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The Effects of Iron Therapy on HbA2 Levels in Patients with Iron Deficiency Anaemia; A Study in Khyber Pakhtunkhwa

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Abstract

Objectives: This study aimed to determine the effect of iron treatment in a post-therapy group of patients with Iron Deficiency Anemia (IDA) in the population of Khyber Pakhtunkhwa (KPK).
Methodology: This quasi-interventional study was conducted from January 2021 to January 2022 at Hayatabad Medical Complex (HMC) and the Institute of Pathology and Diagnostic Medicine, Hematology Laboratory. The participants were aged 8–15 years. To assess the response to iron therapy in both pre- and post-therapy iron-deficient groups, an Electronic Particle Counter (EPC) was used to measure Mean Cell Volume (MCV), and a chemiluminescence immunoassay was used to measure serum ferritin levels in biofluids. SPSS version 19.0 was used for data analysis. A paired T-test was performed for the mean/SD of all hematological parameters recorded before and after iron treatment. Pearson correlation was used to determine the strength of the association between pre- and post-therapy hematological parameters. The level of significance was set at P<0.05.
Results: The mean age of the participants was 9.5±3.5 years, with a male-to-female ratio of 2:1.5. A positive correlation was found between pre- and post-therapy hemoglobin levels (Hb1 and Hb2; r = 0.851) and between pre- and post-therapy MCV values (r = 0.806). The mean MCV before treatment was 55.30±7.42 fL, which increased significantly to 75.82±4.66 fL by day 180 (P<0.001). Similarly, the mean hemoglobin level, which was initially 9.22±1.17 g/dL, increased to 11.22±1.21 g/dL by day 180 (6 months) with a high level of significance (P<0.001). The greatest difference between pre- and post-treatment was observed in ferritin levels (19.66±6.79 ng/mL vs. 62.48±4.82 ng/mL, P<0.001). There was a statistically significant increase in hemoglobin levels (P<0.001), MCV (P<0.001), serum ferritin (P<0.001), and hemoglobin A2 levels.
Conclusion: The study demonstrated statistically significant improvements in hematological parameters following iron therapy, both orally and intravenously, validating the effectiveness of iron treatment in IDA patients.
Keywords: Anemia, HbA2, Hemoglobin, Ferritin

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Introduction

Approximately 300 million children globally had anaemia in 2011.[1] Thus, World Health Organization (WHO) has classified iron deficiency as a public health concern due to the morbidity and death associated with it. [2, 3] Low iron stores disrupt normal haemoglobin synthesis.[1] Babies and toddlers are more vulnerable to the detrimental effects of iron deficiency, due to their rapid growth and increased iron requirements.[4]

According to the World Health Organization's classification and the National Blood Authority's Patient Blood Control Guidelines, anaemia is a haemoglobin level of less than 120 g/L in non-pregnant females and 130 g/L in boys. Infants and toddlers most often have iron deficiency anaemia. [1, 2] Iron deficiency anaemia is common in this age range. Thus, early identification and treatment are crucial to avoid long-term growth and development issues.[4]

IDA and iron deficiency are global health concerns. [5, 6] Energy production, respirati on, and cell division need iron.[1] IDA is caused by insufficient iron intake, more significant iron loss, or high iron requirements. [3] Erythropoiesis cannot meet physiological demands. IDA reduces operating performance by making muscles rely more on anaerobic combustion than healthy persons to grow. [4] Thus, afflicted patients cannot work physically. [4, 5]

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Toddlers need iron for erythropoiesis, organ growth, and smooth functioning. The upper digestive tract must absorb it from meals. [1] Iron insufficiency occurs when the ratio of iron ingested, stored, and lost is insufficient to maintain erythrocyte (ID) production. IDA, the most common type of Anaemia, occurs in 30% of untreated ID cases. [5]

The regions with the lowest anaemia rates include Australasia (5.7%), Western Europe (6%), and North America (6.8%). Sub-Saharan Africa and South Asia are currently carrying the heaviest load. [6, 7] In 2021, Western sub-Saharan Africa (47.4%), South Asia (35.7%), and Central sub-Saharan Africa (35.7%) had the highest frequency of anaemia. [6, 8]

The overwhelming majority of the Pakistani population suffers from Iron Deficiency Anemia (IDA). Predictably, almost all pregnant women, nursing mothers, and toddlers in Pakistan are affected by IDA. The prevalence of IDA among newborns and toddlers is as high as 50%.[9,10] When the prevalence of anemia in young children reaches 40% or more, guidelines generally recommend that children of normal birth weight receive oral iron supplementation (2 mg/kg per day of elemental iron for 3 months) [11], and that low birth weight children receive the same amount starting at 2 months of age .[12]

Nutritional supplementation is a critical step in addressing iron deficiency.[6] Public health programs can help increase dietary iron intake while considering local dietary habits.[2,5] Evidence has shown that daily iron supplementation in children aged 6–23 months is associated with a reduced risk of iron deficiency and anemia .[11,12]

There was little information available for IDA subjects in Khyber Pakhtunkhwa. As a result, most nursing mothers were unaware of the importance of iron replacement therapy for IDA in developing children. Thus, this study aimed to determine the effect of iron therapy in post-therapy groups of iron deficiency patients (IDA).

The purpose of this study was to justify supplementing in IDA patients, particularly newborns and preschool-aged children. Even with extended breastfeeding, complementary foods must provide almost 100% of dietary iron for young children because breast milk contains little iron. [6] Following this study, various iron deficiency prevention and control strategies, such as food fortification, dietary modifications, and hookworm and other helminth infection treatment, can be implemented.

Methodology

The quasi-experimental study was conducted over a year (January 2021 to January 2022) with a one-group pretest-posttest design based on non-random assignment of IDA (Serum Ferritin level of ≤12µg/L, Hb g/dl ≤9.0) patients visiting Hayatabad Medical Complex (HMC) and the Institute of Pathology and Diagnostic Medicine haematology laboratory. A non-probability purposive sampling technique was used to collect data from patients who met the inclusion criteria. On the other hand, cases of inflammatory diseases e.g. inflammatory bowel diseases like ulcerative colitis and Crohn's disease, chronic intestinal bleeding, chronic lung diseases, chronic kidney disease and rheumatologic diseases were excluded from this research. The age range selected was 8–13 years old. The calculated sample size with a population proportion of 0.06 [8, 9] and a level of confidence of 95% was 70 participants. Data were obtained using a demographic information and written consent was obtained from the guardians of all the children. 7ml of blood was drawn from each participant, of which 5ml was put into the EDTA tube for performing CBC and HbA2 estimation. 2ml was put into the serum separating gel tube for performing serum Ferritin at day zero in the pretest group. The lab technician performed the requested testing and provided the results of all baseline parameters. Complete blood count was done on Sysmex XN-1000 hematology analyzer which works on both coulter's principle and flow cytometry for hemoglobin/Hb, WBC, Platelets and MCV. Serum ferritin was tested on Cobas e601which runs on electrochemiluminescence method. HbA2 was tested on D-10 ion exchange HPLC system. The intervention of iron supplementation via oral or parenteral, with a dose recommended according to WHO was implemented. The participants were followed –up for 6 months. After 6 months (day 180) in the post-test group, measurements were again collected to determine the effect of iron treatment on HbA2 and all haematological parameters. Subsequently, the dependent (participants) and independent (iron therapy) variables were analyzed by descriptive (mean and standard deviation) and inferential statistics (t-test) and Pearson's correlation coefficient) in SPSS 22. $P<0.05$ indicated a level of significance.

Results

The mean age of the participants in the study was 9.5±3.5 years in the pretest group, and 10.2±3.0 years in the post-test group via descriptive statistics. The male-to-female ratio was 2:1.5. Table I

Table I: Demographics of the study participants (n= 70) using descriptive statistics

Demographics	Frequency (N)	Percentage (%)
Age Groups		
1-5 years	11	15.71
6-10 years	39	55.71
11-15 years	17	24.28
16-17 years	3	4.28
Gender		
Female	30	42.85
Male	40	57.14
Total	**70**	**100**

A positive correlation was found between pre and post-therapy Hb1 and Hb2 (r = 0.851), with linear correlation in Figure I. Even the positive correlation (r = 0.806), was illustrated in Figure II with linear MCV 1 and MCV 2 in pre and post-therapy groups. The high level of significance was recorded for both parameters in pre and post-iron therapy groups. (p<0.001)

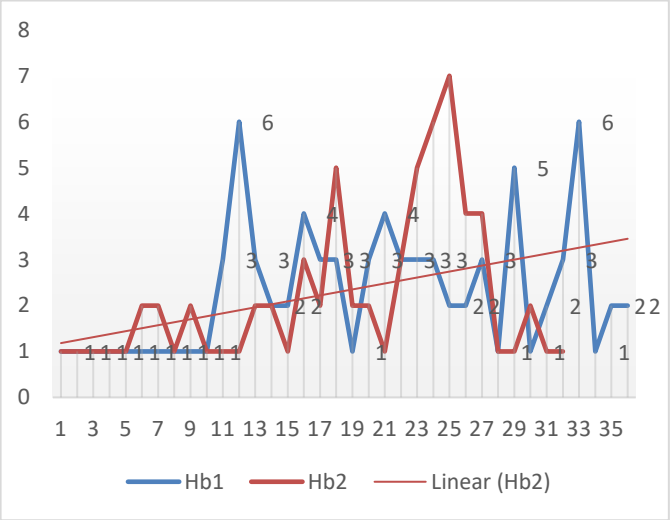

Figure I: Comparison of pre and post-therapy Haemoglobin A2 *Correlation is significant at the 0.001 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed).

The mean corpuscular volume (MCV) before treatment was 55.30±7.42 FL which was raised significantly to 75.82±4.66 FL by day 180 (p<0.001). Similarly, the mean Hb g/dl 9.22±1.17 initially was raised to 11.22±1.21 g/dl at day 180(6 months) in the post-therapy group with a high level of significance (p<0.001). The greatest pre- and post-treatment difference was observed in ferritin levels (19.66±6.79 versus 62.48±4.82, p<0.001). Table II

Table III illustrates the paired comparison of all indices at baseline on day zero and day 180 of follow-up in the pre and post-test group. Pre and Post-therapy means haemoglobin was -1.894 ±1.77 (p<0.001). The pre and post-therapy mean corpuscular Volume concentration was -20.52±6.53Fl (p<0.001) and Pre and Post HbA2% was 0.149±0.290 with p-value <0.001

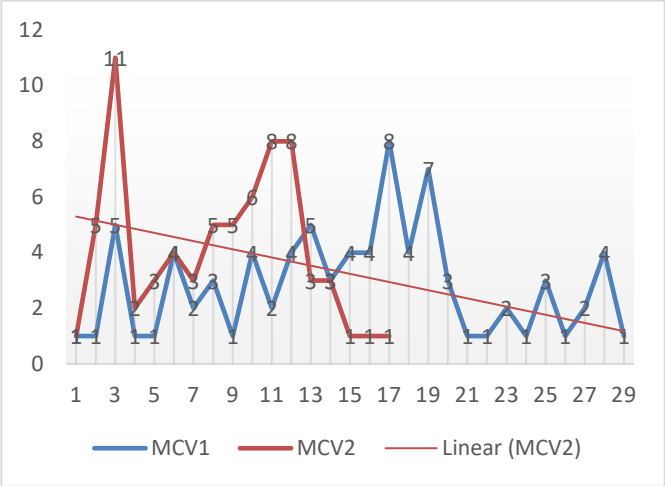

Figure II: Comparison of pre and post-therapy MCV. *Correlation is significant at the 0.001 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed).

Table II: Pre- and post-therapy mean, standard deviation (SD), and relationship of Hematological parameters among both genders using paired t-test (n=70)

Parameters	Pre-therapy (day Zero)	Post-therapy (day 180)	P value
	Mean ± SD	Mean ± SD	
Hb (g/dl)	9.22 ±1.17	11.02± 1.21	**P<0.001
MCV(Fl)	55.30 ±7.92	75.82± 4.66	**P<0.001
HbA2 (%)	2.76 ±1.25	2.91± 1.18	
Serum Ferritin (µg/L)	19.66 ±6.79	62.48±4.82	**P<0.001
Platelets	329.04±104.40	257.54±56.639	**P<0.001

Table III: A paired comparison of pre-and post-therapy mean differences (Paired t-test)

Pairs	Parameters	Mean	SD	P value
Pair 1	Pre Hb - Post Hb	-1.894	1.177	P<0.001
Pair 2	MCV 1 - MCV 2	-20.528	6.531	P<0.001
Pair 3	Pre HbA2% - Post HbA2%	-0.149	0.290	P<0.001
Pair 4	Pre S. Ferritin - Post S. Ferritin	-42.818	98.265	P<0.001
Pair 5	Pre Platelets – Post Platelets	71.00	87.59	P<0.001

Discussion

This present study was able to discuss the beneficial effects of iron therapy on haematological parameters in IDA patients in the population of Khgyber Pukhtunkhawa.

In our study of 70 IDA patients, 55.71% belong to 6-10 years age group. In contrast, to the study of Muhammad et al, [13] showed that IDA is most commonly prevalent in the 0–2-year age group which includes 78%. This observation was regarded due to more hook warm infestation in Nepal which varies from 11% to 100% when compared to the present study. Although the male to female ratio was also 2.12:1 which was similar to our study. Both of the studies showed that male were reporting more with IDA than females.[13]

The study of Habib et al [12] reported the prevalence was 40%, with males being more affected by IDA again corresponds well with our study.

The study by Camaschella[8], using data from the third National Health and Nutrition Examination Survey (NHANES III) in the United States, indicated that 3% of children aged 12–36 months and less than 1% in the 37–60 months age group had IDA. This finding highlights a higher prevalence in younger age groups compared to our study. This great difference was regarded as the overall prevalence of IDA in the population of the United States, recorded to be 6% when compared to the Pakistani population to be 55%.

Our study evaluated the safety and effectiveness of both oral and intravenous iron management of IDA patients. It has increased mean levels of haemoglobin, MCV, serum ferritin and platelets levels when compared to the pre-therapy group. These findings were consistent with the findings of Pinks *ET al.*[14] who noted that following treatment, the levels of haemoglobin rose from 7.43 g/ dl at the time of treatment to 9.27 g/dl on day 14 and 12.4 g/dl after 6 months of therapy almost similar to the study.

One of the local studies conducted by Muhammad et al [13] and Abdullah [15] even showed a more rapid increase in mean haematological values and serum ferritin levels after Intravenous Iron therapy, often similar to the present study.

There was a strong positive linear correlation between haemoglobin and MCV levels in the post-test group on day 180 (6 months) after the iron therapy in the present study. The P-value was also significant for pre and post-iron therapy in IDA subjects. Similar were the findings of Nazir, [16] and colleagues with a positive correlation of 0.891 with a significant p-value of 0.01 between pre and post-therapy Hb (g/%) and MCV.

The mean and deviation for the Blood parameters recorded by Papadoplous ET al.[17] and Kaneva [18] have shown a proportional increase in the values after iron therapy. The findings in this study also derived the mean values for the haematological measures, which corresponded well with all the above conclusive results.

The study of Kumar [19], however, showed more effective Intravenous Iron therapy than orally administered iron management. Although our study has shown the effectiveness of both techniques. However, our study was limited due to the small sample size. Research on a larger population must be conducted to better understand the safety and efficacy of intravenous iron versus oral therapy in our population

Conclusion

The study demonstrated statistically significant improvements in hematological parameters following iron therapy, both orally and intravenously, validating the effectiveness of iron treatment in IDA patients.

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