Bridging the Gap of Iron-Deficient Foods in Low Resource Setting Communities

Mabel Kwofie

Department of Bioresource Engineering

Faculty of Agricultural and Environmental Sciences

Macdonald Campus of McGill University

Sainte-Anne-De-Bellevue, Quebec, Canada

April, 2022

A Thesis Submitted to McGill University in Partial Fulfillment of the Requirement for the Degree of Master of Science

Dedication

I dedicate this master's thesis to God almighty, Ms. Sofia Brault, Dr. Robin Beech, Ms. Edith Breiner, Dr. Russell Steele, Mr. Bryan Salazar Roldan, Mr. Peter Baccin-Smith, and my family for their tremendous support.

Preface and contribution of authors

This master's thesis was written in a manuscript-based format in accordance with McGill University's thesis guidelines and preparation. It consists of five chapters. Three chapters have been scripted for scientific publication as presented below:

- Determinants of Iron Deficiency and Pathways for Improvement Among Populations in Low Resource Setting Communities
- Iron Deficiency and Anemia in Less Developed Countries: Reassessing Trends, Conventional and Evolving Methods of Mitigation
- Curbing Iron Deficiency through Dietary Adjustment of Homemade Infants' Cereal-Based Foods with Heme and Vitamin C for Optimum Iron Availability

Mabel Kwofie carried out the thesis literature review, product development and analysis, results analysis, and the manuscript preparation. The research work was performed at the Food Engineering Laboratory, Bioresource Engineering Department, MacDonald Campus, McGill University.

Dr Michael Ngadi (co-author), James McGill Professor at the Bioresource Engineering Department, McGill University, Macdonald Campus, Sainte-Anne-de-Bellevue, Quebec, was the supervisor for this research work, he provided technical guidance, revision, and correction of the manuscripts.

Signed: Mabel Kwofie

Date: April, 2022

Abstract

Iron deficiency anaemia (IDA) is a global public health issue affecting people in both developed and developing countries. Iron deficiency occurs when dietary iron absorption is insufficient to meet the body's iron requirements and losses. Iron deficiency has numerous implications, impacting not only individual health but also community and social growth. Pregnant women, infants, and adolescents are most susceptible to iron deficiency (ID) since they have increased iron requirements. The main cause of iron deficiency (ID) in most developing countries is low dietary iron bioavailability, this according to studies is due to high intake of cereals, seeds, and grains (plant-based non-heme iron) with limited heme iron and vitamin C (iron absorption enhancers) intake. The absorption of iron from plant-based foods is impeded by the phytate presence in the cereals and grains.

Controlling and preventing iron deficiency and anaemia in all groups of a population with varying iron requirements necessitates coordinating several initiatives. The objectives of this research study were to (1) find out determinants of iron deficiency (ID) and pathways for improvement among populations in low resource setting communities, (2) examine the trends and evolving methods (strategies) of managing iron deficiency anemia and the (3) Evaluation of adjusted infants six-twelve months home-made cereal-based foods with heme and iron absorption enhancers to support optimum iron availability. The main causes of iron deficiency (ID) in low resource setting communities were reviewed and determined, and to better address the iron deficiency (ID) challenge, strategies for its prevention and management were also evaluated. Since iron deficiency's long-term effects on infants and young children are detrimental, cereals and grains such as rice, corn and millet frequently used in infants' complementary foods preparation in low resource setting communities were sampled and developed into iron-rich infant foods, other ingredients such as chicken, pumpkin seeds, fruits, and soya beans were added in the products preparation in accordance with the world health organisation's (WHO) recommendations for the inclusion of at least four items from the seven (7) food groups aimed at dietary diversification to produce adjusted infant porridges which contains heme and vitamin C to support adequate iron absorption from cereal-based infant foods. The study findings suggest iron from adjusted rice porridge is more bioavailable, this is followed by adjusted corn porridge before the adjusted millet porridge.

Resume

L’anémie ferriprive est un problème de santé mondial qui affecte autant les populations des pays industrialisés que celles des pays en voie de développement. Une carence en fer survient quand l’apport alimentaire est insuffisant pour rencontrer les besoins en fer de l’organisme.

Une carence en fer affecte non seulement la santé des individus mais a aussi un impact négatif sur la croissance économique et sociale des communautés. Les femmes enceintes, les bébés, les jeunes enfants et les adolescents dont les besoins en fer sont grands, sont plus susceptibles de souffrir d’une carence en fer. La cause principale de la carence en fer rencontrée dans les pays en voie de développement provient principalement du manque de biodisponibilité du fer alimentaire. En effet, les études montrent une consommation élevée de céréales et de grains ayant un faible contenu en fer hémique et en vitamine C (activateur d’absorption du fer).

De plus, la presence de phytate dans cette alimentation végétarienne, entrave l’absorption du fer. La prévention et le contrôle de la carence en fer et de l’anémie des divers groupes de la population ayant des besoins différents nécessitent la mise en place de plusieurs projets.

Les objectives de cette étude étaient: 1) de définir les déterminants alimentaires qui sont la cause de l’anémie ferriprive chez les populations à faible revenu, 2) d’évaluer les tendances et les stratégies utilisées pour contrer la carence en fer et 3) d’évaluer l’impact sur l’absorption du fer chez les nourrissons de six à douze mois, suite à l’ajout de fer hémique et d’activateurs d’absorption du fer dans les céréales. On a ainsi identifié et déterminé les causes principales d’une carence en fer rencontrée dans les communautés à faible revenu. Cela a permis de mieux comprendre les défis à affronter et d’évaluer les stratégies mises en place pour la prévention et le contrôle de cette situation problématique.

Afin de prévenir les effets négatifs à long terme d’une carence en fer chez les nourrissons et les jeunes enfants, on a enrichi en fer les préparations alimentaires pour bébés composées habituellement de riz, de maïs et de millet. D’autres ingrédients tels le poulet, des graines de citrouilles, des fruits et des fèves de soya ont été ajoutés aux préparations tel que recommandé par l’Organisation Mondiale de la Santé (OMS). En effet, l’OMS recommande d’ajouter aux

préparations de céréales pour bébés, au moins quatre éléments provenant des sept groupes alimentaires afin d’assurer l’ajout de fer hémique et de vitamine C favorisant l’absorption de fer.

Les résultats de l’étude montrent que la biodisponibilité du fer est obtenue principalement dans les céréales de riz enrichies, suivi par les céréales de maïs enrichies et troisièmement dans les céréales de millet enrichies.

Acknowledgement

Countless individuals contributed enormously to the success of my study; I would like to sincerely thank everyone that assisted me. I acknowledge all staff of McGill university student resources that helped in making my completion of the MSc (thesis) program a reality. I gratefully express my gratitude to Dr. Michael Ngadi, my supervisor, Dr. Vijaya Raghavan, the graduate program director, (GPD), and the department of Bioresource Engineering for this opportunity. I thank my supervisor for the academic guidance, and support.

I wish to thank Dr. Robert Kok, Dr. Valerie Orsat, Dr. Katherine Gray-Donald, Dr. Stan Kubow, Dr. Jim Fyles, Dr. Lorraine Chalifour, Dr. Robin Beech, Dr. Russel Steele, Ms. Edith Brenier, Dr. Elham Rahme, Dr. Linda Wykes, Dr. Grace Marquis, Ms. Lise Grant, Ms. Christiane Trudeau, Dr. Li (Laura) Liu, Louise Legault. and family (landlord), Mrs. Ngadi, and family.

I am grateful to all professors at the School of Human Nutrition and the Department of Bioresource Engineering.

Finally, I appreciate my family, colleagues, and friends especially, Ebenezer Miezah Kwofie Dr. for their support.

Table of Contents

List of Figures

List of Tables

Abbreviations

AOAC	Association of Official Agricultural Chemist
Ca	Calcium
CNF	Canadian Nutrient File
CO_2	Carbon Dioxide
CRP	C-reative Protein
DALYs	Disability-Adjusted Life Years
DTT	Dithiothreitol
DV	Daily Value
EDTA	Ethylenediaminetetraacetic acid
EF	Enhancing Factor
FAO	Food and Agricultural Organization
Fe	Iron
FNDDS	Food and Nutrition Database for Dietary Studies
G(g)	Gram (Unit of mass or weight)
HB	Heme Bioavailability
HCI	Hydrochloric Acid
HPLC	High Performance Liquid Chromatography
ICH	International Conference on nutrition
ICP-OES	Inductively Couple Plasma-Optical Emission Spectrometry
ID	Iron Deficiency
IDA	Iron Deficiency Anemia
IF	Intrinsic Factor
LMIC	Low-and-Middle-Income Countries
MFP	Meat, Fish, Poultry
MG (mg)	Milligram
NHB	Non-Heme Bioavailability
NIH	National Institute of Health
pH	Potential of Hydrogen
PVC	Polyvinyl Chloride
RBC	Red Blood Cells

RCF	Relative Centrifugal Force
RDA	Recommended Dietary Allowance
SUN	Scaling Up Nutrition
TFEA	Total Iron (Fe) Absorbed
ULs	Upper Limits
UNICEF	United Nations Children’s Fund
UNU	United Nations University
Vit. C	Vitamin C
WaSH	Water, Sanitation and Hygiene
WFP	World Food Program
WHO	World Health Organization
Zn	Zinc

Chapter 1 - General Introduction

1.1 Background

Iron is a widespread element on earth and a biologically indispensable component of all forms of life, (Kaplan & Ward, 2013; S. Lynch et al., 2018). The importance of iron in human health and disease prevention has been recognized since time immemorial. Egyptians, Hindus, Greeks, and Romans were among the first to use iron as medicine. Iron was used to treat chlorosis (green sickness), a condition caused by iron deficiency (ID) in the 17th century, (Nazanin, Hurrel, & Kelshadi, 2014). However, it was not until 1932 that the significance of iron was recognised, due to compelling evidence that inorganic iron was needed for haemoglobin synthesis, (Yip R, 1996). Iron's role in haemoglobin production and oxygen transport has spurred nutritional interest for many years, (Abbaspour, Hurrell, & Kelishadi, 2014). While insufficient iron intake and bioavailability are now the leading causes of anaemia globally,(Miller, 2013), just about half of the anaemia in less developed nations are caused by iron deficiency (ID); Infectious and inflammatory diseases, particularly malaria, parasitic infections' blood loss, and other nutritional deficiencies such as vitamin A, riboflavin, folic acid, and vitamin B^{12} are all contributing factors to iron deficiency anemia (IDA), (The World Bank Group, 2009; Van Zutphen, Kraemer, & Melse-Boonstra, 2021).

Iron deficiency anaemia is a condition in which the body's iron reserves are depleted, (Naigamwalla, Webb, & Giger, 2012). It is caused by either a shortage of dietary iron or a lack of iron bioavailability which is the proportion of the ingested mineral (iron) which is absorbed and used for normal physiological functions, (R. Hurrell & Egli, 2010b).

Total iron bioavailability is a combination of heme (animal-based) and non-heme (plant-based) iron absorption levels, (Skolmowska & Głąbska, 2019). Non-heme iron absorption is weak and highly variable, while heme iron absorption is stable (approximately 25%). This is due to the impact of different dietary influences on the absorption of non-heme iron, (L. Hallberg, Bjørn-Rasmussen, Howard, & Rossander, 1979; Monsen et al., 1978). Ascorbic acid and animal tissues (chicken/fish/beef, etc.) are two dietary factors that enhance non-heme iron absorption, (E. R. Monsen, 1988). Phytic acids, polyphenols, and calcium salts, are the most common dietary iron inhibitors, (Milman, 2020).

Impact of iron deficiency anemia (IDA) varies among population groups and in different geographical settings, according to the local conditions (*UN Children's Fund 2011; Stevens G. A. et al 2011*).

Iron absorption and bioavailability are severely impeded by high phytate content of unrefined cereals such as corn, millet, and rice which are widely used in low-medium-income-countries (LMICS), (Gupta, Gangoliya, & Singh, 2015).

The main food items used in meal preparations are based on locally accessible staples, however, the choice of individual food item varies greatly amongst groups due to tradition, food availability, and convenience, (Kuyper E, Vitta B, & Dewey KG, 2013). Cereals are common staples with high phytic acid content which inhibit Iron absorption. Cereals, including grains, starchy roots, and its fruits, with 65-75% carbohydrates, 6-12% protein, and 1-5% fat which offers energy, (Gupta et al., 2015), constitute staple foods for most populations globally. Cereals and grains are the main source of energy, ranging 334.4 and 382.2 kcal per 100 g of whole cereal, and provides dietary fibres. Grains make up 70–77 percent of all cereals and are frequently processed before consumption to make the starch digestible but a large amount of it's nutrients are lost during processing, (Oghbaei & Prakash, 2016).

Socioeconomic factors, taboos, and misinformation, potentially influence feeding in several low- and middle-income countries (LMIC), (Mayén, Marques-Vidal, Paccaud, Bovet, & Stringhini, 2014). Infant's complementary meals are usually made into thin cereals-based foods with little to no addition of fish/meat/fish/eggs etc., especially among low-income groups, (Roy et al., 2021) thereby contributing to iron deficiency. Infant's median daily nutritional intakes (per 100 kcal) of energy, iron, calcium, zinc, vitamins C and A when below world health organisation (WHO) recommendations and desirable nutrient levels, is considered unacceptable, (Suthutvoravut et al., 2015).

In some areas of low resource setting communities, underlying illnesses and infections could be a contributing factor to iron deficiency anemia (IDA) which must first be treated before dietary enhancements interventions can be effective. This study focuses on identifying underlying contributions to iron deficiency anemia (IDA), approaches of mitigation, and dietary development that reduces iron deficiency among infants and adults for a continual iron sufficiency and healthy livelihood among at-risk populations that are most affected by iron deficiency anemia (IDA).

1.2 Research Objectives

The research study seeks to:

a) Review determinants of iron deficiency (ID) and pathways for improvement among populations in low resource settings communities.
b) Examine the trends and evolving methods (Strategies) of managing iron deficiency anemia.
c) Evaluation of dietary adjustment of infants 6-12 months home-made cereal-based foods using heme and iron absorption enhancers for optimum iron availability.

1.3 Thesis Organisation

The thesis is structured in five chapters: the general introduction (Chapter one), review of literatures (Chapter two, and three), a research manuscript (Chapter four) and a general conclusion, (Chapter five). The main introduction is made up of the background information of the thesis topic and the research study.

1.4 Connecting text

The preliminary chapter provided a general introduction of the thesis and presented the three main objectives of the study. The next chapter is on the thesis objective one which is a review of determinants of iron deficiency (ID) and pathways for improvement among populations in low resource setting communities.

Chapter 2 - Determinants of Iron Deficiency (ID) and Pathways for Improvement Among Populations in Low Resource Setting Communities

Abstract

Iron deficiency anemia (IDA), although preventable, remains a common nutritional deficiency worldwide, especially in low resource setting regions and developing countries. When the body's absorbed iron is inadequate to satisfy iron requirements and losses, this condition of iron deficiency anemia (IDA) typically develops. Pregnant mothers, babies, young infants, and adolescents are at a high risk of iron deficiency because they have higher iron requirements. The major contributing factor to iron deficiency in developing regions is the diet's poor iron bioavailability. This nutritional deficiency condition (IDA), has several and acute effects, affecting not only human health but also the development of populations and nations. In this review, overview of iron, iron deficiency, and the body's iron regulation are presented. Iron deficiency, nutritional anemia, and its contributing factors in underdeveloped nations are examined. Dietary food patterns and the approaches of tackling of iron deficiency anemia are presented. The paper focuses on methods of making non-heme iron which is commonly found in plant-based foods bioavailable among its frequent users to diminish iron deficiency. Finally, applicable measures for iron status improvement and maintenance in low resource settings areas are discussed.

Key words: Heme, non-heme, anemia, iron-deficient (ID), Iron deficiency anemia (IDA), iron bioavailability, iron absorption enhancers, phytate, polyphenols, vitamin C

2.1 Introduction

Iron deficiency anemia (IDA) is the single micronutrient deficiency affecting people in developed and developing nations. The World Health Organization (WHO) estimates that anemia affects 30% of the world's population which constitutes 5000 million anemia-affected people, hence considered a public health situation (Brannon & Taylor, 2017; Chaparro & Suchdev, 2019; WHO, 1993). Women of reproductive ages are the most affected, with greater than 500 million globally, (Teshale, Tesema, Worku, Yeshaw, & Tessema, 2020). Anemia is a major contributor to perinatal and maternal mortality, disabilities, and loss of work. Among the 26 risk factors of the global burden of diseases (GBD) 2000 project, iron deficiency ranked 9th globally and results in 841,000 deaths and 35,057,000 disability-adjusted life years (DALYs). It accounts for 71% of mortality burden and 65% DALYs in some African countries and parts of Asia (Stoltzfus, 2003). Iron deficiency results in impaired cognitive function in infants, it also contributes to maternal and newborn adverse pregnancy outcomes (Achebe & Gafter-Gvili, 2017); as well as declining cognition in the elderly (Andro, Le Squere, Estivin, & Gentric, 2013). Maternal iron status is crucial for infant life and health. Iron is essential in the early human developmental stages, and it is critical for both fetus and infant growth. Iron is involved in the process of embryogenesis of the nervous system in the first trimester. The fetus forms its iron stores in the last trimester of pregnancy (Burke, Leon, & Suchdev, 2014), hence adequate iron of the mother is helpful. Neurodevelopmental routes that are propelled by iron are also developed in early life stages and persist through the course of life. This refers to brain growth, cognitive development, motor, and psychosocial development, myelination, and synaptogenesis (Radlowski & Johnson, 2013). In full-term infants born to iron sufficient mothers, it is presumed that iron stores accumulated in-utero can meet the iron requirement over the initial six (6) months of the infant's life (Kilbride et al., 1999; Ziegler, Nelson, & Jeter, 2014).

Iron is also an essential nutrient needed for hemoglobin (Hb), and the making of red blood cells (RBC); it forms an important part of the hemoglobin molecule. Several conditions such as the growth of tissue mass of an infant, fetus growth during pregnancy require an upsurge in red blood cells hence increased iron intake and uptake, (Cerami, 2017). Iron deficiency anemia (IDA) awareness and health consequences among women, adolescent and children's development have increased in the past years. The World Health Organization 65th assembly approved an action plan targeting globally, maternal and children's nutrition with a duty to reduce iron deficiency anemia

(IDA) prevalence among reproductive age women by 2025. Interventions such as scaling up nutrition initiatives (SUN) have increased. The iron deficiency anemia factors that adversely affect women and children reduction has been emphasized (Stevens et al., 2013). This review discusses determinants of iron deficiency and pathways of improvement among populations in low resource communities with the objectives to (1) identify iron deficiency anemia (IDA) contributing risk factors in developing nations, (2) ascertain possible dietary choices/patterns in managing iron deficiency anemia (heme and non-heme diets) and to (3) discuss lifestyles and practices for continual iron sufficiency and healthy livelihood in the population.

2.2 Overview of Iron, Iron Deficiency, Anemia and The Body's Iron Regulation

Iron is an essential element that the body uses to produce hemoglobin. Hemoglobin is a protein found in red blood cells (RBCs) and assists in the oxygen transport to different parts of the body. It is also the pigment that gives red blood cells their red colour, (Abbaspour et al., 2014). Low body iron results in a reduction in hemoglobin which develops into iron deficiency anemia (IDA). Iron deficiency is defined by low ferritin <30 µg/mL in a person >15years of age with low C-reactive protein (CRP). Cut-offs of 15 and 20 µg /mL, respectively, are used for children aged 6–12 years and younger adolescents aged 12–15 years, (Clénin, 2017). Iron deficiency anemia occurs from imbalances in iron consumed, iron stores, and the loss of iron from the body, where it becomes inadequate to assist in the production of erythrocytes (red blood cells), (Miller, 2013).

Iron deficiency develops in three stages, that is (1) early depletion of iron stores: in this first stage, there's shrinkage of iron stores without it directly affecting body areas that need iron. (2) Early functional iron deficiency: It refers to decreased iron availability which affects the bodily parts where iron is required. (3) Iron deficiency anemia (IDA) it describes the third stage of iron deficiency, which is caused by nutritional deficiency, with several negative health outcomes (Johnson-Wimbley & Graham, 2011). In the diagnosis of iron deficiency anemia, the measuring of transferrin saturation, serum ferritin, serum soluble transferrin receptors-ferritin index is more precise than red cell indices (Lopez & et al., 2016). For the essence of this review study, the body's physiological handling and regulation of iron is discussed. Transferrin and ferritin are special proteins aid in iron absorption, distribution, and storage processes. During iron transport to the tissues, transferrin binds with iron in blood plasma, iron then no longer exists in its free form after binding with transferrin hence cannot damage cell protein and membranes through the formation of free radicals. Extra iron storage form is ferritin which is normally available in the liver and macrophages in the reticular-endothelial system, (Cleland & Thomas, 2019). Iron differs from other minerals because of the absence of any physiological excretion process (Han, 2011). The elimination of iron from the body, although limited happen through the intestinal endothelial cells shedding into feces (Hunt, Zito, & Johnson, 2009), sweating, and gastrointestinal (GI) blood loss. Anemia of chronic disease has been associated with peptide hepcidin in the liver, the primary regulator of iron homeostasis (Singh, Gruissem, & Bhullar, 2017; Wallace Daniel, 2016). Collective modeling is employed in estimating dietary iron requirements, (Dainty, Berry, Lynch, Harvey, & Fairweather-Tait, 2014; Fairweather-Tait et al., 2017). The components contributing most to iron loss and constraint in low resource setting communities is discussed below.

2.3 Iron Deficiency Anemia Contributing Risk Factors in Developing Countries

The etiology of anemia is multifactorial, and are sometimes described with the local conditions, however, iron deficiency (ID) remains the key underlying cause of anemia among atrisk individuals in low resource setting communities and developing regions (WHO, 1993), owing to high intake of foods low in iron as well as poor iron bioavailability, iron lost through blood loss (menstruation) hence high requirements, etc. In underdeveloped nations, factors such as malaria, hookworm, chronic infection, thalassemia, hemoglobinopathies, and other nutritional deficiencies also contribute to anemia (Balarajan, Fawzi, & Subramanian, 2013). Nutritional anemia occurs due to deficiencies of iron, folate, and vitamin B_{12}, any other nutritional deficiencies may manifest only after the treatment of iron, folate, and vitamin B_{12} deficiencies (Nagao & Hirokawa, 2017; WHO, 1993). The physiological changes such as pregnancy, growth spurt in adolescents, blood loss via menstruation, socio-economic issues, malaria, hookworm, nutritional considerations (iron, vitamin A, folate, vitamin B_{12}), that contributes directly to iron deficiency anemia among populations in developing regions is discussed more specifically below.

2.3.1 Physiological Changes Increased Iron Requirement (pregnancy, menstruation, adolescent growth spurts)

Women's iron needs increase due to their biological changes and the needs that arise. Maternal iron needs are highest in the period of pregnancy and childbirth. Likewise, iron demand is increased during menstruation due to menstrual blood loss (Moschonis & et al., 2013). Estimation of 1000-1200mg of iron is required by the body from pregnancy conception through to delivery (Lee & Okam, 2011), for an average weight of 55kg, (Garzon & et al., 2020). Maternal iron intake and stores must be adequate to sustain fetal and placenta growth with an estimate of 350mg, and the possible blood loss during delivery of 250mg, (Garzon & et al., 2020); J L Miller, 2013, states that the mother's erythrocyte (RBCs) mass increases from 350 to 450 mL (Miller, 2013). The World Health Organization (WHO) suggests 700-800mg increased bodily iron need over a pregnancy duration (WHO, 1993). Maternal iron deficiency anemia at perinatal periods and during pregnancy has detrimental consequences for the infant and the expectant mother, (Abu-Ouf & Jan, 2015). In women, iron deficiency anemia reduces work and energy output; (Coad & Pedley, 2014), that leads to poor pregnancy and delivery outcomes which results in premature delivery, low birth weight, high perinatal mortality (Abu-Ouf & Jan, 2015; T. O. Scholl & Hediger, 1994) and increased maternal death menaces during childbirth and postpartum (Khaskheli & et al., 2016). Also, due to increased dietary requirements for growth and development, adolescence is a critical period of nutritional vulnerability. It is worth indicating that, because of the rapid growth and muscular development that occurs during adolescence, which results in an increase in blood volume, it is critical that the adolescent's iron needs are met through appropriate dietary support (Mesías, Seiquer, & Navarro, 2013).

2.3.2 Socio-Economic issues

Low socioeconomic status contributes to iron deficiency anemia (IDA). Impoverished socio-economic situations and limited access to diverse foodstuffs render people in developing regions susceptible to iron deficiency anemia (IDA) together with malnutrition situations. Parasitic infection in rural, subtropical, and tropical areas contributes to iron deficiency anemia (IDA) through malabsorption and intestinal blood loss (Shaw & Friedman, 2011). Pica is one of the neurological comorbidities with iron deficiency, it a dietary craving for substances that are not eaten as food such as clay. This practice is common in developing countries by some pregnant women residing in high iron deficiency anemia regions (Miller, 2013). Health care providers attentiveness to the iron needs of the population is crucial in reducing iron deficiency anemia (IDA) incidences in low- and middle-income countries. Other drivers of anemia among reproductive aged women in developing regions reported through research studies, includes rural/urban habitation, a woman's education and profession, spouses academic background, water, sanitation, and hygiene (WaSH), and household income. These factors may directly or indirectly influence circumstances that results in iron deficiency anemia among women, (Kothari et al., 2019; Owais, Merritt, Lee, & Bhutta, 2021).

2.3.3 Malaria

Malaria is caused by the parasite genus *Plasmodium*, it results in 600,000 individual deaths yearly (Wassmer et al., 2015). Malaria is a major cause of anemia globally (Kassebaum et al., 2014), appropriate practices and measures in decreasing malaria lessens anemia (Meremikwu, Donegan, Sinclair, Esu, & Oringanje, 2012). Iron functions in determining disease susceptibility, malaria and iron share a complicated relationship. The malaria parasite, *Plasmodium* during its liver stage growth and disease-related phase of erythrocyte infection utilizes iron. The process of the protozoan iron acquisition from humans is not distinctly defined but the malaria pathogens growth is impeded by iron chelators in vivo and invitro models (Spottiswoode, Duffy, & Drakesmith, 2014). Iron deficiency protects humans against malaria; however, iron supplementation during malaria infected stage, rises diseases and infection risks. Malaria interrupts iron distribution and uses procedures such as the release of heme, anemia, hemolysis, and dietary iron absorption inhibition. Upregulated hepcidin at blood-stage parasitemia can mediate iron redispersion that come with infection (Spottiswoode et al., 2014). Malaria prophylaxis and treatment in developing regions and affected areas is essential in reducing iron deficiency anemia (IDA).

Gwamaka, et al. (2012), studied a large group of infants in Tanzania, aged, 0 to 3 years. They observed that, iron deficiency during healthy aparasitemic visits was highly linked to a lower occurrence of parasitemia and acute malaria in this at-risk groups of population, (Gwamaka et al., 2012). In a different study, iron deficiency was predictive of clinical malaria incidents in a year after measurement in a significantly older study group of Kenyan children (eight months–eight years), (Nyakeriga, Troye-Blomberg, Chemtai, Marsh, & Williams, 2004). Jonker et al. (2012), found a similar impact in infants 6 months to 5 years old in Malawi: that is, children who were iron-deficient (defined as serum ferritin <30 ng/mL) had a decreased episodes of clinical malaria the following year, (Jonker et al., 2012).

2.3.4 Hookworm Infestation (Soil-transmitted helminths)

Hookworm and other soil-transmitted infection is a public health issue that contributes to iron deficiency anemia through blood loss, yet a neglected tropical disease (NTD) with 740 million infections worldwide and prevalence in developing countries (Rodriguez-Guardado, Pozo, Fernandez-García, Amo-Fernandez, & Nozal-Gancedo, 2013). It is an intestinal *helminthiasis*, triggered by two species of hookworm: *Necator americanus* and *Ancylostoma duodenale* that feed on blood. Hookworm resides in the small intestine and excretes via human stool; they hatch in soil under appropriate conditions and form larvae. They are transmissible through human skin during exposure and travels into the blood vessels, through to the lungs to the pharynx, and finally to the intestine (Hotez, Bottazzi, Franco-Paredes, Ault, & Periago, 2008). They attach to the mucous wall of the small intestine, soften the intestinal villi wall, break the blood capillaries, and then feed on blood and tissue fragments (Ranjit, Jones, Stenzel, Gasser, & Loukas, 2006). The causes of hookworm infection include poor hygiene and socio-economic factors, living in tropical, subtropical, and rural areas, improper management of biological waste, barefoot walking that allows the skin penetration of the parasite; (Rodriguez-Guardado et al., 2013). Untreated intestinal parasitic infections (IPI's) can potentially result in iron deficiency anemia (IDA) when there is extracorporeal blood loss, (Hossain, Das, Gazi, Mahfuz, & Ahmed, 2019).

2.3.5 Nutritional Considerations

Nutritional anemia is prevalent in low resource settings communities, (Desalegn, Mossie, & Gedefaw, 2014). Limited absorption or low dietary intake of iron, folate, and B vitamins especially vitamin B12 is considered a major iron deficiency anemia (IDA) contributing factor. Recommended daily allowance (RDA) of folate increases from 400mcg for non-pregnant women to 600mcg/day during pregnancy, (National Institute of Health (NIH), 2020a). The prevalent cause of vitamin B_{12} deficiency is improper absorption from intrinsic factor (IF) deficiency, (which is a glycoprotein made in the stomach), (Al-Awami Hashim, 2022). Lack of folate and vitamin B_{12} results in megaloblastic anemia (pernicious anemia), (Carmel, 2008). Proper dietary choices and intake can reduce the incidence of nutritional anemia.

2.4 Dietary Foods Patterns and the Tackling of Iron Deficiency Anemia

2.4.1 Heme and Non-heme Iron

The building blocks of life are proteins. They're also a vital source of nutrients for the body. Amino acids are released into the body when proteins are digested, and they are used for biosynthesis or cellular energy generation. Proteins supply a variety of nutrients, including metals, in addition to amino acids. Iron is the most prevalent metal in the human body, with 3–4 g required by an adult, (Hooda, Shah, & Zhang, 2014).

Dietary irons are derived from two food sources, which are heme (50-60% animal foods iron) and non-heme (plant-based) dietary food sources (Skolmowska & Głąbska, 2019). Heme iron is derived predominantly from animal meat of myoglobin and hemoglobin breakdown, these include beef, poultry, fish, and different kinds of seafood; they constitute protein sources that are well absorbed by the body without the need for absorption enhancing co-factors (Briat, Curie, & Gaymard, 2007). A large proportion of the body's iron is found in heme. Heme is absorbed in the small intestine (Theil et al., 2012). The stomach's low pH and the action of proteolytic enzymes in the stomach and small intestine causes heme to be released from proteins, (Hooda et al., 2014). Non-heme iron is available in both plant and animal food sources, mixed or both heme and non-heme diets eaters have a bioavailability of 14 to 18% whiles vegetarians (non-heme) consumers have 5 to 12% iron bioavailability (Carpenter & Mahoney, 1992). Non-heme iron is present as Fe (II) and Fe (III) in aqueous solutions with a pH of 7.0 or above. Fe (II) easily oxidises to Fe (III), which precipitates as ferric hydroxide from solution or forms soluble hydroxyl-iron dimers that are not readily absorbable, (West & Oates, 2008). Non-heme iron form an essential dietary source for vegetarians, however, due to its limited iron bioavailability requires a balance between dietary enhancers, inhibitors, and dietary iron stores (R. Hurrell & Egli, 2010a). Non-heme dietary sources include whole grains, legumes, beans, dried fruits, nuts, seeds, and dark leafy vegetables (Saunders, Craig, Baines, & Posen, 2012).In developing countries and low resource setting communities, non-heme iron constitutes a greater percentage of the source of iron with minimal heme iron intake. The table 2.1, below provides a distribution in selected cereals and grains that provides non-heme iron.

Table 2.1- Legumes, Cereals, and Seeds(non-heme) Composition and Iron Bioavailability

	Legumes		Millet		Sorghum		Rice		Maize		Wheat	
	Soy	Lentils	whole	decorticated	whole	decorticated	brown	polished	Whole	Degermed	whole	White flour
Kcal/100g	403	116	361	361	332	332	360	363	362	364	336	364
Fat(g/100g)	17.7	0.4	5	4.6	3	2.4	1.9	0.4	4	1.2	1.9	1
Phytate (mg/100g)	2322	358	870	609	618	439	500	255	800	72	800	280
Fe (mg/100g)	2.3	3.3	8	8	4	4	1.6	0.8	3	1	3.3	1.2
Phytate/Fe molar ratio	70	9	9	6	13	9	26	27	25	6	23	20
Bioavail. Fe (%)	1.7	1.2	-	-	3	-	-	3	3.7	5	5	20
Bioavail. Fe (mg/100g)	0.05	0.04	-	-	0.12	-	-	0.02	0.1	0.05	0.16	0.24
Bioavail. Fe density (mg/100 kcal).	0.12	0.34	-	-	0.36	-	-	0.06	0.28	0.14	0.47	0.66

Adapted from, (L H. Allen & Ahluwalia, 1997).   *Dry Weights, *Phytate (g) 660 ÷Fe (mg)/56.

2.4.2 Dietary Iron Bioavailability and Inhibitors

Dietary iron bioavailability which is, the absorption rate of ample amount of iron from heme (animal-based products), ranges between 15%-35% (R. Hurrell & Egli, 2010a); whiles non-heme (plant-based products) have lower iron bioavailability, with an absorption range of 2%-20%, (E. R. E. Monsen, 1988). The chemical context of non-heme iron in foods relates to its bioavailability, that exists in a variety of forms, such as, ferric citrate, ferrous gluconate, ferric dextrans, ferrous fumarate, ferritin, ferric chloride, iron carbonyl, ferric phytate, ferrous sulfate, ferrous carbonate and ferric EDTA (Nielsen, Tetens, & Meyer, 2013; Theil, 2004). Ferritin iron is bioavailable in humans. The key inhibitor of plant-based food's non-heme iron absorption in the body is phytic acid (Myo-inositol (1,2,3,4,4,5,6)-hexa*kis*phosphoric acid), (Luo & Xie, 2014; Theil et al., 2012). Phytate can be found in all seeds and, probably, all plant cells in nature. It's a naturally occurring molecule that forms during the development of plant seeds and grains, and it acts as a cation and high-energy phosphoryl group storage. Mineral availability is lower in plant-based foods than in animal-based foods, according to a significant body of evidence. Phytate chelating cation such as iron occurs because the phosphate groups of phytate are negatively charged in physiologically beneficial conditions (Bohn, Meyer, & Rasmussen, 2008; Schlemmer, Frølich, Prieto, & Grases, 2009). Phytate degradation (removal) is essential for the improvement in iron absorption among population who depend extensively on cereals and grains or plant-based crops as staple foods. These plant-based crops may as well be their main source of iron as in the case of some vegetarians and a proportion of people in low resource setting communities. Studies further indicate Polyphenols (antioxidants present in foods and beverages from plant sources including tea with tannic acid, red wine, oregano, and coffee) decreases iron absorption; (Thankachan, Walczyk, Muthayya, Kurpad, & Hurrell, 2008). Increased concentrated tea has high potency since polyphenols have a dose-dependent impact on iron absorption. According to (R. F. Hurrell, Reddy, & Cook, 1999), the addition of milk to beverages may not change the inhibitory effect of polyphenols (R. F. Hurrell et al., 1999). Likewise, it has also been found that calcium inhibits heme and non-heme iron absorption;(Callister, Gautney, Aguilar, Chan, & Aguilar, 2020; Roughead, Zito, & Hunt, 2005). Single-meal and day studies suggest that fortified and supplemental calcium has an inhibitory effect on iron absorption (Minihane & Fairweather-Tait, 1998)*;* in a study, calcium absorption was reduced by 49% from the intake of 40mg fortificant calcium, (Lim, Riddell, Nowson, Booth, & Szymlek-Gay, 2013). However, enhanced iron absorption theoretically improves iron status, particularly in women.

2.4.3 Dietary Iron Absorption Enhancers

Dietary iron absorption enhancers include Ascorbic acid (Vitamin C) and the MFP factor (meat, fish, poultry). Vitamin C enhances the absorption of iron due to its iron-chelating and reducing properties, that is changing ferric iron to a more solubility form which is ferrous iron, (Teucher, Olivares, & Cori, 2004). Vitamin C also inhibits the effects of phytate, polyphenol, and calcium which act as iron absorption inhibitors, (S. R. Lynch & Cook, 1980; B. Teucher, M. Olivares, & H. Cori, 2004). The addition of ascorbic acid at a 2:1 molar ratio to meals containing low to medium amounts of inhibitors is required (e.g., 20 mg AA: 3 mg iron). When inhibitors are high, ascorbic acid must be given at a molar ratio greater than 4:1 to improve absorption, (Teucher et al., 2004). Meat, fish, poultry (MFP factors) enhances nonheme iron absorption; research evidence suggests an enhanced effect on non-heme iron absorption by heme protein (R. F. Hurrell, Reddy, Juillerat, & Cook, 2006). According to Bjorn-Rasmussen E; Hallberg L 1979; the inclusion of different animal proteins that is poultry, fish, and meat in a meal enhances non-heme iron absorption in multiple folds (Engelmann et al., 1998; R. F. Hurrell et al., 2006). Studies further indicates cysteine-containing peptides in meat inhibit luminal inhibitors by forming luminal carriers in transporting iron (Taylor, Martínez-Torres, Romano, & Layrisse, 1986). The main contributor to iron deficiency anemia (IDA), aside from infections and inflammation is the iron bioavailability of foods consumed as previously stated. Different methods have been introduced to estimate iron bioavailability, to fully understand individuals' iron needs and to address the challenge. Below are the different methods in determining dietary iron bioavailability.

2.4.4 Iron Bioavailability Estimation Approaches

Several methods are used in determining iron bioavailability. Relatively, bioavailability considers absorption, digestion proportion of dietary iron, and its subsequent use by the human body.

2.4.4.1 Chemical Balance Method

This is an indirect approach of measuring iron retention in the body after dietary intake. The approach calculates the differences in intake and fecal matter iron followed by the exclusion of urinary iron to determine iron retained (Wienk, Marx, & Beynen, 1999).

2.4.4.2 Dialyzability Method

In the dialyzability method reported by (Kapsokefalou & Miller, 1991), dialysate bags are used to segment samples which were Casein, bovine serum albumin, plasma, and egg albumin. The dialysate bag has a base like PIPES buffer or $NaHCO_3$ that slowly increases the pH to a suitable level for intestinal enzyme action. The approach estimates dialyzable iron (soluble iron). In a study conducted by Kapsokefalou and Miller, 1991, the researcher's findings indicated the samples did not enhance D-Fe(U) above the control (Kapsokefalou & Miller, 1991).

2.4.4.3 Solubility Studies

Iron solubility approach, an in-vitro research study focuses on non-heme iron since heme iron is readily absorbed by the body. It is started by initial treatment with hydrochloric acid, (HCI) for pH adjustment to two; followed by digestion with pepsin. With the pH modification to six after the pepsin has digested further with pancreatin. After centrifugation, the released soluble iron is estimated in the supernatant (Au & Reddy, 2000).

2.4.4.4 Caco-2 cell model

Human adenocarcinoma cells known as Caco-2 cells are commonly used in this type of iron absorption studies. Cells grown in a cell culture medium at 37°C with a CO_2 concentration of 5% are used in an iron uptake experiment in the cell culture model. In-vitro digestion of the test meal is performed, as is the case with iron solubility. The cells are then given the digested test meal to see how much iron they absorb from the digest, (Au & Reddy, 2000).

2.4.4.5 Hemoglobin repletion approach

Hemoglobin repletion approach is used to compare the relative bioavailability of a test iron compound to ferrous sulphate. Male rats are kept on an iron-deficient diet for a period before being fed an iron replete diet (containing the iron compound to be tested) to increase their iron status. Rats are normally held in stainless steel cages with a wire rim. A 12-hour light-dark cycle is maintained for them. Throughout the study, food and deionized water are always available. Various techniques, such as tail incision, orbital socket blood draw, and cardiac puncture, are used to gather blood before and after repletion. Changes in haemoglobin or haemoglobin iron during the repletion cycle are plotted against either iron consumption or the iron level in the diet when the data is analysed, (Swain, Newman, & Hunt, 2003; WegmüLler et al., 2004).

2.4.4.6 Isotopic methods

The commonest methods for determining iron bioavailability are isotopic methods. Intrinsic labelling is the most precise process. The food is biosynthetically labelled with an iron radioisotope in this process. While the extrinsic tagging process, have two popular methods for measuring iron bioavailability. These are the whole-body counting system and red cell radioisotope iron incorporation. A radioisotope of iron is provided with the test meal or diet in the whole-body counting process, since other radioisotope of iron (Fe), does not emit gamma radiations, it is used. To function as a reference count, a radioisotope count is taken shortly (usually one hour) after the radiolabeled meal or diet is consumed. This count is taken to be 100 percent accurate. After about 10 to 14 days, the counts are taken again. Fe is continuously depleted after the first count because of faecal excretion. With red cell incorporation method, after an overnight fast, the subjects are fed a test meal that is labelled with either radio or stable isotopes of iron. Subjects are expected to fast for 24 hours after eating the test meal (only water is allowed for the next several hours). To measure radioactivity in the blood, blood samples are taken two weeks after the test meal is consumed, (Benito & Miller, 1998; Wienk et al., 1999).

2.4.4.7 Area under the curve for serum ion method

It is a good approach of comparing the absorption of two or three different compounds in the same subject. In the serum iron curve process, a post absorptive serum iron curve is created by taking a baseline blood sample, then administering a test meal/compound, and then taking several blood samples at regular intervals. Serum iron is measured in blood samples, and a curve for serum iron over time is established. Iron bioavailability is measured by the area under the curve for each subject (Wienk et al., 1999).

2.4.5 Algorithms for Prediction of Dietary Iron Bioavailability

Various arithmetical models have been created over the years for the estimation of iron bioavailability of diets. These are necessary because clinical and isotopic absorption measurements are unfeasible in population studies. Algorithms iron bioavailability models are designed considering host iron status, dietary iron-type (heme or non-heme), inflammation, then iron absorption inhibitors and enhancers. Several studies developed varying dietary iron bioavailability algorithms; (Monsen & et al., 1978) developed an algorithm that considered only iron enhancers (MPF: meat, fish, poultry, etc.) and Vitamin C (ascorbic acid)). The study quantified the body’s non-heme and heme iron absorption level for 0, 250, 500, and 1000 mg.

(Tseng, Chakraborty, Robinson, Mendez, & Kohlmeier, 1997), modified (Monsen & et al., 1978) algorithms by including inhibitors (Phytate, tea,) MFP, ascorbate in designing his algorithm. Hallberg and his colleague, (Leif Hallberg & Hulthén, 2000) also developed a detailed algorithm that factored interaction in dietary factors, 23µg/L ferritin absorption of heme and non-heme (constituting 40% absorption of reference dose of 3mg) modified to individual iron status. Furthermore, (Conway, Powell, & Geissler, 2007) used a ten (10) food group-based, animal meat, legumes (beans and lentils), whole grains cereals, dairy, tea, soya, high vitamins, fruits, eggs, and nuts to develop a multiple regression model where results were adjusted to absorption level of 40% of a reference dose of 3-mg. Table 2.2, discusses iron inhibitors and enhancers and their mechanism.

Table 2.2: Dietary Iron enhancers and Inhibitors

Enhancers	***Components/Mechanism***	**Inhibitors**	***Components/Mechanism***
Citric fruits (fruit juices), Vegetables.	**Ascorbic acid**: Creates soluble iron-ascorbate complexes that stay soluble in the intestine; and Fe3+ to Fe2+ reduction. Both support absorption.	Legumes, nuts, whole grain cereals.	**Phytic acid**: In the gut, where insoluble iron-phytate complexes are formed.
Fish	**Animal Tissue/Protein**: Iron binds to digestion components, primarily proteins, forming soluble complexes.	Milk (Cow's), diary Products	**Milk Protein:** Iron is closely bound by whole milk casein and s-casein phosphopeptides, preventing absorption.
Poultry, Meat	**Animal Tissue/Protein**: Iron binds to digestion components, primarily proteins, forming soluble complexes.	Tea, Cocoa, Coffee	**Polyphenols**: Production of insoluble iron complexes in the intestine

Adapted from (Blanco-Rojo & Vaquero, 2019).

2.5 Conventional Food Processing Methods in Making Non-heme Iron Bioavailable

Non-heme iron is the main iron source for vegetarians and several individuals globally. However, the iron absorption rate of non-heme is often inhibited by different substances such as phytic acid, polyphenols, tannins, etc. Approaches in making the iron absorbable to the population that needs it most are necessary. Studies indicate conventional practices such as cereals/whole grains soaking, milling, fermentation, germination/sprouting, and combined practices potentially makes dietary iron from plant-based foodstuffs more bioavailable (Oghbaei & Prakash, 2016). The following discusses some of these practices:

2.5.1 Soaking

Soaking involves the immersion and holding of food crops such as cereals and grains in water to increase its soluble minerals such as iron by passive diffusion and phytate leaching. Ruel and Levin (2000), observed the increase in soluble iron by ten-fold by 24hours soaking of flour. Also, an in-vitro iron bioavailability of sorghum varieties increased iron in ranges of 8.02 to 9.07-10.72% following soaking (Afify, El-Beltagi, Abd El-Salam, & Omran, 2011). Soaking has been reported as a practice that improves plant-based foods' bioavailability as well as the hydrolysis of polyphenols that inhibits iron absorption (Luo & Xie, 2014).

2.5.2 Dehulling

Dehulling is the method of removing the exterior components (hull) of seeds and grains. Dehulling is often followed with other food process practices such as milling, soaking, etc. In their study, (Pal et al., 2017); asserted cereal and grains dehulling reduced the content of tannin, phytate, which inhibited iron absorption. This was attributed to the build-up of a majority of anti-nutrients in the outer covering (hulls) of legumes*: (Pal et al., 2017).*

2.5.3 Germination

During cereal germination, the plant food product is held for 72hours in a dark area, with sporadic water sprinkling on the food crops (grains) to induce sprouting. During cereal germination, phytic acid is broken down as phytase activity increases during the germination. Likewise, tannin and polyphenols impact are reduced during cereal germination. (Laminu, Sheriff, & Alhaji, 2014); observed a 65% reduction in phytic acid and 64% of tannin content with an iron surge of a germinated wheat; (Laminu et al., 2014). Similarly, in a study by (Abioye, Ogunlakin, & Taiwo, 2018), on the germination of finger millet for 0-96 hours, the researchers saw a reduction of 50%

phytate and tannin (Abioye et al., 2018). Germination provides beneficial effects of fermentation on the viscosity and nutrition of cereals for individuals in a population, (Nkhata, Kamau, Ayua, & Bosco, 2018).

2.5.4 Fermentation

Fermentation employs a biochemical modification of food products (cereals and grains) through enzymatic and microbial action. The process metabolises simple sugars such as glucose and lactose through the action of yeast and lactic acid bacteria to produce a product of alcohol, lactic acid, and CO_2 (carbon dioxide). Fermenting of cereals (Pearl millet) is proven to reduce tannin and phytic acid by 71% to 72% distinctly, hence increasing iron concentrations (Laminu et al., 2014). The lowering of inositol phosphate with the action of phytase enzymes during fermentation makes micronutrients bioavailable (Gupta et al., 2015).

2.5.5 Thermal Processing of Food

Thermal food processing employs temperature controls and time, in sterilization or pasteurization of food preparation such as blanching, pressure and microwave cooking. Studies reported a rise in iron bioavailability of cereal-based foods prepared by thermal food processing (Jing, Yuwei, Zhenping, & Qian, 2017; Sreeramaiah, Platel, & Srinivasan, 2007). In their research study, (Sreeramaiah et al., 2007) reported that, heat treatment improved iron bio accessibility in all of the dietary grains examined, including rice, finger millet, sorghum, and wheat. Hence, heat treatment of grains improved iron bioavailability, (Sreeramaiah et al., 2007).

2.5.6 Combined Processes

Combined food processing is the integration of two to more methods of conventional food processing approach. Its processes is reported to improve the bioavailability of cereal/plant-based iron. Luo and Xie (2014) and other research studies indicated a combined food processing technique of soaking before cereal germination decreased phytic acid content, thereby enhancing iron bioavailability (Hemalatha, Platel, & Srinivasan, 2007; Luo & Xie, 2014).

2.6 Measures for Iron Status Improvement and Upkeep in Low Resource Setting Areas

Iron status improvement techniques that can make a substantial impact on the targeted local population’s condition and iron status are the approaches that would possibly succeed. Such approaches ought to be feasible, cost-effective, culturally acceptable, and locally implementable.

2.6.1 Dietary and Staples Based Selection Approaches

2.6.1.1 Millet, sorghum, maize, and Legumes (high in iron as well as phytic acid)

Staples supports the main energy requirements globally and especially in developing nations; millet, sorghum, maize, and legumes which are high in both phytate, and iron are consumed extensively in most African countries and Latin America; forming part of their important diets. To assist in the iron uptake from these crops, strategies in lowing the phytic acid contents and tannins level without losing the iron are essential. Studies suggest germination/leavening and fermentation of these staples could potentially increase the iron bioavailability as well other minerals. The inclusion of ascorbic acid (vitamin C) to meals also increases non-heme iron absorption, (Kathryn Beck, Cath Conlon, Rozanne Kruger, & Jane Coad, 2014; Brazaca & Da Silva, 2003; S. R. Lynch & Cook, 1980). Iron fortification of foods is easier if staples are centrally processed, unfortunately, this is not the case in most low resource setting communities (L H. Allen & Ahluwalia, 1997; Indumadhavi & Agte, 2007; Rollán, Gerez, & Leblanc, 2019).

2.6.1.2 Brown Rice and Wheat (Has moderate iron and phytic acid)

Low socioeconomic populations in several developing countries consume staples such as brown rice and wheat. Milling of brown rice moderately high in both iron and phytate decreases the iron absorption inhibitors content by half (50%) in the brown rice and about two-thirds in wheat. Since the same amount of iron and phytate are removed, the iron molar ratio after milling remains unchanged; rather, the iron content becomes more bioavailable due to the phytate reduction. Unprocessed cereals/grains high in phytate contents affect the efficacy of standard fortification unless vitamin C (ascorbic acid) intake is considered (L H. Allen & Ahluwalia, 1997; Huang, Glahn, Welch, Fukai, & Rerkasem, 2006; Trinidad P. Trinidad et al., 2009).

2.6.1.3 White flour, white rice (moderately high in phytate, low in iron)

White flour made unleavened bread, which are high in phytate and iron is patronized extensively in some places around the world, (Reinhold, 1972; Turksoy, Ozkaya, & Akbas, 2010). Similarly, white rice which has a low iron high phytate fraction, is highly patronized in some Asian countries and some areas of Latin America. Reducing phytate in white flour, can enhance the iron bioavailability, yet the low iron content will remain unchanged, (Sanz-Penella, Laparra Llopis, Sanz, & Haros, 2012). In instances as this, ascorbic acid, utilization will be beneficial, also ways to increase fish, meat, and poultry intake and iron fortification of white wheat flour and rice must be implemented (L H. Allen & Ahluwalia, 1997).

2.6.1.4 Reduction in Phytate Intake, Improved Vitamin C In-take, and other Minerals

To reduce phytic acid intake and improve iron bioavailability, cereals and grains should be fermented at home before large-scale grain flour meal preparation for public consumption. More so, locally available food crops with sufficient vitamin C contents ought to be consumed to enhance iron bioavailability, (B. Teucher et al., 2004). Local ascorbic sources include oranges, grapefruits, guava, pawpaw, mangoes, etc. (L H. Allen & Ahluwalia, 1997). Iron deficiency in some low resource settings communities is often accompanied by micronutrient deficiencies, such as vitamin B12, and folate. The target population's local health and specific micronutrient needs should be assessed and addressed accordingly (L H. Allen & Ahluwalia, 1997; El Ati-Hellal & Hellal, 2021).

2.6.1.5 Adequate Fish, Meat, and Poultry Consumption

Animal products (proteins) consumption is often limited in some low resource settings communities due to price constraints; however, protein intake is necessary to enhance iron bioavailability. The right assessment for a population's regular requirement of protein and amino acid(AA), according to the World Health Organization's (WHO) expert report on human nutrition (2007), is 105 mg nitrogen/kg a day or 0.66 g protein/kg per day, (Schönfeldt & Gibson Hall, 2012). The target population ought to be motivated to practice home/backyard animal farming. These include poultry, rabbits, goats, sheep, grasscutter, and fish farming where produce would be consumed by households and not sold (L H. Allen & Ahluwalia, 1997; Leroy & Frongillo, 2007).

2.6.1.6 Other micronutrients intake

In some parts of developing countries, iron deficiency can be followed by other micronutrient deficiencies. Where appropriate, strategies to enhance iron absorption should be evaluated in terms of their potential to increase total nutritional uptake or bioavailability. This includes higher uptakes of retinol, vitamin B12, riboflavin, and absorbable zinc. When more animal products are consumed; it increases zinc, calcium, and copper absorption, as well as the content of certain B vitamins and higher uptakes of retinol, vitamin B12, riboflavin, and absorbable zinc. (L H. Allen & Ahluwalia, 1997; Bailey, West Jr, & Black, 2015).

2.6.2 Multiple/Combined Methods

There may be several ways to increase the amount of iron consumed from food that is all equally beneficial. For example, adding synthetic ascorbic acid or a similar amount of crops such as cauliflower, ground beef, or ferrous sulfate to meals with high levels of phytate and low levels of enhancing factors increases iron absorption by two to three folds. Similarly, the ascorbic acid intake will need to be increased to allow for better absorption of fortifying iron from staples with high phytic acid content. Multiple methods should be considered wherever possible since the interventions that can be used to improve iron absorption are usually cumulative, (L H. Allen & Ahluwalia, 1997; Leif Hallberg & Hulthén, 2000).

2.6.3 Treatment of anemia of inflammation

Iron deficiency anemia (IDA) prevention methods necessitate the identification and treatment of the underlying sources of inflammation. This requires emphasizing the significance of health resources for chronic inflammation, helminth infections (hookworms, whipworms, and roundworms), and malaria (clinical and subclinical) treatment in reducing anemia in low resource settings communities. Interventions and food-based approaches among affected population and communities can be effective when all contributing health factors of iron deficiency anemia are effectively treated, (Chaparro & Suchdev, 2019; Loukas et al., 2016; Osazuwa, Ayo, & Imade, 2011).

2.6.4 Reduction in tea or coffee intake with meals

Tea and coffee are generally consumed with meals in societies where this practise is prevalent, and efforts must be made to raise awareness about the effects of this practise on iron absorption, (Morck, Lynch, & Cook, 1983). To find appropriate substitutes, ideally juices high in ascorbic acid must be consumed with meals and tea or coffee later. Success with this can be difficult to achieve since this practice requires people to remove conventional drinks or stop consuming them within two hours of a meal. However, it could be effective in populations at high risk of iron deficiency; for example, mothers could be educated about the dangers of giving coffee or certain forms of tea to infants and children, and pregnant women could be encouraged to change their coffee or tea-drinking habits, (L H. Allen & Ahluwalia, 1997; Sung, Choi, Kim, Kim, & Shin, 2018).

2.6.5 Improving ascorbic acid (Vitamin C) consumption

Fruit juices, fruits, and certain vegetables are all potential ascorbic acid sources and should be consumed within communities. For each possible food source, data on acceptability, cost, availability, seasonality, and amount usually consumed versus amount that would need to be added to achieve a substantial increase in iron absorption; the meals with which it is consumed, and the non-heme iron content of those meals must be obtained for appropriate population groups. Ease of preparation; ascorbic acid loss during storage and preparation; and attitudes and opinions regarding its flavour and other desirable or undesirable characteristics must be known. The data can be generated from existing nutritional data, as well as village heads, pilot research, and survey implementation in the population (L H. Allen & Ahluwalia, 1997; Carr & Rowe, 2020).

2.7 Behavioral Change Communications (BCC)

To promote compliance in the use of dietary iron, effective antimalarials, and anthelminthics, behavioural change communications (BCC) are required during contact with mothers, infants, and the community at large. The following should be emphasized in communications: Good breastfeeding practises; full immunisation for women, infants, and families; increased consumption of energy, iron-rich foods (meat), other micronutrients (vitamins A and B-12 and folic acid), and iron enhancers (vitamin C, germinated/fermented foods) intake. Reduced iron inhibitor (tea and coffee at meals) consumption; nightly use of insecticide-treated (ITB) bed nets; modern family planning methods that reduce iron loss; good water and sanitation practises; and awareness of potential complications in pregnancy, delivery, postpartum (bleeding), and childhood diseases, as well as what to do about such situations, (World Bank, 2004).

2.8 Conclusion

In this study, determinants of iron deficiency (ID) and pathways of improvement among populations in low resource setting communities were reviewed. Contributing factors to iron deficiency anemia (IDA), which includes physiological (pregnancy, growth spurt in adolescents, menstruation (blood loss)), socio-economic issues, malaria, hookworm infestations, nutritional considerations such as iron, vitamin A, folate, vitamin B_{12} deficiencies, and the approaches for reducing these incidences especially in developing regions were presented. Consumption of cereals, seeds, and grains that are plant-based foods (non-heme) iron sources were determined to be higher in low resource settings communities than animal products (heme) intake. These plant-based food sources were found to contain high phytic acids that hinder its food’s iron absorption after intake. Iron absorption enhancers, which includes foods high in ascorbic acids, and meat, fish, and poultry (MFP) with heme iron consumed with the plant-based food support better iron bioavailability. Polyphenols, calcium, teas, and coffee were also considered to hinder plant-based foods' iron absorption. Conventional food processing practices such as soaking, milling, fermentation, germination/sprouting, and combined practices was considered effective approaches in reducing phytate contents in cereals, seeds, and grains. It was prudent that underlying health situations contributing to iron deficiency anemia (IDA) in developing regions should first be treated before any dietary-based approach to iron deficiency (IDA) prevention can be effective. Important dietary methods of iron deficiency anemia (IDA) mitigation proposed include adequate fish, meat, poultry, and fruits high in vitamin C consumption, diverse food sources with vitamins A, B^{12}, B^{2}, zinc, calcium, copper intake, with tea, polyphenols, and coffee being replaced with citrus juices or consumed two hours after plant-based non-heme intake.

2.9 Connecting text

The previous chapter focused on the etiology of iron deficiency anemia (IDA) with a major emphasis on dietary contributions to the iron deficiency anemia (IDA) situation especially in low resource setting communities and how the condition can be reduced or prevented through dietary modification approaches besides treatment of underlying health contributions of the condition.

The next chapter is on the thesis objective two (chapter three) which primarily examines the trends and evolving strategies of managing iron deficiency anemia collectively in a population.

Chapter 3 - Iron Deficiency and Anemia in Less Developed Countries: Reassessing Trends, Conventional and Evolving Methods of Mitigation

Abstract

Iron deficiency is a recognized WHO public health issue, with prevalence in both developed and under-developed nations. Iron deficiency and anemia prevention and management in all categories of population with different iron requirements necessitate coordination of various interventions. In this review, current approaches to controlling iron deficiency anemia (IDA), are presented. The prevention approaches which include iron supplementation, food fortification methods, and biofortification, diverse food-based in-take approaches with education, iron ingot and iron pot use in cooking, were investigated. The WHO recommended food fortificants and their food vehicles were also examined. Finally, the impact, toxicity, and recommendation of dietary iron, dietary iron sources, and recommendations for vulnerable groups in developing regions were assessed and presented.

Key Words

Supplementations, fortification, fortified, fortificants, biofortification, food vehicles, iron, dietary

3.1 Introduction

Iron deficiency, an underlying cause of nutritional anemia had 1.62 billion worldwide prevalence, with the highest incidences among pre-school infants (47.4%) and lowest in men (12.7%) from 2008 world health organisation (WHO) data. In 2019, global anaemia prevalence among women of reproductive age was 29.9%, equating to more than half a billion women aged 15 to 49 years. Non-pregnant women of reproductive age had a prevalence of 29.6%, while pregnant women had a prevalence of 36.5 %. Anaemia was found in 39.8% of children aged 6 to 59 months, resulting in 269 million children suffering from anaemia, (WHO, 2008, 2022). Iron deficiency and anemia are the world health organisation (WHO) reported public health challenges, with a major incidence in less developed countries (Chaparro & Suchdev, 2019; WHO, 2008; WHO/UNU/UNICEF, 2001). Africa and South-East Asia, have half of the women population and two-thirds of school-aged infants affected by iron deficiency. African regions has the highest incidences of anaemia in children under the age of five, at 60.2%, (WHO, 2005, 2022). The world health organisation (WHO) estimates one out of every four persons is affected by anemia with the most at-risk group being expectant or pregnant women and preschool-aged infants. Nutritional anemia is referred to pathological circumstances in which human blood hemoglobin levels fall to a low percentage because of several or a single nutrient insufficiency. However, iron deficiency is the main attributing cause of global nutritional anemia; while folic acid and vitamin B_{12} have minimum prevalence (Kotecha, 2011). In several instances, aside from reduced dietary iron intake, pregnant women iron deficiency anemia is reflective of their physiologic expansion thus the high iron demand of the growing fetus from the second to the third trimester, unless the individual's local conditions dictate otherwise, such as in cases of infections, malaria, etc., or some other factors, like hereditary disorders (alpha and beta thalassemia) which could potentially affect iron status (WHO, 2005). Likewise, school-aged children and adolescents need enough dietary iron to support the iron requirement for their rapid growth and development.

Iron is a vital micronutrient; it constitutes an integral component of hemoglobin, necessary for oxygen and CO_2 (carbon dioxide) transport, (Hamamy & Alwan, 2015; Patel Sagar, 2021). Iron forms part of immune system enzymes and energy production cytochromes, (Haschka, Hoffmann, & Weiss, 2021). Iron deficiency detectable indicators are serum ferritin low concentration which is reflective of iron stores, progressive anemia (low blood hemoglobin), (Johnson-Wimbley &

Graham, 2011; Miniero et al., 2019). Iron deficiency reduces work output (energy balance). It is the leading contributor to infants' poor cognitive performance and impaired behavior; prematurity/low birth weight as well as adverse pregnancy outcomes, (Hamamy & Alwan, 2015; Moreno-Fernandez, Ochoa, Latunde-Dada, & Diaz-Castro, 2019).

In populated countries with limited resources, hunger and food inadequacy are avoided through the intake of plant-based food crops and tubers with little consumption of expensive animal products (L.H Allen, 1991; Lindsay H. Allen, 2009; Muller, 2005). The leading contributing factor of diminished iron status in less developed countries and low resource setting communities according to the world bank and the world health organisation (WHO), is the intake of low-quality diet, other than quantity; (WHO, 2020; World Bank, 2004). However, except for the low bioavailability of plant/cereal-based non-heme iron, populations dependent on plant-based diets could potentially meet and even exceed minimum dietary iron requirement than animal products consumers; (Murphy, Beaton, & Calloway, 1992).

Practices directed at the improvement of dietary iron are essential in reducing anemia and iron deficiency prevalence especially in low resource countries where their greater dietary proportion is plant-based.

This paper reviews; trends and evolving methods of iron deficiency and nutritional anemia mitigation in less developed countries. The objectives of the study are (1) to examine the current ways of iron deficiency prevention approaches: that is through iron supplementation, biofortification /iron fortification, dietary enhancement, and food diversifications, etc., (2) evaluate commonly supplemented, biofortified, and fortified foods stuffs and their accessibility and to (3) establish the impact, toxicity, and recommendations of the dietary iron for individuals and at-risk populations.

3.2 Current Approaches of Controlling Iron Deficiency Anemia

Strategies aimed at reducing and preventing iron deficiencies are often selected based on an individual's or the community's peculiar conditions, in some instances, integrated approaches such as underlying health treatment and control measures precede the specific iron interventions. Common practical approaches to iron status improvements include (1) mineral (iron) supplementations, (2) iron fortification/biofortification programs, (3) dietary enhancement, and food diversifications and other methods such as the use of iron pots in cooking, etc. These approaches are discussed below.

3.2.1 Iron Supplementation

Supplementation refers to the giving of oral pills, capsules, syrups as supplements to a specified population either daily (continuously) or at intervals (intermittently). In situations of 40% prevalence of iron deficiency anemia in a community, (WHO/UNICEF/UNU, 1998), recommends a general iron supplementation program for affected groups. Iron supplementation is extensively applied to improve iron status and to avoid iron deficiency and anemia among vulnerable populations such as during antenatal for expectant mothers or iron-deficient newborns and young infants. Oral iron preparations available as supplements are made into different forms: ferric sulphate, ferrous sulphate, ferrous gluconate, ferrous fumarate, amino acid chelate, and ferrous bisglycinate, (Stoffel & et al., 2020). The effectiveness of iron supplementation is largely determined by the iron deficiency and anemia prevalence in the affected community. Anemia at-risk populations such as expectant women benefit from iron supplementation thereby curtailing maternal anemia and iron deficiency possibilities; (Peña-Rosas & et al., 2015). Oral iron supplementations are often limited because of their related side effects such as epigastric gas, nausea, vomiting, and low adherence; (Beutler, Hoffbrand, & Cook, 2003). However, studies indicate that intermittent supplementation or low dosage can minimize the side effects occurrences in oral iron therapy (Cavalli-Sforza Tommaso, 2005).

3.2.1.1 Intermittent and daily supplementation

Iron absorption from supplements dispensed intermittently is recorded as having higher absorption rate, with potential induced changes related to intestinal iron metabolism and transport; (M. Ruivard & et al., 2009; Marc Ruivard et al., 2006). In a systematic review study, on non-pregnant women intermittent (once, twice, or thrice a week) iron supplementation evaluation compared to a non-intervention, found that, intermittent iron supplementation had 4.6g/L and 8.3 mg/L ferritin enhancement of hemoglobin with anemia reduction of 27%. However, in comparison with daily iron supplementation, the researchers reported, a 26% likely anemia risk of the group receiving intermittent iron supplementation in contrast to those taking daily iron supplements: (Fernández-Gaxiola & De-Regil, 2019; Fernández-Gaxiola Ana, 2011).

3.2.1.2 Iron Supplementation and Malaria Rise Risk

The World Health Organization (WHO, 2007) and united nations children's fund (UNICEF 2006), directives suggest that iron supplementations in malaria-endemic communities for young infants who are iron-deficient, or anemic are only effective and diminishes infant mortality when underlying health conditions such as malaria, parasitic infections are first treated; *(WHO, UNICEF, 2006, 2007)*. An increased risk of adverse outcomes following iron supplementations in low resource communities where malaria prevention and primary health care are constrained has been reported*; (Sazawal & et al., 2006)*. Hence, iron supplementation among infants below two years of age residing in malaria-endemic communities requires prior malaria infection screening and treatment for only iron-deficient infants. Iron supplementation is allowed for under six months old low-birthweight and preterm infants in malaria-endemic communities, who sleep beneath beds covered with bed nets that are insecticide-treated, and efficient anti-malaria treatment offered them when they are affected by malaria sickness; *(WHO, UNICEF, 2006, 2007).*

Iron-rich fortified complementary feeding is recommended for infants six months and beyond according to WHO guidelines since complementary foods give functional iron dosages and not higher iron contents; *(WHO, 2011)*. In instances of severe clinical anemia symptoms in low resource communities with limited testing facilities and equipment, oral iron is provided following prompt diagnosis and infection management. Due to folate possible interferences with antifolate antimalaria treatments folate supplementation is not suggested; *(WHO; 2006)*.

3.2.2 Iron Food Fortification

Food fortification is the addition and raising of micronutrient (iron) of processed foods. This is to improve the nutritional values of the food components, to correct and support public nutritional status and wellbeing with less related health risks; *(WHO, 2019)*. Fortification also enriches foods with vitamins, and amino acids, providing sufficient but not an excess of specified nutrients in a diet. Ferrous sulphate, electrolytic iron powder, ferrous fumarate, and ferric pyrophosphate are composites that can be used for iron fortification of foods; (FAO/WHO, 2006).

Food fortification ensures the following (1) *restoration*: adding specific nutrients to a food crop that restores naturally present nutrients in the crops that was lost through processing such as de-branning and milling. (2) *nutritional equivalence*: as in substitute products made to have same nutritive value as the actual food products (3) *The composition of food as a unique purpose food product*: as in iron-fortified complementary foods*;(FAO/WHO, 2006).*

Food fortification is also seen as the addition of single or multiple micronutrients to foods to boost the intake of these micronutrients to attain added health benefits, (Das & et al., 2019). National and regional fortification quantities differs; just a single micronutrient can be used to enhance foodstuffs, as in iron food fortification projects, likewise, a combination of multiple nutrients, such as iron, vitamin B^{12}, and folate fortification, can be applied (Das & et al., 2019; Olson, Gavin-Smith, Ferraboschi, & Kraemer, 2021). The parameters used for public health food fortifications depend mostly on the degree of fortification, fortificants, bioavailability, and the magnitude of consumed fortified foods, (WHO, 2006). Generally, populations extensively benefit from the fortified products through the product's frequent usage.

As revealed in several scientific studies, the public health goal of food fortification program is (1) Averting and minimizing micronutrient deficiency occurrence in a specified group of people or a population (2) Participating in the improvement of a known or identified micronutrient deficiency among a given group of persons (3) nutritional level enrichment potential appropriate for dietary changes and (4) tool for health improvement and maintenance to impede disease occurrence; (Lindsay H. Allen, 2006; FAO/WHO, 2006).

3.2.2.1 Food Fortification Types

Fortification of foods are done in various ways. A large populations' commonly consumed foodstuffs can be fortified, this is referred to as mass fortification, this practice could be mandatory to support the micronutrients needs of the population. Fortification can as well be done for specific subgroups such as in complementary foods iron fortification for iron-deficient children, or targeted fortification for displaced individuals. The food fortification programs could be done voluntarily or mandatorily for health purposes. Manufacturers fortification of food products sold in the marketplace (market-driven fortification) are often required by government regulations; (Lindsay H. Allen, 2006; FAO/WHO, 2006).

3.2.2.2 Mass fortification

Mass fortification is a process of the incorporation of one of several micronutrients into the general public's frequently used foodstuffs, such as cereals and grains, and milk fortifications. These practices are often mandatory, and government regulated. In instances where a population is confronted with undesirable risks to their public health or the deficiency of a particular micronutrient, mass fortification of food is enforced and practiced. In most instances, the micronutrient deficiency could be due to low intake of specific nutrients such as iron deficiency anemia caused by low dietary iron intakes. Such populations usually benefit from iron fortification of foods to prevent iron deficiency negative health outcomes, poor infant cognitive development and function in children, and mortality; (Lindsay H. Allen, 2006; FAO/WHO, 2006).

3.2.2.3 Targeted Food Fortification

In food fortification targeted programs, a subgroup in the population's foods are fortified to enhance the intake of nutrient missing from diets, an example is the instances of foodstuffs made for school feeding programs, iron-fortified bakeries made for expectant mothers (or iron supplements) and meals made for emergency feeding of displaced populations (directed by the world food program (WFP), that targets women (lactating or pregnant) and young infants; (Lindsay H. Allen, 2006; FAO/WHO, 2006).

3.2.2.4 Market-driven food fortification

In market-driven food fortifications, commercial food manufacturers in a business-focused scheme, include specific levels of single or multiple micronutrients to foods being processed. This type of food fortification even though done voluntarily, is implemented based on set governmental regulatory thresholds. Market-driven food fortifications play a substantial public health role by reducing micronutrient deficiencies such as in iron fortifications. It also improves supplies of sufficiently difficult to add micronutrients that are best done through mass fortifications as in condiments and staple foods fortifications with iron, folic acids, or calcium. In developing nations, the market-driven food fortification effect on public health is minimal because of the limited availability of processed foods owing to the cost. Urbanization can increase access to market-driven fortified foods where manufacturers are required to abide by quality control assurance measures in the making of fortified food products for the public; (Lindsay H. Allen, 2006; FAO/WHO, 2006).

3.2.2.5 Other Fortification types (household and community)

In several countries, household food fortification is practiced, in an effort of making and accessing practical ways of micronutrient additions to meals at the household levels especially infant complementary foods preparation. Crushed tablets and micronutrient powder assist in enhancing local foodstuffs for feeding young children in low resources setting communities where mass food fortification may not be applicable. Food fortification at the community level is still at the experimental stage due to the cost of required equipment and the uniformity of micronutrient incorporations; (Lindsay H. Allen, 2006; FAO/WHO, 2006).

3.2.2.6 Staple Foods Biological Fortification (Biofortification)

Staple foods' biological fortification includes genetic modification of crops, agronomic practices, and conventional plant breeding to enhance their nutritive values or their bioavailability. In biofortification, food crops' nutritional contents are boosted during sowing or plant developments, this practice represents sustainable ways of controlling specific nutrient deficiencies; (Malik & Maqbool, 2020). Biofortification constitute a plant breeding potential to rise plant micronutrient standards such as in various legumes, tubers, and cereals. For instance, some cereals like rice and legumes can be biofortified for high iron levels (Lindsay H. Allen, 2006; FAO/WHO, 2006). Biofortification of crops is a feasible strategy of meeting micronutrient needs for a population that is unable to implement food fortification and supplementation programs; such as people residing in developing and low resource communities because agriculture produce often constitutes their main sources of foods and nutrients (Vasconcelos, Gruissem, & Bhullar, 2017). Moreover, the commonest of all the food biofortification approaches is the agronomic practices of improving minerals levels with the addition of inorganic compounds of applicable minerals to the fertilizer. While conventional breeding utilizes natural practices of sexual and nonsexual crop reproduction; in genetic modification method, new genetic plant information is directly inserted into the plant's genome for cultivation; (Salonia et al., 2020; C. Zhu & et al., 2007; Chenqiao Zhu et al., 2019).

Genetic modification can be used in increasing iron accumulation in rice. Iron's concentration of two folds was attained through the ferritin in rice gene expression. Aside from improving iron contents, iron bioavailability factors could also be controlled through the introduction of the phytase gene which yielded a 130-fold increment of the phytase enzyme expression. The bioavailability of iron is further enhanced by cysteine-rich peptides, the gene expression of the encoding cysteine-rich metallothionein-like protein present in rice can help the absorption of iron; (Lucca, Hurrell, & Potrykus, 2002; Welch & Graham, 2002). Similarly, phytic acid is broken down and minerals are released as enhanced through the expression of phytase in crops. Low-phytate crop strains of barley, rice, maize, and soybean are alternative strategies and breeding approaches; (Raboy, 2002).

In a study, during a 9-month double-blind randomised feeding trial in nine convents in Manila, Philippines, the efficacy of eating iron-biofortified rice (Oryza sativa) was investigated. Iron-biofortified rice (3.21 mg/kg Fe) or a local variety of conventional rice (0.57 mg/kg Fe) were given to participants at random. In comparison to the control rice, which provided 0.37 mg of iron per day, the iron-biofortified rice provided 1.79 mg of iron per day to the diet. When compared to regular rice, iron-biofortified rice raised serum ferritin concentrations ($P = 0.02$) and total body iron concentrations ($P = 0.05$) in non-anemic women. After accounting for baseline values and daily rice consumption, the results showed a 20% iron increase. Overall, non-anemic women with the lowest baseline iron status and those who consumed the most iron from rice observed the highest improvements in iron status, (J. L. Finkelstein, Haas, & Mehta, 2017).

3.2.2.7 New method of iron fortification

New iron fortificants are currently being produced according to research studies. Nanotechnology engineering creates nanosized iron that can be absorbed quickly through physiological pathways (Gharibzahedi & Jafari, 2017). However, since too much free iron in biological systems is dangerous, industrial processing must be performed under strict safety conditions (Mahler et al., 2012). It was found that Fe (III) oxide nano particulates were absorbed by the ferric pathway and had no adverse haematological or organ effects in an animal model (Susana Chamorro, 2015), implying that customised iron forms and fractions with the goal of regulating iron solubility and absorption can be produced. Another alternative found in literature is ferritin nanoparticles. Ferritin is a large protein capable of storing large quantities of iron, and it may be a good source of iron, though the exact mechanism of absorption is unknown. Synthetic ferritin-mimetic nano particulates have thus been created and tested in isolated duodenal loops or cultured cells (Latunde-Dada et al., 2014).

3.2.3 Diverse Food-Based Approaches and Education

Food-based approaches focus on strategies to enhance household's nutrition through access to and the intake of micronutrient-rich diverse dietary foodstuffs. It also focuses on the diverse dietary foods' availability, consumption, bioavailability, and enhancement in meals (FAO/UN/CAB International, 2011). The International Conference on Nutrition (ICN) that advocates for the mitigation of malnutrition of micronutrients emphasized the primarily prioritizing and utilization of food-based approaches for a population with iron and vitamin A deficiencies with a focus on available foods and local food traditions (FAO, 1992).

Dietary approaches do not only limit iron deficiency anemia but micronutrient malnourishment from inadequate diverse diet intake and limited absorption of mostly iron, vitamin A, folate, and B12, which are the main causes of nutritional anemia; *(WHO, 2017)*. Behavior changes and applicable dietary education focusing on knowledge impact of more intake of micronutrients absorbable food crops, less consumption of inhibitors of dietary iron, mineral, and vitamin-rich foods intake, as well as meal preparations are important in minimizing iron deficiency anemia; (Allen Lindsay, 2008).

Intake of orange/yellow fruits and dark green leafy vegetables have been reported by studies to enhance vitamin A levels (Debelo, Novotny, & Ferruzzi, 2017); although, dietary carotenoids must be converted to retinol for the body's use (FAO, 2011). The addition of flesh foods (meat and poultry) in a diet can improve the fat content of the food as well as enabling the absorption of carotenoids and vitamin A; (Tontisirin, Nantel, & Bhattacharjee, 2002). Monotonous plant-based (non-heme) diets with less meat in a population result in low dietary iron availability with below 10% iron absorption:(FAO, 2011). Food-based approaches emphasizes dietary quality through increased consumption of vegetables, fruits, and animal protein intake and less intake of low nutritious carbohydrates.

Animal food products support the body with B-12 vitamins, bioavailable iron, retinol, choline, riboflavin, vitamin D, and E; (Allen Lindsay, 2008; FAO, 2011). Plant food sources scarcely meet iron and micronutrient requirements due to non-heme high phytic levels requiring the intake of ascorbic acid-rich foods and beverages to reduce the chelating effect of the phytic acid; (Teucher et al., 2004), and improve absorption and hence iron status. Folate food sources include beans, nuts and grains, fruits and fruit juices, dairy products, dark green leafy vegetables (Debelo et al., 2017).

Since breast milk is limited in iron, infants' complementary foods must be enriched with foods high in iron such as fish, meat, and animal offal (chicken liver). Non-heme food sources such as spinach, green leafy vegetables, and legumes should be incorporated into infants' foods; (Lopes & et al., 2018).

Dietary/food-based approaches education must be directed towards the vulnerable population (pregnant and lactating mothers, young children, and infants) in the society especially in a low resource setting community. According to (Tontisirin et al., 2002), a good daily dietary combination must include staples, pulses, animal food sources, green leafy vegetables or fruits at a single meal, also food preparations of stir fry and steaming are considered good practices that increase micronutrients bioavailability. Guidelines for infant breastfeeding must be observed and followed with complementary food provisions that meet energy, micronutrients, and protein requirements. Delayed complementary feedings result in iron deficiency and stunting among children. Plant-based diets for young children incorporated with fish powder or chicken liver yields increased iron absorption; (Tontisirin et al., 2002).

3.2.4 Other Methods of Iron Deficiency Prevention

In practice in some localities is the use of iron ingots name 'lucky iron fish' or 'happy fish' used in boiling soup or water; (Armstrong, 2017). Iron ingots have been reported to release and meet 40-75% of women of reproductive ages daily iron requirements depending on boiling duration, with no reported toxicity; (Armstrong, 2017; Charles, Dewey, Daniell, & Summerlee, 2011). Also, the cooking of foods in iron-containing cookware in developing and low resource communities have been reported by studies, the iron from the cookware leaches into the meals during the cooking process and supports iron requirements when consumed (Alves, Saleh, & Alaofè, 2019). Table 3.1 provides iron deficiency anemia (IDA) interventions for specific population in low resource setting communities.

Table 3.1:Iron deficiency anemia (IDA) Interventions for Specific Groups in Low Resource Settings

Target Population	Interventions	Study Description	References
Babies	Maternal adequate iron supplementation pre-conception and during conception improving maternal and infant stores.	Newborns accumulate iron stores in-utero for the first few months after birth since breastmilk is low in iron.	*(Cerami, 2017; Parul Christian, 2010a; Theresa O. Scholl, 2011).*
Infants and young children	Iron-fortified complementary foods with ascorbic acid to improve iron absorption	Iron-fortified meat-based complementary meals. Iron-fortified infant complementary foods. Multiple micronutrient powder home fortifications. iron-fortified Oat with Vitamin C	*(Ma et al., 2016)* *(Dobe, Garg, & Bhalla, 2018; Zlotkin et al., 2004).* *(De-Regil & et al., 2011)* *(Trinidad et al., 2014)*
Women of reproductive ages	Iron supplementation, Iron fortification and Iron biofortification, Diverse foods approach	Elemental Iron supplements and folic acid. (20% or higher anemia prevalence). Mixed diets with iron absorption enhancers and fewer iron inhibitors	*(Fernández-Gaxiola Ana, 2011).* *(Nestel, Bouis, Meenakshi, & Pfeiffer, 2006).* *(WHO/UNU/UNICEF, 2001)* *(Pasricha, Drakesmith, Black, Hipgrave, & Biggs, 2013)*
Pregnant Women	Daily Iron Supplementation. Diverse foods approach Multiple powder supplementation	Elemental iron and folic acid. Mixed diets with iron absorption enhancers and fewer iron inhibitors	*(P. Christian et al., 2009)* *(WHO/UNU/UNICEF, 2001)* *WHO (2011)* (Pasricha et al., 2013)
Lactating Mothers	Daily Iron Supplementation Diverse foods approach. Iron fortification Biofortified Crops	Elemental iron and folic acid. Mixed diets with iron absorption enhancers and fewer iron inhibitors	*(WHO/UNU/UNICEF, 2001)* *(Pasricha et al., 2013)* *(Nestel et al., 2006)*
Community-wide/ Households	Adequate healthcare. Fortified Foods Biofortified crops Diverse food approach	*NaFeEDTA-fortified soy sauce.* *Wheat flour iron fortification.* Mixed diets with iron absorption enhancers and fewer iron inhibitors. Maize flour fortification with iron and other micronutrients. Biofortified Crops	(Chen et al., 2005) (Field, Mithra, & Peña-Rosas, 2021) (WHO/UNU/UNICEF, 2001) *(Pasricha et al., 2013)* *(WHO/FAO/UNICEF/GAIN/MI/FFI, 2009)* *(Liberal, Pinela, Vívar-Quintana, Ferreira, & Barros, 2020)*

3.3 Food Vehicles for Dietary Iron Interventions

Dietary iron supplements such as tablets, liquid, and capsules can be gulped directly. However, iron fortification requires a food substance (vehicle) for the application of iron compounds before consumption. Several iron salts used for producing iron-fortified foods have been assessed and applied in various nutritional matrices.

Food fortification with iron is practiced worldwide, although it remains the most complex micronutrient added to foodstuffs for fortified food production. Several Latin American countries have over the years iron-fortified corn or wheat flours. Cereal-based infant complementary foods, soy sauce, fish sauce, milk are examples of frequent iron fortification food vehicles. In some efficacy study trials, table salts have also been iron fortified. Cereal derived flour products such as snacks, bread, and breakfast cereals constitute valuable iron fortification food vehicles, however, the quality of iron made available through these food vehicles usually depends on the fortification level and the volume of the food consumed (R. Hurrell & Egli, 2010a; R. F. Hurrell, 2007; WHO, 2006). Conversely, essential micronutrients such as iron are biofortified in targeted staple crops such as in cereals like rice, wheat, and in root tubers as cassava (Garg et al., 2018). Table 3.2 presents appropriate fortificant compounds for specific food vehicle fortification techniques.

Table 3.2: Recommended iron fortificants for designated food vehicles

Fortificant	Relative Bioavailability	Food vehicle
Ferrous sulphate. Encapsulated ferrous sulfate. Ferrous fumarate. Electrolytic iron (x2 amount). All with vitamin C (≥2:1 molar ratio of Vitamin C: Fe)	100	Cereal-based Complementary foods
Ferrous fumarate with Vitamin C	100	Cocoa Products
Ferric pyrophosphate (x2 amount) with vitamin C	21-74	Cereals, fluid milk
Encapsulated ferrous sulfate	100	Salt
Ferric pyrophosphate (x2 amount)	92	Fruit juice, bouillon cubes
Sodium iron EDTA Ferrous sulfate with citric acid	100	Soy and fish sauce
Sodium Iron EDTA	>100	Sugar, cereals, fish sauce, soy sauce
Ferrous bis-glycinate, ferrous lactate Micronized ferric pyrophosphate	>100	Juice, Soft drinks, cereals, fluid milk
Sodium Iron EDTA Ferrous fumarate (x2 amount) Encapsulated ferrous fumarate	100	Wheat Flour (high extraction)
Micronized ferric pyrophosphate	92	Bouillon cubes
Ferric pyrophosphate (x2 amount)	21-74	Rice
Ferric ammonium citrate Ferrous bis-glycinate Micronized ferric pyrophosphate	>100	Liquid (Fluid) Milk
Dry ferrous sulfate	100	Pasta
Ferrous sulfate with vitamin C	100	Dry Milk
Dry ferrous sulfate Ferrous fumarate Electrolytic iron (x2 amount) Encapsulated ferrous sulfate Encapsulated ferrous fumarate	100	White wheat (low extraction) flour

Adapted from (WHO, 2006), (Blanco-Rojo & Vaquero, 2018; Diego Quintaes, Barberá, & Cilla, 2017; R. Hurrell & Egli, 2010a).

3.4 Impact, Toxicity, and Recommendations of Dietary Iron

The essence of dietary iron being an integral component of regular meals of infants, adolescents, women of reproductive ages, pregnant and lactating women; the effect of iron overdosing (overload); and suggestive recommendations of dietary iron types for vulnerable populations in low resource setting communities is discussed below.

3.4.1 Dietary Iron Impact

Dietary iron requirements are based on the upkeep of normal balance of basal and menstrual iron losses and the iron requirement over the life cycle, that is, an adolescence growth spurt, pregnancy (physiology), birth, and infancy, adulthood. Research studies indicate dietary iron intake supports the body and prevents iron deficiency (ID) and iron deficiency anemia (IDA). Most importantly it enhances motoric, cognitive, and behavioral development in infants and young children, improving concentration and attention in school children and adult women (Domellöf, Thorsdottir, & Thorstensen, 2013; WHO, 2011).

3.4.2 Dietary Iron Toxicity and Overload

Toxicity of iron from accidental or deliberate higher supplemental iron intake can occur and result in poisoning which will be categorized as either cellular or corrosive (Baranwal Arun, 2003). Supplemental iron intake below 20 mg/kg is acceptable (non-toxic) and often taken with orange juice or a meal; supplementation of iron also varies among age and gender. Intake of iron more than 60 mg/mg may cause acute toxicity and result in adverse health consequences such as injury to the gastrointestinal mucosa, vomiting, nausea, diarrhea, abdominal pain, and even mortality. Iron salts formulations differ; with the commonest being 325 mg ferrous sulphate tablets, containing 65 mg (20%) of supplement iron for each tablet, 300 mg ferrous gluconate, containing supplement iron of 36 mg (12%) in each tablet and 100 mg ferrous tablets, having supplement iron of 33 mg (33%) in each tablet (Madiwale & Liebelt, 2006; Sane & et al., 2018; Yuen Ho-Wang, 2021). Among individuals especially in low resource communities with conditions causing non-physiologic increased iron absorption such as chronic hemolytic anemia, homozygote and compound heterozygote thalassemia disorders, and hereditary hemochromatosis iron supplementations intervention's effect and safety on their health is currently not well understood since its related epidemiological studies are still ongoing *(Lemmens-Zygulska et al., 1996; Weatherall, 2010).*

The food and drugs boards authority established tolerable upper limits (ULs) for dietary iron intake which unlikely causes undesirable health effects. ULs apply to healthy young infants and adults. Physicians may prescribe supplemental iron doses based on an individual's peculiar situation (National Institute of Health (NIH), 2020b).

3.4.3 Dietary Iron Sources Recommendation for Vulnerable Groups in Developing Countries

3.4.3.1 Neonates (Newborns).

Maternal iron adequacy during pregnancy supports infants' in-utero nutritional iron needs and helps in preventing intrauterine growth restrictions (IUGR) and low birth weight infants. Preterm infants have depleted iron stores which could translate into iron deficiency anemia. Maternal iron supplementation and infection control during pregnancy is needed (Parul Christian, 2010b; Rao & Georgieff, 2007). According to several studies, delayed placental cramping of maternal umbilical cord following birth for 2-3 minutes allows continued blood flow to the fetus increasing iron levels and red blood cell mass of the newborn (Andersson, Hellstrom-Westas, Andersson, & Domellof, 2011; Arca, Botet, Palacio, & Carbonell-Estrany, 2010; Hutton & Hassan, 2007; Stoltzfus, 2011).

3.4.3.2 Young children and Infants

Iron supply to infants should be done through complementary feedings with the inclusion of animal and ascorbic acid food sources. Education directed at caregivers/parents on iron and to encourage its inclusion in infant meals especially during the critical child development window of 6-24 months can yield positive results. Also, point-of-use micronutrients, fortified cereal products as well as lipid-based nutrient spread can be used in supporting infants' iron needs. Provision of infant foods rich in iron or additives is preferable to infant iron supplementation (Sazawal & et al., 2006; Stoltzfus, 2011).

3.4.3.3 Women of reproductive ages and expectant mothers

Supplementation of folic acid with iron-on weekly bases is essential in women of reproductive ages (to improve their iron status). During pregnancy, daily folic acid and iron supplementation are required to prevent newborn neural tube defects and iron deficiency anemia. Underlying maternal health conditions must be treated, these includes malaria, and hookworm infections which contribute to blood loss. These conditions are common in some endemic communities, and its treatment is to prevent maternal anemia which can negatively affect growing fetus. The World Health Organization (WHO) recommends antenatal care visits at health facilities by expectant women (Stoltzfus, 2011).

3.5 Conclusion

In this research, current methods of iron deficiency and nutritional anemia prevention and management in developing nations and low resource setting communities were reviewed. Controlling iron deficiency has many public health benefits. Iron supplementation, food fortification, and biofortification strategies designed to improve the iron status of populations were presented as remedies to reduce the incidence of iron deficiency anemia (IDA) especially among adolescents, non-pregnant, pregnant women, adults, and infants. Iron supplementation during pregnancy has been recommended for decades to control iron deficiency anemia, and its clinical outcomes is shown to have significant health benefits for both the growing fetus and mother. Iron-fortified complementary foods were proposed after exclusive breastfeeding for lactated children. Iron-fortified meals were also recommended by the World Health Organization (WHO) for children six months and beyond in malaria-endemic communities instead of iron supplementation except in situations where malaria infections are preventable with accessible healthcare services. Food fortification with iron fortificants and genetic plant biofortification, and the intake of foods from diverse food-based groups, were practical approaches found to prevent and reduce iron deficiency anemia (IDA) among at-risk populations in anemia predominant communities. Other iron deficiency anemia prevention strategies discussed included lucky or happy iron fish and iron pots/cookware usage in water boiling and soup preparations for iron status improvement. Food vehicles for iron interventions as well as iron fortificants for designated food vehicles were presented. Finally, dietary iron’s impact, its overload and toxicity, and recommended iron sources for vulnerable populations in low resources setting communities were emphasized.

3.6 Connecting text

Iron deficiency anemia mitigation in a population were examined in the previous chapter.

In the next chapter, which is the objective three of the study, an iron-enriched cereal-based infants food products were developed since the long-term consequence of iron deficiency anemia (IDA) on children, are irreversible cognitive and mental defects which is injurious. The chapter evaluated the potential of dietary adjustment of infants 6-12 months homemade cereal-based foods using heme and iron up-take enhancers in supporting infant optimal iron absorption and availability in low resource setting communities.

Chapter 4 - Curbing Iron Deficiency through Dietary Adjustment of Homemade Infants' Cereal-Based Foods with Heme and Vitamin C for Optimum Iron Availability

Abstract

Human milk, although, low in iron content and high in its bioavailability, is unlikely to be sufficient to meet the rising needs of body tissue and circulation as newborns grow and their blood volume expands. To prevent iron deficiency and anaemia in infants, iron-rich complementary foods should be given in addition to human milk after the exclusive breastfeeding period. Iron deficiency anemia (IDA) is associated with decrease intellect and physical capacity and is an indication of both inadequate nutrition and poor health. Home-made infant weaning foods in low resource setting communities is often limited in heme iron and ascorbic acid therefore has low iron bioavailability, since it is generally made from only cereals and grains. In this study, commonly consumed cereals, and grains in low resource setting communities such as millet, rice and corn were used to prepare infant porridges adjusted for enhanced iron content and bioavailability. This was accomplished by the combination of the cereals and grains with iron absorption enhancers food products, such as chicken (heme), fruits that contain vitamin C, pumpkin seeds, and soyabeans. The objectives of the study were to (1) develop iron-rich food products from locally available ingredients to meet infants' iron needs; (2) measure the total iron contents of the food products and its recommended daily allowance (RDA) of iron contributions, and finally, (3) use an algorithm to establish the iron bioavailability of the infant food products. The study findings suggest that; iron from adjusted rice porridge is more bioavailable, this is followed by adjusted corn porridge before the adjusted millet porridge.

Key words: Complementary foods, Iron deficiency, Adjusted Porridges, Iron, Phytate, Cereals, RDA, Infant

4.1 Introduction

Iron deficiency anemia is prevalent globally with greater incidences in under-developed and low resource setting communities, which is perceived to result in morbidity and mortality among infants (Chaparro & Suchdev, 2019). In 2011, it was reported that 273 million children below age five (5) were anaemic worldwide, with iron deficiency contributing to approximately half of those cases (Stevens et al., 2013; Sundararajan & Rabe, 2021). A recent study found that, in 2019, the global anaemia prevalence was 22.8 percent (95 percent confidence interval: 22.6–23.1), down from 27.0 percent (26.7–27.2) in 1990. It indicated that while the frequency of anaemia has reduced, the number of cases has climbed from 1.42 (1.41–1.43) billion in 1990 to 1.74 (1.72–1.76) billion in 2019. Besides, the incidence was highest among children under the age of five, with a combined prevalence of 39.7% (39.0–40.4), (Gardner & Kassebaum, 2020). Iron deficiency anaemia (IDA) in infants has a negative impact on short-term haematological indices as well as long-term learning and memory functions, resulting in weariness and low economic productivity (Sundararajan & Rabe, 2021). Inadequate infant food consumption, particularly a combination of high anti-nutrient (phytic acids, tannins) intake and low heme iron intake, is a major cause of iron deficiency anaemia in pre-school-aged children, (Mantadakis, Chatzimichael, & Zikidou, 2020). Parasitic infections (Plasmodium falciparum, helminths, and schistosomiasis) and haemoglobin abnormalities are further causes of anaemia (Mantadakis, 2020).

An exclusively breastfed healthy term infant's iron needs are estimated to be met for up to half of the first year owing to the maternal iron endowment. The initial iron stores of 75 mg/kg in term babies, (Domellöf, 2017; Widdowson EM, 1988,) deplete as infancy advances, with steeper declines in more rapidly growing infants, because iron is used to sustain growth and development, (Qasem & Friel, 2015). Human breastfeeding is thought to include highly bioavailable iron, but only in small amounts that are insufficient to meet iron needs as an infant age progresses (Dror & Allen, 2018). Human milk iron values increase in colostrum and thereafter decrease over the first year of lactation (Mastroeni et al., 2006; Samuel & et al., 2020), with reported median values ranging from 0.04 to 1.92 mg/L (Dorea, 2000). As a result, infant weaning meals from 6 months old and beyond must include sufficient bioavailable iron (American Academy of Pediatrics Committee on Nutrition, 2013; Finn et al., 2017). This suggests that iron must be provided by exogenous ways, such as through complementary meals (Abeshu, Lelisa, & Geleta, 2016), food fortification or supplementation (Paganini, Uyoga, & Zimmermann, 2016).

As children get older, the nutritional gap between what they need and what they get from breast milk widens. Thus, at six to eight, nine to eleven, and twelve to twenty-three months, complementary meals are expected to provide 200, 300, and 550 kcal per day, respectively. Likewise, complementary meals must contain significant amounts of micronutrients such iron, vitamin B6, calcium, zinc, magnesium, phosphorus, (Abeshu et al., 2016; World Health Organisation, 2021).

Complementary feeding is still a challenge for children's nutrition in many regions of developing countries. For instance, only 4.2 percent of breastfed toddlers aged 6 to 23 months in Ethiopia had a minimum acceptable meal (Abeshu et al., 2016). During complementary feeding phase (6 to 24 months), the acute need for iron coincides with developmental stages (cognitive and motor) that might be negatively impacted by iron deficiency, especially if it is substantial enough to cause anaemia (Stoltzfus, Heidkamp, Kenkel, & Habicht, 2007). Inadequate nutritional quality or improper feeding methods, if not both, are primarily responsible for the disparities. For low-income earning families, commercially iron-fortified foods are sometimes extremely expensive to purchase. As a result, homemade complementary foods are still widely used. Unfortified cereal-based complementary foods, even when they are made using improved recipes, often provide insufficient essential micronutrients particularly iron to children aged 6–23 months, (Abeshu et al., 2016).

Infants and toddlers' diets often include items with low iron content (e.g., breastmilk, starchy meals) and/or low bioavailability iron (e.g., vegetables, legumes). As a result, in many resource-constrained households, meeting the iron needs of young children is practically difficult without techniques that include high-digestible iron compounds (Stoltzfus et al., 2007). Low iron bioavailability was discovered to be a bigger concern as much as dietary iron consumption in pre-school children’s home-made meals (Evang, Habte, Owino, & Krawinkel, 2021). Iron absorption is impeded by the diets that is low in heme iron and high in phytate and polyphenols. Since non-heme iron crystallises in the small intestine, it naturally has a limited bioavailability (Evang, Habte, Owino, & Krawinkel, 2020); however, vitamin C and heme iron can improve the dietary iron bioavailability (R. Hurrell & Egli, 2010a; S. R. Lynch & Cook, 1980; Teucher et al., 2004). Hence, improving the bioavailability of non-heme iron with vitamin C, heme and other organic acids is one strategy for preventing anaemia and iron deficiencies among children who depend mostly on home-made plant-based (cereals) which are high in anti-nutrients (Balay & et al., 2010; Gibson, Perlas, & Hotz, 2006). Vitamin C inhibits the dose-dependent inhibitory effects of polyphenols and phytates on iron absorption (Dasa & Abera, 2018), and additional research has shown that vitamin C and heme improves non-heme iron absorption (Kathryn Beck, Cathryn Conlon, Rozanne Kruger, & Jane Coad, 2014; Heffernan, Evans, Holmes, & Moore, 2017). Consequently, the general objective of this study is to examine the influence of dietary adjustment of home-made cereal-based Infant's foods with heme, vitamin C, and other essential nutrients in supporting optimum iron availability. The specific objectives are to;(1) develop iron-rich food products from locally available ingredients to meet infants' iron needs; (2) measure the total iron contents of the food products and its iron recommended daily allowance (RDA) contributions, then finally, (3) use an algorithm to establish the iron bioavailability of the developed infant food products.

4.1.1 State of foods frequently used in complementary feeding in some developing regions

Compelling reports on incidences of iron deficiencies among children under five especially in low- and middle-income countries (LMICS) is enormous, (Lutter & Dewey, 2003). The findings attributed the situation to the high intake of low-quality meals or diets with low iron contents and bioavailability. Research revealed that, commonly consumed cereals including corn, millet, and rice are prepared as porridge without the addition of other ingredients such as fruits with ascorbic acid and animal products i.e., chicken/fish/beef that provides heme iron and supports optimum dietary iron absorption after consumption for infants 6-23 months.

For instance, millet (*Pennisetum americanum*), maize (*Zea mays*), and guinea corn (*Sorghum spp.*) are common staple foods in Nigeria, besides, yam (*Dioscorea spp*.), gari (grated dried fermented cassava), rice (*Oryza sativa*) and cocoyam (*Xanthosoma sagittifolium*). These staples are pureed, diluted, or pre-crushed and given to infants as complementary foods. Legumes are introduced relatively later after 6 months of infant age due to the crop's perceived indigestibility, (Ogbonnaya JA, Ketiku AO, Mojekwu CN, Mojekwu JN, & Ogbonnaya JA., 2012 ; Onofiok & Nnanyelugo, 1998). Similarly, Fermented corn porridge (koko) is commonly used for complementary feeding in Ghana since mothers perceive it is readily digestible, (Lartey, Manu, Brown, Peerson, & Dewey, 1999). Young children are fed the family meals consisting of cereal dishes, starchy tubers, legumes, and vegetables, along side breastmilk, (Onofiok & Nnanyelugo, 1998). Allen et al., (2012), stated that, vitamin B complex and vitamin C's nutritional requirements are met through dietary patterns in Guatemala, however, infants' complementary diets are often deficient in minerals such as iron (Fe), zinc (Zn) and calcium (Ca), (Lindsay H Allen, 2012; Vossenaar & Solomons, 2012). Likewise, South African caregivers frequently utilise mushy, thick, and low-nutrient density corn porridges. The corn meals are generally diluted with water to achieve a thin consistency, lowering the nutrient content while increasing the food's volume, (Plessis LM, Kruger HS, & Sweet L, 2013). Additionally, infant's complementary meals are usually made into light rice porridges in the Philippines by low-income families (Jacquier, Angeles-Agdeppa, Lenighan, Toledo, & Capanzana, 2020), resulting in reduced nutrient quantity. Dietary modifications that support ideal iron availability and absorption is important for a healthy child growth and development, (Faleiros, Da Silva, De Assis Carvalho, & Machado, 2016).

4.2 Materials and Methods

4.2.1 Concept for enhancing infant complementary foods

Cereals and grains frequently used in infants' complementary foods preparation in developing regions were sampled and used for this study, these includes rice, corn, millet. The selected cereals constitute the base (main ingredients) of all the food preparation for the research experiment. The individual cereals and grains (i.e., rice, corn, millet) were further developed into an iron-rich foods products through the addition of other nutritious food ingredients such as pumpkin seeds, soya beans, chicken (heme), fruits (mango and cantaloupe) for vitamin C. The practice of adding fruits to a cereal-based food item is not a common practice in several home-made infant food preparation in some low resource setting communities. The indicators used in determining the appropriate ingredients for the adjusted home-made infant porridges were the overall nutrient density; protein (animal products); micronutrients need (iron); serving size; cost; infant's age; seasonality; flexibility; and accessibility. The world health organisation's (WHO) recommendations for the inclusion of at least four items from the seven (7) food groups aimed at dietary diversification, consisting of: (1) legumes and nuts, (2) vitamin-A rich fruits and vegetables, (3) eggs and their products (4) grains, roots, and tubers, (5) dairy products (milk, yogurt, cheese), (6) other fruits and vegetables, (7) meat and meat products (meat, poultry, fish, liver/organ meats), was observed during the ingredients selection for the adjusted recipe development (FAO/WHO GIFT, 2021; World Health Organization et al., 2008.). These recipes are to support lactated infants' dietary intakes for optimum iron availability. AACC approaches were also factored in during the cereals samples preparations with modifications, (American Association of Cereal Chemists., 1984).

4.2.2 Materials

The food ingredients (rice, millet, corn, soybeans, pumpkin seeds, chicken, and fruits) for the recipes development were purchased from an international foods shop in Montreal, Canada, where the ingredients were imported from India, Togo, and Ghana since the study is a low- and middle-income countries (LMICS) focused. All the purchased and packaged fresh food ingredients were transported to the foods and bioprocess laboratory of McGill University, Macdonald campus by the researcher. Upon arrival at the laboratory, the graduate student researcher developed the separate food items (recipes) according to the approved standardized approach, while observing high hygiene standards. The individual cereals and grains (i.e., corn, rice, millet), constituting the base of the foods were measured into three samples of cereals to non-cereals fractions of 1:1, 1.5:1, and 2:1, for each cereal sample, other non-cereal ingredients such as soybeans, fruits, chicken, and pumpkin seeds were added during the processing of the food items except the control product which was 1:0 (only cereals). The quantified food ingredients were prepared, and frozen at -24 ^{o}C, then freeze-dried for 72h (freeze-dryer Modulyo, Edwards, UK). The freeze-dried samples were then examined, homogenized, labelled, and stored at -24^{o}C until analysed. All food samples used for the research experiments were analyzed in dried states within 21 days after preparation and processing.

4.2.3 Standardized Preparation and cooking procedure of the adjusted infant porridges

All the dry ingredients were finely blended, sieved, fruits pureed, protein (chicken) cooked and finely minced, and all ingredients weighed (Table 4.1). Then in a pan, a measured quantity of portable water was brought to a boil. For each selected cereal, all the ingredients for the specific product processing were together in a mixing bowl except the cooked chicken paste/powder and pureed fruits. This was then blended to form a lump-free paste after the addition of minimum water. The heat was lowered beneath the pan following the boiling of the water, and then the smooth paste mixture added, while stirring vigorously to achieve a lump-free texture. The food content was allowed to boil for 30 minutes, then the cooked chicken powder/paste was added. The porridge was simmered for an additional 5 minutes before the pureed fruits was added while stirring continuously. Extra water was added as required to achieve preferred consistency; the porridge was allowed to simmer for few minutes after. The heat was turned off, and the porridge transferred into a bowl.

Table 4.1: Adjusted Infant foods Ingredients and quantities

Ingredient	Unit	Quantities		
Non-cereal ingredients				
Water	ml	118-177	157-236	177-300
Pumpkin seeds	g	5.69	5.69	5.69
Chicken	g	14.3	14.3	14.3
Soya beans	g	14.3	14.3	14.3
Fruits	g	14.3	14.3	14.3
Cereal to non-cereal solid ratio				
Rice		1:1	1.5:1	2:1
Millet		1:1	1.5:1	2:1
Corn		1:1	1.5:1	2:1

4.2.4 Vitamin C Analysis

Fruits (considered as primary source of ascorbic acid) were exclusively added to the developed food products since most of the infants' home-made meals prepared in low- and middle-income countries (LMICS) had little to no ascorbic acids. The addition of the fruits was to support better iron absorption from cereal-based meals which has phytic acids that inhibit iron absorption after consumption.

The extraction method used was modified from (Fracassetti, Costa, Moulay, & Tomás-Barberán, 2013; Odriozola-Serrano, Soliva-Fortuny, & Martin-Belloso, 2008). Two hundred fifty milligrams were mixed with 10ml of 5% methanol, 21g/L citric acid and 0.5g/L EDTA. The samples were sonicated for 1hour and centrifuged at 5000 rcf (relative centrifugal force) for 5 minutes. One milliliter was filtered through a .45µm PTFE syringe filter into a HPLC vial. An additional 0.8ml sample was mixed with 200µl of 20mg/ml 1,4 dithiotreitol (DTT) and incubated at room temperature in the dark. After incubation, these samples were also filtered into HPLC vials, (Fracassetti et al., 2013; Odriozola-Serrano et al., 2008).

The HPLC analysis of the sample extracted were performed using the method of (Furusawa & Kishida, 2001). Separation was performed using a Waters Symmetry C18, 5µm column (4.6 x 250mm). The mobile phase was an isocratic flow of 1ml/min using 2% acetic acid in water. The injection volume used was 20µl, (Furusawa & Kishida, 2001).

4.2.5 Protein, crude fat, and calories determination

The dry matter content was determined by putting a 2 g of the sample in a drying plate and keeping it in a drying oven at 110°C overnight. For chemical evaluation, protein, crude fat, calories were determined in accordance with AOAC methods. The nitrogen content was measured by the Dumas combustion method on a fison's NA2000 Analyzer. The crude fat content was determined using an Ancom XT15 Fat extractor, (Ancom Technology, Fairport, NY, USA) following the instructions of the manufacturer. The caloric content was analysed using a parr 6200 automatic adiabatic bomb calorimeter, ANSI/ASTM method.

4.2.6 Mineral analysis

4.2.6.1 Reagents and sample preparations

A blender was used to grind the food sample into a homogeneous fine powder. Nitric acid purified by sub-boiling distillation in a Milestone Inc., USA, duoPUR acid purification system was used. Daily, analytical calibration standards were generated from stock standard solutions diluted in 2 percent (v/v) nitric acid (Choice Analytical Pty Ltd.), (Phan-Thien, Wright, & Lee, 2012). Using the microwave digester, approximately 0.2500 g of the dry powdered sample were digested in duplicate with 3 mL of 69–71 % (w/w) nitric acid and 1 mL of analytical grade hydrogen peroxide. Deionized water was used to move the transparent digestion to make it up to 25 mL, (Perera, Gunawardana, Jayatissa, & Silva, 2020).

4.2.6.2 Instrumentation

Inductively coupled plasma-optical emission spectrometer (ICP–OES) was used for all mineral determinations (Optima 4300 DV-PerkinElmer, Norwalk, CT, USA). For all mineral analyses, the emission intensities were measured at the most sensitive and spectral interference-free lines (nm).

Signal quantification was done using peak area measurement. A concentric pneumatic nebulizer (Meinhard TR-30-K3, 36 psi) was attached to a 50 mL glass cyclonic spray chamber in the nebulizer/spray chamber system used (both, Glass Expansion, West Melbourne Vic, AU). The nebulization device was filled with sample solution using a peristaltic pump with Solvent-flex® PVC tubing. The quantities of various minerals in the samples were determined by the test results, (Froes & et al., 2009; Phan-Thien et al., 2012).

4.2.7 Iron bioavailability estimation

The iron bioavailability was determined following the predictive algorithm established by (Tseng et al., 1997). The first step was to segregate the iron content of MFP_{Fe} (meat/fish/poultry's iron) into heme and non-heme iron fraction. The heme fraction was estimated to be 40% of MFP_{Fe}. The remaining 60% was assumed to be non-heme. The second step was to estimate non-heme iron content of the meal. The total non-heme iron was estimated as the sum of the non-MFP (other constituents), iron content (100%) and the non-heme iron content of the MFP (60%). The third step was to determine the heme iron bioavailability which was estimated as 23% of the total heme iron. The final step was to determine the non-heme iron bioavailability. The non-heme iron bioavailability was based on the enhancing factors (EF) which is estimated based on MFP (meat/fish/poultry) and Vitamin C content of the food according to equation 4.1, (Tseng et al., 1997).

$$\boldsymbol{EF = MFP\ (g) + Vit\ C\ (mg)} \quad \text{4.1}$$

If EF is greater than 75, non-heme bioavailability (NHB) was estimated to be 8% of total non-heme iron

If EF is less than 75, EF was estimated using equation 4.2:

$$\boldsymbol{NHB = 3 + \left[8.93 \times log\left(\frac{EF+100}{100}\right)\right]} \quad \text{4.2}$$

The Total FE absorbed (TFEA) was estimated using equation 4.3:

$$\boldsymbol{TFEA = HB + NHB} \quad \text{4.3}$$

Considering the impact of phytate on iron absorption, the bioavailability is further adjusted to account for the phytate

The phytate content of the samples were estimated following the modified McCance-Widdowson reported by Wheeler and Ferrel (1971). They established an iron-phytate ratio for grain cereals to be 4 Fe:6 P. Using the iron content of the cereal used, the proportional phytate associated were determined.

In accounting for phytate, the NHB is corrected for as NHB_{pc}

Using the estimated phytate content of the cereal, the phytate correction of the non-heme iron bioavailability is estimated using Tseng, Chakraborty' equation shown in 4.4 :

$$\boldsymbol{Phytate\ correction = 10 \times ([-0.2869 \times log(mphytate)] + 0.1295)} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots . 4.4$$

The corrected non-heme iron content is estimated as NHB_{pc}

$$\boldsymbol{NHB_{pc} = NHB \times phytate\ correction} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 4.5$$

Total FE absorbed TFEA taking into account vitamin C and phytate is estimated as:

$$\boldsymbol{TFEA = HB + NHB_{pc}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots ..4.6$$

4.2.8 Statistical analysis

The JMP Pro 15 Statistical Discovery Software from Statistical Analysis System (SAS) was used to test the statistical significance of the variation observed among the cooked meals. An alpha value of 0.05 was used, and significance was accepted at $p < 0.05$. The Tukey-Kramer HSD was used to test the statistical significance among the mean Fe content of the adjusted infant meals.

4.3 Results and Discussion

4.3.1 Nutrients profiles of raw ingredients

4.3.1.1 Proximate Analysis

The proximate analysis of the ingredients is shown in Table 4.2. As expected, the cereals and the fruits had relatively small amount of protein (less than 10%) compared to the other ingredients. The chicken samples protein were more than seven times higher than cereals. The pumpkin seeds were both rich in protein and crude fats and had the highest amount of calories (6733.9 kcal). The fruits had the least proximate results in protein, fats, and calories. Considering the high protein content of soybean, pumpkin seeds and the chicken, their inclusion in infant complementary food could significantly enhance the protein and caloric value of the meals.

Table 4.2: Proximate analysis of ingredients used for the proposed adjusted infant meals

Food Items	Protein (%)	Crude Fat (%)	Calories
Rice	9.6 ± 0.1	0.2 ± 0.2	3766.9 ± 4.7
Millet	9.8 ± 0.1	4.9 ± 0.3	4213.9 ± 14.1
Corn	7.3 ± 0.1	2.7 ± 0.3	3921.7 ± 3.9
Chicken	78.3 ± 0.2	10.1 ± 0.1	5468.7 ± 63.8
Blended fruits	6.7 ± 0.1	0.3 ± 0.2	3553.1 ± 36.9
Pumpkin seeds	35.5 ± 0.1	47.8 ± 0.1	6733.9 ± 15.2
Soybeans	37.6 ± 0.5	21.8 ± 0.2	5370.0 ± 4.2

4.3.1.2 Mineral analysis

The mineral analysis of ingredients used for the proposed adjusted infant meals are shown in Table 4.3 and 4.4. Table 4.3 reveals the macro minerals including calcium, potassium, magnesium, sodium, phosphorus, and sulphur. Similarly, Table 4.4 shows the micro mineral content of the ingredients including iron, zinc, copper, and manganese. The result shows that among the cereals considered, millet had the highest amount of minerals. Compared to corn, it was more than 5.3, 2.7, 2.4, and 1.6 times higher in iron, zinc, calcium, and magnesium, respectively. It was also 13.9, 1.8, 1.7, and 12.9 times higher in iron, zinc, calcium, and magnesium, respectively, when compared with rice. The results also indicate that the addition of the pumpkin seeds and the soybean could distinctly increase the nutritional quality of the infant meal, considering that the pumpkin seeds were at least 1.2, 1.8, 4.3, and 4.5 times higher in iron, zinc, calcium, and magnesium, respectively, compared to millet.

Table 4.3: Macro mineral analysis of ingredients used for the proposed adjusted infant meals

	Ca	K	Mg	Na	P	S
Rice	54.0 ± 10.9	306.5 ± 5.6	91.8 ± 8.5	41.8 ± 1.6	668.8 ±34.5	2789.9 ± 1848.0
Millet	92.0 ± 3.4	2238.5 ± 48.6	1182.1 ± 32.9	47.6 ± 4.6	3183.1 ± 112.8	2010.6 ± 893.2
Corn	38.8 ± 16.5	1235.0 ± 0.8	760.0 ± 15.4	49.0 ± 1.7	2069.8 ± 28.9	1930.5 ± 1159.5
Chicken	127.8 ± 1.0	8575.4 ± 292.4	1029.1 ± 29.3	1243.0 ± 3.5	7575.6 ± 391.2	9679.4 ± 976.2
Blended fruits	550.1 ± 18.1	11505.3 ± 390.9	577.4 ± 8.5	1142.2 ± 33.3	792.2 ± 25.0	2062.2 ± 1213.2
Pumpkin seeds	399.0 ± 9.1	4632.7 ± 17.1	5290.5 ± 59.5	44.7 ± 3.2	11306.5 ± 479.3	4376.4 ± 1225.4
Soybean	2652.4 ± 47.4	13610.8 ± 144.3	2098.3 ± 35.1	44.0 ± 3.0	5606.3 ± 54.0	4374.1 ± 1390.7

Table 4.4: Micro mineral analysis of ingredients used for the proposed adjusted infant meals

	Cu	Fe	Mn	Zn
Rice	2.7 ± 1.0	5.1 ± 1.0	8.6 ± 0.4	21.3 ± 1.0
Millet	4.7 ± 1.1	70.8 ± 10.1	12.4 ± 0.3	37.4 ± 2.2
Corn	1.3 ± 0.2	13.3 ± 1.3	3.4 ± 0.8	13.9 ± 1.0
Chicken	6.0 ± 5.2	23.1 ± 5.3	1.1 ± 0.8	24.6 ± 3.1
Blended fruits	3.5 ± 0.7	13.1 ± 1.2	5.1 ± 0.6	9.3 ± 0.7
Pumpkin seeds	12.7 ± 0.2	83.0 ± 6.2	44.7 ± 1.1	65.7 ± 0.4
Soybeans	11.0 ± 0.3	67.2 ± 0.1	28.9 ± 0.2	43.3 ± 9.1

4.3.2 *Iron content variation of adjusted porridges*

The Fe content of the cooked meals adjusted for their nutritional quality is shown in figure 4.1 (a-d). Figure 4.1a shows the results of adjusted rice porridge prepared with the varying rice to non-rice solid fractions (1:1, 1.5:1, and 2:1) compared with a conventional refined white rice porridge serving as control. Clearly, the inclusion of the other ingredients significantly improved the iron content by more than three-folds (3.1-5.1 folds). These results indicate that lower ratio of rice to other ingredients (pumpkin seeds, chicken, fruits, soyabeans) for the adjusted porridges improved the iron contents of the food product. The findings also suggest that white refined rice which is consumed extensively around the globe has relatively low iron contents. A statistical comparison of the mean iron content using the Tukey-Kramer HSD test shows that for the adjusted rice porridges prepared using a 1:1 ratio resulted in significantly higher iron content compared to a 2:1. However, the mean iron content of adjusted porridge made from 1.5:1 ratio was not statistically different from that which was prepared with the 1:1 or 2:1 rice to non-rice ratios. The iron content could have been improved if brown rice was used since the bran of brown rice is noted to enhance its nutritional quality. A study conducted by Trinidad P. Trinidad et al. (2009), found that, white refined rice has low iron content in comparison to brown unrefined rice. Generally, white rice has been the preferred rice choice for complementary foods relative to brown rice. This is largely due to the concerns of unpolished (brown) rice being a source of chemical contaminants from pesticides such as inorganic arsenic found on the outer husks of rice grains, (Karagas et al., 2016). Since white refined rice is reported to have low iron content, the inclusion of the other ingredients such as pumpkin seeds, fruits, chicken, and soyabeans can supply or would compensate for the low iron and make the proposed adjusted rice porridge more nutritious.

Figure 4.1b presents the results of iron content from the adjusted millet porridges. The iron content of the adjusted porridges ranged from 39.4-46.3 ppm. A Tukey-Kramer HSD test revealed no statistical difference between the three porridges made with varying millet content. Normal millet porridge without the additional ingredients (1:0 cereal only) had high iron content relative to the adjusted porridges (representing a 38.5 ±2.4% iron content variation). This is supported by other works in the literature. For instance, pearl millet used in the infant food preparation is known to have high iron content, (Anitha et al., 2021). While this result may provide a valid reason for nursing mothers to use the pearl millet in making infant weaning foods in developing countries to combat iron deficiency anemia, the challenge here is how much of the iron present in the control (millet only) porridge can be absorbed after intake considering the high content of phytic acids present in the cereal (millet) which impedes iron absorption. Researchers, (Tako, Reed, Budiman, Hart, & Glahn, 2015) found in their studies that, pearl millets although high in iron, have elevated polyphenols levels that inhibit iron bioavailability. These findings from the study, goes further to support the argument that since the adjusted millet porridges have both heme (chicken) and non-heme iron, as well as the iron absorption enhancer (ascorbic acid from the added fruits), pumpkin seeds and soybean, the adjusted millet porridges iron contents can be readily absorbed after intake than the control which is made of only millet without the heme and iron absorption enhancers. The adjusted porridges can better provide a complete nutrition for the infant from the other added diverse nutritious ingredients, this conclusion from this study is also supported by (Julia L. Finkelstein et al., 2015), who found bio-fortified millet products to diminish iron deficiency anemia among school-aged children than just the control which is only the conventional millet.

The iron content of the corn adjusted porridges are shown in figure 4.1c. The chart shows that the normal corn porridge (corn only - control) is significantly lower in iron than the adjusted porridges. The addition of the other ingredients improved iron content by up to 128.7%. The impact of the amount of corn added is minimal because the comparisons of all pairs using the Tukey Kramer HSD test showed no statistical difference between the samples. More importantly, the heme iron from the added chicken and the ascorbic acids from the fruits will facilitate better iron absorption. In a study, (Glahn, Tako, & Gore, 2019) discussed iron levels in whole kernels of three different corn varieties ranged from 12.5 to 30.8 g/g. Fe density ranged from 51.0 to 141.3 g/g in the germ fractions. They revealed non-germ component of the corn contained iron concentrations of 7.4 to 18.9 g/g. Which explains that the corn variety with the highest Fe bioavailability also had the highest non-germ Fe concentrations, indicating that the corn has a lower Fe bioavailability. In households' levels in some developing nations, infant corn porridges processing requires that the corn's bran, germ, and endosperm are removed or strained and discarded before its use in infant weaning food preparation to prevent the fiber causing infant choking. This practice takes out the essential nutrients and further diminishes the iron contents, (Gwirtz & GarciaCasal, 2014). In maximizing the iron contents of corn porridges, the adjusted corn porridges from this study with the diverse nutritious food ingredients (pumpkin seeds, chicken, fruits, soya beans) incorporation in the corn porridges can better meet infants iron needs when used for weaning besides enhancing the food's iron absorption.

A comparison of all the adjusted porridges is shown in figure 4.1d. The result suggests that the products from the adjusted millet porridges had the highest iron contents, followed by the adjusted corn porridges before the adjusted rice porridges. Consequently, in choosing an infant porridge for weaning, all these products can be useful sources of iron to support infant iron needs extensively in areas where infants are at high risk of iron deficiency anemia.

4.3.3 Contribution of adjusted meals to daily recommended iron

The result also shows that the consumption of the one serving (67 g) of the adjusted rice porridge could provide up to 15.8% of the recommended daily allowance (RDA) of iron compared to the 3.1% offered by the conventional rice porridge which may consist of basically starch and provides energy with a glycemic index of 86, (Ludwig, Hu, Tappy, & Brand-Miller, 2018). Similarly, adjusted corn porridges doubles the percent daily values. However, the adjusted millet porridges had a lower iron content compared to the conventional millet porridges.

Foods that provide 20% or more of the daily value (DV) are considered high sources of that mineral (iron), but foods that provide lower percentages of the DV can nevertheless contribute to a healthy diet, (National Institute of Health (NIH), 2020b).

Table 4.5: Iron content per serving and contribution to Recommended Daily Allowance (RDA)

Porridges	***Iron content per serving (mg)***				***Percent Daily Value (%)***			
	1:0*	***1:1****	***1.5:1****	***2:1****	***1:0****	***1:1****	***1.5:1****	***2:1****
Rice Porridge	0.34	1.73	1.43	1.08	3.1	15.8	13.0	9.8
Millet Porridge	4.78	2.93	3.07	2.75	43.4	26.7	28.0	25.0
Corn Porridge	0.89	1.78	2.05	1.74	8.1	16.2	18.6	15.9

*Represent the cereal to non-cereal ratio used in preparing the adjusted porridges

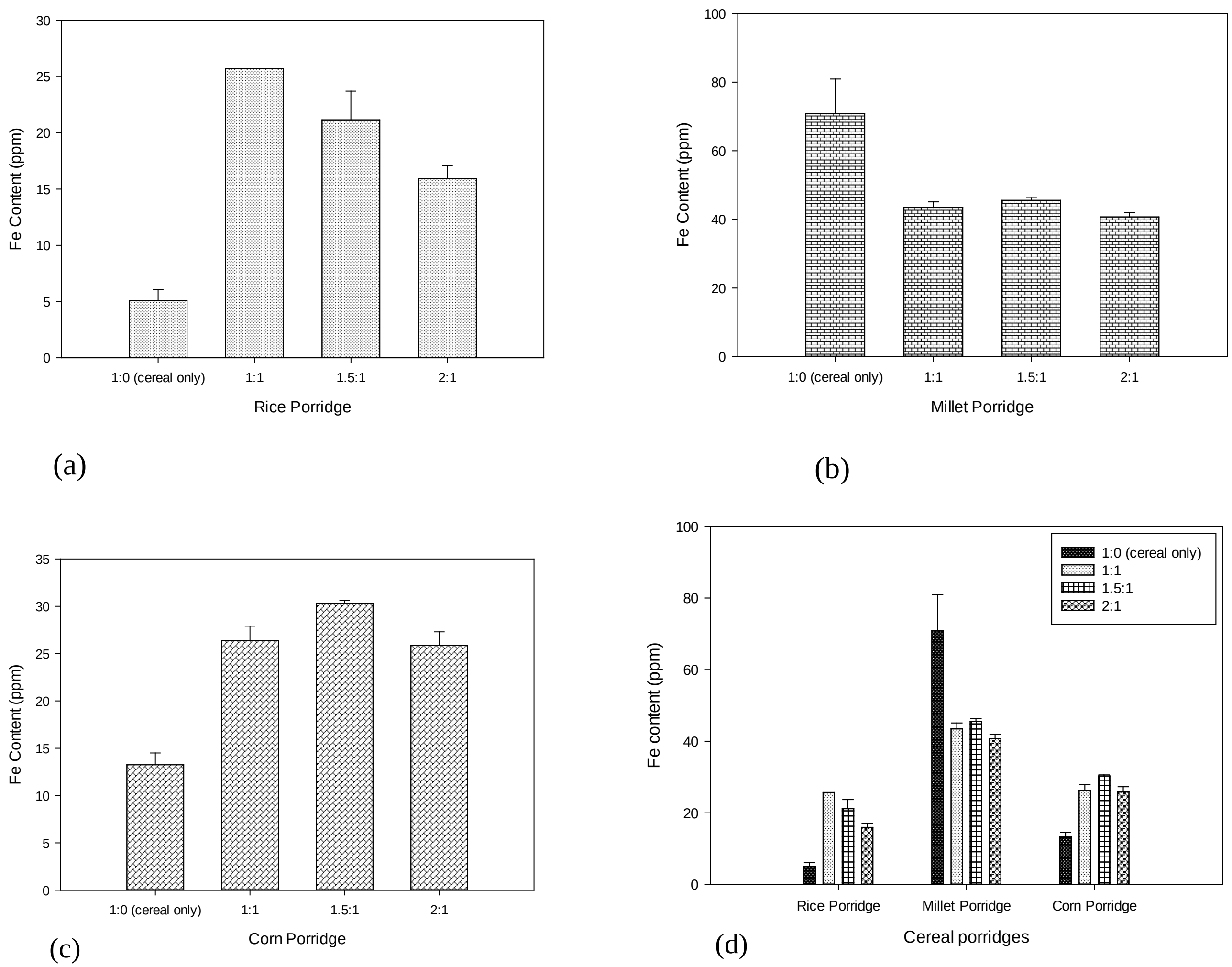

Figure 4.1: Variation of cereal-non cereal amount with overall iron contents (a) rice porridge (b) millet porridge (c) corn porridge (d) comparison

4.3.4 Vitamin C content of adjusted porridges

The total vitamin C measured as the sum of the Ascorbic Acid and the Dehydro Ascorbic Acid is shown in figure. 4.2. As anticipated, higher cereal content reduced the amount of total vitamin C since the vitamin C content of the controls were relatively small. In all adjusted porridges, the vitamin C content of porridges prepared using a fraction of 1:1 of cereal was significantly higher than the ratio of 1.5:1 and 2:1 cereal content. Among the three adjusted porridges, corn porridges had the highest vitamin C contents, confirming the relatively higher amount of natural occurring vitamin C in corn (Siyuan, Tong, & Liu, 2018), because the same quantity of fruits (vitamin C enhancers) were used in the preparation of all the adjusted infant products. Higher vitamin C contents in the product suggests better iron absorption after intake; hence the adjusted corn porridge's iron contents could be easily absorbed after intake compared with the others.

Cereals are known to provide very little to no vitamin C for the body. Many food composition tables including that of the United States Department of Agriculture's Food and Nutrition Database for Dietary Studies (FNDDS) and the Canadian Nutrient File (CNF) reports 0mg/100 g vitamin C for raw millet, millet flour, raw rice, cooked rice. It is evident that, the inclusion of the other ingredients will significantly improve the overall vitamin C content of the food products. This is essential in two ways: (1) it will provide decent level of antioxidants for the infants being fed these adjusted meals and serve as a guard protecting them from oxidation and disease (2) it will enhance the iron absorption and reduce the risk of iron deficiency anemia (IDA). As have been indicated by other researchers, it is important that the practice of adding fruits to infant porridges is observed and applied in developing nations and in iron deficiency anemia (IDA) endemic communities. Since cereals generally have low vitamin C contents which are possibly caused by its processing which can diminish iron absorption through phytate inhibition from the cereals, (Gibso, 1999). The developed adjusted porridges from this study had adequate vitamin C contents for enhancing infant iron absorption after intake.

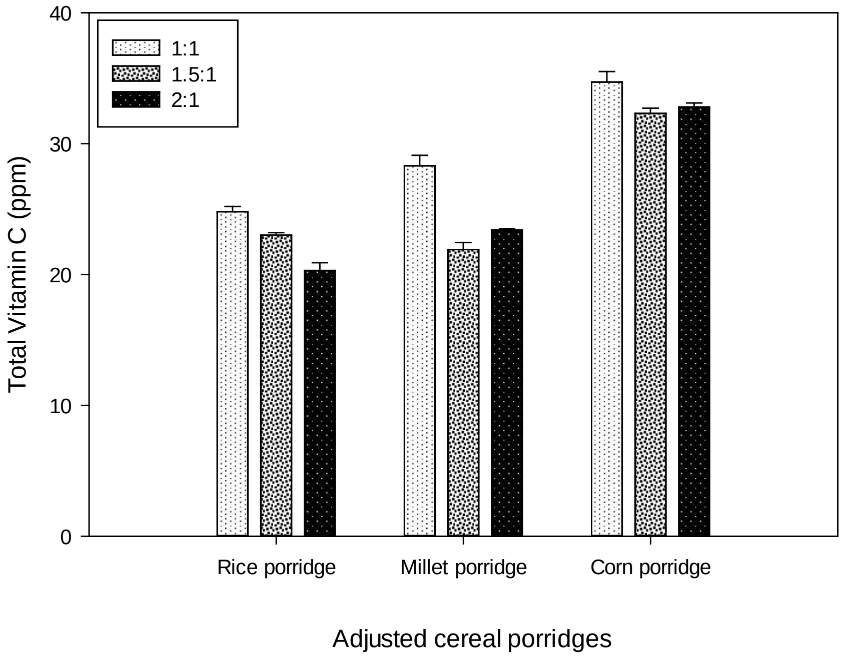

Figure 4.2: Total Vitamin C content of adjusted porridge

4.3.5 Iron Bioavailability

The estimated percent iron availability of the adjusted porridges is shown in figure 4.3. The percent bioavailability of rice was relatively higher that millet (by at least 11%) and corn (at least by 6%). For rice, a 14% bioavailability is observed, which is relatively lower than the 17-28% reported by T. P. Trinidad et al. (2009). This may be due to over estimation of the phytate. The results also suggest a higher bioavailability of the adjusted rice meals (15.1-21.6%). These results were similar to those reported by (Tuntawiroon et al., 1990). It must be pointed out that even though the variation in percent iron bioavailability among the rice porridges may be low, the total iron content in the control rice porridge was only 20% that of the adjusted meals, hence, the seemly similar percent bioavailability to the adjust porridges is not the reflective of the actual bioavailable iron. Similarly, the control corn and millet had significantly lower percent iron compared to the adjusted porridges. This was expected since the iron bioavailability depends on the total iron content.. Although, the adjusted millet porridges had the highest iron content, it had the lowest iron bioavailability. This is largely due to the phytate concentration in millet. The phytate content is a function of the iron content in a ratio of 4:6 (iron: phytate), (Wheeler & Ferrel, 1971). This implies that, the higher the iron content, the higher the phytate, hence the lower the iron bioavailability.

Phytate are known to inhibit iron absorption. The relatively lower percent iron of the control millet porridge is due to two reasons. First, it had the highest iron content (70.8 ± 10.1 ppm) hence high phytate and lower bioavailability. This implies that expressing the bioavailable iron as a percentage of the total iron present will be very small. Second, millet had no vitamin C which is considered as iron absorption enhancer which led to the lower bioavailability. This second reason also explains why the adjusted corn porridges had relatively higher iron bioavailability compared to millet. Corn has a naturally occurring vitamin C which increases its iron bioavailability.

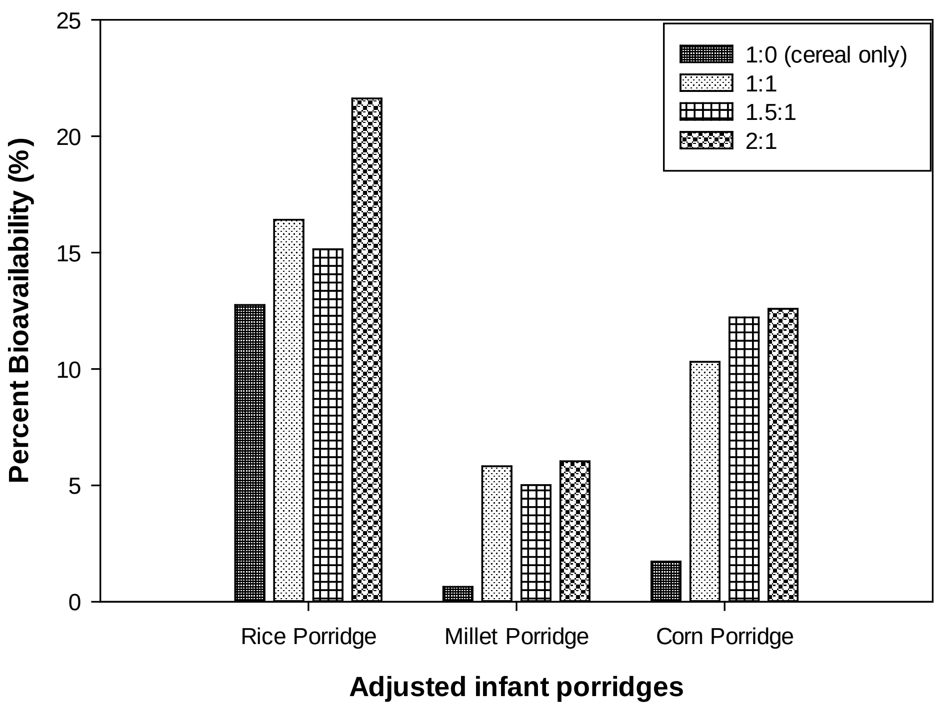

Figure 4.3: Iron bioavailability of adjusted cereal porridges with varying cereal content

4.4 Conclusion

In this study, cereal-based complementary porridges for infants were enhanced using other ingredients including, fruits, chicken, pumpkin seeds, and soybeans to improve the iron contents and its absorption. The results showed that normal conventional rice and corn porridges are low in iron, and the addition of mineral rich ingredients will significantly enhance the nutritional quality of the porridges to be used as infants' complementary foods. The low phytate content of rice implied relatively higher content of its iron could be absorbed compared to millet which has higher iron and phytate contents. This also means iron bioavailability of millet could significantly be impeded by the presence of the phytate, however, the addition of fruits which contains vitamin C to the meals will improve the iron absorption after intake. Corn although had relatively higher iron and phytate content than rice, had natural occurring vitamin C which acts as iron absorption enhancer. Overall, the inclusion of the key nutritious ingredients significantly improved the infant complementary foods iron and nutrient values and will further support adequate iron assimilation.

4.5 Connecting text

The previous chapter studied infant iron-rich porridge processing potential from cereal-based products, chicken, fruits with vitamin C and other nutritious ingredients for adequate infant foods iron availability and absorption. This was aimed at reducing iron deficiency anemia (IDA) among infants and school-aged children in low resource setting communities and iron deficiency (IDA) affected areas who depend on home-made cereal -based food products to thrive.

The next chapter presents the study summary, conclusion, recommendations, and the implication for future studies.

Chapter 5 - Conclusion and Recommendation

In this chapter, the study summary, conclusion, recommendations, and a future research suggestion is presented.

5.1 Summary and Conclusions

This research study explored determinants of iron deficiency (ID) and pathways of improvement among populations and examined the trends and evolving strategies of managing iron deficiency anemia in low resource setting communities. The study also developed iron-enriched cereal-based infant foods using heme and iron enhancers as well as other nutritious ingredients in supporting iron needs of infants in limited resources and deprived communities who depend extensively on home-made complementary foods which often have limited heme iron with low iron bioavailability. The study findings indicate limited dietary iron intake and low iron bioavailability are the major contributors to iron deficiency anemia in low resource settings communities. These communities have dietary patterns of high cereals and grains intake, which are non-heme iron that contains phytic acid and hinders dietary iron absorption. Some other contributing factors to iron deficiency anemia in low resource setting communities found in the cause of the studies are infectious and inflammatory diseases, malaria, blood loss from parasitic infections, other nutritional deficiencies such as vitamin A, riboflavin, folic acid, vitamin B12, and haemopoiesis.

In conclusion, the study found that, approaches of making non-heme iron bioavailable through heme iron intake and the introduction of iron absorption enhancers such as food sources with vitamin C into household foods preparation is essential. Iron supplementation, food fortification, and biofortification strategies designed to improve the iron status of a population were determined to reduce the incidences of severe iron deficiency anemia (IDA) especially among vulnerable populations. It was evident that underlying health conditions contributing to iron deficiency anemia in developing regions should first be treated before any dietary-based approach for iron deficiency anemia (IDA) prevention can be effective.

5.2 Broader implications of the study findings

The results and findings of the study strongly suggest that the adjusted infant porridges can improve nutritional and iron status of maternal and paediatrics populations in low resource setting communities who depend extensively on cereal-based food product as their primary source of nourishment. This would in fact assist in diminishing iron deficiency (ID) in areas that are most affected by the nutritional deficiency. Nutritional intervention trials or study could be conducted in the nearest future to determine the applicability and practicality of the findings of this study and to also validate the results.

5.3 Limitations of the Study

While the study has demonstrated that the inclusion of other ingredients such as chicken (heme), pumpkin seeds, fruits and soya beans to infant home-made cereal porridges could improve the overall iron contents and the iron availability of the product, there were identifiable limitations also to the study. These important limitations include:

- Lack of consideration of polyphenol content: Iron bioavailability are known to be impeded by the phytic acids and polyphenol contents particularly in cereals and grains. However, the polyphenol content was not included in the bioavailability estimation of this research study.
- Also, the impact of the use of different cereal cultivars on iron bioavailability was not accounted for or factored into the research: As expected, different cereal cultivars will contain different iron content, thus, resulting in a varying iron bioavailability outcome. It would have been interesting to account for the variation of to the cultivars used for the product development and preparation.

5.4 Recommendations

The study recommends that, important dietary methods of iron deficiency anemia (IDA) mitigation should include adequate fish, meat, poultry, and fruits high in vitamin C intake. Diverse food sources with vitamins A, B^{12}, B^{2}, zinc, calcium, copper intake must be emphasized; with tea, polyphenols, and coffee replaced with citrus juices or consumed two hours after plant-based non-heme products intake. Furthermore, since human breastmilk is iron-inadequate and cannot meet an infant's rapid iron needs after the first six months of life, iron-fortified complementary foods containing heme and vitamin C are recommended after exclusive breastfeeding.

5.5 Suggestions for future work

Implications for future studies is research into the extent phytic acid influences iron absorption among specific individuals within a population at different life stages, that is during pregnancy, lactation, infancy, adolescence, adulthood, and old age. Since interpersonal variability could contribute to non-heme iron absorption.

References

Abbaspour, N., Hurrell, R., & Kelishadi, R. (2014). Review on iron and its importance for human health. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences, 19*(2), 164-174. Retrieved from https://pubmed.ncbi.nlm.nih.gov/24778671 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3999603/

Abeshu, M. A., Lelisa, A., & Geleta, B. (2016). Complementary Feeding: Review of Recommendations, Feeding Practices, and Adequacy of Homemade Complementary Food Preparations in Developing Countries - Lessons from Ethiopia. *Frontiers in Nutrition, 3*, 41-41. doi:10.3389/fnut.2016.00041

Abioye, V., Ogunlakin, G., & Taiwo, G. (2018). Effect of Germination on Anti-oxidant Activity, Total Phenols, Flavonoids and Anti-nutritional Content of Finger Millet Flour. *Journal of Food Processing & Technology, 09*. doi:10.4172/2157-7110.1000719

Abu-Ouf, N. M., & Jan, M. M. (2015). The impact of maternal iron deficiency and iron deficiency anemia on child's health. *Saudi Medical Journal, 36*(2), 146-149. doi:10.15537/smj.2015.2.10289

Achebe, M. M., & Gafter-Gvili, A. (2017). How I treat anemia in pregnancy: iron, cobalamin, and folate. *Blood, 129*(8), 940-949. doi:10.1182/blood-2016-08-672246

Afify, A. E.-M. M. R., El-Beltagi, H. S., Abd El-Salam, S. M., & Omran, A. A. (2011). Bioavailability of Iron, Zinc, Phytate and Phytase Activity during Soaking and Germination of White Sorghum Varieties. *PLOS ONE, 6*(10), e25512. doi:10.1371/journal.pone.0025512

Al-Awami Hashim, M. H. (2022). Physiology, Gastric Intrinsic Factor.

Allen, L. H. (1991). Ending Hidden Hunger: The History of Micronutrient Deficiency Control https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.490.6054&rep=rep1&type=pdf.

Allen, L. H. (2006). New Approaches for Designing and Evaluating Food Fortification Programs. *The Journal of Nutrition, 136*(4), 1055-1058. doi:10.1093/jn/136.4.1055

Allen, L. H. (2009). The Nutrition CRSP: What Is Marginal Malnutrition, and Does It Affect Human Function? *Nutrition Reviews, 51*(9), 255-267. doi:10.1111/j.1753-4887.1993.tb03117.x

Allen, L. H. (2012). Adequacy of family foods for complementary feeding. *The American Journal of Clinical Nutrition, 95*(4), 785-786. doi:10.3945/ajcn.112.035675

Allen, L. H., & Ahluwalia, N. (1997). *Improving Iron Status Through Diet The Application of Knowledge Concerning Dietary Iron Bioavailability in Human Populations*.

Allen Lindsay, H. L. (2008). To what extent can food-based approaches improve micronutrient status? *Asia Pacific Journal of Clinical Nutrition, 17*, 103-105.

Alves, C., Saleh, A., & Alaofè, H. (2019). Iron-containing cookware for the reduction of iron deficiency anemia among children and females of reproductive age in low- and middle-income countries: A systematic review. *PLOS ONE, 14*(9), e0221094. doi:10.1371/journal.pone.0221094

American Academy of Pediatrics Committee on Nutrition. (2013). *Pediatric Nutrition, 7th Edition (Sponsored Member Benefit)*: <p>American Academy of Pediatrics</p>.

American Association of Cereal Chemists. (1984). AACC Methods, Approved Methods of Analysis; The American Association of Cereal Chemists: St. Paul, MN, USA, ; p. 280.

Andersson, O., Hellstrom-Westas, L., Andersson, D., & Domellof, M. (2011). Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months: a randomised controlled trial. *BMJ, 343*(nov15 1), d7157-d7157. doi:10.1136/bmj.d7157

Andro, M., Le Squere, P., Estivin, S., & Gentric, A. (2013). Anaemia and cognitive performances in the elderly: a systematic review. *European Journal of Neurology, 20*(9), 1234-1240. doi:10.1111/ene.12175

Anitha, S., Kane-Potaka, J., Botha, R., Givens, D. I., Sulaiman, N. L. B., Upadhyay, S., . . . Bhandari, R. K. (2021). Millets Can Have a Major Impact on Improving Iron Status, Hemoglobin Level, and in Reducing Iron Deficiency Anemia-A Systematic Review and Meta-Analysis. *Frontiers in Nutrition, 8*, 725529-725529. doi:10.3389/fnut.2021.725529

Arca, G., Botet, F., Palacio, M., & Carbonell-Estrany, X. (2010). Timing of umbilical cord clamping: New thoughts on an old discussion. *The Journal of Maternal-Fetal & Neonatal Medicine, 23*(11), 1274-1285. doi:10.3109/14767050903551475

Armstrong, G. R. (2017). The Lucky Iron Fish: a simple solution for iron deficiency. *Blood Advances, 1*(5), 330-330. doi:10.1182/bloodadvances.2016000521

Au, A. P., & Reddy, M. B. (2000). Caco-2 Cells Can Be Used to Assess Human Iron Bioavailability from a Semipurified Meal. *The Journal of Nutrition, 130*(5), 1329-1334. doi:10.1093/jn/130.5.1329

Bailey, R. L., West Jr, K. P., & Black, R. E. (2015). The Epidemiology of Global Micronutrient Deficiencies. *Annals of Nutrition and Metabolism, 66*(Suppl. 2), 22-33. doi:10.1159/000371618

Balarajan, Y. S., Fawzi, W. W., & Subramanian, S. V. (2013). Changing patterns of social inequalities in anaemia among women in India: cross-sectional study using nationally representative data. *BMJ Open, 3*(3), e002233. doi:10.1136/bmjopen-2012-002233

Balay, K. S., & et al. (2010). Orange But Not Apple Juice Enhances Ferrous Fumarate Absorption in Small Children. *Journal of Pediatric Gastroenterology and Nutrition, 50*(5), 545.

Baranwal Arun, K. A. (2003). Acute iron poisoning: management guidelines. *Indian pediatrics, 40*(6), 534-540.

Beck, K., Conlon, C., Kruger, R., & Coad, J. (2014). Dietary Determinants of and Possible Solutions to Iron Deficiency for Young Women Living in Industrialized Countries: A Review. *Nutrients, 6*, 3747-3776. doi:10.3390/nu6093747

Beck, K., Conlon, C., Kruger, R., & Coad, J. (2014). Dietary Determinants of and Possible Solutions to Iron Deficiency for Young Women Living in Industrialized Countries: A Review. *Nutrients, 6*(9), 3747-3776. doi:10.3390/nu6093747

Benito, P., & Miller, D. (1998). Iron absorption and bioavailability: An updated review. *Nutrition Research, 18*(3), 581-603. doi:10.1016/s0271-5317(98)00044-x

Beutler, E., Hoffbrand, A. V., & Cook, J. D. (2003). Iron Deficiency and Overload. *Hematology, 2003*(1), 40-61. doi:10.1182/asheducation-2003.1.40

Blanco-Rojo, R., & Vaquero, M. P. (2018). Iron bioavailability from food fortification to precision nutrition. A review. *Innovative Food Science & Emerging Technologies, 51*. doi:10.1016/j.ifset.2018.04.015

Blanco-Rojo, R., & Vaquero, M. P. (2019). Iron bioavailability from food fortification to precision nutrition. A review. *Innovative Food Science & Emerging Technologies, 51*, 126-138. doi:10.1016/j.ifset.2018.04.015

Bohn, L., Meyer, A. S., & Rasmussen, S. K. (2008). Phytate: impact on environment and human nutrition. A challenge for molecular breeding. *Journal of Zhejiang University SCIENCE B, 9*(3), 165-191. doi:10.1631/jzus.b0710640

Brannon, P., & Taylor, C. (2017). Iron Supplementation during Pregnancy and Infancy: Uncertainties and Implications for Research and Policy. *Nutrients*, *9*(12), 1327. doi:10.3390/nu9121327

Brazaca, S. G. C., & Da Silva, F. C. (2003). Enhancers and inhibitors of iron availability in legumes. *Plant Foods for Human Nutrition, 58*(3), 1-8. doi:10.1023/b:qual.0000041140.50758.72

Briat, J. F., Curie, C., & Gaymard, F. (2007). Iron utilization and metabolism in plants. *Current Opinion in Plant Biology, 10*(3), 276.

Burke, R., Leon, J., & Suchdev, P. (2014). Identification, Prevention and Treatment of Iron Deficiency during the First 1000 Days. *Nutrients, 6*(10), 4093-4114. doi:10.3390/nu6104093

Callister, A., Gautney, J., Aguilar, C., Chan, J., & Aguilar, D. (2020). Effects of Indigenous Diet Iron Content and Location on Hemoglobin Levels of Ghanaians. *Nutrients, 12*(9), 2710. doi:10.3390/nu12092710

Carmel, R. (2008). How I treat cobalamin (vitamin B12) deficiency. *Blood, 112*(6), 2214-2221. doi:10.1182/blood-2008-03-040253

Carpenter, C. E., & Mahoney, A. W. (1992). Contributions of heme and nonheme iron to human nutrition. *Critical Reviews in Food Science and Nutrition, 31*(4), 333-367. doi:10.1080/10408399209527576

Carr, A. C., & Rowe, S. (2020). Factors Affecting Vitamin C Status and Prevalence of Deficiency: A Global Health Perspective. *Nutrients, 12*(7), 1963. doi:10.3390/nu12071963

Cavalli-Sforza Tommaso, T. (2005). Weekly iron-folic acid supplementation of women of reproductive age: impact overview, lessons learned, expansion plans, and contributions toward achievement of the millennium development goals. *Nutrition Reviews, 63*(12), 152-158.

Cerami, C. (2017). Iron Nutriture of the Fetus, Neonate, Infant, and Child. *Annals of Nutrition and Metabolism, 71*(Suppl. 3), 8-14. doi:10.1159/000481447

Chaparro, C. M., & Suchdev, P. S. (2019). Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. *Annals of the New York Academy of Sciences*. doi:10.1111/nyas.14092

Charles, C. V., Dewey, C. E., Daniell, W. E., & Summerlee, A. J. S. (2011). Iron-deficiency anaemia in rural Cambodia: community trial of a novel iron supplementation technique. *The European Journal of Public Health, 21*(1), 43-48. doi:10.1093/eurpub/ckp237

Chen, J., Zhao, X., Zhang, X., Yin, S., Piao, J., Huo, J., . . . Chen, C. (2005). Studies on the Effectiveness of Nafeedta-Fortified Soy Sauce in Controlling Iron Deficiency: A Population-Based Intervention Trial. *Food and Nutrition Bulletin, 26*(2), 177-186. doi:10.1177/156482650502600201

Christian, P. (2010a). Micronutrients, Birth Weight, and Survival. *Annual Review of Nutrition, 30*(1), 83-104. doi:10.1146/annurev.nutr.012809.104813

Christian, P. (2010b). Prenatal Micronutrient Supplementation and Intellectual and Motor Function in Early School-aged Children in Nepal. *JAMA, 304*(24), 2716. doi:10.1001/jama.2010.1861

Christian, P., Stewart, C. P., Leclerq, S. C., Wu, L., Katz, J., West, K. P., & Khatry, S. K. (2009). Antenatal and Postnatal Iron Supplementation and Childhood Mortality in Rural Nepal: A Prospective Follow-up in a Randomized, Controlled Community Trial. *American Journal of Epidemiology, 170*(9), 1127-1136. doi:10.1093/aje/kwp253

Cleland, S. R., & Thomas, W. (2019). Iron homeostasis and perioperative management of iron deficiency. *BJA Education, 19*(12), 390-397. doi:10.1016/j.bjae.2019.09.003

Clénin, G. E. (2017). The treatment of iron deficiency without anaemia (in otherwise healthy persons). *Swiss Med Wkly, 147*, w14434. doi:10.4414/smw.2017.14434

Coad, J., & Pedley, K. (2014). Iron deficiency and iron deficiency anemia in women. *Scandinavian Journal of Clinical and Laboratory Investigation, 74*(sup244), 82-89. doi:10.3109/00365513.2014.936694

Conway, R. E., Powell, J. J., & Geissler, C. A. (2007). A food-group based algorithm to predict non-heme iron absorption. *International Journal of Food Sciences and Nutrition, 58*(1), 29-41. doi:10.1080/09637480601121250

Dainty, J. R., Berry, R., Lynch, S. R., Harvey, L. J., & Fairweather-Tait, S. J. (2014). Estimation of Dietary Iron Bioavailability from Food Iron Intake and Iron Status. *PLOS ONE, 9*(10), e111824. doi:10.1371/journal.pone.0111824

Das, J. K., & et al. (2019). Food fortification with multiple micronutrients: impact on health outcomes in general population. *Cochrane Library, The*.

Dasa, F., & Abera, T. (2018). Factors Affecting Iron Absorption and Mitigation Mechanisms: A review. *International Journal of Agricultural Science and Food Technology*, 024-030. doi:10.17352/2455-815x.000033

De-Regil, L. M., & et al. (2011). Intermittent iron supplementation for improving nutrition and development in children under 12 years of age. *The Cochrane library.*

Debelo, H., Novotny, J. A., & Ferruzzi, M. G. (2017). Vitamin A. *Advances in Nutrition: An International Review Journal, 8*(6), 992-994. doi:10.3945/an.116.014720

Desalegn, A., Mossie, A., & Gedefaw, L. (2014). Nutritional Iron Deficiency Anemia: Magnitude and Its Predictors among School Age Children, Southwest Ethiopia: A Community Based Cross-Sectional Study. *PLOS ONE, 9*(12), e114059. doi:10.1371/journal.pone.0114059

Diego Quintaes, K., Barberá, R., & Cilla, A. (2017). Iron bioavailability in iron-fortified cereal foods: The contribution of in vitro studies. *Critical Reviews in Food Science and Nutrition, 57*(10), 2028-2041. doi:10.1080/10408398.2013.866543

Dobe, M., Garg, P., & Bhalla, G. (2018). Fortification as an effective strategy to bridge iron gaps during complementary feeding. *Clinical Epidemiology and Global Health, 6*(4), 168-171. doi:10.1016/j.cegh.2017.11.001

Domellöf, M. (2017). Meeting the Iron Needs of Low and Very Low Birth Weight Infants. *Annals of Nutrition and Metabolism, 71*(Suppl. 3), 16-23. doi:10.1159/000480741

Domellöf, M., Thorsdottir, I., & Thorstensen, K. (2013). Health effects of different dietary iron intakes: a systematic literature review for the 5th Nordic Nutrition Recommendations. *Food & Nutrition Research, 57*(1), 21667. doi:10.3402/fnr.v57i0.21667

Dorea, J. G. (2000). Iron and copper in human milk. *Nutrition, 16*(3), 209-220. doi:10.1016/s0899-9007(99)00287-7

Dror, D. K., & Allen, L. H. (2018). Overview of Nutrients in Human Milk. *Advances in Nutrition, 9*(suppl_1), 278S-294S. doi:10.1093/advances/nmy022

El Ati-Hellal, M., & Hellal, F. (2021). Food Supplementation with Vitamins and Minerals: An Overview. In: IntechOpen.

Engelmann, M. D. M., Davidsson, L., Sandström, B., Walczyk, T., Hurrell, R. F., & Michaelsen, K. F. (1998). The Influence of Meat on Nonheme Iron Absorption in Infants. *Pediatric Research, 43*(6), 768-773. doi:10.1203/00006450-199806000-00009

Evang, E. C., Habte, T.-Y., Owino, W. O., & Krawinkel, M. B. (2020). The Nutritional and Micronutrient Status of Urban Schoolchildren with Moderate Anemia is Better than in a Rural Area in Kenya. *Nutrients, 12*(1), 207. doi:10.3390/nu12010207

Evang, E. C., Habte, T.-Y., Owino, W. O., & Krawinkel, M. B. (2021). Can the supplementary consumption of baobab (Adansonia digitata L.) fruit pulp improve the hemoglobin levels and iron status of schoolchildren in Kenya? Findings of a randomized controlled intervention trial. *European Journal of Nutrition, 60*(5), 2617-2629. doi:10.1007/s00394-020-02447-2

Fairweather-Tait, S. J., Jennings, A., Harvey, L. J., Berry, R., Walton, J., & Dainty, J. R. (2017). Modeling tool for calculating dietary iron bioavailability in iron-sufficient adults. *Am J Clin Nutr, 105*(6), 1408-1414. doi:10.3945/ajcn.116.147389

Faleiros, F. T. V., Da Silva, V. N., De Assis Carvalho, M., & Machado, N. C. (2016). Intake, bioavailability, and absorption of iron in infants aged 6 to 36 months: an observational study in a Brazilian Well Child Clinic. *Nutrire, 41*(1). doi:10.1186/s41110-016-0011-0

FAO. (1992). INTERNATIONAL CONFERENCE ON NUTRITION (ICN). http://www.fao.org/3/u9265e/u9265e00.pdf.

FAO. (2011). VITAMIN A: MOVING THE FOOD-BASED APPROACH FORWARD. http://www.fao.org/fileadmin/user_upload/agn/pdf/Greiner_VITAMIN_A_Final.pdf.

FAO/UN/CAB International. (2011). Combating Micronutrient Deficiencies: Food-based Approaches, http://www.fao.org/3/am027e/am027e00.htm.

FAO/WHO. (2006). GUIDELINES ON FOOD FORTIFICATION WITH MICRONUTRIENTS,https://www.who.int/nutrition/publications/guide_food_fortification_micronutrients.pdf Accessed February, 2021.

FAO/WHO GIFT. (2021). Global Individual Food Consumption. https://www.fao.org/gift-individual-food-consumption/methodology/food-groups-and-sub-groups/en/.

Fernández-Gaxiola, A. C., & De-Regil, L. M. (2019). Intermittent iron supplementation for reducing anaemia and its associated impairments in adolescent and adult menstruating women. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.cd009218.pub3

Fernández-Gaxiola Ana, C. (2011). Intermittent iron supplementation for reducing anaemia and its associated impairments in menstruating women. *Cochrane Database of Systematic Reviews*.

Field, M. S., Mithra, P., & Peña-Rosas, J. P. (2021). Wheat flour fortification with iron and other micronutrients for reducing anaemia and improving iron status in populations. *The Cochrane library*.

Finkelstein, J. L., Haas, J. D., & Mehta, S. (2017). Iron-biofortified staple food crops for improving iron status: a review of the current evidence. *Current Opinion in Biotechnology, 44*, 138.

Finkelstein, J. L., Mehta, S., Udipi, S. A., Ghugre, P. S., Luna, S. V., Wenger, M. J., . . . Haas, J. D. (2015). A Randomized Trial of Iron-Biofortified Pearl Millet in School Children in India. *The Journal of Nutrition, 145*(7), 1576-1581. doi:10.3945/jn.114.208009

Finn, K., Callen, C., Bhatia, J., Reidy, K., Bechard, L., & Carvalho, R. (2017). Importance of Dietary Sources of Iron in Infants and Toddlers: Lessons from the FITS Study. *Nutrients, 9*(7), 733. doi:10.3390/nu9070733

Fracassetti, D., Costa, C., Moulay, L., & Tomás-Barberán, F. A. (2013). Ellagic acid derivatives, ellagitannins, proanthocyanidins and other phenolics, vitamin C and antioxidant capacity of two powder products from camu-camu fruit (Myrciaria dubia). *Food Chem, 139*(1-4), 578-588. doi:10.1016/j.foodchem.2013.01.121

Froes, R. E., & et al. (2009). Exploratory analysis and inductively coupled plasma optical emission spectrometry (ICP OES) applied in the determination of metals in soft drinks. *Microchemical Journal, 92*(1), 68.

Furusawa, N., & Kishida, K. (2001). High-performance liquid chromatographic procedure for routine residue monitoring of seven sulfonamides in milk. *Fresenius J Anal Chem, 371*(7), 1031-1033. doi:10.1007/s00216-001-1098-5

Gardner, W., & Kassebaum, N. (2020). Global, Regional, and National Prevalence of Anemia and Its Causes in 204 Countries and Territories, 1990–2019. *Current Developments in Nutrition, 4*(Supplement_2), 830-830. doi:10.1093/cdn/nzaa053_035

Garg, M., Sharma, N., Sharma, S., Kapoor, P., Kumar, A., Chunduri, V., & Arora, P. (2018). Biofortified Crops Generated by Breeding, Agronomy, and Transgenic Approaches Are Improving Lives of Millions of People around the World. *Frontiers in Nutrition, 5*. doi:10.3389/fnut.2018.00012

Garzon, S., & et al. (2020). Iron Deficiency Anemia in Pregnancy: Novel Approaches for an Old Problem. *Oman Medical Journal, 35*(5), 166.

Gharibzahedi, S. M. T., & Jafari, S. M. (2017). The importance of minerals in human nutrition: Bioavailability, food fortification, processing effects and nanoencapsulation. *Trends in Food Science & Technology, 62*, 119-132. doi:https://doi.org/10.1016/j.tifs.2017.02.017

Gibso, S. A. (1999). Iron intake and iron status of preschool children: associations with breakfast cereals, vitamin C and meat. *Public Health Nutrition, 2*(4), 521-528. doi:10.1017/s1368980099000701

Gibson, R. S., Perlas, L., & Hotz, C. (2006). Improving the bioavailability of nutrients in plant foods at the household level. *Proceedings of the Nutrition Society, 65*(2), 160-168. doi:10.1079/pns2006489

Glahn, R., Tako, E., & Gore, M. A. (2019). The Germ Fraction Inhibits Iron Bioavailability of Maize: Identification of an Approach to Enhance Maize Nutritional Quality via Processing and Breeding. *Nutrients, 11*(4), 833. doi:10.3390/nu11040833

Gupta, R. K., Gangoliya, S. S., & Singh, N. K. (2015). Reduction of phytic acid and enhancement of bioavailable micronutrients in food grains. *Journal of Food Science and Technology, 52*(2), 676-684. doi:10.1007/s13197-013-0978-y

Gwamaka, M., Kurtis, J. D., Sorensen, B. E., Holte, S., Morrison, R., Mutabingwa, T. K., . . . Duffy, P. E. (2012). Iron Deficiency Protects Against Severe Plasmodium falciparum Malaria and Death in Young Children. *Clinical Infectious Diseases, 54*(8), 1137-1144. doi:10.1093/cid/cis010

Gwirtz, J. A., & GarciaCasal, M. N. (2014). Processing maize flour and corn meal food products. *Annals of the New York Academy of Sciences, 1312*(1), 66.

Hallberg, L., Bjørn-Rasmussen, E., Howard, L., & Rossander, L. (1979). Dietary heme iron absorption. A discussion of possible mechanisms for the absorption-promoting effect of meat and for the regulation of iron absorption. *Scand J Gastroenterol, 14*(7), 769-779. doi:10.3109/00365527909181403

Hallberg, L., & Hulthén, L. (2000). Prediction of dietary iron absorption: an algorithm for calculating absorption and bioavailability of dietary iron. *The American Journal of Clinical Nutrition, 71*(5), 1147-1160. doi:10.1093/ajcn/71.5.1147

Hamamy, H., & Alwan, N. (2015). Maternal Iron Status in Pregnancy and Long-Term Health Outcomes in the Offspring. *Journal of Pediatric Genetics, 04*(02), 111.

Han, O. (2011). Molecular mechanism of intestinal iron absorption. *Metallomics, 3*(2), 103. doi:10.1039/c0mt00043d

Haschka, D., Hoffmann, A., & Weiss, G. (2021). Iron in immune cell function and host defense. *Seminars in Cell & Developmental Biology, 115*, 27-36. doi:https://doi.org/10.1016/j.semcdb.2020.12.005

Heffernan, A., Evans, C., Holmes, M., & Moore, J. B. (2017). The Regulation of Dietary Iron Bioavailability by Vitamin C: A Systematic Review and Meta-Analysis. *Proceedings of the Nutrition Society, 76*(OCE4). doi:10.1017/s0029665117003445

Hemalatha, S., Platel, K., & Srinivasan, K. (2007). Influence of germination and fermentation on bioaccessibility of zinc and iron from food grains. *European Journal of Clinical Nutrition, 61*(3), 342-348. doi:10.1038/sj.ejcn.1602524

Hooda, J., Shah, A., & Zhang, L. (2014). Heme, an Essential Nutrient from Dietary Proteins, Critically Impacts Diverse Physiological and Pathological Processes. *Nutrients, 6*(3), 1080-1102. doi:10.3390/nu6031080

Hossain, M. S., Das, S., Gazi, M. A., Mahfuz, M., & Ahmed, T. (2019). Ascaris lumbricoides infection: Still a threat for iron deficiency anaemia in 2-year-old Bangladeshi slum-dwelling children. *The Journal of Infection in Developing Countries, 13*(10), 933-938. doi:10.3855/jidc.11340

Hotez, P. J., Bottazzi, M. E., Franco-Paredes, C., Ault, S. K., & Periago, M. R. (2008). The Neglected Tropical Diseases of Latin America and the Caribbean: A Review of Disease Burden and Distribution and a Roadmap for Control and Elimination. *PLoS Neglected Tropical Diseases, 2*(9), e300. doi:10.1371/journal.pntd.0000300

Huang, L., Glahn, R., Welch, R., Fukai, S., & Rerkasem, B. (2006). Iron (Fe) bioavailability and the distribution of anti-Fe nutrition biochemicals in the unpolished, polished grain and bran fraction of five rice genotypes. *Journal of the Science of Food and Agriculture, 86*, 1209-1215. doi:10.1002/jsfa.2471

Hunt, J. R., Zito, C. A., & Johnson, L. K. (2009). Body iron excretion by healthy men and women. *The American Journal of Clinical Nutrition, 89*(6), 1792-1798. doi:10.3945/ajcn.2009.27439

Hurrell, R., & Egli, I. (2010a). Iron bioavailability and dietary reference values. *The American Journal of Clinical Nutrition, 91*(5), 1461S-1467S. doi:10.3945/ajcn.2010.28674f

Hurrell, R., & Egli, I. (2010b). Iron bioavailability and dietary reference values. *The American Journal of Clinical Nutrition, 91*, 1461S-1467S. doi:10.3945/ajcn.2010.28674F

Hurrell, R. F. (2007). Iron Fortification: Its Efficacy and Safety in Relation to Infections. *Food and Nutrition Bulletin, 28*(4_suppl4), S585-S594. doi:10.1177/15648265070284s411

Hurrell, R. F., Reddy, M., & Cook, J. D. (1999). Inhibition of non-haem iron absorption in man by polyphenolic-containing beverages. *British Journal of Nutrition, 81*(4), 289-295. doi:10.1017/s0007114599000537

Hurrell, R. F., Reddy, M. B., Juillerat, M., & Cook, J. D. (2006). Meat Protein Fractions Enhance Nonheme Iron Absorption in Humans. *The Journal of Nutrition, 136*(11), 2808-2812. doi:10.1093/jn/136.11.2808

Hutton, E. K., & Hassan, E. S. (2007). Late vs Early Clamping of the Umbilical Cord in Full-term Neonates. *JAMA, 297*(11), 1241. doi:10.1001/jama.297.11.1241

Indumadhavi, M., & Agte, V. (2007). Effect of fermentation on ionizable iron in cereal-pulse combinations. *International Journal of Food Science & Technology, 27*, 221-228. doi:10.1111/j.1365-2621.1992.tb01198.x

Jacquier, E. F., Angeles-Agdeppa, I., Lenighan, Y. M., Toledo, M. B., & Capanzana, M. V. (2020). Complementary feeding patterns of Filipino infants and toddlers lack diversity, especially among children from poor households. *BMC Nutrition, 6*(1). doi:10.1186/s40795-020-00376-1

Jing, L., Yuwei, L., Zhenping, H., & Qian, W. (2017). Impact of heat processing on the bioavailability of zinc and iron from cereals and pulses. *International Food Research Journal, 24*, 1980-1985.

Johnson-Wimbley, T. D., & Graham, D. Y. (2011). Diagnosis and management of iron deficiency anemia in the 21st century. *Therapeutic Advances in Gastroenterology, 4*(3), 177-184. doi:10.1177/1756283x11398736

Jonker, F. A. M., Calis, J. C. J., Van Hensbroek, M. B., Phiri, K., Geskus, R. B., Brabin, B. J., & Leenstra, T. (2012). Iron Status Predicts Malaria Risk in Malawian Preschool Children. *PLOS ONE, 7*(8), e42670. doi:10.1371/journal.pone.0042670

Kaplan, J., & Ward, D. M. (2013). The essential nature of iron usage and regulation. *Current Biology, 23*(15), R642-R646. doi:10.1016/j.cub.2013.05.033

Kapsokefalou, M., & Miller, D. D. (1991). Effects of Meat and Selected Food Components on the Valence of Nonheme Iron duringIn VitroDigestion. *Journal of Food Science, 56*(2), 352-355. doi:10.1111/j.1365-2621.1991.tb05278.x

Karagas, M. R., Punshon, T., Sayarath, V., Jackson, B. P., Folt, C. L., & Cottingham, K. L. (2016). Association of Rice and Rice-Product Consumption With Arsenic Exposure Early in Life. *JAMA Pediatrics, 170*(6), 609. doi:10.1001/jamapediatrics.2016.0120

Kassebaum, N. J., Jasrasaria, R., Naghavi, M., Wulf, S. K., Johns, N., Lozano, R., . . . Murray, C. J. L. (2014). A systematic analysis of global anemia burden from 1990 to 2010. *Blood, 123*(5), 615-624. doi:10.1182/blood-2013-06-508325

Khaskheli, M., & et al. (2016). Iron deficiency anaemia is still a major killer of pregnant women. *Pakistan Journal of Medical Sciences, 32*(3).

Kilbride, J., Baker, T. G., Parapia, L. A., Khoury, S. A., Shuqaidef, S. W., & Jerwood, D. (1999). Anaemia during pregnancy as a risk factor for iron-deficiency anaemia in infancy: a case-control study in Jordan. *International Journal of Epidemiology, 28*(3), 461-468. doi:10.1093/ije/28.3.461

Kotecha, P. (2011). Nutritional anemia in young children with focus on Asia and India. *Indian journal of community medicine, 36*(1), 8.

Kothari, M. T., Coile, A., Huestis, A., Pullum, T., Garrett, D., & Engmann, C. (2019). Exploring associations between water, sanitation, and anemia through 47 nationally representative demographic and health surveys. *Annals of the New York Academy of Sciences*. doi:10.1111/nyas.14109

Kuyper E, Vitta B, & Dewey KG. (2013). Novel and underused food sources of key nutrients for complementary feeding. . *A&T Tech Brief, 6:1–8.*

Laminu, H., Sheriff, M., & Alhaji, M. (2014). Evaluation of the chemical composition, anti-nutrients and mineral element level of a composite meal from pearl millet, wheat, cowpea and groundnut. *Sky Journal of Food Science, 3*, 34-40.

Lartey, A., Manu, A., Brown, K. H., Peerson, J. M., & Dewey, K. G. (1999). A randomized, community-based trial of the effects of improved, centrally processed complementary foods on growth and micronutrient status of Ghanaian infants from 6 to 12 mo of age. *The American Journal of Clinical Nutrition, 70*(3), 391-404. doi:10.1093/ajcn/70.3.391

Latunde-Dada, G. O., Pereira, D. I., Tempest, B., Ilyas, H., Flynn, A. C., Aslam, M. F., . . . Powell, J. J. (2014). A Nanoparticulate Ferritin-Core Mimetic Is Well Taken Up by HuTu 80 Duodenal Cells and Its Absorption in Mice Is Regulated by Body Iron. *The Journal of Nutrition, 144*(12), 1896-1902. doi:10.3945/jn.114.201715

Lee, A. I., & Okam, M. M. (2011). Anemia in Pregnancy. *Hematology/Oncology Clinics of North America, 25*(2), 241.

Lemmens-Zygulska, M., Eigel, A., Helbig, B., Sanguansermsri, T., Horst, J., & Flatz, G. (1996). Prevalence of α-thalassemias in northern Thailand. *Human Genetics, 98*(3), 345-347. doi:10.1007/s004390050220

Leroy, J. L., & Frongillo, E. A. (2007). Can Interventions to Promote Animal Production Ameliorate Undernutrition? *The Journal of Nutrition, 137*(10), 2311-2316. doi:10.1093/jn/137.10.2311

Liberal, Â., Pinela, J., Vívar-Quintana, A. M., Ferreira, I. C. F. R., & Barros, L. (2020). Fighting Iron-Deficiency Anemia: Innovations in Food Fortificants and Biofortification Strategies. *Foods, 9*(12), 1871. doi:10.3390/foods9121871

Lim, K., Riddell, L., Nowson, C., Booth, A., & Szymlek-Gay, E. (2013). Iron and Zinc Nutrition in the Economically-Developed World: A Review. *Nutrients, 5*(8), 3184-3211. doi:10.3390/nu5083184

Lopes, K. D. S., & et al. (2018). Nutrition-specific interventions for preventing and controlling anaemia throughout the life cycle: an overview of systematic reviews. *The Cochrane library.*

Lopez, A., & et al. (2016). Iron deficiency anaemia. *The lancet., 387*(10021), 907.

Loukas, A., Hotez, P. J., Diemert, D., Yazdanbakhsh, M., McCarthy, J. S., Correa-Oliveira, R., . . . Bethony, J. M. (2016). Hookworm infection. *Nature Reviews Disease Primers, 2*(1), 16088. doi:10.1038/nrdp.2016.88

Lucca, P., Hurrell, R., & Potrykus, I. (2002). Fighting Iron Deficiency Anemia with Iron-Rich Rice. *Journal of the American College of Nutrition, 21*(sup3), 184S-190S. doi:10.1080/07315724.2002.10719264

Ludwig, D. S., Hu, F. B., Tappy, L., & Brand-Miller, J. (2018). Dietary carbohydrates: role of quality and quantity in chronic disease. *BMJ*, k2340. doi:10.1136/bmj.k2340

Luo, Y., & Xie, W. (2014). Effect of soaking and sprouting on iron and zinc availability in green and white faba bean (Vicia faba L.). *Journal of Food Science and Technology, 51*(12), 3970-3976. doi:10.1007/s13197-012-0921-7

Lutter, C. K., & Dewey, K. G. (2003). Proposed Nutrient Composition for Fortified Complementary Foods. *The Journal of Nutrition, 133*(9), 3011S-3020S. doi:10.1093/jn/133.9.3011s

Lynch, S., Pfeiffer, C. M., Georgieff, M. K., Brittenham, G., Fairweather-Tait, S., Hurrell, R. F., . . . Raiten, D. J. (2018). Biomarkers of Nutrition for Development (BOND)—Iron Review. *The Journal of Nutrition, 148*(suppl_1), 1001S-1067S. doi:10.1093/jn/nxx036

Lynch, S. R., & Cook, J. D. (1980). INTERACTION OF VITAMIN C AND IRON. *Annals of the New York Academy of Sciences, 355*(1 Micronutrient), 32-44. doi:10.1111/j.1749-6632.1980.tb21325.x

Ma, J., Sun, Q., Liu, J., Hu, Y., Liu, S., Zhang, J., . . . Hambidge, K. M. (2016). The Effect of Iron Fortification on Iron (Fe) Status and Inflammation: A Randomized Controlled Trial. *PLOS ONE, 11*(12), e0167458. doi:10.1371/journal.pone.0167458

Madiwale, T., & Liebelt, E. (2006). Iron: not a benign therapeutic drug. *Current Opinion in Pediatrics, 18*(2), 174.

Mahler, G. J., Esch, M. B., Tako, E., Southard, T. L., Archer, S. D., Glahn, R. P., & Shuler, M. L. (2012). Oral exposure to polystyrene nanoparticles affects iron absorption. *Nature Nanotechnology, 7*(4), 264-271. doi:10.1038/nnano.2012.3

Malik, K. A., & Maqbool, A. (2020). Transgenic Crops for Biofortification. *Frontiers in Sustainable Food Systems, 4*. doi:10.3389/fsufs.2020.571402

Mantadakis, E. (2020). IRON DEFICIENCY ANEMIA IN CHILDREN RESIDING IN HIGH AND LOW-INCOME COUNTRIES: RISK FACTORS, PREVENTION, DIAGNOSIS AND THERAPY. *Mediterranean Journal of Hematology and Infectious Diseases, 12*(1), e2020041. doi:10.4084/mjhid.2020.041

Mantadakis, E., Chatzimichael, E., & Zikidou, P. (2020). Iron Deficiency Anemia in Children Residing in High and Low-Income Countries: Risk Factors, Prevention, Diagnosis and Therapy. *Mediterranean Journal of Hematology and Infectious Diseases, 12*(1), e2020041-e2020041. doi:10.4084/MJHID.2020.041

Mastroeni, S. S., Okada, I. A., Rondó, P. H., Duran, M. C., Paiva, A. A., & Neto, J. M. (2006). Concentrations of Fe, K, Na, Ca, P, Zn and Mg in maternal colostrum and mature milk. *J Trop Pediatr, 52*(4), 272-275. doi:10.1093/tropej/fmk004

Mayén, A.-L., Marques-Vidal, P., Paccaud, F., Bovet, P., & Stringhini, S. (2014). Socioeconomic determinants of dietary patterns in low- and middle-income countries: a systematic review.

The American Journal of Clinical Nutrition, 100(6), 1520-1531. doi:10.3945/ajcn.114.089029

Meremikwu, M. M., Donegan, S., Sinclair, D., Esu, E., & Oringanje, C. (2012). Intermittent preventive treatment for malaria in children living in areas with seasonal transmission. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.cd003756.pub4

Mesías, M., Seiquer, I., & Navarro, M. P. (2013). Iron Nutrition in Adolescence. *Critical Reviews in Food Science and Nutrition, 53*(11), 1226.

Miller, J. L. (2013). Iron Deficiency Anemia: A Common and Curable Disease. *Cold Spring Harbor Perspectives in Medicine, 3*(7), a011866-a011866. doi:10.1101/cshperspect.a011866

Milman, N. T. (2020). A Review of Nutrients and Compounds, Which Promote or Inhibit Intestinal Iron Absorption: Making a Platform for Dietary Measures That Can Reduce Iron Uptake in Patients with Genetic Haemochromatosis. *Journal of Nutrition and Metabolism, 2020*, 1-15. doi:10.1155/2020/7373498

Miniero, R., Talarico, V., Concetta Galati, M., Giancotti, L., Saracco, P., & Raiola, G. (2019). Iron Deficiency and Iron Deficiency Anemia in Children. In: IntechOpen.

Minihane, A. M., & Fairweather-Tait, S. J. (1998). Effect of calcium supplementation on daily nonheme-iron absorption and long-term iron status. *The American Journal of Clinical Nutrition, 68*(1), 96-102. doi:10.1093/ajcn/68.1.96

Monsen, E. R. (1988). Iron nutrition and absorption: dietary factors which impact iron bioavailability. *J Am Diet Assoc, 88*(7), 786-790.

Monsen, E. R., & et al. (1978). Estimation of available dietary iron. *American Journal of Clinical Nutrition, The, 31*(1), 134.

Monsen, E. R., Hallberg, L., Layrisse, M., Hegsted, D. M., Cook, J. D., Mertz, W., & Finch, C. A. (1978). Estimation of available dietary iron. *The American Journal of Clinical Nutrition, 31*(1), 134-141. doi:10.1093/ajcn/31.1.134

Monsen, E. R. E. (1988). Iron nutrition and absorption: dietary factors which impact iron bioavailability. *Journal of the American Dietetic Association, 88*(7), 786-790.

Morck, T. A., Lynch, S. R., & Cook, J. D. (1983). Inhibition of food iron absorption by coffee. *The American Journal of Clinical Nutrition, 37*(3), 416-420. doi:10.1093/ajcn/37.3.416

Moreno-Fernandez, J., Ochoa, J. J., Latunde-Dada, G. O., & Diaz-Castro, J. (2019). Iron Deficiency and Iron Homeostasis in Low Birth Weight Preterm Infants: A Systematic Review. *Nutrients, 11*(5), 1090. doi:10.3390/nu11051090

Moschonis, G., & et al. (2013). Association of Iron Depletion with Menstruation and Dietary Intake Indices in Pubertal Girls: The Healthy Growth Study. *BioMed Research International, 2013*, 1.

Muller, O. (2005). Malnutrition and health in developing countries. *Canadian Medical Association Journal, 173*(3), 279-286. doi:10.1503/cmaj.050342

Murphy, S. P., Beaton, G. H., & Calloway, D. H. (1992). Estimated mineral intakes of toddlers: predicted prevalence of inadequacy in village populations in Egypt, Kenya, and Mexico. *The American Journal of Clinical Nutrition, 56*(3), 565-572. doi:10.1093/ajcn/56.3.565

Nagao, T., & Hirokawa, M. (2017). Diagnosis and treatment of macrocytic anemias in adults. *Journal of General and Family Medicine, 18*(5), 200-204. doi:10.1002/jgf2.31

Naigamwalla, D. Z., Webb, J. A., & Giger, U. (2012). Iron deficiency anemia. *The Canadian veterinary journal = La revue veterinaire canadienne, 53*(3), 250-256. Retrieved from https://pubmed.ncbi.nlm.nih.gov/22942439
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3280776/

National Institute of Health (NIH). (2020a). Folate. https://ods.od.nih.gov/factsheets/Folate-HealthProfessional/.

National Institute of Health (NIH). (2020b). Iron.https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/.

Nazanin, A. N., Hurrel, R., & Kelshadi, R. (2014). Review on iron and its importance for human health. *Journal of Research in Medical Sciences, 19*(2), 164-174.

Nestel, P., Bouis, H. E., Meenakshi, J. V., & Pfeiffer, W. (2006). Biofortification of Staple Food Crops. *The Journal of Nutrition, 136*(4), 1064-1067. doi:10.1093/jn/136.4.1064

Nielsen, A., Tetens, I., & Meyer, A. (2013). Potential of Phytase-Mediated Iron Release from Cereal-Based Foods: A Quantitative View. *Nutrients, 5*(8), 3074-3098. doi:10.3390/nu5083074

Nkhata, S., Kamau, E., Ayua, E., & Bosco, S. (2018). Fermentation and germination improve nutritional value of cereals and legumes through activation of endogenous enzymes. *Food Science & Nutrition, 6*, 1-13. doi:10.1002/fsn3.846

Nyakeriga, A. M., Troye-Blomberg, M., Chemtai, A. K., Marsh, K., & Williams, T. N. (2004). Malaria and nutritional status in children living on the coast of Kenya. *The American Journal of Clinical Nutrition, 80*(6), 1604-1610. doi:10.1093/ajcn/80.6.1604

Odriozola-Serrano, I., Soliva-Fortuny, R., & Martin-Belloso, O. (2008). Phenolic acids, flavonoids, vitamin C and antioxidant capacity of strawberry juices processed by high-intensity pulsed electric fields or heat treatments. *European Food Research and Technology, 228*, 239-248. doi:10.1007/s00217-008-0928-5

Ogbonnaya JA, Ketiku AO, Mojekwu CN, Mojekwu JN, & Ogbonnaya JA. (2012). Energy, iron and zinc densities of commonly consumed traditional complementary foods in Nigeria. . *Br J Appl Sci Technol (2012) 2(1):48–57. doi:10.9734/*

Oghbaei, M., & Prakash, J. (2016). Effect of primary processing of cereals and legumes on its nutritional quality: A comprehensive review. *Cogent Food & Agriculture, 2*(1), 1136015. doi:10.1080/23311932.2015.1136015

Olson, R., Gavin-Smith, B., Ferraboschi, C., & Kraemer, K. (2021). Food Fortification: The Advantages, Disadvantages and Lessons from Sight and Life Programs. *Nutrients, 13*(4), 1118. doi:10.3390/nu13041118

Onofiok, N. O., & Nnanyelugo, D. O. (1998). Weaning Foods in West Africa: Nutritional Problems and Possible Solutions. *Food and Nutrition Bulletin, 19*(1), 27-33. doi:10.1177/156482659801900105

Osazuwa, F., Ayo, O. M., & Imade, P. (2011). A significant association between intestinal helminth infection and anaemia burden in children in rural communities of Edo state, Nigeria. *North American journal of medical sciences, 3*(1), 30-34. doi:10.4297/najms.2011.330

Owais, A., Merritt, C., Lee, C., & Bhutta, Z. A. (2021). Anemia among Women of Reproductive Age: An Overview of Global Burden, Trends, Determinants, and Drivers of Progress in Low- and Middle-Income Countries. *Nutrients, 13*(8), 2745. doi:10.3390/nu13082745

Paganini, D., Uyoga, M., & Zimmermann, M. (2016). Iron Fortification of Foods for Infants and Children in Low-Income Countries: Effects on the Gut Microbiome, Gut Inflammation, and Diarrhea. *Nutrients, 8*(8), 494. doi:10.3390/nu8080494

Pal, R. S., Bhartiya, A., Yadav, P., Kant, L., Mishra, K. K., Aditya, J. P., & Pattanayak, A. (2017). Effect of dehulling, germination and cooking on nutrients, anti-nutrients, fatty acid composition and antioxidant properties in lentil (Lens culinaris). *Journal of Food Science and Technology, 54*(4), 909-920. doi:10.1007/s13197-016-2351-4

Pasricha, S.-R., Drakesmith, H., Black, J., Hipgrave, D., & Biggs, B.-A. (2013). Control of iron deficiency anemia in low- and middle-income countries. *Blood, 121*(14), 2607-2617. doi:10.1182/blood-2012-09-453522

Patel Sagar, S. (2021). Physiology, Oxygen Transport And Carbon Dioxide Dissociation Curve.

Peña-Rosas, J. P., & et al. (2015). Daily oral iron supplementation during pregnancy. *The Cochrane library.*

Perera, D. R. G., Gunawardana, D., Jayatissa, R., & Silva, A. B. G. (2020). Estimation of Iron Content and Its Contribution in Iron-Fortified Food Products Consumed by School Children in Sri Lanka. *Journal of Food Quality, 2020*, 6079379. doi:10.1155/2020/6079379

Phan-Thien, K.-Y., Wright, G. C., & Lee, N. A. (2012). Inductively coupled plasma-mass spectrometry (ICP-MS) and -optical emission spectroscopy (ICP–OES) for determination of essential minerals in closed acid digestates of peanuts (Arachis hypogaea L.). *Food Chemistry, 134*(1), 453-460. doi:https://doi.org/10.1016/j.foodchem.2012.02.095

Plessis LM, Kruger HS, & Sweet L. (2013). Complementary feeding: a critical window of opportunity from six months onwards. *S Afr J Clin Nutr 26(3 Suppl):S129–40.*

Qasem, W. A., & Friel, J. K. (2015). An Overview of Iron in Term Breast-Fed Infants. *Clinical Medicine Insights: Pediatrics, 9*, CMPed.S26572. doi:10.4137/cmped.s26572

Raboy, V. (2002). Progress in Breeding Low Phytate Crops. *The Journal of Nutrition, 132*(3), 503S-505S. doi:10.1093/jn/132.3.503s

Radlowski, E. C., & Johnson, R. W. (2013). Perinatal iron deficiency and neurocognitive development. *Frontiers in Human Neuroscience, 7*. doi:10.3389/fnhum.2013.00585

Ranjit, N., Jones, M. K., Stenzel, D. J., Gasser, R. B., & Loukas, A. (2006). A survey of the intestinal transcriptomes of the hookworms, Necator americanus and Ancylostoma caninum, using tissues isolated by laser microdissection microscopy. *International Journal for Parasitology, 36*(6), 701-710. doi:10.1016/j.ijpara.2006.01.015

Rao, R., & Georgieff, M. K. (2007). Iron in fetal and neonatal nutrition. *Seminars in Fetal and Neonatal Medicine, 12*(1), 54-63. doi:10.1016/j.siny.2006.10.007

Reinhold, J. G. (1972). Phytate concentrations of leavened and unleavened Iranian breads†. *Ecology of Food and Nutrition, 1*(3), 187-192. doi:10.1080/03670244.1972.9990288

Rodriguez-Guardado, A., Pozo, E., Fernandez-García, R., Amo-Fernandez, J., & Nozal-Gancedo, T. (2013). [Hookworm as cause of iron deficiency anemia in the prison population.]. *Revista espanola de sanidad penitenciaria, 15*, 63-65.

Rollán, G. C., Gerez, C. L., & Leblanc, J. G. (2019). Lactic Fermentation as a Strategy to Improve the Nutritional and Functional Values of Pseudocereals. *Frontiers in Nutrition, 6*.

Roughead, Z. K., Zito, C. A., & Hunt, J. R. (2005). Inhibitory effects of dietary calcium on the initial uptake and subsequent retention of heme and nonheme iron in humans: comparisons using an intestinal lavage method. *The American Journal of Clinical Nutrition, 82*(3), 589-597. doi:10.1093/ajcn/82.3.589

Roy, S. K., Jahan, K., Iqbal Kabir, A. K. M., Keya, N. A., Khatoon, S., Mannan, M. A., & Bhattacharjee, L. (2021). Improved recipes provide better complementary feeding in young children: findings of community-based trials in Bangladesh. *European Journal of Clinical Nutrition*. doi:10.1038/s41430-021-00936-z

Ruivard, M., & et al. (2009). Iron absorption in dysmetabolic iron overload syndrome is decreased and correlates with increased plasma hepcidin. *Journal of Hepatology, 50*(6), 1219.

Ruivard, M., Tournilhac, O., Montel, S., Fouilhoux, A.-C., Quainon, F., Lénat, A., . . . Philippe, P. (2006). Plasma exchanges do not increase red blood cell transfusion efficiency in severe autoimmune hemolytic anemia: A retrospective case-control study. *Journal of Clinical Apheresis, 21*(3), 202-206. doi:10.1002/jca.20096

Salonia, F., Ciacciulli, A., Poles, L., Pappalardo, H. D., La Malfa, S., & Licciardello, C. (2020). New Plant Breeding Techniques in Citrus for the Improvement of Important Agronomic Traits. A Review. *Frontiers in Plant Science, 11*. doi:10.3389/fpls.2020.01234

Samuel, T. M., & et al. (2020). Nutritional and Non-nutritional Composition of Human Milk Is Modulated by Maternal, Infant, and Methodological Factors. *Frontiers in Nutrition, 7*.

Sane, M., & et al. (2018). Fatal iron toxicity in an adult: Clinical profile and review. *Indian Journal of Critical Care Medicine, 22*(11), 801.

Sanz-Penella, J., Laparra Llopis, J. M., Sanz, Y., & Haros, C. M. (2012). Assessment of Iron Bioavailability in Whole Wheat Bread by Addition of Phytase-Producing Bifidobacteria. *Journal of Agricultural and Food Chemistry, 60*, 3190-3195. doi:10.1021/jf205048r

Saunders, A. V., Craig, W. J., Baines, S. K., & Posen, J. S. (2012). Iron and vegetarian diets. *The Medical Journal of Australia, 1*(2), 11-16. doi:10.5694/mjao11.11494

Sazawal, S., & et al. (2006). Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial. *Lancet, The, 367*(9505), 133.

Schlemmer, U., Frølich, W., Prieto, R. M., & Grases, F. (2009). Phytate in foods and significance for humans: Food sources, intake, processing, bioavailability, protective role and analysis. *Molecular Nutrition & Food Research, 53*(S2), S330-S375. doi:10.1002/mnfr.200900099

Scholl, T. O. (2011). Maternal iron status: relation to fetal growth, length of gestation, and iron endowment of the neonate. *Nutrition Reviews, 69*, S23-S29. doi:10.1111/j.1753-4887.2011.00429.x

Scholl, T. O., & Hediger, M. L. (1994). Anemia and iron-deficiency anemia: compilation of data on pregnancy outcome. *The American Journal of Clinical Nutrition, 59*(2), 492S-501S. doi:10.1093/ajcn/59.2.492s

Schönfeldt, H. C., & Gibson Hall, N. (2012). Dietary protein quality and malnutrition in Africa. *British Journal of Nutrition, 108*(S2), S69-S76. doi:10.1017/s0007114512002553

Shaw, J. G., & Friedman, J. F. (2011). Iron Deficiency Anemia: Focus on Infectious Diseases in Lesser Developed Countries. *Anemia, 2011*, 1.

Singh, S. P., Gruissem, W., & Bhullar, N. K. (2017). Single genetic locus improvement of iron, zinc and β-carotene content in rice grains. *Scientific Reports, 7*(1). doi:10.1038/s41598-017-07198-5

Siyuan, S., Tong, L., & Liu, R. (2018). Corn phytochemicals and their health benefits. *Food Science and Human Wellness, 7*(3), 185.

Skolmowska, D., & Głąbska, D. (2019). Analysis of Heme and Non-Heme Iron Intake and Iron Dietary Sources in Adolescent Menstruating Females in a National Polish Sample. *Nutrients, 11*(5), 1049. doi:10.3390/nu11051049

Spottiswoode, N., Duffy, P. E., & Drakesmith, H. (2014). Iron, anemia and hepcidin in malaria. *Frontiers in Pharmacology, 5*. doi:10.3389/fphar.2014.00125

Sreeramaiah, H., Platel, K., & Srinivasan, K. (2007). Influence of heat processing on the bioaccessibility of zinc and iron from cereals and pulses consumed in India. *Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS), 21*, 1-7. doi:10.1016/j.jtemb.2006.10.002

Stevens, G. A., Finucane, M. M., De-Regil, L. M., Paciorek, C. J., Flaxman, S. R., Branca, F., . . . Ezzati, M. (2013). Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. *The Lancet Global Health, 1*(1), e16-e25. doi:https://doi.org/10.1016/S2214-109X(13)70001-9

Stoffel, N. U., & et al. (2020). Oral iron supplementation in iron-deficient women: How much and how often? *Molecular Aspects of Medicine, 75*, 100865.

Stoltzfus, R. J. (2003). Iron Deficiency: Global Prevalence and Consequences. *Food and Nutrition Bulletin, 24*(4_suppl2), S99-S103. doi:10.1177/15648265030244s206

Stoltzfus, R. J. (2011). Iron Interventions for Women and Children in Low-Income Countries. *The Journal of Nutrition, 141*(4), 756S-762S. doi:10.3945/jn.110.128793

Stoltzfus, R. J., Heidkamp, R., Kenkel, D., & Habicht, J.-P. (2007). Iron Supplementation of Young Children: Learning from the New Evidence. *Food and Nutrition Bulletin, 28*(4_suppl4), S572-S584. doi:10.1177/15648265070284s410

Sundararajan, S., & Rabe, H. (2021). Prevention of iron deficiency anemia in infants and toddlers. *Pediatric Research, 89*(1), 63-73. doi:10.1038/s41390-020-0907-5

Sung, E. S., Choi, C. K., Kim, N. R., Kim, S. A., & Shin, M.-H. (2018). Association of Coffee and Tea with Ferritin: Data from the Korean National Health and Nutrition Examination Survey (IV and V). *Chonnam Medical Journal, 54*(3), 178. doi:10.4068/cmj.2018.54.3.178

Susana Chamorro, L. G., María Pilar Vaquero, Dolores Verdoy, Gorka Salas, Yurena Luengo, Agustín Brenes and Francisco José Teran,. (2015). Safety assessment of chronic oral exposure to iron oxide nanoparticles. *Nanotechnology, Volume 26, Number 20,*.

Suthutvoravut, U., Abiodun, P. O., Chomtho, S., Chongviriyaphan, N., Cruchet, S., Davies, P. S. W., . . . Koletzko, B. (2015). Composition of Follow-Up Formula for Young Children Aged 12-36 Months: Recommendations of an International Expert Group Coordinated by the Nutrition Association of Thailand and the Early Nutrition Academy. *Annals of Nutrition and Metabolism, 67*(2), 119-132. doi:10.1159/000438495

Swain, J. H., Newman, S. M., & Hunt, J. R. (2003). Bioavailability of Elemental Iron Powders to Rats Is Less than Bakery-Grade Ferrous Sulfate and Predicted by Iron Solubility and Particle Surface Area. *The Journal of Nutrition, 133*(11), 3546-3552. doi:10.1093/jn/133.11.3546

Tako, E., Reed, S., Budiman, J., Hart, J., & Glahn, R. (2015). Higher iron pearl millet (Pennisetum glaucum L.) provides more absorbable iron that is limited by increased polyphenolic content. *Nutrition Journal, 14*, 11. doi:10.1186/1475-2891-14-11

Taylor, P. G., Martínez-Torres, C., Romano, E. L., & Layrisse, M. (1986). The effect of cysteine-containing peptides released during meat digestion on iron absorption in humans. *The American Journal of Clinical Nutrition, 43*(1), 68-71. doi:10.1093/ajcn/43.1.68

Teshale, A. B., Tesema, G. A., Worku, M. G., Yeshaw, Y., & Tessema, Z. T. (2020). Anemia and its associated factors among women of reproductive age in eastern Africa: A multilevel mixed-effects generalized linear model. *PLOS ONE, 15*(9), e0238957. doi:10.1371/journal.pone.0238957

Teucher, Olivares, & Cori. (2004). Enhancers of Iron Absorption: Ascorbic Acid and other Organic Acids. *International Journal for Vitamin and Nutrition Research, 74*(6), 403.

Teucher, B., Olivares, M., & Cori, H. (2004). Enhancers of Iron Absorption: Ascorbic Acid and other Organic Acids. *International journal for vitamin and nutrition research. Internationale Zeitschrift für Vitamin- und Ernährungsforschung. Journal international de vitaminologie et de nutrition, 74*, 403-419. doi:10.1024/0300-9831.74.6.403

Thankachan, P., Walczyk, T., Muthayya, S., Kurpad, A. V., & Hurrell, R. F. (2008). Iron absorption in young Indian women: the interaction of iron status with the influence of tea and ascorbic acid. *The American Journal of Clinical Nutrition, 87*(4), 881-886. doi:10.1093/ajcn/87.4.881

The World Bank Group. (2009). Anemia. http://web.worldbank.org/archive/website01213/WEB/0__CO-50.HTM. Retrieved 2021-10-26.

Theil, E. C. (2004). IRON, FERRITIN, AND NUTRITION. *Annual Review of Nutrition, 24*(1), 327-343. doi:10.1146/annurev.nutr.24.012003.132212

Theil, E. C., Chen, H., Miranda, C., Janser, H., Elsenhans, B., Núñez, M. T., . . . Schümann, K. (2012). Absorption of Iron from Ferritin Is Independent of Heme Iron and Ferrous Salts in Women and Rat Intestinal Segments. *The Journal of Nutrition, 142*(3), 478-483. doi:10.3945/jn.111.145854

Tontisirin, K., Nantel, G., & Bhattacharjee, L. (2002). Food-based strategies to meet the challenges of micronutrient malnutrition in the developing world. *Proceedings of the Nutrition Society, 61*(2), 243-250. doi:10.1079/pns2002155

Trinidad, T. P., Kurilich, A. C., Mallillin, A. C., Walcyzk, T., Sagum, R. S., Singh, N. N., . . . Fletcher, J. (2014). Iron absorption from NaFeEDTA-fortified oat beverages with or without added vitamin C. *International Journal of Food Sciences and Nutrition, 65*(1), 124-128. doi:10.3109/09637486.2013.836739

Trinidad, T. P., Mallillin, A. C., Sagum, R. S., Briones, D. P., Encabo, R. R., & Juliano, B. O. (2009). Iron absorption from brown rice/brown rice-based meal and milled rice/milled rice-based meal. *International Journal of Food Sciences and Nutrition, 60*(8), 688-693. doi:10.3109/09637480701830404

Trinidad, T. P., Mallillin, A. C., Sagum, R. S., Briones, D. P., Encabo, R. R., & Juliano, B. O. (2009). Iron absorption from brown rice/brown rice-based meal and milled rice/milled rice-based meal. *Int J Food Sci Nutr, 60*(8), 688-693. doi:10.3109/09637480701830404

Tseng, M., Chakraborty, H., Robinson, D. T., Mendez, M., & Kohlmeier, L. (1997). Adjustment of Iron Intake for Dietary Enhancers and Inhibitors in Population Studies: Bioavailable Iron in Rural and Urban Residing Russian Women and Children. *The Journal of Nutrition, 127*(8), 1456-1468. doi:10.1093/jn/127.8.1456

Tuntawiroon, M., Sritongkul, N., Rossander-Hultén, L., Pleehachinda, R., Suwanik, R., Brune, M., & Hallberg, L. (1990). Rice and iron absorption in man. *Eur J Clin Nutr, 44*(7), 8.

Turksoy, S., Ozkaya, B., & Akbas, S. (2010). The effect of wheat variety and flour extraction rate on phytic acid content of bread. *J. Food Agr. Env., 8*.

Van Zutphen, K. G., Kraemer, K., & Melse-Boonstra, A. (2021). Knowledge Gaps in Understanding the Etiology of Anemia in Indonesian Adolescents. *Food and Nutrition Bulletin, 42*(1_suppl), S39-S58. doi:10.1177/0379572120979241

Vasconcelos, M. W., Gruissem, W., & Bhullar, N. K. (2017). Iron biofortification in the 21st century: setting realistic targets, overcoming obstacles, and new strategies for healthy nutrition. *Current Opinion in Biotechnology, 44*, 8.

Vossenaar, M., & Solomons, N. (2012). The concept of "critical nutrient density" in complementary feeding: The demands on the "family foods" for the nutrient adequacy of young Guatemalan children with continued breastfeeding. *The American Journal of Clinical Nutrition, 95*, 859-866. doi:10.3945/ajcn.111.023689

Wallace Daniel, F. D. (2016). The Regulation of Iron Absorption and Homeostasis. *Clinical Biochemist Reviews, The, 37*(2), 51-62.

Wassmer, S. C., Taylor, T. E., Rathod, P. K., Mishra, S. K., Mohanty, S., Arevalo-Herrera, M., . . . Smith, J. D. (2015). Investigating the Pathogenesis of Severe Malaria: A Multidisciplinary and Cross-Geographical Approach. *The American Journal of Tropical Medicine and Hygiene, 93*(3_Suppl), 42-56. doi:10.4269/ajtmh.14-0841

Weatherall, D. J. (2010). Thalassemia as a global health problem: recent progress toward its control in the developing countries. *Annals of the New York Academy of Sciences, 1202*(1), 17-23. doi:10.1111/j.1749-6632.2010.05546.x

WegmüLler, R., Zimmermann, M. B., Moretti, D., Arnold, M., Langhans, W., & Hurrell, R. F. (2004). Particle Size Reduction and Encapsulation Affect the Bioavailability of Ferric Pyrophosphate in Rats. *The Journal of Nutrition, 134*(12), 3301-3304. doi:10.1093/jn/134.12.3301

Welch, R. M., & Graham, R. D. (2002). *Plant and Soil, 245*(1), 205-214. doi:10.1023/a:1020668100330

West, A. R., & Oates, P. S. (2008). Mechanisms of heme iron absorption: Current questions and controversies. *World Journal of Gastroenterology, 14*(26), 4101. doi:10.3748/wjg.14.4101

Wheeler, E. L., & Ferrel, R. E. (1971). A method for phytic acid determination in wheat and wheat fractions. *Cereal Chemistry, 48*, 312-320.

WHO. (1993). Iron Deficiency Anaemia Assessment, Prevention, and Control,https://www.who.int/nutrition/publications/en/ida_assessment_prevention_control.pdf, Accessed January 2021.

WHO. (2005). Worldwide prevalence of anaemia 1993–2005, WHO Global Database on Anaemia.

WHO. (2006). Guidelines on food fortification with micronutrients. https://www.who.int/nutrition/publications/guide_food_fortification_micronutrients.pdf. Accessed, February 2021.

WHO. (2008). Worldwide prevalence of anaemia 1993-2005. WHO Global Database on Anaemia Geneva, World Health Organization, https://www.who.int/vmnis/anaemia/prevalence/summary/anaemia_data_status_t2/en/. Accessed February 2021.

WHO. (2011). Anaemia. https://www.who.int/health-topics/anaemia#tab=tab_1.

WHO. (2020). Global anaemia reduction efforts among women of reproductive age: impact, achievement of targets and the way forward for optimizing efforts. .https://apps.who.int. Retrieved on 2022-01-22.

WHO. (2022). Anemia in women and children: https://www.who.int/data/gho/data/themes/topics/anaemia_in_women_and_children#:~:text=Summary%20findings&text=In%202019%2C%20global%20anaemia%20prevalence,women%20aged%2015%2D49%20years. Retrived on 2022-01-22.

WHO/FAO/UNICEF/GAIN/MI/FFI. (2009). Recommendations on Wheat and Maize Flour Fortification. https://www.who.int/nutrition/publications/micronutrients/wheat_maize_fort.pdf?ua=1. Accessed February 2021.

WHO/UNICEF/UNU. (1998). IDA: Prevention, Assessment and Control. Report of a joint WHO/UNICEF/UNU consultation. World Health Organization, Geneva.

WHO/UNU/UNICEF. (2001). Iron Deficiency Anaemia Assessment, Prevention, and Control, https://www.who.int/nutrition/publications/en/ida_assessment_prevention_control.pdf.

Widdowson EM, S. D., Hey E: . (1988,). Fetal growth and body composition; in Lindblad BS (ed): Perinatal Nutrition. Bristol-Myers Nutrition Symposia. 6. . *New York, Academic Press,*, pp 3-14.

Wienk, K. J. H., Marx, J. J. M., & Beynen, A. C. (1999). The concept of iron bioavailability and its assessment. *European Journal of Nutrition, 38*(2), 51-75. doi:10.1007/s003940050046

World Bank, h. w. w. o. a. w. W. C.-H. R. o.-.-. (2004).

World Health Organisation. (2021). https://www.who.int/news-room/fact-sheets/detail/infant-and-young-child-feeding.

World Health Organization, UNICEF, USAID, AED, UCDAVIS, & IFPRI. (2008.). Indicators for assessing infant and young child feeding practices, Part 1- Definitions. Washington, DC, US: http://apps.who.int/iris/bitstream/handle/10665/43895/9789241596664_eng.pdf;jsessionid=53110D56E7DDAD8366D7457CC305A062?sequence=1.

Yip R, D. P. (1996). *Iron. Present knowledge in nutrition. Ziegler EE, Filer LJ, editors. Washington DC: ILSI Press, 7th ed.*

Yuen Ho-Wang, H. W. (2021). Iron Toxicity.

Zhu, C., & et al. (2007). Transgenic strategies for the nutritional enhancement of plants. *Trends in Plant Science, 12*(12), 548.

Zhu, C., Zheng, X., Huang, Y., Ye, J., Chen, P., Zhang, C., . . . Deng, X. (2019). Genome sequencing and CRISPR /Cas9 gene editing of an early flowering Mini-Citrus (Fortunella hindsii). *Plant Biotechnology Journal, 17*(11), 2199-2210. doi:10.1111/pbi.13132

Ziegler, E., Nelson, S., & Jeter, J. (2014). Iron Stores of Breastfed Infants during the First Year of Life. *Nutrients, 6*(5), 2023-2034. doi:10.3390/nu6052023

Zlotkin, S. H., Christofides, A. L., Hyder, S. M. Z., Schauer, C. S., Tondeur, M. C., & Sharieff, W. (2004). Controlling iron deficiency anemia through the use of home-fortified complementary foods. *The Indian Journal of Pediatrics, 71*(11), 1015-1019. doi:10.1007/bf02828118