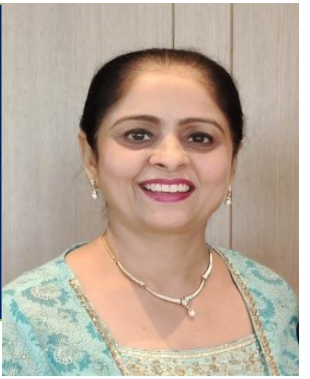
Name : Dr Pikee Saxena , Dept of Obstetric & Gynecology LHMC , New Delhi, India

Designation : Director Professor of Obstetrics & Gynecology, FICOG, MNAMS, FMAS, FIMCH, PGCC (Hospital Management), PGDCR (Clinical Research)



- Winner of 32 gold medals, including C.S Dawn award twice, Corion award, BEST paper in FOGSI Journal
- Abdul Kalam Appreciation award in 2022
- Editor of 6 books, published more than 230 articles/chapters & > 250 invited talks
- Citations > 2279, h index- 17, i10 index 28
- Expert Group member- Drug Controller General of India
- Governing Council Member, DIPSI
- General Secretary of Board of Management of Delhi Diabetic Forum (2016-19)
- Executive Member of Indian Fertility Society (IFS), Convener of Special Interest Group, Early Pregnancy ,IFS
- Editor of NARCHI Bulletin 2022-2024, Associate Editor of IJDDC
- Reviewer for 14 indexed journals
- In-charge of Infertility clinic and IUI Lab, LHMC ;Nodal Officer of National Skills Lab , LHMC
- Principal Investigator for 5 funded Research Projects including ICMR, DST
- Executive member of Delhi Diabetic Forum (DDF), ISAR, Endocrinology Committee of FOGSI; Safe Motherhood & Reproductive Endocrinology committee of AOGD 2020-2022
- Senior Executive editor, Indian Journal of Medical Specialties & Pan Asian Journal of Obstetrics & Gynecology, Editor of DDF Journal, Member of endometriosis & multipurpose committee 2018-2020, Co Editor AOGD,2018-19, Joint Secretary , NARCHI Delhi

APPROACH TO A PREGNANT WOMAN WITH DIABETES MELLITUS

Dr Pikee Saxena

Director Professor of Obstetrics & Gynaecology

Lady Hardinge Medical College & Associated hospitals, New Delhi

HIP is a major global health problem

Hyperglycemia is one of the **most common medical conditions women encounter during pregnancy**

1 in 6 live births occur to women with some form of hyperglycemia

84% *of which are due to GDM*

HYPERGLYCEMIA/GDM IS ASSOCIATED WITH:

- Leading causes of **maternal mortality**
- Higher incidence of **maternal morbidity**
- Higher incidence of **perinatal and neonatal morbidity**
- **Later long term consequences** for both mother and child

Significance for global health

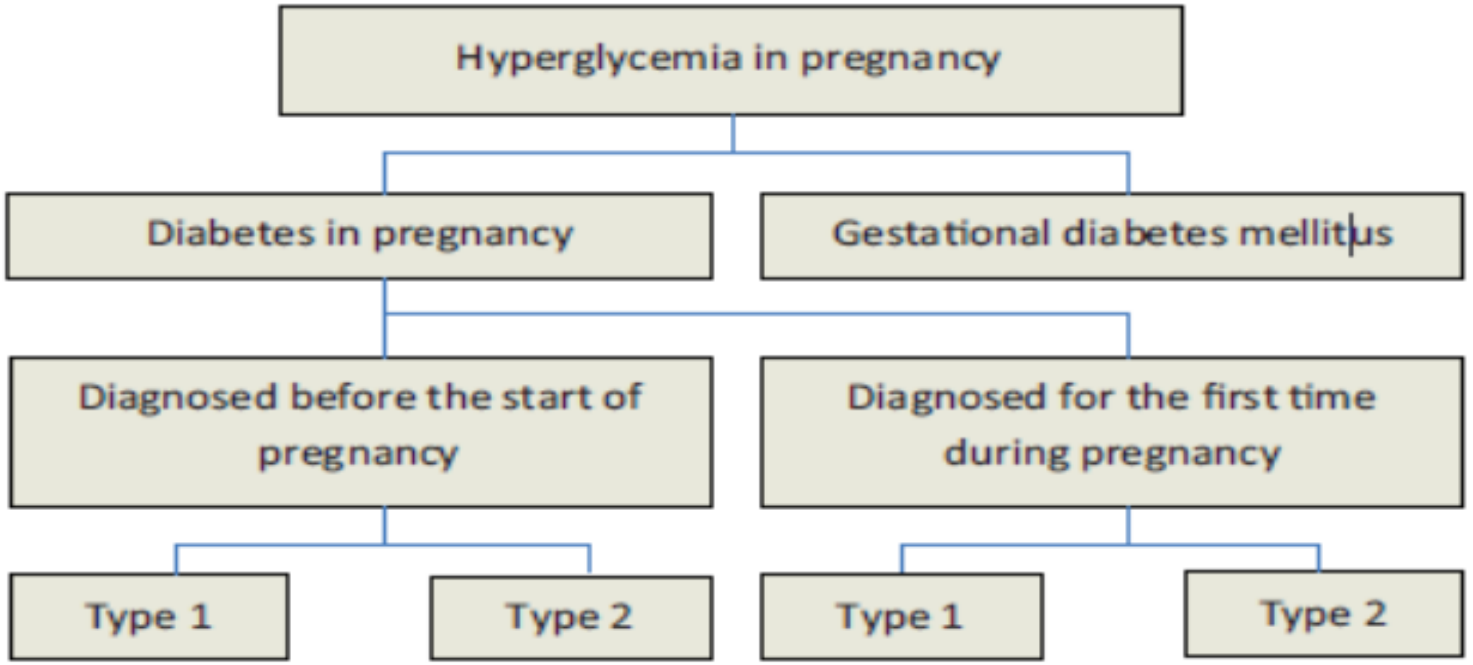
Table 3
Maternal and fetal morbidity associated with gestational diabetes mellitus.

Maternal morbidity	Fetal/neonatal/child morbidity
Early pregnancy	Stillbirth
Spontaneous abortions	Neonatal death
Pregnancy	Nonchromosomal congenital malformations
Pre-eclampsia	Shoulder dystocia
Gestational hypertension	Respiratory distress syndrome
Excessive fetal growth (macrosomia, large for gestational age)	Cardiomyopathy
Hydramnios	Neonatal hypoglycemia
Urinary tract infections	Neonatal polycythemia
Delivery	Neonatal hyperbilirubinemia
Preterm labor	Neonatal hypocalcemia
Traumatic labor	Erb's palsy (as consequence of birth injury)
Instrumental delivery	Programming and imprinting; fetal origins of disease: diabetes, obesity, hypertension, metabolic syndrome
Cesarean delivery	
Postoperative/postpartum infection	
Postoperative/postpartum hemorrhage	
Thromboembolism	
Maternal morbidity and mortality	
Hemorrhage	
Puerperium	
Failure to initiate and/or maintain breastfeeding	
Infection	
Long-term postpartum	
Weight retention	
GDM in subsequent pregnancy	
Future overt diabetes	
Future cardiovascular disease	

FIGO Boxes highlight salient points

- FIGO recommends and supports the call for greater attention and focus on the links between maternal health and noncommunicable diseases in the sustainable developmental agenda.

Different terminology used for HIP



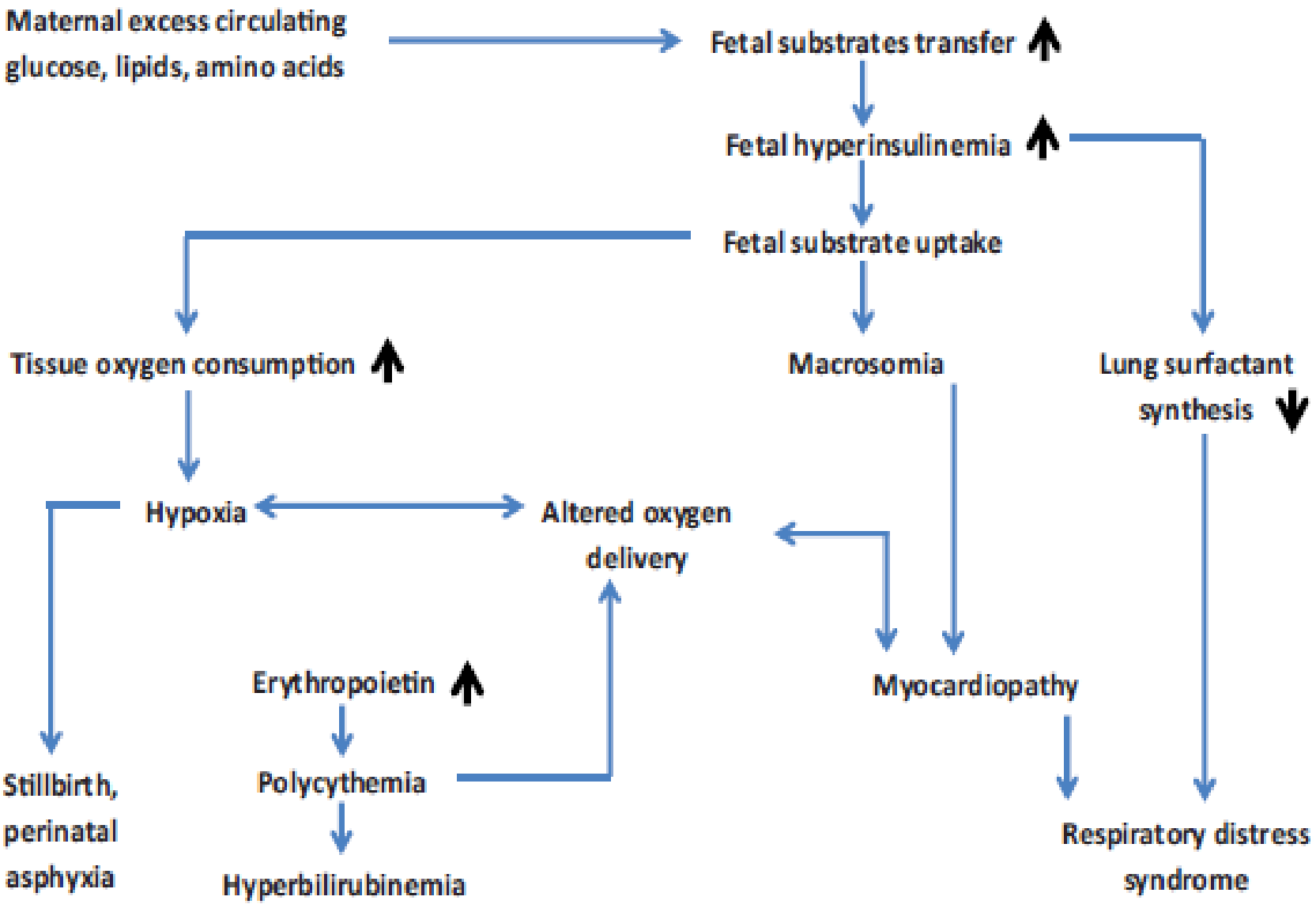
Diabetes in pregnancy/ pregestational diabetes/overt diabetes/
Type 1 or Type 2 Diabetes

Fasting - ≥ 126mg/dl
Random or 2 hrs post glucose load -> 200mg/dl

GDM- 2hrs post glucose load-≥ 140 to 199 mg/dl

FIGO 2015

Pathophysiology of perinatal complications



Villous oedema in placenta of diabetic pregnancies can also impair oxygen transport resulting in foetal hypoxemia.

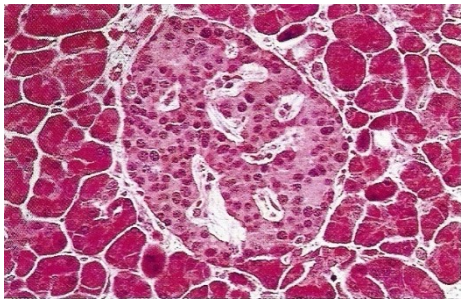
Endless controversy : Screening and diagnosis of GDM

- Multiple guidelines have been proposed by reputed authorities but they vary widely and there is no uniform consensus regarding the best approach.

- Indian women have 11 fold increased risk of developing glucose intolerance during pregnancy.

- Hence **universal screening** for GDM is essential amongst women of Asian origin and especially ethnic Indians

In a hyperglycemic mother



Each islet cell functions as an endocrine organ

Develop at 10-11 weeks of gestation

Maternal hyperglycemia:

β-cell hyperplasia →hyperinsulinemia → macrosomia → Type 2 DM

Early maternal metabolic imprinting occurs by 7-8 wks. may affect fetal growth. Therefore, universal early screening is recommended

The Barker Hypothesis

Adult Disease originates in fetal life

Textbook of diabetes & pregnancy . Gareth williams and John

How to screen- Which Diagnostic criteria to be used?

1 or 2 step?
50gm/75gm/100gm?
How many blood samples?
Threshold values?

Different Diagnostic thresholds for GDM

Approach	Glucose load gms	Diagnostic criteria	Glucose Threshold	mg/dl			Abnormal values n
			Fasting	1-h	2-h	3-h	
2-step Somogyi-Nelson method	100	NDDG (1979) ACOG	105	190	165	145	2
2-Step Glucose oxidase method	100	CC(1982) ACOG	95	180	155	140	2
1-step	75	WHO 1999	126		140		1
1-Step	**75**	**DIPSI (2004)**	**-**	**-**	**140**	**-**	**1**
1-Step	**75**	**IADPSG/ ADA/ WHO 2013**	**92**	**180**	**153**	**-**	**1**
1-Step	75	NICE 2015	101		140		1

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 8, 2008 VOL. 358 NO. 19

Hyperglycemia and Adverse Pregnancy Outcomes

The HAPO Study Cooperative Research Group*

- 23,316 pregnant women without overt diabetes -15 centres in 9 countries over 6 years (July 2000 – April 2006) →75 g OGTT at 24 – 32 wks

- HAPO study indicated a continuous positive correlation between maternal plasma glucose levels (Fasting/1hr/2hr) with birth weight > 90th centile, cord C peptide levels > 90th centile, need for caesarean section and neonatal hypoglycemia.

- Adverse maternal & fetal outcomes were observed at levels even below the diagnostic cut offs *(Diatetes Care2013)*

Indian Guidelines -2018

DIPSI test is the recommended, low cost, reliable, 1 step screening and diagnostic test for all pregnant women

Timing:

- Should be done in the first visit
- Repeat at 24-28 wks (if 1st test is negative and **4 wks gap b/w two**)

If vomiting occurs within 30 minutes of oral glucose intake, the test has to be repeated the next day, or else refer to a facility. If vomiting occurs after 30 minutes, the test continues.

DIPSI Procedure

- 75 g oral glucose load*, irrespective of fasting or nonfasting state and without regard to the time of the last meal in 300 ml water over 5-10 mins
- A venous blood sample is collected at 2 hours for estimating plasma glucose. GDM is diagnosed if 2-hour PG is ≥ 140 mg/d or plasma calibrated glucometer may be used to give report at the same time
- If 75 g glucose packet is not available, remove and discard 5 level teaspoons (not heaped) of glucose from a 100 g packet

In the Indian Scenario with high diabetic burden: universal, early screening with single step, DIPSI criteria is convenient and evidence based.

THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India
DOI 10.1007/s13224-017-0962-y

ORIGINAL ARTICLE

Comparison of Diagnostic Accuracy of Non-fasting DIPSI and HbA1c with Fasting WHO Criteria for Diagnosis of Gestational Diabetes Mellitus

Pikee Saxena[1] · Puja Verma[1] · Binita Goswami[2]

DIPSI with W.H.O GTT for diagnosis of GDM on 800 women

Prevalence of GDM (WHO): 6.25%
Sensitivity of DIPSI: 98.04% ; Specificity : 98.26%
Positive predictive value: 79.37%;
Negative Predictive value : 99.86%
Diagnostic accuracy of DIPSI : 98.25%
kappa(agreement) :0.868

The Journal of Obstetrics and Gynecology of India
https://doi.org/10.1007/s13224-021-01486-x

ORIGINAL ARTICLE

Diagnostic Accuracy of Diabetes in Pregnancy Study Group of India with Carpenter–Coustan and National Diabetes Data Group Criteria for Diagnosis of Gestational Diabetes Mellitus and Correlation with Fetomaternal Outcome

Pikee Saxena[1] · Tanya Shubham[1] · Manju Puri[1] · Anju Jain[2]

Received: 20 September 2020 / Accepted: 15 April 2021

Abstract

Background No previous study compared ACOG and DIPSI criteria for diagnosing gestational diabetes (GDM). This study compared diagnostic accuracy of Diabetes in pregnancy study group of India (DIPSI) with Carpenter–Coustan (CC) and National Diabetes Data Group (NDDG) criteria for diagnosis of GDM and correlation with fetomaternal outcome.

Methods A total of 1029 pregnant women underwent 2 h 75 g OGTT in non-fasting state. After 3–7 days, women were called in fasting state and subjected to 100 g OGTT and fasting, 1, 2, 3 h samples were taken. GDM was diagnosed using DIPSI, CC and NDDG criteria. All women were followed till delivery, and fetomaternal outcome was noted.

Results 10.4% (107) women were diagnosed as GDM by DIPSI, 6.4% (66) by CC and 3.1% (32) by NDDG criteria. Sensitivity of DIPSI with CC was 98.48%, specificity was 95.64%, and diagnostic accuracy was 95.82%. Sensitivity of DIPSI with NDDG was 99.89%, specificity was 92.38%, and diagnostic accuracy was 95.52%. Sensitivity of NDDG with CC was 48.48%, specificity was 100%, and diagnostic accuracy was 96.7%. Women with GDM by all three criteria were seen to have a significantly higher proportion of LSCS, higher birth weight and macrosomia compared to normoglycemic women (p value < 0.001).

Conclusion Diagnostic accuracy, sensitivity and specificity of DIPSI are comparable to CC and NDDG criteria; therefore, DIPSI can be recommended for diagnosing GDM with added advantage of low cost, simplicity and convenience. Women diagnosed as GDM by DIPSI, CC and NDDG had significantly higher rate of cesarean delivery, higher birth weight and macrosomia as compared to women with normoglycemia.

Targets plasma glucose levels?

FIGO 2015, ACOG 2017, ADA 2021

Fasting: ≤95 mg/dl

1-h postmeal: ≤140 mg/dl or

2-h postmeal: ≤120 mg/dl

HbA1c -6-6.5% (if possible<6%) ADA ; <6% NICE

During labour- 70- 120mg/dl

If target plasma glucose thresholds are exceeded, lifestyle changes including MNT & exercise are initiated

Is There a Role for HbA1c in Pregnancy?

- During pregnancy, role of HbA1c is not yet established
- 1st trimester - identifies pregestational DM
- Later pregnancy- Poor concordance with OGTT
- The sensitivity of HbA1c with respect to WHO GTT was 47.06%,specificity 97.86%, and diagnostic accuracy 94.63% in 800 pregnant women *(Saxena et al, 2017)*
- Gives control over 3mths whereas in pregnancy day to day tight glycemic control is desired.

Preconception care

- **Education:** risks / diet / exercise / hypoglycemia /**Self-monitoring** of plasma glucose
- **Folic acid** supplements (4 mg/day)
- Treat **hypertension** before pregnancy, optimal BP control (130/80mmHg).
- Discontinue use of oral hypoglycemics, ACE inhibitors, ARB's, statins and fibrates.
- **Retinal assessment** by fundoscopy (unless carried out in previous 6 months)
- **Renal assessment** (including microalbuminuria)
- **Thyroid functions** (5-10% incidence with type I diabetes)
- Evaluate for **Neuropathy/foot examination**
- **Effective contraception till weight and HBA1c optimization before pregnancy**

(NICE 2015)

Work Up

Blood sugar profile needs to be done to start her on MNT along with oral antidiabetic agent or Insulin – Wt, BP,Bl S, Urine alb/ketones

Diabetes complications & comorbidities, including -

- ECG in women starting at age 35 years who have cardiac signs/symptoms or risk factors
- BP control - < 135/85 mm hg
- Lipid profile
- Comprehensive renal/ ophthalmologic examination
- Examination of foot

ADA 2023

Referral to Nephrologist :

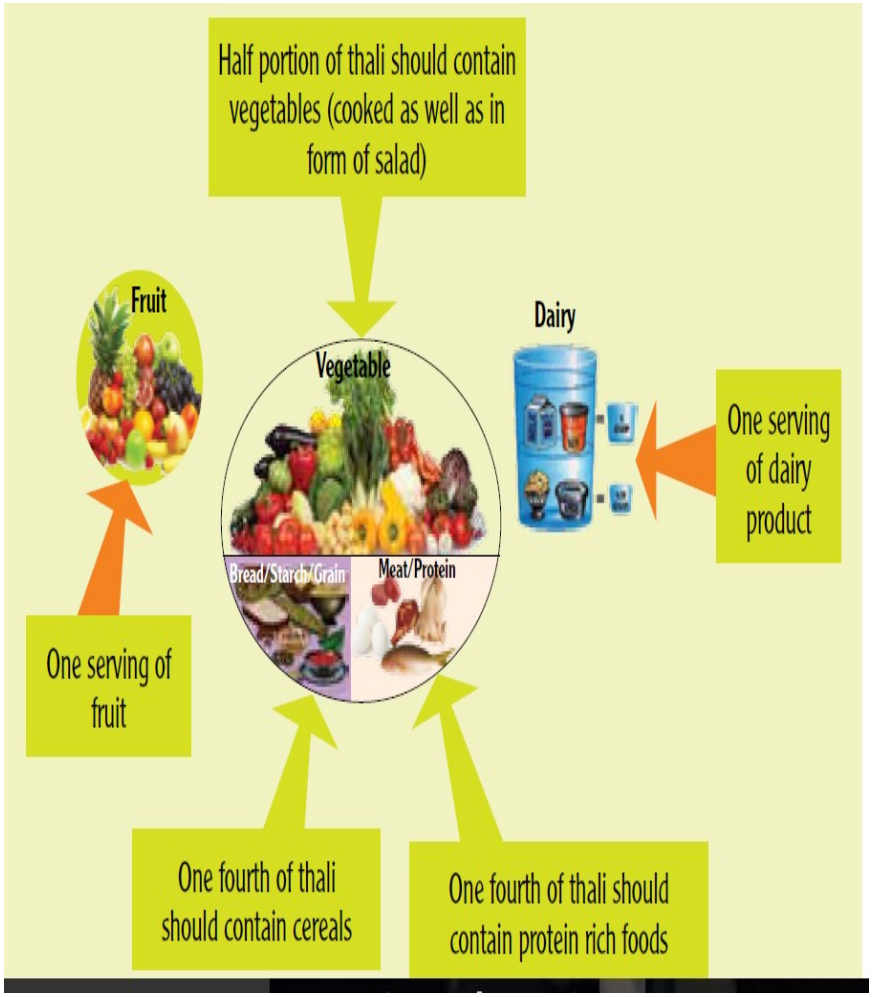
- S. Cr > 1.36 mg/dl (120 micromol/L)
- Albumin: creatinine ratio - > 30mg/mmol
- eGFR < 45 ml/min/1.73m2

NICE2015

Medical Nutrition therapy (ADA 2019)

Goals of MNT

1. Optimal nutrition for developing fetus & mother
2. Maternal euglycemia without ketosis and hypoglycemia
3. Individualizing weight gain and calorie need
4. Carbohydrate – quantity, quality (Glycemic Index) and distribution
5. Protein, fat and micronutrient distribution



The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

- A moderate exercise program is recommended as part of the treatment plan for women with GDM.
- 30 minutes of moderate-intensity aerobic exercise at least 5 days a week or a minimum of 150 minutes per week.
- Simple exercise such as walking for 10–15 minutes after each meal can lead to improved glycemic control and is commonly recommended.

July, 2017

When should pharmacotherapy be considered?

If diet and exercise fail to achieve blood glucose targets within 2 weeks in 2nd trimester or within1wk during third trimester

↓

Pharmacotherapy-

Insulin or Antidiabetic Agent??

Indications for initiating insulin therapy for women with GDM: 1st line therapy

- FBS >110 mg/dl
- 1 hr PP> 140 mg/dl
- POG < 20wks or >30 wks
- Fetal macrosomia — FIGO 2015
- USG: AC > 75th percentile at 29-33wks — ACOG 2016
- FBS> 126mg/dl ; RBS/PP> 200 mg/dl (Overt Diabetes)
- During labour for strict glycemic control
- Diabetes with organ dysfunction
- Ketoacidosis/Medical complications
- Steroids for fetal lung maturity

Types of Insulins

- **Basal insulin** suppresses hepatic glucose production and maintains near normoglycemia in the fasting state- intermediate and long acting inulin- NPH (Neutral Protamine Hagedorn), Detemir, Degludec
- **Bolus insulin** covers the extra requirements after food is absorbed, decreasing postprandial glucose excursions- Regular, Aspart, Lispro
- Insulin type, injection technique, insulin antibodies, site of injection and individual patient response differences can affect the onset, degree and duration of insulin activity.

Safety and level of evidence for Insulin use during pregnancy

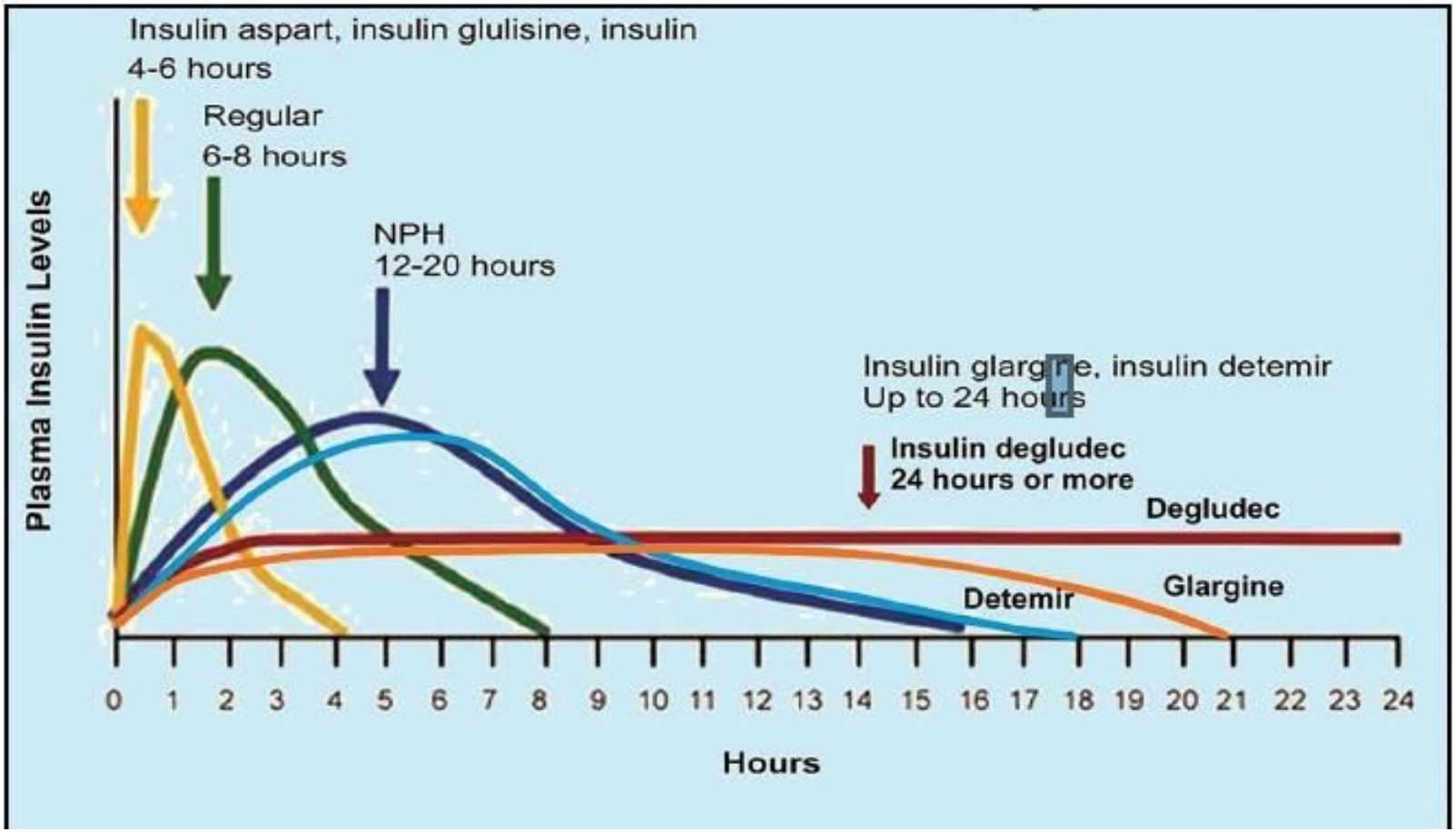
Class	Medication	Pregnancy class	Fetal exposure	LOE & grade of recommendation
Insulin	Lispro	B	Unlikely	LOE1 grade A
	Aspart	B	Unlikely	LOE1 grade A
	Glulisine	C	Unlikely	LOE4 grade D
	Regular	B	Unlikely	LOE1 grade A
	NPH	B	Unlikely	LOE2 grade A
	Detemir	B	Unlikely	LOE1 grade A
	Glargine	C	Unlikely	LOE2 grade B
	Degludec	C	Unlikely	----

Insulin therapy

Insulin shown to be safe in pregnancy

Insulin name	Type	Onset	Peak effect	Duration	Dosing interval
Aspart	Rapid acting	15 min	60 min	3-5 hr	At start of each meal
Lispro	Rapid acting	15 min	60 min	3-5 hr	At start of each meal
Regular	Short acting	60 min	2-4 hr	6-8 hr	60-90 minutes before meal
NPH	Intermed. Acting	2 hr	4-6 hr	12-20 hr	Every 8-12 hr
Insulin detemir	Long acting	2 hr	-	24 hr	Every 24 hr

Insulin Profiles After Subcutaneous Injections



How to initiate insulin therapy: General principles

Blood sugar profile is done : 7 point

Fasting, 2 hr Post BF, Pre-lunch, 2 hr Post lunch, pre dinner, 2 hr post dinner, 3 am

- If only FPG is high, NPH/basal should be started at bed time (Grade A; EL 4)
- If postprandial BG is higher, short/rapid acting insulin should be added before that meal based on blood glucose monitoring
- Premix (Mixtard) insulin may be used before breakfast and before dinner (Grade A; EL 1)
- Depending on SMBG, multiple dose injection regimens are also recommended for achieving euglycemia (Grade A; EL 3)
- Rapid-acting bolus analogue insulin may be used over regular insulin for postprandial glucose control, although perinatal outcomes are similar [Grade B, Level 2].
- Split mix: morning (2/3 IAI, 1/3 SAI);
  pre dinner (SAI); bed time IAI

Seshiah V,et al. Diabetes in Pregnancy Study Group. Gestational diabetes mellitus guidelines. *J Assoc Physicians India 2006;54:622-628.*

Insulin Therapy

Pregnant Woman with GDM

MNT for 2 weeks

2 hr PPBS ≥ 120 mg/dL

2 hr PPBS < 120 mg/dL

Start Human Insulin premix 30:70

- Subcutaneous injection, 30 mins before breakfast, once a day
- Dose of insulin calculated by blood sugar level

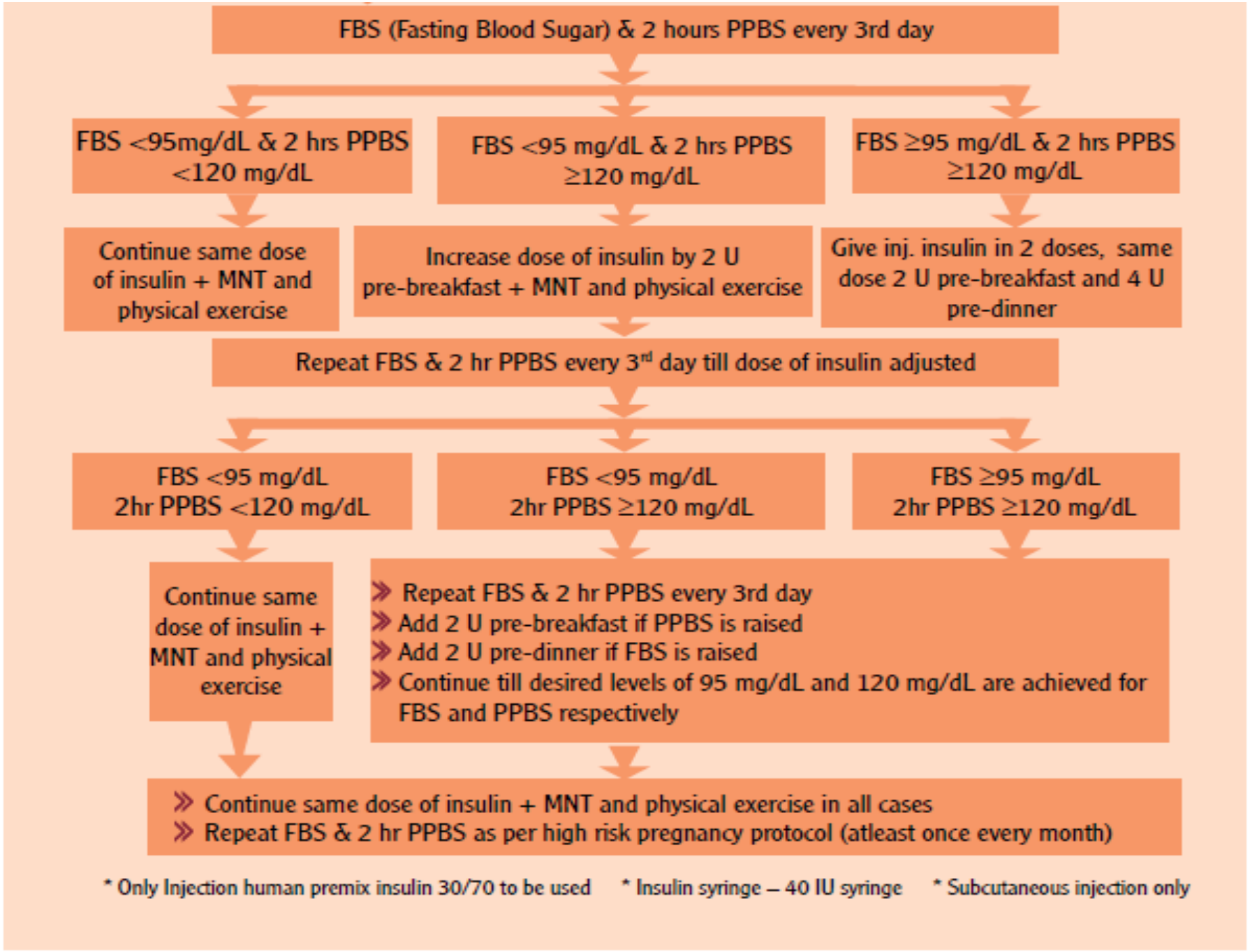
Blood sugar	Dose of insulin
Between 120-160	4 units
Between 160-200	6 units
More than 200	8 units

Continue MNT and physical exercise, repeat 2 hr PPBS as per high risk pregnancy protocol or as advised by the physician (at least once monthly)

≥120 mg/dL

<120 mg/dL

FBS (Fasting Blood Sugar) & 2 hours PPBS every 3rd day


FBS (Fasting Blood Sugar) & 2 hours PPBS every 3rd day
FBS <95mg/dL & 2 hrs PPBS <120 mg/dL
FBS <95 mg/dL & 2 hrs PPBS ≥120 mg/dL
FBS ≥95 mg/dL & 2 hrs PPBS ≥120 mg/dL
Continue same dose of insulin + MNT and physical exercise
Increase dose of insulin by 2 U pre-breakfast + MNT and physical exercise
Give inj. insulin in 2 doses, same dose 2 U pre-breakfast and 4 U pre-dinner
Repeat FBS & 2 hr PPBS every 3rd day till dose of insulin adjusted
FBS <95 mg/dL 2hr PPBS <120 mg/dL
FBS <95 mg/dL 2hr PPBS ≥120 mg/dL
FBS ≥95 mg/dL 2hr PPBS ≥120 mg/dL
Continue same dose of insulin + MNT and physical exercise
» Repeat FBS & 2 hr PPBS every 3rd day
» Add 2 U pre-breakfast if PPBS is raised
» Add 2 U pre-dinner if FBS is raised
» Continue till desired levels of 95 mg/dL and 120 mg/dL are achieved for FBS and PPBS respectively
» Continue same dose of insulin + MNT and physical exercise in all cases
» Repeat FBS & 2 hr PPBS as per high risk pregnancy protocol (atleast once every month)
* Only Injection human premix insulin 30/70 to be used
* Insulin syringe – 40 IU syringe
* Subcutaneous injection only

Prevention of Hypoglycemia

A. Inform patients of increased risk of severe hypoglycemia during early pregnancy

A. Educate patients on hypoglycemia prevention:
   - Frequent SMBG
   - Regular meal timing
   - Accurate medication administration
   - Careful management of exercise programs

HOW TO RECOGNISE AND MANAGE HYPOGLYCEMIA?

- Hypoglycemia : Plasma glucose level is **< 70 mg/dl.**
- Educate PW and her family regarding recognition & treatment of hypoglycemia
- **Early symptoms** - Tremors of hands, sweating, palpitations, hunger, easy fatigability, headache, mood changes, irritability, low attentiveness, tingling sensation around the mouth/lips or any other abnormal feeling.
- **Severe** - Confusion, abnormal behavior or both, visual disturbance, nervousness or anxiety, abnormal behavior.
- **Uncommon** - Seizures and loss of consciousness

Treatment of hypoglycaemia

- 3 TSF of glucose powder (15- 20 grams) in a glass of water.
- After taking oral glucose, she must take rest & avoid any physical activity for 15 minutes
- After taking glucose, she must eat one chapati with vegetable/rice/one glass of milk/idli/fruits/anything eatable which is available
- If glucose is not available, take one of the following: Sugar - 6 TSF in a glass of water/fruit juice/honey/anything which is sweet/any food

Once blood sugar levels are controlled, how frequently would you repeat the blood sugar tests?

Which levels are more important to be measured during pregnancy-Pre or post meal?

Frequency of plasma glucose monitoring

- Once controlled, monitor every 3rd day –FPG & 2hrs post meal
  For Metformin-biweekly -FPG & 2hrs post meal

MOHFW 2018

- Once controlled, monitor with 3-4 samples/day- including FBG + 2-3 post meal at least twice a week/ staggering approach

FIGO 2015 /ACOG

- Postprandial glucose levels are associated with adverse pregnancy outcomes

Assoc Physicians India 2006;54:622-628, ADA 2018, FIGO 2015

- ANC every two weeks with blood sugar profile reports or earlier if values are deranged

NICE ,FIGO 2015

ORAL ANTIDIABETIC AGENTS

Should Metformin be continued in PCOS pts?

Systematic Review and Meta-Analysis

Medicine®

OPEN

Effects of metformin on pregnancy outcomes in women with polycystic ovary syndrome

A meta-analysis

Xian-Ling Zeng, MD[a], Ya-Fei Zhang, MD[b], Quan Tian, PhD[a], Yan Xue, PhD[a], Rui-Fang An, PhD[a,*]

Abstract

Aim: The aim of the study is to evaluate the effects of metformin on pregnancy outcomes in women with polycystic ovary syndrome (PCOS).

Methods: We searched electronic databases and bibliographies of relevant papers to identify studies comparing the pregnancy outcomes in the metformin group with those in the placebo or blank control group. Then, we did this meta-analysis based on the PRISMA guidelines. The primary outcomes included early pregnancy loss (EPL), preterm delivery, term delivery, and gestational diabetes mellitus (GDM). Secondary outcomes included pregnancy-induced hypertension (PIH), intrauterine growth restriction (IUGR), fetal malformation, vaginal delivery (VD), cesarean section (CS), and metformin's side effects, such as nausea or gastrointestinal discomfort. Certainly, data about neonatal death and macrosomia were analyzed if data available.

Results: Finally, 13 studies including 5 randomized controlled trials (RCT) and 8 cohort studies involving 1606 pregnant women with PCOS were analyzed. The pooled OR of EPL was 0.19 with obvious statistical significance, manifesting that metformin help to lower the rate of EPL (95% CI 0.12–0.28, $P < 0.00001$). Simultaneously, metformin showed the advantage of reducing the prevalence of preterm delivery (OR 0.37, 95% CI 0.20–0.68, $P = 0.002$). In addition, metformin could promote term delivery greatly and the pooled OR was 5.23 with sharp statistical difference (95% CI 3.12–8.75, $P < 0.00001$).

Conclusion: Metformin treatment in women with PCOS throughout pregnancy could increase the possibility of term delivery, VD and reduce the risk of EPL, preterm labor, pregnancy complications such as GDM and PIH, with no serious side effects. Moreover, metformin was not teratogenic based on the limited data. So we may recommend metformin treatment for women with PCOS during the whole pregnancy period for it is quite beneficial and safe for both mothers and babies.

ADA 2022 : Metformin may not be continued in PCOS patients after 12 weeks

Advantages of oral ADA in pregnancy

- 2nd line if pt. is not willing to take insulin or stays in remote area
- More convenient, less expensive
- Less monitoring is required
- If preferred by patient it may enhance treatment adherence.
- Metformin is useful for obese women or for women who are already on high doses of insulin.
- It reduces weight gain during pregnancy
- Lower chances of hypoglycaemia

Safety of OAD during pregnancy

Class	Medication	Pregnancy class	Fetal exposure	LOE & grade of recommendation
Secretogogues	Glipizide	C	Crosses placenta	LOE4 grade D
	Glyburide	B	Crosses placenta	LOE2 grade B
	Glimepiride	C	Crosses placenta	LOE4 grade D
	Repaglinide	C	Unknown	LOE4 grade D
	Nateglinide	C	Unknown	LOE4 grade D
Biguanides	Metformin	B	Crosses placenta	LOE3 grade C

Comparative safety & efficacy of Metformin vs. Glyburide

Metformin

Dose

500mg to 2gm/day

Safety

- 1.5 to 1.7 times higher risk of preterm birth

Efficacy

- Approx. 30-50% failure rate requiring substitution with insulin

Glyburide

Dose

2.5mg to 20mg/day

Safety

- > 2.5 times higher risk of macrosomia
- >2 times higher risk of neonatal hypoglycemia

Efficacy

Approx. 16% failure rate requiring substitution with insulin

PLoS One 2013
BMJ. 2015
British Journal of Clinical Pharmacology 2015
Obstet Gynecol. 2010

Authority	Insulin	OAD
MoHFW 2018	Recommended	Recommended
DIPSI 2023	Recommended	NOT RECOMMENDED
Australian 2015	Recommended	Not recommended
ACOG 2017	Recommended	Offer Metformin to those who deny insulin although long term safety not established. Glyburide not recommended.
ADA 2023	Recommended	Metformin and glyburide should not be used as first-line agents as both cross the placenta & long term safety not established.
NICE 2015	Recommended	Recommended

Regulatory body-US FDA ,Australia or Drug Controller General India

Not approved Metformin for use in pregnancy.

Animal reproduction studies have failed to demonstrate a risk to the fetus, but there are no adequate and well controlled studies in pregnant women

Package Insert: GLUCOPHAGE® (metformin hydrochloride) Tablets

- **Pregnancy Teratogenic Effects:** Pregnancy Category B Recent information strongly suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities. Most experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible. Because animal reproduction studies are not always predictive of human response, **GLUCOPHAGE and GLUCOPHAGE XR should not be used during pregnancy unless clearly needed.**

- Pediatric Use: The **safety and effectiveness of GLUCOPHAGE** for the treatment of type 2 diabetes have been established **in pediatric patients ages 10 to 16 years and not below 10 yrs**

Foetal surveillance in GDM

Fetal monitoring: (ACOG, 2017)

GDM A1 category - well controlled on diet-

Routine monitoring , no special monitoring required

GDM A2 category -medication requiring

Start fetal surveillance earlier

Gestational Age	Fetal Monitoring
First trimester	Dating ultrasound, s-PAPP-A & s-βHCG, NT-NB scan, uterine artery Doppler for PE
18-20 wk	Anomaly scan: 18 - 20 weeks including examination of the fetal heart (4 chambers, outflow tracts & 3 vessels
20+ wk	Fetal echocardiogram if indicated at 22-24 wks
Third trimester	Serial growth ultrasound every 3-4 wkly for macrosomia/ polyhydramnios, earlier as needed. For FGR- weekly or 2 times a week
32 wk	Initiate DFMC, NST, BPP 2-3 times/wk for insulin –requiring DM; Doppler has limited value in GDM A good BPP score is reassuring but cannot predict sudden fetal death

Macrosomia

Fetal weight >90th percentile, a B.Wt $\geq$ 4000 g or $\geq$2 SD of mean weight by POG.

In Indian population average baby weight is less, **Birth Wt. >90th Centile i.e. 3.45 kg is considered as macrosomia**. (*Balaji V. Indian J Endocr Metab. 2011)*

- **Predictive value of USG is 40- 64 % ; Clinical evaluation is 10-53%**

- **Serial USG & individualized growth curve do not improve detection rate**

Serial fetal AC >90th percentile -84% sens; Estimated fetal weight - 74% ; EFW+AC - 88% ; Transverse fetal thigh diameter, 3-dimensional USG, fractional limb volume, S/C fat over arm, abdomen

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FIGO COMMITTEE REPORT

WILEY

Good clinical practice advice: Antenatal corticosteroids for fetal lung maturation☆

FIGO Working Group on Good Clinical Practice in Maternal–Fetal Medicine*,a

April 2018

Shared decision making taking the patient and her relatives into confidence and explain the risk and benefits of steroid cover for lung maturity in case of preterm delivery

For women with **insulin-treated diabetes** who are taking steroids for fetal lung maturation, **give additional insulin according to sliding scale over and above the required insulin ; monitor plasma glucose 4 hrly.**

National Institute for Health and Care Excellence. Diabetes inPregnancy:Management From Preconception to the Postnatal Period(NG3). London: NICE; 2015.

Termination of pregnancy

Condition	Timing of Delivery	
GDM on diet	After 39 wks till 41 wks Not before 39 weeks	ACOG,2017 Indian Guidelines,2018
GDM controlled on insulin	39-39+6 wks	ACOG 2017
Pregestational diabetes -	37 - 38+6 wks	NIH 2011, NICE 2015
Complicated/uncontrolled diabetes	Early termination (after 34 wks)	

Antenatal steroids if elective CS is planned before 37wks

Induction at 38-39 weeks gestation may be slow or unsuccessful due to unfavorable bishops but this has to be balanced against the poorly defined and 5 times higher risk of late IUD beyond 38 wks.

In Indian set up, termination is planned between 38-39 wks

Termination of pregnancy

GDM on diet : After 39wks till 41 weeks

(ACOG 2017, Indian Guidelines ,2018)

GDM controlled on insulin : 39-39+6 wks (ACOG 2017)

Pregestational diabetes or poorly controlled GDM- 37 to 38+6 wks (NIH2011, NICE 2015).

Complicated diabetes: earlier termination after 34 wks.

Antenatal steroids if elective CS is planned before 38wks

In Indian set up, termination is planned between 38-39 wks

Immediate Postpartum Glycemic Control

- **GDM women -** stop insulin therapy after delivery; monitor F & PP for 1-3 days
- **Type 2 DM** who are breast feeding -resume metformin and glibenclamide immediately after birth and monitor fasting and PP levels
- **Overt diabetes who were on insulin** -reduce insulin dose by 20-40% and monitor blood glucose levels carefully to establish appropriate dose
- Metformin and Glyburide may be used during lactation as their levels in breast milk have been negligible. They have not been shown to have hypoglycemia or developmental abnormality in the neonate.

J Hum Reprod Sci. 2012 May-Aug; 5(2): 166–169
Gynecol Endocrinol 2006
FIGO
2015

Post-Partum Follow-up

	Short term Follow up	Test	Long term Follow up
MoHFW	**6 To 12 weeks**	**75 G OGTT**	**Every year**
ADA 2017	**4–12 Weeks Postpartum with 75mg OGTT**	**75 G OGTT**	**Every 1-3 years**
ACOG 2013	**6-12 Weeks**	**FPG OR 75 G-2hr OGTT**	**Every 1-3 years**
NICE 2015	**6-13 Weeks**	**FPG**	**Annual HbA1c**
	After 13 Weeks	**FPG Or HbA1c**	

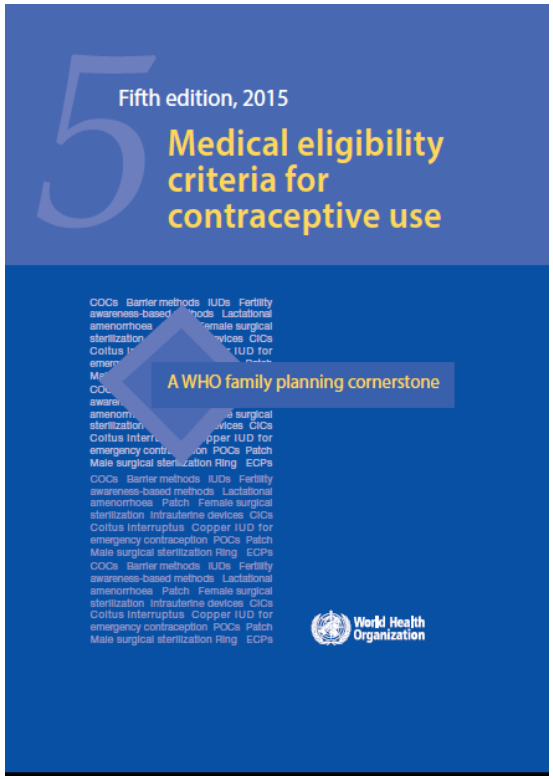
Breastfeeding > 3mths v.s. women who did not breastfeed

↑ median time to diabetes to 12.3 years v.s. 2.3 year*(Diabetes 2012 Dec;61(12): 3167-71)*

Counsel: next pregnancy after preconception evaluation

GDM and contraceptive advice

Risk of an unplanned pregnancy outweighs the risk of any given contraception option



Any contraceptive method is safe for a woman with DM

Except

CHC and injectable progestin only contraceptives are category 4 /3 for women with complicated DM or DM> 20 yrs duration

Cu IUD and barrier are category 1

Rest all category 2

Interconceptional Care

Advise on lifestyle
- **Diet**
- **Exercise**
- **Weight reduction**

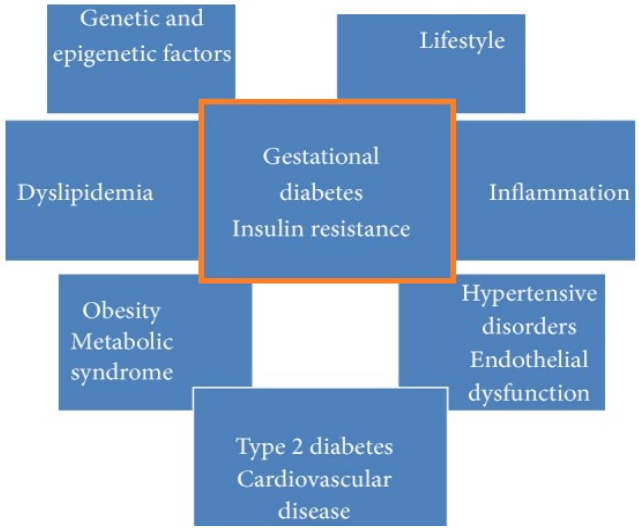
Breastfeeding

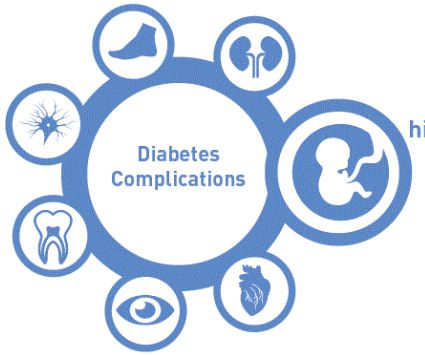
Metformin

Periodic Monitoring
- **Lipids**
- **BP**
- **Glycemia**

Contraception

Next pregnancy after preconception counselling & optimisation





Children who are exposed to **high blood glucose** in the womb are at higher **risk** of developing **type 2 diabetes** later in life

To Conclude,

- Maintaining **euglycemia with supervised**, **multidisciplinary care** will avoid short and long term complications for mother/fetus
- **Early diagnosis** , **patient education, lifestyle management with MNT & exercise** forms the backbone of treatment.
- **Insulin is the Gold Standard for treatment of diabetes in pregnancy** with unparalleled and unquestionable efficacy and safety.
- No oral agent is FDA-approved & their use is off label in pregnancy.
- Metformin:2nd line approach; Counsel women about increased risk of **preterm birth, 26% to 46% failure rate, placental transfer of the drug, and lack of long-term data in exposed offsprings**.

Thank You

Induction of Labour

- Induction with PGE2 gel starting from late evening or early morning
- 50% dose of intermediate or long acting insulin is given at bedtime
- Morning dose of insulin is withheld
- Clear oral fluids are allowed during early labour
- Blood sugar monitoring is done every hourly & is maintained between 70-120mg%
- Both hypo & hyperglycemia by capillary blood glucose measurements should be confirmed by venous sample
- Anytime, the blood sugars < 70mg%, infusion of 5% dextrose is started at a rate of 100-150 cc/hr to maintain blood sugars in target range
- Regular insulin is administered by intravenous infusion at a rate of 1.25u/hr if blood sugars exceed 120 mg% OR subcutaneous insulin is given at 1 unit for every 20mg increase of blood sugar beyond upper targets
- Continuous fetal heart monitoring throughout labour

SPECIAL PRECAUTIONS DURING LABOUR

- **The morning dose of Insulin is withheld on the day of induction/labour** and the PW should be started on 1-2 hourly monitoring of plasma glucose by a glucometer; urine ketones 4 hourly

- IV infusion with normal saline (NS) to be started & regular insulin to be added according to plasma glucose levels as per the table below:

Plasma glucose (mg/dl)	Insulin in 500ml NS	Rate of NS infusion
90 – 120	0	100 ml/hr(16 d/min)
120 – 140	4 U	100 ml/hr(16 d/min)
140 – 180	6 U	100 ml/hr(16 d/min)
>180	8 U	100 ml/hr(16 d/min)

Intrapartum Fetal Monitoring

A normally oxygenated foetus with good placental respiratory reserve tolerates uterine contractions well but macrosomic foetus of a diabetic mother has placental oedema , maternal vascular disease with relative hypoxia → uteroplacental insufficiency

Fetal Monitoring

Continuous intrapartum electronic foetal monitoring or

Intermittent Auscultation -After uterine contraction

First stage of labour	Every 15 minutes
Second stage	Every 5 minutes

- Avoid repeated PV exams, descent of head to be monitored
- Higher risk for prolonged labour, 2nd stage arrest, shoulder dystocia, instrumental delivery, infection, foetal injury
- Experienced paediatrician and obstetrician to take delivery

Preoperative management

- LSCS should be scheduled early in the morning.
- Give night dose of intermediate-acting insulin, short- or rapid-acting insulin or continuous insulin infusion
- Decrease the dose of long-acting basal insulin at night (detemir, glargine, or basaglar) by 50 percent
- Fasting : NPO for 8 hours (solids) and 2 hours (clear liquids)
- FBS & S. electrolytes on morning of surgery
- Withhold morning dose of insulin, if surgery is delayed, give basal insulin (approx. 1/3rd of morning NPH dose in 5 % dextrose infusion to avoid ketosis)

Postoperative care

- Tight control ‘relaxed’ .
- Early ambulation , thromboprophylaxis
- Type I – revert to pre-pregnancy schedule
- Type II- oral hypoglycemics
- GDM – will not require any antidiabetic drug.
- Wound care .