

# Soluble Transferrin Receptor-Ferritin Indices as Diagnostic Tool for Iron Deficiency Anemia in Chronic Kidney Disease in Children

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## **Abstract**

**Background:**Chronic kidney disease is an important chronic, non-communicable epidemic disease. Up to 80% of patients with Chronic kidney disease may have anaemia. Soluble serum transferrin receptor (sTfR) was introduced as a promising new diagnostic tool of iron status. The main objective of this study was to assess the utility of soluble transferrin receptor-Ferritin Indices as markers of iron deficiency anemia in chronic kidney disease patient.**Methods:** This was a cross-sectional study was conducted at Department of Pediatric Nephrology at Zagazig University Hospital including 45 anemic children. The duration of the study ranges from 6 to 12 months.Soluble serum transferrin receptor andSoluble serum transferrin receptor index were measured.**Results:**There was no significant difference among groups regard age or BMI distribution. There was no significant difference regard sex distribution among studied groups.regard s TIR and s TIR index IDA group were significantly higher than other two groups then mixed and finally ACD were significantly lower.**Conclusion:** Soluble transferrin receptor value was useful tool for assessment of iron status in patients with CKD.

**Key words:** Soluble transferrin receptor- assessment- anemia-CKD.

## **I. Introduction:**

Anemia is a common complication of chronic kidney disease. It has multiple causes, but the main pathological process is hypoproliferative erythropoiesis resulting from insufficient erythropoietin (EPO) production by the kidneys, whereas iron deficiency is the most common cause of resistance to recombinant human erythropoietin (rHuEPO) therapy <sup>(1)</sup>.

Normal iron homeostasis is maintained by compensating daily loss through duodenal absorption of dietary iron. Due to increased blood losses, especially in hemodialysis patient , as well as decreased

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gastrointestinal iron absorption, the total body iron stores in CKD patients are likely to be depleted resulting in absolute iron deficiency. In addition, many CKD patients suffer from functional iron deficiency, defined as the inability to deliver sufficient iron amount to the site of erythroblast production, even in presence of adequate stores, due to reticuloendothelial cell iron blockade. <sup>(2)</sup>.

Because of the insufficient sensitivity and specificity of conventional hematologic and biochemical parameters in assessing the iron status of anemic patients with CKD, many attempts have been made to evaluate new diagnostic parameters of the iron status of anemic patients with CKD <sup>(3)</sup>.

The best diagnostic tool to identify IDA in CKD is still iron stained bone marrow aspiration (BMA) but because BMA is invasive, could not be used as a standard of care in daily practice. Therefore, more convenient non-invasive and reliable enough method to detect iron status is needed. <sup>(4)</sup>.

Soluble serum transferrin receptor (sTfR) was introduced as a promising new diagnostic tool of iron status. Human transferrin receptor (TfR) is a transmembranedimeric glycoprotein expressed on the surfaces of nearly all types of cells, in particular, rapidly proliferating cells and cells with special iron requirements, such as erythropoietic cells of bone marrow. Thus, the number of TfRs on a cell is tightly regulated by both the cell's iron status and proliferative status. The physiological function of TfR is uptake of erythroid iron by receptor-mediated endocytosis <sup>(5)</sup>.

The main objective of this study was to assess the utility of soluble transferrin Receptor-Ferritin Indices as markers of IDA in chronic kidney disease patient.

## **II. Patients and Methods**

### **Technical Design:**

Cross section study was conducted in Pediatric Nephrology Unit at Zagazig University Hospital and Clinical Pathology Department from October 2019 to October 2020.

Our study included 45 anemic children (both male and female) Chronic kidney disease was diagnosed 3 months ago at least by laboratory investigation

### **Methodology**

#### **All patients subjected to the following**

1. Full history taking
2. Complete clinical examination :-
3. Laboratory Investigations :
  - Iron indices (ferritin, total iron binding capacity (TIBC), transferrin saturation (TAST)
4. Specific investigation
  - **Soluble serum transferrin receptor**

### STATISTICAL ANALYSIS

A collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean  $\pm$  SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test ( $X^2$ ). Differences between quantitative independent groups by t test, correlation by Pearson's correlation or Spearman's. A receiver operating characteristic (ROC).P value was set at  $<0.05$  for significant results &  $<0.001$  for high significant results. Data were collected and submitted to statistical all the following statistical tests and parameters were used.

### III. Results:

- There was no significant difference among groups regard age or BMI distribution (**Table 1**).
- There was no significant difference regard sex distribution among studied groups (**Table 2**).
- Regard s TfR and s TfR index IDA group were sig higher than other two groups then mixed and finally ACD werev sig lower(**Table 3**).

**Table1: Age,weight and duration distribution among studied groups**

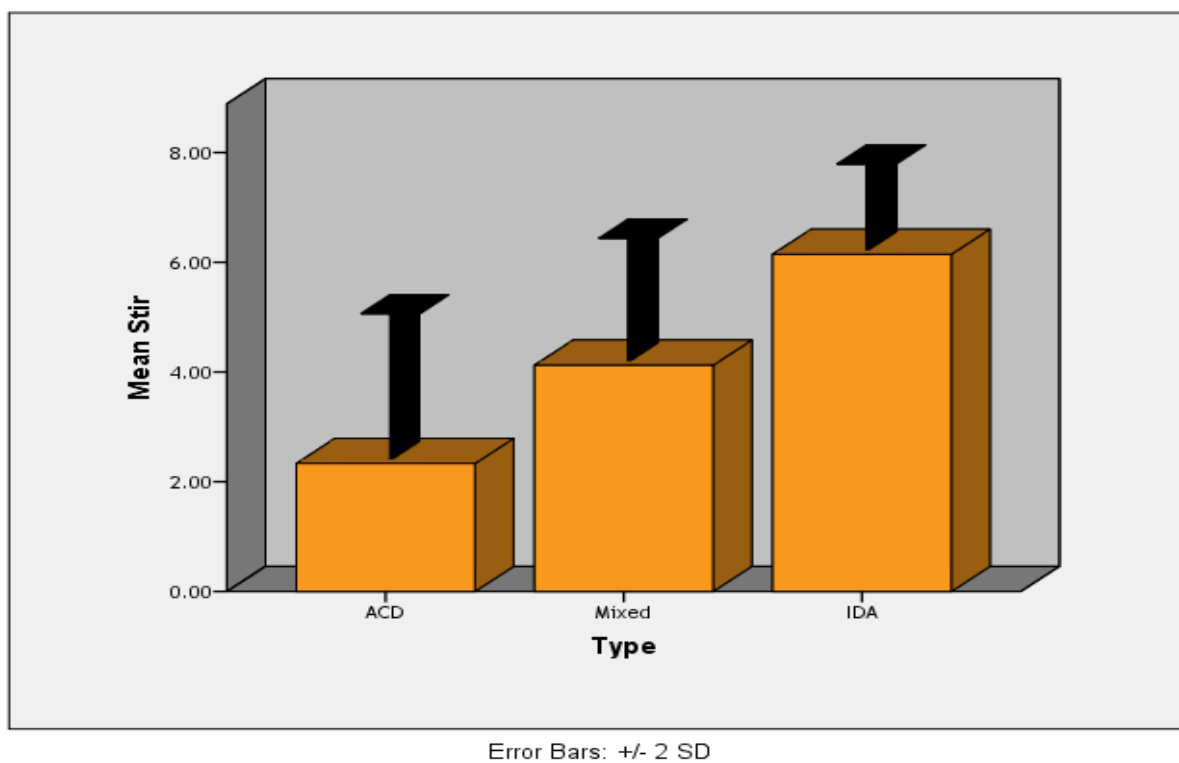
	ACD	Mixed	IDA	KruskalWalis	P
<b>Age</b> <b>(years)</b>	8.24 $\pm$ 2.68	8.3 $\pm$ 2.9	6.38 $\pm$ 2.12	1.592	0.215
	1.2-12.0	1.5-11.2	1.0-12		
<b>Weight</b> <b>(kg)</b>	25.39 $\pm$ 8.59	28.76 $\pm$ 9.85	20.01 $\pm$ 7.58	1.520	0.230
	13.5-48.0	14.0-46.0	13.7-44.0		
<b>Duration</b> <b>(years)</b>	5.11 $\pm$ 3.35	4.90 $\pm$ 3.11	7.38 $\pm$ 3.52	2.328	.110
	1.0-12.0	1.0-11.0	2.0-15.0		

**Table 2: Sex distribution among studied group**

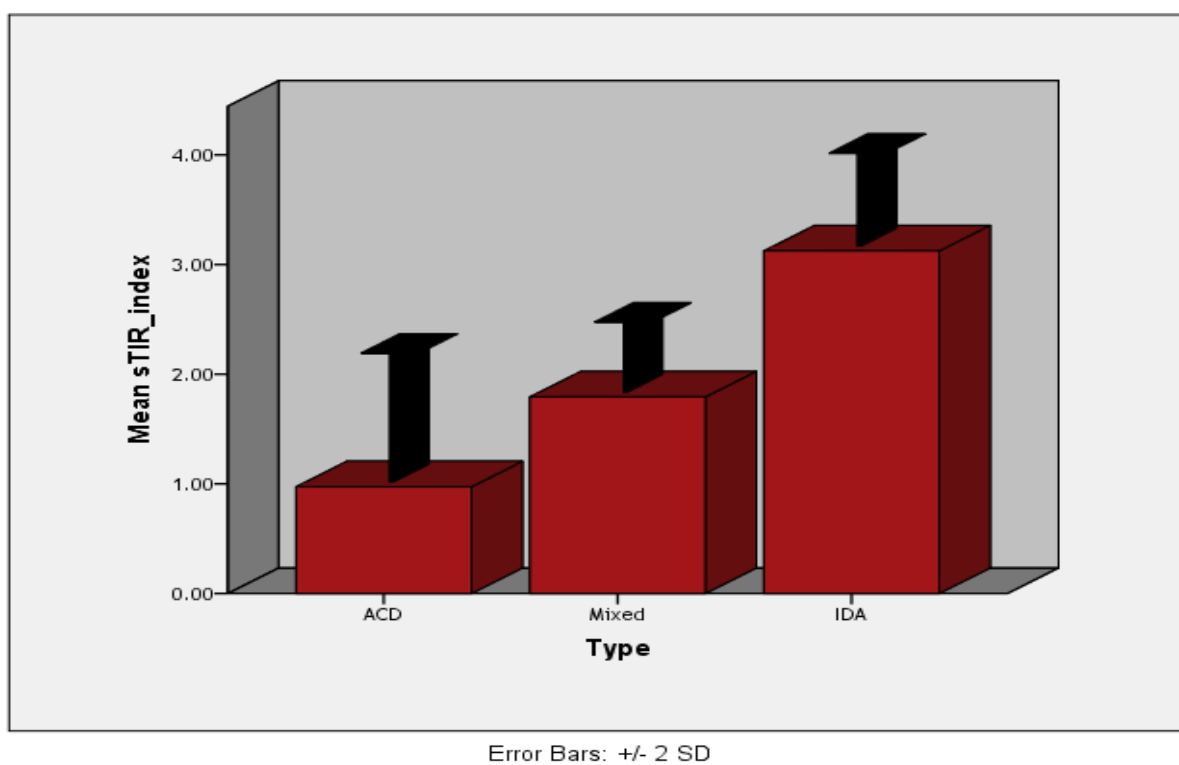
			Type			Total	X <sup>2</sup>	P
			ACD	Mixed	IDA			
Sex	Male	N	6	7	9	22		
		%	31.6%	53.8%	69.2%	48.9%	4.55	0.102
	Female	N	13	6	4	23		
		%	68.4%	46.2%	30.8%	51.1%		
Total		N	19	13	13	45		
		%	100.0%	100.0%	100.0%	100.0%		

**Table 3: sTfR and Index distribution among studied groups**

	ACD	Mixed	IDA	KruskalWallis	P
sTfR (µg/ml)	2.33±1.08	4.12±1.12	6.14±0.79	42.953	0.00**
	0.4-6.5	3.1-7.4	4.9-7.2		
sTfR index	0.97±0.41	1.89±0.34	3.12±0.43	75.914	0.00**
	0.24-2.62	1.47-2.69	2.56-3.75		



**Figure (1):** Mean distribution of s TfR among studied groups.



**Figure (2):** Mean distribution of sTfR index among studied groups.

#### IV. Discussion

The current study showed no significant difference among groups regard age, sex, duration of illness or BMI distribution.

The result of this study were in agreement with study of **Alzahrani et al.**,<sup>(6)</sup> as they reported that there was no significant difference among groups regard age, sex and duration of illness.

In recent years, soluble transferrin receptor (sTfR) has been introduced as a sensitive, early and valuable marker of iron depletion. sTfR is a truncated form of the transferrin receptor present on erythroblasts in bone marrow and many other cells. sTfR concentration is not affected by inflammation or infection rather in conditions where iron deficiency co-exists with ACD, sTfR raises secondary to underlying iron deficiency. Moreover, sTfR levels also reflect the rate of erythropoiesis. So, its specificity decreases as a sole marker of iron deficiency. Synthesis of transferrin receptor and the iron storage protein ferritin are reciprocally linked to cellular iron content. Thus, because of this reciprocal relationship between sTfR and serum ferritin, the sTfR /ferritin ratio reflects the iron status over the entire range<sup>(7)</sup>.

In this study , regard s TIR and s TIR index IDA group were significantly higher than other two groups then mixed and finally ACD were significantly lower.

Our results were supported by study of **Latif et al.**,<sup>(8)</sup> as they revealed that Mean sTfR level was higher ( $4.81 \pm 1.64$  µg/ml) in patients with IDA than ( $2.89 \pm 1.40$  µg/ml) in patients with ACD ( $p < 0.0001$ ). Mean ferritin level was  $599.59 \pm 449.15$  µg/L in ACD patients whereas  $101.23 \pm 119.42$  in IDA patients ( $p < 0.0001$ ). Total iron binding capacity (TIBC) was more in ACD patients with sTfR $\geq 3$  µg/ml as compared to ACD patients with sTfR $< 3$  µg/ml. Transferrin saturation (TSAT) level was significantly decreased in ACD patients with sTfR $\geq 3$  µg/ml as compared to ACD patients with sTfR $< 3$  µg/ml. sTfR and ferritin indices between group A (IDA) and group B (ACD) shows mean sTfR:logSF level was significantly ( $P < 0.001$ ) high in group A ( $2.71 \pm 1.13$ ) in comparison to group B ( $1.08 \pm 0.54$ ). Mean log sTfR:SF was also significantly higher ( $P < 0.05$ ) in group A ( $0.001 \pm 0.0008$ ) compared to group B ( $0.013 \pm 0.012$ ).

In another study by **Gupta et al.**,<sup>(9)</sup> found that the mean value of serum iron in CKD patients was higher than IDA patients, whereas TIBC was lower in CKD patients with higher TSAT values. They showed that a ratio of sTfR/Log ferritin  $> 1.4$  indicates co-existence of iron deficiency anemia with anemia of chronic disease, while ratio of up to 1.3 indicates anemia of chronic disease only.

Regarding **Jain et al.**,<sup>(10)</sup> ferritin level was significantly higher in ACD patients than IDA patients. In this study mean ferritin level was  $599.59 \pm 449.15$  µg/L in ACD patients whereas  $101.23 \pm 119.42$  µg/L in IDA patients and also ferritin is lower in control group ( $83.73 \pm 45.09$  µg/L) than IDA group. It has been shown that, ferritin values increased in IDA with CKD patients; may be due to chronic inflammatory process.

TfR-F index has been found to have close, linear relationships with stored iron expressed as per kg body weight. This finding resulted from the experimental study that performs repeated phlebotomy of 14 healthy subjects where sTfR and ferritin were measured consecutively in serial<sup>(11)</sup>.

Soluble transferrin receptor (sTfR) and the ratio of sTfR/log ferritin (TfR-F index) as a new promising indicator that can differentiate IDA with others especially anemia of chronic disease (ACD). These two markers not entirely influenced by concurrent chronic disease as well as inflammation <sup>(12)</sup>.

## V. Conclusion:

Soluble transferrin receptor value was useful tool for assessment of iron status in patients with CKD

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