Keep the Tank Full Anemia in Pregnancy

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Disclosures

- No conflict of interest
- Practicing Maternal-Fetal Subspecialist

Goals and Objectives

- Recognize iron deficiency and distinguish from other causes of anemia
- Discuss the importance of treating iron deficiency in pregnancy
- Know the treatment options of iron deficiency

Anemia in Pregnancy

- Preventable and treatable
- One of the most undertreated disorders in pregnancy
  - Occurs in about 13% of all pregnancies
  - About 30% in low SES populations
  - Defined as Hb < 11g/dl
  - Risk of transfusion doubled
  - Increased length of hospital stay at delivery
  - Increased PP depression

In the fetus/baby

- Increased PTB
- Increased FGR
- Increased NND
- Neonatal anemia
- Developmental delay

Anemia in Pregnancy
Absence of Iron Can Alter Brain Development

- Brain metabolism
- Neurotransmission
- Epigenetics
- Myelination

Lozoff, B Food Nutr Bull 2007;130:1402

Anemia in Pregnancy
Absence of Iron Can Alter Brain Development

- Poor Cognitive function
- Behavioral abnormalities
- Poor Motor, social and emotional development

Lozoff, B Food Nutr Bull 2007;130:1402

Anemia

- Anemia is a sign, not a diagnosis
- Anemia Hgb < 11.9 g/dl or Hct < 35%
- Secondary to :

  Decreased production

  Increased destruction

  Acute or chronic blood loss

Diagnosis of Iron Deficiency

- How severe is the anemia?
- Is this a new problem?
- What is the MCV?
- Is the Reticulocyte response appropriate

  Calculate absolute retic count (ARC): RBC count/L x % retic=ARC

  ARC 100K/mcL indicates lots of activity
- Do the RBCs or other cells have morphologic changes

Causes of Anemia

- **Decreased RBC Production**
  - Iron deficiency
  - B12 deficiency
  - Folic acid deficiency
  - Bone marrow disorders/suppression
  - Low EPO (renal disorders)
  - hypothyroidism

Increased RBC destruction

Inherited hemolytic anemias

- Sickle cell
- Thalassemia major
- Hereditary spherocytosis

Acquired hemolytic anemias

- Autoimmune hemolytic anemia
- TTP
- HUS
- Malaria

Hemorrhagic anemia

Differential Diagnosis of Anemia Major Causes

	Microcytic (MCV <80)	**Normocytic MCV (80-100)**	**Macrocytic MCV (>100)**
Production Problem (Normal to low retic count)	Iron Def Anemia of Chronic Disease	Early Fe Def B12 and Folate Def Chronic disease Bone Marrow Supp Endocrine dysfunction Chronic Renal Dz Hypothyroidism	Folate Def B12 Def Ethanol abuse Liver Disease Myelodysplastic Synd
Destruction Problem (Elevated retic Count)	Thalassemia Sideroblastic anemia	Hemorrhagic Anemia Drug induced Hereditary Spherocytosis Autoimmune Hemolytic **Paroxysmal Nocturnal Hemoglobinuria**	Drug induced (AZT) Reticulocytosis

Iron Deficiency v Thalassemia

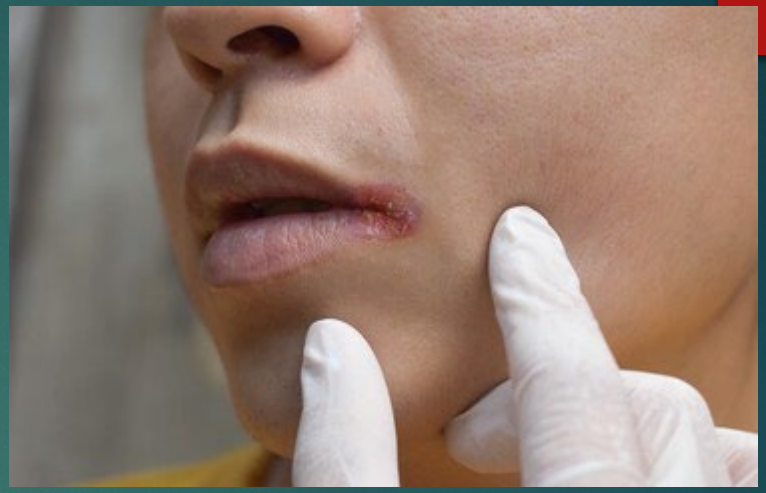
Iron Deficiency	Alpha Thalassemia	Beta Thalassemia
Low RBC count	Increased RBC count	Increased RBC count
Low Ferritin	Fe normal or slightly increased	Fe normal or slightly increased
Retic count low	Retic count increased	Retic count increased
Hgb A2 2-3%	Hgb A2 <3.5%	Hgb A2 (>3.5%) Hgb F (5-95%)

Symptoms of Iron Deficiency

- Fatigue
- Generalized weakness
- Decreased exercise tolerance
- Exertional dyspnea
- PICA (ice, paper, raw rice, dirt)
- Restless leg syndrome
- Headache
- Weakness

Suspect Iron Deficiency

- Angular cheilitis (cracking at mouth corners)
- Koilonychia (spoon shaped fingernail)
- Depapilation of the tongue
- Dry rough skin
- Pallor, tachycardia, flow murmur



Iron Deficiency Anemia

- Anemia is associated with an increased risk of SGA, PTB, Stillbirth and perinatal asphyxia
- Small RCT in low- and medium-income countries have shown a reduction in SGA and PTB with iron & folic acid supplementation
- 30-50% of SMM and MM are preventable

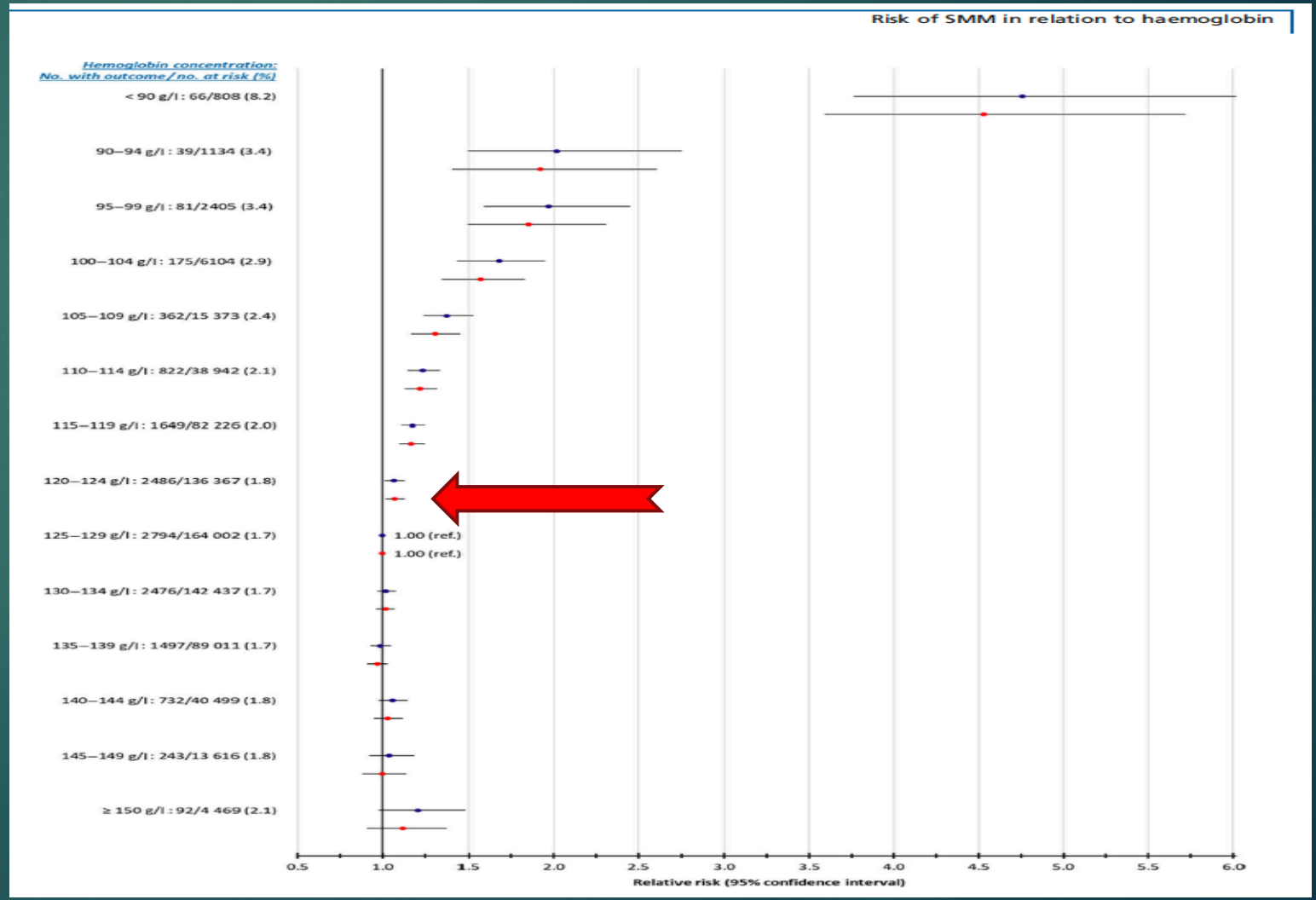
Iron Deficiency Anemia Ontario Canada

- 737,393 births with Hgb available at 2-16 weeks
- 13,514 (1.8%) cases of Severe Maternal Morbidity/Mortality 23 weeks to 42 days postpartum
- Mean Hgb 12.7 (.9 g/dL)
- 0.8% required a transfusion

Ray JG BJOG 2020;127:1154

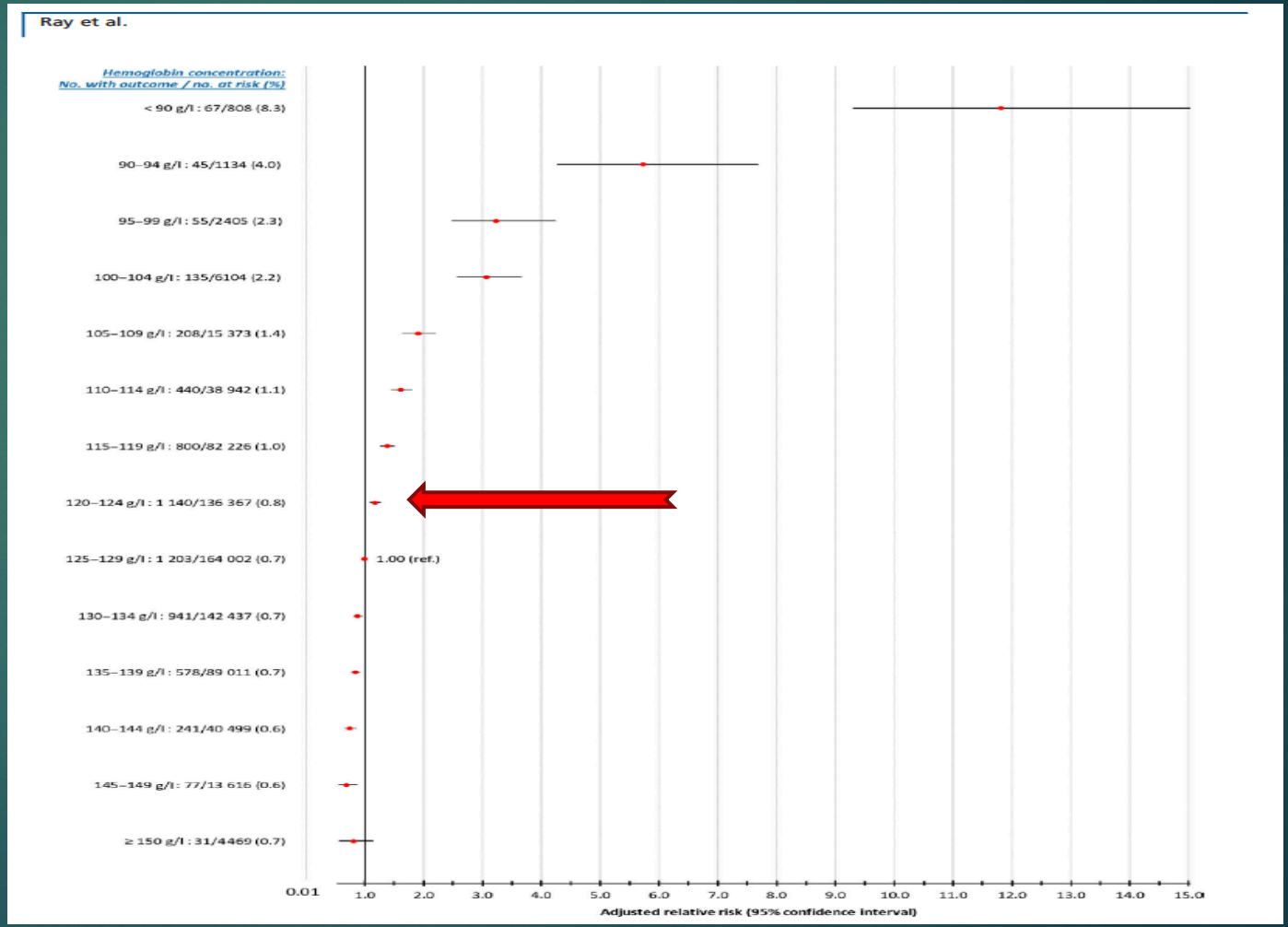
Anemia and Severe Maternal Morbidity

- Hgb at 2-16 weeks and risk of Severe Maternal Morbidity



Anemia and Risk of Transfusion

- Hgb Level at 2-16 weeks and risk of Transfusion



Iron Deficiency Anemia
Risk of SMM or MM

Hgb Concentration	SMM/MM	Transfusion
12.5-12.9 g/dl	1.7%	0.7%
12.0-12.4 g/dl	1.8% RR 1.07	0.8%
10.5-10.9 g/dl	2.4% RR 1.4	1.4% RR 1.9
<9.0 g/dl	8.2% RR 4.53	8.3% RR 11.8

Ray JG BJOG 2020;127:1154

Iron Deficiency Anemia

Hgb and Serum ferritin	% with SMM or MM	Adjusted relative risk
Hgb > 11.0 and ferritin > 15 mcg/l	1.7	1.00
Hgb > 11.0 and ferritin < 15 mcg/l	1.9	1.23
Hgb < 11.0 and ferritin > 15 mcg/l	2.6	1.37
Hgb <11.0 and ferritin < 15 mcg/l	2.8	1.72

Ray JG BJOG 2020;127:1154

Disparities in SMM and Anemia

- 3,863,594 births in California 2011 to 2020
- Anemia defined as Hgb < 11.0 g/dL
- Blacks had the highest incidence of antepartum anemia (21.5%)
- Whites had the lowest (9.6%)

Igbinosa, II Obstet Gynecol 2023;142:845

Disparities in Anemia
Association between Anemia and SMM

Race & Ethnicity	Adjusted RR (95% CI)	Adj Population Attributable Risk %
Native American	3.27 (2.46-4.34)	16.7 (5.2-29.0)
Asian	2.57 (2.43-2.71)	11.3 (8.9-13.3)
Black	2.81 (2.64-3.00)	20.9 (18.1-23.4)
Hispanic	3.63 (3.54-3.73)	20.9 (19.9-22.1)
Multiple races	2.94 (2.59-3.32)	21.4 (17.5-25.0)
Pacific Islander	3.37 (2.67-4.24)	16.4 (7.3-26.4)
White	2.96 (2.83-3.09)	14.7 (13.3-16.0)

Obstet Gynecol 2023;142:845

Anemia
Response to Iron Therapy

- N = 20,690 in population-based cohort (2011-2019) in 2 hospitals
- 35.8% anemic (Hgb < 11.0 g/dL)
- 17.8% refractory to therapy, 36.3% successful response and 45.9% untreated
- Successfully treated group had a lower PTB rate (5.1% v 8.3%), preeclampsia rate (5.9 v 8.3%)

Detlefs SE. AJOG MFM 2022;4

100569. doi:10.1016/j.ajogmf.2022.100569.

Treatment of Anemia

Outcome	Refractory to Treatment	Successful Treatment	Untreated	Nonanemic	P-value
Preterm Birth	11.0%	5.1%	12.3%	8.3%	<.0001
Preeclampsia	11.5%	5.9%	12.4%	8.3%	<.0001
Blood transfusion	5.5%	1.5%	3.5%	1.0%	<.0001

Detlefs SE. AJOG MFM 2022

Iron Deficiency Anemia Recommendations

- If Hgb <12.0 g/dl in first trimester check serum ferritin level, iron saturation (TIBC) , B 12 and Folic acid
- If Ferritin < 30 ng/mL, (90% sensitive) or Transferrin Sat < 20 %, start iron therapy (Ferrous Fumarate 325 mg or Ferrous sulfate 325 mg po QOD)
- In 2-4 weeks Hgb should be half way back to normal or at least increased 1-2 g/dl
- Nonadherence to oral iron is high
- Absorption of Fe is decreased in the third trimester
- Serum hepcicin increased with iron ingestion which decreases absorption and utilization,

Refractory to Oral Iron Therapy

- Celiac disease (5%)
- Autoimmune gastritis
- Helicobacter pyloris
- Bariatric surgery
- Genetic: Iron refractory iron deficiency anemia, (IRIDA)

Intravenous Iron

- LMW iron dextran (INFeD) 100 mg
- Ferric gluconate (Ferrlecit) 125 mg multiple doses 125-250 mg
- Iron Sucrose (Venofer) 200-300 mg
- Ferumoxyton (Feraheme) 510 mg
- Iron isolamtoside (Monoferric) 20 mg/kg
- Ferric carboxymaltose (Ferinject) 20 mg/kg
- Iron dextran, ferric carboxymaltose, ferumoxytol, and isomaltoside can be given in 1000 mg dose in 15-60 minutes
- Iron sucrose and ferric gluconate require 4-5 doses of 200-250 mg

Intravenous Iron Treatment

- Ferric carboxymaltose (Injectafer): Single dose 1000mg
- Ferric derisomaltose (Monoferric) Single dose 1000mg
- Ferric gluconate (Ferrlecit) Multiple doses 125-250 mg
- Ferumoxytol (Feraheme) Single dose 1020mg or 2 doses 510mg
- Iron Dextran, LMW (Infed) Single dose 1000mg after test dose
- Iron Sucrose (Venofer) Multiple doses 100-300mg

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IV Iron

- > 24 weeks
- Severe anemia < 8 gm/dL
- Side effects from po iron
- Poor compliance
- Inflammatory bowel disease
- History of gastric bypass
- Consider strongly prior to discharge postpartum Hgb < 9.0

Why Aggressively Screen and Treat Anemia

- Reduce transfusion of PRBC
- Reduce severe maternal morbidity
- Reduce hospital stay
- Increase breastfeeding
- Decrease PP depression
- Possibly decrease FGR and PTD


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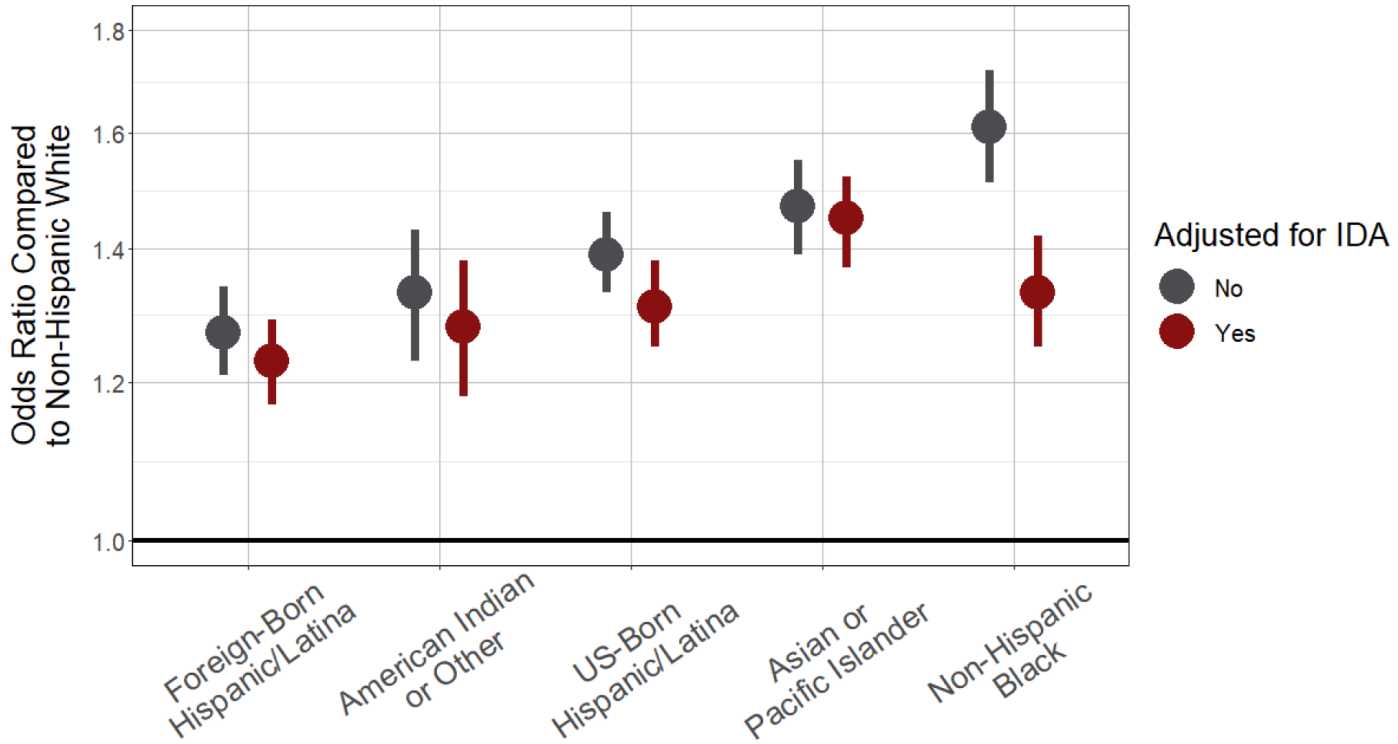
IV Iron

- Hgb iron deficit (mg)- BW x (14-Hgb) x 2.145 + iron to replenish stores
- 2.14 is a constant: 65 (ml/kg blood volume) x 3.3 mg Fe/g Hgb ÷ 100ml/dl
- Generally, around 1500-2000 mg

Risk of Transfusion During Delivery by Race and Iron Deficiency Anemia (IDA)



Igbinosa I, Leonard SA, Butwick AJ, etal. Antepartum anemia and racial/ethnic disparities in blood transfusion in California. Am J Obstet Gynecol 2020;222:S304.

Refractory to Oral Iron Therapy

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Disparities in SMM and Anemia

Race and Ethnicity	Patient with Anemia (%)	Patients w/o Anemia (%)	Crude RR	Adjusted RR
Native American	6.3	1.7	1.85 (1.64-2.08)	1.53 (1.35-1.73)
Asian	3.8	1.3	1.29 (1.25-1.33)	1.33 (1.30-1.37)
Black	5.1	1.6	1.91 (1.85-1.98)	1.27 (1.22-1.32)
Hispanic	4.6	1.2	1.31 (1.28-1.33)	1.17 (1.14-1.20)

Obstet Gynecol 2023;142:845

Anemia in Pregnancy

- Iron deficiency is the number one cause of anemia
- 30% of all women of reproductive age have iron deficiency anemia (IDA)
- Increased blood volume (500 mg of Fe) Fetus and placenta (350 mg of Fe)
- 38% of pregnant women have iron deficiency anemia
- Low maternal ferritin leads to IDA in the neonate

Tran PV Pediatr Res 2009;65:493
Shao J J Nutr 2012;142:2004