

REVIEW ARTICLE

Preconceptional Care

¹K Aparna Sharma, ²Alka Kriplani

How to cite this article: Sharma KA, Kriplani A. Preconceptional Care. J Mahatma Gandhi Univ Med Sci Tech 2017;2(2):85-93.

Source of support: Nil

Conflict of interest: None

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).

¹Associate Professor, ²Professor and Head

^{1,2}Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, India

Corresponding Author: Alka Kriplani, Professor and Head Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, India, Phone: +911126588500 e-mail: kriplaniaalka@gmail.com

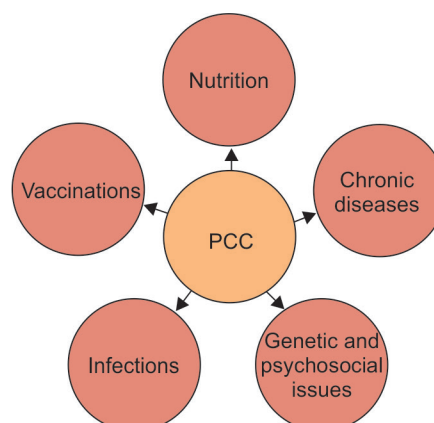


Fig. 1: The whorl of PCC

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 study⁹ 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 studies¹² 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 effective 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 India²⁷ 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 women²⁹

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 analysis³⁰ 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 al³¹ 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 conception³² 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/m² with comorbidities, and in women with BMI above 37.5 kg/m² 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/m²) 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 study⁴⁸ 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 study⁵⁰ 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 ($2,593 \pm 480$ *vs* $2,294 \pm 620$ 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 intra-uterine 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 mmHg 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 pre-pregnancy 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. Non-immune 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.

REFERENCES

1. Singh S, Sedgh G, Hussain R, Unintended Pregnancy: World-wide Levels, Trends, and Outcomes, 2010. *Stud Fam Plann* 2010 Dec;41(4):241-250.
2. World Health Organization. Meeting to develop a global consensus on preconception care to reduce maternal and childhood mortality and morbidity. Geneva: World Health Organization; 2013.
3. Dean SV, Lassi ZS, Imam AM, Bhutta ZA. Preconception care: closing the gap in the continuum of care to accelerate improvements in maternal, newborn and child health. *Reprod Health* 2014 Sep 26;11 (Suppl 3):S1.
4. Lassi ZS, Bhutta ZA. Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes. *Cochrane Database Syst Rev* 2015 Mar;3:CD007754.
5. Lewycka S, Mwansambo C, Rosato M, Kazembe P, Phiri T, Mganga A, Chapota H, Malamba F, Kainja E, Newell ML, et al. Effect of women's groups and volunteer peer counseling on rates of mortality, morbidity, and health behaviours in mothers and children in rural Malawi (MaiMwana): a factorial, cluster-randomised controlled trial. *Lancet* 2013 May;381(9879):1721-1735.
6. Elsinga J, de Jong-Potjer LC, van der Pal-de Bruin KM, le Cessie S, Assendelft WJ, Buitendijk SE. The effect of preconception counselling on lifestyle and other behaviour before and during pregnancy. *Womens Health Issues* 2008 Nov-Dec;18(6 Suppl):S117-S125.
7. More NS, Bapat U, Das S, Alcock G, Patil S, Porel M, Vaidya L, Fernandez A, Joshi W, Osrin D, et al. Community mobilization in Mumbai slums to improve perinatal care and outcomes: a cluster randomized controlled trial. *PLoS Med* 2012 Jul;9(7):e1001257.
8. Tripathy P, Nair N, Barnett S, Mahapatra R, Borghi J, Rath S, Rath S, Gope R, Mahto D, Sinha R, et al. Effect of a participatory intervention with women's groups on birth outcomes and maternal depression in Jharkhand and Orissa, India: a cluster-randomised controlled trial. *Lancet* 2010 Apr;375(9721):1182-1192.

9. MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet* 1991 Jul;338(8760):131-137.
10. Czeizel AE, Dudas L. Prevention of the first occurrence of neural tube defects by periconceptional vitamin supplementation. *N Engl J Med* 1992 Dec;327(26):1832-1835.
11. De-Regil LM, Peña-Rosas JP, Fernández-Gaxiola AC, Rayco-Solon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database Syst Rev*. 2015 Dec;12:CD007950.
12. Kim MW, Hong SC, Choi JS, Han J-Y, Oh MJ, Kim HJ, Nava-Ocampo A, Koren G. Homocysteine, folate, and pregnancy outcomes. *J Obstet Gynaecol* 2012 Aug;32(6):520-524.
13. Lassi ZS, Salam RA, Haider BA, Bhutta ZA. Folic acid supplementation during pregnancy for maternal health and pregnancy outcomes. *Cochrane Database Syst Rev* 2013 Mar 28;3:CD006896.
14. Selhub J, Morris MS, Jacques PF. In vitamin B12 deficiency, higher serum folate is associated with increased total homocysteine and methylmalonic acid concentrations. *Proc Natl Acad Sci U S A*. 2007 Dec;104(50):19995-20000.
15. Goh YI, Bollano E, Einarson TR, Koren G. Prenatal multivitamin supplementation and rates of congenital anomalies: a meta-analysis. *J Obstet Gynaecol Can* 2006 Aug;28(8):680-689.
16. Simpson JL, Shulman LP, Brown H, Holzgreve W. Closing the folate gap in reproductive-age women. *Contemp Ob Gyn* 2010;55:34-40.
17. Yang L, Jiang L, Bi M, Jia X, Wang Y, He C, Yao Y, Wang J, Wang Z. High dose of maternal folic acid supplementation is associated to infant asthma. *Food Chem Toxicol* 2015 Jan;75:88-93.
18. Fodinger M, Horl WH, Sunder-Plassmann G. Molecular biology of 5,10-methylenetetrahydrofolate reductase. *J Nephrol* 2000 Jan-Feb;13(1):20-33.
19. Varga EA, Sturm AC, Misita CP, Moll S. Cardiology patient pages. Homocysteine and MTHFR mutations: relation to thrombosis and coronary artery disease. *Circulation* 2005 May;111(19):e289-e293.
20. Houghton LA, Sherwood KL, Pawlosky R, Ito S, O'Connor DL. [6S]-5-Methyltetrahydrofolate is at least as effective as folic acid in preventing a decline in blood folate concentrations during lactation. *Am J Clin Nutr* 2006 Apr;83(4):842-850.
21. Lamers Y, Prinz-Langenohl R, Moser R, Pietrzik K. Supplementation with [6S]-5-methyltetrahydrofolate or folic acid equally reduces plasma total homocysteine concentrations in healthy women. *Am J Clin Nutr* 2004 Mar;79(3):473-478.
22. Obeid R, Holzgreve W, Pietrzik K. Is 5-methyltetrahydrofolate an alternative to folic acid for the prevention of neural tube defects? *J Perinat Med* 2013 Sep;41(5):469-483.
23. NFHS-3. National Nutrition Monitoring Bureau Survey (NNMBS), 2006.
24. Ezzati M, Lopez AD, Rodgers A, Murray CJL. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva: World Health Organization; 2004.
25. Lone FW, Qureshi RN, Emanuel F. Maternal anaemia and its impact on perinatal outcome. *Trop Med Int Health* 2004 Apr;9(4):486-490.
26. Rahman MM, Abe SK, Rahman MS, Kanda M, Narita S, Bilano V, Ota E, Gilmour S, Shibuya K. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr* 2016 Feb;103(2):495-504.
27. National Iron + Initiative. Guidelines for Control of Iron Deficiency Anemia. Adolescent Division Ministry of Health and Family Welfare Government of India; 2013.
28. Berger J, Thanh HT, Cavalli-Sforza T, Smitasiri S, Khan NC, Milani S, Hoa PT, Quang ND, Viteri F. Community mobilization and social marketing to promote weekly iron-folic acid supplementation in women of reproductive age in Vietnam: impact on anemia and iron status. *Nutr Rev* 2005 Dec;63(12 Pt 2):S95-S108.
29. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, Joshi SR, Sadikot S, Gupta R, Gulati S, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. *J Assoc Physicians India* 2009 Feb;57:163-170.
30. Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, Regan L, Robinson S. Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. *Int J Obes Relat Metab Disord* 2001 Aug;25(8):1175-1182.
31. Kumari P, Gupta M, Kahlon P, Malviya S. Association between high maternal body mass index (BMI) and fetomaternal outcome. *J Obes Metab Res* 2014;3:143-144.
32. Forsum E, Brantsaeter AL, Olafsdottir AS, Olsen SF, Thorsdottir I. Weight loss before conception: a systematic literature review. *Food Nutr Res* 2013;57.
33. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. *Lancet* 2006 Sep;368(9542):1164-1170.
34. Glazer NL, Hendrickson AF, Schellenbaum GD, Mueller BA. Weight change and the risk of gestational diabetes in obese women. *Epidemiology* 2004 Nov;15(6):733-737.
35. Kjaer MM, Nilas L. Pregnancy after bariatric surgery—a review of benefits and risks. *Acta Obstet Gynecol Scand* 2013 Mar;92(3):264-271.
36. Dornhorst A, Paterson CM, Nicholls JS, Wadsworth J, Chiu DC, Elkeles RS, Johnston DG, Beard RW. High prevalence of gestational diabetes in women from ethnic minority groups. *Diabet Med* 1992 Nov;9(9):820-825.
37. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational diabetes mellitus in India. *J Assoc Physicians India* 2004 Sep;52:707-711.
38. Wahabi HA, Esmaeil SA, Fayed A, Al-Shaikh G, Alzeidan RA. Pre-existing diabetes mellitus and adverse pregnancy outcomes. *BMC Research Notes* 2012;5:496.
39. Murphy HR, Roland JM, Skinner TC, Simmons D, Gurnell E, Morrish NJ, Soo SC, Kelly S, Lim B, Randall J, et al. Effectiveness of a regional prepregnancy care program in women with type 1 and type 2 diabetes: benefits beyond glycemic control. *Diabetes Care* 2010 Dec;33(12):2514-2520.
40. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. *Indian J Endocrinol Metab* 2013 Jul-Aug;17(4):647-652.
41. El Baba KA, Azar ST. Thyroid dysfunction in pregnancy. *Int J Gen Med*. 2012;5:227-230.
42. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N Engl J Med* 1999 Aug;341(8):549-555.
43. Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. *Arch Gynecol Obstet* 2010 Feb;281(2):215-220.

44. Kriplani A, Buckshee K, Bhargava VL, Takkar D, Ammini AC. Maternal and perinatal outcome in thyrotoxicosis complicating pregnancy. *Eur J Obstet Gynecol Reprod Biol* 1994 May;54(3):159-163.
45. Luewan S, Chakkabut P, Tongsong T. Outcomes of pregnancy complicated with hyperthyroidism: a cohort study. *Arch Gynecol Obstet* 2011 Feb;283(2):243-247.
46. Spencer L, Bubner T, Bain E, Middleton P. Screening and subsequent management for thyroid dysfunction pre-pregnancy and during pregnancy for improving maternal and infant health. *Cochrane Database Syst Rev* 2015 Sep;9:CD011263.
47. Li M, Yao Q, Xing A. A clinical analysis of 188 cases of pregnancy complicated with critical heart disease. *Zhong Nan Da Xue Xue Bao Yi Xue Ban* 2014 Nov;39(11):1145-1150.
48. Bhatla N, Lal S, Behera G, Kriplani A, Mittal S, Agarwal N, Talwar KK. Cardiac disease in pregnancy. *Int J Gynaecol Obstet* 2003 Aug;82(2):153-159.
49. Gelson E, Curry R, Gatzoulis MA, Swan L, Lupton M, Steer P, Johnson M. Effect of maternal heart disease on fetal growth. *Obstet Gynecol* 2011 Apr;117(4):886-891.
50. Arora N, Kausar H, Jana N, Mandal S, Mukherjee D, Mukherjee R. Congenital heart disease in pregnancy in a low-income country. *Int J Gynaecol Obstet* 2015 Jan;128(1):30-32.
51. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol* 2000 Jul;183(1):S1-S22.
52. Agency for Healthcare Research and Quality. Management of chronic hypertension during pregnancy. Evidence Report/Technology Assessment no.14. AHRQ publication no. 00-E011. Rockville, MD: Agency for Healthcare Research and Quality; 2000.
53. Ferrer RL, Sibai BM, Mulrow CD, Chiquette E, Stevens KR, Cornell J. Management of mild chronic hypertension during pregnancy: a review. *Obstet Gynecol* 2000 Nov;96(5 Pt 2): 849-860.
54. Sridharan R, Murthy BN. Prevalence and pattern of epilepsy in India. *Epilepsia* 1999 May;40(5):631-636.
55. Viale L, Allotey J, Cheong-See F, Arroyo-Manzano D, McCorry D, Bagary M, Mignini L, Khan KS, Zamora J, Thangaratinam S, et al. Epilepsy in pregnancy and reproductive outcomes: a systematic review and meta-analysis. *Lancet* 2015 Nov;386(10006): 1845-1852.
56. Smyth A, Oliveira GH, Lahr BD, Bailey KR, Norby SM, Garovic VD. A systematic review and meta-analysis of pregnancy outcomes in patients with systemic lupus erythematosus and lupus nephritis. *Clin J Am Soc Nephrol* 2010 Nov;5(11):2060-2068.
57. Hazes JM, Coulie PG, Geenen V, Vermeire S, Carbonnel F, Louis E, Masson P, De Keyser F. Rheumatoid arthritis and pregnancy: evolution of disease activity and pathophysiological considerations for drug use. *Rheumatology (Oxford)* 2011 Nov;50(11):1955-1968.
58. Velu PP, Gravett CA, Roberts TK, Wagner TA, Zhang JS, Rubens CE, Gravett MG, Campbell H, Rudan I. Epidemiology and aetiology of maternal bacterial and viral infections in low- and middle-income countries. *J Glob Health* 2011 Dec;1(2):171-188.
59. UNAIDS: UNAIDS report on the global AIDS epidemic. 2010. Available from http://www.unaids.org/globalreport/Global_report.htm
60. Ioannidis JP, Abrams EJ, Ammann A, Bulterys M, Goedert JJ, Gray L, Korber BT, Mayaux MJ, Mofenson LM, Newell ML, et al. Perinatal transmission of human immunodeficiency virus type 1 by pregnant women with RNA virus loads <1000 copies/ml. *J Infect Dis* 2001 Feb;183(4):539-545.
61. Anglemeyer A, Rutherford GW, Horvath T, Baggaley RC, Egger M, Siegfried N. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. *Cochrane Database Syst Rev* 2013 Apr;4:CD009153.
62. Rimoin DL, Connor JM, Pyeritz RE, Korf BR. Emery and Rimoin's principles and practice of medical genetics. Churchill Livingstone Elsevier; 2007.
63. Verma IC, Puri RD. Global burden of genetic disease and the role of genetic screening. *Semin Fetal Neonatal Med* 2015 Oct;20(5):354-363.
64. White SJ, Boldt KL, Holditch SJ, Poland GA, Jacobson RM. Measles, mumps, and rubella. *Clin Obstet Gynecol* 2012 Jun;55(2):550-559.
65. American College of Obstetricians and Gynecologists. ACOG educational bulletin: viral hepatitis in pregnancy. *Int J Gynaecol Obstet* 1998 Nov;63:195-202.
66. Geeta MG, Riyaz A. Prevention of mother to child transmission of hepatitis B infection. *Indian Pediatr* 2013;50:189-192.
67. Swamy GK, Beigi RH. Maternal benefits of immunization during pregnancy. *Vaccine* 2015 Nov;33(47):6436-6440.
68. Sukumaran L, McCarthy NL, Kharbanda EO, McNeil MM, Naleway AL, Klein NP, Jackson ML, Hambidge SJ, Lugg MM, Li R, et al. Association of Tdap vaccination with acute events and adverse birth outcomes among pregnant women with prior tetanus-containing immunizations. *JAMA* 2015 Oct;314(15):1581-1587.
69. Singru SA, Tilak VW, Gandham N, Bhawalkar JS, Jadhav SL, Pandve HT. Study of susceptibility towards Varicella by screening for the presence of IgG antibodies among nursing and medical students of a Tertiary Care Teaching Hospital in Pune, India. *J Glob Infect Dis* 2011 Jan-Mar;3(1):37-41.
70. Nathwani D, Maclean A, Conway S, Carrington D. Varicella infections in pregnancy and the newborn. A review prepared for the UK Advisory Group on Chickenpox on behalf of the British Society for the Study of Infection. *J Infect* 1998;36 (Suppl 1): 59-71.
71. Michaan N, Amzallag S, Laskov I, Cohen Y, Fried M, Lessing JB, Many A. Maternal and neonatal outcome of pregnant women infected with H1N1 influenza virus (swine flu). *J Matern Fetal Neonatal Med* 2012 Feb;25(2):130-132.
72. Smith NM, Bresee JS, Shay DK, Uyeki TM, Cox NJ, Strikas RA. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006 Jul;55(RR-10):1-42.