. After a child with CHB, the risk of recurrence of neonatal lupus in subsequent children is much higher.

Lupus flares present as fever, malaise, arthritis, rash or lymphadenopathy. Lab test will reveal low C3, C4 complement, active sediments in urine, elevated anti-ds DNA antibody titer, low platelets and leucopenia. HCQ, oral glucocorticoids, azathioprine, cyclosporine, and tacrolimus can be used to prevent or manage SLE flares duringpregnancy. Moderate-to-severe flares can be managed with methylprednisolone pulse therapy, intravenous immunoglobulin andplasmapheresis. Mycophenolic acid, cyclophosphamide, leflunomide and methotrexate should be avoided.

SLE patients with antiphospholipid antibodies, diabetes mellitus, or a previous episode of preeclampsia and those with lupus nephritis are at risk of pre-eclampsia. Such patients should receive low-dose aspirin (LDA). In women with SLE associated APS or primary APS, combination treatment with LDA and heparin is recommended to decrease the risk of adverse pregnancy outcomes.

Patients who are already taking warfarin because of a past venous or arterial thrombotic event should be switched to LMWH as soon as the pregnancy is diagnosed. Such women should continue anticoagulants for 3-6 months postpartum.

Fetal growth must be monitored by serial sonography from 24 weeks onward. Weekly NST and biophysical profile can be started from 28 weeks. In presence of IUGR, color Doppler should be performed and if

delivery before 34 weeks is anticipated, corticosteroids for fetal lung maturity are administered. Fetal loss is much higher in SLE patients. First-trimester losses are associated with APLA and with markers of lupus activity (low complement concentrations and increasedanti-double stranded DNA antibodies) and renal disease. Late losses are associatedwith antiphospholipid antibodies. Women with SLE and APLA should be managed with combination of low dose aspirin and LMWH to decrease fetal loss.

In the PROMISSE Study (Predictors of pregnancy outcome: Biomarkers in antiphospholipidantibody Syndrome and Systemic Lupus Erythematosus), circulating angiogenic factorsmeasured during early gestation proved to have a high negative predictive value for ruling out thedevelopment of severe adverse outcomes among patients with SLE and/or antiphospholipid syndrome.

For breast feeding mothers immunosuppressive agents are contraindicated and long-acting NSAIDs areinadvisable. Short-acting NSAIDs, antimalarials, low-dose prednisone, warfarin, and heparin seemto be safe.Hydroxychloroquine is also secreted in breast milk and may cause kernicterus in neonate. Low dose Prednisone can be used safely during breastfeeding.

Combined oral contraception carry risk of venous thrombosis and use is controversial.Progestinonly pill or LNG IUS are safe and efficacious.

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COVID 19 AND PREGNANCY

Novel corona virus (SARS-COV-2) is a new strain of corona virus causing COVID-19, It's characteristics especially those of person to person transmission were documented in December 2019.Shortly after, it was declared as a pandemic. Global Figures have been steadily climbing ever since then the number of cases in India is also growing.

The primary route for the spread of COVID-19 is thought to be through aerosolized droplets that are expelled during coughing, sneezing, or breathing, but there are also concerns about possible airborne transmission. Faeco-oral transmission has also been reported in a few cases, with viral isolation from the faeces of some patients.

SCREENING AND TRIAGE FOR COVID-19

1.	H/o Fever	☐ YES	☐ NO
2.	Any one of the following: a) H/o Cough b) H/o difficulty in breathing c) Or any **signs** of respiratory disease	☐ YES	☐ NO
3.	Any one of the following: a) H/o Travel to or residence in a country/ area or territory reporting local transmission in the last 14 days prior to onset of symptoms b) H/o contact with COVID-19 confirmed case in the last 14 days prior to onset of symptoms c) Severe Acute Respiratory Infection (SARI) **AND** requiring hospitalization **AND** with no other etiology that fully explains the clinical presentation (including health care provider)	☐ YES	☐ NO

TESTING

Testing for COVID-19 in Pregnancy Current testing strategies in India – at present, pregnant women are tested according to same criteria as other adults. It is essentially meant for acute respiratory illness with exposure, travel, contact or a HCW. Test methods and facilities – presently the RT-PCR test from nasopharyngeal swab is used for diagnosis.

SYMPTOMS

Most pregnant women will have mild to moderate FLu-like symptoms of cough, sore throat, and fever. Few may have difficulty in breathing or shortness of breath. These have been classified as features of severe acute respiratory illness (SARI) by the WHO. Pregnant women, especially those with associated medical diseases (diabetes, asthma, etc) may present with pneumonia and marked hypoxia. Immuno compromised and elderly pregnant women may present with atypical features such as fatigue, malaise, body ache and/or gastrointestinal symptoms like nausea and diarrhea

Pregnant women should be tested in the following circumstances

1. A pregnant woman who has acute respiratory illness with one of the following criteria: a history of travel abroad in the last 14 days (6 March 2020 onwards).

In addition to testing, these individuals (with or without symptoms) and their household contacts should home quarantine for 14 days.

2. A pregnant woman who is presently asymptomatic should be tested between 5 and 14 days of coming into direct and high risk contact of an individual who has been tested positive for the infection

LAB FINDING

Other laboratory findings are leucopenia, lymphocytopenia, mild thrombocytopenia, mild elevation of liver enzymes and other acute infection markers.

CT scan and other imaging modalities usually show patterns consistent with atypical pneumonia.

In cases where an X-Ray is taken or a CT scan is needed for a pregnant woman, there should be provision of an abdominal shield to protect the fetus from radiation exposure. An informed consent for the imaging should be taken from the pregnant woman and her relative

EFFECT ON PREGNANCY

Effects of COVID-19 infection on mother and fetus: maternal disease does not get aggravated by pregnancy unless there are co-morbidities. There is no evidence of transplacental spread to the fetus at present and fetal abnormalities or compromise have not been seen.

IN PATIENT

Arrangements in existing healthcare facilities to manage COVID-19 exposed and infected pregnant women Hospitals should have isolation zones which

should include outpatient, ward, ICU, labour rooms and operation theatres demarcated for COVID-19 infected women.

Pregnant women (not in labour) with COVID-19 infection– Most women will not need hospitalization or critical care.

ICU

Intensive Care (to be managed by critical care specialist) Pregnant women who meet any of the following criteria: ·

respiratory rate > 30 breaths/min; oxygen saturation < 93% at a rest; arterial partial pressure of oxygen (PaO2)/oxygen concentration (FiO2) < 300 mm Hg , Patients with > 50% lesions progression within 24 to 48 hours in lung imaging

Quick Sequential Organ Failure Assessment Score (qSOFA) score can be a useful adjunct to decision making for ICU management

MANAGEMENT OF COVID

The principle evidence based guidelines for ARDS include: ·

Conservative Intravenous Fluid strategies ·

Empirical early antibiotic for possible bacterial pneumonia ·

Early invasive ventilation may be needed ·

Lung protective ventilation strategies ·

Periodic prone/Left lateral positioning during mechanical ventilation

LABOUR

Management of Labour and Delivery in women with COVID-19 infection There is no rationale to induce labour or deliver a woman early because of COVID-19 infection. Decisions regarding route of delivery should be as per standard obstetric practice in most situations.

Labour Analgesia and Anesthesia in Pregnant Women with COVID-19 infection Regional analgesia and anesthesia can be used in women with COVID-19 infection. Specialized techniques should be adopted for general anesthesia. Pre oxygenate the patient for 5minutes with 100% O2 and perform rapid sequence induction (RSI) to avoid manual ventilation of the patient's lungs. Use a video-laryngoscope to improve intubation success. Place a high efficiency hydrophobic filter between the facemask and breathing circuit or between the facemask and reservoir bag to avoid contaminating the atmosphere

DRUGS USED

Hydroxychloroquine 600 mg (200 mg thrice a day with meals) and Azithromycin (500 mg once a day) for 10 days has been used successfully.

Antiviral therapy (Lopinavir + Ritonavir or Oseltamavir) may be used in high risk groups (immune compromised, chronic disease, uncontrolled diabetes).

Other supportive care should include rest, supplemental oxygen and paracetamol.

Patients Stay at home as much as possible unless there is a medical need related to development of symptoms of infection or related to pregnancy.

NEWBORN

Newborn care should be practiced as per routine. At present, testing is recommended if the mother has COVID-19 infection or if the baby is symptomatic. Breastfeeding can be given with good hygiene practices.

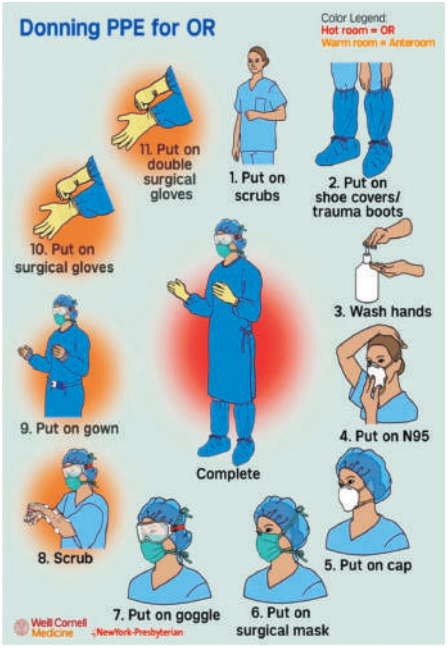
Cleaning, maintenance of facilities and medical equipment should be done with adequate PPE to the HCW. 1% sodium hypochlorite solution with contact time of 30 minutes can be used

TESTING FOR NEONATES

Insert a swab into nostril parallel to the palate. Swab should reach depth equal to distance from nostrils to outer opening of the ear. Leave swab in place for several seconds to absorb secretions. Slowly remove swab while rotating it. Place swabs immediately into sterile tubes containing 2-3 ml of viral transport media. Oropharyngeal swab (e.g., throat swab): Swab the posterior pharynx, avoiding the tongue. Nasopharyngeal wash/aspirate or nasal aspirate Collect 2-3 mL into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container.

TRAINING

Training and managing the healthcare cadre is essential to prevent them from getting infected. Shift arrangements and transport need to be arranged. It is important to keep up morale.



TRIAGE

Triage stations with adequately trained staff should be allotted at the entrance of each health care facility. Physical barriers (glass/plastic barriers) should be installed at these stations to limit close contact between triage personnel and potentially infectious patients. At these triage points, all patients must be assessed for possible COVID-19 infection and suspects

MASK

The HCWs involved in patient care should use a N-95 mask, eye protection (goggles) or face shield to prevent contamination of mucus membranes, clean non sterile long sleeved gown and gloves. Instructions in correct doffing and disposal of PPE is essential.

Dedicated equipment (thermometers, sphygmo-manometers and stethoscopes) should be used after proper cleaning and disinfection with 70% ethyl alcohol before and after attending each patient

According to the efficiency of filtration these are usually graded as-95, 99 and 100Means these respirator masks are capable of traping 95%, 99% and 99.9% of particles, smaller up to the 0.3 micron size.This grading can also be done asP1 (FFP1) - 80%P2 (FFP2) - 95%P3 (FFP3) - 99.95%Filtration efficiency.

Few respirator masks have valve, That valve is nothing but a simple exhalation port with one way valve mechanism, it reduces effort of expiration, reduce heat inside the mask, dissipate humidity and reduce Co2.

APPOINTMENT

For women who have had symptoms, appointments can be deferred until 7 days after the start of symptoms, unless symptoms (aside from persistent cough) persevere.

For women who are self-isolating because someone in their household has possible symptoms of COVID-19, appointments should be deferred for 14 days.

OPD

Routine OPD work should be kept to a minimum. No relatives should be allowed in unless unavoidable.

Social distancing must be practiced within clinics and hospitals, with waiting-room chairs placed six feet apart. Patients with respiratory symptoms made to wear a paper mask in the waiting area and instructed on cough and sneeze hygiene. Doctors clinics should be well ventilated The doctor should wear a surgical mask and scrub hands with soap and water and use an alcohol-based disinfectant after each patient interaction

ISOLATION & QUARANTINE

Isolation - Separation of individuals who are ill and suspected or confirmed to have COVID-19 infection

Quarantine - Separation of individuals who are not yet ill but have been exposed to COVID-19 and therefore have a potential to become ill

Active quarantine -All the HCWs, while on duty for seven days, will be mandatorily staying in in-house quarantine

In-house quarantine means the quarantine facility developed and provided by the institute at various places. single accommodation if facilities are available high-risk category will be given preference for single accommodation and those with low risk category will be accommodated on sharing basis

Passive quarantine - All the HCWs, after completion of their 7 days of duty will be mandatorily staying in quarantine facility for 14 days at a quarantine facility provided (in campus or outside campus)

All the HCWs (Medical Team Members), regardless of their risk category and level of work, will preferably be accommodated in single accommodation facility with separate toilet.

If there is a minor query, it can be sorted out telephonically. At present, telephonic consultations are permitted by the Medical Council of India till the situation comes under control

Keep the home visitors including homecare personnel, maids, and staff members to a minimum or avoid completely if possible.

HAND WASH

Washing their hands frequently and properly with soap and water or an alcohol based hand rub for minimum 20 seconds

Elbow Covering their mouth and nose with their bent elbow, handkerchief or tissue while coughing or sneezing. Then the used tissue should be disposed immediately. This is an important component of respiratory hygiene.

Avoid touching face, eyes, nose and mouth with hands.

Space Keep a distance of at least 1 meter from the next person outside and in the house

General advice in OT

Elective/planned obstetric procedures (e.g. cervical cerclage or Caesarean) should be scheduled at the end of the operating list.

Non-elective procedures should be carried out in a second obstetric theatre, where available, allowing time for a full postoperative theatre clean as per local health protection guidance.

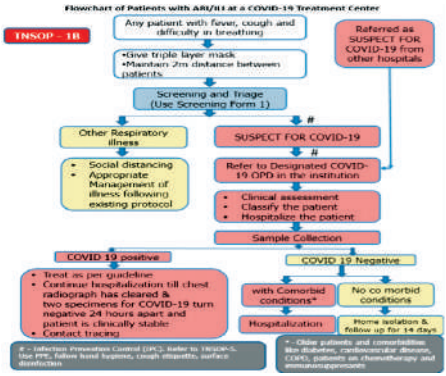
The number of staff in the operating theatre should be kept to a minimum, and all must wear appropriate PPE.

All staff (including maternity, neonatal and domestic) should have been trained in the use of PPE so that 24-hour emergency theatres are available and possible delays reduced.

CONCLUSION

Pregnancy patient is categorized as normal patient, suspected cases(SARI & from contaminated zone), COVID 18 POSITIVE. Receiving OP, Labour ward & OT should be separate with separate team. Labour management & Iscs indication nothing special. PPE KIT is must for positive patient & treating team. Hand wash & social distancing is must for all to avoid spread.

FLOW CHART



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SURGICAL SITE INFECTIONS IN PUERPERIUM

Fever in puerperal period may be due to surgical site infection, UTI, respiratory infection, breast inflammation and abscess. This article explores various facets of surgical site infection (SSI) including incidence, causative factors, types, prevention and treatment.

Incidence

The incidence of LSCS is around 13.7% in public sector and 37.9% private sector in a study by NHRM which included 24,398 deliveries. Optimal rate of LSCS is around 5-20% according to WHO. Higher incidence is seen in private health care facility and urban areas. Common causes for LSCS are increased maternal age, hypertension and breech presentation. The incidence of LSCS has also increased probably due to at request LSCS by women who are on the wealthier sector and had higher education [1, 2, 3]. Women who had greater than 4 antenatal visits had 1.23 times higher risk of CS.

Incidence of surgical site infection seen among 7235 LSCS was around 1.7 – 2.95% in a study from Kuwait [4].World-wide surgical site infection is found to be around 3 – 15% [5, 6, 7]. Surgical site infection contributes to 20% healthcare associated infections. Incidence in Sub Saharan African countries illustrated an average of 7.3%. Complex surgical site infections are declining from 0.84% to 0.15% as observed by Ferraro et al. Incidence is higher in under developed countries as compared to developed countries (7.3% vs 1.75% - 4.78%).

In a study performed in India, the incidence of SSI following Gynaecologic surgeries was found to be greater than that of Obstetric surgeries. (10.3% vs 1.2%) [8]

Surgical site infection complicates a significant number of patients who undergo LSCS. 2-7% experience superficial infection and 2 – 16% will develop endometritis [9].Incidence of Necrotizing Fasciitis is 0.18% [10].

Definition

Surgical site infection is defined as infection which occurs within 30 days of post-surgical procedure involving skin, sub cutaneous tissue, soft tissue or organ/space[11].

The incidence is decreasing due to improvement of hygiene conditions, administration of prophylactic antibiotics and following standard infection control protocol [12, 13].Although post LSCS surgical site infections are not very serious, this can cause pain, discomfort, morbidity, stress, financial strain and extended stay [12].

Risk Factors

1) Increased maternal age
2) Nulli parity
3) Twin gestation
4) PROM
5) Diabetes Mellitus
6) Hypertension
7) Medical diseases like cardiac diseases, renal diseases and liver diseases. Pre-existing medical disorders increases the risk by six folds [8]
8) Obesity
9) Smoking
10) Malnutrition
11) Immuno suppression, especially on corticosteroids
12) Repeated vaginal examination [8]
13) Presence of vaginal discharge [8]
14) Prolonged stay in the hospital prior to surgery leading to susceptibility for nosocomial infection
15) More than one-hour surgery doubles the risk of surgical site infection [8]
16) Inappropriate antibiotic prophylaxis increases the surgical site infection by five folds [8]
17) Depth of sub-cutaneous plane
18) Prolongation of post-surgical stay increases the risk by 5% each day [8]
19) Hematoma formation in the post-operative period due to cough and anti- coagulants is seen in 2 – 5% [14, 15]

Causes of surgical site infection

Surgical site infections are known to be caused by microbes from patient's own body rather than those

that are outside. They can be transmitted from the OT, surgeon and staff. Most of the surgical site infections are preventable.

Common Organisms are Staphylococcus aureus (MRSA), Klebsiella pneumonia (ESBL), E. coli (ESBL) and Pseudomonas. Infections could be nosocomial or iatrogenic.

Necrotizing Fasciitis (NF) is characterized by rapid and progressive necrosis of subcutaneous tissue and fascia [10]. Type 1 NF has a polymicrobial etiology whereas Type 2 NF is caused by single organism (Group A Streptococcus).

Post-partum endometritis is caused due to polymicrobial infection of decidua.

Classification of surgical site infection

Clean

Clean contaminated – Eg: LSCS

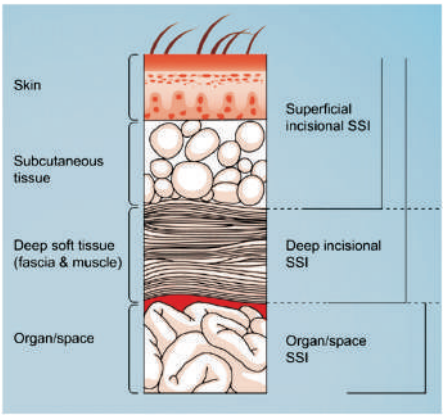
Contaminated

Infected / Dirty

Types of surgical site infection

Based on layer of involvement it is classified into

1) Superficial infection - Skin /Sub cutaneous layer involvement with purulent discharge
2) Deep incisional infection – Deep tissue involvement with purulent discharge in the myo-fascial layer
3) Organ / Space infection – Combination of deep infection which extends beyond myo-fascial layer into the peritoneal cavity.



Signs and symptoms of surgical site infections

Time taken to develop surgical site infection is between 2 – 30 days post operatively. The signs and symptoms observed are:

a) Fever, local tenderness, warmth, redness and swelling on the fourth day after discharge

b) Wound gaping and pus discharge

c) Severe intra peritoneal infection usually present with systemic signs like high fever, tachycardia, dehydration, tachypnoea and local signs like abdominal distention and pain. Patient will be invariably sick requiring hospitalisation.

d) Necrotizing Fasciitis usually presents with severe pain, woody induration of the sub – cutaneous tissue and vesiculo-bullous lesions. Rapid progression of clinical signs and symptoms is a classical feature [16-18]

e) Post-partum endometritis is characterised by spiking fever, abdominal tenderness and purulent vaginal discharge in 2 – 16% of women. Especially when surgery is done following trial of labour / PROM

Prevention of Surgical Site Infections

Decreasing the primary CS rate is the vital mode of prevention. Other preventive measures include:

1. Preparation
   a) Pre-operative shower using soap/chlorhexidine on the day before and/or on the day of surgery.
   b) Shaving with razors to be avoided. Electric clippers with single use head can be used on the day of surgery.
   c) Vaginal cleansing with Povidone Iodine solution [9]
2. Theatre wear for the patient

   Specific clean theatre wear for the appropriate surgery should be used. Use of theatre gowns is ideal. Legs, eyes, mouth and head should be covered appropriately.
3. Theatre wear for the staff
   a) It is ideal for all staff to wear non sterile pant and shirt, leg covers, cap and mask. Once dressed up, OT staff should minimize their movements.
   b) OT staff should avoid use of artificial nails, nail enamels and jewellery.
4. Antibiotic prophylaxis

   LSCS comes under clean / contaminated surgery. Antibiotics, preferably third generation cephalosporins should be given intravenously before induction of anaesthesia.

   Addition of 500mg Azithromycin intra venouslywith third generation cephalosporins (1 - 2g Cefazolin depending on the patient weight) reduces the incidence of surgical site infection from 15% to 3%, endometritis from 8% to 2% and post-operative febrile morbidity from 17% to 3%[19, 20].

   Second dose can be repeated depending upon the situations like PROM and prolonged surgery. Dose is calculated according to the weight of the patient.

5. Intra operative phase

a) Team should wash with antiseptic surgical scrub. Nails and hand should be clean. Alcoholic hand rub can be added before surgery.

b) Operating team should use sterile gowns and double gloves should be worn.

6. Preparation of skin

Antiseptic should be used with alcohol / aqueous based chlorhexidine oralcohol / aqueous based solution of povidone iodine and skin should be cleaned meticulously. Chlorhexidine may be used in the place of povidone iodine in patients who are allergic to iodine [21].

If cautery is used to cut the skin, evaporate the alcohol. It is better to avoid use of cautery to cut the skin as there is an increase in associated surgical site infections.

7. Maintaining patient's homeostasis

a) Temperature should be maintained to avoid too much hypothermia

b) Maintain oxygenation and perfusion

c) In diabetic patients, intra operative and post-operative blood glucose levels to be monitored and insulin should be added.

8. Wound irrigation

Wound irrigation and intra cavity lavage should be restricted to decrease the incidence of surgical site infection.

9. Uterine Exteriorization

It has not been found to increase the incidence of SSI. Hence avoidance of uterine exteriorization is not suggested as a preventive measure.

10. Removal of Placenta

Manual removal of the placenta was associated with a higher risk of endometritis compared to removal with traction of umbilical cord

11. Application of antiseptic

Application of antiseptic or antibiotic to the wound before closure is only under research setting (NICE Guidelines 2019).

12. Closure Method

Antimicrobial triclosan coated sutures may be of use in closing uterine and fascial wound. Skinclosure method should be ideally suturing rather than staples to reduce surgical site infections (NICE Guidelines 2019). Preferred method of suturing being simple interrupted. Sub cutaneous closure is done if theplane is greater than 2cm and sub cutaneous drain is placed if the plane is greater than 4cm [22, 23]. However, sub cutaneous drain placement is not of much use in prevention of surgical site infection.

Negative pressure wound therapy after LSCS is gaining popularity, especially in obese women. It reduces excess fluid accumulation and protects the wound from irritation caused by reducing the frequency of dressing changes to only every 3 – 5 days [9]. It has also been reported that negative pressure wound therapy is only beneficial if the risk of surgical site infection is greater than 14% [24].

13. Post-operative phase

a) Use aseptic, non-contact technique for changing or removing surgical wound dressing.

b) Change of dressings can be done after 48 hours to 72 hours. Regular bath can be given after 72 hours

c) Additional dose of antibiotics in appropriate cases such as prolonged surgical time, obesity and PROM may be required.

Patient can be febrile upto 48 hours. Temperature > 100.4 ° F is considered to be febrile morbidity. If temperature persists beyond that period, think of two possibilities in a post LSCS patients. It may be either due to surgical site infection or breast engorgement and inflammation. Rarely, thrombophlebitis may also be considered.

In such incidences, patient has to be clinically evaluated. Wound should be evaluated and observed for signs of inflammation, dehiscence or pus. Antibiotics and anti-inflammatory drugs may be continued as required.

If there is pus, samples should be sent for culture and sensitivity. One or two stitches can be opened in the wound and pus can be drained. Plane of infection should be identified, if it is superficial, deep or extension into the cavity and management should be planned accordingly.

Management

98.3 % of surgical site infections observed are superficial. These Infections are common and often observed after the patient goes home. They may be treated at home with antibiotics and anti-inflammatory drugs with cleaning of the infected site with chlorhexidine gluconate soap and clean water after removal of dressing. Daily bathing must also be advised. They usually do well with domiciliary treatment.

For deep fascial lesion, the stitch is opened and irrigated with clean water and betadine solution, three to four times a day and dressing done. Wound is allowed to heal by secondary intention or re-suturing can be done when the wound is clean. Follow with appropriate anti biotics according to culture and sensitivity.

In case of intra- peritoneal surgical site infection, patients may need hospitalization. Patient has to be

clinically evaluated, wound has to be inspected. USG, CT/MRI can help in diagnosis. If there is evidence of intraperitoneal pus collection, surgical drainage should be done either by laparoscopy or laparotomy. Broad spectrum antibiotics which covers both gram positive and negative organisms along with anaerobic coverage is needed.

In severe cases like necrotizing fasciitis, help of other specialty is needed and early extensive wound debridement should be done. The wound should be re-explored every 24 – 36 hours. Type 1 NF with polymicrobial etiology is managed with Vancomycin (MRSA), Piperacillin – tazobactam, metronidazole and clindamycin and Type 2 NF caused by Streptococcus is managed medically with a combination of Penicillin and Clindamycin. Role of intra venous immunoglobulin (IVIG) is unclear. In case of Clostridium infection, a combination of Penicillin and Clindamycin may be administered. Role of hyperbaric oxygen therapy in Clostridium infection is unclear.Supportive measures are needed. Maintain hydration, oxygenation and correct anaemia. Electrolyte and acid base balance to be corrected in case of severe sepsis and need to take the help of intensivists.If not treated properly, mortality goes up to 25 – 50%.

Post-partum endometritis should be managed with a combination therapy with Clindamycin and Gentamicin. Ampicillin may also be added for better coverage of Enterococcus. If fever persists, imaging is needed to rule out pelvic abscess.

Patients should be followed up to 30 days, to detect all surgical site infections. Superficial surgical site infections need homecare whereas complex surgical site infections require impatient care.

Surgical site infection can remain chronic at times. In such situations we have to think about atypical Mycobacterial infection. Recent work recorded surgical site infection with atypical mycobacterium. Mycobacterium has long incubation period. These organisms are found in natural tap water or ordinary water and soil.

Non- tuberculous rapidly growing mycobacterium, (RGM) are opportunistic pathogens that are found in the environment. M. fortuitum, M. chelonae and M. abscessus are human pathogens. They can cause wound infection, disseminated cutaneous disease and purulent infection. In post laparoscopic wound, mesh site infections and other surgical site infections can happen due to M. fortuitum and M. chelonae. They cause delayed onset of infections and do not respond to routine antibiotics. Identification is quite difficult, unless we think about it [25].

Patients undergo drainage of wound abscess, debridement and daily dressing. There is often a delay in diagnosis up to 60 days. They may need liquid chromatography, DNA probe or PCR for diagnosis, pus for gram stain and AFB stain and culture and sensitivity. Pus from the surgical site infection can demonstrate the acid-fast bacillus. Occasionally, culture with LJ (Lowenstein- Jensen) media can grow this organism.

These patients respond well to Clarithromycin, amikacin, doxycycline and ciprofloxacin for 2 – 3 months. Some patients may need administration of these antibiotics for an extended period of 6 - 12 months.

Strict sterilization procedures are needed. Instead of glutaraldehyde, ethylene oxide gas and autoclaving are best methods [26].

Conclusion

1) Surgical site infections are increasing with increase in LSCS rates, which should be decreased adhering to practice protocols in the OT.
2) Surgical site infections are usually diagnosed after discharge where the patients are discharged at 72 hours.
3) Emergency LSCS has higher risk of surgical site infection.
4) Improper anti-biotic prophylaxis is an important factor.
5) With emergence of MDR organisms,there is an urgent need to implement revised skin preparationand antibiotic prophylaxis.
6) They lead to severe morbidity if not detected earlier.
7) Chronic non-healing surgical site infection should arise the suspicion of atypical mycobacterial infection and treatment should be directed towards it.

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CHICKEN POX (VARICELLA) IN PREGNANCY

General Consideration

Varicella Zoster Virus (VZV) is a highly contagious infectious agent. Chicken Pox is a common child hood illness, vaccination for VZV is not included in national immunization program. In this scenario pregnant women can often be exposed to contagious individual. VZV infection in pregnancy can cause significant feto-maternal morbidity and sometimes even mortality. So, the obstetrician should be knowledgeable of basics of VZV infection and management protocol in case of exposure to chicken pox patient as well infection by VZV.

Pathophysiology –

VZV is a highly contagious DNA virus of herpes family. Virus is transmitted by respiratory droplets and by direct contact with vesicle fluid or indirectly by fomites. Humans are the only source and virus enters the host through the conjunctivae and mucous membrane of the nasopharynx. Incubation period is 10-21 days. Infection rate in susceptible individual after exposure can be as high as 60-90 %. [1] It is relatively benign and self-limiting disease in childhood. It is important to note that infection is more severe in adults. [2]

At the end of second viraemic phase, nonspecific prodromal symptoms such as headache, malaise, fever occur which is followed by pruritis and a maculopapular rash. Rash becomes vesicular before crusting which occurs about 5 days later. Affected individuals are infectious from 2 days prior to rash appearance till vesicular lesion has crusted over. Primary infection usually confers lifelong immunity yet symptomatic reinfection has been reported.

Following the primary infection, the virus remains dormant in sensory nerve root ganglion. It can be reactivated to cause a vesicular erythematous skin rash in segmental distribution known as herpes Zoster (HZ) or shingles. In non-exposed sites risk of acquiring infection is less, however exposed Zoster should be considered to be infectious

Chicken Pox in Pregnancy –

Varicella approximately affects 1/2000 of pregnancies.

Effect of pregnancy on infection course – In pregnant women VZV infection may be associated with high risk of maternal morbidity and mortality. Nearly 2-5 % of pregnant women can develop pneumonia.[3] Risk factor for VZV pneumonia are smoking, more than 100 cutaneous lesions.

Symptoms of VZV pneumonia are fever, tachypnoea, dry cough, dyspnoea and pleuritic pain.

Hepatitis and Encephalitis are rare but potentially very serious complications.

Effect of VZV infection on fetus and new-born

VZV infection in early pregnancy VZV does not cause spontaneous abortion. However, virus can cross the placenta and may result in fetal infection causing fetal varicella syndrome.[4,5] The risk of FVS is 0.4 % in first trimester, 2 % in second trimester and virtually zero in the third trimester infection. Highest risk is between 13-20 Weeks. Features of FVS are Chorioretinitis, Microphthalmia, Cerebral Cortical Atrophy, IUGR, Limb defect and or non-immune hydrops.[6,7] Diagnosis of FVS is mainly based on ultrasound findings which appear about 5 weeks after maternal primary infection. USG should be done by expert.

Table : Clinical features of congenital varicella syndrome[6] (%)

Skin lesions (scarring, skin loss)	76
Neurological defects (cortical atrophy, limb hypoplasia, seizures, microcephaly, Horner's syndrome, encephalitis, dysphagia)	60
Eye disease (microphthalmia, chorioretinitis, cataract, nystagmus, optic atrophy)	51
Limb hypoplasia	49
Intrauterine growth restriction	21
Muscle hypoplasia	22
Gastrointestinal abnormalities	15
Developmental delay	12
Genitourinary abnormalities	12
Cardiovascular defects	8
Defects of other organs	7

Amniocentesis and viral PCR on amniotic fluid confirm fetal infection, but it is important to keep in mind that all affected fetus may not develop FVS. Thus, a detailed ultrasound examination remains the main stay of diagnosis. [8]

Infection with VZV in later stage of pregnancy can cause premature delivery and also neonatal chicken pox infection. Neonatal chicken pox infection is characterized by severe pneumonia and fulminant hepatitis can occur if mother is infected 5 days before to 2 days after delivery. Attack rates range from 25-50 % and neonatal mortality rate can approach 30 %. In some cases, neonate can develop disseminated visceral and CNS disease which can be fatal.

Diagnosis

Diagnosis is usually clinical with its characteristic vesicular rash. Infection can be confirmed with PCR or NAAT of vesicular fluid or from samples taken from unroofed skin lesion. HSV 11 and coxsackie virus may cause symptoms similar to Congenital varicella syndrome and should be considered in differential diagnosis.

When there is doubt regarding past history of infection i pregnant women with varicella exposure, serum IgG for varicella should be checked.

Management

A. Pre-conceptional – All women in reproductive age group and planning conception immune status should be checked either by history of chicken pox, if in doubt by checking serum varicella antibodies. If seronegative she can be offered varicella vaccination. She should also be advised to avoid pregnancyfor 3 months. However, if pregnancy occurs in this period there is no need or indication for termination of pregnancy

B. During Pregnancy – In all patients, previous history of chicken pox infection should be elicited. Positive history of chicken pox infection is predictive of immune status. If no history she should be advised to avoid contact with person with chicken pox or shingles.

If women give with H/O or concern for exposure to person having chicken pox or shingles, timing of exposure and closeness and duration of contact should be carefully noted.

Exposed women should be given Varicella Zoster Immunoglobulin (VARI ZIG). Immunoglobulin is best given within 36 hours of exposure; its use is approved for up to 10 days to prevent or attenuate varicella infection.[9,10] The dosage is 125 U /10Kg to maximum of 625 U I/M or 1mg/Kg body weight Intravenously. It is a human product and limited supply, so must be used judiciously.

However, in women with positive history of varicella Van ZIG is not indicated.

Irrespective of whether VZIG given or not, the pregnant women should be managed as potentially infectious for 3-4 weeks. They should be instructed to report to doctor immediately if they develop rash. There is no role of VZIG, once clinical disease has developed.

C. Maternal Infection-

Chickenpox infection in pregnancy is associated with high morbidity and mortality so they should be treated with Acyclovir 800mg five times a day for one week within 24 hours of development of rash. [4,5] Acyclovir has not been found to be teratogenic, and should be considered even in first trimester infection.

Famciclovir is category B drug; its dosage is 500-1000mg twice a day for 7 days. Its compliance due to less frequent administration is more.

Antiviral therapy has been shown to decrease duration and severity of infection. Beside supportive treatment for fever, hydration and personal hygiene is essential.

Women who develop pneumonia, they should be admitted and given I/V Acyclovir in dosage of 10-15 mg/kg body weight. The women with complicated VZV infection should be managed by multidisciplinary team.

D. Obstetric Management –

When infection occurs in early pregnancy the mother should be counselled of no risk of miscarriage and low risk of 1% for fetal Varicella Syndrome. A follow up ultrasound is warranted but not less than 5 weeks following VZV infection. If severe fetal defect are found option of termination can be given with due consideration of legal limits.

If infection occurs near term, delivery should be delayed by at least 5-7 days following rash appearance. This period allows transfer of protective antibodies IGG to fetus. The initial body response is IgM but it does not cross placenta.

Delivery during viraemic phase is hazardous. Maternal risk are bleeding, Thrombocytopenia, Coagulopathy and hepatitis. However, if women present in active labor or need delivery due to other obstetric indication, neonate should be given VZIG. If neonate has developed rash VZIG is not helpful and neonate should be given Acyclovir to treat VZV infection.

E. Precaution for health care worker – Health care worker caring for women and neonate with VZV infection, their immune status should be determined by history or serological testing. Non immune health care worker should be offered vaccination. If they have had significant exposure to infection, they should be reallocated to minimise patient contact from 8-21 days.Vaccination

Varicella vaccine is alive attenuated vaccine given in 2 dosage 4 month apart. It is recommended for non-pregnant adolescent and adults with no history of chicken pox/ Seroconversion is 98 %.[2] It is important to keep in mind that vaccine induced immunity diminishes over time and breakthrough infection rate can be approx. 5 % over 10 years.[11]

Vaccine is not recommended for pregnant women or for those who can become pregnant within a month of vaccination. However, no case of FVS or congenital malformation have noted with use of vaccine in pregnancy within 1-3 month.[12]

The vaccine is not secreted in breast milk. So postpartum vaccine can always be given and should not be delayed in sero negative women.[13]

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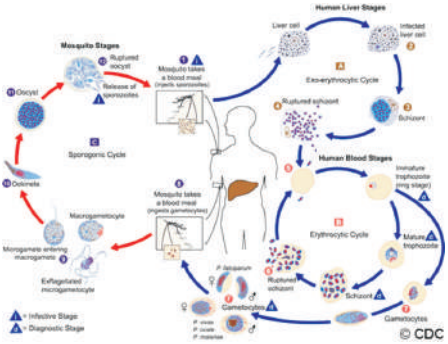
PARASITIC INFECTIONS IN PREGNANCY

P.falciparum is more common in Africa while P.vivax is more common in India. P.vivax and P.ovale cause relapsing malaria while P.malariae can present with late recrudescence.

Malaria infection affects mother and baby which leads too miscarriage, stillbirth, prematurity, low birth weight, maternal mortality.

Pathogenesis:



The parasites P.falciparum, P.malariae, P.ovale, P.vivax are transmitted to humans by the bite of female anopheles mosquito. They undergo development to schizont stage in liver and enter red blood cells. In RBC, they get attached to hemoglobin and alter the red cell membrane. These altered RBC's become sticky and aggregate in small blood vessels of organs causing damage. In P.falciparum the parasites apart from damaging maternal organs, infect the placenta causing placental parasitemia.

Terms in malaria infection:

Uncomplicated malaria: Malaria infection with no severity or complications.

Severe complicated malaria: Present with >2% parasitemia which in turn causes severe features.

Congenital malaria: Infection in infant or newborn which occurs due to transfer through placenta in utero. There is no role for bite of anopheles mosquito in this congenital malaria.

Clinical features:

Symptoms:

Fever, Chills and rigors, Headache, Nausea, vomiting, Cough & Myalgia

Signs:

Pallor, Icterus, Increased temperature & Respiratory distress

Features of severity:

Respiratory system: respiratory distress, pulmonary edema

Cardiovascular system: Shock, hypotension

Hematological: Jaundice, hemoglobinuria, D

Central nervous system: Convulsions

Laboratory features:

Hb <8g/dl, Thrombocytopenia, pH <7.3, hyperlactatemia, hypoglycemia, renal impairment

P.falciparum

HIGH TRANSMISSION: In these areas, due to diffuse infection, there happens to high level of immunity. This leads to asymptomatic presentation in cases of P.falciparum infection. There is no peripheral parasitemia. But pregnant mothers can have anemia and localization of parasites in placenta which in turn causes low birth weight in babies.

LOW TRANSMISSION: In these areas, there is lack of immunity leading to maternal anemia and severe malaria infection, which in turn causes abortion, prematurity, stillbirth, low birth weight.

P.vivax

P.vivax infection causes chronic anemia, localization in placenta causing low birth weight and neonatal death.

PREVENTION: Avoid travel to malaria endemic regions by postponing travel.

Follow the ABCD protocol:

Awareness of risk: Know about level of transmission, season at the area, resistant strains, missing chemoprophylaxis.

Bite prevention:

- Repellent creams – 50% DEET, PMD, 20% picardin – these creams require frequent applications to reduce risk of bite
- Mosquito sprays- pyrethroids kill and permethrin repel and kill mosquitoes
- Insecticide treated bed nets- long lasting pyrethrioid nets need to be used when outdoors, if it's not long lasting net needs to be re impregnated every 6 months. These nets provide 50% protection
- Clothing protection- use long sleeves, long trousers, socks impregnated with pyrethroid, permethrin
- Room protection with electric bats, mosquito coils

Chemoprophylaxis: There is no chemoprophylaxis that is 100% effective. Causal prophylaxis is against liver schizont stage and is to be continued for 7 days after leaving endemic area. Suppressive prophylaxis against RBC stage needs to be continued for 4 weeks after leaving endemic area.

In women taking prophylaxis while attempting pregnancy, it is better to avoid pregnancy for a while. If they do get pregnant, there is no need to terminate pregnancy.

Chloroquine sensitive areas: Chloroquine300mg/ proguanil 200mg daily and once weekly. Folic acid supplementation is necessary in women taking proguanil.

Chloroquine resistant areas: Mefloquine 5mg/kg once weekly. Contra indicated to those with depression, neuropsychiatric disorders.

Doxycycline which will impair fetal bone and cartilage, primaquine which causes hemolysis in fetus are contraindicated as chemoprophylaxis.

Diagnosis:

Diagnostic tests include microscopic analysis and rapid diagnostic tests. However these rapid tests are based on detection of specific antigen or enzyme can become false negative in low levels of parasitemia. So rapid tests are unreliable in pregnancy and insensitive in P.vivax infection. The gold standard for diagnosing malaria is by microscopic examination of thick and thin blood smears. Women who have taken chemoprophylaxis or with high levels of immunity may have low levels of parasitemia on microscopic examination. Still they can present with placental parasitemia and needs to be monitored adequately.

Treatment:

Malaria in pregnancy should be considered as an emergency condition. Patients with uncomplicated malaria need to be admitted to hospitals while those with severe complicated malaria need intensive care admission. Prefer intravenous route in severe cases. Avoid oral drugs if there is vomiting to ensure successful treatment.

Malaria	Causative agent	Drug of choice
Uncomplicated malaria	P.vivax, P.ovale, P.malariae	Oral chloroquine 600mg f/b 300mg 48 hours later, day 2, day 3
	Resistant P.vivax	Follow P.falciparum
	P.falciparum	Oral quinine 600mg tds + Oral clindamycin 450mg tds – 7 days (or) Atovaquone proguanil 4 tablets daily for 3 days
	Vomiting + P.falciparum	Quinine 10mg/kg in 5%D over 4 hours, later tds + IV clindamycin 450mg tds. Switch over to oral regimen when patient is stable
Severe malaria	Any species	IV artesunate 2.4mg/kg at 0, 12, 24 hours and then daily. When patient is stable oral artesunate 2mg/kg or IM artesunate 2.4mg/kg od + clindamycin. Else follow oral regimen for uncomplicated falciparum infection.
	Artesunate allergy	IV quine 20mg/kg in 5%D over 4 hours f/b 10mg/kg in 5%D over 4 hours, later tds + IV clindamycin 450mg tds. When patient is stable switch over to oral regimen.
Maintenance during pregnancy		Chloroquine 300mg weekly till delivery
Maintenance after delivery		Withhold drugs for 3 months postpartum and perform G6PD testing
Fever can cause preterm labour, fetal distress		Paracetamol 1g qid
Recurrent malaria		Aretesunate 2mg/kg or 100mg + clindamycin 450mg tds - 7 days

If woman develops fever of ≥ 38°C, rule out other causes of fever, evaluate and proceed with fever investigations. In case of vomiting within 30 minutes of oral tablets, repeat full dose; if vomit occurs after 30-60mins, repeat half dose. Can administer metoclopramide to treat vomiting.

Adverse effects of oral quinine: CINCHONISM – headache, nausea, tinnitus, blurred vision, diarrhea. Caution needed when using quinine as it can cause hypoglycemia in pregnancy due to hyper insulinemia. Also alter iv quine dosing to bd instead of tds in women with impaired renal or liver function.

Effect of pregnancy on malaria treatment: non compliance due to vomiting, lower efficacy due to lower anti malarial concentration in blood, increased risk of recurrence. They might require weekly blood film screening to assess parasitemia and possibility of recurrence.

Effect of malaria on pregnancy:

Hypoglycemia: can cause fetal bradycardia, fetal distress, lactic acidosis. Monitor blood glucose levels. If <40mg/dl, administer dextrose infusions.

Pulmonary edema: Serious complication which can have 50% mortality. Avoid fluid overload. Monitor respiratory rate, urine output, JVP, CVP. Treat patient by propped up position, oxygen, diuretics and fluid restriction. If needed intubate and administer PEEP /CPAP

Severe anemia: Risk of postpartum hemorrhage, maternal and perinatal mortality. Monitor hemoglobin levels. If Hb <8g/dl, arrange transfusion.

Shock: Rule out secondary bacterial infection. Increased risk of Gram negative sepsis. Perform blood

cultures and start on empirical broad spectrum antibiotics. Switch over to sensitive antibiotics after blood culture reports. Maintain hemodynamic status by proper fluid management.

DIC: treat coagulopathy with blood component transfusion and vitamin K injection

Convulsions: maintain airway. Administer intravenous or recta diazepam.

Obstetric management:

During antenatal period follow routine visits, monitor hemoglobin, platelet count, blood glucose levels, growth scan.

Risk of preterm labour, fetal growth restriction, fetal distress, fetal bradycardia in malaria complicating pregnancy. Rule out hypoglycemia and increased temperature in cases of fetal distress and treat accordingly.

Arrange a multidisciplinary team with obstetrician, neonatologist, anaesthetist, intensive care management. Administer tocolytics and steroid therapy in preterm pregnancies. Ensure prompt delivery to avoid stillbirth. Monitor thrombocytopenia and ensure adequate platelet count to avoid risk of hemorrhage and associated morbidity. Advise placental blood film to check for placental parasitemia suggestive of congenital malaria.

Monitor 4th hourly PR, BP, RR, JVP, Oxygen saturation, urine output. Perform daily CBC, LFT, Urine examination.

Inform patients of risk of vertical transmission. It can occur even after treating the mother. So in cases with placental parasitemia, advise weekly monitoring of newborn with thick and thin blood smears till 28 days.

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VIRAL INFECTIONS IN PREGNANCY

Maternal pyrexia is defined as body temperature of 38^{0}C or above on a single reading or 37.5^{0}C or above on two consecutive readings one hour apart[1]. It may be caused by both infectious and non-infectious aetiologies. The effects on pregnancy depend on the extent of temperature elevation, duration and the stage of foetal development. Severe exposure during embryonic and foetal development can result in miscarriage, preterm labour, growth restriction and stillbirth. It can also lead to a wide range of foetal structural and functional defects particularly affecting the CNS. Pregnant women with febrile illness are more likely to develop a critical outcome than the general population[2]. There is an increased severity of infections in pregnancy as a result of normal physiological changes in the immune system. We shall discuss some rare infectious causes of fever during pregnancy that has important implications for the mother and foetus.

Ebola virus disease

The Democratic Republic of Congo (DRC) is currently experiencing the second largest Ebola outbreak since 2014[3]. Ebola virus was first discovered in 1976 in Yambuku, DRC along the Ebola River as a zoonotic RNA virus and a member of the Filoviridae family. It caused small outbreaks in Africa till 2014. The Ebola outbreak of 2014-2016 in West Africa had profound and lasting effects. It highlighted the importance of screening for travel history to avoid import of disease. The virus is transmitted from person-to-person through direct contact with blood or body fluids, sexual contact with semen,through breast milk and by unsafe burial practices[4].

Clinical course

Signs and symptoms include fever, severe headache, muscle pain, abdominal pain, diarrhoea, vomiting and unexplained haemorrhage. The incubation period from exposure to the development of symptoms is 2-21 days[4]. A diagnosis of EVD is initially based on clinical presentation in the context of potential exposure history. Laboratory testing via reverse transcriptase polymerase chain reaction (RT-PCR) of blood or oral swabs to detect Ebola virus RNA may be positive within the first 24 hours after onset of symptoms or delayed upto 72 hours[4]. Enzyme linked immunosorbent assay (ELISA) can also be performed to detect Ebola Virus specific IgM or IgG, with antibodies developing as early as 2 days and 6 days after symptom development and persisting for up to 6 months and 10 years for IgM and IgGrespectively. Prolonged detection of Ebola virus has been demonstrated in certain body fluids including semen and vaginal secretions. Following the initial phase of illness, patients often progress to severe disease and may develop hypovolemia, oliguria, hypoalbuminemia, elevated creatinine, leukopenia, thrombocytopenia and multi-organ failure.

The clinical presentation and disease course of EVD appears to be similar among pregnant and non-pregnant women. There is no evidence of increased susceptibility during pregnancy and very few pregnant women have been reported in the literature[4]. Maternal mortality rate has been reported historically to be about 90% with 100% adverse perinatal outcome.There is limited information regarding specific care and treatment recommendations for pregnant women. Thus supportive care recommendations to maintain plasma volume and blood pressure including liberal use of blood products, correction of electrolyte imbalances, coagulopathy and maintaining adequate oxygenation is suggested[4].

Current Recommendations

The Guideline Development Group of the WHO in February 2020 published a guideline regarding management of pregnant women with Ebola virus disease[5].

RECOMMENDATION 1: Clinical management of all pregnant women should include optimized supportive care. This includes systematic assessment, fluid resuscitation, electrolyte monitoring and correction, glucose monitoring and management, treatment of potential co-infections and nutritional support. Prevention and management of complications should be provided.

RECOMMENDATION 2: Investigational therapies REGN-EB3 or mAb114 may be offered to pregnant

women. Pregnant women with acute EVD who are not treated with investigational agents experience very high rates of spontaneous miscarriage, foetal or neonatal death.

RECOMMENDATION 3: Labour should not be induced for foetal indications in pregnant women with acute EVD. Pregnant women recovering from the disease should be provided with counselling pertaining to the effect on pregnancy outcomes, risk for persistent infectivity of pregnancy-related fluids even after recovery. If a woman chooses to terminate the pregnancy, safe abortion services should be provided. Termination of pregnancy with drugs is preferred over surgical evacuation. PPE and standard precautions should be taken while handling products of conception. Products should be tested for Ebola virus and disposed off safely.

RECOMMENDATION 4: Invasive procedures should not be performed for foetal indications in pregnant women with acute EVD.

RECOMMENDATION 5: All pregnant women should be managed using standard precautions and Ebola-specific measures.

RECOMMENDATION 6: All pregnant women who have recovered should attend frequent Antenatal Care. During childbirth and pregnancy, Ebola infection prevention control measures should be used in addition to standard precautions.

RECOMMENDATION 7: Post-mortem Caesarean is not recommended in view of higher risk of transmission of disease to healthcare workers.

RECOMMENDATION 8: Breastfeeding should be stopped if acute EVD is suspected or confirmed. The child should be separated from the breastfeeding woman and provided a breastmilk substitute. The child should undergo monitoring for signs and symptoms of EVD for 21 days. Post-exposure prophylaxis can be considered for exposed children.

RECOMMENDATION 9: A woman who has recovered and cleared viremia and wants to continue breastfeeding should wait until she has had two consecutive negative RT-PCR breastmilk tests for EBOV 24 hours apart.

RECOMMENDATION 10: Pregnant and breastfeeding women should be offered vaccination with the prequalified Ervebo live-replicating rVSV-ZEBOV-GP vaccine during an active Zaire EBOV outbreak in affected areas.

ZIKA Virus

Zika virus is considered endemic in the Americas and Caribbean following the 2015- 16 outbreak as well as in much of Africa and Asia. The majority of people infected with Zika virus have minimal symptoms. Zika virus tends to cause a mild, short-lived (2 to 7 days) illness. WHO has concluded that Zika virus infection during pregnancy is a cause of Congenital Zika Syndrome, which encompasses congenital brain abnormalities and microcephaly. Zika virus has also been recognised as a trigger of Guillain-Barré syndrome[6].

Zika virus is predominantly transmitted by the bite of infected female Aedes mosquito. After an infected mosquito bites a human, the first symptoms can develop in 3 to 12 days but it can be shorter or longer in some. Sexual transmission hasalso been reported. The virus has been shown to be present in semen, vaginal secretions and menstrual blood. Zika virus can be transmitted by blood transfusion. Standard precautions for ensuring safe blood donations and transfusions should be done[6].

Cases of maternal fetal transmission have been confirmed. Viable virus has been detected in breast milk but Zika virus transmission through breast milk has not been confirmed. Therefore, the benefits of breastfeeding are likely to outweigh the risks of Zika virus infection in infants.

The diagnosis of Zika virus infection should be considered in individuals who experience symptoms suggestive of acute Zika virus infection within 2 weeks of leaving an area with risk for Zika virus transmission. Serum sample along with urine may be tested for the presence of virus by PCR[6]. Although amniotic fluid can be tested for the virus, there is no recommendation to routinely perform it in order to detect the chance of foetal anomaly.

In India 157 cases including 63 pregnant womenhave been identified in Rajasthan, Gujarat and Tamilnadu. To date no cases of microcephaly or congenital Zika syndrome have been reported.

Prevention

There is no drug or vaccine at present to prevent the disease. Measures to reduce the chance of mosquito bite by using repellents or mosquito net is recommended. Non-essential travel to areas with recent outbreaks should be avoided[6].

Treatment

There is no specific antiviral treatment available. Supportive nursing care including rest, plenty of fluid intake and treatment of symptoms are the standard treatment. The woman should receive a baseline foetal ultrasound and be referred to a foetal medicine service for further assessment. If foetal microcephaly or brain abnormality, such as intracranial calcification is diagnosed consideration should be given to performing an amniocentesis to test for the virus using RT-PCR. When a significant brain abnormality or microcephaly is confirmed in the presence of Zika virus infection, the option of termination of pregnancy should be discussed with the woman[6].

Rubella virus

Rubella is a mild viral disease that typically occurs in childhood. In 1941, an Australian ophthalmologist established the relationship between congenital defects and rubella during pregnancy. Rubella crosses

the placenta of infected pregnant women and can cause miscarriage, fetal death or congenital rubella syndrome. Congenital rubella syndrome includes auditory, sensorineural, cardiac and ocular abnormalities. The incidence of rubella has significantly decreased in many countries because of vaccination, since 1969.

The virus belongs to the Togaviridae family and is an enveloped, positive single-stranded RNA virus.

Clinical features

More than 50% of cases are asymptomatic. In clinically apparent cases, after an incubation period of 13 to 20 days, a prodromal illness that includes fever, malaise and postauricular lymphadenopathy. A maculopapular rash develops that typically lasts 1 to 3 days and is characterized by small pink papules. Polyarthralgia is also seen.

Diagnosis

In developed countries, women of childbearing age are routinely screened for rubella antibodies by measuring the RV-IgG with enzyme immunoassays. Susceptible women are vaccinated and pregnancy deferred for a month.

Laboratory diagnosis is essential to confirm a recent rubella infection and is based on the observation of a seroconversion, on the kinetics of RV-IgG, RV-IgM and RV-IgG avidity and on the detection of rubella virus in nasopharyngeal secretions by reverse transcription/polymerase chain reaction[7].

Diagnosis of foetal infection

The risks of congenital infection and defects depend on the gestational age at infection. Before 12-weeks, the congenital infection and anomaly rate approaches 90%, decreases to 30% between 24 and 26-weeks[7]. Fetal anomalies rarely occur after 20 weeks. A prenatal diagnosis of congenital infection is recommended when a maternal infection is diagnosed and is based on the detection of RV-IgM in foetal blood or on the detection of the viral genome in AF, foetal blood or chorion villus biopsy. A postnatal diagnosis of congenital infection is based on the detection of a specific RV□IgM by immunocapture ELISA. Performing a postnatal diagnosis of a congenital infection is important to provide a specific follow-up care plan if an infection is discovered since a child infected in utero could excrete the virus in saliva and urine for several months or years[7].

Management

Infection before 18 weeks: The fetus is at high risk for infection and severe symptoms. Termination of pregnancy could be discussed after a detailed ultrasound examination and assessment of amniotic fluid viral RNA.

Infection after 18-weeks: The pregnancy should be continued with ultrasound monitoring. A specific paediatric examination of the newborn and testing for RV-IgM are recommended.

The new strategic plan that aims to eliminate rubella and measles by MMR vaccination by the end of 2020 is generating new hope for the eradication of these diseases[7].

With international travel, it is essential for OGicians to know about uncommon viral infections and treat them appropriately.

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2. "Fever in pregnancy" Dr. D. Maharaj, Infectious disease and antimicrobial agents, http://www.antimicrobe.org/e42.asp
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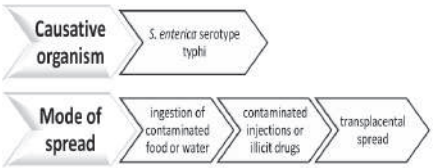
BACTERIAL INFECTIONS IN PREGNANCY

Bacterial infections may affect a woman from conception to delivery and peripartum period, they may either have an adverse effect on pregnancy and fetus or pregnancy may affect the course of infection, also all antibiotics may not be safe in pregnancy thus hindering the treatment. Most common infections caused by bacteria are urinary tract infections, group B streptococcal infections, bacteria vaginosis which result in preterm labour, other bacterial infections like typhoid fever , tuberculosis and infectious endocarditis are rare but may have pronounced effect on mother and fetus.

Typhoid fever

Enteric fever is caused by group D salmonellae, *Salmonella enterica* serotype typhi, pregnant woman are at risk compared to general population due to decreased peristaltic activity in gastrointestinal and biliary tract, and increased prevalence of biliary sludge and concretions, worldwide each year around 22 million of cases and 2 lakhs death occur due to typhoid fever[1]

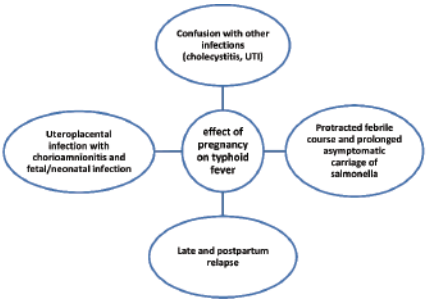


Risk factors for typhoid fever in pregnancy[2]

Signs and symptoms:

At the onset of bacteraemia patient usually experiences malaise, myalgia, vague abdominal discomfort, cough, and fever usually without rigors: may be mistaken for a viral illness in the beginning or cholecystitis. The temperature is high (39–40°C) in second week and sustained. The 'rose spot' rash (blanching erythematous rash) is reported in only 5–30% of all cases. Persistent high fever and hyperthermia are the hallmark of typhoid fever; Adverse fetal effects may be seen if infection occurs in first trimester. Those women who have been ill for more than 2 weeks may have serious complications in 10-15%.

Pregnancy effects on the course of typhoid fever[3]



Typhoid fever during pregnancy can result in uteroplacental infection, miscarriage and vertical intrauterine transmission leading to neonatal typhoid. Bleeding and perforation of necrotic Peyer's patches can occur in cases of delayed diagnosis and poor treatment, however they are rare nowadays due to advanced methods of diagnosis and better antimicrobial options.

Diagnosis :

Blood cultures are essential for diagnosis, although bone marrow culture is more sensitive. Stool or rectal swab cultures are less reliable earlier in the course, but the rate of positive cultures increases with duration of the illness.

Treatment:

For acutely ill patients empiric antibiotic therapy with cephalosporin combined with an aminoglycoside may be desired and can be changed when culture and sensitivity results are available.

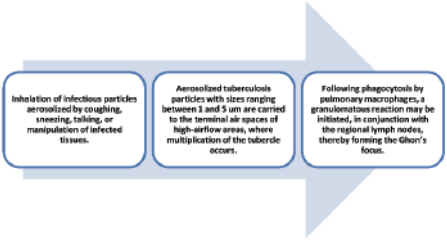
Prevention: strict hygiene to be maintained before consuming food and water. The Vi capsular polysaccharide vaccine provides effective immunity for two years with a single dose. It is safe to use during pregnancy since it is not a live vaccine[4]. Due to relatively short duration of protection, boosters are needed every 3rd year, oral vaccines have no role in pregnancy due to delayed gastrointestinal motility.

Tuberculosis:

Tuberculosis is major health concern especially in developing countries, it accounts for nearly 4500 deaths per day and prevalence of tuberculosis is 1.75 billion (1/3rd of world population), it is prevalent in those of low income group and age group of 15-45 years, thus affecting reproductive age group, so pregnant woman with pulmonary tuberculosis is not uncommon, though prevalence of extrapulmonary tuberculosis is rare in pregnant woman as infertility is common in such cases. People living with HIV/AIDS are high risk for tuberculosis due to weakened immune system

Microbiology: Mycobacterium tuberculosis, is an aerobic, non-spore-forming, nonmotile bacillus, belongs to Mycobacterium tuberculosis complex, others being M. bovis, M. ulcerans, M. Africanum, and M. microti, though M. tuberculosis is the major human pathogen. It belongs to the family Mycobacteriaceae. Other Mycobacterium species that may infect humans include Mycobacterium leprae, M. avium, M. Intracellulare, and M. scrofulaceum.

Pathophysiology:



Effect of pregnancy on tuberculosis

Factors influencing effect of tuberculosis on pregnancy are:
Severity of the disease
Period of gestation
Presence of extrapulmonary spread
HIV coinfection

Pulmonary cavities due to tuberculosis were believed to collapse as a result of the increased intra-abdominal pressure due to growing fetus and therapeutic abortion was adviced in 19th century, but it is no longer valid. Prognosis is same now as in non pregnant patients except diagnosis of tuberculosis may be delayed due to masking of symptoms due to pregnancy.

Effect of tuberculosis on pregnancy and fetus[5]

The worst prognosis is recorded in women in whom a diagnosis of advanced disease is made in the puerperium as well as those with HIV coinfection. Lack of compliance for treatment also worsens the prognosis.

Obstetric complications[6] due to tuberculosis are higher rate spontaneous abortion, decreased weight gain in pregnancy, small for dates fetus, preterm labour and increased neonatal mortality. Congenital tuberculosis is a rare complication of in utero tuberculosis infection. It may occur as a result of haematogenous spread through the umbilical vein to the foetal liver or by ingestion and aspiration of infected amniotic fluid. A primary focus subsequently develops in the liver, with involvement of the peri-portal lymph nodes. The tubercle bacilli infect the lungs secondarily, unlike in adults where over 80% of the primary infections occur in the lungs. Congenital tuberculosis may be difficult to distinguish from other neonatal or congenital infections from which similar symptoms may arise in the second to the third week of life. These symptoms include hepato-splenomegaly, respiratory distress, fever, and lymphadenopathy. Nearly half of the neonates delivered with congenital tuberculosis may eventually die, especially in the absence of treatment.

Diagnosis of Tuberculosis in Pregnancy

History of exposure and presence of chronic cough is important, other symptoms like progressive weight loss, nausea or malaise may be masked by pregnancy symptom. In pregnant women with signs and symptoms suggestive of TB, a tuberculin skin test should be carried out. A chest radiograph with abdominal lead shield may be done after 12 weeks, Microscopic examination of sputum(early morning sample) for Acid-fast bacilli (AFB) remains the cornerstone of laboratory diagnosis of TB in pregnancy. Culture on Lowenstein-Jensen's medium may take 4–6 weeks to obtain a result. Molecular Line Probe Assay (LPA) as well as the use of polymerase chain reaction (PCR) are presently facilitating the specific identification of the tubercle bacilli.

Treatment

The management of tuberculosis in pregnancy is a multidisciplinary approach, with the team comprising the obstetrician, communicable disease specialist, neonatologists, and public health officials. According to RNTCP 2018[7] guidelines principle of treatment has been shifted towards daily regimen with administration

of daily fixed dose combination of first line ATD as per appropriate weight bands.

Treatment in intensive phase consists of daily dosages of INH, rifampicin pyrazinamide and ethambutol for 8 weeks according to weight band categories, and 16 weeks of INH, rifampicin and ethambutol in continuous phase. In previously treated cases 12 weeks of HRZE in intensive phase and 20 weeks of HRE in continuous phase. Streptomycin is contraindicated in pregnancy.

Weight category	No of tablets (FDC) HRZE (75, 150, 400, 275)mg
25-39kg	2
40-54 kg	3
55-69 G	4
>70 kg	5

Follow up to be done according to RNTCP guidelines.

INH causes hepatotoxicity, follow up to be done and it should be supplemented with pyridoxine, rifampicin may cause hemorrhagic disorders and few may opt to give vit K in last few days before delivery, pyrazinamide may cause teratogenicity but risk benefit ratio to be analysed.

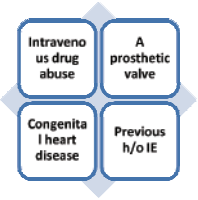
Treatment of TB in Lactating Women: Breastfeeding is better option as to prevent ill effects in babies due to malnutrition, however neonatologist to be consulted. The American Academy of Pediatrics recommends that women with tuberculosis who have been treated appropriately for two weeks or more and who are not considered contagious may breastfeed , while the RNTCP recommends breast-feeding of neonates regardless of the mother's TB status . Antituberculous drugs are excreted into breast milk, though the dose is less compared with the therapeutic dose for infants. Breastfed infants may receive as much as 20% of the therapeutic dose of INH for infants, while other antituberculous drugs are less excreted. No toxicity has been reported from this small concentration in breast milk. Pyridoxine deficiency may cause seizures in the newborn. Supplemental pyridoxine should, therefore, be administered to infants on INH or whose mother is taking the drug.. In the absence of evidence of congenital tuberculosis, isoniazide (10 mg/kg/day) should be commenced at birth and continued for six months.

Prevention of Tuberculosis: The BCG vaccine is contraindicated in pregnancy . Improved living condition and good ventilation to be encouraged, and overcrowding should be avoided. Improvement in nutritional status is also important.

Infective endocarditis

Though infective endocarditis is rare in pregnancy with an overall reported incidence of 1 in 100,000 pregnancies, it has high maternal morbidity and mortality(33%) and high fetal mortality (up to 29%). It may arise following bacteraemia in a patient with a predisposing cardiac lesion. Over past 50 years to prevent IE, at-risk patients aregiven antibiotic prophylaxis before dental and certain non-dental interventional procedures[8].

Risk factors for infectious endocarditis



Pathogenesis : The normal heart is relatively resistant to infection. Development

of endocarditis requires both a predisposing abnormality of the endocardium like prosthetic valves(more in mechanical) or congenital heart diseases and microorganisms in the bloodstream (bacteraemia). The three most common causative organisms are Streptococcus viridans, staphylococci and enterococci.

Infective endocarditis has been classified into acute and subacute. Subacute bacterial endocarditis (SBE) usually develops insidious onset and slow progression. Often, no source of infection is evident. It is caused most commonly by S. viridans and enterococci and less commonly by S. aureus. Subacute infective endocarditis often develops on abnormal valves after asymptomatic bacteraemia due to periodontal, gastrointestinal and genitourinary infections. In contrast, acute bacterial endocarditis develops abruptly and progresses rapidly, with a source of infection evident. It is usually caused by S. aureus, group A haemolytic streptococci, pneumococci or gonococci.

Clinical features: any pregnant woman with history of cardiac disease with presence of fever and features of embolism should evoke a strong suspicion of IE

Modified Duke's criteria[9]

Major Criteria
A. Supportive laboratory evidence ➢ Typical microorganism for infective endocarditis from two separate blood cultures: viridians streptococci, *Staphylococcus aureus, Streptococcus bovis*, HACEK group (*Haemophilus spp. Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella spp., and Kingella kingae*) or ➢ Community-acquired enterococci, in the absence of a primary focus
➢ Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from blood cultures drawn more than 12 hours apart or ➢ Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from all of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart.
➢ Single positive blood culture for *Coxiella burnetti* or phase I antibody titer >1:800

B. Evidence of endocardial involvement ➢ Echocardiogram supportive of infective endocarditis. 1. Type of study Transesophageal echocardiography recommended as first test in the following patients: a) prosthetic valve endocarditis; or b) those with at least "possible" endocarditis by clinical criteria; or c) those with suspected complicated endocarditis, such as paravalvular abscess. TTE recommended as first test in all other patients 2. Definition of positive findings: Oscillating intracardiac mass, on valve or supporting structures, or in the path of regurgitant jets, or on implanted material, in the absence of an alternative anatomic explanation or myocardial abscess or new partial dehiscence of prosthetic valve
C. New valvular regurgitation (increase or change in pre-existing murmur not sufficient).

Minor Criteria
➢ Predisposing heart condition or intravenous drug use
➢ Fever >= 38.0 C (100.4 F)
➢ Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhage, Janeway lesions
➢ Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor
➢ Positive blood culture not meeting major criterion as noted previously (Excluding single positive cultures for coagulase-negative staphylococci and organisms that do not cause endocarditis) or serologic evidence of active infection with organism consistent with infective endocarditis

Diagnosis: Echocardiography plays a key role in diagnosis, management and follow up of patients, usually Transthoracic Echocardiography is done.

Treatment

IE during pregnancy often causes embolic events and mycotic aneurysms. Two-thirds of IE in the pregnant patients requires timely or urgent cardiac surgery to alleviate patients' deterioration. At least a 3-week antibiotic therapy is mandatory before cardiac surgery aiming at improving the patients' conditions. During cardiac surgery, fetal heart rates may temporarily be slowed down but may gradually recover to normal after the operation, combination of penicillin and gentamycin is preferred, in patients who are term, elective caesarean section to be done first followed by definitive cardiac surgery[10].

Antibiotic Prophylaxis: Pregnant woman with cardiac disease undergoing dental procedures, instrumental delivery, caesarean section, those with 3rd or 4th degree perineal tear require antibiotic prophylaxis with ampicillin and gentamycin, according to NICE guidelines, women at risk admitted for normal delivery do not require antibiotic prophylaxis[11].

Proper and adequate antibiotic treatment is key in management of bacterial infections, keeping in mind of potential side effects both to mother and fetus and to be mindful of possibility of emergence of antibiotic resistance with inappropriate dose and interval of antibiotic therapy.

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H_1N_1 IN PREGNANCY

Introduction:

Pandemic swine – origin influenza A (H_1N_1) emerged as a threatening pathogen in March 2009. Although this specific strain of influenza is dangerous to many group of individuals, including the very young or people with chronic medical conditions. **It has targeted pregnant women at an alarming rate and with potential serious sequelae.** For these reason, it is imperative that prenatal care providers should become familiar with the diagnosis and treatment of pregnant women with suspected H1N1 influenza. In addition health care providers should understand the importance of vaccinating all pregnant patients against influenza.

Influenza like illness caused by Influenza A (H_1N_1) was reported from Mexico on 18th March, 2009 and rapidly spread to all continents.

India reported its first case on 13th may, 2009.

What is H1N1?

It is an Orthomyxovirus that contains glycoproteins: Haemagglutinin and Neuraminidase

For this reason they are described as H_1N_1, H_1N_2 etc depending upon the type of antigens they express. Haemagglutinin causes red blood cells to clump together and binds the virus to the infected cells.

Neuraminidase is a type of glycoside hydrolase enzyme which helps to move the virus particle through the infected cell and assist in budding from the host cells.

Epidemiology:

- Incubation period: 1-7 days
- Transmission by droplet infection and fomites
- Communicability from 1 day before to 7 days after onset of symptoms

High risk groups:

- Children ≤2 years
- Adults ≥65 years
- pregnant women
  - chronic medical conditions
  - person with immunosuppression

Clinical presentation:

- acute respiratory influenza like illness
- cough, sore throat, rhinorrhoea
- Fever
- Shortness of breath
- Other symptoms
  - Bodyache
  - Headache
  - Vomiting
  - Diarrhea
  - Fatigue

Investigations:

- CBC , LFTs, RFTs, coagulation profile
- X Ray chest, CT Scan (when required)
- Real Time Reverse Transcriptase(RT-PCR) is done for confirmation of diagnosis
- Clinical Specimen such as nasopharyngeal swab, throat swab, nasal swab, tracheal aspirate (for intubated patients) are to be obtained preferably before administration of antiviral drug.
- Specimen should be placed in sterile virus transport media (VTM) and immediately placed on ice or cold packs or at 4 degree C (refrigerator) for transport to the laboratory.

Pregnancy at risk:

Pregnancy does not predispose women to an increased risk of acquiring influenza infection. However pregnant women are at increased risk of morbidity and mortality as compared to women who are not pregnant. This is due to changes in their immune system to accommodate the developing fetus and adaptation in body as a result of the hormonal and physical changes. Other factors such as family commitments, lack of awareness, Gender discrimination have been identified to cause delay in seeking health care.

Complication:

- Compared to non-pregnant individuals, pregnant women are more likely to develop influenza-associated complications, severe disease, and death, especially if they have co-morbidities.

- It is associated with increased risk of adverse pregnancy outcomes such as spontaneous abortion, preterm birth, and fetal distress.
- The risk of complications in newborn infants increases, if their nutritional status is poor and fluid intake is low because of prolonged vomiting, diarrhea, or inability to feed.
- Newborn infants less frequently present with typical influenza signs, such as cough and fever. Influenza or its complications in newborn infants may manifest as apnoea, low grade fever, fast breathing, cyanosis, excessive sleeping, lethargy, feeding poorly, and dehydration.

Management:

Prevention is always better than cure. The main route for transmission of pandemic (H1N1) 2009 influenza virus is, via droplets that are expelled while speaking, sneezing, or coughing. People can avoid infection by taking the following measures:

- Cover your mouth and nose while sneezing
- Washing hands frequently with soap and hot running water or utilize alcohol based sanitizer.
- Maintain 1 m distance if infected or have flu like symptoms to refrain from affecting others
- Do not shake hands, hugs or kiss when greeting anyone.
- Dispose of used tissues immediately after using.
- Do not touch eyes, mouth and nose without washing hands.
- It is advisable to practice additional good health habits, including getting adequate sleep, eating nutritious food, and staying physically active.

Special considerations for pregnant women and new mothers and their babies:

- Avoid crowded public places whenever possible
- Avoid providing care for those with confirmed, probable, or suspected influenza infection except for their own newborns.
- Anyone with respiratory symptoms should not provide antenatal care for a pregnant woman or a mother or a newborn baby.

Antenatal care:

- Reduce antenatal clinic visits to the minimum required and advise women with low-risk pregnancies to postpone clinic visits during early pregnancy for a few weeks.
- Advise pregnant women to avoid crowded places, whenever possible.
- When attending pregnant women, use all preventive measures to avoid transmission of infection.
- Provide adequate information on the prevention of influenza and steps to take in case of symptoms that suggest influenza infection.
- Vaccination is recommended for all healthcare workers.

Intra partum care:

- Protect the infant from exposure to respiratory secretions during or immediately after delivery.
- Mother should use face mask throughout labor, as tolerated.
- Adherent to current infection control guidance.
- During delivery all persons should use face mask, gloves and gown.
- Allow birth companions, but screen them for influenza infection (i.e. take their history, measure body temperature, and look for signs of influenza infection).
- Immediate separation of newborn to an open warmer by a distance of > 6 ft.
- Bath infant as soon as the temperature is stable.

Post natal care:

Temporary separation of the infected mother from the newborn within her room or in a separate room until, the risk of infection transmission is reduced, which is when ALL of the following criteria are met:

- The mother is without fever for 24hrs without antipyretics.
- The mother has received Antiviral Medications for at least 48hrs.
- The mother can control cough and respiratory secretions.

Once these criteria are met, the mother and the newborn can initiate close contact throughout the postpartum period with droplet precautions and mother can start breast-feeding.

Breast-feeding:

- Mothers should be encouraged to begin breastfeeding within one hour of giving birth and to breastfeed frequently and exclusively including a period of pandemic (H1N1).
- Infants who are not breastfed are more vulnerable to infectious diseases, including severe respiratory tract infection.

Care of the Newborn:

- Washing hands frequently with soap and water and cleaning soiled surfaces to keep the environment free from virus, especially since infants have a tendency to place their hands in their mouth.
- Adherence to respiratory etiquette i.e.; covering their mouth and nose, when coughing or sneezing.
- If a tissue is used, it should be discarded in a bin with a lid and then hands should be washed.

Implementation of infection control measures:

- Preferably isolation room should be there, if not available then patients can be kept in well-ventilated isolation ward with beds kept one meter apart.
- All those entering the room must wear high efficiency masks, gowns, goggles, gloves, cap and shoe cover.
- Restrict number of visitors
- Use of face mask by patient when outside the room.
- Diagnostic testing and empirical antiviral therapy immediately.
- Do not delay antiviral treatment pending diagnostic results.

Drug Treatment (Neuraminidase Inhibitor): Oseltamivir (TAMIFLU):

- Safe drug both for prophylaxis and treatment.
- FDA Category-C
- Dose -75 mg BD for 5 days for adults.
- Safe in pregnancy in all trimester

Zanamivir:

- Inhaled as Powder.
- Dose: 10 mg BD for 5 days.
- Contraindicated in asthmatic patients

Supportive therapy:

- Symptomatic treatment, IV Fluids, parenteral nutrition, Oxygen therapy/ventilator support.
- Paracetamol is prescribed for fever, myalgia and headache.
- Antibiotics should be administered, if required.
- Explain the importance of adequate nutrition and fluid intake to the woman and her family.

Chemoprophylaxis:

Chemoprophylaxis is recommended for contacts of suspected, probable and confirmed cases. Contacts include household /social contacts, family members, workplace or school contacts, fellow travelers, and health care worker. It should be provided till 10 days after last exposure. Oseltamivir (TAMIFLU) is the drug of choice with dose of 75 mg OD for 10 days for adults. Oseltamivir is extensively metabolized by placenta and minimally accumulated by fetus. Benefits outweigh the theoretical risks.

Vaccination:

5 key target populations to be vaccinated on first-come, first-served basis

- Pregnant women
- People who live or care for children <6 months old
- Health care and emergency services personnel
- Persons aged 6 months through 24 years
- People aged 25-64 yrs at higher risk due to chronic disease or compromised immune systems.

H_1N_1 Vaccine:

- FDA has approved the H_1N_1 monovalent vaccine as intramuscular injection (inactivated) and an intranasal spray (Live). It is safe and recommended for pregnant women.
- Inactivated vaccine should not be administered to those having history of anaphylaxis to any constituents of vaccine, moderate to severe illness with fever and children below 6 months.
- Live intranasal vaccine should not be administered to pregnant women, individuals below 2 years and above 50 years, those having chronic illness and fever.
- If delivered before vaccination she should still receive vaccine to protect herself and newborn (because vaccine is contraindicated before 6 months of age.)

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PANDEMICS IN THE PAST

What is a Pandemic?

A pandemic is the global outbreak of a disease. Pandemics are generally classified as epidemics first, which is the rapid spread of a disease across a particular region or regions. COVID-19 began as an epidemic in China, before making its way around the world in a matter of months and becoming a pandemic. But epidemics don't always become pandemics, and it's not always a fast or clear transition.

The first cholera pandemic occurred in 1817 and originated in Russia, where 1 million people died, according to History.com. The bacterium was transmitted to British soldiers, who carried it into India and eventually the rest of the world.

The 1957-1958 Asian flu pandemic was triggered by a new strain of influenza A virus (H2N2) that emerged in East Asia. The virus killed an estimated 1.1 million people worldwide, which corresponded to an estimated death rate of 0.019%.

The 1968 Hong Kong flu pandemic was caused by a new strain of the H3N2 virus that arose in Southeast Asia. Again, the pandemic earned its name because of where initial news reports of the outbreak originated, and not because of where the virus originated. The Hong Kong flu killed an estimated 1 million people worldwide

The H1N1 swine flu pandemic of 2009 -10 was caused by a new strain of the same virus that caused the Spanish flu — the H1N1 virus. The swine flu infected an estimated 700 million to 1.4 billion people. But the mortality rate was far less.

And the other pandemics that rattled the world are:

The Black Death: 1346-1353

The Black Death traveled from Asia to Europe, leaving devastation in its wake. Some estimates suggest that it wiped out over half of Europe's population. It was caused by a strain of the bacterium *Yersinia pestis* that is likely extinct today and was spread by fleas on infected rodents. The bodies of victims were buried in mass graves.

The plague changed the course of Europe's history. With so many dead, labor became harder to find, bringing about better pay for workers and the end of Europe's system of serfdom. Studies suggest that surviving workers had better access to meat and higher-quality bread. The lack of cheap labor may also have contributed to technological innovation.

Flu pandemic: 1889-1890

In the modern industrial age, new transport links made it easier for influenza viruses to wreak havoc. In just a few months, the disease spanned the globe, killing 1 million people. It took just five weeks for the epidemic to reach peak mortality.

The earliest cases were reported in Russia. The virus spread rapidly throughout St. Petersburg before it quickly made its way throughout Europe and the rest of the world, despite the fact that air travel didn't exist yet.

Spanish Flu: 1918-1920

An estimated 500 million people from the South Seas to the North Pole fell victim to Spanish Flu. One-fifth of those died, with some indigenous communities pushed to the brink of extinction. The flu's spread and lethality was enhanced by the cramped conditions of soldiers and poor wartime nutrition that many people were experiencing during World War I.

Despite the name Spanish Flu, the disease likely did not start in Spain. Spain was a neutral nation during the war and did not enforce strict censorship of its press, which could therefore freely publish early accounts of the illness. As a result, people falsely believed the illness was specific to Spain, and the name Spanish Flu stuck.

Asian Flu: 1957-1958

The Asian Flu pandemic was another global showing for influenza. With its roots in China, the disease claimed more than 1 million lives. The virus that caused the pandemic was a blend of avian flu viruses.

The Centers for Disease Control and Prevention noted that the disease spread rapidly and was reported in Singapore in February 1957, Hong Kong in April 1957, and the coastal cities of the United States in the summer of 1957. The total death toll was more than 1.1 million worldwide.

AIDS pandemic and epidemic: 1981- present day

DS has claimed an estimated 35 million lives since it was first identified. HIV, which is the virus that causes AIDS, likely developed from a chimpanzee virus that e

transferred to humans in West Africa in the 1920s. The virus made its way around the world, and AIDS was a pandemic by the late 20th century. Now, about 64% of the estimated 40 million living with human immunodeficiency virus (HIV) live in sub-Saharan Africa.

For decades, the disease had no known cure, but medication developed in the 1990s now allows people with the disease to experience a normal life span with regular treatment. Even more encouraging, two people have been cured of HIV as of early 2020.

H1N1 Swine Flu pandemic: 2009-2010

The 2009 swine flu pandemic was caused by a new strain of H1N1 that originated in Mexico in the spring of 2009 before spreading to the rest of the world. In one year, the virus infected as many as 1.4 billion people across the globe and killed between 151,700 and 575,400 people, according to the CDC.

The 2009 flu pandemic primarily affected children and young adults, and 80% of the deaths were in people younger than 65, the CDC reported. That was unusual, considering that most strains of flu viruses, including those that cause seasonal flu, cause the highest percentage of deaths in people ages 65 and older. But in the case of the swine flu, older people seemed to have already built up enough immunity to the group of viruses that H1N1 belongs to, so weren't affected as much. A vaccine for the H1N1 virus that caused the swine flu is now included in the annual flu vaccine.

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