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REVIEW ARTICLE

Preconceptional Care

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INTRODUCTION

Pregnancy is one of the most cherished experiences in a woman's life. However, oftentimes, the outcome is less than ideal. The interventions aimed at improving the outcomes are usually focused on pregnancy and delivery. The problem is, however, not addressed because the genesis of the adverse pregnancy outcomes is much before the pregnancy actually occurs. Around 3 million mothers die every year and 2 million neonates die every year. If 4 out of 10 pregnancies in India are unplanned,[1] perinatal deaths are 50% higher in adolescents, and 50% of girls are anemic and underweight.[2] Any amount of interventions during pregnancy cannot bring about the requisite positive change. Preconceptional care (PCC) provides a window of opportunity to optimize the conditions in which conception occurs to have a desirable maternal and fetal outcome.

EVIDENCE FOR PCC

Numerous studies reported that PCC substantially reduced the adverse pregnancy outcomes.[3-6] Two large interventional studies aimed at improving maternal and perinatal care in India witnessed positive outcomes.[7,8]

COMPONENTS OF PCC

Umbrella of PCC covers the aspects of problem identification, educating the couple regarding the problem and planning an intervention if required before pregnancy for an optimal outcome. Hence, all the aspects of PCC need to be discussed under the broad categories of Identify (Preempt); Educate (Counsel), and Intervene (Cure).

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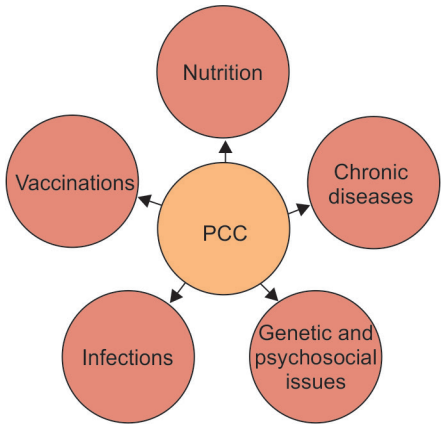

Fig. 1: The whorl of PCC

The whorl of PCC encompasses nutritional interventions, chronic diseases, infections, genetic and psychosocial issues, and vaccinations (Fig. 1).

Nutritional Interventions in PCC

Role of Folic Acid

Preconceptional folic acid (FA) intake is currently the classical example of a preconceptional intervention which is known to have a profound impact on the fetal outcomes. Two landmark trials, the Medical Research Council vitamin study[9] and the randomized controlled trial (RCT) by Criezal and Dudas,[10] emphasized on the relationship between folate intake and the neural tube defects (NTDs).

Folate and Other Malformations

In a Cochrane meta-analysis,[11] there was no evidence of any preventive or negative effects on cleft palate [relative risk (RR) 0.73, 95% confidence interval (CI) 0.05–10.89; three studies; 5,612 births; low-quality evidence], cleft lip [(RR 0.79, 95% CI 0.14–4.36; three studies; 5,612 births; low-quality evidence], congenital cardiovascular defects (RR 0.57, 95% CI 0.24–1.33; three studies; 5,612 births; low-quality evidence), miscarriages (RR 1.10, 95% CI 0.94–1.28; five studies; 7,391 pregnancies; moderate quality evidence), or any other birth defects (RR 0.94, 95% CI 0.53–1.66; three studies; 5,612 births; low-quality evidence).

Folate and Adverse Pregnancy Outcomes

Although certain studies[12] have shown some beneficial impact of maternal folate on preeclampsia, a Cochrane review in 2013 did not find conclusive evidence of benefit.[13]

Folate and Multivitamins

In a study, among people with low serum vitamin B12 concentrations, high plasma folate was found to be associated with higher concentrations of the two functional indicators of impaired B12 status, homocysteine and methylmalonic acid.[14] In the Cochrane analysis, the protective effect of folate on NTDs was not affected by addition of multivitamins.[13] Certain studies, however,[15-17] have shown that fortification with multivitamins reduced heart defects, urinary tract anomalies, oral facial clefts, and limb defects.

Folate and Methylene Tetrahydrofolate Reductase

Folic acid is converted to its active form, 5-methyltetrahydrofolate (5-MTHF), by the enzyme methylene tetrahydrofolate reductase (MTHFR) in the body.[18] Some people could inherit a natural genetic variation in the MTHFR gene, which damages its ability to process folate.[19] However, despite the genetic variation, there is some activity in the enzyme that can process folate if taken in sufficiently high doses. Various controlled trials using different doses have shown that supplementation with 5-MTHF is at least as effective as FA in improving folate status in women of childbearing age.[20-22] Use of 5-MTHF can prevent the masking hematological symptoms of severe vitamin B12 deficiency, which can occur with the excessive use of FA.

The Practice Points

All women of childbearing age should take FA 0.4/0.5 mg daily for at least 3 months before conception up to 3 months after conception. Women who are at moderate risk of NTDs (e.g., family history of NTD in a first or second-degree relative, personal positive or family history of other folate-sensitive congenital anomalies, maternal diabetes (type I or II), malabsorption syndrome) should take FA 1 mg daily for at least 3 months before conception up to 3 months after conception. Women who are at high risk of NTDs (personal or history of NTDs in previous pregnancies) should take a higher dose (4 mg) of folate. The role of other micronutrients is not very clear. Some studies have shown improvement in birth weight, preterm labor, and congenital malformations. Methyltetrahydrofolate is at least as affective as folate according to the available trials. It may have an advantage in patients with MTHFR gene mutation. However, more evidence needs to be generated.

IRON SUPPLEMENTATION

Iron deficiency anemia is a mammoth problem that is responsible for considerable maternal morbidity and mortality.

The Problem of Iron Deficiency Anemia

Nutritional anemia in India is primarily due to iron deficiency. The National Family Health Survey-3 (NFHS-3)[23] data suggest that anemia is widely prevalent among all age groups, and is particularly high among the most vulnerable—nearly 58% among pregnant women, 50% among nonpregnant nonlactating women, and 56% among adolescent girls (15–19 years).

The Consequences of Iron Deficiency Anemia

Anemia during pregnancy increases the risk of maternal mortality, perinatal mortality, low birth weight (LBW), preterm birth, and lower Apgar score babies.[24-26] A recent meta-analysis concluded that maternal anemia could be associated with significant health problems, such as LBW (RR: 1.31; 95% CI: 1.13, 1.51), preterm birth (RR: 1.63; 95% CI: 1.33, 2.01), perinatal mortality (RR: 1.51; 95% CI: 1.30, 1.76), and neonatal mortality (RR: 2.72; 95% CI: 1.19, 6.25).[26]

Role of PCC in Iron Deficiency Anemia

The iron supplementation programs in pregnancy have been instituted in our country since many years but have failed to show any improvement in the prevalence of anemia. Keeping this in mind, the Government of India[27] now advocates the life-cycle approach where the reproductive lifespan is considered to an extension of the well-being during childhood and adolescence, and the iron supplementation should continue from the early years throughout the reproductive years.

A study by Berger et al,[28] weekly 60 mg iron and 3.5 mg FA during 3 to 6 months of preconception period, and weekly 120 mg iron and 3.5 mg FA during conception, demonstrated the effectiveness and safety of the preventive approach of weekly iron FA supplementation.

The Practice Points

All women in reproductive age group, including those planning conception, can be advised to take weekly 100 mg elemental iron and 500 mcg of FA. Along with this, albendazole (400 mg) should be prescribed for biannual de-worming and for helminthic control.

Overweight and Obesity

Optimal weight before pregnancy is a prerequisite for a desirable outcome of pregnancy. The ideal body mass index (BMI) categories are shown in Table 1.

The Problem of Obesity

In India, more than 30 million of people are either overweight or obese (NFHS, 2005–2006). Prevalence of

Table 1: Reference ranges for BMI in Indian women[29]

Class	*BMI (kg/m^2)*
Underweight	<18
Normal	18.0–22.9
Overweight	23.0–24.9
Obesity	>25

overweight/obesity among women is increasing over the years in India.

The Consequences of Obesity

In a retrospective data analysis[30] undertaken in 287,213 pregnancies (normal weight mothers = 61.7%, moderately obese mothers = 27.5% and very obese mothers = 10.9%), it has been showed that compared with women with normal BMI, gestational diabetes mellitus (GDM), preeclampsia, induction of labor, cesarean section, postpartum hemorrhage, thromboembolism, genital tract infection, wound infection, and intrauterine death were significantly more common in obese pregnant women.

Many of the published studies including data by Kumari et al[31] have shown that obesity during pregnancy increases both maternal and fetal morbidity.

Preconceptional Care in Obesity

A meta-analysis conducted for investigating the effects of weight loss due to dietary interventions before conception[32] demonstrated a reduced risk for large-for-gestational age infants in women with a BMI above 25 who lost weight before pregnancy.[33,34]

A recent review concluded that pregnancy after bariatric surgery was associated with lower birth weight, a reduced risk of macrosomia, and a lower risk of metabolic pregnancy complications compared with presurgery pregnancies and BMI-matched pregnancies.[35]

The Practice Points

Overweight and obese women in the preconceptional period should be counseled about the increased risk of adverse maternal and perinatal outcomes, especially NTDs, macrosomia, preterm delivery, stillbirth, gestational diabetes, hypertensive, and thromboembolic disorders. Focused counseling sessions combined with multipronged interventions consisting of nutritional modification along with aerobic and strength-conditioning exercises should be the first line approach to achieve the target weight loss. Emphasis on either or both (diet and exercise) should be individualized according to the patient profile.

Irrespective of the prepregnancy weight, weight loss during pregnancy is not recommended, and hence, counseling during preconception should be done to achieve a realistic target of 5 to 10% over a period of 6 months. Bariatric surgery is suggested in women with BMI above 32.5 kg/m^2 with comorbidities, and in women with BMI above 37.5 kg/m^2 without comorbidities. Patients should be advised to avoid pregnancy for at least 12 to 18 months after the surgery.

Underweight

Weight below average is also a high risk for adverse pregnancy outcome. Timely identification and intervention can ameliorate these affects to a certain extent. The preconceptional aspects can be summarized.

Underweight women (BMI <18 kg/m^2) should be informed about the increased risk of adverse perinatal outcomes like preterm birth, LBW, and increased risk of birth defects like gastroschisis. Health care providers should examine the food choices and provide nutritional advice to underweight women. Underweight women should also be screened and treated for eating disorders like anorexia nervosa and bulimia.

CHRONIC ILLNESSES

Diabetes Mellitus (DM)

Diabetes is literally the new age epidemic of certain ethnic populations like the Indians. Compared with Caucasian women, Indian women have an 11-fold increased risk of developing glucose intolerance during pregnancy.[36] In India, GDM is prevalent in 16.5% of pregnant women.[37]

Numerous studies have shown that preconceptional glycemic control can help in improving the pregnancy outcome in these women. In an RCT, PCC was associated with improved pregnancy preparation in terms of taking FA ($p < 0.0001$), lower glycated hemoglobin (HbA1c) levels ($p < 0.0001$), and reduced risk of adverse pregnancy outcomes ($p = 0.009$) in type I and type II DM.[38,39]

All women should be screened for diabetes as per World Health Organization criteria in preconception. A fasting of ≥126 mg/dL and postprandial value of ≥200 mg/dL should be taken as the cut-offs. Women should be counseled on diabetes self-management skills and the importance of maintaining good glycemic control before and throughout pregnancy. The HbA1c of 6.5% and fasting glucose of 60 to 100 mg/dL should be achieved before conception.

Thyroid Disorders

Thyroid disorders are another group of ubiquitous conditions that have a profound impact on the pregnancy outcome and yet if controlled in time they have a near normal maternal and fetal outcomes. They are

second most common disorders affecting women in the reproductive age group. Both hypothyroidism and hyperthyroidism have implications on the reproductive function, but hypothyroidism is more common than hyperthyroidism.

In a prevalence study from India,[40] the overall prevalence of hypothyroidism was 10.95% with a significantly higher ($p < 0.05$) proportion of females *vs* males (15.86 *vs* 5.02%). Hyperthyroidism is less common than hypothyroidism and occurs in only 0.2% of pregnancies.[41]

The Consequences of Hypothyroidism

Hypothyroidism during pregnancy is associated with adverse maternal (gestational hypertension and preeclampsia postpartum hemorrhage, abortion, and preterm delivery), fetal, and neonatal consequences.[42,43] In addition to thyroid dysfunction, the presence of maternal antithyroperoxidase antibodies (TPO Ab) also increases the risk of miscarriage and preterm delivery. Hyperthyroidism is associated with increased risk of spontaneous abortion, premature labor, LBW, stillbirth, and preeclampsia.[44,45]

Role of PCC

Currently, the evidence on universal screening for thyroid dysfunction during preconception is not very clear. A recent Cochrane review, which included two RCTs, concluded that universal screening for thyroid dysfunction increases the number of women diagnosed with hypothyroidism who can subsequently be treated but it does not clearly impact (benefit or harm) maternal and infant outcomes.[46]

Practice Points

Universal screening for hypothyroidism should be offered wherever feasible. A case finding approach can be an alternative method of screening women who are symptomatic, are from an area of known moderate-to-severe iodine insufficiency, who have a family or personal history of thyroid disease type I or type II diabetes, who have a history of miscarriage/preterm delivery, a history of head and neck radiation, or are morbidly obesity (BMI > 40).

Women with overt hypothyroidism [thyroid stimulating hormone (TSH) > 2.5–3 mIU/L with low free thyroxine (FT4) levels or TSH > 10 mIU/L irrespective of FT4] should be treated. Women with subclinical hypothyroidism (serum TSH between 2.5 and 10 mIU/L with normal FT4 concentration) detected during preconception should be referred to an endocrinologist for further evaluation and management. Anti-TPO Ab should be advised and treatment may be offered in their presence.

Increase in levothyroxine dose (by around 30%) at the time of confirmation of pregnancy is recommended for women with hypothyroidism.

HEART DISEASE

Heart disease in pregnancy poses a significant risk to the mother and fetus. Preconception is the ideal time to detect any previously asymptomatic cardiac conditions or optimize the existing known conditions.

Common cardiac complications include rheumatic heart disease (RHD), congenital heart disease (CHD), arrhythmias, and cardiomyopathy.[47] A retrospective study[48] reported 88% prevalence of RHD among pregnant women with cardiac disease in developing countries and observed a fewer maternal complications and higher birth weight babies in patients with New York Heart Association (NYHA) class I/II than NYHA class III/IV (84.54 *vs* 15.45%).

The Consequences of Cardiac Disorders in Pregnancy

Women with CHD and acquired heart disease compared with controls are associated with higher neonatal complications (34 *vs* 15%) and lower median birth weight percentile (31 *vs* 49; $p < 0.05$).[49] An Indian prospective observational study[50] also reported 56% LBW, 15% preterm birth, and 11% neonatal death in women with pre-existing CHD. In addition, mean birth weight was higher in women with corrected heart lesions than in those with uncorrected ones (2,593 ± 480 *vs* 2,294 ± 620 gm; $p = 0.22$).

Practice Points

A basic clinical cardiac assessment should be done in the preconceptional period for all women and they should be subsequently referred if required. Conditions like severe pulmonary arterial hypertension of any cause, severe systemic ventricular dysfunction, women with NYHA III–IV, or left ventricular ejection fraction <30%, previous peripartum cardiomyopathy with any residual impairment of left ventricular function, severe left heart obstruction, Marfan syndrome with aorta dilated >40 mm, aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve or native severe coarctation should be identified and these women should be strongly advised against getting pregnant. In a woman with known cardiac condition, detailed cardiac assessment should be carried out to assess the baseline cardiac condition, to review the medications, and to evaluate the requirement for corrective surgery. Genetic counseling should be offered for women with CHD. Medication review should be done

for the mechanical valve replacement patients who are on anticoagulation therapy.

Hypertensive Disorders

Preexisting hypertensive disorders are prone to be worsened during pregnancy and also lead to maternal complications like preeclampsia, eclampsia, pulmonary edema, cardiovascular accidents. The fetal risks include preterm deliveries, growth restriction, and even intrauterine death.[51-53]

Practice Points

All women should be screened for hypertensive disorders before pregnancy, especially those with previous hypertensive disorders in pregnancy, renal disease, autoimmune disorders, or thrombophilias. Women with hypertension for several years should be assessed for renal disease, ventricular hypertrophy, and retinopathy. All women with preexisting hypertension should be advised to achieve a target blood pressure of 150/100 mm Hg in the case of uncomplicated chronic hypertension and below 140/90 mm Hg in the presence of target organ damage. Angiotensin converting enzyme inhibitors and angiotensin receptor blockers should be avoided in women planning pregnancy.

Seizure Disorders

There are more than 10 million living with epilepsy in India.[54] It is one of the most common neurological disorder. The adverse impact of antiepileptics is not just because of the disease per say but also due to the drugs which are widely known to be teratogenic.

A recent systematic review found that women with epilepsy *vs* those without had increased odds of spontaneous miscarriage [odds ratio (OR) 1.54, 95% CI 1.02–2.32; I^2 = 67%], antepartum hemorrhage (1.49, 1.01–2.20; I^2 = 37%), postpartum hemorrhage (1.29, 1.13–1.49; I^2 = 41%), hypertensive disorders (1.37, 1.21–1.55; I^2 = 23%), induction of labor (1.67, 1.31–2.11; I^2 = 64%), cesarean section (1.40, 1.23–1.58; I^2 = 66%), any preterm birth (<37 weeks of gestation; 1.16, 1.01–1.34; I^2 = 64%), and fetal growth restriction (1.26, 1.20–1.33; I^2 = 1%).[55]

Practice Points

A women with known epileptic disorder should be offered effective contraception till the disease is optimized. Hormonal contraceptive failure may occur at standard doses in the presence of hepatic cytochrome P-450 inducing antiepileptics like carbamazepine, phenytoin, phenobarbital, and topiramate. Hence, low-dose pills should be avoided.

All the commonly used antiepileptic drugs (AEDs) are teratogenic. Drugs like valproate, phenytoin, carbamazepine, phenobarbital, and topiramate have higher baseline rates. Newer drugs like levetiracetam have a lower risk of major malformations. Antiepileptic drugs should be given at the lowest dose and lowest plasma level, multiple agents, especially combinations involving valproate, carbamazepine, and phenobarbital should be avoided. Valproate and carbamazepine should be avoided if there is a family history of NTDs. In established pregnancy, AEDs should not be changed solely to reduce teratogenic risk as changing AEDs may precipitate seizures and overlapping AEDs during the change exposes the fetus to additional AEDs. Woman should be on a stable anticonvulsant regimen for at least 6 months (after dose modification or withdrawal) prior to conception.

A higher dose of FA up to 4 mg can be given to women on AEDs, especially those known to cause NTDs like valproate and carbamazepine.

Autoimmune Disorders (AID)

Autoimmune diseases are a heterogeneous group of disorders which can complicate pregnancy. A woman with a known AID should use effective contraception till the disease is optimized. The management of such patients should be a multidisciplinary with active involvement of the concerned physicians. Rheumatoid arthritis and systemic lupus erythematosus (SLE) are the more common AIDs which are seen in pregnancy.

Women with known AID can have an improvement, worsening, or no change when they become pregnant depending on their specific AID. Pregnancies in women with SLE are at high risk for maternal and fetal complications, including spontaneous abortion and premature delivery, intrauterine growth retardation, and superimposed preeclampsia.[56]

There is spontaneous amelioration of RA during pregnancy and an increased risk of flare after delivery.[57] Women with SLE who wish to get pregnant should be advised to achieve quiescent SLE at least 6 months before conception. Methotrexate and leflunomide are extremely teratogenic and should be discontinued in women planning a pregnancy.

INFECTIONS

Infections are an important cause of maternal and fetal morbidity and mortality. The list of infections that can have an effect on the outcome of pregnancy is quite exhaustive. The priority in the preconception period is to screen for the relevant infections and provide appropriate treatment. A systematic review with respect to the maternal infections found the following median prevalence

rates in low- and middle-income countries: *Treponema pallidum* (2.6%), hepatitis B virus (4.3%), and hepatitis C virus (1.4%).[58] Globally, there are about 15.9 million women who are human immunodeficiency virus (HIV) positive currently could possibly transfer the virus to their future children.[59] Once detected, HIV positive women on antiretroviral therapy (ART) have very low chances perinatal transmission if the ART is instituted on time. In an international registry, the rate of perinatal HIV-1 transmission was only 1% among ART-treated mothers whose virus load at delivery or measurement closest to delivery was <1,000 copies/mL, and the transmission was significantly lower than those women who did not receive any ART.[60] Further, a review analyzed 1 RCT and 9 observational studies found that ART use in an HIV-infected member as HIV-discordant couple is associated with lower risk of HIV transmission to the uninfected partner compared with untreated discordant couples.[61]

Practice Points

Universal screening is desirable for HIV, hepatitis B surface antigen (HBsAg), and Venereal Disease Research Laboratory. For HIV positive woman, ART should be initiated and continued throughout her reproductive lifespan. Effective contraception should be provided till the viral load is suppressed. For serodiscordant couples, in whom the woman is HIV-positive, it is preferable to attempt home insemination with the partner's sperm during ovulation for 3 to 6 months before considering other methods. If the male partner is HIV positive, then a referral to a fertility specialist should be considered and an option of sperm washing with intrauterine insemination should be given.

GENETIC DISORDERS

Preconception is the ideal time to identify, understand, and prevent genetic disorders in the fetus. The prevalence of chromosomal, single gene, and multifactorial disorder has been reported to be 0.6, 0.56, and 2% respectively at the time of birth.[62] Large population, high birth rate, and consanguineous marriage favor a high prevalence of genetic disorders in India. It was reported that approximately 495,000 neonates with congenital malformations, 390,000 with glucose-6-phosphate dehydrogenase deficiency, 21,400 with Down syndrome, 9,760 with amino acid disorders, 9,000 with β-thalassemia, and 5,200 with sickle cell disease are born each year in India.[63]

Preconceptional care can identify couples at high risk of genetic disorders in the fetus. A thorough family medical history needs to be taken and a complete three-generation family tree including ethnicity information should be constructed during the preconceptional period in order to identify couples who have genetic predisposition to an adverse pregnancy outcome. A history of consanguinity, hereditary disorder in family, advanced parental age, teratogen exposure or infection, birth defects, intellectual disability, and recurrent pregnancy loss are some of the indications for a referral to a geneticist.

A preconceptional visit to the geneticist can provide a detailed overview of the likelihood of affection. Depending on the type of disorder, the likelihood of affection in the next pregnancy (e.g., 25% for autosomal recessive disorders like thalassemia) can be predicted and also the impact of the affection of the underlying genetic disorder (degree of disabilities, e.g., Down's syndrome) can be understood. Also, during the preconceptional evaluation, it can be determined if there is a possibility of modifying the impact or likelihood of occurrence of the disorder (e.g., prenatal diagnosis; thalassemia).

VACCINATIONS

Vaccination is an important aspect of PCC as it brings to the fore the preventive aspect of PCC. Some vaccines benefit by preventing the congenital infection, while others are useful in preventing the perinatal transmission.

Strongly Advisable

Measles, Mumps, and Rubella

Measles, mumps, and rubella (MMR) are associated with spontaneous abortions, prematurity, LBW, and other birth defects.[64]

Women in reproductive age group should be screened for rubella immunity and immunized if nonimmune. Serological testing for rubella, however, is not absolutely essential before vaccinating. The MMR is preferred over rubella vaccine alone. Patients should be counseled to avoid pregnancy for 3 months after vaccination. Accidental vaccination in pregnancy does not pose a substantial risk to the fetus.

Hepatitis B Vaccine

India presents "intermediate to high endemicity" for HBV with approximately 40 million chronic HBV carriers, contributing about 11% to global burden of disease.[65] Hepatitis B can be transmitted to the neonate from the mother and the neonatal infections have a very high chances of chronic infection which predisposes to cirrhosis and hepatocellular carcinoma. The neonatal transmission occurs in 10% if infection occurs in the first trimester, while it is up to 90% if the infection occurs in the third trimester. The presence of hepatitis B e-antigen increases the infectivity and the neonatal transmission.[66]

This vaccine provides high protective efficacy (95%) against perinatal transmission.[67] Immunization in

prepregnancy should be offered to at least for those who are at risk, e.g., having more than one sex partner during the previous 6 months, been evaluated or treated for a sexually transmitted disease, recent or current injection-drug use, or having had an HBsAg—positive sex partner is a practical option.

Desirable

Tetanus, Diphtheria, and Pertussis

Tetanus, diphtheria, pertussis (Tdap) vaccination in prepregnancy would be of benefit because passive immunity is protective against neonatal tetanus. There are definite advantages of Tdap vaccine during pregnancy.[67,68] In a systematic review of impact of PCC for adolescents, women and couples of reproductive age on maternal, neonatal, child health outcomes demonstrated reduction in neonatal deaths (including those specifically due to tetanus) when compared with placebo in women receiving more than 1 dose of the vaccine (OR 0.52; 95% CI: 0.29–0.91).[69]

Tdap should be given in the preconceptional period if the tetanus vaccination schedule is not up-to-date (no booster in the last 2 years). Also, even if the woman has been vaccinated in the preconception, the pregnancy schedule should be followed.

Varicella

The Varicella or chicken pox in children is a mild disease but can be very severe in adults and neonates. In a study from India,[70] the susceptibility proportion was found to be 25.4% with a CI of 15.8 to 35.4%.

Infection in pregnancy can cause varying manifestations depending on the gestation of affection. Early pregnancy infection may result in fetal varicella syndrome characterized by fetal scarring of the skin and affected limb(s), limb deformities (hypoplasia), eye damage, LBW, brain atrophy and mental retardation, sometimes fetal death, or spontaneous abortion,[71] while infection in the third trimester leads to chances of neonatal disease.

With the availability of varicella vaccine, preconception is a good time to screen for varicella immunity by a history of infection, immunization, or serology. Nonimmune women should receive two doses of varicella vaccine with a gap of at least 4 weeks and should be counseled to avoid pregnancy for 3 months.

Influenza

In a recent review of 100 studies published between 1961 and 2015, investigators reported that, compared with the general population, pregnant women are more often hospitalized and admitted to an Intensive Care Unit due to influenza virus infection. Infection during pregnancy has been associated with an approximately 5-fold increase in perinatal mortality, including miscarriages, stillbirths, and early neonatal diseases and death.[72]

Vaccination is 70 to 90% effective in preventing influenza. Vaccination of pregnant women against influenza is recommended especially during influenza season, to reduce the risk of complications and to provide passive protection to the neonate regardless of gestational age during influenza season.

Human Papillomavirus

Women in the preconceptional period should be advised to carry out the routine protocol for vaccination against human papillomavirus and preferably complete the vaccination schedule before conception. If they conceive before completing the schedule, the rest of the doses can be given after delivery.

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