DETECTION OF TRANSFERRIN RECEPTOR 1 SINGLE NUCLEOTIDE VARIANT RS- 3817672 IN PEDIATRIC IRON DEFICIENCY ANAEMIA

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INTRODUCTION

Iron deficiency anemia (IDA) is the most common cause of anemia worldwide. It is one of the main causes of increased maternal and childhood morbidity and mortality.(1) According to WHO, around 50 % of anemia cases diagnosed with IDA.(2) Several iron regulatory genes encode proteins that control iron hemostasis; *HFE* gene, *TFR2* gene, *TFR1*gene and *HJV* gene. Variations in these genes are reported to be associated with iron homeostasis imbalance causing either IDA or overload. Genetic variations that interfere with the TFR1-HFE interaction will probably lead to high hepcidin and IDA.(3) *TFR1* gene, encodes for transferrin receptor 1 protein, genetic polymorphism rs3817672 was selected to study its association with IDA.

AIM OF THE WORK

The aim of the study was to detect the presence of *TFR1* gene variant rs3817672 (p.S142G) in children diagnosed with iron deficiency anemia and assess the relation of this variant with their iron profiles.

SUBJECTS AND METHODS

Subject: The current case control study is conducted on 50 children diagnosed with IDA and 50 age and sex matched healthy controls. Children diagnosed with thalassemia, anemia of chronic illness, acute infection and gastrointestinal problems causing chronic blood loss were excluded.

Methods: -DNA was extracted from EDTA blood using QIA amp DNA Mini Blood (QIAGEN). TFR1 rs3817672 SNP genotyping was performed by real time PCR.. The detected fluorescence signal was interpreted as shown in figures below.

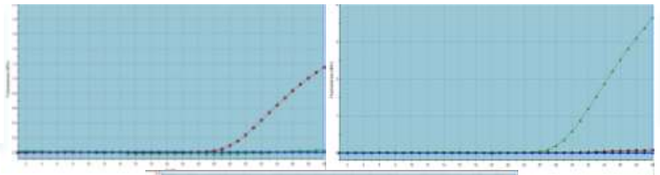

Figure 1: Amplification plot for homozygous (CC) genotype.

Figure 2: Amplification plot of homozygous (TT) genotype.

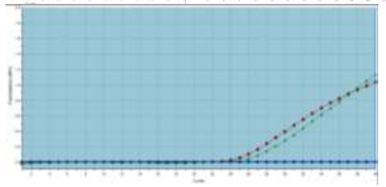

Figure 3: Amplification plot of heterozygous (CT) genotype.

RESULTS

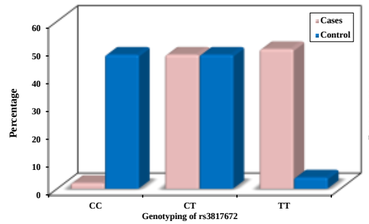

Figure 4: Comparison between the two studied groups according to *TFR1* rs3817672 SNP genotypes.

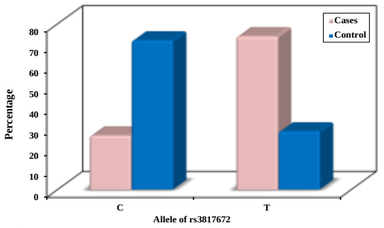

Figure 5: Comparison between the two studied groups according to *TFR1* rs3817672allele frequency

Table 1: Relation between *TFR1* rs3817672 SNP genotypes and CBC parameters in total sample (cases and controls)

CBC	Total sample (n=100)			F	P
	TFR1 rs3817672 SNP Genotypes				
	CC (n = 25)	CT (n = 48)	TT (n = 27)		
Hb (g/dl)					
Min. – Max.	9.30 – 14.70	7.80 – 14.70	8.30 – 12.0	22.468*	<0.001*
Mean ± SD.	12.63 ± 0.98	11.33 ± 1.72	10.08 ± 0.89		
RBCs(million/ul)					
Min. – Max.	3.40 – 5.50	3.40 – 5.30	3.17 – 5.20	0.415	0.662
Mean ± SD.	4.46 ± 0.43	4.49 ± 0.40	4.40 ± 0.40		
MCV(fl)					
Min. – Max.	65.0 – 91.70	56.70 – 84.70	56.60 – 83.60	25.262*	<0.001*
Mean ± SD.	81.86 ± 5.85	72.90 ± 9.07	66.94 ± 6.0		
MCH(pg)					
Min. – Max.	20.80– 31.60	18.0 – 30.50	19.30 – 29.0	18.929*	<0.001*
Mean ± SD.	27.88 ± 2.41	24.67 ± 3.54	22.83 ± 2.37		
MCHC(g/dl)					
Min. – Max.	31.70 –36.60	29.90 –39.90	30.70 –34.70	6.742*	0.002*
Mean ± SD.	34.08 ±1.19	33.14 ±1.79	32.60 ±1.04		
RDW (%)					
Min. – Max.	12.10 –17.40	11.90 –26.20	13.70 –22.10	14.939*	<0.001*
Mean ± SD.	13.95 ±1.37	16.10 ±3.31	18.07 ±2.42		
Reticcount(%)					
Min. – Max.	0.80 – 2.30	0.50 – 2.40	0.50 – 1.60	22.745*	<0.001*
Mean ± SD.	1.73 ± 0.35	1.43 ± 0.54	0.93 ± 0.27		
PLTs (×10³/µl)					
Min. – Max.	185.0 – 402.0	175.0 – 591.0	232.0 – 545.0	6.247*	0.003*
Mean ± SD.	290.92 ± 62.31	351.77 ± 100.41	373.70 ± 84.46		

Table 2: Relation between *TFR1* rs3817672 SNP genotypes and iron profile in total sample (cases and controls)

Iron profile	Total sample (n=100)			Test of Sig.	p
	TFR1 rs3817672 SNP Genotypes				
	CC (n = 25)	CT (n = 48)	TT (n = 27)		
Serum iron (µg/dl)					
Min. – Max.	19.30 – 130.0	14.90 – 139.20	15.30 – 70.50	H= 44.576*	<0.001*
Mean ± SD.	86.94 ± 22.26	59.29 ± 32.46	26.77 ± 13.51		
Median	87.80	56.45	22.0		
TIBC (µg/dl)					
Min. – Max.	243.0 – 452.0	245.0 – 476.0	296.0 – 473.0	F= 32.910*	<0.001*
Mean ± SD.	306.72 ± 51.52	371.40 ± 62.16	426.89 ± 34.60		
Median	293.0	387.50	430.0		
Transferrin Saturation					
Min. – Max.	4.30 – 52.80	3.10 – 42.20	3.30 – 23.80	H= 43.786*	<0.001*
Mean ± SD.	29.72 ± 10.37	17.64 ± 11.57	6.56 ± 4.36		
Median	26.10	14.95	5.30		

CONCLUSION

- *TFR1*rs3817672 T (alternative) allele is the predominant allele in IDA cases.
- Subjects with TT genotype showed statistically significant low hemoglobin level, MCV, MCH, MCHC, reticulocyte count, serum iron and transferrin saturation compared to CT and CC genotypes.
- *TFR1* rs3817672 might have a role in the pathophysiology of IDA.

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