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Evaluation of brain iron content in Egyptian Patients with Sickle cell disease and its impact on Neurocognitive functions

A Thesis

Submitted For partial fulfillment of Master degree in pediatrics

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ABSTRACT

Background: Sickle cell disease (SCD) is considered the most prevalent monogenic diseases worldwide. Iron overload is one of its major complications especially those who required frequent transfusion. MRI is a reliable and non-invasive method for quantifying iron concentration in many organs as the liver and heart. Children with SCD are at a high risk for neurocognitive impairment; they often scored lower on general IQ measures than healthy children which may be due to iron overload in brain tissue.

Primary objective: To assessed brain iron content (using R2* values) in the caudate and thalamic regions through quantitative brain MRI study in SCD patients in comparison to age and sex-matched healthy controls. **Secondary objective:** To evaluate the impact of brain iron content on neurocognitive functions assessed by neurocognitive examinations.

Methods: 32 children and young adults (19 males, 13 females) with SCD and 11 control persons (5 males, 6 females) were recruited. Brain MRI study using multi-echo fast gradient echo sequence was performed for only 15 SCD patients and 11 controls. Brain R2* values of both caudate and thalamic regions (right and left sides) were calculated. All SCD patients were examined for the neurocognitive functions; Wechsler IV Intelligence Scale (verbal, perceptual, memory, processing and total IQ) and Benton Visual Retention Test.

Results: No statistically significant differences were found between SCD and control group in all regions of interests in brain MRI. No statistically significant differences were found between the two subgroups ($p>0.05$) in right thalamus, left and right caudate regions. 62.5% SCD patients had anxiety; 4.2%, 8.3% and 50% had severe, moderate and mild anxiety respectively.

Conclusion: Although children and young adults with SCD had high prevalence of neurocognitive dysfunction, this could not be explained by brain iron overload alone which might be slowly accumulating iron.

Keywords: Brain iron overload, Sickle cell disease, T2* values.

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List of Abbreviations

Abb.	Full term
ACS	Acute chest syndrome
ALT	Alanine amino trasnferese
AST	Aspartate amino transferese
BBB	Blood brain barrier
BCECs	Brain capillary endothelial cells
BPRS	Brief Psychiatric Rating Scale
CBC	Complete blood count
CNS	Central nervous system
CSSCD	Cooperative Study of Sickle Cell Disease
CVAs	Cerebrovascular accidents
DFO	Deferoxamine
DFP	Deferiprone
DFX	Deferasirox
DNA	Deoxyribonucleic acid
GI	Gastrointestinal
GSH	Glutathione
Hb	Hemoglobin
HbA	Hemoglobin A
HbA2	Hemoglobin A2
HbF	Hemoglobin F
HbS	Hemoglobin S
HCV	Hepatitis C virus
HPLC	High-Performance Liquid Chromatography
IQ	Intelligence Quotient
Kg	Kilogram
LDH	Lactate dehaydrogenese
LIC	Liver Iron Concentration

List of Abbreviations (Cont...)

Abb.	Full term
MRA	Magnetic resonance angiogram
MRI	Magnetic Resonant Imaging
MTD	Maximum tolerated dose
NADPH	Nicotinamide adenine dinucleotide phosphate
NTBI	Non transferrin bound iron
RBCs	Red Blood Cells
ROC	Receiver Operating Characteristic
ROI	Region of Interest
ROS	Reactive oxygen species
SCA	Sickle cell anemia
SCD	Sickle cell disease
SCI	Silent cerebral infarction
SDS	Standard deviation score
SWI	Weighted Images Sequence
TF	Transferrin
TfR1	Transferrin receptors
TIQ	Total Intelligence Quotient
TLC	Total Leucocytic Count
UT	Under threshold (UT)
VOC's	Vaso-occlusive crises
WAIS-IV	Wechsler Adult Intelligence Scale-Fourth Edition
WBC	White blood cell
α	Alpha
β	Beta
γ	Gamma