



## Evaluation of serum electrolyte levels in iron deficiency anemia patients.

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### Article received on:

20/07/2020

### Accepted for publication:

03/10/2020

## INTRODUCTION

Low concentrations of red blood cells (RBCs) or hemoglobin in blood circulation characterized by depleted capacity of oxygen transport by RBCs is called anemia. Anemia is associated with pallor, fatigue, suboptimal mental functioning and impaired development, which leads to high morbidity and mortality.<sup>1</sup> There are more than 400 types of anemia with diverse nature of etiologies, though most important classes include nutritional deficiencies, inherited problems, and effect of environmental pollutants, poverty, demography and chronic diseases.<sup>2</sup> Iron deficiency anemia (IDA) has been the commonest type among nutritional anemia globally which is estimated to occupy 50% load of anemia alone, posing a major health issue especially in under-developed nations.<sup>3</sup> Prevalence of IDA is high amongst Pakistani women especially during adolescence.<sup>4</sup> Risk of IDA is high during adolescence among

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**ABSTRACT... Objectives:** To evaluate electrolytes levels in patients suffering from iron deficiency anemia and to compare it with patients without anemia. **Study Design:** Descriptive Cross Sectional study. **Setting:** Department of Pathology, Sahiwal Medical College Sahiwal. **Period:** November, 2019 to May, 2020. **Material & Methods:** After taking informed consent, five milliliter of blood was drawn from each patient. Blood sample was analyzed for electrolytes, complete blood counts and serum ferritin levels. Results were compared in normal and iron deficiency anemic groups. **Results:** A total of 287 clinically anemic suspects including 181 (63.0%) female and 106 (37.0%) male with mean age of patients as  $36.11 \pm 12.23$  were included in this study. A total of 205 (71.4%) of the suspects had anemia whereas frequency of anemia remained higher among females (78.5%) as compared to males (59.5%) in this study. On the basis of serum ferritin levels a total of 178 (62.0%) patients had iron deficiency. Mean values of Sodium ( $130.41 \pm 0.59$ ) and Bicarbonate ( $24.10 \pm 0.31$ ) remained low while mean Potassium ( $4.33 \pm 0.07$ ) and Chloride ( $103.93 \pm 0.47$ ) levels of Iron Deficiency Anemia (IDA) group remained high as compared to non-anemic group. **Conclusion:** Levels of sodium and bicarbonate are found to be on the lower side while potassium and chloride remained on higher side in patients with Iron deficiency Anemia in this study. Thus these findings indicate close monitoring of electrolytes to evade impediments during management of patients.

**Key words:** Electrolytes, Ferritin, Iron Deficiency Anemia (IDA).

**Article Citation:** Rafiq M, Arooj A, Tahir Q, Fayyaz N, Samad A, Bashir S. Evaluation of serum electrolyte levels in iron deficiency anemia patients. Professional Med J 2021; 28(5):691-696. <https://doi.org/10.29309/TPMJ/2021.28.05.5702>

both genders, as the demand of iron increases two to three folds due to growth spurt, pubertal developments and physical activity.<sup>5</sup> Prolonged and negative dietary imbalances with respect to individual's physical demands of iron intake lead to iron deficiency.<sup>6</sup> Iron being a dynamic element for health plays vital role in optimal body functioning and any disturbances in its homeostasis may cause serious pathologies, one of which is serum electrolytes imbalance in patients of IDA.<sup>7</sup>

Electrolytes which include sodium, potassium, chloride and bicarbonate make 1% of plasma in circulation. They play important role in fluid and acid base balance, nerve conduction, muscle contraction and blood clotting. Electrolyte balance is essential for maintaining the shape of RBCs, exchange of oxygen/carbon dioxide between tissue and red cells.<sup>8</sup> Regulation of erythrocyte apoptosis is triggered by calcium

sensitive potassium channels.<sup>9</sup> Red cell cationic homeostasis is regulated mainly by sodium-potassium ATPase (Na-K ATPase) enzyme bound to the cell membrane involving sodium-potassium pump which obtains energy from ATP.<sup>10</sup> Exchange of two potassium with three sodium ions by Na-K ATPase plays a vital role to maintain circulatory system.<sup>11</sup>

Studies have indicated the enhanced activity of sodium-potassium ATPase due to IDA in the past<sup>12</sup> while recent studies revealed the alteration of membrane bound enzyme which directly affect the sodium and potassium in the serum.<sup>13</sup> Prior studies have reported that anemia patients show elevated sodium/potassium ATPase activities. This increase compensates the process by which patients adopt low levels of oxygen for physiological functioning of cells. Therefore sodium/potassium ATPase activity is altered and this alteration affects the electrolytes levels in the plasma.<sup>13</sup> Though the contradiction regarding electrolyte imbalance among IDA patients exists in different reports.<sup>7</sup>

Furthermore scarce data is published specifically in this regard. Electrolyte imbalance is root cause of many health issues including lethargy, fatigue, irregular heartbeat, muscle cramping, confusion, irritability and convulsions etc.<sup>14</sup> Thus it is necessary to take up the issue for better clinical understanding and timely management. Therefore aim of present study is to observe electrolytes imbalance among patients suffering from iron deficiency anemia.

## MATERIAL & METHODS

This descriptive cross sectional study was undertaken in Department of Pathology, Sahiwal Medical College, Sahiwal during October 2019 to April 2020. Patients suffering from anemia, aged eighteen and above of either gender were included in this study. Patients suffering from chronic diseases like diabetes mellitus, tuberculosis, viral hepatitis, cancers, pregnant women and patients already using micronutrient supplements were not included in this study. A sample size of 287 anemic patients was calculated by taking confidence level as 95%, level of precision as 5%

and prevalence of anemia in general population as 24.8%.<sup>15</sup>

After obtaining ethical clearance from institutional ethical review committee and taking the informed consent from each patient, demographic data including name, age, gender, area of residence and other related information was noted on a pre-designed questionnaire. Each patient was asked to provide five milliliter of blood. For this purpose aseptic procedure was used and sample was drawn in sterile disposable syringe and divided in two vacutainers. Half of the sample was put in pre-labeled ethylene-diamine-tetra-acetate (EDTA) anti-coagulated tube and other half was placed in gel tube.

Each anti-coagulated sample was tested for hemoglobin, RBC count, hematocrit (HCT), mean corpuscular volume & hemoglobin (MCV & MCH) and mean corpuscular hemoglobin concentration (MCHC) on an automated hematology analyzer Sysmex KX-21. Further smears were prepared, fixed and stained by hematoxylin/eosin stain to observe morphology of RBCs. Serum was drawn by centrifugation of clotted samples to analyze the quantification of serum ferritin levels using an automatic immunoassay analyzer Beckman Coulter Access 2. Patients having hemoglobin levels <12.5 g/dl were considered and confirmed as anemic while patients with normal hemoglobin served as control group. Norms of red cell indices were observed and MCV of <76 fL was considered as microcytic, MCH <27 pg & MCHC <32g/dl was reported as hypochromic. Serum ferritin level  $\leq 15$  ng/ml was considered iron deficient while reference ranges of electrolytes were 135-143 meq/L for sodium, 3.5-5 meq/L for potassium, 98-107 meq/L for chloride and 22-26 meq/L for bicarbonate.

Data was entered and analyzed in statistical package for social sciences (SPSS) version 20. Qualitative variables like gender and normality of variables was presented as frequency and percentages. Quantitative data like age and quantification of variables was presented as mean  $\pm$  standard deviation. Data was further characterized in various groups and comparison

was presented by using t-test where p value <0.05 was considered as significant.

## RESULTS

A total of 287 anemic suspects including 181 (63.0%) females and 106 (37.0%) males with a male to female ratio of 1:1.7 were recruited in this study. Mean age of patients was  $36.11 \pm 12.23$  years. Most of the patients (35.2%) lied in the age range of 36-45 years of age while minimum (10.1%) lied in age group of 18-25 years. Educational status of the patients was also recorded and most of the patients were found to be in  $\leq$ Primary (36.6%) level while few (12.2%) had completed their middle school and rest had higher education levels. Similarly most of the patients belonged to the rural ethnicity (65.8%) and lower-middle class (43.5%) remained pre-dominant socio-economic class in this study. Demographic characteristics of patients are presented in Table-I.

Characteristics		N	%
Gender	Male	106	37.0
	Female	181	63.0
Age Range (In Years)	18-25	29	10.1
	26-35	47	16.4
	36-45	101	35.2
	46-55	71	24.7
	>55	39	13.6
Education	$\leq$ Primary	105	36.6
	Middle	35	12.2
	High School	83	28.9
	Higher Above	64	22.3
Ethnicity	Rural	189	65.8
	Urban	98	34.2
Socio-economic Status	Lower	53	18.5
	Lower-middle	125	43.5
	Middle	64	22.3
	High	45	15.7

**Table-I. Demographic characteristics of patients (N = 287)**

Sign and symptoms of the patients were also noted and presented in Table-II. Pale presentation of skin was present in all patients further fatigue (88.2%) remained the most predominant symptom while syncope was present only among 2.1% patients. Similarly exercise intolerance, lethargy, muscle cramps, confusion, bounding pulses and other symptoms were also shown to be present.

Sign & Symptoms	N	%
Pale presentation	286	100
Exercise Intolerance	108	37.6
Fatigue	253	88.2
Dyspnea at rest	48	16.7
Bounding pulses	63	22.0
Lethargy	98	34.2
Confusion	93	32.4
Muscle Cramps	113	39.4
Dizziness	87	30.3
Syncope	6	2.1

**Table-II. Frequency of sign and symptoms among patients (N = 287)**

A total of 205 (71.4%) of suspects had anemia whereas frequency of anemia remained higher among 142 females (78.5%) as compared to 63 males (59.5%) in this study. On the basis of serum ferritin levels, a total of 178 (62.0%) patients had iron deficiency as all of these were from anemic group therefore proportion of iron deficiency anemia among this group was remained to be 86.8% (178/205). Normal distribution of anemia and iron deficiency among both genders on the basis of serum ferritin levels are shown in Table-III.

Comparison of mean electrolyte levels among non-anemic and IDA groups was done by applying t-test and p-value <0.05 denoted significant difference among both groups.

Parameter		Male (N = 106)		Female (N = 181)		Total (N = 287)	
		N	%	n	%	n	%
Anemia	Present	639	59.5	142	78.5	205	71.4
	Absent	43	40.5	39	21.5	82	28.6
Serum Ferritin Level	$\leq 15$ ng/ml	52	49.1	126	69.6	178	62.0
	>15 ng/ml	54	50.9	55	30.4	109	38.0

**Table-III. Normal distribution of anemia and iron deficiency.**

Mean values of Sodium ( $130.41 \pm 0.59$ ) and Bicarbonate ( $24.10 \pm 0.31$ ) remained low in IDA group as compared to non-anemic group where as significant difference was observed in case of sodium while no significant difference was present in case on bicarbonate among both groups. Mean Potassium ( $4.33 \pm 0.07$ ) and Chloride

( $103.93 \pm 0.47$ ) levels of IDA group remained high as compared to non-anemic group where difference was found to be significant among both groups. Mean electrolyte levels on the other hand remained within the defined normal ranges. All the values were calculated by taking a confidence interval of 95% as depicted in Table-IV.

Electrolytes	IDA (N = 178)	Non-anemic (N = 82)	95% C. I.*	t-test value	P-Value
	Mean $\pm$ Standard Deviation (meq/L)				
Sodium	$130.41 \pm 0.59$	$134.57 \pm 0.39$	4.016 - 4.303	57.019	<0.0001
Potassium	$4.33 \pm 0.07$	$4.04 \pm 0.05$	0.272 - 0.307	33.063	<0.0001
Chloride	$103.93 \pm 0.47$	$101.97 \pm 0.42$	1.838 - 2.081	31.694	<0.0001
Bicarbonate	$24.10 \pm 0.31$	$24.17 \pm 0.33$	0.015 - 0.155	1.630	0.1043

**Table-IV. Comparison of electrolytes among IDA and non-anemic groups.**  
\*Confidence Interval

## DISCUSSION

A total of 71.4% suspects had anemia while proportion of IDA was found to be 62.0% on the basis of serum ferritin level in this study. Similarly on the basis of gender 49.1% of the total male patients had IDA while a higher proportion of 69.6% of females were found to be suffering from IDA in this study. A recent study undertaken in Yemen on university students showed a prevalence of IDA as 30.4% of which 54.0% were females and 46.0% were males<sup>4</sup> thus not in agreement as the present study was undertaken on people suspected to have anemia while the former had focused on general students of specified younger age group. Prior studies on the other hand have reported a variable and higher prevalence of IDA as 73.5% and 81% among children and pregnant women respectively.<sup>2,16</sup>

A Bengali study had shown comparable results regarding prevalence of IDA as 55.3% in general and higher proportion of 63.3% among females and 36.7% among males showing significant difference.<sup>17</sup> Although various studies are showing variable proportions of IDA but all the studies are presenting higher proportions of IDA among females. Factors related to this difference though are not studied currently but others have revealed the possible factors including inadequate dietary intake of iron, poor nutritional status, compromised bioavailability, socioeconomic status, and customs of gender biases.<sup>18,19</sup> Currently, lower

education level, middle age group, rural ethnicity and lower-middle education of patients remained the pre-dominant risk factors of IDA in this study.

Red cell cationic homeostasis is regulated mainly by sodium-potassium ATPase enzyme bound to the cell membrane.<sup>10</sup> Studies have indicated the enhanced activity of sodium-potassium ATPase due to IDA in the past<sup>12</sup> while recent studies revealed the alteration of membrane bound enzyme which directly affect the sodium and potassium in the serum.<sup>13</sup> Same is the case in present study which showed decrease in serum sodium level among IDA patients while increase in potassium among same group and vice versa for non-anemic group. Although mean values of both groups for serum sodium and potassium remained within the normal range but a significant difference (p-value <0.05) could be observed among both groups.

Electrolyte imbalance and IDA have high prevalence in developing countries especially in Subcontinent. Various reports have shown the association of altered serum electrolytes with iron deficiency anemia which made the issue debatable and of clinical importance.<sup>13</sup> Since, a minor alterations in electrolytes among IDA patients is observed yet the inconsistency among results of various studies are also of great concern.<sup>20,21</sup> Normally RBCs have been reported to maintain high levels of intracellular potassium and low levels

of sodium in plasma whilst the case is vice versa in present study and in agreement with another study<sup>7</sup> thus, the sodium-potassium ATPase may facilitate both ions to move to and from across the membrane. These findings of change in activities of erythrocyte membrane have strengthened the belief in modulation of sodium-potassium ATPase causing hematological disorders due to IDA.<sup>13</sup> This hike in ATPase activity has been supposed to compensate the process adapting low levels of oxygen and their functions in the red cell.

Various mechanisms have been reported to be involved in electrolyte imbalance in anemia other than IDA. In sickle cell anemia for example potassium chloride activated abnormally to cause dehydration due to loss of free potassium.<sup>22</sup> Similarly, de-oxygenation in sickle cell anemia has been known to elevate permeability of sodium, potassium and calcium through membrane whereas reduction in sodium-potassium pump has been reported to be reduced in thalassemia like cells among patients suffering from disease.<sup>23-24</sup>

## CONCLUSION

In conclusion serum electrolyte levels have shown variations among IDA as compared to normal control group. Serum sodium & bicarbonate are found to be on lower side of normal range while potassium & chloride were on higher side in this study. Thus the findings indicate close monitoring of electrolytes in IDA patients to evade impediments during management. Mechanism of electrolyte imbalance though could not be studied presently and recognized as limitation while improvements in electrolyte changes may be studied after iron replacement therapy of patients is suggestive to be a future goal of this study.



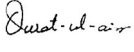

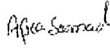
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### AUTHORSHIP AND CONTRIBUTION DECLARATION

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3	Qurrat-ul-Ain Tahir	Data collection and manuscript writing.	
4	Nudrat Fayyaz	Data collection and manuscript writing.	
5	Afra Samad	Review and final approval of manuscript.	
6	Sibgha Bashir	Review and final approval of manuscript.	