IMPACT OF PHYSICAL ACTIVITY ON COGNITIVE FUNCTION IN WOMEN WITH IRON DEFICIENCY ANEMIA

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ABSTRACT

Background: *Iron deficiency anemia (IDA) is associated with cognitive impairment in women, yet the potential role of physical activity (PA) in mitigating these deficits remains unexplored. This study aimed to investigate the impact of physical activity on cognitive function among women with IDA.*

Methods: *A cross-sectional study was conducted on 228 women aged 18–45 years diagnosed with IDA for at least six months to 1 year. Participants were categorized into Inactive, Moderate, and Active groups based on the International Physical Activity Questionnaire (IPAQ)-Long Form. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) Version 8.1. Descriptive and inferential statistics, including chi-square tests, MANOVA, and one-way ANOVAs, were used to evaluate the association between physical activity levels and cognitive performance.*

Results: *The mean age of participants was 27.57 ± 7.50 years, with a mean BMI of 23.28 ± 2.92 kg/m². Physical activity was significantly associated with global cognitive performance (χ^2 (6, N = 228) = 178.24, $p < .001$). The Active group exhibited the highest proportion of normal cognition (54.2%), while the Inactive group had the greatest prevalence of moderate (89.4%) and severe (100%) cognitive impairment. Significant differences were observed across multiple cognitive domains, including Attention, Orientation, Naming, Language Abstraction and Delayed Recall ($p < .001$), whereas Visuospatial/Executive function did not differ significantly between both groups.*

Conclusion: *Higher physical activity levels are strongly associated with better cognitive performance in women with IDA, suggesting that regular physical activity may act as a protective factor against cognitive decline. While causality cannot be confirmed due to the cross-sectional design, these findings support the integration of physical activity into holistic management strategies for women with IDA. Future longitudinal and interventional studies are recommended to establish causal relationships, optimize exercise interventions, and explore underlying physiological mechanisms.*

Keywords: *Iron deficiency anemia, physical activity, cognitive function, MoCA, IPAQ, women*

INTRODUCTION

Anemia is an international public health problem (Loechl et al., 2023) that affect those living in both developed and developing countries (Sharief et al., 2019) (ELMoslemany et al., 2019) and has a strong negative influence on women's quality of life (Firquet et al., 2017). Anemia is a global health problem in which the size and/or number of red blood cells (RBC) or the concentration of hemoglobin (Hb) falls below healthy values (Bahrami et al., 2020) (Turner et al., 2018) (Chaudhry & Kasarla, 2017) (Yilmaz & Shaikh, 2020) (Mahar et al., 2024) (Tang & Sholzberg, 2024) (Chaparro & Suchdev, 2019). Anemia was defined according to World Health Organization criteria: hemoglobin concentrations lower than 13 g/ dl for men and lower than 12 g/dl for women (Soliman et al., 2017) who are not pregnant, and below 11.0 g/dL in pregnant women (Jimenez et al., 2015) (Yilmaz & Shaikh, 2020) (More et al., 2013).

Anemia occurs in 1.62 billion individuals worldwide (Yunanci et al., 2023) (Abd–Allah et al., 2018) (Devi & Mageshwari, 2015), which is equivalent to 24.8 percent of the total population (Devi & Mageshwari, 2015). Despite global advancements in science and medicine, anemia continues to be one of the most prevalent conditions recorded globally (Pivina et al., 2019). Anemia is a worldwide public health issue that affects people of all ages, it occurs in almost all geographic regions & in most age groups although it is more common in females than men (Kausar et al., 2023) (Chaparro & Suchdev, 2019). The World Health Organization (WHO) estimates anemia affects 37% (32 million) of pregnant women, and 30% (32 million) of non- pregnant women 15–49 years of age (Tang & Sholzberg, 2024). According to the National Nutritional Survey Pakistan (NNS) in 2011, Moderate to severe anemia can result from inadequate nutritional consumption (Mahar et al., 2024). According to reports, anemia affects 50% of Pakistani women who are of reproductive age, and in Punjab, a province in Pakistan, 21% of women in the 9–29 age group also struggle with quality of life (Kausar et al., 2023). A survey in the 2011 Sindh Province revealed a greater prevalence of anemia in both groups, with 59.7% in pregnant females and 62.0% in the adolescent/WRA group; however, in the survey in the 2018 Baluchistan Province, the highest prevalence was 53.9% and 61.8%, respectively (Mahar et al., 2024).

At a biological level, anemia develops because of an imbalance in erythrocyte loss relative to production; this can be due to ineffective or deficient erythropoiesis (e.g., from nutritional deficiencies, inflammation, or genetic Hb disorders) and/or excessive loss of erythrocytes (due to hemolysis, blood loss, or both) (Chaparro & Suchdev, 2019; Turner et al., 2018). Reduced hemoglobin in the RBCs decreases the amount of oxygen delivered to the peripheral tissues leading to tissue hypoxia (Chaudhry & Kasarla, 2017).

Etiology of anemia identifying how distal factors contribute to more proximate determinants of anemia, such as food insecurity, clean water, and sanitation, and, ultimately, the most immediate causes of anemia (e.g., nutritional deficiencies, disease, inflammation, and Hb disorders) (Chaparro & Suchdev, 2019). Poor socioeconomic position and low education level is linked to a greater risk of anemia among women (Chaparro & Suchdev, 2019). In developing countries most common cause of anemia is malnutrition and poor dietary intake (Mawani et al., 2016). In a study of Malawian PSC, factors associated with severe anemia included malaria, bacteremia, hookworm infection, HIV infection, TB, glucose-6-phosphate dehydrogenase (G6PD) deficiency, and vitamin A (VA) and B12, folates deficiencies (Chaparro & Suchdev, 2019) (Loechl et al., 2023). Sickle cell disorders were the fifth and seventh top causes of anemia among females and males, respectively (Chaparro & Suchdev, 2019). Heavy menstrual bleeding (HMB) is an important cause of anemia in peri-menopausal women (Firquet et al., 2017). Anemia may have multiple etiologies, but iron deficiency (ID) is categorized as the most common cause and the major contributing factor to 50 % of all types of anemia among reproductive-age women (Sekhar et al., 2016) (Warner & Kamran, 2023).

Mild anemia may be asymptomatic (Turner et al., 2018). The critical role of Hb to carry oxygen to the tissues explains the most common clinical symptoms of anemia, which include fatigue (Jimenez et al., 2015), shortness of breath (Turner et al., 2018), bounding pulses or palpitations (Mawani et al., 2016), conjunctival and palmar pallor (Chaparro & Suchdev, 2019), impaired cognitive function, diminished well-being (Jimenez et al., 2015), lethargy (Turner et al., 2018), slow development, difficulty in maintaining body temperature, decreased immune function, inflamed tongue, headache, dizziness, emotional instability, depression and restlessness (Mawani et al., 2016), weakness, and tiredness, restless legs, syncope, chest pain, reduced exercise tolerance-with more severe anemia, Pica- desire to eat unusual and non-dietary substances (Turner et al., 2018).

Anemia affects an individual's physical and mental development, which decreases their ability to work, which ultimately impacts the development of the whole country (Devi & Mageshwari, 2015). Systematic reviews have indicated that anemia is related to reduction in cognitive performance (Kim et al., 2019). Numerous epidemiological studies have highlighted and association between anemia and the increased risk of developing cognitive impairment (Kung et al., 2021). The risk of CI was significantly higher in patients when compared to those who did not have any kind of anemia (Kung et al., 2021). Patients who had anemia were more likely to develop mild cognitive impairment (MCI) compared to those who did not have any kind of anemia (Kung et al., 2021). Anemic girls have significantly reduced levels of cognitive abilities (Bahrami et al., 2020). Anemia is associated with increased morbidity and mortality in women, poor birth outcomes, decreased work productivity in adults, and impaired cognition & behavior (Chaparro & Suchdev, 2019) (Kausar et al., 2023). Some of the studies have established a strong correlation between Hgb levels and CI (Marzban et al., 2021), while others have shown no meaningful relationship between anemia and CI (Marzban et al., 2021). It is also established that increased levels of hemoglobin lead to improved CNS functions (Sharief et al., 2019).

Most anemias have a characteristic RBC appearance, which can provide insights to the diagnosis of anemia (Chaparro & Suchdev, 2019). At the population level and in clinical practice, Hb concentration is the most common hematological assessment method used and the most common indicator used to define anemia (Chaparro & Suchdev, 2019) (Friedman et al., 2015) (Chaudhry & Kasarla, 2017). Clinical signs and medical history are used to diagnose anemia when hematological data are unavailable, but they are limited in their ability to detect anemia (Chaparro & Suchdev, 2019). The cutoff values of Hb concentrations have been defined by the World Health Organization (WHO) for various population groups (Bahrami et al., 2020). The diagnosis of anemia patients was based on WHO criteria, i.e., men: Hb < 13 g/dL, women: Hb <12 g/dL, measured in blood samples (Kung et al., 2021) (Marzban et al., 2021) (Bahrami et al., 2020) (Lee, 2020) (Sekhar et al., 2016). Hb levels may vary across age and race (Cappellini et al., 2022), so care must be taken, particularly in the interpretation of borderline values (Turner et al., 2018).

Approach to anemia includes identification of the type of anemia (Turner et al., 2018). Identifying the cause of anemia and treating it appropriately is very crucial in the management of anemia (Turner et al., 2018).

Anemia, if undiagnosed or left untreated for a prolonged period of time can lead to multiorgan failure and can even death (Turner et al., 2018). Anemia has been linked with increased prevalence of cardiovascular diseases, cognitive impairment, reduced physical performance, quality of life and increased fall risk and fractures (Abd–Allah et al., 2018) (Mawani et al., 2016).

Efforts are needed to further understand how the principal causes of anemia, including ID and other nutritional deficiencies, disease, and Hb disorders, contribute to anemia so that appropriate interventions in specific settings can be implemented (Chaparro & Suchdev, 2019). The early identification of a patient's conditions and the proper management of anemia patients might contribute to the prevention of CI risk (Kung et al., 2021). The 2019 United Kingdom guidelines recommend initiating oral iron without delay to anemic patients (Tang & Sholzberg, 2024). Precise screening and treatment of anemia in adolescent girls is recommended (Bahrami et al., 2020). The Centers for Disease Control and Prevention (CDC) recommends testing "all nonpregnant women for anemia every 5–10 years throughout their childbearing years during routine health examinations" (Sekhar et al., 2016) (Weyand et al., 2023).

The WHO Global Nutrition Target 2025 on anemia aims to reduce anemia in women with reproductive age by 50% by 2025.(Chaparro & Suchdev, 2019) (Benson et al., 2021). Based on a global prevalence of 29.38% anemia among WRA (nonpregnant and pregnant, respectively) as of 2011, a reduction of 1.8-2.4 percentage points per year would be required to meet this target. (Chaparro & Suchdev, 2019). Without addressing the gaps in knowledge and implementation science, the global goals to reduce anemia burden are likely to fail (Chaparro & Suchdev, 2019). For all age groups and both sexes, anemia is estimated to have decreased roughly seven percentage points between 1990 and 2016, from 40% to 33%(Chaparro & Suchdev, 2019).

The basic and important function of iron (as a part of hemoglobin) is to transport oxygen (Coad & Pedley, 2014) from lungs to cells in our body and is an essential requirement of the body (Mawani et al., 2016). Iron is essential for synthesis of hemoglobin, cell growth and differentiation, neurotransmission, immunity and cardiopulmonary function (Benson et al., 2021). The function of central nervous system (CNS) processes is highly dependent on iron containing enzymes and proteins (Sekhar et al., 2016) (Firquet et al., 2017). Iron status has an impact on cognitive performance (including spatial ability, attention, memory, learning, reasoning ability and executive functioning) in women of reproductive age (Firquet et al., 2017). Iron is crucial to biologic functions (Clark, 2008) including respiration, energy production (Cook et al., 2017) (McClung & Murray-Kolb, 2013), DNA synthesis, and cell proliferation (Camaschella, 2015).

A considerable body of evidence has established that appropriate levels of brain iron are necessary for optimal brain development and functioning (McClung & Murray-Kolb, 2013). Iron is the main component of hemoglobin and is the prime carrier of oxygen (Chaudhry & Kasarla, 2017) (Warner & Kamran, 2023). The growth of the brain and the preservation of its neural connections and function depend heavily on iron, which is also essential for myelination (Sharief et al., 2019) and brain development (Cook et al., 2017). Iron is required by the enzymes involved in brain function, including myelination (Sharief et al., 2019) (Can et al., 2018) (McClung & Murray-Kolb, 2013). Moreover, it also plays an important character in the mechanisms of brain development, such as: The brain's development, intelligence, attention span, and sensory perception functions in the brain (Sharief et al., 2019).

Depending on the type of intervention and the context, we will need to consider and address different priority factors, including the timing, safety, and efficacy of interventions to improve iron status (Loechl et al., 2023). The recommended dietary allowance (RDA) for iron is 8 mg/day for adult postmenopausal women and 18 mg/day for premenopausal women (Coad & Pedley, 2014) (McClung & Murray-Kolb, 2013) (Sekhar et al., 2016) (DeLoughery, 2017) (Tang & Sholzberg, 2024). A sensible approach to oral iron replacement is to start with a single ferrous sulfate taken with a meal that (if not vegetarian) contains meat (DeLoughery, 2017). Avoiding tea and coffee plus taking 500 units of vitamin C with that meal will also aid iron absorption (DeLoughery, 2017). Iron should be continued until iron stores are replete with a goal ferritin of 50 to 100 ng/Dl (DeLoughery, 2017).

ID is a visible reduction in the overall iron content in the body or having less than normal iron stores for physiological status (Yunanci et al., 2023). According to CDC (centers for disease control and prevention), "Iron deficiency is a condition resulting from too little iron in the body" (Mawani et al., 2016). The topic of ID in peri-menopausal women is rarely addressed in the literature (Firquet et al., 2017).

Iron deficiency is a major cause of anemia and is more prevalent in developing countries (Mawani et al., 2016). Iron deficiency affects more than 2 billion people worldwide (Camaschella, 2015) (Dziembowska et al., 2019). Fifty percent of anemia cases are caused by ID across the globe and is a world health issue. (Sharief et al., 2019) (Marzban et al., 2021; Yunanci et al., 2023) (ELMoslemany et al., 2019) (Lopez et al., 2016) (Mawani et al., 2016) (Mahar et al., 2024). Recent statistics shows a prevalence of around 45% of Iron deficiency anemia in Pakistan (Mawani et al., 2016). ID is considered the most common nutritional deficiency leading to anemia, though other nutritional deficiencies can also cause anemia, including deficiencies of vitamins A, B12, B6, C, D, E, folate, riboflavin, copper, and zinc.(Chaparro & Suchdev, 2019) (Tang & Sholzberg, 2024) (Mawani et al., 2016) (Dziembowska et al., 2019) (Coad & Pedley, 2014) (McClung & Murray-Kolb, 2013). The prevalence of ID and IDA is often greater in premenopausal women than other population demographics (McClung & Murray-Kolb, 2013). It is also well documented that the incidence of iron deficiency, with and without anemia, is greater in female athletes than male athletes compared with the less active population (Clark, 2008).

In general, iron deficiency results when iron demands by the body are not met by iron absorption (Clark, 2008). Iron deficiency may result from a single or a combination of several major factors: insufficient dietary iron consumption and/or decreased dietary bioavailability (Mahar et al., 2024) Reduced amounts of iron storage in the body are associated with deficiency that results in a deteriorating trend in the number of RBC and a decrease in the supply of iron in tissues (Yang et al., 2023).

Several conditions have been identified in the literature as risk factors for ID in women (Firquet et al., 2017). Risk factors that healthcare professionals should be aware of include vegetarian or vegan diets, teenage pregnancy, previous anemia, multiple gestation and short inter-pregnancy interval (< 1 year) (Benson et al., 2021).The high-risk group consists of females and children but comparatively it is higher in females due to physiological reasons (Mawani et al., 2016) (Clark, 2008). For women, the risk of iron deficiency and iron deficiency anemia increases due to iron demands during pregnancy and regular iron losses due to menstruation during reproductive years (Tang & Sholzberg, 2024) (Dziembowska et al., 2019) (Clark, 2008) (Coad & Pedley, 2014). Cross-sectional studies in industrialized countries have shown that obese individuals are at increased risk of iron deficiency (Mawani et al., 2016). Gastrointestinal conditions, such as celiac disease and inflammatory bowel disease (IBD), as well as chronic kidney disease (CKD), cancer, and chronic heart failure (CHF) increase the risk for anemia and iron deficiency (Jimenez et al., 2015) (Clark, 2008). People of low socioeconomic status are at higher risk of iron deficiency due to low intake of expensive iron-rich foods, and decreased access to healthcare (Tang & Sholzberg, 2024).

The most common causes of iron deficiency are bleeding (menstrual, gastrointestinal), impaired iron absorption (atrophic gastritis, celiac disease, bariatric surgical procedures), inadequate dietary iron intake, and pregnancy (Tang & Sholzberg, 2024) (Leung et al., 2024) (Firquet et al., 2017). ID develops when [dietary iron intake cannot meet iron needs over a period of time, especially during periods of life when iron requirements are particularly high or when iron losses exceed iron intake. (Cook et al., 2017) (Tang & Sholzberg, 2024) (More et al., 2013). The patient's diet can also affect the efficacy of supplementation, as many foods and drinks contain inhibitors of iron absorption (Loechl et al., 2023) (Benson et al., 2021). Phytic acid, which is found in cereals and legumes, is a well-known potent inhibitor of iron absorption and the cause of iron deficiency (Loechl et al., 2023) (Mawani et al., 2016) (Tang & Sholzberg, 2024) (Coad & Pedley, 2014). Coffee, black tea, herbal teas, red wine, and hot chocolate contain polyphenols, which also impair iron bioavailability (Loechl et al., 2023) (Coad & Pedley, 2014) (DeLoughery, 2017) (Benson et al., 2021). Vegetarians and vegans have a greater risk of ID as their heme iron intake is almost nil (Firquet et al., 2017) (Benson et al., 2021). Peri-menopausal women are vulnerable to ID due to low dietary iron intake resulting from restrictive dieting aimed at losing weight (Firquet et al., 2017). The use of copper IUDs is also a risk factor; 28% of women using copper IUDs were found to be iron depleted (Firquet et al., 2017). Female athletes, and especially long distance runners, suffer ID due to insufficient iron intake, menstruation or increased blood losses due to exercise (sweating, hemolysis, hematuria or GI bleeding (Firquet et al., 2017). Bleeding associated with anticoagulants/ aspirin/non-steroidal anti-inflammatory drugs (NSAIDs), proton pump inhibitors may contribute to ID (Firquet et al., 2017) (Benson et al., 2021). Obesity, a chronic inflammatory condition with an increasing prevalence, also has the potential to compromise iron status (Firquet et al., 2017).

Symptoms highly suggestive of ID include generalized fatigue (Soliman et al., 2017) (DeLoughery, 2017) (Tang & Sholzberg, 2024) (Jimenez et al., 2015) (Coad & Pedley, 2014) (McClung & Murray-Kolb, 2013) (Benson et al., 2021), often independent of anemia, ingestion of non-nutritive materials such as clay, dirt, paper, laundry starch (amylophagia), and others (pica) (Auerbach & Adamson, 2016) (DeLoughery, 2017) (Benson et al., 2021), pagophagia (ice craving), brittle nails, hair loss (Benson et al., 2021), and restless legs syndrome (Auerbach & Adamson, 2016) (DeLoughery, 2017) (Jimenez et al., 2015) (Turner et al., 2018) (Lee, 2020) (Benson et al., 2021), weakness, impaired immune function, and reduced cognitive function (Soliman et al., 2017) (Tang & Sholzberg, 2024) (Jimenez et al., 2015) (More et al., 2013) (Coad & Pedley, 2014), tachycardia, lack of endurance, cold intolerance (DeLoughery, 2017), reduced physical and mental endurance (Dziembowska et al., 2019) (More et al., 2013) (Coad & Pedley, 2014), impaired development, poor health-related quality of life (Tang & Sholzberg, 2024) (Jimenez et al., 2015), infertility (Jimenez et al., 2015), esophageal webs (Turner et al., 2018), depressed immune function (More et al., 2013), sleep disturbance (Lee, 2020), depression, apathy, irritability, depression/low mood (Benson et al., 2021), problems with concentration (brain fog) (Coad & Pedley, 2014) (McClung & Murray-Kolb, 2013) (Al-Sayes et al., 2011) (Benson et al., 2021), headache (Al-Sayes et al., 2011), aching, reduced exercise tolerance, anxiety, poor work performance (Benson et al., 2021). Signs of ID include pallor (with anemia), decreased population of the tongue, cheilosis (cracking at the corners of the mouth), and prominent defects in the nail beds including Mees lines and koilonychia, spooning of the nails (Auerbach & Adamson, 2016). A common complaint in iron-deficient women is hair loss, with increased loss reported in women with ferritins less than 100 ng/dL (DeLoughery, 2017).

The impact of ID on CF is sufficiently documented (Selvi Öztorun et al., 2018). Iron deficiency, which has a significant role in oxygen delivery and storage, could result in cerebral hypoxia and mental decline (Marzban et al., 2021; Sharief et al., 2019; Yavuz et al., 2012). ID in women and decreased serum iron associated with psychological effects and decreased dopamine production (Coad & Pedley, 2014) that adversely effects on cognitive memory (Coad & Pedley, 2014) (El Nahas & Gabr, 2017) (Mawani et al., 2016), cognitive performance, motor performance (Coad & Pedley, 2014) (Can et al., 2018), delay in mental and motor development (Camaschella, 2015) (Mawani et al., 2016) (Can et al., 2018), cognitive (McClung & Murray-Kolb, 2013) (Auerbach & Adamson, 2016) (Coad & Pedley, 2014), behavioral (McClung & Murray-Kolb, 2013) (Can et al., 2018), and executive planning functions (Lopez et al., 2016) (Coad & Pedley, 2014), attention disorder (Coad & Pedley, 2014), emotional disorders, intellectual ability disorder, sensory perception issues (Coad & Pedley, 2014) (Pivina et al., 2019) (Firquet et al., 2017), spatial ability, reasoning abilities, learning, motivation, memory, addiction (Coad & Pedley, 2014), increased anxiety and depressive symptoms (Can et al., 2018), affective and neurophysiological declines have been associated with poor iron status in premenopausal women (McClung & Murray-Kolb, 2013). The collective impact of HMB and mild iron deficiency in females of reproductive age may be connected with CNS function that negatively impacts quality of life (Can et al., 2018), decrements in energy, activity, (Can et al., 2018), productivity (Tang & Sholzberg, 2024), sexual function, and work productivity (Auerbach & Adamson, 2016), increased fatigue (Mawani et al., 2016), altered endurance, stimulus seeking behavior (Dziembowska et al., 2019), pre-menopausal women with ID were found to have poorer results on tests of attention, learning and memory when compared to iron sufficient participants. (Can et al., 2018). Therefore, more attention should be paid to preventing even mild iron deficiency, particularly among young women (Dziembowska et al., 2019).

The most recent guidelines from the WHO published in April 2020 recommend a ferritin cut-off of < 15 μg.l-1 for diagnosing iron deficiency (Benson et al., 2021), and ID was defined as hemoglobin (Hb) concentrations < 12g/dl in adults (Wenger et al., 2019). Multiple factors like age, parity, socioeconomic status and diet can determine the stores of iron in the women of reproductive age group (Mawani et al., 2016). The laboratory diagnosis includes several tests, each of which requires some degree of interpretation to be accurately applied (Auerbach & Adamson, 2016). No single test, serum iron value is diagnostic of ID (Auerbach & Adamson, 2016) (Camaschella, 2015). Iron levels can be detected via blood works of Hemoglobin, Hematocrit, CBC, serum iron, ferritin (DeLoughery, 2017) (Lee, 2020) (Tang & Sholzberg, 2024), transferrin saturation and transferrin receptor (Mawani et al., 2016). Ferritin values, which represent the iron stores, seem a better candidate for screening (Firquet et al., 2017) (Coad & Pedley, 2014) (Camaschella, 2015). A low ferritin value confirms ID (Firquet et al., 2017).

There are several success stories of countries implementing interventions and getting a good outcome (Mawani et al., 2016). Groups like young children, adolescent girls, women of reproductive age, pregnant and lactating women should be an area of focus for interventions (Mawani et al., 2016). A recent Cochrane review concluded "Daily iron supplementation effectively reduces the prevalence of anemia and ID, raises Hb and iron stores, improves exercise performance and reduces symptomatic fatigue." (Firquet et al., 2017). Oral iron is considered first line therapy (Tang & Sholzberg, 2024) and is a cheap and effective way of treating iron deficiency (Benson et al., 2021). For patients intolerant of, or unresponsive to, oral iron, intravenous (IV) administration is the preferred route (Auerbach & Adamson, 2016). The currently available IV iron formulations are equally safe, effective (Auerbach & Adamson, 2016) (Camaschella, 2015) well-tolerated, and adverse reactions are rare (Tang & Sholzberg, 2024) 3 to 6 months of treatment are required for the repletion of iron stores and the normalization of serum ferritin levels (Camaschella, 2015). Interventions range from primary prevention that involves a focus on a healthy diet (includes diet low in saturated fats, trans fats, cholesterol, sugars and salt) and including good sources of iron (fruits, vegetables, whole grains, milk and milk products, lean meat, fish, dry beans, egg, nuts) (Mawani et al., 2016). Proper management improves quality of life, alleviates the symptoms of iron deficiency, and reduces the need for blood transfusions (Jimenez et al., 2015).

WHO recommends that in high-risk populations, iron supplements should be given to adolescents and women for 2 to 4 months per year to ensure that women have reasonable iron stores when they become pregnant (Mawani et al., 2016). Considering the economic impact of ID and the large range of ferritin values observed, all health care authorities should recommend this additional marker as a screening test in middle aged women at risk of ID (Firquet et al., 2017). Frequent follow-ups and reminders would be beneficial. The door-to-door approach should be implemented, keeping in mind the cultural implications and lack of access to medical facilities for women. Pakistan has a male dominating society; hence male member of the family should be made aware of this problem (Mawani et al., 2016).

Realizing the importance and deficiencies of iron, the Government of Pakistan in its 9th 5- year plan has committed for the control of this problem (Mawani et al., 2016).

Iron deficiency anemia was defined as Hb concentration less than 12 g/L for women, a mean corpuscular volume less than 80 fL, and a serum ferritin level less than 20 ng/ml (Can et al., 2018). Iron deficiency anemia refers to low red blood cell production that happens due to iron scarcity within the body (ELMoslemany et al., 2019) and the presence of microcytic hypochromic red cells (Camaschella, 2015).

Anemia occurs in numerous forms, but anemia caused by iron deficiency is the most frequently occurring form of anemia (Yunanci et al., 2023) (DeLoughery, 2017) (Mahar et al., 2024). Over 25 % of the total world population suffers from anemia of which over 50% are due to IDA (Pivina et al., 2019) (Kung et al., 2021) (Soliman et al., 2017) (Kausar et al., 2023) (Lee, 2020). IDA is the most frequent dietary deficit, reported by the World Health Organization (Yavuz et al., 2012) (Cook et al., 2017) (Lopez et al., 2016) (Wenger et al., 2019) (Soliman et al., 2017) (Leung et al., 2024) (Clark, 2008) (Al-Sayes et al., 2011) among adolescent girls (ELMoslemany et al., 2019) (Wenger et al., 2019), both in developed and developing nations (Cook et al., 2017), (ELMoslemany et al., 2019) (Soliman et al., 2017) (Mawani et al., 2016). For women aged 15 to 44 (El Nahas & Gabr, 2017) (Devi & Mageshwari, 2015), iron deficiency anemia is currently the third leading cause of disability-adjusted loss of life years worldwide (Sharief et al., 2019) (Lopez et al., 2016). In a different study that included data from 23 different nations for women of reproductive age, IDA was delineated in 37.0% of the women (95% CI: 28.0, 46.0) (Petry et al. 2016) (Pivina et al., 2019). Iron deficiency anemia is the most common form of anemia in Pakistan, and is more common in females (Mawani et al., 2016).

Anemia resulting from iron-restricted erythropoiesis occurs through several mechanisms. In pure iron deficiency, depleted iron stores are due to an imbalance between iron uptake and utilization. (Jimenez et al., 2015). The persistence of a negative balance leads to microcytic and hypochromic anemia (Jimenez et al., 2015).

Published risk factors for IDA are race, lack of proper diet, restrictive dietary practices, poor socioeconomic status education, iron mal-absorption or low iron intake, heavy menses, high parity of women, pregnancy, access to poor health, fatigue or impaired exercise capacity, genetic, and a previous diagnosis of IDA, are based on all women of reproductive age, (Sekhar et al., 2016) (Mawani et al., 2016) (Tang & Sholzberg, 2024) (Can et al., 2018; Firquet et al., 2017) (Harrabi et al., 2021) (More et al., 2013) (Lee, 2020) (Clark, 2008) (Al-Sayes et al., 2011) Additional risk factors include use of non-steroidal anti-inflammatory drugs (Coad & Pedley, 2014) inflammatory bowel disease (IBD [13%-90%]), and other chronic inflammatory conditions, such as CKD (24%-85%), Chronic HF (37%-61%), and cancer (18%-82%) (Leung et al., 2024) (Mahar et al., 2024).

The cause of iron-deficiency anemia varies based on age, gender, and socioeconomic status (Warner & Kamran, 2023). Despite best diagnostic efforts, approximately 29% to 47% of patients with IDA lack a definitive etiology (Clark, 2008). In developing countries, iron deficiency and iron-deficiency anemia typically result from insufficient dietary intake, excessive blood loss during surgery (Lopez et al., 2016) (Chaudhry & Kasarla, 2017) (Warner & Kamran, 2023), intestinal worm colonization, or both. In high income countries, certain eating habits (e.g., a vegetarian diet or no intake of red meat) (Camaschella, 2015), Pica, tea consumption, low consumption of red meat, vegetables, cereals and fruits and lesser intake of hem-iron sources (Mawani et al., 2016) (Al-Sayes et al., 2011), chronic disorders (e.g: chronic heart failure, inflammatory bowel disease, cancer, and chronic kidney disease) (Lopez et al., 2016) and pathologic conditions (e.g., chronic blood loss or mal absorption) are the most common causes. (Camaschella, 2015). Gastrointestinal parasites (including Trichuris trichiura and Necator americanus) (Lopez et al., 2016) (Lee, 2020), schistosomiasis can contribute to IDA (Chaparro & Suchdev, 2019). There are numerous medications implicated in iron deficiency anemia, either by promoting increased blood loss (e.g., non-steroidal anti-inflammatory drugs) or suppressing iron absorption (e.g., proton-pump inhibitors and H2 receptor antagonists) (Lopez et al., 2016) (Firquet et al., 2017) (Lee, 2020). The most prevalent etiologic factors of IDA in women are menorrhagia (Jimenez et al., 2015) (Lee, 2020) (Coad & Pedley, 2014) lack of proper diet , reduced dietary iron and reduced absorption of iron (Chaudhry & Kasarla, 2017) (Clark, 2008), pregnancy (Kumar et al., 2022), (ELMoslemany et al., 2019) (Can et al., 2018) (Leung et al., 2024; Warner & Kamran, 2023).

The symptoms of IDA may range widely (Lopez et al., 2016). IDA-related signs and symptoms are nonspecific and are often underestimated or overlooked by patients (Leung et al., 2024). In IDA patient the signs and symptoms caused by hypoxic metabolism are; Weakness, fatigue, palpitations, irritability, paleness, exertional dyspnea leading to breathlessness at rest, pallor of the conjunctiva and skin, vertigo, syncope, lightheadedness, headache, tachycardia, cold intolerance, poor capillary refilling, decreased appetite, pica (such as pagophagia and geophagia), poor concentration, depression, poor aerobic physical fitness and endurance capacity, poor work productivity, restless leg syndrome, worsening heart failure (HF). and susceptibility to infection (Lopez et al., 2016) (Firquet et al., 2017) (Camaschella, 2015) (Can et al., 2018; Harrabi et al., 2021; Warner & Kamran, 2023) (Leung et al., 2024) (Leung et al., 2024) (Lee, 2020) (Clark, 2008) (Coad & Pedley,

2014) (Al-Sayes et al., 2011). In mild to moderate iron deficiency anemia, poor appetite, fatigability, lassitude, lethargy, exercise intolerance, irritability, and dizziness may be seen (Leung et al., 2024). In severe iron deficiency anemia, tachycardia, shortness of breath, diaphoresis, and poor capillary refilling, symptoms of heart failure may occur (Leung et al., 2024) (Clark, 2008). Additional clinical findings include koilonychias, blue sclera, esophageal webbing, dysphagia, angular stomatitis, and glossitis (Clark, 2008).

There is significant evidence that ID and IDA are associated with psychomotor development and cognitive impairment (ELMoslemany et al., 2019) (Pivina et al., 2019) (Wenger et al., 2019) (Can et al., 2018) (Leung et al., 2024) (Al-Sayes et al., 2011), lower math exam scores, decreased exercise tolerance (ELMoslemany et al., 2019). There is a plethora of studies in literature describing adverse effects (such as affecting mental health (Dziembowska et al., 2019), muscle power, nutritional status, physical functioning (Al-Sayes et al., 2011), quality of life, fatigue) (Can et al., 2018) (Selvi Öztorun et al., 2018), which may not always be fully reversible even following the correction of iron deficiency anemia (Leung et al., 2024). IDA has been proved to bring emotional and cognitive effects like emotional instability, depression, anxiety, reduced cognition (Can et al., 2018) (Friedman et al., 2015). Reproductive-age women are at higher risk for ID and IDA, with both involved in reduced CF (Cook et al., 2017). IDA women scored significantly low on attention than those unaffected (Cook et al., 2017). MurrayKolb et al. showed that iron sufficient women performed better on cognitive tests than IDA women who aged 18-35years (Can et al., 2018). However, there are only a few studies to investigate the effects of IDA on cognitive functioning in women of reproductive age in the literature (Can et al., 2018).

Most patients are asymptomatic (Camaschella, 2015) and identified through a blood test (Lee, 2020) (Warner & Kamran, 2023) Iron-deficiency anemia is chronic and thus may often go undiagnosed (Camaschella, 2015). IDA is diagnosed in terms of reduced levels of hemoglobin (Lee, 2020) (Warner & Kamran, 2023) (Benson et al., 2021) 11.0g/dL (Firquet et al., 2017), hematocrit, or red blood cell count per cubic millimeter (ELMoslemany et al., 2019), reduced or inappropriate mean corpuscular volume (Warner & Kamran, 2023)(less than 100 fL), a lower serum ferritin level (Warner & Kamran, 2023) (Leung et al., 2024) (Lee, 2020) (Benson et al., 2021) (less than 15 mg/L) (Clark, 2008) (Firquet et al., 2017), and/or a lower transferrin saturation level (Lee, 2020) (less than 20%) (Friedman et al., 2015), serum iron, soluble transferrin receptor, hepcidin level, zinc protoporphyrin (Lee, 2020) (Clark, 2008). On physical exam, a patient may present with pallor (Warner & Kamran, 2023), evident on hands as well as conjunctivitis (Warner & Kamran, 2023), tachycardia (Warner & Kamran, 2023), increased respiratory rate, exhaustion, koilonychia (spoon-shaped nails) (Chaudhry & Kasarla, 2017), congestive heart failure, and guaiac-positive stool (Warner & Kamran, 2023). From a clinical perspective, focusing on common symptoms (e.g., fatigue, depression, poor concentration) linked to IDA could be an important step in the development of an IDA screening tool (Sekhar et al., 2016).

When the prevalence of anemia is greater than 40%, the WHO and UNICEF strongly recommend that universal supplementation be implemented (Lee, 2020) (Mahar et al., 2024). The purpose of treatment of IDA, is to normalize hemoglobin concentration and replenish iron stores to improve symptoms, quality of life (Jimenez et al., 2015), and the prognosis of chronic diseases (Lee, 2020). Iron supplementation improves cognitive function regardless of whether the person suffers from ID or IDA (Firquet et al., 2017). Oral iron supplementation is the first line treatment of iron deficiency and IDA in women (Loechl et al., 2023) (Firquet et al., 2017) (Tang & Sholzberg, 2024) (Turner et al., 2018) (Leung et al., 2024). Ferrous iron is preferred because of its high bioavailability; however, the least expensive (Jimenez et al., 2015) (Lee, 2020) (Leung et al., 2024), effective (Lee, 2020) (Warner & Kamran, 2023) and most commonly used form for replenishing. Hb in patients with IDA is ferrous sulfate (Loechl et al., 2023). The total iron consumption period is about 3 to 6 months (Lee, 2020). When oral therapy is unsuccessful, parenteral iron therapy is then indicated (Clark, 2008). The efficacy of intravenous (IV) iron has already been demonstrated in dozens of randomized clinical trials and meta-analysis (Lee, 2020). Intravenous iron is indicated for patients with oral iron intolerance, poor absorption (celiac disease, post-bariatric surgical procedure), chronic inflammatory conditions (CKD, HF, IBD, cancer), ongoing blood loss, or when rapid correction of the iron deficit is required (Loechl et al., 2023) (Firquet et al., 2017) (Auerbach & Adamson, 2016) (Jimenez et al., 2015) (Lee, 2020) (Turner et al., 2018) (Warner & Kamran, 2023) (Leung et al., 2024). Dietary counseling is usually necessary for management (Warner & Kamran, 2023). Foods such as green leafy vegetables, tofu, red meats, raisins, and dates and iron-fortified milk formulas contain a lot of iron (Warner & Kamran, 2023) (Turner et al., 2018). Patients must be advised to avoid excess tea or coffee, as these can decrease iron absorption (Turner et al., 2018).

Iron preparations vary in their bioavailability, efficacy and side effects (Firquet et al., 2017). Use of oral iron is limited by side effects, including nausea, vomiting, diarrhea, constipation, and metallic taste, gastric cramping and thick, green, tenacious stool. (Camaschella, 2015) (Auerbach & Adamson, 2016) (Tang & Sholzberg, 2024) (Turner et al., 2018) (Chaudhry & Kasarla, 2017) (Warner & Kamran, 2023) (Lee, 2020). Oral iron may not be tolerated or may not be effective in some women (Tang & Sholzberg, 2024). The transient side effects of intravenous iron supplementation include nausea, vomiting, pruritus, headache, hypertension, flushing and injection site reactions, myalgia, arthralgia, and back and chest pain, wheezing, stridor, or periorbital edema usually resolve within 48 hours, even after total dose administration (Camaschella, 2015) (Tang & Sholzberg, 2024; Warner & Kamran, 2023) (Lee, 2020) (Benson et al., 2021).

The complications of iron deficiency anemia include: 1: Increased risk of infections 2: Heart conditions 3: Developmental delay in children 4: Pregnancy complications 5: Depression (Warner & Kamran, 2023) Some consequences of IDA are growth retardation, exercise intolerance, behavioral changes, and abnormal thermogenesis (Al-Sayes et al., 2011).

Early detection and treatment of IDA is essential to prevent cognitive impairment and to improve quality of life in adult women (Can et al., 2018). The CDC guidelines to test nonpregnant reproductive-age women at low risk for IDA every 5–10 years versus annual testing for high-risk women (Sekhar et al., 2016). The government must act decisively to improve educational standards, the socioeconomic status of women, the availability of health professionals, and the intensity of public education (Mahar et al., 2024). Cognitive performance has been linked to nutrition and physical determinants (Scott et al., 2017). The sensation of lowered energy levels may affect an individual's motivation to finish a given task, increase anxiety and depressed mood and thus deplete endurance and cognitive capacity (Dziembowska et al., 2019). A randomized controlled trial showed that a complex multimodal activity intervention helped to reduce the risk of CI in patients who were at a higher risk of IDA (Kung et al., 2021). In addition to promoting social relationships, improving sleep, elevating cognitive performance, regulating neurotransmitters, and lowering the risk of diseases like depression and anxiety, it also contributes to long-term mental well-being (Kausar et al., 2023) (Keeley & Fox, 2009). Physical activity reduce mortality and prevent many chronic diseases such as hypertension, diabetes, stroke, and cancer, it can promote healthy cognitive and psychosocial function (Kausar et al., 2023). There has also been growing interest in the benefits of physical activity for mental health and a strong evidence base shows that regular activity and improved fitness increase psychological well-being (Keeley & Fox, 2009). Anemia has a detrimental impact on physical performance, especially work productivity in adults (Lopez et al., 2016). IDA is linked to Quality-of-life impairments; reduced physical functioning, compromised performance at work, depression, tiredness, vitality loss (Friedman et al., 2015) (Dziembowska et al., 2019) (Can et al., 2018), voluntary activity (observed as an increase in sedentary behavior), fatigue and athletic performance (Coad & Pedley, 2014) (McClung & Murray-Kolb, 2013). IDA results in reduced maximal oxygen consumption (VO2 max) so aerobic physical fitness and endurance capacity are compromised, in premenopausal women affecting physical performance and work tolerance (Coad & Pedley, 2014) (McClung & Murray-Kolb, 2013). Even mild iron deficiency (ID) may result in decreased endurance, increased irritability and withdrawal behavior among women (Dziembowska et al., 2019). Patterson et al. reported that physical and mental health were significantly impaired in women aged 18-50 years with ID (Can et al., 2018). A study reported that aerobic exercise increased hemoglobin (Hb) concentration and hematologic factors in young females (Kausar et al., 2023). Moderate physical activity has a positive impact on mental health, lowering stress through the production of endorphins, elevating mood through the increase of serotonin and dopamine, and regulating cortisol (Kausar et al., 2023). "Anemia control produces an immediate increase in physical work output, higher productivity outside the workplace, improved quality of leisure time, increased learning capacity, and a greater sense of well-being" (Firquet et al., 2017).

As iron is an important component of many enzymes involved in cellular energy metabolism and neurotransmitter synthesis, inadequate energy production and alterations in neurotransmitter metabolism may be the underlying mechanisms of decreased quality of life (Can et al., 2018). Red cell mass and total hemoglobin will increase with exercise training, which helps to improve the oxygen-carrying capacity (El Nahas & Gabr, 2017) (Kausar et al., 2023). In correlation analysis, it has been detected that serum iron, ferritin, and hemoglobin levels were significantly correlated with both physical and mental health quality (Can et al., 2018). Neurogenesis is the growth of new nerve cells in the nervous system, and provides a potential mediating mechanism by which physical activity and fitness could improve cognitive efficiency (Keeley & Fox, 2009). To our knowledge, there is no study to evaluate the physical function using a specific assessment tool in subjects with IDA (Can et al., 2018). Although a limited number of human studies have investigated the physiologic effects of ID on physical performance (McClung & Murray-Kolb, 2013). Literature shows there is a lack in any defined physical activity, which can affect the Hb concentration and stress (Kausar et al., 2023).

Iron Deficiency Anemia (IDA) is reported to affect cognitive function, but few studies address the correlation between PA & CF in IDA women. The present study will examine the impact of PA on CF in IDA women, which will shed new light pertaining to possible advantages of physical activity in treating cognitive impairment associated with IDA. Many studies on cognitive functioning and physical functioning have focused on infants and early childhood. Less research had focused on the effects of IDA in women of reproductive age (Can et al., 2018).

LITERATURE REVIEW

THEORETICAL BACKGROUND:

Iron deficiency anemia (IDA) is a nutritional disease that has continued to be the most common in the world, with women of reproductive age bearing the brunt of this anemia because of menstruation, pregnancy, and improper intake of iron during their diets. The World Health Organization (WHO) states that about 30 percent adults in the world carry IDA, and it is the most widespread of all nutritional deficiencies (Kumar et al., 2022). Iron is an essential component of physiology because of its role in transporting oxygen, enzyme processes and generating energy via the mitochondrion.

The loss of iron stores compromises iron hemoglobin production, causing tissue hypoxia, which may present as fatigue, palpitations and, above all, cognitive impairment. According to Kumar et al. (2022), severe cognitive impairments and diminished attention and memory of these individuals may be because of central hypoxia caused by IDA and improve after hemoglobin levels normalize.

In clinical terms, it is important to note that Lee (2020) states that IDA can be diagnosed in 30 -50 percent of all people on the planet, the majority of whom have malnutrition, menstrual bleeding, issues with the gastrointestinal tract, and genetics affecting hepcidin balance. This paper has pointed out that weakness, fatigue, decreased appetite, and impaired neurocognitive function are some of the common symptoms of IDA that usually improve with iron supplementation. Nevertheless, clinically, diagnosis and management of IDA have been poorly understood, and there is a need to ensure the advancement of the knowledge on iron metabolism and harmonious diagnostic profiles to reduce its cognitive and system effects.

In the same light, Coad and Pedley (2014) provide that iron deficiency comes in phases of slight depletion and later on to anemia, where production of hemoglobin is hampered, as well as the release of oxygen. The authors point out that, because of low levels of enzymes and neurotransmitters that require iron, even subclinical iron deficiency, preceding the onset of anemia, can impact the neurocognitive performance. They also note that the menstrual losses, pregnancy and elevated physiological demands expose women of fertility age to a high risk.

Besides, the risk of cognitive and physical fatigue, which may adversely influence daily functioning and physical activity levels, may be aggravated by such conditions as obesity and inflammation, which can worsen iron absorption and use.

On the population level, Mawani et al. (2016) find iron deficiency anemia as a long-standing public health concern of developing nations, as it occurs in 26-50% of urban women and up to 90% of rural women. They put this blame on socioeconomic inequality, improper dietary consumption, and elevated parity. The research places IDA as a cause of not only poor physical health but also mental lethargy and lack of concentration, particularly in childbearing women. These consequences are also aggravated by low levels of access to medical care and nutrition education, which highlights the necessity of targeted work with the population.

Similarly, Tang and Sholzberg (2024) address the topic of IDA in women in the health equity paradigm, which uncovers barriers of systemic health concern that can be used to hinder appropriate diagnosis and treatment. They stress that the lack of diagnosis of iron deficiency under-diagnosis, especially where anemia is not apparent, continues disparities in the health of women and their quality of life. The authors touch upon the idea that iron deficiency has become normalized in menstruating and pregnant women when even its negative effects on fatigue, mood, and mental ability are known. Moreover, the differences are worsened by the cultural taboos related to the health of the menstrual period and the lack of screening, where the frequency of deficiency and low developmental results in children reach intergenerational levels.

To supplement the literature on the topic, the regional evidence by the study (Qadir et al., 2022) confirms the statistical finding that 25 percent of women of childbearing age in Quetta have different levels of anemia, with moderate-intense IDA cases being the most common in adolescents aged between 15 and 19 years. The article indicates that awareness about iron supplementation is still poor even with the health consequences of anemia on physical endurance, mental alertness and productivity as a whole that are now known. This local evidence highlights the importance of increased recognition of the importance of public health campaigns that will raise awareness of preventative measures against IDA as well as cognitive consequences of this disease, especially in young women.

More to the regional background, the research (Masood et al., 2019) (2018) also offers strong evidence that Pakistani females with IDA complain of significantly worse quality of life and higher severity of symptoms than males. The study was carried out on 300 patients in Lahore and revealed that women participants registered greater instances of exhaustion and muscle pain as well as reduced physical activity as a result of fatigue due to anemia. The results demonstrated that limited activity patterns and deteriorated daily functioning had a high correlation with anemia, highlighting the fact that both physical and mental health are undermined by the lack of iron. The authors concluded that anemia does not only reduce the work capacity and social well-being but also leads to the increase of emotional distress, and thus, the combination of psychoeducation and lifestyle interventions is likely to significantly improve the quality of life among women with IDA.

Furthermore, Jamil et al., 2016, offer information regarding the susceptibility of young and educated women to IDA. The researchers considered 390 female medical students aged between 19 and 24 years and found that 6.66 percent of the population had IDA, whereas 41.54 percent had an iron deficiency without anemia. Although the students are health-conscious individuals, a large number of students showed low hemoglobin and ferritin levels, indicating stress, dietary constraints, and overworking to be the contributing factors. The authors of the research came to the conclusion that even in such a comparatively privileged and educated population, iron deficiency was also frighteningly widespread. This has highlighted the fact that IDA is not only a consequence of poverty or unawareness but also that of lifestyle and physiological demands, and both of them have a potential impact on bodily performance and cognitive ability. All of these studies are drawn to the conclusion that IDA not only deteriorates physiological and haematological parameters but also affects cognitive functioning that is particularly pronounced in women of reproductive age. Iron is very important in the metabolism of the neurons, the production of nerve transmitters, and the supply of oxygen to the brain. Deficiency results in reduced mental performance, attention, and executive function, whereas iron repletion was demonstrated to enhance physical endurance with cognitive results. Considering the interaction between physical activity and brain functional activity, the neurophysiological processes of IDA would provide the basis on which to investigate how physical activity would alleviate cognitive impairment in women with this disorder.

REVIEW OF RELEVANT STUDIES:

The iron deficiency anemia (IDA) occurs at a large rate among women, especially in the reproductive age, and is always linked to poor cognitive and physical functioning. A review of the literature by Yunanci et al. (2023) between 2014 and 2021 revealed that iron deficiency causes adverse effects on attention, memory and executive functions. Moreover, a low-iron state was associated with low physical exercise, which was probably caused by the fact that low iron levels prevent the maximum supply of oxygen to tissues, which may worsen cognition further.

This is a significant review of how iron deficiency should be addressed to prevent deterioration of both the cognitive level and the activity level among young women.

A cross-sectional study by Scott et al. (2017) examined 105 women aged between 18 and 35 years, and the results revealed that women with normal ferritin levels who had better aerobic fitness had the best cognitive and academic performance compared to women who have normal ferritin with low fitness and those who have low ferritin but have high fitness. The relationship between aerobic fitness and academic performance was mediated by working memory, which showed that the iron status and increased physical activity have a combined effect on cognition.

The paper (El Nahas and Gabr, 2017) involved 17-year-old and 22-year-old girls who took iron supplementation and did aerobic exercise or iron supplementation only. The exercise group had more improvements in the total symptoms of anemia and fatigue, which points to physical activity as a way to complement the positive results of iron supplementation and, consequently, to the cognitive functions by decreasing fatigue and improving energy levels.

Systematic review and meta-analysis (Kim et al., 2019) reviewed 16 observational studies and discovered that cognitive impairment is significantly related to anemia (OR/RR 1.51; 95% CI: 1.32–1.73), which includes dementia. This underscores the direct detrimental effect of low hemoglobin on cognitive ability in adults and underscores the necessity of interventions among women at risk of IDA.

The study (Cook et al., 2017) evaluated cognitive performance amongst 299 females aged 18–35. Female IDA scored substantially lower on attention tasks than female iron deficiency alone, which may indicate that full-blown anemia affects particular areas of cognition such as attention.

In the study (Wenger et al., 2019), the researchers compared behavioral, EEG, and metabolic responses of college students with iron deficiency and iron sufficiency to cognitive tasks. Results indicated that cognitive demands resulted in increased brain activity and energy expenditure, and this effect was regulated by ferritin and hemoglobin levels, demonstrating a physiological relationship between iron status and cognitive effort. (Link)

Interestingly, the opposite study by Alzahrani et al. involved 198 female students and did not find any significant relationship between IDA and cognitive abilities, such as immediate memory, working memory, speed, and accuracy of attention, although the prevalence of IDA was 27.4%. This points to the fact that not all groups might present any measurable cognitive deficits even with anemia being present, which is indicative of possible work of compensatory processes, diet, or other confounders.

In the study (Can et al., 2018), 33 women with IDA and 32 controls without anemia were studied to evaluate the level of cognitive functioning, physical functioning, fatigue, and quality of life.

The score of cognitive tests, physical functioning, and fatigue was lower, and the degree of anxiety and depression was worse in women with IDA. Cognitive performance and overall well-being had a positive correlation with serum iron, ferritin and hemoglobin.

In Dziembowska et al. (2019), young and healthy women who had exhausted iron stores exhibited reduced activity levels and endurance, tested EEG, which suggested the withdrawal tendencies, and took longer to complete their cognitive tasks. This implies that slight iron deficiency can impair cognitive endurance and energy, but this may have an indirect effect on cognitive performance and behavior.

They showed that moderate exercise led to a higher level of hemoglobin in young women, but there were no significant effects on perceived stress (Kausar et al., 2023). This evidence suggests that physical exercising will be able to enhance the haematological condition, which can be a factor in enhancing cognitive functions and health in general.

Lastly, McClung & Murray-Kolb (2013) performed a review regarding the effect of iron deficiency and IDA on premenopausal women. Iron deficiency was linked to depressed physical functioning, work efficiency, voluntary activity, cognition and behavior. It is important to note that nutritional interventions were emphasized to avoid iron deficiency and to improve physical and cognitive functions.

GAPS IN LITERATURE:

Even though a substantial level of research has proven that iron deficiency anemia (IDA) is strongly associated with cognitive impairment among women, the present body of knowledge has certain gaps. Research (Scott et al., 2017; Yunanci et al., 2023) involving studies all indicate that low levels of iron stores adversely influence attention, memory, executive functioning and overall academic performance, especially when accompanied by low physical fitness (Scott et al., 2017; Yunanci et al., 2023). Also, there are interventions that combine iron supplementation and aerobic exercise which have been reported to improve fatigue in anemia and physical symptoms (El Nahas and Gabr, 2017), indicating that physical activity can potentially be used as a supportive supplement.

However, in spite of these results, most of the literature is devoted to one of the things: Iron deficiency and direct effect on cognitive functioning or the positive effect of physical activity on the general state of health or hematological parameters. Although research-like (Kausar et al., 2023) proves that physical activity has the ability to enhance the level of hemoglobin, its direct impact on the cognitive performance of women with IDA has not been studied.

Further, despite meta-analyses and observational studies (Cook et al., 2017; Kim et al., 2019) asserting that IDA compromises cognitive functions of attention and memory, they scarcely consider physical activity as a moderating factor. Even the studies that measure the use of cognitive energy or neural activity during iron deficiency (Wenger et al., 2019) also give the mechanistic evidence but fail to test the hypothesis that structured physical activity might help people to overcome the deficits.

Moreover, inconsistent results like those of Alhazmi et al. (2024) point out that not all the population demonstrates negative cognitive functioning with IDA, indicating that other variables (e.g., physical activity) may play a role in results, but no such interaction has been directly examined.

In conclusion, although the relationship between IDA and cognitive impairment is well established, none of the studies has actually dealt with the effects of physical activity on the cognitive abilities of IDA women. This is a serious gap in the literature that the current study intends to fill by offering new knowledge to understand whether physical activity could be considered a possible intervention for improving the cognitive outcomes of women with IDA.

METHODOLOGY

STUDY DESIGN:

The present study employed a cross-sectional study design to evaluate the impact of physical activity on cognitive function among women with iron deficiency anemia. Data were collected at a single point in time to identify the relationship between levels of physical activity and corresponding cognitive performance within the target population. This design was thought to be adequate because it enabled the determination of the relationship between the exposure (physical activity) and the outcome (cognitive function) in an efficient manner within a specified period of time. The methodology was appropriate to the purpose of the study, which made it efficient in gathering data and offered a wholesome picture of the current trends and associations among iron-deficient anaemic women.

STUDY SETTING:

The research was carried out in the different hospital and institutional facilities to get the representative sample of women diagnosed with iron deficiency anemia. The data was gathered in several tertiary care hospitals in Karachi. The selection of these study sites were because they availed access to women who had known diagnoses of iron deficiency anemia, where they are in treatment, or they are in follow-up. Conducting the research across multiple hospitals and clinical centres strengthened the validity and reliability of the findings by including participants from diverse healthcare settings. These settings also ensured the feasibility of data collection and supported the study's objective of evaluating the impact of physical activity on cognitive function among women with iron deficiency anemia.

DURATION OF STUDY:

The research was finished in a period of approximate nine months having been initiated in March 2025 and finished in November 2025. It took this period of time to conduct the entire research process including the data collection, analysis as well as interpretation. This time was adequate to meet the study objectives and be able to collect all the required data in all the selected settings.

POPULATION AND SAMPLING:

The study population comprised women aged 18 to 45 years who were clinically diagnosed with iron deficiency anemia for a duration of at least six months to one year. The purposive non-probability sampling method was used in the selection of eligible participants as per the inclusion criteria. This method enabled effective gathering of data of those individuals available in the definite population, where the sample group effectively represented women suffering iron deficiency anemia in the specified age range.

SAMPLE SIZE AND TECHNIQUE:

SAMPLE SIZE:

The sample size for this study was calculated using the OpenEpi calculator, keeping a 95% confidence interval and a 5% margin of error. According to the National Nutrition Survey (NNS-2018) that stated that 18% of females aged between 15 years and 49 years' experience iron deficiency anemia, the sample size to be used was calculated as 227. Nevertheless, the sample size was then modified to 228 participants in order to achieve equal allocation among the two groups of the study; i.e. 114 physically active and 114 sedentary women The calculation was based on the standard formula $n = Z^2 \times p \times (1-p) / d^2$, ensuring adequate power and representation of the target population.

SAMPLING TECHNIQUE:

The study used a purposive non-probability sampling technique, as it was feasible and cost-effective for engaging participants who met the specified inclusion criteria. This approach enabled the researchers to select women aged 18-45 years old who had iron deficiency anemia for at least six months to one year to make them relevant to the study objectives. The purposive approach was appropriate for targeting individuals with specific characteristics necessary to assess the impact of physical activity on cognitive function among women with iron deficiency anemia.

INCLUSION/EXCLUSION CRITERIA:

INCLUSION CRITERIA:

Participants included in the study met the following criteria:

• Sex: Only women were included in the study.

• Age limit: Participants were between 18 and 45 years of age.

Diagnosis: Participants diagnosed with iron deficiency anemia (IDA) for at least six months to one year, confirmed through medical records or laboratory tests showing hemoglobin levels below 12 g/dl and ferritin levels below 15 ng/ml.

• Health status: Participants did not have any severe chronic illnesses that could affect cognitive function

• Consent: All participants were capable of providing informed consent and completing the cognitive assessments.

• Mental status: Only mentally healthy adults were included.

• Physical activity: Participants had been engaging in a defined level of physical activity for at least six months to one year.

• Body Mass Index (BMI): Only women with a BMI (<18.5 To >30.0 kg/m²) were included.

• Dietary habits: Participants who were not consuming a balanced or regular diet.

• Medication: Participants were taking prescribed medication and iron supplements as per their physician's advice.

• Physical activity classification: Participants were categorized according to the International Physical Activity Questionnaire-Long Form (IPAQ) into three groups:

• Sedentary women: Low physical activity (<600 MET-min/week).

• Moderately active women: Moderate physical activity (≥600–3000 MET-min/week).

• Active women: High physical activity (>3000 MET-min/week).

EXCLUSION CRITERIA:

Participants were excluded from the study based on the following criteria:

• Age: Women below 18 years and above 45 years of age were excluded.

• Type of anemia: Participants with anemia due to causes other than iron deficiency (e.g., thalassemia, sickle cell anemia, or anemia of chronic disease) were excluded.

• Cognitive or neurological history: Women with a history of cognitive impairment, dementia, or any neurological condition affecting cognition were excluded.

• Pregnancy: Pregnant women were excluded from the study.

• Medication use: Participants using drugs that significantly affect cognition or physical activity levels (e.g., sedatives, antidepressants, or stimulants) were excluded.

• Substance use: Heavy smokers and those with alcohol or substance abuse habits affecting cognitive function were excluded.

• Musculoskeletal or physical limitations: Women with musculoskeletal disorders, injuries, or other medical conditions that restricted movement or prevented regular physical activity were excluded.

• Chronic illnesses: Women with chronic diseases influencing cognitive function (e.g., diabetes, cardiovascular, inflammatory bowel diseases) were excluded.

• Dietary patterns: Participants following restrictive or extreme diets (e.g., vegan, keto, or intermittent fasting) were excluded.

• Physical activity level: Women engaging in extreme physical activity levels, such as professional athletes, individuals performing high-intensity interval training (HIIT), were excluded to avoid skewed results.

• Undefined activity level: Women who did not fit into either of the IPAQ-defined categories for sedentary, moderately active & active groups were excluded.

• BMI range: Obese women (BMI ≥ 30.0 kg/m²) and underweight women (BMI < 18.5 kg/m²) were excluded from the study.

DATA COLLECTION TOOLS AND PROCEDURE:

DATA COLLECTION TOOLS:

Data were collected using standardized and validated tools to ensure accuracy and reliability. Cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) -Version 8.1 English while physical activity levels were measured through the International Physical Activity Questionnaire (IPAQ)-Long Form. Additionally, a self-administered questionnaire was used to gather basic demographic information and verify inclusion and exclusion criteria. All assessments were conducted under proper supervision, and participant responses were recorded systematically for analysis.

RELIABILITY & VALIDITY OF TOOLS:

MoCA Scale:

The MoCA has high internal consistency (Cronbach = 0.83), high test-retest reliability (ICC= 0.92), high interrater reliability (ICC= 0.81), high correlation (0.87, p <0.001) for content validation. Sensitivity is excellent (90%) & specificity is good (87%).

IPAQ-LONG FORM:

The IPAQ (Long Form) presents satisfactory relative to excellent test-retest reliability with overall scores generally possessing an intraclass correlation coefficient (ICC) of around 0.7 to 0.9. Validity scores are more valid as they normally exhibit a moderate to good correlation.

IPAQ has been found to have moderate to good concurrent validity.

DATA COLLECTION PROCEDURE:

This survey-based cross-sectional study was conducted on a total of 228 participants. All the participants had to complete standardized questionnaire and assessments to determine the level of cognitive function as well as physical activity. The measures taken in the study were:

(1) A self-administered questionnaire to record demographic and other health-related details depending on inclusion and exclusion criteria.

(2) Physical activity evaluation using the International Physical Activity Questionnaire (IPAQ)-Long Form.

(3) Cognitive function assessment using the Montreal Cognitive Assessment (MoCA)- Version 8.1 English Scale.

(4) Laboratory blood tests to determine the hemoglobin and ferritin levels in order to confirm iron deficiency anemia.

VARIABLES (INDEPENDENT, DEPENDENT&CONFOUNDERS):

INDEPENDENT VARIABLE:

Physical activity level was the independent variable used in this study and measured using the International Physical Activity Questionnaire (IPAQ) Long Form. All the participants had to self-report about their physical activity during the past seven days and based on the information they provided, they were classified as three distinct levels of physical activity

1: Inactive
2: Moderate
3: Active

based on the standardized scoring guidelines.

DEPENDENT VARIABLE:

The dependent variable cognitive function was measured with the help of the Montreal Cognitive Assessment (MoCA)-Version 8.1 English scale. The scale provided a maximum score of 30, where higher scores indicated better cognitive performance, while scores below 26 suggested possible cognitive impairment among participants.

CONFOUNDING VARIABLES:

Several confounding variables were considered in this study as they could influence both physical activity and cognitive function. These included neurological or psychiatric conditions, dietary habits (such as vegan or keto diets), substance use (alcohol or drugs), pregnancy, use of medications affecting cognition and activity levels, chronic diseases (e.g., diabetes, cardiovascular, inflammatory bowel diseases), medical conditions or injuries limiting mobility, BMI-underweight and obese women which could impact both cognitive performance and physical activity levels.

DATA ANALYSIS PLAN:

Statistical Package of the Social Sciences (SPSS) version 27.0 was used to analyze the data. To summarize the data and to compare the cognitive functioning of physically active and sedentary females with iron deficiency anemia, descriptive and inferential statistics were used. Appropriate statistical tests were used to determine the relationship and significance between physical activity levels and cognitive performance. All results were interpreted at a 95% confidence interval with a p-value ≤ 0.05 considered statistically significant.

ETHICAL CONSIDERATIONS:

The research was carried out according to the principles of ethics as supported by the Declaration of Helsinki. Ethical approval was obtained from the relevant institutional research ethics committee prior to data collection. All participants were informed about the purpose, benefits, and potential risks of the study, and written informed consent was obtained from each participant before inclusion. Participants were also assured of the confidentiality and anonymity of their data, which were used solely for research purposes.

RESULT

1: DEMOGRAPHICS OF PARTICIPANTS:

A total of 228 women diagnosed with iron deficiency anemia (IDA) participated in the study. The mean age of the sample was 27.57 years (SD = 7.50), indicating a predominantly young adult population. The average Body Mass Index (BMI) of participants was 23.28 kg/m² (SD = 2.92), which falls within the normal weight range.

Regarding iron supplementation habits, the majority of participants (75.4%, n = 172) reported taking supplements occasionally, while 24.6% (n = 56) adhered to daily supplementation. Physical activity levels varied widely within the sample. Exactly half of the participants (50%, n = 114) reported no physical activity during the week. Among those who engaged in activity, 12.7% (n = 29) were active for 1 day/week, 11.8% (n = 27) for 2 days/week, and 10.5% (n = 24) for 3 days/week. A smaller proportion reported engaging in activity for 4 days/week (4.8%, n = 11), or more than 5 days/week (10.1%, n = 23). Participation in a structured physical activity program was evenly distributed, with 114 participants (50%) in each category.

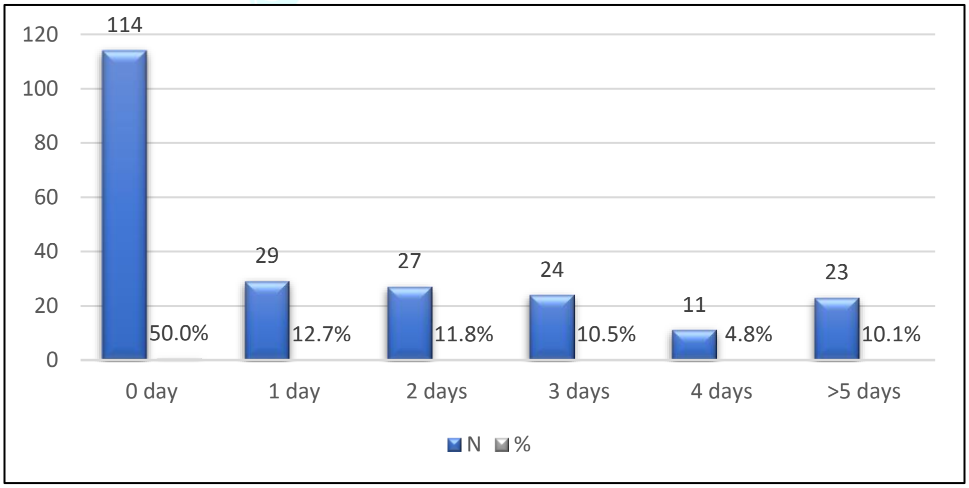

Figure:1
Days per week participants engaged in structural physical activity program.

Symptomatically, a high proportion of participants reported IDA-related complaints. The most commonly reported symptom was weakness experienced by 96.9% of participants (n = 221). Other frequently reported symptoms included pale skin or inner eyelids (91.7%, n = 209), shortness of breath during regular activities (86.8%, n = 198), dizziness or light-headedness (78.5%, n = 179), and feeling cold in hands and feet (78.1%, n = 178). Additionally, 62.7% (n = 143) reported cravings for non-nutritive substances such as ice or raw rice, consistent with pica commonly associated with IDA.

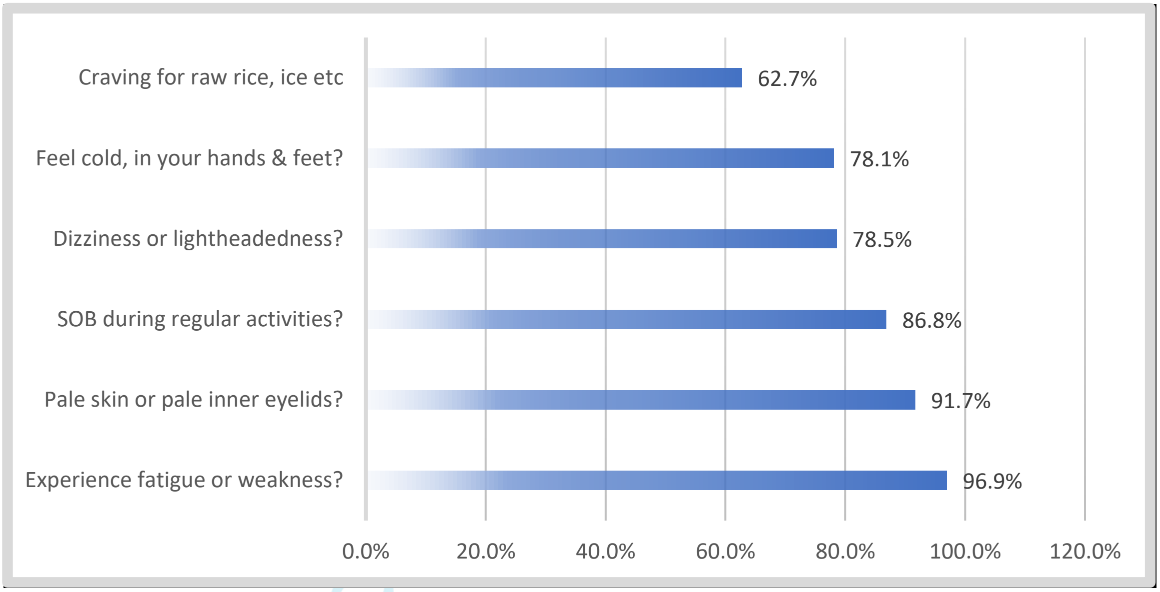

Figure :2
Percentage Breakdown of Symptoms

2: DESCRIPTIVE STATISTICS:
Descriptive statistics were calculated to summarize physical activity levels and cognitive function scores among women with iron deficiency anemia (IDA). A total of 228 participants were included in the analysis, with no missing data reported.

2.1 Physical Activity Levels (IPAQ Categories):
The International Physical Activity Questionnaire (IPAQ) results indicated that the mean physical activity score of the total sample was M = 1.61, SD = 0.69, reflecting generally low-to-moderate activity levels. Based on IPAQ categorical classifications, 50.0% of participants (n = 114) were classified as inactive, 38.6% (n = 88) as moderately active, and 11.4% (n = 26) as active.
These distributions suggest that a large proportion of women with IDA demonstrate insufficient physical activity, aligning with the study's need to compare cognitive function between physically active and inactive groups.

2.2 Cognitive Function (MoCA Scores):
Cognitive performance was assessed using the Montreal Cognitive Assessment (MoCA). The overall mean MoCA score was M = 23.42, SD = 2.24, indicating generally borderline-normal cognitive performance among the cohort.
When MoCA scores were summarized categorically:

- Normal cognition: 10.5%
- Mild cognitive impairment: 46.9%
- Moderate cognitive impairment: 41.2%
- Severe cognitive impairment: 1.3%

These findings show variability in cognitive functioning across participants, providing a basis for inferential comparison between active and inactive groups.
2.3 Group-Based Descriptive Patterns:
When IPAQ scores were compared across cognitive categories:

Table :1
IPAQ Mean Scores Across Cognitive Status Groups

Cognitive Status	M	SD
Normal cognition	2.46	0.66
Mild impairment	1.88	0.59
Moderate impairment	1.12	0.35
Severe impairment	1.00	0.00

Note. M = Mean; SD = Standard deviation; IPAQ = International Physical Activity Questionnaire.

These results show that participants with better cognitive function (Normal) had higher IPAQ scores indicating higher physical activity, whereas those with lower cognitive performance (Moderate or Severe impairment) tended to show lower IPAQ scores, reflecting lower physical activity levels.

3: INFERENTIAL STATISTICS:
3.1: Relationship between Physical Activity and Cognitive Function: To examine the association between physical activity level and cognitive function among women with iron deficiency anemia (IDA), a Chi-square test of independence was conducted. Participants were categorized into Inactive, Moderate, and Active groups based on their IPAQ scores, and cognitive function was classified as Normal, Mild, Moderate, or Severe impairment according to MoCA scores.
Crosstabulation results are shown in Table 2.

Table: 2
Crosstabulation of Physical Activity Level and Cognitive Impairment Category (N = 228)

Physical Activity Level	Normal	Mild	Moderate	Severe	Total
Inactive	2 (8.3%)	25 (24.3%)	84 (89.4%)	3 (100.0%)	114 (50.0%)
Moderate	10 (37.5%)	68 (63.6%)	10 (9.5%)	0 (0.0%)	88 (38.6%)
Active	12 (54.2%)	13 (12.1%)	1 (1.1%)	0 (0.0%)	26 (11.4%)
Total	24 (100%)	106 (100%)	95 (100%)	3 (100%)	228 (100%)

Note. IPAQ = International Physical Activity Questionnaire; MoCA = Montreal Cognitive Assessment. Percentages indicate column-wise distribution of participants across physical activity levels.

A Chi-square test of independence revealed a significant association between physical activity level and cognitive impairment, $\chi^2(6, N = 228) = 178.24$, $p < .001$. This indicates that higher physical activity is associated with better cognitive function among women with IDA. Specifically:

- Participants in the Active group predominantly exhibited normal cognition (54.2%) or mild impairment (12.1%), with very few showing moderate or severe impairment.
- The moderate activity group showed a mixed distribution, with a majority having mild impairment (63.6%), but fewer with moderate or severe impairment.
- The inactive group had the highest prevalence of moderate (89.4%) and severe (100%) cognitive impairment, with very few participants exhibiting normal cognition (8.3%).

3.2 Relationship between Physical Activity and Specific Cognitive Domains
A one-way multivariate analysis of variance (MANOVA) was conducted to examine the differences between the three physical activity groups (Inactive, Moderate, Active) on the seven sub-domains of the MoCA.
The MANOVA revealed a statistically significant difference in the combined cognitive sub-domain scores based on physical activity level ($p< .001$).
Following the significant MANOVA, a series of one-way ANOVAs were conducted on each dependent variable. The ANOVA results for each sub-domain are presented in Table 3.

- Attention: The one-way ANOVA showed a statistically significant difference in scores between the physical activity groups, F (2, 225) = 70.13, *p* < .001. Post-hoc analyses using Tukey HSD indicated that the Active group (M = 5.44, SD = 0.93) scored significantly higher than both the Moderate (M = 4.82, SD = 1.39) and Inactive (M = 3.04, SD = 1.20) groups. The Moderate group also scored significantly higher than the Inactive group.
- Orientation: A significant main effect was found for orientation, F(2, 225) = 96.72, *p* < .001. Post-hoc tests showed that the Active group (M = 5.89, SD = 0.32) and the Moderate group (M = 5.57, SD = 0.66) both scored significantly higher than the Inactive group (M = 3.70, SD = 1.38).

Naming: The effect on naming was significant, F (2, 225) = 14.03, *p* < .001. Post-hoc analysis revealed that both the Active (M = 2.67, SD = 0.48) and Moderate (M = 2.54, SD = 0.59) groups scored significantly higher than the Inactive group (M = 2.18, SD = 0.56).

Language: A significant difference was found for language, F (2, 225) = 10.73, *p* < .001. Post-hoc tests indicated that the Active group (M = 1.67, SD = 0.78) and the Moderate group (M = 1.46, SD = 0.93) scored significantly higher than the Inactive group (M = 1.01, SD = 0.78).

Delayed Recall: The effect on delayed recall was significant, F (2, 225) = 22.85, *p* < .001. Post-hoc analysis revealed that the Active group (M = 3.74, SD = 1.38) and the Moderate group (M = 3.24, SD = 1.45) demonstrated better recall than the Inactive group (M = 2.20, SD = 1.23).

Abstraction: A significant difference was found for abstraction, F (2, 225) = 6.45, *p* = .002. Post-hoc tests indicated that the Active group (M = 1.96, SD = 0.65) scored significantly higher than the Inactive group (M = 1.46, SD = 0.71). The Moderate group (M = 1.64, SD = 0.68) did not differ significantly from either group.

Visuospatial/Executive Function: The one-way ANOVA for visuospatial/executive function was not statistically significant. F (2, 225) = 2.44, *p* = .089.

Table: 3

One-Way ANOVA Results for MoCA Sub-domains by Physical Activity Level (IPAQ)

MoCA Sub-domain	Inactive (n=114)	Moderate (n=88)	Active (n=26)	F	P
	M (SD)	M (SD)	M (SD)		
Attention	3.04 (1.20)	4.82 (1.39)	5.44 (0.93)	70.13	< .001
Orientation	3.70 (1.38)	5.57 (0.66)	5.89 (0.32)	96.72	< .001
Naming	2.18 (0.56)	2.54 (0.59)	2.67 (0.48)	14.03	< .001
Language	1.01 (0.78)	1.46 (0.93)	1.67 (0.78)	10.73	< .001
Delayed Recall	2.20 (1.23)	3.24 (1.45)	3.74 (1.38)	22.85	< .001

MoCA Sub-domain	Inactive (n=114)	Moderate (n=88)	Active (n=26)	F	P
Abstraction	1.46 (0.71)	1.64 (0.68)	1.96 (0.65)	6.45	.002
Visuospatial/Executive	2.30 (1.53)	2.26 (1.29)	2.93 (1.33)	2.44	.089

Note: MoCA = Montreal Cognitive Assessment. IPAQ = International Physical Activity Questionnaire M = Mean; SD = Standard Deviation.

Summary of Inferential Findings:

Collectively, the inferential statistics provide strong evidence supporting a significant relationship between physical activity and cognitive function in women with IDA. The highly significant chi-square test confirms a global association, with more active individuals showing less severe cognitive impairment. Furthermore, the analysis of specific cognitive domains reveals that this relationship is robust across multiple domains. Specifically, higher physical activity levels were associated with significantly better performance in Attention, Orientation, Naming, Language, abstraction and Delayed Recall. The effect on Visuospatial/Executive function was not statistically significant. These results indicate that physical activity is associated with broad cognitive benefits in this clinical population particularly in areas of attention, memory, and orientation.

DISCUSSION

MAIN FINDINGS:

The present study exploed the impact of physical activity on cognitive function among 228 women diagnosed with iron deficiency anemia (IDA). The findings demonstrated a strong and statistically significant association between physical activity levels and overall cognitive performance.

Participants who engaged in higher levels of physical activity consistently exhibited better MoCA scores and a lower prevalence of cognitive impairment. Specifically, more than half of the Active group (54.2%) demonstrated normal cognition, whereas the Inactive group showed the highest proportion of moderate (89.4%) and severe (100%) cognitive impairment, highlighting a clear gradient of cognitive decline with decreasing activity levels.

In addition to global cognitive scores, physical activity significantly influenced several specific cognitive domains. Women in the Active and Moderate groups performed significantly better in Attention, Orientation, Naming, Language, and Delayed Recall ($p < .001$). These patterns indicate that physical activity supports both memory-related and executive cognitive processes. However, the Visuospatial/Executive domain did not show a statistically significant difference between activity groups.

Overall, the study's main finding is that higher physical activity levels are strongly associated with better cognitive functioning in women with IDA, reinforcing the role of regular movement as a protective factor against cognitive decline in this vulnerable population.

COMPARISON WITH LITERATURE:

The findings of the present study, which demonstrate a significant positive association between higher physical activity levels and better cognitive function in women with iron deficiency anemia (IDA), are strongly supported by existing literature. Most previous studies consistently highlight that IDA impairs cognitive performance, particularly attention, memory, and executive functioning. Our results parallel these conclusions, especially the observation that inactive women exhibited the highest rates of moderate and severe cognitive impairment, which aligns with the work of Cook et al. (2017), who reported significantly poorer attention scores among women with IDA compared to iron-deficient but non-anemic women.

Similarly, the strong performance of the Active and Moderate physical activity groups across MoCA subdomains—especially Attention, Orientation, Naming, Language, and Delayed Recall—is consistent with findings from Yunanci et al. (2023) and Can et al. (2018), both of whom identified that reduced iron stores are linked to declines in attentional capacity, memory, and overall cognitive processing. Our results also support the physiological basis described by Kumar et al. (2022) and Coad & Pedley (2014), who explain that iron deficiency disrupts oxygen delivery and neurotransmitter function, contributing to cognitive impairment—effects that may be partially offset by increased physical activity due to improved cerebral blood flow and metabolic efficiency.

Further support comes from interventional evidence such as El Nahas & Gabr (2017), who reported that combining iron supplementation with aerobic exercise led to significantly greater improvements in anemia symptoms compared to supplementation alone. This reinforces the idea that physical activity acts as an additional therapeutic factor, consistent with our findings demonstrating better cognitive performance among women who reported higher activity levels.

The significant relationship found in our study also aligns with broader epidemiological evidence. For example, Kim et al. (2019) concluded through meta-analysis that anemia increases the risk of cognitive impairment, while Wenger et al. (2019) demonstrated that iron deficiency increases the cognitive energy cost during mental tasks suggesting that physical activity may help mitigate these deficits by improving metabolic efficiency and reducing cognitive strain.

However, the literature also presents contrasting findings. Studies such as Alhazmi et al. (2024) reported no significant association between IDA and cognitive scores in university students.

Although differing from the majority of evidence, such contradictory findings may be explained by population-specific factors, compensatory cognitive strategies, or higher baseline cognitive reserve highlighting the possibility that physical activity could be a key moderating factor. Our results support this interpretation, as cognitive impairment was most pronounced among inactive women, suggesting that inactivity may amplify the cognitive effects of IDA.

Collectively, the comparison demonstrates that the findings of the present study are largely consistent with international and local research, strengthening the evidence that physical activity plays an important role in mitigating cognitive deficits associated with iron deficiency anemia.

STRENGTHS OF THE STUDY:

The present study demonstrates several notable strengths that enhance its scientific rigor and contribution to the existing body of knowledge. First, it includes a large and well-defined sample of 228 women diagnosed with iron deficiency anemia (IDA), offering strong statistical power and improving generalizability to women of reproductive age. Compared to earlier studies that often-used smaller samples, the size and specificity of this cohort strengthen the reliability of the findings.

Second, the study employed validated and standardized assessment tools, including the International Physical Activity Questionnaire (IPAQ) to measure physical activity levels and the Montreal Cognitive Assessment (MoCA) to evaluate cognitive function. The use of these widely recognized instruments enhances the accuracy of measurements and facilitates meaningful comparisons with prior research. Additionally, evaluating individual cognitive subdomains allowed for a more precise understanding of which cognitive areas such as attention, orientation, naming, language, and delayed recall benefit most from physical activity.

Another major strength lies in the comprehensive statistical analysis, including chi-square tests for categorical comparisons and MANOVA with subsequent ANOVAs to assess differences across cognitive subdomains. This multi-tiered analytic approach increases the robustness of the findings and ensures that the relationship between physical activity and cognitive performance is examined from multiple angles.

A unique and significant strength of this study is that it addresses a critical gap in the literature. While many international and local studies have documented the association between IDA and cognitive impairment, no prior study has specifically examined the impact of physical activity on cognitive function among women with IDA. Existing research either focuses on the cognitive consequences of IDA alone or on the general health benefits of physical activity, but none investigate the combined interaction of these two variables. The present study is the first to demonstrate this relationship, providing novel evidence that higher physical activity levels are associated with better cognitive outcomes in women affected by IDA.

Finally, the inclusion of real-life variables, such as weekly physical activity patterns, iron supplementation habits, and symptom profiles, enhances ecological validity. This makes the findings more reflective of actual experiences of women living with IDA and increases the practical relevance of the study for clinicians, physiotherapists, and public health professionals.

LIMITATIONS OF STUDY:

1: Sample Size and Time Constraints: Due to limited time, the study could not include a larger number of participants. A larger sample would have enhanced the statistical power and generalizability of the findings.

2: Incomplete Medical Records: Many individuals remained undiagnosed, and complete medical reports were not available for all participants. This limitation may have affected the accuracy of participant classification.

3: Diagnostic Uncertainty: In some cases, participant identification was based on observable signs and symptoms rather than confirmed diagnostic reports, which may have introduced variability in the study population.

4: Limited Representativeness: The study population does not represent the entire female population with IDA, as data were collected only from selected hospitals and clinics. Only those women meeting the study's inclusion criteria were considered, potentially limiting the applicability of the findings to broader populations.

5: Cross-Sectional Design: The study employed a cross-sectional design, which provides a snapshot of the relationship between physical activity and cognitive function but does not establish causality. Longitudinal or experimental studies would be needed to confirm causal effects.

6: Absence of Structured Physical Activity Guidelines: Although the study demonstrated a relationship between physical activity and cognitive function, it did not include a structured exercise plan or day-wise guideline for participants, limiting practical recommendations for intervention.

IMPLICATIONS FOR PHYSIOTHERAPY PRACTICE:

The findings of this study have several important implications for physiotherapy practice, particularly in the management of women with iron deficiency anemia (IDA):

1. Incorporating Physical Activity as a Supportive Intervention:

Since the study indicates a positive relationship between physical activity and cognitive function, physiotherapists can incorporate structured physical activity programs as part of the holistic management of women with IDA.

2. Early Screening for Cognitive Impairment:

Physiotherapists working with women diagnosed with IDA should consider early screening for cognitive difficulties. Identifying attention, memory, or concentration issues can guide the selection of appropriate treatment strategies.

3. Designing Individualized Exercise Plans:

Although this study did not include a formal exercise protocol, the results support the development of personalized exercise programs focusing on aerobic and low-to-moderate intensity activities, which may help improve both physical health and cognitive performance.

4. Multidisciplinary Collaboration:

The relationship between physical activity and cognition highlights the need for collaboration between physiotherapists, physicians, nutritionists, and psychologists to create comprehensive care plans for women with IDA.

5. Patient Education and Lifestyle Counseling:

Physiotherapists can play a key role in educating women about the benefits of regular physical activity not only for physical well-being but also for mental alertness, cognitive clarity, and daily functioning.

6. Promoting Adherence to Exercise:
Encouraging consistent physical activity through tailored programs, motivational strategies, and follow-up sessions may help patients achieve better outcomes in managing IDA symptoms and cognitive challenges.

7. Contribution to Preventive Health:
By emphasizing the cognitive benefits of physical activity, physiotherapists can help prevent long-term cognitive decline in women at risk due to prolonged or untreated IDA.

RECOMMENDATIONS FOR FUTURE RESEARCH:

Based on the findings and limitations of this study, several recommendations can guide future research in this area:

1. Conduct Longitudinal or Experimental Studies:
Future studies should use longitudinal, randomized controlled, or interventional designs to establish a causal relationship between physical activity and cognitive function in women with IDA.

2. Include Larger and More Diverse Samples:
Increasing the sample size and recruiting participants from multiple regions, hospitals, and socioeconomic backgrounds will enhance the generalizability of findings.

3. Utilize Confirmed Diagnostic Reports:
Researchers should ensure that all participants have complete medical documentation, including laboratory-confirmed IDA, to improve accuracy in participant selection.

4. Develop and Test Structured Physical Activity Programs:
Future studies should include standardized exercise protocols or day-wise activity plans to evaluate the direct effects of specific types and intensities of physical activity on cognitive outcomes.

5. Investigate Underlying Mechanisms:
Future work should explore physiological mechanisms linking IDA, physical activity, and cognition such as oxygen transport, neural metabolism, and neuroplasticity.

6. Include Male Participants or Compare Genders:
Although this study focuses on women, future research could examine whether similar patterns exist in men or conduct gender-comparative analyses.

7. Evaluate the Role of Iron Supplementation Combined with Exercise:
Studies combining physical activity with medical or nutritional interventions may offer deeper insights into synergistic effects on cognitive function.

CONCLUSION

The present study is the first to examine the impact of physical activity on cognitive function specifically among women diagnosed with iron deficiency anemia (IDA). The findings revealed a strong and statistically significant association between higher physical activity levels and better cognitive performance, both globally and across specific cognitive domains such as attention, orientation, language, naming, and delayed recall. Women who reported higher levels of physical activity demonstrated notably better MoCA scores, while inactive participants showed the highest prevalence of moderate to severe cognitive impairment. These results suggest that physical activity may act as a protective factor against cognitive decline in women with IDA. Although the cross-sectional design does not allow causal conclusions, the study provides new evidence supporting the integration of regular physical activity as a supportive, non-pharmacological approach in the management of cognitive difficulties associated with IDA.

Future research should employ longitudinal, randomized controlled, or interventional designs to establish causality and further clarify the direction of this relationship. Larger and more diverse samples, along with complete diagnostic reports, are recommended to strengthen generalizability. Studies should also aim to develop and test structured, standardized physical activity programs to determine the most effective types and intensities of exercise for cognitive improvement in IDA populations. Investigating underlying physiological mechanisms such as oxygen transport, neural metabolism, and neuroplasticity, may deepen understanding of how physical activity influences cognitive outcomes in iron-deficient individuals. Gender- comparative studies and research combining physical activity with iron supplementation could further expand insights into synergistic interventions. Overall, the present study highlights the potential of physical activity as a valuable component in the holistic care of women with IDA and encourages future work to advance this promising area of research.

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