Recurrent Pregnancy loss Relation between Serum ferritin level and number of previous pregnancy losses

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Approximately 8%–12% of couples experience infertiliy .

15-20% of pregnancies are lost.

Recurrent pregnancy loss (RPL) affects 1%–3% of couples trying to conceive according to the European Society of Reproductive Medicine.

RPL is defined as the loss of three or more pregnancies before 22 weeks of gestation not necessary to be consectutive
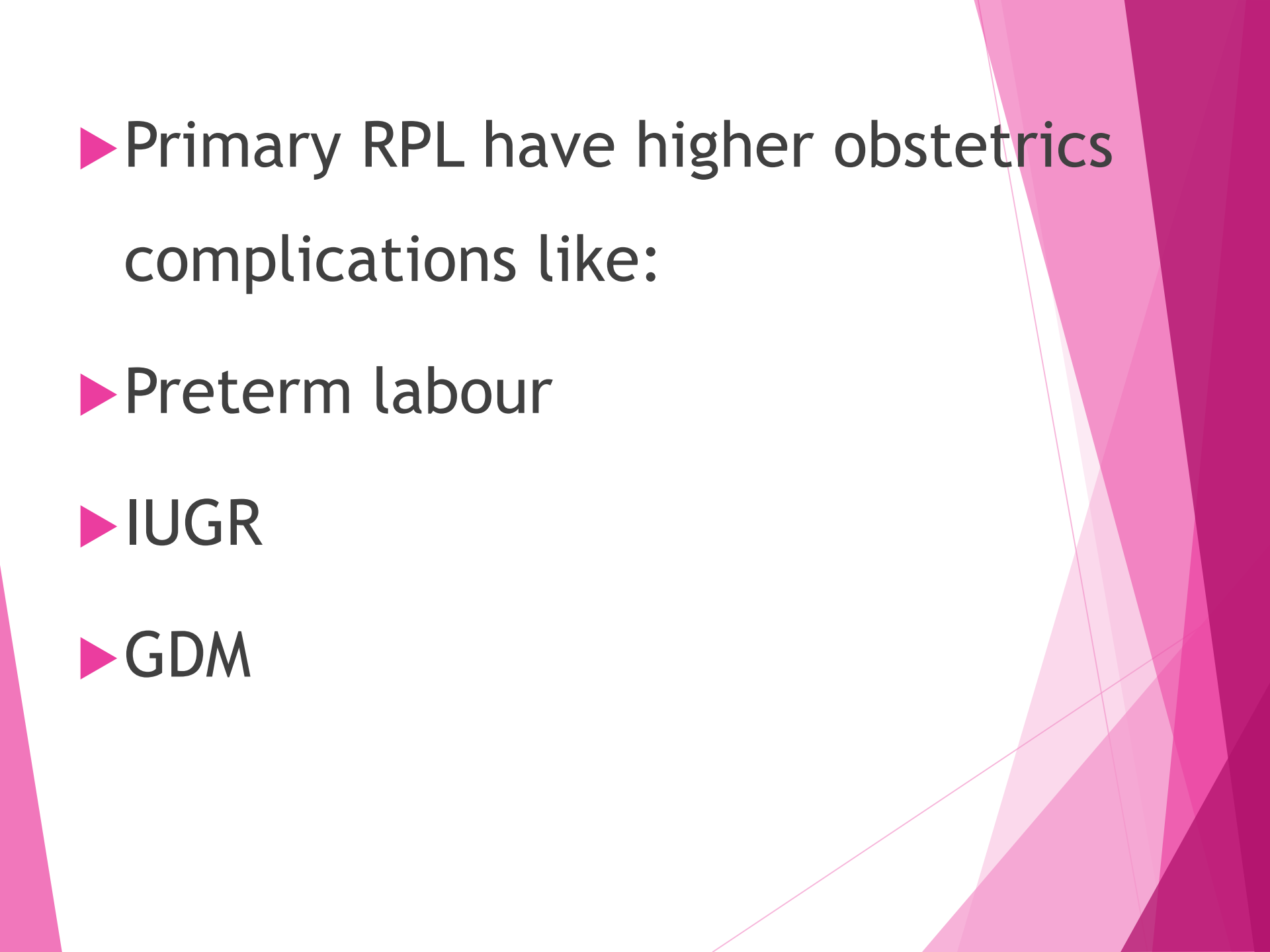
OR

two or more losses late in pregnancy (>12 weeks of gestation).

Evaluation is recommended in couples with

▶ Presence of FHR before abortion

▶ Normal karyotype of conceptus

▶ female age>35

▶ infertility

▶ Family history of RPL

Primary RPL VS.secondary RPL

- Primary is defined as recurrent pregnancy loss with no previous live birth

- Secondary refers to women with pregnancy loss with at least one live birth.

► Primary RPL have higher obstetrics complications like:

► Preterm labour

► IUGR

► GDM

The prognosis is different in different patients

▶ **Late** pregnancy losses have a worse prognosis than early .

▶ **Euploid** abortions are associated with a worse prognosis than **aneuploid** abortions.

▶ There may not be one approach to treatment.

RPL is associated with multiple risk factors :

- antiphospholipid antibody syndrome

- parental chromosomal aberrations

- uterine anatomic abnormalities

  the majority of cases remain unexplained after standard evaluation

Other causes Of Recurrent pregnancy loss:

▶ Thrombophilia

▶ Infections

▶ Endocrine factors : PCO , Thyroid Dx

▶ Systemic diseases :DM

▶ Incompetent cervix

▶ Unexplained

- A significant proportion of cases of recurrent miscarriage remain unexplained

- These women and their partners can be reassured that the prognosis for a successful future pregnancy with supportive care alone is in the region of 75%.

What are the Risk factors for RPL

- Marenal Age
- Number of previous miscarriages

What is the new guideline for miscarriage risk factor?

 -Increasing paternal age is a risk factor for recurrent miscarriage, although not as markedly as with maternal age.

-having previous miscarriages

 - BMI (being underweight or overweight)

-smoking

-excess caffeine intake

what is the chance of a future successful pregnancy?

Two factors are main for prognosis:

1-the number of **preceding pregnancy losses**

2-**maternal age**

3- **Lifestyle** factors such as cigarette smoking

4-**paternal age**

5-previous conceptions **by IVF/ICSI** treatment
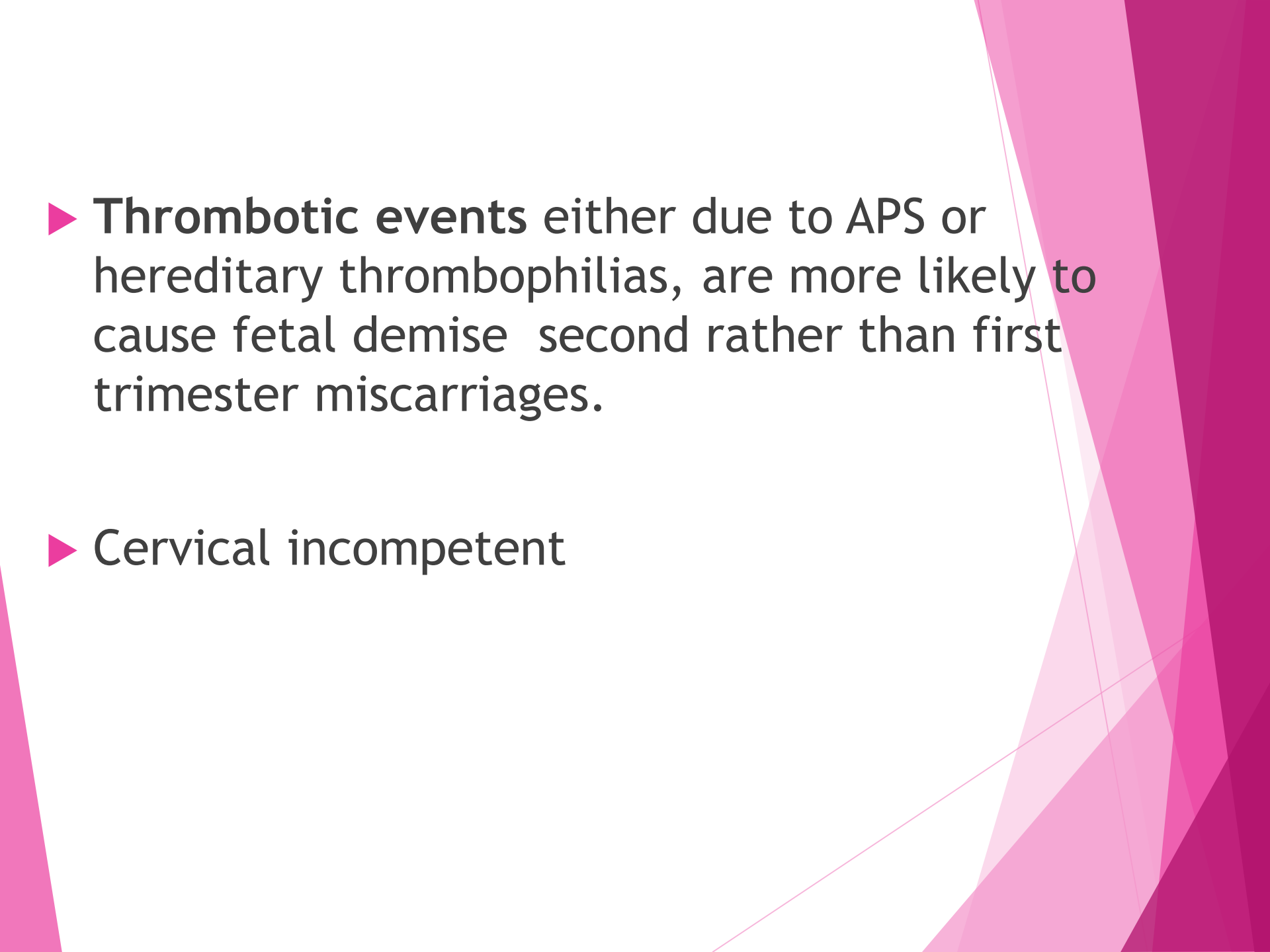
6-maternal and paternal BMI.

- *Maternal age* is strongly associated with a higher risk of fetal aneuploidy

- Advanced *paternal* age has been linked to increased levels of sperm deoxyribonucleic acid (DNA) fragmentation, which is associated with (recurrent) pregnancy loss

- *paternal obesity* may cause excessive oxidative stress and affect pregnancy outcome by damaging DNA integrity of the spermatozoa

Maternal BMI

▶ Couples with unexplained RPL demonstrated a U-shaped relationship between miscarriage rate and maternal prepregnancy BMI.

▶ the highest risk of miscarriage is in women underweight BMI of <20 kg/ m2

and in obese women (BMI > 30)

Specific Forms of Pregnancy Loss

- **Second trimester pregnancy loss**
- The chance of a second trimester loss being due to **chromosomal aberrations** is less than in first trimester miscarriages.
- There may be **fetal structural anomalies**. (ultrasound)and Diabetes should be excluded.

- **Thrombotic events** either due to APS or hereditary thrombophilias, are more likely to cause fetal demise second rather than first trimester miscarriages.

- Cervical incompetent

Losses of Live Embryos and different type of abortions

▶ Each pregnancy loss may have a different clinical presentation. Blighted ova

▶ Abortion of a live fetus in the second trimester

▶ missed abortion.

Blighted Ovum

▶ Genetic

▶ More in PCO ,APS(antiphospholipid syn.)

▶ High TPO ,low ovarian reserve

▶ Antiovarian Ab ?

▶ Sperm abnormality

▶ Infections like TB.

▶ Uterine structural abnormalities.

Unexplained RPL and DOR

DOR (decreased Ovarian Reserve)

Some women with RPL have DOR

It was shown that DOR patients with either RPL or Infertility have increased risk of **aneuploid** fetuses.

BUT

Ovarian Reserve is not a marker for oocyte quality.

- The relationship of DOR and RPL is controversial But it is more confirmed in age over 35 y/o .

Thyroid Problem

- Autoimmunity (high TPO /anti thyroglobulin) is important even if TSH is normal

- Subclinical Hypothyroid TSH >4 mIU/

- if patient is pregnant or planning for pregnancy treatment should be considered.

- **Anti-thyroid antibodies** may directly interfere with trophoblast differentiation and proliferation.

- Multiple studies have confirmed that Thyroid autoimmunity without overt thyroid dysfunction is associated with a **three- to five-fold increase in overall miscarriage rate**

ESHRE Recommendation

▶ Thyroid screening (TSH and TPO antibodies) is recommended in women with RPL.

    (Strong +++)

▶ Abnormal TSH and TPO-antibody levels should be followed up by T4 testing in women with RPL.
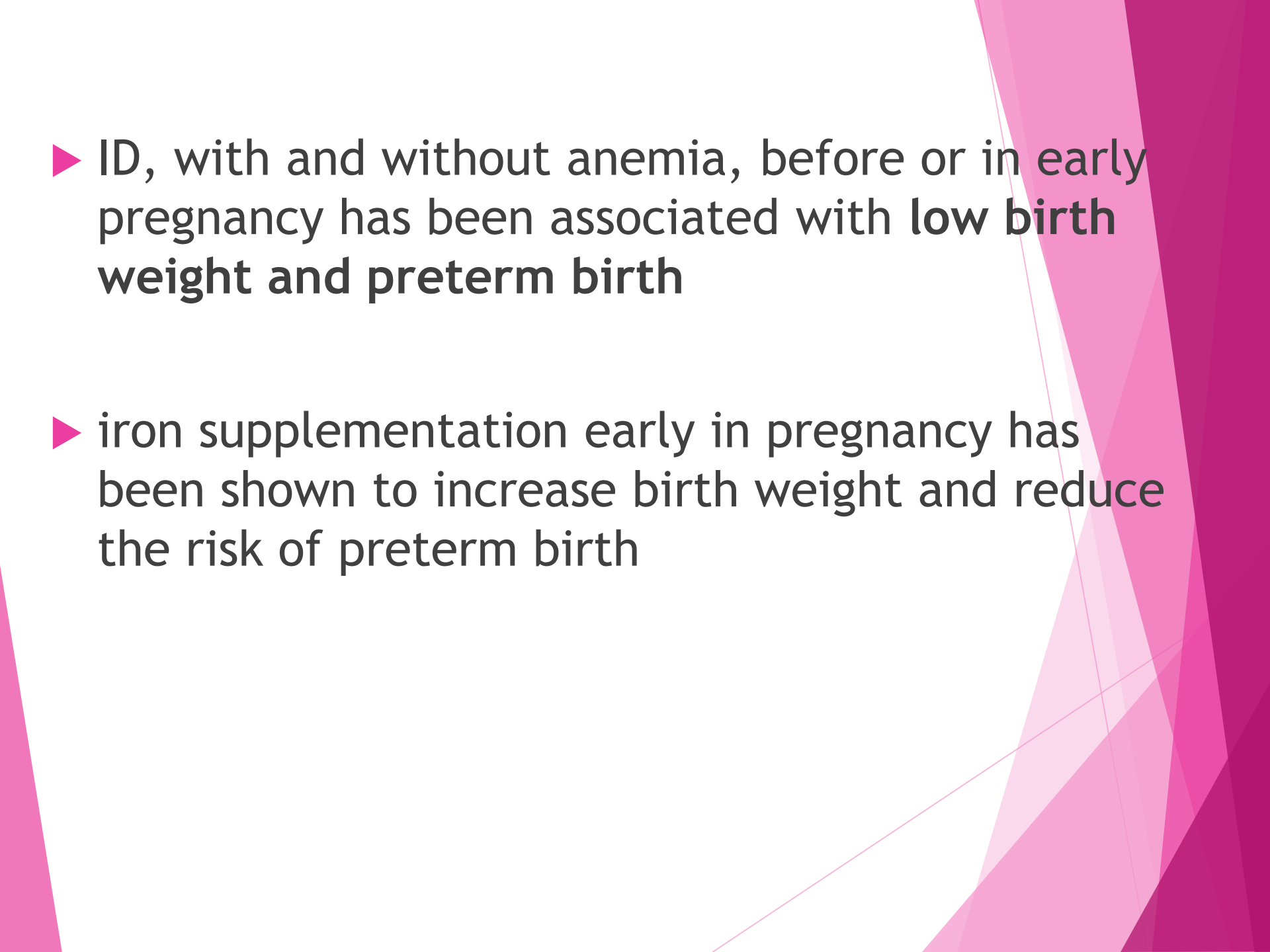
- ▶ Iron deficiency (ID) is the leading single nutrient deficiency in the world.

- ▶ Serum ferritin (s-ferritin) reflects the iron stores in the body and is widely used to detect Iron deficiency.
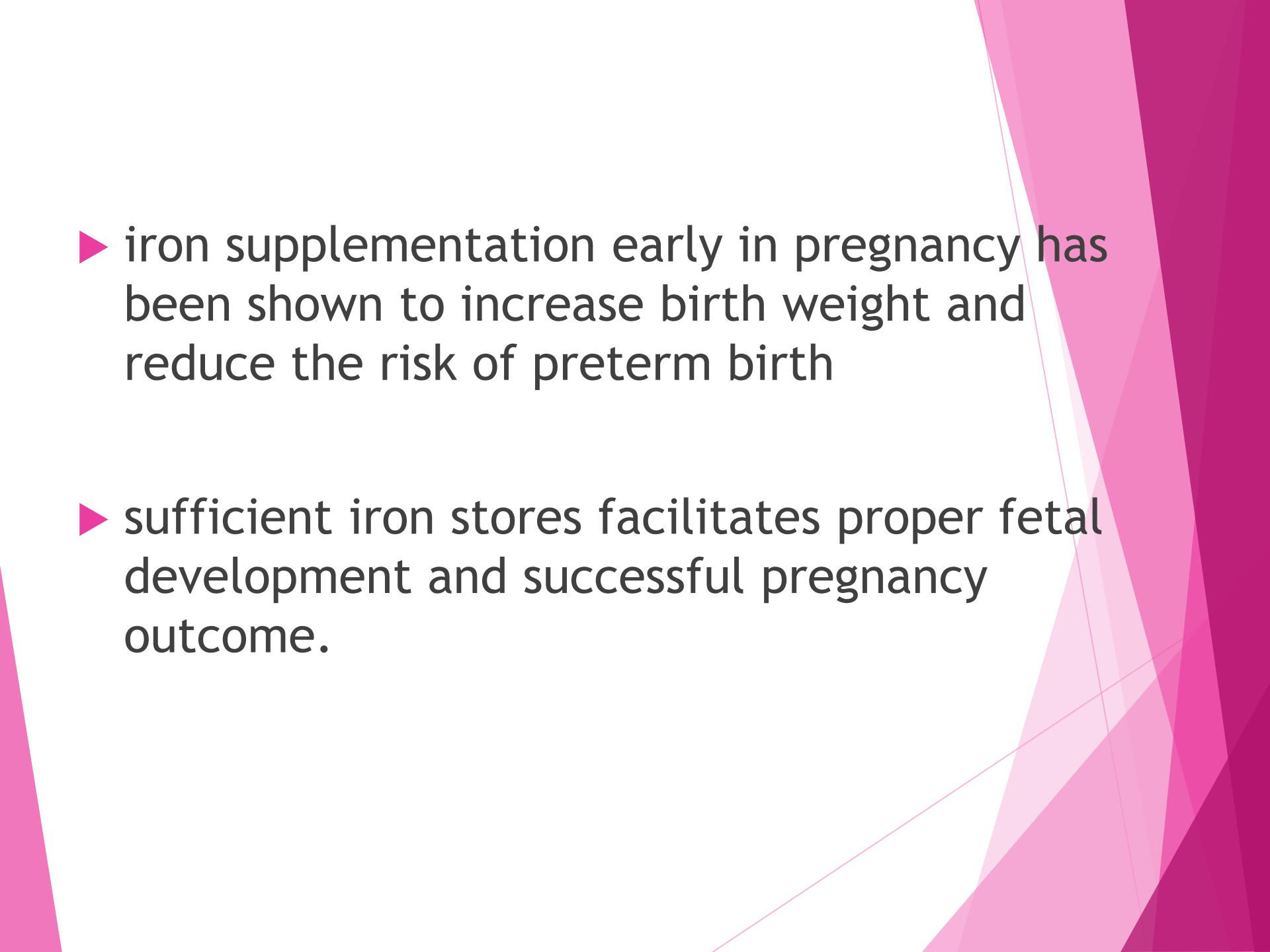
According to WHO

- ▶ If s-ferritin <15 microgram /L ID is diagnosed.

- ▶ But it is suggested to change the cutoff to 30 microgram/L

- prevalence of ID among women of reproductive age ranges from 10% to 33% in European countries .

- The high prevalence of ID suggests that many women may be iron depleted when planning to become pregnant.

- Iron supplementation is recommended by researchers to all pregnant women from gestational week 10.

- Iron is essential for the production of hemoglobin, cellular metabolism, and immune system function

- iron demands are increasing in the developing follicle, thereby affecting maturation of the follicle and ovum.

- Iron requirements are higher during preg- nancy owing to fetal growth and the expansion of the maternal blood volume to meet the increased maternal and fetal oxygen requirements

- ID, with and without anemia, before or in early pregnancy has been associated with **low birth weight and preterm birth**

- iron supplementation early in pregnancy has been shown to increase birth weight and reduce the risk of preterm birth

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- sufficient iron stores facilitates proper fetal development and successful pregnancy outcome.

Study

▶ In this study, it was found that women with RPL had lower s-ferritin compared with women with no known fertility problem, supporting hypothesis.

▶ women with RPL had a greater prevalence of iron deficiency.

▶ s-Ferritin decreased in a dose- dependent manner with increasing number of previous pregnancy losses.