Diabetes Mellitus with Pregnancy

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Definitions

Diabetes mellitus (DM): Chronic metabolic disorder in CHO metabolism with impact on fat & protein metabolism due to insulin dysfunction (deficiency or resistance).

Gestational DM (GDM): DM first discovered during current pregnancy.

DM in pregnancy: Gestational DM + pregnancy in patients known to be diabetic.

Epidemiology

Incidence: 2-5% of all pregnancies (80-90% are GDM).

Stages of DM:

A) Potential DM: Normal glucose tolerance but high risk to develop DM.

B) Latent DM: Abnormal GTT under stress only.

C) Subclinical (chemical) DM: Abnormal GTT without manifestations of DM.

D) Clinical (overt) DM: Symptomatic or complicated DM.

National Diabetes Data Grouping (NDDG) of WHO classification of DM

A) Type I: Insulin-dependant DM (IDDM).

B) Type II: Non insulin-dependant DM (NIDDM).

C) Type III: Gestational DM (GDM).

D) Type IV: 2ry DM (due to genetic disorders, endocrino-pathies, drugs or infection).

CLASSIFICATION [American Diabetic Association 2020]

Diabetes can be classified into the following general categories:

1. Type I diabetes; (due to autoimmune β- cell destruction ,usually leading to absolute insulin deficiency).

2. Type 2 diabetes ; (due to a progressive loss of adequate β-cell insulin secretion frequently on the background of insulin resistance)

3. Gestational diabetes mellitus; (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)

4. Specific types of diabetes; due to other causes, e.g.,

a). monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young),

b). diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis),

c). drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation).

Modified White's classification of DM in pregnancy:

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Class	Age of onset	Duration	Vascular disease	Treatment
A	Any	Any	None	Diet alone
A_1	During pregnancy		None	Diet alone
A_2	During pregnancy		None	Diet, insulin
B	>20 yrs	<10 yrs	None	Diet, insulin
C	10–19 yrs or	10–19 yrs	None	Diet, insulin
D	<10 yrs or	>20 yrs	Benign hypertension, background retinopathy	Diet, insulin
F	Any	Any	Nephropathy	Diet, insulin
R	Any	Any	Proliferative retinopathy	Diet, insulin
H	Any	Any	Cardiac disease	Diet, insulin
T	Any	Any	Renal transplant	Diet, insulin

Risk factors for GDM:

1. Past history of GDM.
2. Family history of DM in 1st degree relatives.
3. Advanced maternal age: > 35 years.
4. Multiparity.
5. Bad obstetric history:
   a) Previous polyhydramnios, macrosomia, unexplained IUFD or congenital anomalies.
   b) Previous traumatic or operative delivery.
   c) Previous neonatal metabolic changes (hypoglycemia, hypocalcemia or jaundice).
6. Maternal obesity.

Effects of pregnancy on DM

A) Pregnancy is diabetogenic: DM is aggravated during pregnancy & clinical diabetes may appear for 1st time during pregnancy (GDM) due to:

1) Anti-insulin effect of pregnancy hormones (as HPL, estrogen & progesterone).
2) Increased peripheral insulin resistance.
3) Secretion of insulinase enzyme by placenta.

B) Change in insulin requirements according to GA: → Difficult diabetic control.

1) In 1st trimester: ↓↓ dose for fear of maternal hypoglycemia.
2) Second & third trimesters: ↑↑ dose due to diabetogenic effect of pregnancy hormones.
3) During labor: ↓↓ dose to avoid hypoglycemia (due to muscular effort).
4) During puerperium: ↓↓ dose due to withdrawal of pregnancy hormones.

Effects of pregnancy on DM

C) Diabetic complications increase:

1- Hypoglycemia: Blood glucose level < 60 mg/dl.

2- Diabetic ketoacidosis (DKA).

3- Starvation ketosis.

4- Diabetic comas: Hyperglycemic or hypoglycemic.

5- Aggravation of retinopathy & nephropathy.

Effects of DM on pregnancy (MATERNAL)

1- Maternal / During pregnancy:

a) **Abortion:** Due to Ag-Ab reaction associating DM or chromosomal abnormalities.

b) **Preterm labor:** 3-4 times higher in diabetics ($MgSO_4$ is the tocolytic of choice).

c) **Polyhydramnios:** Pathogenesis isn't clear but may be due to increased osmotic pressure of AF, or increased fetal urination, or increased transudate from large placenta, or associated congenital anomalies as NTDs.

d) **Hypertensive disorders:** Due to vasculopathy or nephropathy.

e) **Infection:** UTI, vulvovaginitis (specially monilia) or chorioamnionitis (after ROM).

Effects of DM on pregnancy (MATERNAL)

2- Maternal / During labor:

(a) Obstructed labor & dystocia: Due to macrosomia & congenital anomalies.

(b) Increased incidence of instrumental deliveries & CS.

3- Maternal / During puerperium:

a) PPH & puerperal sepsis.

b) Abnormal lactation: Due to changes in glucose level.

4- Maternal /Late complication: 50% of cases with GDM will develop overt DM later on.

Effects of DM on pregnancy (FETAL)

1) Fetal / Congenital anomalies: 5-10 times > normal.

a) *CNS:* Anencephaly & spina bifida.

b) *CVS:* Specially VSD (commonest).

c) *GIT:* Tracheo-esophageal fistula or imperforate anus.

d) *Renal:* Renal agenesis or polycystic kidney.

e) *Sacral agenesis (caudal regression or caudal dysplasia):* Most specific fetal anomaly for DM (mothers of all reported cases were diabetic).

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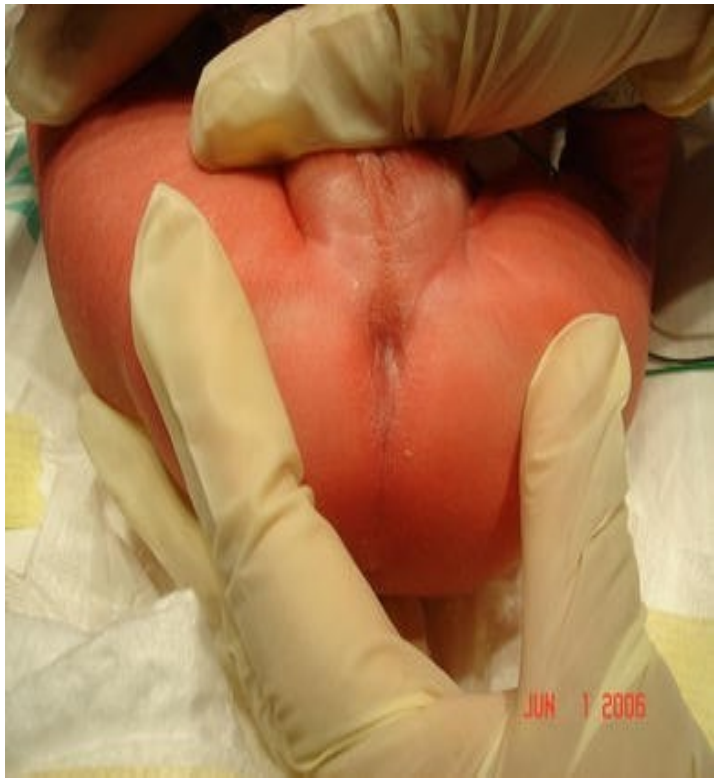
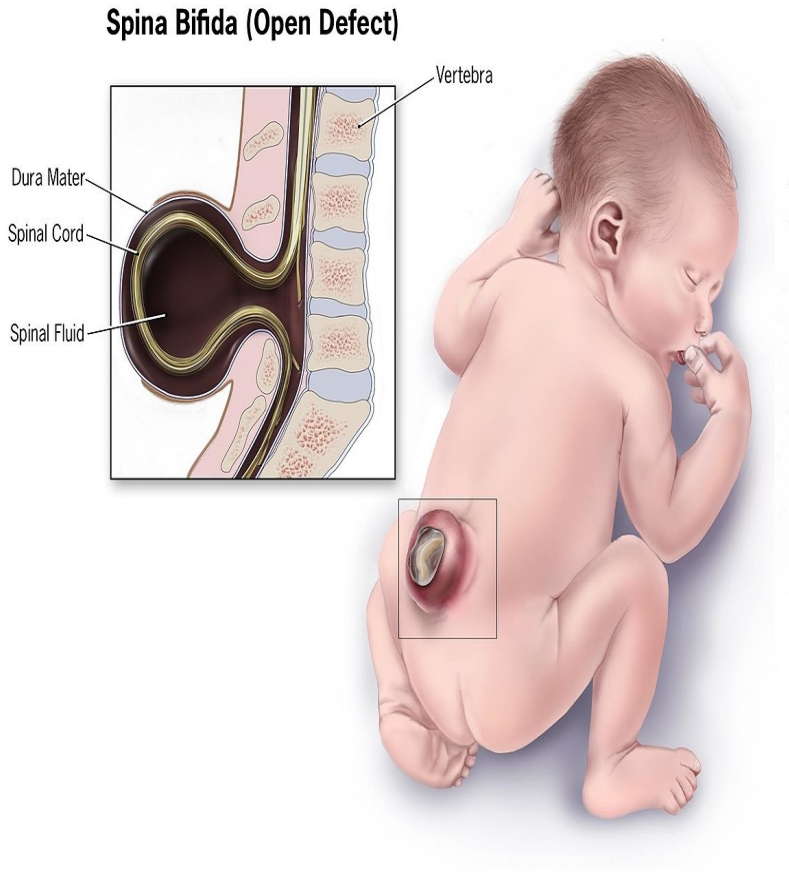


Imperforate anus



Effects of DM on pregnancy (FETAL)

2- Fetal / Macrosomia: 10- fold more than non- diabetics. . Caused by fetal hyperinsulinemia (lipogenesis effect of insulin) in response to fetal hyperglycemia (from maternal hyperglycemia). It can be prevented by strict diabetic control before the second trimester.

3- Fetal / IUGR: Due to chronic placental insufficiency (due to vasculopathy).

4- Fetal / IUFD: Causes may be:

a) Preeclampsia. b) Congenital anomalies.

c) Severe maternal hypoglycemia.

d) Unexplained IUFD .

Effects of DM on pregnancy (NEONATAL)

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1) Respiratory distress syndrome (RDS): Due to delayed lung maturity (because hyperinsulinemia inhibits secretion of pulmonary surfactant).

2) Hypoglycemia: Blood glucose level < 40 mg/dl (due to hyperinsulinemia).

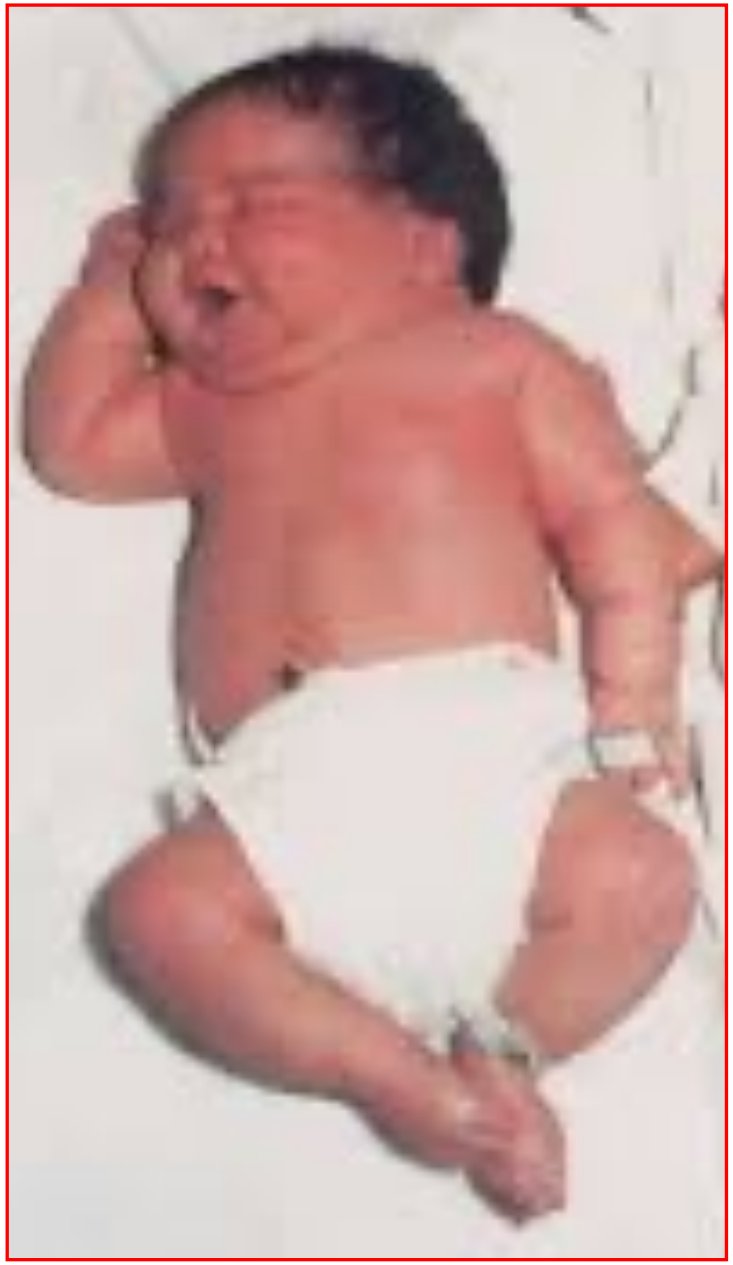
3) Hypocalcemia & hypo-magnesemia. 4) Hyperbilirubinemia: Due to delay in liver maturation.

5) Polycythemia: Hematocrit > 65%. 6) Hypertrophic cardiomyopathy.

7) Poor suckling: Due to prematurity, RDS or congenital anomalies.

8) birth injuries : due to macrosomia

9) Late complication: increased risk of development of type I DM later in life (1-3% if mother only is diseased & 6% if father is diseased also).



Infant of diabetic mother

- ***Size:*** Long, large, fatty, > 4 kg, with broad shoulders.
- ***Color:*** Cyanosed (RDS), plethoric (polycythemia), yellow (jaundice).
- ***Congenital anomalies.***
- ***Hypoglycemia.***

Diagnosis

A. History

1. *Risk factors for GDM*: See before.
2. *Symptoms of DM*: Polyuria, polydepsia, polyphagia & pruritus.
3. *Symptoms of complications*: Maternal or fetal.

B) Examination: Signs of maternal or fetal complications (see before).

World Health Organization

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Diabetes in pregnancy should be diagnosed by the 2006 WHO criteria for diabetes if one or more of the following criteria are met:

- **fasting plasma glucose ≥ 7.0 mmol/l (126 mg/ dl)**
- **2-hour plasma glucose ≥ 11.1 mmol/l (200 mg/dl) following a 75g oral glucose load**
- **random plasma glucose ≥ 11.1 mmol/l (200 mg/ dl) in the presence of diabetes symptoms.**

Gestational diabetes mellitus should be diagnosed at any time in pregnancy if one or more of the following criteria are met:

- **fasting plasma glucose 5.1-6.9 mmol/l (92 -125 mg/dl)**
- **1-hour plasma glucose ≥ 10.0 mmol/l (180 mg/dl) following a 75g oral glucose load***
- **2-hour plasma glucose 8.5-11.0 mmol/l (153 -199 mg/dl) following a 75g oral glucose load**

****there are no established criteria for the diagnosis of diabetes based on the 1-hour post-load value***

Diagnosis

- *100 gm 3-hours OGTT:*
- Results: GDM is diagnosed if at least 2 values exceed the following values:

Time	*Plasma glucose level*
Fasting	105 mg/dl
After 1 hour	190 mg/dl
After 2 hours	165 mg/dl
After 3 hours	145 mg/dl

Key Points

GDM diagnostic threshold values from various organizations

		Plasma glucose concentration thresholds (mg/dl)			
Organization	**OGTT glucose load**	**Fasting**	**1-hour**	**2-hour**	**3-hour**
ADA*	100 g	95	180	155	140
ACOG*	100 g	105	190	165	145
WHO§	75 g	126	-	140	-
IADPSG§	75 g	92	180	153	-

*Diagnosis of GDM if two or more glucose values equal to or exceeding the threshold values §Diagnosis of GDM if one or more glucose values equal to or exceeding the threshold values GDM: Gestational Diabetes Mellitus, OGTT: Oral Glucose Tolerance Test, ADA: American Diabetes Association, ACOG: American Council of Obstetricians and Gynecologists, WHO: World Health Organization, IADPSG: International Association of Diabetes and Pregnancy Groups

- According to these criteria the diagnosis of GDM is made if there is at least one abnormal value (≥**92, 180 and 153 mg/dl** for fasting, one-hour and two-hour plasma glucose concentration respectively), after a 75 g oral glucose tolerance test (OGTT).

Diagnosis

*C) **Investigations**:*

1. Oral glucose tolerance tests (OGTTs):

a). 50 gm 1-hour OGTT: The best screening test.

Method: Measuring plasma glucose level 1 hour after ingestion of 50 gm glucose.

Results: Values ≥ 140 mg/dl are abnormal & 100 gm 3-hours OGTT is indicated.

b). 100 gm 3-hours OGTT: The gold standard for diagnosis of GDM.

Method: Measuring FBS (after 8 hours fasting) & plasma glucose level 1 & 2 & 3 hours after ingestion of 100 gm glucose (next slide)

Diagnosis

C) Investigations:

3) Glycosylated HbA_1 (HbA_1c):

The normal range of HbA1c was **4.7–6.3%** in nonpregnant women, 4.5–5.7% in early pregnancy, and 4.4–5.6% in late pregnancy.

HbA1c in the first and second trimesters was significantly lower than that in non-pregnant women. (O'Connor et al 2014)

Values: Reflects glycemic control for the past 4-8 weeks & it can determine the risk of congenital anomalies (è high levels).

4) Investigations to detect complications: Maternal & fetal.

Management

- PRECONCEPTIONAL: history &exam, diabetic control before pregnancy, folic acid, and health education.
- DURING PREGNANCY: ANC, glycemic control (diet, insulin, oral hypoglycemics), observation, and management of complications.
- DURING DELIVERY;
- POSRPARTUM; THE NEOBORN, THE MOTHER, POSTPARTUM CONTRACEPTION

Management

A) Pre-conceptional care

1. History & examination (to evaluate patient's condition & her fitness for pregnancy).
2. Diabetic control before pregnancy: Prevents abortion & congenital anomalies.
3. Folic acid supplementation before pregnancy.
4. Health education programs.

Management

B) Management during pregnancy:

1) Adequate antenatal care:

Frequency of visits: being high risk pregnancy; every 2 weeks till 28 weeks then every week till 36 weeks. Hospitalization in the following conditions :

i) For adjusting insulin dose.

ii) At 36 weeks in uncomplicated cases.

iii) At 32 weeks in patients è vasculopathy: Due to high incidence of hypertensive disorders & IUGR.

iv) At any time when complications occur.

Supervision: By obstetrician & internist.

Management

B) Management during pregnancy:

2) Glycemic control (control of DM):

a) Dietary recommendation:

- Total caloric intake: 30 calories/kg/day (normal BMI) & 24 calories/kg/day (for obese).

- Components of diet: 35-55% CHO, 25% proteins & 20% fat.

-Number of meals/day:

In type I DM: 6 meals/day (3 meals + 3 snacks inbetween meals).

In type II DM & GDM: 4 meals/day (3 meals + bed -time snack).

Management

b) Insulin therapy: The standard treatment for DM with pregnancy.

Goals: Keeping FBS < 105 mg/dl & 2 hours PPS < 120 mg/dl.

Insulin preparations: Ultra-short, short, intermediate & long acting.

Route of administration: SC.

Calculation of total dose/day:

1- In 1st half of pregnancy: Body weight × 0.6 units/day.

2- In 2nd half of pregnancy: Body weight × 0.7 units/day.

Management

Regimens: Total dose/day can be given by one of the following regimens:

1-Conventional regimen/ 2-doses regimen: Before breakfast :2/3 total dose (1/3 short acting & 2/3 intermediate acting insulin). Before dinner. 1/3 total dose (1/3 short acting & 2/3 intermediate acting insulin).

2- Four-doses regimen: Preferred in pregnancy (due to meticulous control). 3/4 total dose is given as short acting insulin as follows: [40% before breakfast, 30% before lunch, and 30% before dinner.] 1/4 total dose is given as intermediate acting insulin at bed time.

Management

c) Oral hypoglycemics:

Insulin is the gold standard for treatment of hyperglycemia during pregnancy when lifestyle measures do not maintain glycemic control during pregnancy.

However, recent studies have suggested that certain oral hypoglycemic agents (**metformin and glyburide**) may be safe and be acceptable alternatives in patients with type II DM.

Management

3) Observation: ***a)*** **Maternal:**

1- Monitoring of weight gain.

2- Monitoring of blood glucose level.

3- Urine analysis: For proteinuria, glucosuria, acetone & pus cells.

4- Fundus examination: At 1st ANC visit & repeated monthly when needed.

5- Observation for development of any complication.

Management

Observation

b) Fetal:

1- Confirmation of fetal viability (by ultrasound).

2- Diagnosis of congenital anomalies: double marker test for screening trisomy (11-14 weeks), nuchal translucency, triple marker test for trisomy (16-18 weeks), fetal echocardiography (19-22 weeks).

3. Fetal biophysical profile (starting 32-34 weeks)may be as early as 28 weeks in complicated cases, determination of fetal maturity after that.

Management

C) Management of delivery:

When to deliver?

1) At 40 weeks (EDD): Only in class A_1.

2) At 38 weeks: In other classes if diabetic state is controlled & pregnancy isn't complicated.

3) Earlier delivery (< 38 weeks): In the following conditions: Uncontrolled DM, Maternal complications indicating termination (hydramnios or severe preeclampsia.), Fetal complications (anomalies, IUGR or IUFD), and previous unexplained IUFD (Fetus is delivered 1 week earlier than date of death of previous fetus).

Management

Method of delivery: (vaginal versus cesarean)

1) Vaginal delivery:

Prerequisites for induction of labor:

a) No indication for CS & everything is ready for CS at any moment if needed.

b) Hospitalization at least 1 week before induction.

c) Good diabetic control.

d) Ensure fetal maturity before induction.

Management

Precautions:

a) During 1st stage:

1- Glycemic control: Daily dose of insulin is replaced by insulin infusion monitored by blood glucose level to keep blood glucose level at 80-110 mg/dl.

2- Avoid EROM. 3- Prophylactic antibiotics: Specially if ROM occurred.

4- Partogram & continuous fetal monitoring.

b) During 2nd stage: Only easy vaginal delivery is allowed (no instrumental delivery) with anticipation & proper management of shoulder dystocia.

c) During 3rd stage: Guard against PPH.

Management

2) Cesarean section: DM isn't indication for CS but it is associated with increased incidence of CS (CS rate reaches 47%).Indications of CS include:

a) Associated hydramnios or preeclampsia. b) Macrosomia (> 4kg) or IUGR.

c) Bad obstetric history. d) Other indications of CS.

D) Neonatal care

1) No milking of cord (to avoid hypervolemia). 2). NICU for at least 24-hours.(for close observation).

3) Proper examination to exclude any congenital anomaly.

4) Early diagnosis & treatment of any neonatal complication (as RDS, hypoglycemia & hypocalcemia).

5) Perinatal mortality: 2-5% (50% of them are due to congenital anomalies).

Management

E) Postnatal care:

1) Give prophylactic antibiotics: Because these cases are more liable to infection.
2) Encourage patient to take highly nutritive light fluids.
3) Adjust insulin dose: Usually reduced by 1/3 (keep on hyperglycemic side).
4) Encourage breast feeding.
5) Contraceptive advice (see next slide)

Management

Post partum Contraceptive advice

1. ***Physiological methods:*** Can be used safely but have high failure rate.
2. ***Barrier methods:*** Can be used safely but have high failure rate.
3. ***Combined hormonal contraceptives:*** Contraindicated (affect glycemic control).
4. ***Progesterone only contraceptives:*** Can be used.
5. ***IUCD:*** Relatively contraindicated (increase infection) but if used → complete antiseptic technique + antibiotic course with insertion + short threads + regular follow up + awareness of alarming symptoms of infection.
6. ***Female sterilization:*** Excellent method for woman completed her family.

شكرا لحسن استماعكم

Thanks