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PREGNANCY & SAFE MEDICINE: A REVIEW

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ABSTRACT

The study in this paper is an attempt to cover what is hepatitis, influenza, and zika aids its types, the history, different types of diseases affecting the womb with special emphasis on prevention of diseases in pregnancy with safe use of medicines. Swine flu (swine influenza) is a respiratory disease caused by viruses, hepatitis affects the liver, diabetes affecting the pancreatic activity, hypertension, and zika virus causing the birth of microcephaly child. The immature adaptive immune systems of neonates and premature infants make them particularly vulnerable to morbidity and mortality due to infection. Immunization of pregnant women can protect them directly against vaccine-preventable infections, and in so doing potentially protect the fetus.

Key words: Hepatitis, H1N1, Zika, ZIKV, HAV, HBV.

INTRODUCTION

Pregnancy is a unique period in a woman's life. Many changes are happening to her body that may affect the pharmacology of medications. During pregnancy, a woman's gastric pH is increased and gastric motility is reduced which may interfere with the rate and extent of medication absorption. Maternal plasma volume is increased leading to changes in the volume of distribution. In addition, increases in progesterone and estradiol levels may affect the hepatic metabolism of some medications. Glomerular filtration rate is increased due to increase renal blood flow which may affect renally cleared medications. Despite the changes, the pharmacology of most medications is not altered enough to require dosing changes [1]. The placenta is an organ of exchange allowing the mother to pass nutrients and medications to the fetus; therefore, medications administered to pregnant women have the potential to affect the growing fetus. The fetus is generally at the greatest risk of developing teratogenic effects from medications during the first trimester, but it is drug specific. The use of medications in pregnancy should be evaluated for the benefits and risks to both the mother and fetus. Upon evaluation, some medications may be used sparingly during some trimesters and contraindicated in others [2]. All efforts should be made to optimize the risk benefit ratio. Drugs with low molecular weight, low maternal protein binding, low ionization, and high lipophilicity are more likely to cross the placenta and cause pharmacologic affects. The developing fetus's body systems are not mature; therefore, the fetus may lack the ability to metabolize medications causing teratogenic effects [2].

Hepatitis and Pregnancy

Pregnancy is generally considered to be an immune suppressed state; however, the impact of pregnancy on mothers with viral hepatitis (Table 1) and the impact of viral hepatitis on fetuses/infants (Table 2) are not the same for all types of hepatitis. Pregnant women with acute hepatitis due to hepatitis E virus (HEV) or herpes simplex virus (HSV) have an increased risk of acute liver failure compared to persons who are not pregnant. Flares of chronic hepatitis B may occur during pregnancy and in the postpartum period, but hepatic decompensation is rare. The risk of vertical transmission of hepatitis viruses is higher in pregnant women with acute versus chronic infection. In general, the risk is not increased with amniocentesis, fetal monitoring, or vaginal birth, and cesarean should not be recommended to prevent transmission of hepatitisviruses [3]. Breastfeeding is safe for women with chronic hepatitis B virus (HBV) or chronic hepatitis C virus (HCV) infections— unless they have cracked nipples [4, 5]. Hepatitis A and B vaccines are safe to be administered during pregnancy.

Swine flu & pregnancy

Most pregnant women will have an

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uncomplicated course, but there have been reports of adverse pregnancy outcome, including maternal death. The h1n1 virus infected pregnant women have been lead to increased rate of morbidity. In keeping with previous influenza pandemics, mortality also appears to be higher in pregnant women, especially if infection occurs in the third trimester [10-12]. Pregnancy-related complications of novel H1N1 infection include non reassuring fetal testing (most commonly fetal tachycardia) and febrile morbidity. Hyperthermia in early pregnancy has been associated with neural tube defects and other congenital anomalies, and fever during labor and birth is a risk factor for neonatal seizures, newborn encephalopathy, cerebral palsy, and death [13-15]. In a series of 5 pregnant women recently hospitalized for pandemic H1N1, the CDC reported that 2 women developed complications including spontaneous abortion (at 13 weeks) and premature rupture of membranes (at 35 weeks) [16].

Zika virus and pregnancy

Transmission cycles between humans and *Aedes aegypti* mosquitoes in urban settings can cause large-scale epidemics of ZIKV infection. Asian ZIKV strains directly into the lateral left ventricle of fetal brains at E13.5 (equivalent to the late second trimester of pregnancy in humans) and analyzed tissues before8 or after9 birth. Both groups observed a reduction in the number of cortical neural progenitors in the dorsal ventricular and subventricular zones, and this loss was associated with cell death. Wu et al. also injected ZIKV through an intraperitoneal route into pregnant immunocompetent mice at E13.5. They found that ZIKV could cause a transient viremia with seeding of the placenta in a subgroup of pregnant mice. Somewhat unexpectedly, they found ZIKV RNA in the dorsal ventricular zone of the fetal brain but in no other brain regions. They concluded that ZIKV can cross the fetal–placental barrier and specifically target the cortical neural progenitors of fetal mice.

Follow up of pregnant women infected with ZIKV

Pregnant women tested positive for Zika virus infection (identified by RT-PCR or detection of IgM/IgG immunoglobulin) should be referred for high-risk prenatal care. There are no studies with appropriate design plan for the monitoring of pregnant women diagnosed with Zika virus aiming to assess prognosis or quality of life. Howev-er, if the fetal ultrasound examination is normal in women tested positive for Zika virus infection, both physician and patient should considerer scheduling ultrasounds serially every 3 to 4 weeks to monitor fetal anatomy and growth [21].

Prevention In ZIKV

There are no medicines to treat Zika. If you have signs or symptoms, you can:

• Get plenty of rest.

• Drink plenty of fluids.

• Take acetaminophen (Tylenol®) to relieve fever and pain.

HIV and pregnancy

According to the Centers for Disease Control and Prevention (CDC), about 50,000 people get infected with HIV each year in the United States. In 2010, of the 1.1 million people in the United States living with HIV, 47,500 people had new HIV infections and one in four people were women [22]. About 80% of new cases in women in the United States are contracted through heterosexual intercourse, 20% by contaminated needles and the remaining cases through blood transfusions (no longer occurring as transmission factor due to universal screening of blood products for HIV) and maternal-child transmission. In the United States, African American and Hispanic women represent 25% of the female population but 82% of the total number of women with AIDS. Furthermore, black women alone account for 80% of newly diagnosed HIV/AIDS cases.28 Eventually, most people infected with HIV develop AIDS and die from opportunistic disease or malignancy. Without treatment, 90% of people with HIV progress to AIDS after 10–15 years. Treatment with antiretroviral medication prolongs life expectancy even after progression to AIDS such that the average survival with antiretroviral treatment exceeds 15 years [23, 24]. The most common clinical manifestations of the acute retroviral syndrome include fever, lymphadenopathy, sore throat, rash, myalgia/arthralgia, and headache. Diagnosis is made with HIV immunoassay (ELISA or Western blot) and HIV viral RNA detection. If left untreated levels of CD4 T cells decline The reduction in mother-to-child transmission of human immunodeficiency virus (HIV) is regarded as one of the most effective public health initiatives in the United States. While pregnancy does not affect disease course, HIV infection in pregnancy includes a risk of vertical transmission. The exact mechanism of mother-to-child transmission of HIV remains unknown at this time. This transmission may occur during intrauterine life, delivery, or breastfeeding. The greatest risk of transmission is attributed to advanced maternal disease, likely due to a high maternal HIV viral load. The hormonal status, the regulation of the mucosal environment in the female reproductive tract, and the morphological changes in the female reproductive tract associated with pregnancy play a critical role in the susceptibility to HIV. This is an area that we have only begun to understand and involves multiple complex biological and clinical factors that need to be carefully evaluated [25].

Prevention of mother-to-child transmission (PMTCT)

The critical determinants of transmission risk in the ART era are maternal viral load and duration of maternal ART. In the absence of ART, viral load is proportionate to the risk of mother-to-child transmission among pregnant women.

High-risk scenarios include

• Incident HIV infection in a pregnant or breastfeeding woman (defined as new HIV diagnosis in a pregnant or breastfeeding woman with a prior negative HIV test during pregnancy).

• HIV exposure first identified at delivery or in the postpartum period in a breastfed infant.
• Pregnant women whose viral load exceeds 1000 copies/mL within four weeks prior to delivery (if viral load testing is available).
• Pregnant women on ART for less than four weeks (if viral load testing is not available).

Prolonged rupture of membranes, preterm delivery and low birth weight are no longer associated with increased risk of transmission when mothers are receiving ART.

Safe drug therapy

Strategy	Research Projects
A: Antiretroviral Therapy	Phase III: 1. PETRA: ZDV & 3TC 2. ZDV alone in short-course in breastfeeding women 3. Nevirapine (HIVNET 012 & PACTG 316) Phase I/II: Drugs under investigation include: ddi, d4T, Nevirapine, Melfinavir, Ritonavir, Indinavir, Saquinavir, PMPA, MKC-442
B: Active Immunisation	1. Recombinant Gp120 vaccine to pregnant women (PACTG 235). 2. Recombinant Gp 120 to newborns; phase I/II (PACTG 230) 3. Canary pox vaccine to newborns (PACTG 327)
C: Passive Immunisation	1. HIVIG (Uganda) 2. Phase I Katinger antibody
D: Micronutrients	1. Vitamin A (Malawi: 10 000IU) 2. Vitamin A South Africa (5000 IU + B Carotene 30 mg) 3. 13 Vitamin A 10 000 IU and N 12 other vitamins and minerals (Zimbabwe) 4.Factorialdesign Vitamin A & B Carotene (Tanzania) (Zimbabwe) postpartum and to children 5. VitaminA (Zvitambo).
E: Vaginal Cleansing	Chlorhexidine (Kenya)
F: Infant Feeding	Randomised trial of breast vs formula feeding (Kenya).

Table 1. Types and Risk Of Hepatitis In Pregnancy

TYPES	POTENTIAL RISK TO MOTHER	TIMING OF PREGNANCY WITH HIGHEST RISK
Hepatitis A	Gestational complication;preterm labor	2nd half of pregnancy, especially 3rd trimester
Hepatitis B	Flares of chronic hepatitis B	Can occur during pregnancy or postpartum period
Hepatitis C	None	Cholestasis, neonatal abstinence
Hepatitis E	Acute liver failure	eclampsia 2nd and 3rd trimester
HSV hepatitis	Acute liver failure	3rd trimester

Table 2. Risks of Viral Hepatitis on Fetus/Infant and Preventive Measures

Types	Potential Risks to Fetus=Infant	Preventive Measures
Hepatitis A	Fetal ascites; meconium peritonitis. Rare, mainly if mother is infected during 1st trimester	Vaccinate pregnant women who will be traveling to endemic areas Administer immune globulin to pregnant women who had contact with persons with

		acute hepatitis A
Hepatitis B	Perinatal infection. Risk higher if mother is HBeAg1 or has high HBV DNA	Passive/active prophylaxis HBIG and HBV vaccination within 12 hours of birth for all newborns of HBsAg1 mothers Antiviral therapy for mothers with high HBV DNA in 3rd trimester of pregnancy
Hepatitis C	Perinatal infection. Risk higher if mother is coinfected with HIV or has high HCV RNA	None
Hepatitis E	Spontaneous abortion; premature delivery. Risk higher if mother is infected during 3rd trimester	None
HSV hepatitis	Neonatal HSV: Skin lesions, keratoconjunctivitis, cataracts, chorioretinitis, ulcerative lesions in mouth/tongue, central nervous system disease, disseminated HSV (hepatitis, hemorrhagic pneumonitis, necrotizing enterocolitis, meningoencephalitis)	Treat mother with primary or first episode of genital HSV infection with acyclovir Consider suppressive therapy for recurrent infections at 36 weeks of pregnancy Consider cesarean section delivery if predicted risk of transmission is high.

Table 3. Clinical Studies of Oral Antiviral Therapy in HBsAg1 Pregnant Women to Decrease Risk of Perinatal Transmission of Hepatitis B

Author, Year, Country (ref)	Study Design	No. of Pregnant Women	Maternal HBV DNA	Antiviral Drug and Start Time During Pregnancy	% Infants BsAg1Ve Treated vs Control (time of assessment)	*P* Value
WM Xu et al, 2009, China [6]	Randomized double-blinded, placebo controlled	56 treatment vs 59 placebo	> 109 cp/ml	Lamivudine week 32	18% vs 39% (52 week)	0.014 (intention to treat analysis) vs 0.37 (per protocol analysis)
GR Han et al, 2011, China [7]	Prospective, not randomized	135 treatment vs 94 untreated control	> 107 cp/ml	Telbivudine weeks 20-32	0% vs 8% (28 week)	0.001
CQ Pan et al, 2012, China [8]	Prospective, open-label	53 treated vs 35 untreated control	> 106 cp/ml	Telbivudine weeks 12-30	0% vs 8.6% (28 week)	0.03
MK Celen et al, 2013, Turkey [9]	Retrospective	45 treatment vs. 24 controls	> 107 cp/ml	Tenofovir weeks 18-27	0% vs 8% (28 week)	0.022

Table 4. Causative agent, clinical manifestations, pathological test, symptoms , treatment

Causative agent	Symptoms develop	Clinical manifestations	Pathological test/investigations	Treatment In Pregnant Women
RNA viruses belonging to the family *Orthomyxoviridae*	within 1 week of exposure(headache, fatigue, body aches, vomiting, and diarrhea.)	acute respiratory illness, including cough, sore throat, rhinorrhea, and fever. Other complaints may include headache, fatigue, body	RT-PCR CBC, LFTs, RFTs, Coagulation profile, X-ray Chest, CT scan	oseltamivir (75 mg twice daily for 5 days) or zanamivir (2 5-mg inhalations twice daily

		aches, vomiting, and diarrhea. Their clinical presentation can be complicated by development of a secondary bacterial infection (such as pneumonia).		for 5 days)

Table 5. Development Stages Of Zikv In Pregnancy

Zika infection in pregnancy	Deformities in neonatal	Affects the specific site
Early in pregnancy	severe placental vascular damage and a reduction in fetal blood vessels and blood flow	Infects And Injures Neuronal Progenitor Cells (microcephaly)

Table 6. Comparative Study Of Zika Infection In America

WHO study on ZIKV pregnancies	Detection of ZIKV	Rate of infection in pregnant women with ZIKV	Care for pregnant women with possible Zika virus related fetal brain/ other abnormalities
Abdominal circumference, biparietal diameter, femur length, head circumference (HC), and Occipito-frontal diameter (OFD)	The diagnostic odds ratios were statistically significant and increased considerably as the standard deviations below the mean increased.	OFD and HC were more consistent in specificity and sensitivity	Fetuses and infants with CMV or toxoplasmosis infections but with normal ultrasound findings are expected to have an excellent prognosis [18-20].

Table 6. Provides viral infection in pregnancy, teratogens, prevention with safe use of drugs.

VIRAL DISEASES (TYPE)	TERATOGENS (WOMB/FETUS)	PREVENTION WITH SAFE DRUG USE
Hepatitis A	Fetal ascites; meconium peritonitis. Rare, mainly if mother is infected during 1st trimester	Vaccinate pregnant women who will be traveling to endemic areas Administer immune globulin to pregnant women who had contact with persons with acute hepatitis A
Hepatitis B	Perinatal infection. Risk higher if mother is HBeAg1 or has high HBV DNA	Passive/active prophylaxis HBIG and HBV vaccination within 12 hours of birth for all newborns of HBsAg1 mothers Antiviral therapy for mothers with high HBV DNA in 3rd trimester of pregnancy
Hepatitis C	Perinatal infection. Risk higher if mother is coinfected with HIV or has high HCV RNA	None
Hepatitis E	Spontaneous abortion; premature delivery. Risk higher if mother is infected during 3rd trimester	None
HSV hepatitis	Neonatal HSV: Skin lesions, keratoconjunctivitis, cataracts, chorioretinitis, ulcerative lesions in mouth/tongue, central nervous system disease, disseminated HSV (hepatitis, hemorrhagic pneumonitis, necrotizing enterocolitis, meningoencephalitis)	Treat mother with primary or first episode of genital HSV infection with acyclovir Consider suppressive therapy for recurrent infections at 36 weeks of pregnancy Consider cesarean section delivery if predicted risk of transmission is high.
H1N1 infection	include non reassuring fetal testing (most commonly fetal tachycardia) and febrile morbidity. Hyperthermia in early pregnancy has been associated with neural tube	oseltamivir (75 mg twice daily for 5 days) or zanamivir (2 5-mg inhalations twice daily for 5 days)

	defects and other congenital anomalies, and fever during labor and birth is a risk factor for neonatal seizures, newborn encephalopathy, cerebral palsy, and death	
ZIKV	Fetuses and infants with CMV or toxoplasmosis infections but with normal ultrasound findings are expected to have an excellent prognosis, MICROCEPHALY(FETUS WITH REDUCED VOLUME OF BRAIN,INCOMPLETE DEVELOPMENT OF BRAIN)	NO SPECIFIC DRUG THERAPY • Get plenty of rest. Drink plenty of fluids. Take acetaminophen (Tylenol®) to relieve fever and pain. Use of preventives during safe sexual contact. Avoid travelling to zika infected areas
HIV	Preterm lobour, abruptio placentaintra-partum, intra-uterine death	ART, HAART, avoidance of breast feeding from mother to child.

The only interventions proven to be effective in reducing mother-to-child transmission (MTCT The only interventions proven to be effective in reducing mother-to-child transmission (MTCT) of HIV at present are the use of zidovudine (either as long-course through pregnancy, labor and for six weeks to the infant, or as short-course), and the avoidance of breastfeeding. Research continues into a number of other alternatives, with a major focus on interventions active at the time of labor and delivery, when much of the transmission is believed to occur. Studies that are completed and in the analysis stage include a vitamin A study in Malawi, a randomized formula feeding study conducted in Nairobi and a self-selection study looking at the effects of breastfeeding on transmission in Soweto. Other studies on the effect of vitamin A administration (South Africa, Zimbabwe and Tanzania), vaginal disinfection (Kenya), and short-course antiretroviral are ongoing.

CONCLUSION

Pregnancy is a divine stage of women life. Various diseases affecting womb may cause abnormalities in neonatal infants and such fetus are prevented by safe use of medicine. Hepatitis and its types are prevented from fetal attack by proper clinical manifestations and effective medicine use. Swine flu the most covering the influenza H1N1all over the population causes the prenatal illeffects.ZIKV the most dangerous virus affecting the womb If untreated, leading to microcephaly. The research and vaccines on ZIKV is emerging day by day.THE FOLLOWING

Thus medicines serves divine in pregnancy to prevent the fetus from infection with safe medicine use and cherrish the fetus with nourishment.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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