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# Managing Hypertension in Diabetic Pregnancy

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## Abstract

Last few decades have observed increase in Diabetes in pregnancy which may be attributed to urbanisation sedentary lifestyle, obesity, hypertension, prediabetes, alcohol consumption, and immigration. On the other hand hypertension in pregnancy in another significant condition resulting in substantial maternal and fetal/neonatal morbidity and mortality. It's prevalence is 3-10% globally but is reported as high as 18% in Indians. Preeclampsia and gestational diabetes mellitus (GDM) are two diseases that affect a significant number of pregnancies and responsible for adverse perinatal outcomes of both the mother and child. Although preeclampsia and GDM seem to be unrelated disease entities as their clinical manifestation and diagnostic criteria do not overlap but many researchers have shown a correlation between preeclampsia and GDM. Women with history of preeclampsia or gestational hypertension may be at increased risk of developing diabetes and vice versa. Co-existence of both diseases significantly increases the adverse pregnancy outcome.
**Keywords:** Hypertension, Pregnancy, Diabetes.

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## 1. Introduction

Last few decades have observed increase in Diabetes in pregnancy which may be attributed to urbanisation sedentary lifestyle, obesity, hypertension, prediabetes, alcohol consumption, and immigration. On the other hand hypertension in pregnancy in another significant condition resulting in substantial maternal and fetal/neonatal morbidity and mortality. It's prevalence is 3-10% globally but is reported as high as 18% in Indians [1]. Preeclampsia and gestational diabetes mellitus (GDM) are two diseases that affect a significant number of pregnancies and responsible for adverse perinatal outcomes of both the mother and child . Although preeclampsia and GDM seem to be unrelated disease entities as their clinical manifestation and diagnostic criteria do not overlap but many researchers have shown a correlation between preeclampsia and GDM [2]. Women with history of preeclampsia or gestational hypertension may be at increased risk of developing diabetes and vice versa. Co existence of both diseases significantly increases the adverse pregnancy outcome.

## 2. Diabetes in pregnancy

**Etiologic classification of Diabetes mellitus (ADA 2006)**

**I. Type 1 diabetes (insulin dependent DM)**

A. Immune mediated

B. Idiopathic

**II. Type 2 diabetes (Non insulin dependent DM)**

**III. Other specific types**

-Genetic defects of ß-cell function

-Genetic defects in insulin action

-Diseases of the exocrine pancreas

-Endocrinopathies

-Drug- or chemical-induced

**IV. Gestational diabetes mellitus (GDM)**

**V. Impaired glucose tolerance and impaired fasting glucose.**

**FBG>100mg/dl, but <126 mg/dl and 2 hour value in OGTT>140 mg/dl but <200 mg/dl**

Gestational Diabetes is defined as Carbohydrate intolerance of variable severity with onset or first recognized during pregnancy. It is regardless of whether insulin is used for treatment or the condition persists after

pregnancy. It does not exclude unrecognized glucose intolerance before pregnancy. Its incidence varies according to ethnicity, selection criteria and diagnostic test. According to NICE Guidelines [2008], its global prevalence is somewhere 1% to 14%. Asian population is more prone for diabetes in pregnancy and its prevalence is 5-8%. Reported prevalence in Indian population is varies from 3.8% in Kashmir to 41% [3,4].

**2.1. Complications of diabetes in pregnancy**

**2.1.1 Maternal**

1) Miscarriage
2) Polyhydramnios
3) Preterm labour
4) Worsening of diabetic retinopathy, nephropathy, vasculopathy
5) Pre-eclampsia
6) Hyperglycemia
7) Subinvolution of uterus'
8) Puerperal sepsis
9) Shoulder dystocia
10) PPH

**2.1.2 Fetal**

1) Neural tube defects
2) Microcephaly
3) Sacral agenesis
4) Cardiovascular defects: common is endocardiac cushion defects
5) Renal agenesis
6) Duodenal and anal atresia
7) Oro-facial defects

## 3. Hypertensive disorders of pregnancy

It is the syndrome of high blood pressure with or without proteinuria during gestation. It develops after 20 weeks of gestation [5]. Hypertensive disorder of pregnancy complicates 5-10 % of pregnancies and can result in variety of fetal and maternal complications [6]. The pathogenesis of pregnancy induced hypertension is poorly understood, but likely multifactorial.

Race and ethnicity are important risk factors for GDM and it is more prevalent in Asians.

**3.1Classification of hypertensive disorders of pregnancy**

**3.1.1 Gestational Hypertension (GH)**

Systolic BP 140 mmHg or more and/ or diastolic BP 90 mmHg or more on two consecutive readings taken at least 4 hours apart with patient at rest without proteinuria after 20 weeks of gestation

**Pre-eclampsia**

BP ≥ 140/90 on at least two occasions 4 hours apart with proteinuria after 20 weeks of pregnancy

**Severe Pre-eclampsia**

- Hypertension BP ≥ 160/110 mmHg + Proteinuria ≥ +3 **OR**
- Pre-eclampsia (BP ≥ 140/90 mmHg) with any one of these symptoms-severe headache, blurring of vision, difficulty in breathing, severe pain in upper abdomen, passing less urine

The woman will have swelling of face, hands, lower back

**Eclampsia**

Convulsions with Pre-eclampsia

Prevalence in different parts of world of hypertensive disorders of pregnancy, gestational hypertension and preeclampsia are 5.2-8.2%, 1.8-4.4% and 0.2-9.2%, respectively [7].

**3.2 Risk factors of hypertension in pregnancy**

1) Family history
2) Immune response
3) Genetic variation
4) Unprotected sexual intercourse
5) Anti-phospholipid antibodies
6) Age of maternity
7) Multiple pregnancy
8) Race
9) Ethnicity
10) Smoking
11) Stressful environment
12) Assisted reproductive technology

**3.3Complications of hypertensive disorder of pregnancy**

**3.3.1 Maternal**

1) During pregnancy-Eclampsia, Abruptio placentae, oliguria, anuria, preterm labour, cerebral haemorrhage, ARDS, HELLP syndrome.
2) During labour- Eclampsia, PPH
3) During puerperium- eclampsia, PPH, sepsis
4) Remote complications- recurrent pre-eclampsia, chronic hypertension, chronic nephritis, increased cardiovascular morbidity.

**3.3.2 Fetal**

1) FGR
2) Sudden IUD
3) Oligohydramnios
4) Prematurity
5) Placental infarction

## 4. Diabetes in pregnancy complicated hypertensive disorder of pregnancy

Co-existance of diabetes in pregnancy and hypertensive disorder of pregnancy are common, and their relationship is not well understood. Some studies have quoted Pregnancy induced hypertension and gestational diabetes mellitus together affects 25-30% of pregnancies, resulting in variety of complications of fetus and mother [8]. Overt Diabetes Mellitus has higher risk of preeclampsia as compared to GDM that is 25% versus less than 20% [9]. Presence of microvascular disease increases the risk by 3 fold .In IDDM women poor glycemic control in first trimester is fairly accurate predictor of development of

preeclampsia after 20 weeks of gestation [10]. Various studies are under trial but could not able to find the exact relationship between the two diseases. It has been concluded the prevalence as follows [11].

Diabetes with Severe PE - 4.5%
Diabetes with Gestational Hypertnsion and PE - 4.4%
Diabetes with Eclampsia - 3.9%

There is increased risk of hypertension with GDM in women who tend to be younger, primigravida with increased BMI and received inadequate prenatal care [12].

**4.1 Pathogenesis**

Both etiopathogenesis of diabetes and hypertension in pregnancy is multifactorial. The pathogenesis of gestational hypertension is multifactorial with vascular, immune, genetic and placental factors but endothelial dysfunction plays an important and significant role. Pre-existing hypertension, metabolic syndrome, and renal disease, which also involve endothelial dysfunction and are more common seen in diabetic patients. In other words Diabetes increases women risk for both pre-eclampsia and CVD. Although some degree of insulin resistance is characteristic of normal pregnancy due to multiple physiologic hormone changes, including production of placental lactogen, placental growth hormone, and high level of estradiol, progesterone, and cortisol. Women with significantly high level of fasting insulin are at increased risk for developing hypertension of pregnancy, and during pregnancy, there is a temporal relationship between peak maternal insulin resistance and the first manifestation of gestational hypertension or pre-eclampsia[13]. Even in non diabetic women, a positive correlation exists between both fasting glucose and subclinical abnormalities in response to glucose challenge and pre-eclampsia [14]. Conversely another researcher concluded that hypertension during pregnancy also have a 3 fold elevated risk of developing type 2 diabetes mellitus in future [15]. Identifying relationship between Preeclampsia and GDM is important since preeclampsia is most common during a first pregnancy and assessment of the risk of developing GDM after preeclampsia may help in early management and favourable outcome in subsequent pregnancy. Complications which are aggrevated by coexistence of both diseases are primarily affects the fetus, including :

1) Macrosomia
2) Stillbirth
3) Jaundice
4) Respiratory distress syndrome
5) FGR- only seen in diabetes with vasculopathy
6) Increased Congenital malformations

Pre-existing micro vascular disease in mother also worsens in co existence of these 2 diseases.

**4.2 Hypertension in pregnancy related to diabetic renal disease**

Numbers of patients suffering from diabetes renal disease plan pregnancy, Such Women should be counselled about the risks of pregnancy and emphasized strict control of blood sugars and Blood Pressure for minimizing pregnancy complications, Management of diabetes renal disease prior to conception and during pregnancy is both complex and controversial .In non pregnant individuals , the mainstay of management is inhibition of Renin angiotensin system with Angiotensin converting enzyme (ACE) inhibitors or Angiotensin receptor blocker (ARBs) but these drugs are teratogenic during pregnancy resulting in anuria, skeletal dysplasia, FGR and pulmonary hypoplasia[16]. Pregnancy itself complicates diabetic nephropathy resulting in early progression of end stage renal disease. Pre-existing nephropathy is associated with significant fetomaternal morbidity including preeclampsia, low birth weight, increase incidence of respiratory distress syndrome and perinatal infant death. In women with IDDM and nephropathy ACE inhibitors and ARBs started 6-12 months prior to pregnancy and immediate discontinuation as soon as pregnancy is achieved improves fetomaternal outcome [17]. The nondihydropyridine CCBs (diltiazem and verapamil), when used as alternatives or adjuncts to ACE inhibitors or ARBs among diabetics although data on their benefits in pregnancy is limited [18]. Minimizing progression of diabetic nephropathy and other microvascular disease during pregnancy is essential to reduce the risk of GH or preeclampsia and associated adverse maternal/fetal outcomes.

## 5. Management of hypertension in diabetic women during pregnancy

Although line management of Diabetes remains the same but co existence of these two complications adds further risk to that posed by diabetes alone. Obstetricians are thus challenged with controlling maternal glucose levels and blood pressure (BP) in ways that optimize both maternal and fetal outcome. Chronic hypertension may be masked in first and early second trimester due to physiologic pregnancy-induced vasodilation. High index of suspicion and regular recording of blood pressure is the key to early detection. Chronic hypertension is usually well tolerated during pregnancy and do not require any additional treatment but require discontinuation of preconception antihypertensive drugs. Consideration of medications if BP > 150/100 mmHg, with a goal of preventing maternal cerebrovascular and cardiovascular events at the same time balancing the risk of even transient hypotension resulting in compromised uteroplacental blood

flow and foetal distress [19]. The only definitive treatment of GH or pre-eclampsia is delivery. Delaying delivery only to be done when fetus is remote from term. Expectant management to prolong pregnancy to be decided by senior obstetrician on case to case basis. Decision should be based on close monitoring of both maternal condition and fetal well-being. It may improve outcomes in carefully selected cases at 25 to 34 weeks as lung maturity is delayed due to diabetes [20]. Teratogenic medications to be avoided during pregnancy like ACE inhibitors and ARBs [10]. Diuretics can be considered only in case of renal disease and heart failure [21]. Systolic Blood pressure higher than 155 mmHg poses risk of cerebrovascular accident in pregnancy [22] .

**Pharmacological treatment of hypertensive disorder of pregnancy**

| Medication class | Treatment | Teratogenicity | Formulation | Consideration in DM patients |
|---|---|---|---|---|
| Alpha adrenergic agonists | 1st line | None | Methyldopa Clonidine | No maternal renal protection |
| Beta blockers | 1st line | Fgr, fetal bradycardia | Labetolol | Maternal hypoglycaemia unawareness |
| Vasodilators | 2nd line | Neonatal thrombocytopenia (hydralazine) Cyanide toxicity (nitroprusside) | Hydralazine Nitroprusside | |
| Calcium channel blockers | 2nd line | None | Nifedipine Nicardipine Verapamil | Decrease maternal albuminuria and CVD |
| Ace inhibitors/ ARBs | Contraindicated | Renal failure, anuria, pulmonary hyperplasia | Any | May slow dm renal disease |
| Diuretics | 3rd line | Decrease uteroplacental blood flow | Lasix | Avoid spironolactone due to anti androgenic effect in fetus |

## 6. Future risk analysis

Hypertension in pregnancy alone is alone is a risk for development of chronic hypertension by 3 fold and subsequent cardiovascular events including stroke, thromboembolic disease, congestive heart failure, and ischemic Heart Disease by 2 fold [23]. Of all women with Gestational Diabetes, approximately 50% will develop Type 2 Diabetes within 10 years postpartum and risk OD cerebrovascular disease increases by 70% [24,25]. We recommend that all diabetic women who had hypertension in pregnancy should be counselled regarding their increased CVD risk Emphasis should be given on preventative lifestyle habits, such as caloric limitation and regular exercise and prevention of obesity. Women should be told to be compliant with medications prescribed to control blood glucose, BP, and plasma lipids and follow up.

## 7. Conclusion

Hypertension increases the risk of both fetal and maternal complications in already high risk diabetic patients. Women with diabetes or those predispose to gestational diabetes mellitus are more prone to Hypertensive disorder of pregnancy (HDP). Minimizing both maternal and fetal complications in hypertensive diabetic patients are often challenging to medical field. All the diabetic women who had a history of HDP experience a higher cardiovascular mortality later in life. Increase understanding of pathophysiology of hypertension and improvement in the treatment modalities helps in reducing morbidity and mortality due to HDP. Adequate prenatal visits and follow up help in improving both maternal and fetal outcome.

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