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Iron Deficiency in Infants—What Nurse Practitioners Need to Know

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A B S T R A C T

Iron deficiency anemia (IDA) in infancy is associated with negative, potentially irreversible impacts on cognitive and socioemotional development that persist into adulthood and may result in reduced potential and decreased quality of life. Infants are at particularly high risk of IDA due to rapid growth rates and high iron requirements during this stage of life. There are currently no universal screening programs for IDA. Existing screening guidelines in Canada and the United States provide multiple, conflicting recommendations. Primary care nurse practitioners are uniquely situated to improve accessibility to quality health care and screen, diagnose, and treat IDA at routine well-baby visits.

Iron deficiency is the most common nutritional deficiency and cause of anemia worldwide, affecting up to 43% of all children younger than 5 years old.[1] In the United States (US), infants 12 to 17 months old from low-income families were reported to have a high prevalence of anemia at 18.2%.[2] In Canada, the prevalence of anemia in 6- to 59-month-old children has been steadily increasing since the early 2000s, reaching rates of 13.2% in 2019.[3] The prevalence among Indigenous infants is even higher, with rates of iron deficiency anemia (IDA) ranging from 14% to 50%.[4] The World Health Organization (WHO) classifies IDA as a public health problem when prevalence rates exceed 5%.[1]

IDA is associated with negative, potentially irreversible impacts on cognitive and socioemotional development that can persist from infancy into adulthood and may result in reduced potential and decreased quality of life.[5] Primary care nurse practitioners (NPs) are ideally situated to screen and treat high-risk infants during routine visits and provide families with health and nutrition education to prevent negative outcomes of IDA. The purpose of this article is to address the risk factors, diagnosis, and treatment of IDA, with a focus on the role of the NP.

Clinical Presentation and Diagnosis

Iron deficiency is the state of having insufficient iron to maintain the normal physiological functions of tissues, such as the blood, brain, and muscles.[6] Infants born at term generally have enough iron stores to last 4 to 6 months, at which point they need to receive iron-rich foods.[6,7] The WHO recommends using a serum ferritin value of <12 μg/L to define iron deficiency in infants and children 0 to 59 months old.[1] Anemia is usually defined as a hemoglobin level that is 2 SDs below normal for age and sex. In infants, a hemoglobin of <110 g/L (<11 g/dL) indicates that the iron deficiency is affecting erythropoiesis. Patients can be diagnosed with IDA when they have both low hemoglobin and low serum ferritin, with or without a clinical history of symptoms.

Most infants with IDA will have no clinical symptoms or only nonspecific complaints.[1,2] Therefore, a combination of clinical history, laboratory markers, and response to treatment are required for diagnosis. Potential signs and symptoms include poor feeding, lethargy, irritability, failure to thrive, frequent infections (indicating a compromised immune response), and lowered motor and cognitive function compared with healthy infants.[7] Moderate to severe anemia may present with pallor of the palms, conjunctiva, tongue, and nail beds and may lead to congestive heart failure (tachypnea, cardiomegaly) and death.[8]

In a 25-year longitudinal study in Costa Rica, Lozoff et al[9] correlated that screening for and treating iron deficiency in infancy led to better educational, employment, and socioemotional outcomes compared with the group with chronic iron deficiency. As a result, it is critical that primary care NPs identify and screen for IDA during routine well-baby visits, particularly among high-risk infants.

Risk Factors and Causes

Many complex and interconnected factors (Table 1) contribute to the prevalence of IDA in infants. Because most of the fetal iron stores accumulate in the third trimester of pregnancy,[2,6] factors that affect this trimester have the greatest impact on initial iron stores. These factors include preterm birth, low birth weight or small for gestational age, maternal anemia, and frequent pregnancies, especially if they progressed to full-term births.[7] The timing of umbilical cord clamping at birth affects infant iron stores and can be improved by delayed cord clamping.[2]

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Table 1
Risk Factors for Iron Deficiency in Infants

Risk factor
Preterm birth/low birth weight/small for gestational age
Maternal anemia, frequent births
Prolonged exclusive breastfeeding (≥6 months)
Early supplemental cow's milk (before 12 months)
Low intake of iron-rich foods
Food insecurity
Low maternal education level
Low household income
Altered iron absorption (eg, *Helicobacter pylori)*
Increased iron loss (eg, bleeding)
Chronic inflammation or infection
Lead exposure

By age 6 months, the infant's original iron stores are depleted, and breast milk alone is no longer adequate to meet the nutritional requirements for this period of rapid growth.[7] After age 6 months, infants require dietary intake of iron and may experience iron deficiency with prolonged exclusive breastfeeding, early ingestion of plain cow's milk without added formula, and low intake of iron-rich foods. The recommended daily intake of iron from all sources is 11 mg for infants aged 7 to 12 months and 7 mg for children aged 1 to 3 years.[7,10] Although cow's milk and evaporated milk will satiate an infant, these foods are deficient in absorbable iron and increase the infant's risk of developing IDA, particularly when used as a main source of nutrients.[8] Current recommendations stipulate that infants should be exclusively breastfed for the first 6 months of life and be introduced to complementary iron-rich foods (eg, meat, meat alternatives, or fortified infant cereals) between 4 and 6 months old, depending on infant readiness cues.[7]

It is critical that NPs provide education and raise awareness of IDA while also supporting families that are unable to follow current recommendations. For example, food insecurity can be a significant issue in remote and rural geographic areas, where food supplies may be limited due to availability and affordability. Infants, toddlers, and adult women living in mild to moderately food insecure households are at significantly higher risk of anemia.[11] The risk of developing anemia is also higher for mothers with low educational levels and children in the lowest quintile of household wealth compared with those in the highest quintile.[12] In the Canadian Indigenous population, reduced access to traditional iron-rich foods and increased consumption of low-iron convenience foods contributes to reduced intake and bioavailability of iron in children.[7]

Less common causes of IDA in infancy include altered absorption, as with *Helicobacter pylori* infection or chronic inflammation, lead exposure, and loss of iron through bleeding. Indigenous populations tend to have a high prevalence of *Helicobacter pylori* infection (up to 30% in some communities), which may be related to contaminated water sources and inadequate sanitation.[13]

Screening

NP practice is guided by current, evidence-based recommendations of respected professional health organizations. Unfortunately, there are no cohesive routine screening recommendations for IDA in infants in Canada or the US. As a result, the decision to screen is often left to the discretion of health care providers. Most health care authorities across the US and Canada have indicated that further research is required to develop IDA screening guidelines. Some authorities have recommended selective screening for high-risk infants between 6 and 12 months (Table 2).[4,6,7,14-19] In the presence of conflicting recommendations, it is important that NPs examine the quality of evidence and consider the patient's situation as part of a shared decision-making approach.

Hemoglobin is commonly used to screen for anemia but does not provide information about a patient's iron status and needs to be measured alongside serum ferritin. Screening of ferritin levels can detect iron deficiency before the condition progresses to IDA. Because ferritin is an acute-phase reactant, it can be elevated during infections and chronic inflammatory states, such as obesity and liver disease.[1,20] Therefore, some guidelines recommend using C-reactive protein levels to rule out the presence of inflammation.[1,6] High ferritin may also indicate hemochromatosis, a disorder of increased iron absorption and deposition into joints and tissues.

Mean cell volume (MCV) can also be assessed, because the most common cause of low MCV (microcytic red blood cells) is iron deficiency. However, a normal MCV may be present in early iron deficiency or in a mixed anemia.[20] A microcytic anemia could also be representative of a hemolytic anemia that would not respond to or worsen with iron supplementation. Therefore, it is important to identify the specific cause of the anemia before initiating treatment.

Early screening and treatment of IDA can effectively reduce the health care costs and long-term health effects of IDA. In general, universal screening is more cost-effective than selective screening. However, due to the poor functional outcomes associated with IDA, research has shown it is more cost-effective to use selective screening among high-risk infants rather than no screening at all.[5] Screening programs can be improved through use of technology-based reminders and coordinated electronic medical record systems. Integrated screening tools and interactive charting forms can aid in identifying high-risk populations and ensuring screening and follow-up are completed.[6]

Treatment

Iron deficiency should be treated with a multifaceted approach before the condition progresses to IDA (Table 3). NPs need to provide support to mothers/infants in the prenatal and postnatal periods with the goal of maintaining iron levels through dietary sources and pharmaceutical supplementation as needed. It is important that NPs also discuss contraception and family planning at routine appointments, because frequent pregnancies/births can deplete maternal iron.

Exclusive breastfeeding is recommended by the Canadian Paediatric Society, WHO, and the American Academy of Pediatrics until complementary iron-rich foods can be introduced at age 4 to 6 months.[6] Infants who are not breastfed should receive iron-containing formulas, with higher iron formulas for high-risk groups. Cow's milk, evaporated milk, and other types of milk should be avoided until after age 12 months because they do not supply absorbable nutrients and may lower the intake of other nutrient-dense foods.[7]

The introduction of iron-rich foods at age 4 to 6 months is paramount to supplying the required iron during this period of growth. NPs need to be aware of iron-rich foods that can be recommended to parents and should have educational handouts or resources available; traditional iron-rich foods should be encouraged in Indigenous communities as much as possible.[7] In addition, NPs should advise parents to pair vitamin C-containing foods with iron-rich foods to increase iron absorption.[6,7]

Oral iron supplementation should be discussed with parents of infants diagnosed with iron deficiency and IDA as part of a shared decision-making approach, especially when they have already implemented an iron-rich diet. Although supplementation is generally not recommended for prevention, the Canadian Paediatric Society and American Academy of Pediatrics have recommended iron supplementation by age 2 weeks for preterm and low

Table 2
Iron Deficiency Screening Recommendations (United States and Canada)

Guideline/Group	Screening Recommendation	Recommended Laboratory Screening Tests
American Academy of Family Physicians (AAFP)[14]	The AAFP supports the US Preventive Services Task Force (USPSTF) Screening for Iron Deficiency Anemia in Young Children: Recommendation Statement.	Insufficient evidence to recommend screening
American Academy of Pediatrics (2015)[6]	Universal anemia screening recommended at 12 months, including assessment of risk factors. Selective screening at any age when risk factors present.	Hgb
Canadian Pediatric Society (2019)[7]	There is insufficient evidence to recommend routine iron supplementation or laboratory screening for iron deficiency in healthy term infants with no risk factors who are exclusively breastfed for 6 months. Assessment of risk factors at each well-child visit, with attention to high-risk individuals, and screen appropriately with CBC, serum ferritin.	CBC count, serum ferritin for high-risk individuals
Canadian Task Force on Preventive Health Care (previously the Canadian Task Force on Periodic Health Examination; 1994)[15]	There is insufficient evidence to recommend the inclusion of routine early detection of anemia by hemoglobin measurement between ages 6 and 12 months. For infants of all high-risk groups, physicians are recommended to take particular care to determine the nutritional intake and consider a Hgb measurement between ages 6 and 12 months, perhaps optimally at 9 months old. An Hgb measurement in any infant between ages 6 and 12 months where there is suspicion of poor iron and overall nutritional intake is prudent even if the child is not from a high-risk group.	Hgb between 6 and 12 months for high-risk groups or suspicion of poor iron or nutritional intake
Centers for Disease Control (1998)[16]	Screening recommended for iron deficiency anemia at ages 9 to 12 months, 6 months later, and then annually from ages 2 to 5 years in infants and preschool-aged children who are at high risk for iron deficiency anemia.	Hgb
First Nations and Inuit Health Branch, Health Canada (2011)[4]	Screening for anemia recommended for Indigenous infants between age 6 and 12 months, preferably 9 months.	CBC
Rourke Baby Record (2020) [17]	Consider anemia screening for high-risk groups between age 6 and 18 months: Low socioeconomic status, Indigenous communities, newly arrived refugee, internationally adopted and immigrant children from resource-poor countries; low birth weight and premature infants; infants/children fed whole cow's milk before 9 months old or at quantities >500 mL/ d; prolonged bottle feeding beyond 15 months old; or suboptimal intake of iron-containing foods.	Hgb (high-risk groups)
United States Preventive Services Task Force (2015)[18]	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for iron deficiency anemia in asymptomatic children ages 6 to 24 months.	Insufficient evidence to recommend screening
World Health Organization (2001)[19]	Universal screening at 12 months when prevalence of anemia in the country is between 5% and 20%.	Hgb

CBC = complete blood count; Hgb = hemoglobin.

birth weight (<2,500 g) breastfed infants.[6,7] For formula-fed infants, a high-iron formula should supply enough iron to meet the infants' needs.[7] Children aged 1 to 3 years should be able to achieve their daily iron requirements through diet alone.[2]

There are several options for iron supplementation, the most popular being ferrous salts that are available in liquid formulations for infants where the recommended dose is age and weight dependent. Micronutrient powders or "sprinkles" are another option discussed in the literature; these powders can be mixed into home-prepared foods and have been shown to be safe and effective.[13,21] More studies are needed to determine the feasibility, safety, and efficacy of iron-containing cookware and iron ingots for reducing IDA, especially among children.[22]

Infants receiving iron supplementation should have a follow-up assessment after 4 weeks of initiating the treatment to confirm the diagnosis and assess compliance, adverse effects, and efficacy.[20] Diagnosis of IDA or iron deficiency is confirmed if the infant's hemoglobin increases by >10 g/L (1 g/dL) or the hematocrit increases >3% with supplementation.[2] These clinical indicators verify the improvement of anemia with iron supplementation, even if serum ferritin was not initially tested.

Follow-up blood work (complete blood count, serum ferritin) should be drawn 3 months after iron supplementation is initiated to allow for hematopoiesis and assess the need for continued treatment[7] Follow-up should continue at 3-month intervals while the infant is receiving iron supplementation, until ferritin and hemoglobin levels are within the normal range and the infant is eating a sufficient variety of iron-rich foods.

The most common adverse effects of iron supplementation include nausea, vomiting, constipation, stomach upset, diarrhea, dark stools, and staining of teeth with liquid formulations.[20] Other barriers to treatment include cost, availability, lack of education for care providers and patients, and fear of iron overload.[6] NPs play an important role in providing patient-centered care and supporting their patients by connecting them to educational resources, such as nutritional handouts or websites, financial/nutritional supports, and interdisciplinary services. Further research is required to study the implementation of screening and treatment recommendations in high-risk groups as well as to identify any barriers to screening/treatment and explore the perspectives of different primary care providers.

Conclusion

IDA is a major public health concern in infants, especially those in high-risk groups such as Canadian Indigenous communities. As a result, consistent screening recommendations for select groups or a

Table 3
Factors to Evaluate in Iron Deficiency Anemia

Health history:
- Altered or impaired gastrointestinal absorption
- Delayed timing of cord clamping affects iron store
- Failure to thrive
- Frequent/chronic infections (indicating a compromised immune response)
- Frequent pregnancies (especially if they progressed to full-term births)
- Increased consumption of low-iron 'convenience' foods
- Irritability
- lethargy
- Low birth weight or small for gestational age
- lowered motor and cognitive function compared with healthy infants
- maternal anemia
- low maternal education level
- low socioeconomic status
- poor feeding
- preterm birth
- Indigenous or newly arrived immigrant/refugee from resource-poor country
- Reduced access to traditional iron-rich foods

Physical examination:
- Developmental milestones not reached
- Fatigue, poor concentration, lethargy, irritability, weakness
- Nails—thin, brittle, coarse ridges, concave shape
- Pallor of the palms, conjunctiva, oral mucosa, nail beds
- Increased heart rate and breathing rate (severe anemia)
- Congestive heart failure (tachypnea, cardiomegaly)

Laboratory tests at initial visit and 3 months after iron supplementation:
- Complete blood count, including hemoglobin and mean cell volume
- Serum ferritin
- Other tests: C-reactive protein (if inflammation suspected to be causing hyperferritinemia), lead level (if risk factors)

Treatment:
- Introduction of iron-rich foods at 4 to 6 months old
- Avoid cow's milk, evaporated milk, and other types of milk until after 12 months old
- Cow's milk should be limited no more than 20 ounces (500 mL) per day using a cup in those 1 to 5 years old
- Oral iron supplementation (based on age and weight) if anemic or continued poor intake of iron-rich foods
- Education: iron-rich foods, foods that increase/decrease iron absorption, potential adverse effects of iron supplements: nausea, vomiting, constipation, stomach upset, diarrhea, dark stools, and staining of teeth with liquid formulations
- Follow-up assessment at 4 weeks to assess compliance and adverse effects
- Follow-up blood work (complete blood count, serum ferritin) at 3 months of iron supplementation
- Monitor other barriers to treatment such as cost

universal screening strategy are needed to promote early diagnosis and treatment of IDA. Primary care NPs play a particularly important role in screening, diagnosing, and treating IDA in the prenatal and postnatal periods. They are able to identify and treat IDA in infancy to prevent potentially irreversible negative neurodevelopment and socioemotional outcomes. Primary care NPs are also uniquely situated to provide essential services and improve accessibility to health care in rural and remote areas, where rates of IDA in infants are particularly high. NPs play an important role in educating families about IDA and empowering them to achieve the best possible outcomes for their children.

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