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Effect of Iron Deficiency Anemia on Hearing: Review Article

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ABSTRACT

Background: More and more evidence suggest a connection between the most prevalent kind of anemia, which is caused by low iron levels, and hearing loss. Hearing loss was found to be twice as common in people with iron-deficiency anemia (IDA) as it was in those without the blood condition.

Objective: Review of the literature on effect of iron deficiency anemia on hearing.

Methods: We looked for data on Iron Deficiency Anemia and Hearing in medical journals and databases like PubMed, Google Scholar, and Science Direct. However, only the most recent or extensive study was taken into account between November 2011 and October 2022. References from related works were also evaluated by the writers. There are not enough resources to translate documents into languages other than English, hence those documents have been ignored. It was generally agreed that documents such as unpublished manuscripts, oral presentations, conference abstracts, and dissertations did not qualify as legitimate scientific study.

Conclusion: The prevalence of sensorineural hearing loss (SNHL) is higher in children with IDA. Screening for and treating IDA in children will enhance their health, regardless of whether or not it is associated with better hearing outcomes in those who are hard of hearing.

Keywords: Iron-deficiency anemia (IDA), Pediatrics, Haemoglobin, Hearing.

INTRODUCTION

Most doctors ignore nutritional anaemia, especially iron deficiency anaemia (IDA), in otherwise healthy children because they are overwhelmed by its prevalence. Most of these kids are "apparently normal," however the terminology may also be to blame for this situation. Given the importance of iron to human health, nature has provided us with abundant sources of this mineral. Myoglobin and haemoglobin, two heme proteins, bind up to 75% of the iron in the human body. The enzyme systems cytochromes, catalases, and peroxidases account for about 3%, while the storage proteins ferritin and hemosiderin account for about 20% **(1).**

Recycled iron is accessible from the destruction of old red blood cells by macrophages of the reticuloendothelial system, so the body may meet most of its own iron needs from within. Only around 5% of an adult's daily iron requirements come from the diet, and that's just what's lost in the digestive process. For proper development and muscle growth, children and newborns require an additional 30 milligrams of iron each day from their food. A full-term newborn is in a condition of "iron feast" from the time of birth until the time of their fourth month. This is due to the fact that the concentration of haemoglobin drops from a mean of 17 g/dl at birth to a low of 11 g/dl at 2 months of age, and that iron is supplemented through haemoglobin breakdown. Iron "feast" changes to iron "famine" at roughly 4 months of age when nature switches some responsibility of iron balance to nurture. This susceptibility is due to the substantial quantity of iron required to support a mean haemoglobin concentration of 12.5 g/dl, which is reached swiftly during the period of rapid blood volume expansion between 4 and 12 months of age. Having a diet low in bioavailable iron or high in iron that cannot be absorbed by the body just makes the situation worse. Especially in underdeveloped regions, iron deficiency is a major public health issue

. Given that anaemia is the most reliable sign of iron deficiency, the two conditions are frequently used interchangeably. However, iron deficiency can occur even in the absence of anaemia, and it can negatively impact tissue health. Inadequate intake, quick growth, low birth weight, and gastrointestinal losses due to increased intake of cow's milk are the most common causes of iron insufficiency in children. Patients with iron insufficiency, especially older children, should have blood loss evaluated if inadequate intake has been ruled out and there has been a lack of response to oral iron treatment. Management of iron deficiency anaemia centres on four key tenets: identifying and treating the underlying cause of the condition, replacing lost iron, boosting the patient's diet, and educating the family. Our center's experience with diagnosing and treating iron deficiency is highlighted, along with other practical ways **(2).**

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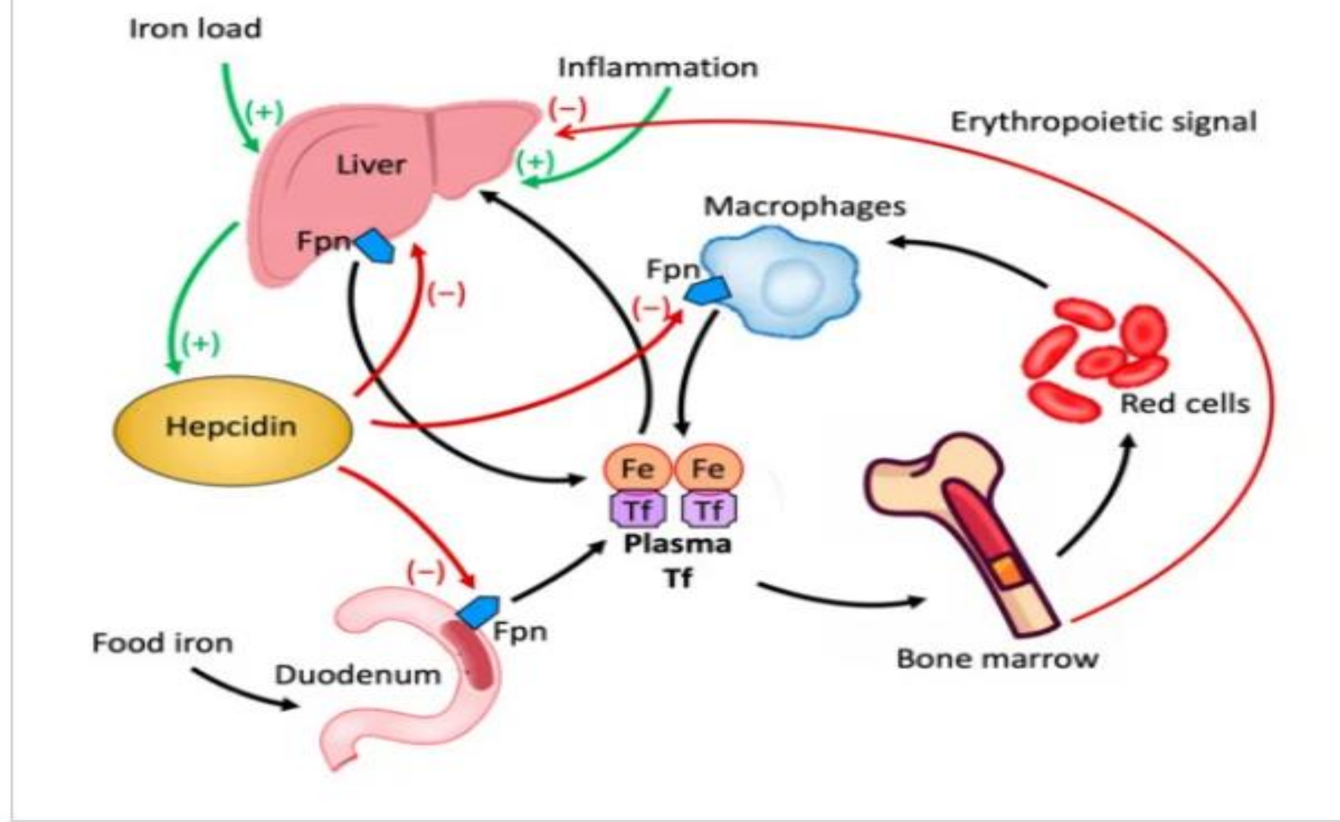

Figure (1): Process of iron deficiency anemia [(2)].

A loss of hearing might be temporary or permanent. Conductive hearing loss (CHL) and sensorineural hearing loss (SN HL) subcategories exist here. Hearing loss due to CHL occurs when the outer ear is unable to effectively transport sound waves to the ear drum and middle ear ossicles. Otitis media, a ruptured eardrum, and congenital defects in the external or middle ear are only few of the diseases that can cause this symptom. Medical or surgical interventions are usually viable choices for treating CHL [(3)].

However, SNHL is defined by injury to the inner ear or cochlea, which prevents the proper transduction of vibrations of the ossicles to neural impulses or the transmission of these impulses from the ear, through the vestibulocochlear nerve, to the brainstem. Hearing loss caused by ototoxic drugs, genetic predisposition, or traumatic/health-related causes is almost always permanent, and hence SNHL is a form of irreversible hearing impairment [(4)].

Sudden onset SNHL occurs in rare cases and is characterized by quick onset and typically unilateral involvement. Many factors influence prognosis, including age, duration of hearing loss, and hearing loss pattern. Nonetheless, in cases of idiopathic abrupt SNHL in which no therapy was attempted, the prognosis is poor. It is believed that between 45% and 65% of people will regain some degree of hearing, with that number rising to 90% with prompt medical attention [(5)].

A subset of anaemia, iron deficiency anaemia (IDA) is characterised by low haemoglobin levels, low serum ferritin levels, low blood iron levels, and/or an elevated soluble transferrin receptor. Oral iron supplementation is a simple and effective way to address this condition. Children at high risk for IDA include those who were born prematurely, who were given just breast milk or formula without iron fortification, who had a restricted diet or poor nutrient absorption, and who had experienced severe blood loss [(6)].

Iron is a cofactor in many cellular processes, including those involved in neurotransmitter metabolism, DNA synthesis, and DNA repair. Iron plays a role in the development, learning, and long-term memory of children because of its involvement in the central and peripheral nervous systems [(7)].

The vascular system also benefits from iron. It's an essential part of the protein in red blood cells called haemoglobin, which transports oxygen throughout the body. Significant heterogeneity exists by sex, socioeconomic class, body mass index, and race in the estimated prevalence of IDA. In the United States, IDA ranges from 2%–3% among toddlers up to age 3 and 5% among adolescent girls [(8)].

Chung *et al.* [(9)] presented the results of a large case-control research in Taiwan that looked at the link between IDA and abrupt SNHL in adults. It was postulated that IDA contributed to the development of sudden sensorineural hearing loss (SNHL) by decreasing blood flow to the inner ear, which is already vulnerable to ischemia damage. Common forms of childhood hearing loss may be related to iron's role in the vascular and neurological systems. Due to age-related differences in the prevalence of hearing loss, SNHL is less common in children [(4)].

SNHL has been associated in some research to a higher risk of sickle cell anaemia in children. It is hypothesised that the sickled red cells obstruct the blood arteries, leading to ischemia [(10)]. Although the sickle cell shape is characteristic of those with sickle cell anaemia, this method would not apply to those with IDA because sickle cell anaemia patients have normal iron levels. Despite the known association between sickle cell anaemia and hearing loss, data on how IDA may affect the risk of hearing loss in children who are no longer infants is scant. Although there has been a lot of research done on the topic of IDA and children's brain development, there is still much more to learn [(11)].

There is scant human evidence linking IDA and childhood hearing loss. Striatal atrophy and a reduction in spiral ganglion cells are two examples of the inner ear changes seen in iron-deficient rat models (including young rats), which have been linked to the development of SNHL. Iron deficiency may have a crucial role in the auditory maturation stage during infancy, as data shows that children in Chile with IDA have abnormal myelination and enhanced auditory brainstem responses at age 4 compared to those without IDA as a baby [(12)].

The theory postulated that in children, IDA would be more strongly associated with SNHL than with CHL. A greater knowledge of the effects of iron status on neurological and vascular function, as well as earlier detection of hearing loss through improved screening protocols, could result from establishing a link between IDA and hearing loss [(4)].

These findings raise questions about screening for IDA in a preventative care context and routine examination for children and adolescents diagnosed with SNHL, despite the fact that a connection between the correction of IDA and better hearing outcomes has not yet been shown. No "standard" workup for SNHL in children and adolescents emerged from a survey of paediatric otolaryngologists. Routine laboratory examinations, such as complete blood count, were requested less frequently than specialized imaging tests, genetic analysis, and electrocardiograms [(13)].

The national paediatric preventive care standard-setting organization bright futures currently suggests a newborn hearing screen before the baby is released from the hospital. In addition to a hearing test at birth, children should receive follow-up testing for hearing loss at 4, 6, and 10 years old as part of their well-child checkups. Adolescents at high risk for IDA are interviewed or screened using questionnaires every 9-12 months [(14)]. This would mean that screening and treatment are built into standard operating practices. Although there is no concrete evidence that treating IDA can also enhance hearing health. It is well established that both IDA and hearing loss have detrimental impacts on focus and academic performance that can be ameliorated by treatment [(15)].

Considering that the study's definition of IDA relied on readings for both haemoglobin and serum ferritin, it's possible that the true prevalence of IDA was underreported. In order to increase the analysis's specificity, those people whose laboratory values did not indicate IDA (based on serum ferritin or haemoglobin levels) were counted as IDA-free. Patients in our sample who did not have IDA may have an underlying medical condition that was not taken into account because serum ferritin and haemoglobin are not regularly checked in the clinic. Presumptive treatment with iron is common in clinical practice for patients with low haemoglobin, and a serum ferritin level is not often needed [(16)].

Our results did not uncover this when we stratified by sex, despite the fact that it would be convincing if the link between IDA and hearing loss could be shown for both sexes. This is probably because our rigorous criteria cut down on the effectiveness of our analysis. Because we needed laboratory values to identify IDA, the full population of paediatric patients in the database is not shown here [(16)].

Patients were not included if they lacked any laboratory values, which reduced the size of the study's sample population and thus its statistical power. The data found a significant relationship between IDA and SNHL for boys aged 4-11 years and male patients aged 4-21 years, suggesting that the original analysis showed reduced power to address this association in the male sex, but this is not thought to be affecting the results. Both SNHL and CHL were less common than previously claimed. However, it's possible that varying definitions of hearing loss in various studies account for part of the variation [(16)].

Lin *et al.* [(17)] employed data from the National Health and Nutrition Examination Survey (NHANES) 2001-2008 and found a prevalence of 2.3% (95% CI [1.5-3.1 percent]) of bilateral and unilateral hearing loss > 25 dB among 12- to 19-years-old, which is similar to the prevalence of 1.7% found in this research [(17)]. The prevalence of hearing loss in children is significantly higher than reported in several research that used NHANES data [(18)]. The NHANES data are distinct from the clinical criteria used by the i2b2 database since they are based on objective audiogram measures. We believe that differences in diagnostic criteria account for the observed range of prevalence rates. However, we are unaware of any published objective criteria that would allow for direct comparison [(18)].

Iron-deficiency nearly half of all instances of anaemia in the globe can be attributed to this frequent form of the disease. Inadequate iron intake and/or absorption and/or iron loss due to haemorrhage in the gastrointestinal, genitourinary, or other systems are to blame for this condition. It's easy to see how a drop in haemoglobin levels in the blood could lead to decreased oxygen supply to tissues. IDA has also been inferentially linked to an increased risk of ischemic stroke in other studies. Further, many studies have shown that low haemoglobin levels have negative consequences on the heart and brain [19].

A temporal bone histopathological investigation suggests a viral origin rather than a vascular origin for SSNHL, which seems counterintuitive given that the disturbance in hemodynamics in IDA may contribute to the traditional SSNHL idea of vascular compromise. New processes involving the pathologic activation of cellular stress pathways are hypothesised, and the traditional explanations of idiopathic SSNHL, such as membrane breaches, perilymphatic fistulae, and vascular occlusions, are called into question. The increased risk of SSNHL in individuals with IDA may be due to factors other than vascular disease, such as an abnormality in iron metabolism [20].

Sun *et al.* [20] new data linked iron deficit to cochlear injury in a rat model. They used an iron-deficient diet to further cause SSNHL in developing rats. Infected rats showed a dramatic decline in spiral ganglion cells and an immediate involvement of stereocilia in both the outer and inner hair cells. The same research team also found that iron therapy significantly improved clinical outcomes for SSNHL patients, lending credence to these findings. Their small case numbers, however, indicate that the connection between IDA and SNHL still needs more elucidation, and their clinical effectiveness only warrants the use of iron treatment in controlling SNHL.

Since IDA has been linked to autoimmunity for a long time, it is also assumed that the immune system may have a non-hemodynamic role in linking IDA and SSNHL. In addition, immune-mediated diseases, like those resulting in SSNHL, have started to receive more attention in recent years. Six patients with SLE or a lupus-like condition developed SSNHL, and it was reported that these individuals had abnormally high levels of anticardiolipin antibodies. Recently, a connection between SSNHL and different autoantibodies was identified in prospective research comprising 51 individuals. Antinuclear antibodies, antithyroid antibodies, rheumatoid factor, and anticardiolipin were all found to be higher in the patients than in the controls. These results suggest that immune-related diseases may contribute to both IDA and SSNHL [21].

It is well-established that IDA is associated with a higher risk of mortality and disability in the elderly. Intriguing, but puzzling, is the correlation between SSNHL and younger age in IDA patients. This study's findings suggest that the processes linking SSNHL and IDA are not directly related to the causes of most cases of IDA in the elderly, such as gastrointestinal bleeding. The results provide circumstantial evidence for an underlying immune-mediated mechanism, which is significant given that most autoimmune diseases strike the young and middle-aged. However, additional research is required to determine the true connection between IDA and SNHL [22].

Second, we don't know how IDA is treated, and it's plausible that some IDA cases were under control until SSNHL emerged. Because of this, it's possible that the anaemia treatment itself is to blame for the higher risk of SNHL [9].

Third, the database's origin in a health insurance system meant that information on several critical predisposing factors for SSNHL was not full, despite the fact that a large number of individuals were enrolled through the population-based database. Prior infections, concomitant otologic problems, noise exposure, and hereditary conditions were difficult to assess for their presence and severity. A degree of bias may have resulted from the inclusion of subjects with SSNHL for which the underlying cause is known. However, the incidence of such instances would be low in comparison to idiopathic SSNHL. We can possibly shift the data toward the null hypothesis if we include cases of SSNHL with a known cause. Consequently, the results wouldn't have changed much even if this bias had been present [23].

People with vascular disease are also at a higher risk for developing SNHL suddenly. Therefore, it is evident that blood supply plays a significant role in hearing loss. Myelin, the waxy substance that coats nerves and is critical for the proper passage of impulses along nerve fibers, is a second possible mechanism. Myelin synthesis and energy production are negatively impacted by iron deficiency because of the breakdown of lipid saturase and desaturase. Damage to the myelin sheath of the auditory nerve can lead to diminished hearing [23].

CONCLUSION

In kids and teenagers, IDA and SNHL go hand in hand. A logical addition to current practice would be to think about screening for IDA for children and young adults aged 4-21 who have been diagnosed with SNHL. Next steps will need to determine if treating the underlying IDA improves hearing health in afflicted children and adolescents, despite the fact that doing so will improve their overall health.

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