Screening, Management and Prevention of Anemia in Pregnancy

An Evidence Based Approach

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Life Cycle: Nutrition, Health and their Consequences

Impaired immunity

Higher mortality rate

Impaired mental development

Reduced capacity to care for baby

Increased risk of adult chronic disease

Baby
Low Birth Weight

Untimely / inadequate weaning

Elderly Malnou rished

Inadequate fetal nutrition

Frequent infections

Inadequate cat ch up growth

Inadequate food, health & care

Anemia

Infection e.g. malaria

Inadequate food, health & care

Anemia

Child Stunted

Reduced mental capacity

Woman
Malnourished

Pregnancy
Low Weight Gain
Micronutrient deficiencies

Adolescent St unted

Inadequate food, health & care

Higher maternal mortality

Inadequate food, health & care

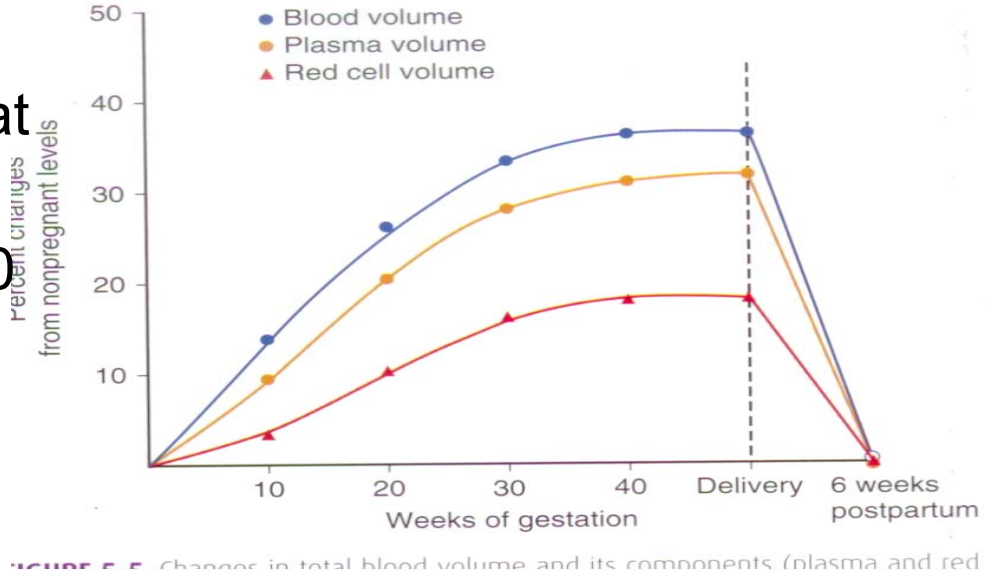
Reduced mental capacity

Objectives

- Understand the physiological blood changes in pregnancy
- Know the maternal and effect of anemia
- Understand the cause of anemia in pregnancy
- Be able to screening, manage and prevent anemia in pregnancy

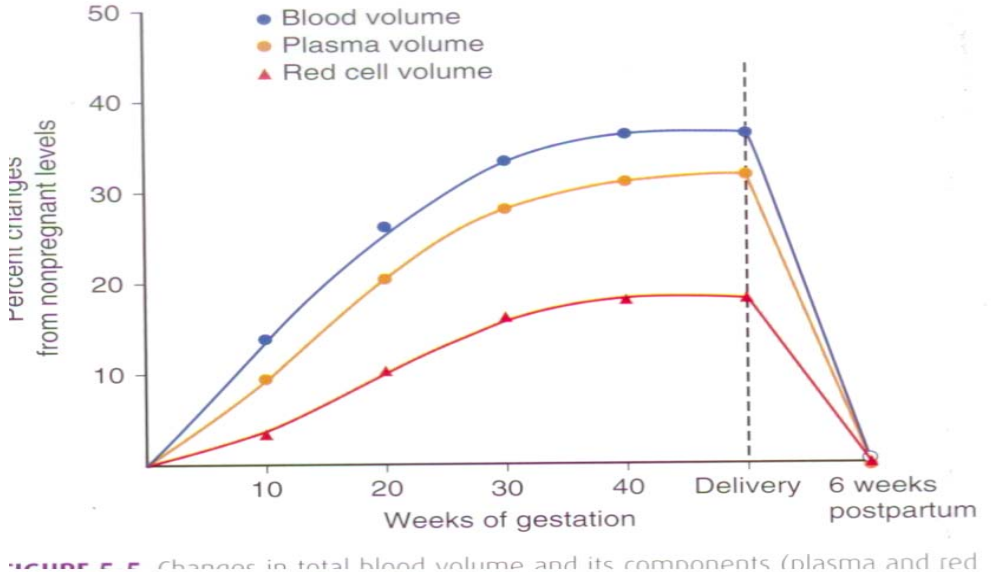
Physiological Changes

- Hypervolemia
  - Start from 6-8 weeks
  - Max volume 4700-5200 mL at 32-34 weeks
  - An increase of 40-45% (1200 -1600 mL)
- Blood volume expansion
  - Plasma ↗
  - Erythrocyte ↗ (450 mL)



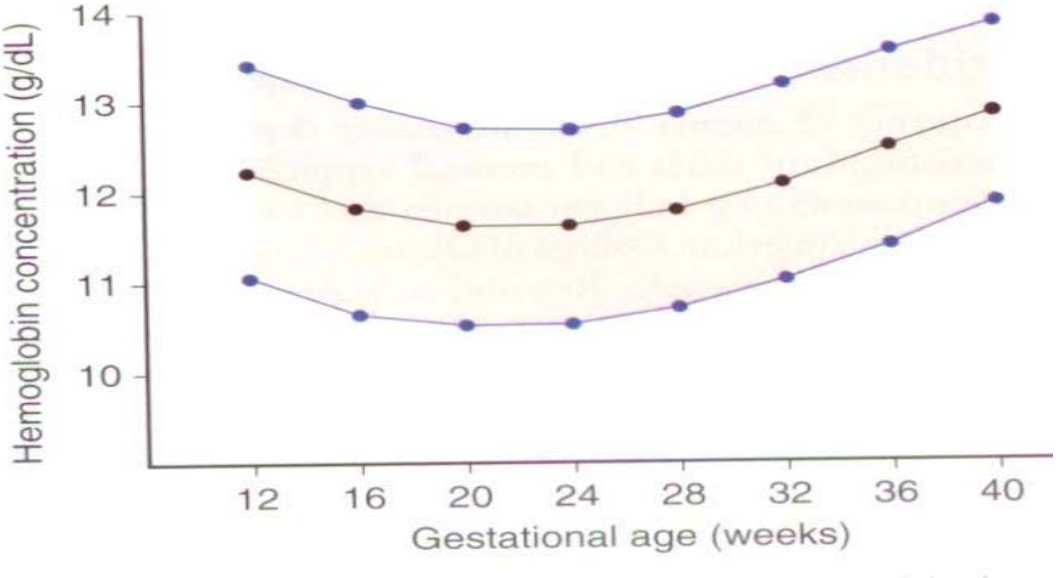
Physiological Changes

- Mechanism unclear
- Nitric oxide mediated vasodilatation →
  - Induces renin angiotensin aldosterone system
  - Stimulates sodium and water retension



Physiological Changes

- Plasma erythropoetin ↗
  - Moderate erythroid hyperplasia
  - Reticulocyte ↗
- Erythropoiesis ↗
  - Placental chorionic somatomammotropin
  - Progesterone
  - Prolactin



Physiological Changes

Pregnancy induced hypervolemia

- To meet the demands on the enlarge **uterus** with greatly hypertrophied vascular system
- To provide an abundance of nutrients and elements to support the rapidly growing **placenta and fetus**
- To protect the mother and in turn the fetus, against the deleterious effect of impaired **venous return** in the supine and erect position
- To safeguard the mother against the adverse effects of blood loss associated with **parturition**

Physiological Changes

- Consequent of hemodilution: ↓ in Hb, Hct, RBC
- MCV (size of RBC) and MCHC (Hb concentrate per RBC) remains stable
  - The MCV ↑ secondary to erythropoiesis
  - These indices decrease progressively in IDA
- Serum iron & ferritin ↓ secondary to ↑ utilization
- Total iron-binding capacity ↑

Iron Metabolism

- Storage Iron
  - Normal adult women 2000-2500 mg
- Iron Requirements: 1000 mg
  - 300 mg: fetus and placenta
  - 200 mg: lost through various normal routes of excretion
  - 500 mg: due to the expanding red cell mass
    - total volume of circulating erythrocytes 450 mL
    - 1 mL of erythrocytes ≈ 1.1 mg of iron
- Iron absorption ↑ moderately

Iron Metabolism

- Maternal iron demand ↑
  - Used mostly during the latter half of pregnancy
  - Iron requirements ↑ after midpregnancy, ± 6-7 mg/day
  - Not available from storage iron

- Without iron supplementation
  - Hemoglobin and hematocrit ↓ → as the blood volume ↑
  - Fetal red cell production in not impaired → because the placenta transfers iron even the mother has severe IDA

Anemia

Definition:

- A pathological condition in which the oxygen-carrying capacity of RBC in insufficient to meet the body's need

Diagnosis is based on the Hb concentration:

- WHO: < 11g/dL at any time during pregnancy
- Clinicians:
  - Trim I and III : < 11 g/dL
  - Trim II : < 10.5 g/dL

Incidence

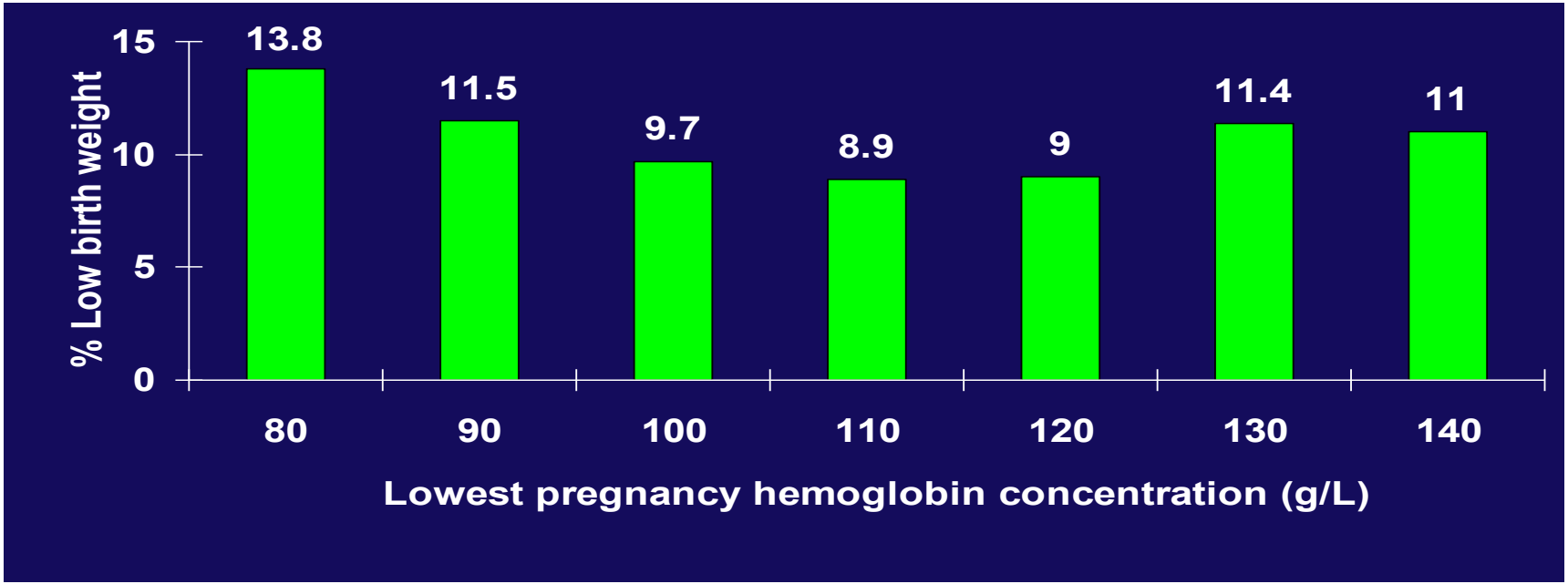
- The commonest medical disorder of pregnancy
- 41.8% world wide (WHO, 2012) → 30-50%
- Mostly due to nutritional anemia
  - 90% iron deficiency
  - 5% folate, vit B12 or vit A deficiencies
  - 5% chronic inflammation, parasitic infections and inherited disorders

Causes of Anemia during Pregnancy

- Acquired
  - Nutritional anemia: Iron deficiency
  - Megaloblastic anemia: Folate and Vit B12 deficiency
  - Anemia caused by acute blood loss
  - Anemia of inflammation or malignancy
  - Acquired hemolytic anemia
  - Aplastic or hypoplastic anemia
- Herediter
  - Thalassemias
  - Sickle-cell hemoglobinopathies
  - Other hemoglobinopathies
  - Hereditary hemolytic anemias

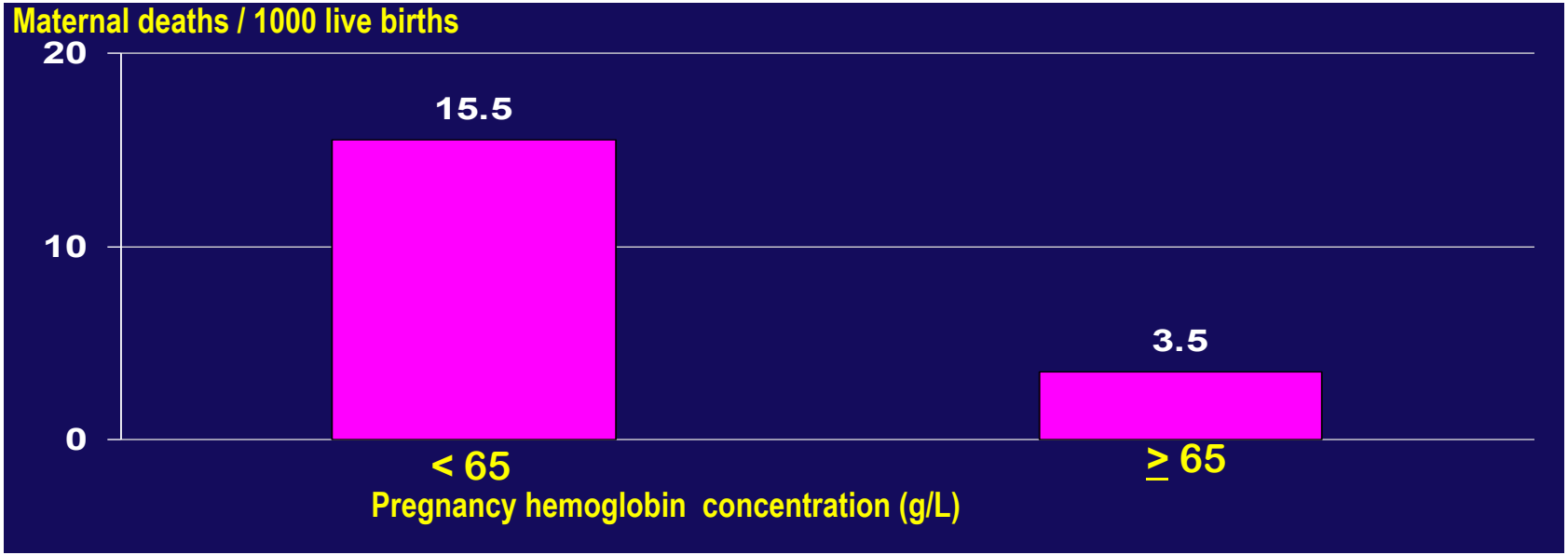
Pregnancy Hemoglobin and Low Birth Weight

Hb >13 g/dL → premature delivery and LBW



Consequences of Maternal Anemia

- Reduced physical capacity
- Maternal mortality



Anemia and Obstetrical Hemorrhage

- Anemia does not cause obstetrical hemorrhage
- Etiology of obstetric hemorrhage
  - Early pregnancy: Abortion complications
  - Mid/late pregnancy to delivery: Previa, abruption, atony, retained placenta, birth canal laceration
- Primary factors affecting outcome:
  - Rapid intervention to prevent exsanguination
  - Availability of skilled provider, drugs, blood and fluids
- There is no evidence that high levels of Hb are beneficial in withstanding a hemorrhagic event.

Enkin et al 2000; Mahomed 2000a.

Iron Deficiency Anemia

Microcytic, hypochromic anemia

- Reduced of MCV (size of RBC)
- Reduced of MCHC (Hb concentrate per RBC)

Iron Deficiency Anemia

Significant iron demands during pregnancy

- Secondary to expanding red cell mass and fetal requirements
- Can only be met by a limited increase in iron absorption and by the utilization of iron stores
- If the iron stores already depleted → anemia will develop rapidly
- The total iron-binding capacity (TIBC) increases secondary to the increased plasma volume and the serum iron falls
- As iron demands exceed during the pregnancy, ferritin levels fall
- Decreased Hb concentration is a late event in iron deficiency anemia

Concequences

The impaired function of iron-dependent enzymes

- Causes alterations in muscle neurotransmitter activity and epithelial changes throughout the body
- The basis explanation for the apparent link between IDA and preterm delivery, infection medical intervention during labour and postpartum hemorrhage

Fetal perspective

- Increased risk of preterm delivery and IUGR
- Increased risk the low neonatal iron status, the impairment of cognitive development and behaviour of babies

Diagnosis

Iron deficiency

- can be present in the absence of anemia
- parameter of the full blood count (reduced MCV and MCHC) are not accurate during pregnancy

The diagnosis test for Iron deficiency

- Ferritin concentration → not affected by pregnancy
- The concentration of <12 ug/L is diagnostic

Treatment

Oral iron replacement

- Effective if there is enough time
  - maximum increase HB: 0.8 g/dL per week
- Recommended dose: 120-240 of elemental iron per day
- Increase the replacement
  - Ferrous salts are absorted better than ferric salts
  - Vit C aids the iron absorption
  - Vit A aids the iron metabolism
- 40% increased of side effect
  - mainly gastrointestinal → effect on compliance

Treatment

Intramuscular Iron

- Iron sorbitol injection has a low molecular → rapid absorption

Intravenous iron

- Iron sucrose → total dose iron replacement in the trim 2 & 3
- More effective & less side effect

Blood transfusion

- Towards the end of pregnancy
- Rapid increase of Hb concentration but not iron stores

Erythropoietin

- Anemia associated with erythropoietin deficiency in CRF
- Increase the autologous production in normal individuals

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Evidence Insufficient to Screen for Iron Deficiency Anemia in Pregnancy

USPSTF Final Recommendation Also Says Evidence Insufficient to Screen Young Children

September 09, 2015 11:22 am News Staff – On Sept. 8, the U.S. Preventive Services Task Force (USPSTF) released its final recommendation statements on screening for the prevention of iron deficiency anemia (IDA) in pregnant women (www.uspreventiveservicestaskforce.org) and children ages 6 to 24 months. (www.uspreventiveservicestaskforce.org)

The USPSTF concluded that there is not enough evidence (www.uspreventiveservicestaskforce.org) to determine the balance of benefits and harms of routine screening for IDA in pregnant women or for the use of iron supplements during pregnancy to prevent adverse maternal health and birth outcomes, with both recommendations receiving I statements. (www.uspreventiveservicestaskforce.org)

Additionally, the task force reviewed evidence (www.uspreventiveservicestaskforce.org) on the benefits and harms of screening for IDA in young children ages 6 to 24 months. It found there is not

Routine Iron Supplementation and Screening for Iron Deficiency Anemia in Pregnant Women: A Systematic Review to Update the U.S. Preventive Services Task Force Recommendation [Internet].

McDonagh M[1], Cantor A[1], Bougatsos C[1], Dana T[1], Blazina I[1].

Rockville (MD): Agency for Healthcare Research and Quality (US); 2015 Mar. Report No.: 13-05187-EF-2.
U.S. Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews.

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Final Recommendation Statement

Iron Deficiency Anemia in Pregnant Women: Screening and Supplementation

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Recommendation Summary

Population	Recommendation	Grade (What's This?)
Pregnant women	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in pregnant women to prevent adverse maternal health and birth outcomes.	I
Pregnant women	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of routine iron supplementation for pregnant women to prevent adverse maternal health and birth outcomes.	I

Go to the Clinical Considerations section for suggestions for practice regarding the I statements.

Clinical Considerations

Patient Population Under Consideration

This recommendation addresses screening and supplementation in pregnant women and adolescents living in the United States who do not have symptoms of iron deficiency anemia. It does not address pregnant women who are malnourished, have symptoms of iron deficiency anemia, or have special hematologic conditions or nutritional needs that may increase their need for iron. Screening for iron deficiency anemia in young children is addressed in a separate recommendation statement (available at www.uspreventiveservicestaskforce.org).

Suggestions for Practice Regarding the I Statement

Potential Preventable Burden

Based on older data, estimates of the prevalence of iron deficiency anemia in pregnant women in the United States range from 2% to 27%, with higher rates in later trimesters and minority populations.[2] Based on calculations of total body iron from 1999 to 2006 National Health and Nutrition Examination Survey (NHANES) data, the estimated prevalence of iron deficiency in pregnant women is 18.6%; of these, 16.2% also have anemia.[1] However, given the physiologic hemodilution that normally occurs during the later stages of pregnancy, determining exact prevalence rates of anemia in pregnant women may be difficult.

Several factors have been identified that may increase a pregnant woman's risk for iron deficiency anemia, including a diet lacking in iron-rich foods (for example, a vegetarian diet with inadequate sources of iron), gastrointestinal disease and/or medications that can decrease iron absorption (for example, antacids), and a short interval between pregnancies. Non-Hispanic black and Mexican American women have higher prevalence rates of iron deficiency than white women and women with parity of 2 or more. Evidence on additional risk factors, such as lower educational level and family income, has been less consistent. On the basis of a literature scan, the USPSTF found limited evidence on the use of risk prediction tools to identify pregnant women who are at increased risk for iron deficiency anemia.

Many observational studies have explored the association between adverse maternal and infant health outcomes (such as postpartum hemorrhage, preterm birth, low birthweight, and perinatal death) and iron deficiency or iron deficiency anemia in pregnancy, but findings have been inconclusive.[2]

Rukuni et al. BMC Pregnancy and Childbirth (2015) 15:269
DOI 10.1186/s12884-015-0679-9

BMC Pregnancy & Childbirth

RESEARCH ARTICLE Open Access

Screening for iron deficiency and iron deficiency anaemia in pregnancy: a structured review and gap analysis against UK national screening criteria

Ruramayi Rukuni[1*], Marian Knight[1†], Michael F Murphy[2†], David Roberts[2†] and Simon J Stanworth[2†]

Abstract

Background: Iron deficiency anaemia is a common problem in pregnancy despite national recommendations and guidelines for treatment. The aim of this study was to appraise the evidence against the UK National Screening Committee (UKNSC) criteria as to whether a national screening programme could reduce the prevalence of iron deficiency anaemia and/or iron deficiency in pregnancy and improve maternal and fetal outcomes.

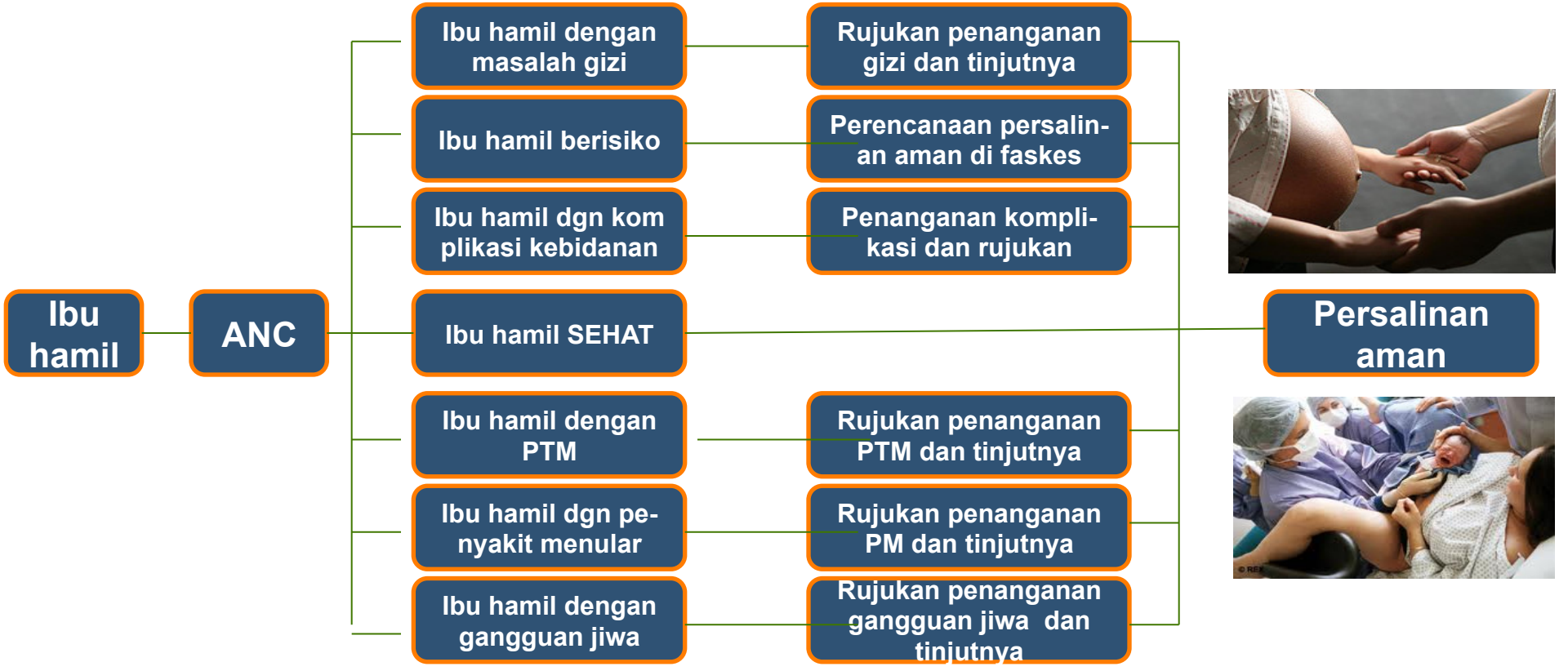
Methods: Search strategies were developed for the Cochrane library, Medline and Embase to identify evidence relevant to UK National Screening Committee (UKNSC) appraisal criteria which cover the natural history of iron deficiency and iron deficiency anaemia, the tests for screening, clinical management and evidence of cost effectiveness.

Results: Many studies evaluated haematological outcomes of anaemia, but few analysed clinical consequences. Haemoglobin and ferritin appeared the most suitable screening tests, although future options may follow recent advances in understanding iron homeostasis. The clinical consequences of iron deficiency without anaemia are unknown. Oral and intravenous iron are effective in improving haemoglobin and iron parameters. There have been no trials or economic evaluations of a national screening programme for iron deficiency anaemia in pregnancy.

Conclusions: Iron deficiency in pregnancy remains an important problem although effective tests and treatment exist. A national screening programme could be of value for early detection and intervention. However, high quality studies are required to confirm whether this would reduce maternal and infant morbidity and be cost effective.

Keywords: Anaemia, iron, iron deficiency, pregnancy, screening

Kerangka Konsep Pelayanan Antenatal Terpadu



Konsep Alur
Pelayanan Antenatal Terpadu di Puskesmas

Pulang

Apotik

RS

Ibu hamil

LOKET

Poli KIA

Poli Umum

Anemia
Malaria
TB
HIV
IMS
Sifilis
KEK
DM
HT
dll

Polindes, POSKESDES, BPS

Laboratorium

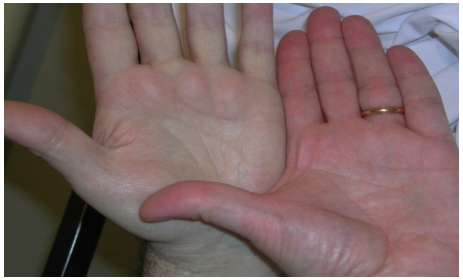
Langkah-langkah ANC Terpadu.....

Pemeriksaan

No	Jenis Pemeriksaan	Trim I	Trim II	Trim III	Ket
1	Keadaan umum	✓	✓	✓	rutin
2	Suhu tubuh	✓	✓	✓	rutin
3	Tekanan darah	✓	✓	✓	rutin
4	Berat badan	✓	✓	✓	rutin
5	LILA	✓			rutin
6	TFU		✓	✓	rutin
7	Presentasi janin		✓	✓	rutin
8	DJJ		✓	✓	rutin

Langkah-langkah ANC Terpadu.....

Pemeriksaan



No	Jenis Pemeriksaan	Trim I	Trim II	Trim III	Ket
10	Hemoglobin	✓		✓	rutin
11	Golongan darah	✓			rutin
12	Protein urin		*	*	atas indikasi
13	Gula darah/reduksi	*	*	*	atas indikasi
14	Darah malaria	*	*	*	atas indikasi
15	BTA sputum	*	*	*	atas indikasi
16	Darah sifilis	*	*	*	atas indikasi
17	Serologi HIV	*	*	*	atas indikasi
18	USG	*	*	*	atas indikasi

Pemeriksaan kecacingan pada faeces belum masuk

Prevention

- Iron supplementation
- Fortification of staple foods with iron
- Health and nutrition education
- Control of parasitic infections
- Improvement in sanitation
- Delayed umbilical cord clamping → preventing IDA among infants and young children

Prevention

- Prevention before pregnancy
  - Balanced diet in the absence of ongoing blood loss
  - Identification and treatment of IDA prior to pregnancy

- Prevention during pregnancy
  - Routine iron supplementation 60 mg/day elemental iron
  - Improvement in hematological indices

Some Facts on Micronutrient Deficiencies

- Common among WRA (15-49 years of age)
- Women in low-middle-income countries often have limited intake
    - animal products,
    - Fruits and vegetables
    - fortified foods
- ↑ Risk among pregnant women → because of the increased requirements.

Micronutrients & Pregnancy Outcomes

Micronutrients	Pregnancy Outcomes
Folic Acid	Neural Tube Defect
Iron	Anemia, Hemorrhage
Iodine	Cretinism
Calcium	Hypertension, Preeclampsia
Zinc	Anemia, NTD, LBW, Anencephaly
Vitamin A	Infant: Vertical transmission of HIV & Survival Maternal: Anemia, Infection, Mortality

Micronutrients & Pregnancy Outcome

Micronutrients	Pregnancy Outcomes
Vitamin D	Neonatal Hypocalcemia
Vitamin K	Hemorrhage
Copper	Anemia, Anencephaly, LBW
Selenium	NTD, Disfunction of brain and cardiovascular system
Magnesium	Increased blood coagulability, Preeclampsia, Preterm birth.

Multiple-Micronutrient Supplementation

Outcome	RR (95% CI)	No of Participants (Studies)	Grade of Evidence
Preterm births	0.96 (0.90-1.03)	90892 (15 RCTs)	High
SGA	0.92 (0.86-0.98)	67036 (14 RCTs)	Moderate
LBW	0.88 (0.85-0.91)	70044 (15 RCTs)	High
Perinatal mortality	1.01 (0.91-1.13)	94780 (12 RCTs)	High
Stillbirths	0.97 (0.87-1.09)	98808 (15 RCTs)	High
Neonatal mortality	1.06 (0.92-1.22)	83103 (11 RCTs)	High

Haider BA & Bhutta ZA, 2017

Folic Acid Supplementation

Outcome	RR (95% CI)	No of Participants (Studies)	Grade of Evidence
Preterm	1.01 (0.73-1.38)	2959 (3 RCTs)	*
Stillbirths	1.33 (0.96-1.85)	3110 (3 RCTs)	*
Birth weight	135.75 (47.85-223.68)	3110 (3 RCTs)	*
Pre-delivery Hb	-0.03 (-0.25-0.19)	1806 (12 RCTs)	*
Pre-delivery anemia	0.62 (0.35-1.10)	4149 (8 RCTs)	*
Megaloblastic anemia	0.21 (0.11-0.38)	3839 (4 RCTs)	*

Lassi et al, 2015)

Daily Iron Supplementation

Outcome	RR (95% CI)	No of Participants (Studies)	Grade of Evidence
Anemia at term	0.30 (0.19-0.46)	2199 (14 RCTs)	Low
Iron Deficiency at term	0.43 (0.27-0.66)	1256 (7 RCTs)	Low
IDA at term	0.33 (0.16-0.69)	1088 (6 RCTs)	Low
Severe Anemia	0.22 (0.01-3.20)	2125 (9 RCTs)	Very Low
Maternal Infection	1.21 (0.83-2.02)	2423 (11 RCTs)	Very Low

- More likely having higher Hb at term and postpartum period
- Increased risk of Hb concentration > 130 g/L during pregnancy

Peña-Rosas et al, 2015

Daily Iron Supplementation

Outcome	RR (95% CI)	No of Participants (Studies)	Grade of Evidence
Preterm	0.93 (0.84-1.03)	19286 (13 RCTs)	Moderate
LBW	0.84 (0.69-1.03)	17613 (11 RCTs)	Low
Birth weight	23.75 (3.02-50.51)	18590 (15 RCTs)	Moderate
Neonatal Death	0.91 (0.71-1.18)	16603 (4 RCTs)	Low
Congenital Anomalies	0.88 (0.58-1.33)	14.636 (4 RCTs)	Low
Megaloblastic anemia	0.21 (0.11-0.38)	3839 (4 RCTs)	*

Peña-Rosas et al, 2015

Intermittent VS Daily Iron Supplementation

Outcome	RR (95% CI)	No of Participants (Studies)	Grade of Evidence
Preterm	1.03 (0.76-1.39)	1177 (5 RCTs)	Low
LBW	0.82 (0.55-1.22)	1898 (8 RCTs)	Low
Birth weight	5.13 (-29.46-39.72)	3110 (3 RCTs)	Low
Neonatal death	0.49 (0.04-5.42)	795 (1 RCT)	Very Low
Anemia at term	1.22 (0.84-1.80)	676 (4 RCTs)	Very Low
IDA at term	0.71 (0.08-6.63)	156 (1 RCTs)	Very Low

Peña-Rosas et al, 2015

Intermittent VS Daily Iron Supplementation

Outcome	RR (95% CI)	No of Participants (Studies)	Grade of Evidence
Side Effects	0.56 (0.37-0.84)	1777 (11 RCTs)	Very Low

- Fewer side effects
- Reduced the risk of high levels of hemoglobin in mid and late pregnancy
- Increased risk of mild anemia near term
- intermittent may be a feasible alternative among those pregnant women who are not anaemic and have adequate antenatal care.

Peña-Rosas et al, 2015

WHO Recommendation

Daily iron and folic acid supplementation in pregnant women

Supplement Composition	Iron: 30-60 mg of elemental iron* Folic acid: 400 ug (0.4 mg)
Frequency	One supplement daily
Duration	Throughout pregnancy. Iron dan folic acid supplementation should begin as early as possible
Target Group	All pregnant adolescents and adult women
Settings	All settings If anaemia in pregnancy ≥40% → 60 mg of elemental iron.

*30 mg of elemental iron ≈ 150 mg of ferrous sulfate heptahydrate, 90 mg of ferrous fumarate or 250 mg of ferrous gluconate.

WHO Recommendation

Intermittent iron & folic acid suppl in non-anaemic pregnant women

Supplement Composition	Iron: 120 mg of elemental iron* Folic acid: 2800 ug (2.8 mg)
Frequency	One supplement once a week
Duration	Throughout pregnancy. Iron dan folic acid supplementation should begin as early as possible
Target Group	Non-anaemic** pregnant adolescents and adult women
Settings	Countries where prevalence of anaemia among pregnant women is lower than 20%

*120 mg of elemental iron ≈ 600 mg of ferrous sulfate heptahydrate, 360 mg of ferrous fumarate or 1000 mg of ferrous gluconate.
**Hb should be measured prior to the start of supplementation to confirm non-anaemic status.

Vitamin A Supplementation

Outcome	RR (95% CI)	No of Participants (Studies)	Grade of Evidence
Maternal mortality	0.88 (0.65-1.20)	154039 (4 RCTs)	High
Perinatal Mortality	1.01 (0.95-1.07)	75176 (1 RCTs)	High
Preterm Birth	0.98 (0.94-1.01)	49007 (5 RCTs)	High
Maternal Anemia	0.64 (0.43-0.94)	15649 (3 RCTs)	Moderate
Maternal Infection	0.45 (0.20-0.99)	17313 (5 RCTs)	Low

- Good evidence that antenatal vitamin A supplementation reduces maternal anaemia for women who live in areas where vitamin A deficiency is common or who are HIV-positive.

McCauley et al, 2015

Vitamin C Supplementation

Outcome	RR (95% CI)	No of Participants (Studies)	Grade of Evidence
Decreases in Hb	1.02 (0.98-1.07)	252 (1 RCTs)	Moderate
Ferritin	1.42 (1.16-1.75)	252 (1 RCTs)	Moderate
Body iron	2.57 (1.71-3.43)	252 (1 RCTs)	Moderate

- No systematic review on Vitamin C supplementation during pregnancy
- Fermented soyabean and vitamin C-rich fruit: a possibility to circumvent the further decrease of iron status among iron-deficient pregnant women in Indonesia.

Wijaya-Erhardt et al, 2011

Killing me softly…

… a full acceptance of the fetal origins hypothesis idea would have radical implications for individual decisions and policy alike, suggesting for example, that the optimum time **to intervene to improve children's life chances is before they are born, and perhaps before mothers even realize that they are pregnant.**

Almond D & Currie J, 2011

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