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Impact of Iron Deficiency Anemia on Nerve Conduction Velocity and Cognitive Function: Insights from North Indian Patients

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Abstract:
Anemia is a medical condition characterised by a deficiency of red blood cells, leading to an inadequate supply of oxygen to meet the physiological requirements of the body. Iron deficiency anemia specifically results when the body lacks sufficient iron to generate haemoglobin. A case-control study has been conducted to explore the association between iron deficiency anemia (IDA) and nerve conduction functions in a rural population setting in Uttar Pradesh state of India. The cognitive test was conducted using MoCA questionnaires. For the nerve conduction velocities, sensory nerve conduction velocity (SNCV), motor nerve conduction velocity (MNCV), and Montreal cognitive assessment (MoCA) scores are estimated. The study shows that there is a significant association between iron deficiency anemia (IDA) and nerve conduction functions. There was a decrease in nerve conduction velocities of all the motor and sensory nerves in iron-deficient anemic patients as compared to controls.

Keywords: Iron deficiency anemia (IDA), nerve conduction functions, Montreal cognitive assessment, sensory nerve conduction velocity (SNCV)

Introduction

Anemia is a medical condition characterised by a deficiency of red blood cells, leading to an inadequate supply of oxygen to meet the physiological requirements of the body. Iron deficiency anemia specifically results when the body lacks sufficient iron to generate hemoglobin. Hemoglobin is a crucial component of red blood cells responsible for imparting the characteristic

red color to blood and facilitating the transportation of oxygenated blood across the body [8]. Iron Deficiency Anemia poses a significant public health issue, particularly impacting young children, pregnant and postpartum women, as well as menstruating adolescent girls and women. Similarly, those people who have a history of excessive cow's milk consumption and/or low iron-containing foods, are among the others [17]. The issue is particularly pronounced in low and lower-middle-income countries with limited access to formal education [17].

The association between iron deficiency anemia (IDA) and cognitive decline is an interesting area of research. Research shows IDA is associated with tissue hypoxia and lack of oxygen, particularly to the brain, could contribute to cognitive decline [19]. Furthermore, studies indicate that IDA might lead to mitochondrial dysfunction within brain cells. When iron is deficient, cytochrome oxidase function may be compromised, potentially leading to cognitive impairments [20]. Sufficient iron levels are essential for maintaining the integrity of the nervous system by supporting the production of myelin, the protective layer that surrounds nerve fibers. A deficiency of iron can affect the biosynthesis of myelin, leading to slower nerve transmission and changes in sensory and motor abilities. Moreover, iron is essential for a range of cognitive functions in the central nervous system, such as neurotransmitter production, energy metabolism, and myelination. Therefore, a lack of iron caused by IDA can have negative impacts on cognitive abilities like memory, attention, and executive function [3, 4].

According to WHO in 2023, South- East Asia is one of the most vulnerable areas affected by IDA [17]. The effects of IDA on hematological parameters are well-known. The focus is now shifting towards its impact on neurological and cognitive functions, such as nerve conduction velocity and cognitive performance [2]. Most of the studies related to IDA are from Western countries and the effect of IDA particularly on the North Indian population is not well explored. No research so far has focussed on the effect of IDA especially on socio-economically disadvantaged community people. Examining how IDA affects Conduction Velocity (NCV) and cognitive function in North Indian patients is important to fully understand the neurological impact of the disease due to specific diets, genetics, and other environmental factors in this region [5, 6, 7].

This article aims to assess the Impact of IDA on NCV and Cognitive Function. In India, there is a notable research gap in understanding the connection between Iron Deficiency Anemia (IDA), Neurocognitive Variables (NCV), and cognitive function, despite progress in medical research. Existing research emphasizes the physiological effects of IDA on general cognitive impairments, neglecting certain important neurocognitive factors that could offer a more comprehensive insight. In addition, there needs to be more studies connecting IDA to NCVs such as attention deficit, memory, and executive function.
Moreover, most studies on this topic come from Western countries, with very few research studies conducted specifically on Indian populations. Current studies often fail to adequately take into account factors like genetic predispositions, dietary habits, and environmental influences specific

to India. This research was conducted to explore if there is a link between IDA and NCV, along with cognitive function, in a group of North Indian individuals. By understanding how IDA affects the neurocognitive symptoms in this group, we can guide medical practices and public health interventions to reduce the neurological consequences of iron deficiency, ultimately enhancing the general health and cognitive results of those impacted.

Material & Methods

The study design refers to a case-control (analytical) study design, conducted in the Department of Physiology and Psychiatry, Government Medical College and associated teaching hospital, Kannauj in East U.P, India, that caters to the rural population in and around the surrounding locality. We calculated the required sample size for our study using the sample size formula for case-control studies [13, 14]. The details of the sample size estimation are given in the supplementary file. The estimated sample size for this study is 60 (30 cases and 30 controls). The data was collected from September 2023 to March 2024.

The data includes 6 males and 24 females in the age group of 23 to 40 years in the case group whereas 12 males and 18 females in the control group. The cases were newly clinically diagnosed untreated patients with iron-deficiency anemia. A comprehensive clinical examination and clinical history of all the participants were taken. Diagnosis of IDA was made based on the findings of a complete blood cell count examination done using a Swelab Alfa Plus 3-part hematology analyzer. The hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), Mean corpuscular hemoglobin concentration (MCHC), and Serum ferritin levels were estimated in cases and controls. The Hb levels less than 13g/dL and 12 g/dL in males and females respectively are assumed to be the criterion of IDA [8]. Similarly, MCV<80fL, MCH <27pg, and MCHC <31 g/dL in both males and females confirmed the diagnosis of IDA [8]. Serum ferritin levels were estimated using an Immunoassay analyzer.

A nerve conduction study was performed using the NeuraStim EMG/NCV (NS2 EMG) machine of the right upper limb median nerve. Three disc surface electrodes were used with surface stimulators - Recording electrode, reference electrode, and ground electrode. The electrodes were placed after applying jelly to reduce resistance in the air between the electrode and the skin surface. The nerve was stimulated, usually with surface electrode patches attached to the skin. Two electrodes were placed on the skin over the nerve. One electrode stimulates the nerve with a very mild electrical impulse and the other electrode records it. The resulting electrical activity was recorded by another electrode. This is repeated for each nerve being tested. The nerve conduction velocity (speed) was then calculated by measuring the distance between electrodes and the time it takes for electrical impulses to travel between electrodes. The cognitive test was conducted using MoCA questionnaires. For the nerve conduction velocities, sensory nerve conduction velocity (SNCV), motor nerve conduction velocity (MNCV), and Montreal cognitive assessment (MoCA) were calculated using the machine NeuraStim EMG/NCV (NS2 EMG) [1, 4, 9].

Results and Discussion

The comparison of RBC indices is presented in Table 1. The mean (±SD) of parameters Hb, MCV, MCH, MCHC, and S.ferritin in cases of the control group are presented in Table 1. The student t-test (independent) is used to check the significance of mean differences between cases and controls. The mean (+SD) difference between cases and control for Hb (8.35±2.34 vs 3.36±0.93), for MCV (72.02±10.54 vs 84.03±5.21), for MCH (23.91±3.39 vs 28.12±1.36), and for S. ferritin (8.50±3.13 vs 26.66±3.42) are statistically significant (p<0.0001). However, for MCHC, the mean difference between cases and controls (33.05±4.30 vs 33.42±1.95) is statistically insignificant (p value= 0.669). A similar study by Neelima et al. also reported a significant decrease in mean ±SD of Hb, MCV, MCHC and S. Ferritin among anemic groups [10].

Table 1: Comparison of RBC indices

Parameters	Cases (n=30)	Controls (n=30)	significance (p-value)
Hb	8.35±2.34	13.36±0.93	<0.0001
MCV	72.02±10.54	84.03±5.21	<0.0001
MCH	23.91±3.39	28.12±1.36	<0.0001
MCHC	33.05±4.30	33.42±1.95	0.6694
S. ferritin	8.50±3.13	26.66±3.42	<0.0001

The comparison of nerve conduction velocities and MoCA scores is presented in Table 2. The study parameters SNCV, MNCV, and MoCA were estimated for cases and controls. We used the student's t-test (independent) to check the statistical significance of mean differences between the two groups. The mean (+SD) difference between cases and control for SNCV (37.20±14.38 vs 57.34±1.54), for MNCV (20.93±3.68 vs 27.53±0.89), and MoCA (20.93±3.68 vs 27.53±0.89) are statistically significant (p <0.0001).

Table 2: Comparison of nerve conduction velocities and MoCA score

Parameters	Cases	Control	significance (p-value)
SNCV	37.20±14.38	57.34±1.54	<0.0001
MNCV	35.08±13.62	57.03±1.97	<0.0001
MoCA	20.93±3.68	27.53±0.89	<0.0001

Iron deficiency, whether or not accompanied by anemia, is a significant health issue [15,16,18]. Iron is essential for brain development from a human physiology standpoint. It is crucial for synthesizing neurotransmitters and forming myelin, both of which are vital for learning and

memory functions [9]. As a consequence, IDA seems to be linked to motor and cognitive dysfunction and socio-emotional problems [7]. Iron deficiency affects oxygen-carrying capacity and can also have an impact on immunity, growth and development [11]. Anemia has been shown to affect both emotional and behavioural disturbances [12]. Iron is the component of the main enzymes that involve essential oxidation and reduction reactions, synthesis of neurotransmitters, catabolism of neurotransmitters and synthetic processes such as the production of myelin. By discussing the functions of iron on CNS, we surely can expect cognitive dysfunction in IDA. Several clinical studies suggest a significant influence of IDA on dynamic properties and functional features of the central nervous system activity.

In the current study, there was a decrease in nerve conduction velocities of all the motor and sensory nerves in iron-deficient anemic patients as compared to controls. Degirmenci et al. [13] and Neelima et al [10] also observed similar findings.

Conclusion

Iron deficiency starts gradually, leading to delayed diagnosis, which is usually delayed due to a delay in overt symptoms. IDA may last for months or even years, with neuropathic symptoms often overlooked for an extended period. Screening and early diagnosis of IDA, and treatment for correction of even mild IDA is required. It would be appreciated if electrophysiological examinations were conducted on anemic individuals at an early stage of the illness to identify any impact on the nervous system. Identification of iron-related neuropathic conditions (such as PNP and CTS) in patients with IDA indicates that IDA might lead to peripheral nervous system complications. Highlighting the importance of screening for IDA in treatment planning for neuropathy patients is crucial. There is a need for further investigation to determine if iron replacement therapy can reverse neurological dysfunction in cases of iron deficiency.

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