SPECTRUM OF HEMATO-BIOCHEMICAL PARAMETERS OF THE ODISHA SICKLE CELL DISEASE PATIENTS

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Abstract

Objective: Regular monitoring of the haematological and biochemical parameters, gives prognostic and diagnostic information regarding the health status of the patients. The prevailing observation evaluated the impact of hematobiochemical parameters at the pathophysiology of the Sickle Cell Disorder (SCD) cases.

Materials and Methods: Eventually, the hemato-biochemical parameters of 167 homozygous SCD cases are studied in Odisha.Data including clinical and laboratory characteristics and treatment strategies of SCD patients were collected retrospectively from SCD centers in Odisha.

Results: Spectrum of hemato-biochemical parameters of SCD is validated by the application of One Way ANOVA, Pearson Correlation and Mann Whitney U Test. One Way ANOVA emphasised that the hemato-biochemical parameters are significant factors and aids in determining the severity of SCD. The Pearson Correlation of paediatrics sub-samples show that SGOT-SGPT, Hb-HbF, Retics (%) – BID exhibit a relationship. The Pearson Correlation of adult sub-samples show that SGOT-SGPT, LDH-SGOT and BID-SGPT, exhibit a relationship. The bayes factor analysis for the paediatrics patients shows the potential relationship between SGOT-Hb, SGOT-HbF, SGOT- RETICS (%),SGPT- RETICS (%), SGPT-LDH, SGPT-Hb, SGPT-HbF, LDH-HbF, LDH-BIT, LDH-SGPT, BIT-Hb, BIT- RETICS(%), BIT-HbF, BID-Hb, BID-HbF, RETICS (%) - SGOT,RETICS (%) – SGPT, RETICS (%) – LDH, RETICS (%) – BIT, and RETICS (%) – HbF. While for the adult patents shows the potential relationship between SGOT-Hb, SGOT-HbF, SGOT-RETICS (%),SGPT- RETICS (%), SGPT-LDH, SGPT-Hb, SGPT-HbF, LDH-HbF, LDH-BIT, LDH-SGPT, BIT-Hb, BIT- RETICS(%), BIT-HbF, BID-Hb, BID-HbF, RETICS (%) - SGOT,RETICS (%) – SGPT, RETICS (%) – LDH, RETICS (%) – BIT, and RETICS (%) – HbF. Mann Whitney U Test summarises that the distribution of SGOT, SGPT, Hb, HbF, and RETICS(%) is same for both adult and paediatrics.

Conclusion: SCD patients in Odisha are found to have lower haemoglobin with abnormally higher retics, HBF and LDH. Despite having high HbF, the proposed study show that patients from Odisha experience severe Vaso-Occlusive Crisis (VOC) symptoms.

Keywords – Hemoglobin, Sickle RBC, Hematological, Biochemical, Vaso- Occlusive

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Introduction

Haemoglobin (Hb) serves an imp role in carrying oxygen in the blood. Sickle Cell Disease (SCD) or Sickle Cell Anemia is a congenital haemoglobin disorder caused due to mutation in gene. This mutation is caused by the translocation of the amino acid in position 6 of a normal beta globin chain inside the 11th chromosome of the q arm of the β-chain of beta globin gene (adenine to thymine (GAG to GTG)).This as a result, changes the characteristics of the hemoglobin tetramer, with an inclination to polymerization and vaso-occlusive crisis. This vaso occlusive crisis causes panic pain attacks in sickle patients. This pain attack continues for two to three days. That'swhy, regular monitoring of the hemato-biochemical parameters gives prognostic and diagnostic information regarding the health status of sickle cell disorder patients. Here, the haematological parameters are Haemoglobin (Hb), Haemoglobin Factor (HbF) and Retics. The biochemical parameters are Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), Lactate Dehydrogenase (LDH), Bilirubin Total (BIT), and Bilirubin Direct (BID).

The monitoring of the hemato-biochemical parametershelps to predict the severity of the disease that helps to manage them easily. The anemia levels are determined by the concentration of Hb in blood. The anemia level predicts the severity of the SCD. Lower level of Hb indicates severe anemia while moderate and a higher value indicates moderate and milder anaemia. Retics are the immature RBCs. The retics count correlates with future sickle cell disease severity. It serves as a useful marker for predicting the degree of erythropoiesis and bone marrow health in response to iron - deficiency anemia. HbF is the main oxygen career in foetus. But HbF inhibits Sickle Haemoglobin (HbS) polymerization that plays a vital role in vaso-occlusive crisis. SGOT and SGPT are transaminases. These are liver enzymes. Due to vaso- occlusion in liver, these enzymes were significantly increased in sickle patients. Severity of the disease can be managed by the early prediction of the parameters. LDH is an enzyme in the glycolytic pathway that catalyses the conversion of pyruvate to lactate while also converting NADH to NAD+. It is an enzyme that's present in all tissues. LDH is usually elevated in sickle patients due to hyperhemolysis. LDH has been used as a marker of haemolysis. Billirubin is the metabolic by product of Hb. Bilirubin levels are high due to hyperhemolysis. Since, blood biochemistry has a critical role for early diagnosis of pathophysiology in the human body regular monitoring of the haematological and biochemical parameters, gives prognostic and diagnostic information regarding the health status of the patients in order to handle the disease crisis more effectively and correlate the severity of the disease. The objective of the present study is to determine the activity of biochemical parameters in reference to the hematological parameters in males and females and different age groups of all sickle cell disease patients found throughout Odisha. Sickle cell disorder is prevalent in Central India and western Odisha. Indian SCA patients have reportedly higher HbF concentration with higher retics and lower LDH. Many researchers had worked on Odisha sickle patients and have drawn inferences like Low Hb, High HbF ,High Retics , High SGPT and High SGOT , High LDH , High Billirubin . Above findings are true but nobody has yet studied on the pathophysiology of the Odisha sickle patients. So, I approached on the darker area of this research. The main objective of this article is to evaluate the distribution and impact of different hemato- biochemical parameters among adults and paediatrics sickle patients in order to study the pathophysiology of sickle patients. The pathophysiology of the sickle patients is very complicated. Patients differ from individual to individual. Even if two sickle patients present in a common environmental conditions, behaves differently, that is called the pathophysiology of the sickle patients.

Methodology

167 sickle blood samples were collected from different district hospitals all over Odisha, after getting the approval of ethical committee. Samples were collected by using EDTA (Ethylene diamine Tetraacetic acid) as anticoagulant. Samples were collected from both male and female subjects for study .This study was carried out from April 2017 to Mar 2020. 167 sickle blood samples were collected from different district hospitals all over Odisha, through interaction with the patients and after getting the approval of the ethical committee. Samples were collected by using EDTA (Ethylenediamine Tetraacetic acid) as anticoagulant. Samples were collected from both male and female subjects for study. Screening was done for all the patients and they were detected as sickle cell homozygous patients. Out of 167 patients, 103 were male and 64 Female patients. 95 Adults (60 male & 35 Female) and & 72 pediatrics (43 male & 29 Female) patients. Patients were grouped as 01-10 years (61 patients) 11 - 20 years

(58 patients) 21 - 30 years (32 patients) 31 - 40 years (7patients) & 40 years (9 patients). All the patients were suffering from common symptoms like joint pains, fever, swelling of hand and pain, delayed growth, delayed puberty, Frequent infections, pain crisis, liver enlargement and Splenomegaly. Further research work was carried out at P. G. Dept of Biosciences and Biotechnology, Fakir Mohan University, Balasore. Confirmative sickling tests were done by following the method of Daland and castle (1948). One drop of whole blood was mixed with one drop of freshly prepared 2 % metabisulphite solution on a microslide. After mixing, a cover slip was placed properly and then sealed with molten wax to make it air tight. The slides were observed under the microscope using high power lens after one hr and after 24 hrs of sealing. Hematological parameters were calculated by using Automated Hematology Analyzer by Sysmex.

The Automated Hematology Analyzer from Sysmex was used to calculate the haematology parameters. Hematology analyzers are frequently used to count blood cells for disease detection and monitoring in patient and research settings. Basic analyzers provide a three-part differential white blood cell (WBC) count along with a complete blood count (CBC). Hematologyanalyzers primarily employ three physical technologies: electrical impedance, flow cytometry, and fluorescent flow cytometry.

To increase the measurable parameters, these are combined with chemical reagents that lyse or modify blood cells. For instance, electrical impedance can separate red blood cells (RBCs), white blood cells (WBCs), and platelets according to volume. It is feasible to distinguish lymphocytes by nucleating an agent that shrinks lymphocytes more than other WBCs.

Electrical impedance, also known as Coulter's principle, is the traditional method for counting cells. In nearly all hematology analyzers, complete blood flows between the two electrodes via an opening so small that he can only bypass one cell at a time. Impedance changes as cells bypass through. The change in impedance is proportional to cell size, resulting in cell variety and quantity measurements. Impedance analysis yields CBC and WBC tripartite variations (granulocytes, lymphocytes, and monocytes), but distinguishes similarly sized granular leukocytes (eosinophils, basophils, and neutrophils). According to 2nd, a matter charge of up to 10,000 cells can be achieved, and a standard impedance analysis can be completed in much less than one minute**.**

Spectrophotometric analysis was done on the biochemical samples.

In contrast to a reference or blank sample, the number of discrete wavelengths of UV or visible light absorbed or transmitted by a sample can be determined using the analytical method of UV-Vis spectroscopy. The sample composition has an impact on this feature, potentially revealing what is in the sample and at what concentration. The energy of light has a fixed value which is inversely correlated with its wavelength. As a result, shorter light wavelengths carry more energy than longer wavelengths. Absorption is a physical phenomenon that occurs when a substance's electrons are promoted to a state with a higher energy level. In a substance, electrons in various bonding conditions require different amounts of energy to move them to higher energy states. This explains why different substances absorb light at different wavelengths. The light then travels through a sample in the spectrophotometer, using whichever wavelength selector is employed. It is crucial to measure a reference sample, sometimes known as the "blank sample," for all analyses. This reference sample might be a cuvette filled with the same solvent that was used to create the sample. Due to quartz's transparency to the majority of UV rays, quartz sample holders are necessary. Because molecular oxygen in the air absorbs light with wavelengths less than 200 nm, one may also consider air to be a filter. For observations with wavelengths less than 200 nm, a unique and more expensive setup is needed, typically containing a pure argon gas-filled optical system. From approximately 380 nanometers, which we perceive as violet, to 780 nanometers, which we perceive as red, humans are able to see a range of visible light. The wavelengths of UV light are about 100 nm shorter than those of visible light. Since light can be defined by its wavelength, UV-Vis spectroscopy, which seeks out the precise wavelengths that correlate to maximal absorbance, can be used to evaluate or identify various substances. The light is then converted into a recognisable electronic signal using a detector. after it has passed through the sample. Detectors are often built using semiconductors or photoelectric coatings.

Value of LDH activity has been calculated by using LDH Kit method established by Weishaar H. D. et. al. (1975). Pyruvate is reduced with NADH by LDH to produce NAD. An increase in absorbance, which is proportional to the sample's

LDH activity, indicates the rate at which NADH is being converted to NAD. Absorbance was taken by using UV spectrophotometer at 340 nm. (Weishaar, 1975)
SGPT - ALT catalyzed the conversion of alpha ketoglutarate to pyruvate and L - glutamate.
Reduced cofactor was oxidised with the aid of LDH. The rate of the reaction mixture's absorbance decreasing at 340 NM as a result of the reduced cofactor's oxidation is directly proportional to the ALT activity.
(J. Clin. Chem. Clin. Biochem., 1986, Vol 24:481)

SGOT - In animal tissues, aminotransferases are found in abundance. Normal distribution of AST and ALT in human plasma.
L-aspartate and 2-oxaloglutarate are transformed by AST into Oxaloacetate and L-glutamate.
The rate of oxidation of the reduced cofactor, which causes the reaction mixture's absorbance to decrease at 340 NM, is directly proportional to the AST activity. (Burtis, C.A., Ashwood, E.R., 1994)

Bilirubin-Bilirubin are broken down in the reticuloendothelial system through apoptosis. This gives Bilirubin as their metabolic by product upon removal of Iron.This billirubin is transferred to the liver and is referred to as indirect bilirubin.
The enzyme Uridyldiphosphateglucuronyl transferase combines bilirubin with glucuronic acid in the liver to create direct bilirubin or conjugated bilirubin.
Total Bil is the sum total of direct and Indirect bilirubin. The concentration of the bilirubin is measured, based on the reaction of bilirubin with diazo reagent to form a colored compound called azobilirubin. The solubilizing agent surfactant is added to the diazo reaction to speed it up. The amount of total bilirubin is directly proportional to the rise in absorbance at 546 nm brought on by azobilirubin.
The quantity of bilirubin in the sample directly correlates to the intensity of the colour that is produced. (Jendrassik L. &Grof P., 1938)

Results
The sample of 167 patients is statistically analysed in table-1. The mean Hb is low in total sickle patients. The mean Hb for male is significantly more than females. The mean HbF is high in total cases and the mean HbF of females is higher than males. The mean retics for total cases is high and the mean retics for male is higher than female patients. The mean SGOT is high in total sickle cases. Males show higher SGOT levels while females show normal SGOT levels. The mean SGPT level is lower in total sickle cases and males have higher SGPT levels than females. The LDH is higher in sickle cases but males have higher LDH than females. The total Bilirubin is higher in sickle cell cases while males have higher bilirubin levels than females. The Direct bilirubin is high in total sickle cases while males show higher values than females.

Table 1 Statistical analysis of sample

	parameters	TOTAL CASES	TOTAL CASES	
			MALE	FEMALE
sample size		167	103	64
MEAN (SD)	Hb	9.12 (1.93)	9.18 (1.93)	9.02 (1.94)
MEAN (SD)	Hb F	16.42 (7.59)	16.21 (5.64)	16.76 (6.06)
MEAN (SD)	RETICS	9.14 (5.6)	9.73 (5.58)	8.2 (5.09)
MEAN (SD)	SGOT	43.22 (23.4)	45.58 (25.31)	39.29 (19.78)
MEAN (SD)	SGPT	27.88 (28.38)	29.36 (33.07)	24.62 (17.77)
MEAN (SD)	LDH	919.44 (541.15)	988.07 (609.77)	808.98 (386.68)
MEAN (SD)	BIT	2.55 (1.88)	2.84 (2.02)	2.03 (1.47)
MEAN (SD)	BID	0.56 (0.66)	0.65 (0.78)	0.45 (0.38)

Table 2 portraits the statistical Analysis of data for adults and paediatrics. This classification gives a vivid insight into the spread of samples. The mean Hb for Adults group is higher than paediatrics sickle patients. Adults male show high Hb counts than adults female. Paediatrics female shows high Hb value than paediatrics male group. Paediatrics group show high HbF value than adults group. Adults male shows high HbF than adults female. Paediatrics female shows high HbF than paediatrics male. Paediatrics group shows high retics count than adults group. Adults male and paediatrics male shows high retics than adults female and paediatrics female respectively. Adults group shows higher SGOT than paediatrics group. Adults male and paediatrics male shows higher SGOT than adults female and paediatrics female respectively. SGPT of paediatrics group is higher than adults group. Adults male shows higher SGPT than adults female. Paediatrics male shows higher SGPT value than paediatrics female. Adults group shows higher LDH than paediatrics group. Adults

male and paediatrics male shows high LDH than adults female and paediatrics female respectively. Total billirubin is higher in adults group than paediatrics group. Adults male and paediatrics male shows higher total billirubin than adults female and paediatrics female respectively. Direct billirubin is high in adults group than paediatrics group. Adults male and paediatrics male shows higher direct billirubin than adults female and paediatrics female respectively.

Table 2 Statistical Analysis of data for adults and paediatrics

	parameters	TOTAL ADULTS	`TOTAL ADULTS		TOTAL PEDIATRICS	TOTAL PAEDIATRICS	
			MALE	FEMALE		MALE	FEMALE
sample size		95	60	35	72	43	29
MEAN (SD)	Hb	9.18(2.23)	9.5 (2.3)	8.62 (2.01)	9.05 (1.46)	8.74 (1.13)	9.51(1.77)
MEAN (SD)	Hb F	16.38(5.88)	17.27(5.72)	14.87(5.92)	16.47(5.72)	14.73(5.23)	19.05(5.5)
MEAN (SD)	RETICS	8.99 (5.42)	9.32 (5.68)	8.43 (4.97)	9.35 (5.86)	10.31(6.9)	7.92(5.3)
MEAN (SD)	SGOT	43.64 (24.24)	46.24(27.31)	39.17(17.23)	42.67(22.41)	44.86(22.14)	39.43(22.8)
MEAN (SD)	SGPT	26.81 (22.87)	29.04 (26.71)	22.98(13.59)	28.52 (34.2)	29.81(40.66)	26.6 (21.89)
MEAN (SD)	LDH	959.26 (547.23)	1014.68(609.44)	864.26(410.72)	866.896(532.24)	950.95(615.47)	742.25 (350.94)
MEAN (SD)	BIT	3.05 (2.02)	3.36 (2.1)	2.47(1.77)	1.88(1.42)	2.1(1.68)	1.52(0.75)
MEAN (SD)	BID	0.69 (0.82)	0.77(0.98)	0.54(0.43)	0.4 (0.29)	0.44(0.32)	0.34(0.25)

The sample of 167 patients is plotted with respect to age. The metrics are plotted in the figure 1(a-h).Figure 1(a) plots the graph between Haemoglobin (Hb) and age. It clearly shows that SCD is lethal with lower age. The Hb is high in >40 age group followed by 11- 20 age group, 21-30 age group, 1 -10 year age group and 31 – 40 age group. In Hb 13.17% of sickle cases found severely anaemic, 37.12 % of cases found mild anaemic, 34.73% of sickle cases found within the normal range and 14.97 % of sickle cases found above normal range. This is predicted with very less number of cases in age above 40 years. HbF or Fetal Haemoglobin versus age is plotted in Figure 1(b). It indicates that abnormally higher values of HbF are seen in sickle cell patients. The HbF level is high in >40 age group followed by 31 -40 age group , 1 – 10 age group, 21-30 group and 11-20 age group. Retics (%) versus age plot is plotted in Figure 1(c). It indicates that the abnormally higher retics (%) is seen amongst sickle cell patients. In Retics count, no sickle cases come below the normal case, 4.79% of cases come within the normal case and 95.2 % of cases found above the normal range. Retics (%) is seen not to change with age. Retics is high in 21-30 year age group followed by >40 year group, then, 31- 40 group, 1-10 year age group and 11-20 year age group. Figure 1(d) indicates the relationship between Serum Glutamic-Oxaloacetic Transaminase (SGOT) and age. SGOT is high in 31-40 age group followed by 11-20 year group, 1-10 year group, 21-30 group and lastly >40 group. In SGOT, 0.59% of sickle cases found below normal range, 52.69% of cases found within the normal range and 46.7 % of cases found above normal range. Sickle cell patients shows inverse relationship with age, while Serum Glutamic Pyruvic Transaminase (SGPT) is seen not vary or deviate much from normal. SGPT was seen to be abnormally lower. SGPT versus age is plotted in Figure 1(e). In SGPT, no sickle cases found below the normal range, 80.83% of cases found within the normal range and 19.16 % of cases found above normal range. SGPT is high in 11-20 year age group, followed by 1-10 year age group, 31-40 group, 21-30 age group, and lastly >40 age group. Figure 1(f) represents the plot between lactate dehydrogenase (LDH) and age. LDH is high in >40 age group, followed by 11-20 year group, 31-40 year group, 1-10 year group and lastly 21-30 age group. In LDH, no sickle cases found below the normal range, 12.57% of cases found within the normal range and 87.42% of sickle cases found above the normal range. Figure 1(g) represents the plot between Bilirubin Total (BIT) and age. In BIT, no sickle cases found in less than normal range, 16.56% found in between the normal range and 83.43 % of cases found above normal range.BIT is high in 11-20 year group followed by 21-30 year group, 31-40 group, >40 group then lastly 1-10 group. Figure 1(h) represents the plot between Bilirubin Direct (BID) and age. BID is high in 11-

20 year followed by 21-30 year group, >40 year group, 31-40 year group and lastly 1-10 year group. In BID, 1.81% of cases found below normal range, 18.18% of cases found within the normal range and 80% of cases found above normal range.

Pair wise correlations uncover the potential relations of interest. Based upon the prior knowledge, the potential relationships must be investigated. Bayes factor constitutes a natural ratio to compare likelihoods between potential relationships. A Bayes factor value predicts the existence of any potential relationships between variables. A Bayes factor of more than 10 indicates a strong relationship. A Bayes factor of more than 3 but less than 10 indicates a moderate relationship. A Bayes factor of more than 1 but less than 3 indicates a feeble relationship .A Bayes factor of 1 indicates no evidence of relationship. A bayes factor between 0.33 and 1 indicates a smaller likelihood of any relationship. A bayes factor between 0.1 and 0.33 indicates a moderate likelihoods of any relationship. A bayes factor of less than 0.1 indicates a strong likelihood of no relationship.

From table 3, it is evident that LDH has a strong relationship with HbF, Retics (%), and SGPT.LDH experiences a moderate relationship with BID and BIT. LDH shows a high likelihood of no relationship with Hb and SGOT. Similarly, for Hb, there exists a high likelihood of relationship with SGPT, SGOT, BIT and BID. A moderate relationship exists between Hb and HbF, Retics (%). This is evident from the data placed in table 3. HbF shows a potential relationship with LDH, SGOT, SGPT and BID. It shows moderate relationship with retics (%) and BIT. It shows a small likelihood of relationship with Hb.This is evident from the data placed in table 3. Similarly, Retics (%) shows a strong relationship with LDH and BIT. In contrast, it shows a moderate relationship with Hb, HBF, SGOT and SGPT. It shows a smaller likelihood of no relationship with BID. This is evident from the data placed in table 3. SGOT shows a strong relationship with Hb and HBF. It shows a weaker relationship with retics (%). Table 3 indicates SGOT has no relationship with LDH, SGPT, BIT and BID. SGPT shows a strong relationship with LDH, Hb and HbF. It shows a weaker relationship with retics (%). It shows no relationship with SGOT and BID. BIT shows a strong relationship with Hb and Retics (%), while it shows moderate relationship with LDH and HbF, no relationship with other variables. This is evident from the data placed in table 3. Lastly, BID shows a strong relationship with Hb and HbF, while, showing a moderate relationship with LDH. It shows no relationship with other variables. The type of relationship, whether directly related, indirectly related, no relation is evident from the Pearson correlation coefficient (r). LDH is inversely proportional to Hb and Hb F but directly proportional to Retics, SGPT, SGOT, BIT and BID. Hb is inversely proportional to LDH, Retics, SGOT and BIT but directly proportional to HbF, SGPT and BID. HbF is inversely related to LDH, retics, SGOT, SGPT, BID and BIT. And directly proportional to Hb. Retics is inversely proportional to Hb, HbF and directly proportional to LDH, SGOT, SGPT, BIT and BID. SGOT is inversely proportional to Hb and HbF and directly proportional to LDH, Retics (%), SGPT, BID and BIT. SGPT is inversely proportional to HbF and directly proportional to LDH, Hb, Retics (%), SGOT, BID and BIT. BIT is inversely proportional to Hb and HbF but directly proportional to LDH, Retics (%), SGOT, SGPT and BID. BID is inversely proportional to HbF and directly proportional to LDH, Hb, Retics (%), SGPT, SGOT and BIT.

Table 3 Bayes Factor Inference on Pairwise Correlations[a]

		SGOT	SGPT	LDH	BIT	BID	Hb	Hb F
SGOT	Pearson Correlation	1	.667	.311	.256	.303	-.068	-.064
	Bayes Factor		.000	.004	.072	.007	11.135	11.656
	N	167	167	167	163	165	167	167
SGPT	Pearson Correlation	.667	1	.064	.194	.384	.043	-.008
	Bayes Factor	.000		11.681	.748	.000	13.992	16.201
	N	167	167	167	163	165	167	167
LDH	Pearson Correlation	.311	.064	1	.105	.153	-.268	-.020
	Bayes Factor	.004	11.681		6.661	2.396	.037	15.789
	N	167	167	167	163	165	167	167
BIT	Pearson Correlation	.256	.194	.105	1	.311	-.029	-.125
	Bayes Factor	.072	.748	6.661		.005	15.085	4.545
	N	163	163	163	163	161	163	163
BID	Pearson Correlation	.303	.384	.153	.311	1	.036	-.030

	Bayes Factor	.007	.000	2.396	.005		14.563	15.026
	N	165	165	165	161	165	165	165
Hb	Pearson Correlation	-.068	.043	-.268	-.029	.036	1	.171
	Bayes Factor	11.135	13.992	.037	15.085	14.563		1.411
	N	167	167	167	163	165	167	167
Hb F	Pearson Correlation	-.064	-.008	-.020	-.125	-.030	.171	1
	Bayes Factor	11.656	16.201	15.789	4.545	15.026	1.411	
	N	167	167	167	163	165	167	167
RETICS (%)	Pearson Correlation	.081	.091	.061	.025	.205	-.133	-.078
	Bayes Factor	9.439	8.248	11.968	15.323	.501	3.766	9.937
	N	167	167	167	163	165	167	167

A one way ANOVA is used when there is a need to compare whether two samples' (Adult & Paediatrics) means are significantly different or not. The ANOVA tests the null hypothesis which states that both groups have the same mean. The F ratio is the ratio of two means square values. If the null hypothesis is true, the value of F is close to 1 most of the time. The F value and significance is inversely proportional. From table 4, it is evident that, the F value is close to 1, thus, the null hypothesis is true. It means, that sickle cell disease affects equally to paediatrics and adults.

Table 4 ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
Hb	Between Groups	147.467	40	3.687	0.981	0.512
	Within Groups	473.402	126	3.757		
	Total	620.869	166			
Hb F	Between Groups	1330.178	40	33.254	0.987	0.503
	Within Groups	4246.980	126	33.706		
	Total	5577.158	166			
RETICS (%)	Between Groups	1010.395	40	25.260	0.756	0.845
	Within Groups	4208.120	126	33.398		
	Total	5218.515	166			
SGOT	Between Groups	22002.449	40	550.061	1.005	0.474
	Within Groups	68941.542	126	547.155		
	Total	90943.991	166			
SGPT	Between Groups	28333.702	40	708.343	0.858	0.706
	Within Groups	104017.254	126	825.534		
	Total	132350.956	166			
BIT	Between Groups	196.255	40	4.906	1.589	0.029
	Within Groups	376.612	122	3.087		
	Total	572.867	162			
BID	Between Groups	11.741	40	0.294	0.592	0.971
	Within Groups	61.510	124	0.496		
	Total	73.251	164			
LDH	Between Groups	16171435.787	40	404285.895	1.570	0.031
	Within Groups	32439748.917	126	257458.325		
	Total	48611184.703	166			

Paired Samples Statistics							
		Mean	N	Std. Deviation	Std. Error Mean	Correlation(R)	Sig.(p)
Pair 1	Hb	9.1269	167	1.93395	.14965	.171	.027
	Hb F	16.4260	167	5.79632	.44853		
Pair 2	Hb	9.1269	167	1.93395	.14965	-.133	.087
	RETICS (%)	9.1493	167	5.60686	.43387		
Pair 3	Hb	9.1269	167	1.93395	.14965	-.068	.382
	SGOT	43.2263	167	23.40631	1.81123		
Pair 4	Hb	9.1269	167	1.93395	.14965	.043	.578
	SGPT	27.5504	167	28.23641	2.18500		
Pair 5	Hb	9.1269	167	1.93395	.14965	-.268	.000
	LDH	919.4428	167	541.14551	41.87510		

Pair 6	Hb	9.1589	163	1.91394	.14991	-.029	.718
	BIT	2.5504	163	1.88048	.14729		
Pair 7	Hb	9.1242	165	1.94460	.15139	.036	.644
	BID	.5688	165	.66832	.05203		
Pair 8	Hb F	16.4260	167	5.79632	.44853	-.078	.319
	RETICS (%)	9.1493	167	5.60686	.43387		
Pair 9	Hb F	16.4260	167	5.79632	.44853	-.064	.412
	SGOT	43.2263	167	23.40631	1.81123		
Pair 10	Hb F	16.4260	167	5.79632	.44853	-.008	.915
	SGPT	27.5504	167	28.23641	2.18500		
Pair 11	Hb F	16.4260	167	5.79632	.44853	-.020	.802
	LDH	919.4428	167	541.14551	41.87510		
Pair 12	Hb F	16.5089	163	5.76791	.45178	-.125	.111
	BIT	2.5504	163	1.88048	.14729		
Pair 13	Hb F	16.4203	165	5.79481	.45113	-.030	.698
	BID	.5688	165	.66832	.05203		
Pair 14	RETICS (%)	9.1493	167	5.60686	.43387	.081	.295
	SGOT	43.2263	167	23.40631	1.81123		
Pair 15	RETICS (%)	9.1493	167	5.60686	.43387	.091	.243
	SGPT	27.5504	167	28.23641	2.18500		
Pair 16	RETICS (%)	9.1493	167	5.60686	.43387	.061	.432
	LDH	919.4428	167	541.14551	41.87510		
Pair 17	RETICS (%)	9.0125	163	5.46951	.42841	.025	.753
	BIT	2.5504	163	1.88048	.14729		
Pair 18	RETICS (%)	9.1457	165	5.63857	.43896	.205	.008
	BID	.5688	165	.66832	.05203		
Pair 19	SGOT	43.2263	167	23.40631	1.81123	.667	.000
	SGPT	27.5504	167	28.23641	2.18500		
Pair 20	SGOT	43.2263	167	23.40631	1.81123	.311	.000
	LDH	919.4428	167	541.14551	41.87510		
Pair 21	SGOT	43.4864	163	23.56376	1.84566	.256	.001
	BIT	2.5504	163	1.88048	.14729		
Pair 22	SGOT	42.8516	165	23.19039	1.80537	.303	.000
	BID	.5688	165	.66832	.05203		
Pair 23	SGPT	27.5504	167	28.23641	2.18500	.064	.414
	LDH	919.4428	167	541.14551	41.87510		
Pair 24	SGPT	27.8491	163	28.51238	2.23326	.194	.013
	BIT	2.5504	163	1.88048	.14729		
Pair 25	SGPT	27.3408	165	28.32874	2.20539	.384	.000
	BID	.5688	165	.66832	.05203		
Pair 26	LDH	924.2880	163	543.57796	42.57631	.105	.183
	BIT	2.5504	163	1.88048	.14729		
Pair 27	BID	.5748	161	.67505	.05320	.311	.000
	T	2.5479	161	1.88769	.14877		

The correlation of Hb & HbF is significant (p= 0.02) and the correlation coefficient is, R = 0.17. The correlation of Hb & Retics is not significant (p = 0.12) and the correlation coefficient is R = -11.85. The correlation of Hb and SGOT is not significant, p=0.38, correlation coefficient is R = -0.06804. The correlation of Hb and SGPT is not significant, p = 0.5, correlation coefficient is R = 0.043387. The correlation of Hb and LDH is significant, p = 0.0005, correlation coefficient is R = -0.26754. The correlation of Hb &BIT is not significant, p = 0.71, correlation coefficient is R= -0.02852. The correlation of Hb &BID is not significant, p = 0.64, correlation coefficient is R=0.036213. The correlation of HbF & Retics is not significant, p = 0.31, correlation coefficient is R = -0.07752. The correlation of HbF & SGOT is not significant, p = 0.41, correlation coefficient is R=-0.06383. The correlation of HbF & SGPT is not significant, p = 0.91, correlation coefficient is R = -0.00832. The correlation of Hb & LDH is not significant, p = 0.8, correlation coefficient is R = -0.01959. The correlation of HbF & BIT is not significant, p = 0.1, correlation coefficient is R=-0.12521. The correlation of HbF & BID is not significant, p= 0.6, correlation coefficient is R = -0.03042. The correlation of Retics & SGOT is not significant, p = 0.29, correlation coefficient is R=0.081441. The correlation of Retics & SGPT is not significant, p = 0.24, correlation coefficient is R=0.09091. The correlation of Retics & LDH is not significant, p=0.43, correlation coefficient is R=0.061267. The correlation of Retics & LDH is not significant, p = 0.75, correlation coefficient is

R=0.024856. The correlation of Retics & BID is significant, p =0.008, correlation coefficient is R=0.204933. The correlation of SGOT & SGPT is significant, p <0.0001, correlation coefficient is R=0.66. The correlation of SGOT & LDH is significant, p <0.0001, correlation coefficient is R=0.311. The correlation of SGOT &BIT is significant, p= 0.001, correlation coefficient is R=0.26. The correlation of SGOT & BID is significant, p <0.0001, correlation coefficient is R=0.28. The correlation of SGPT& LDH is not significant, p = 0.41, correlation coefficient is R=0.064. The correlation of SGPT &BIT is significant, p = 0.01, correlation coefficient is R=0.193955. The correlation of SGPT &BID is significant, p <0.0001, correlation coefficient is R=0.384277. The correlation of LDH &BIT is Not significant, p = 0.18, correlation coefficient is R=0.11 The correlation of LDH &BID is not significant, p =0.05, correlation coefficient is R=0.12 .The correlation of BIT&BID is significant, p <0.0001, correlation coefficient is R =0.311.

Paediatrics

Paired Samples Test

		Paired Differences									
					95% Confidence Interval of the Difference						
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	Sig. (2-tailed)	Correlation	Sig.
Pair 1	SGOT - SGPT	15.98095	25.73129	2.63997	10.73922	21.22268	6.053	94	0	0.638	0
Pair 2	SGOT - LDH	-997.901	644.4285	66.11697	-1129.18	-866.624	-15.093	94	0	0.32	0.002
Pair 3	SGOT - BIT	43.74491	23.44396	2.444202	38.88981	48.60002	17.897	91	0	0.342	0.001
Pair 4	SGOT - BID	44.41411	23.32581	2.418774	39.61022	49.21801	18.362	92	0	0.32	0.002
Pair 5	SGOT - Hb	36.75905	24.10139	2.47275	31.84935	41.66876	14.866	94	0	-0.085	0.414
Pair 6	SGOT - Hb F	28.65326	24.83381	2.54789	23.59436	33.71217	11.246	94	0	-0.041	0.696
Pair 7	SGOT – RETICS (%)	36.17442	24.18427	2.48125	31.24783	41.10101	14.579	94	0	0.076	0.463
Pair 8	SGPT - LDH	-1013.88	651.6094	66.85371	-1146.62	-881.142	-15.166	94	0	0.027	0.791
Pair 9	SGPT - BIT	27.79828	33.28961	3.470682	20.9042	34.69237	8.009	91	0	0.238	0.022
Pair 10	SGPT - BID	28.7197	33.19006	3.441649	21.88429	35.55512	8.345	92	0	0.421	0
Pair 11	SGPT - Hb	20.77811	33.25587	3.411981	14.00354	27.55267	6.09	94	0	0.025	0.807
Pair 12	SGPT - Hb F	12.67232	33.57797	3.44503	5.83213	19.5125	3.678	94	0	0.034	0.743
Pair 13	SGPT – RETICS (%)	20.19347	33.26264	3.41267	13.41753	26.96942	5.917	94	0	0.09	0.387
Pair 14	LDH - BIT	1050.866	654.8764	68.27559	915.2446	1186.487	15.392	91	0	0.208	0.047
Pair 15	LDH - BID	1036.983	654.5929	67.87813	902.171	1171.795	15.277	92	0	0.171	0.1
Pair 16	LDH - Hb	1034.66	652.1759	66.91184	901.8052	1167.515	15.463	94	0	-0.266	0.009
Pair 17	LDH - Hb F	1026.554	652.0701	66.90098	893.721	1159.388	15.344	94	0	-0.062	0.552
Pair 18	LDH – RETICS %)	1034.076	651.0596	66.79731	901.448	1166.703	15.481	94	0	0.106	0.309
Pair 19	BIT - BID	1.69145	1.779559	0.187582	1.318729	2.064171	9.017	89	0	0.342	0.001
Pair 20	BIT - Hb	-6.58828	2.759296	0.287677	-7.15972	-6.01685	-22.902	91	0	-0.106	0.314
Pair 21	BIT - Hb F	-14.8084	6.215628	0.648024	-16.0956	-13.5212	-22.852	91	0	-0.035	0.743
Pair 22	BIT – RETICS (%)	-6.9072	6.106443	0.636641	-8.1718	-5.64259	-10.849	91	0	0.033	0.752
Pair 23	BID - Hb	-8.25788	2.078012	0.21548	-8.68584	-7.82991	-38.323	92	0	-0.047	0.655
Pair 24	BID - Hb F	-16.3756	6.034738	0.625773	-17.6185	-15.1328	-26.169	92	0	-0.046	0.662
Pair 25	BID – RETICS (%)	-8.85293	5.972372	0.619306	-10.0829	-7.62293	-14.295	92	0	0.307	0.003

Pair 26	Hb - Hb F	-8.10579	5.764066	0.591381	-9.27999	-6.93159	-13.707	94	0	0.254	0.013
Pair 27	Hb – RETICS (%)	-0.58463	6.869491	0.704795	-1.98402	0.814755	-0.83	94	0.409	-0.281	0.006
Pair 28	Hb F - RETICS (%)	7.52116	9.17106	0.94093	5.65292	9.3894	7.993	94	0	-0.158	0.126

Paediatrics

The correlation of SGOT & SGPT is significance p = 0 and the correlation coefficient is, 0.638. The correlation of SGOT & LDH is significance p=0.002 and the correlation coefficient is 0.32 .The correlation of SGOT& BIT is significance p= 0.001 and the correlation coefficient is, R= 0.342. The correlation of SGOT & BID is significance p=0.002 and the correlation coefficient is , R= 0.32.

The correlation of SGOT& Hb is not significance p=0.414 and the correlation coefficient is , R= - 0.085.The correlation of SGOT& HbF is not significance p = 0.696 and the correlation coefficient is , R= - 0.041.The correlation of SGOT & Retics is not significance p= 0.46 and the correlation coefficient is , R= 0.076 .The correlation of SGPT & LDH not significance p= 0.79 and the correlation coefficient is , R= 0.027.The correlation of SGPT& BIT is significance p= 0.02 and the correlation coefficient is R=0.238.The correlation of SGPT & BID is significance p= 0 and the correlation coefficient is , R= 0.421. The correlation of SGPT& HB is not significance p= 0.8 and the correlation coefficient is , R=0.025.The correlation of SGPT & HbF is not significance p= 0.74 and the correlation coefficient is 0.034.The correlation of SGPT& Retics is not significance p= 0.38 and the correlation coefficient is ,R = 0.09.The correlation of LDH& BIT is significance p= 0.04 and the correlation coefficient is R=0.208.The correlation of LDH& BID is significance p=0.1 and the correlation coefficient is R= 0.171.The correlation of LDH& Hb is significance p= 0.009 and the correlation coefficient is R= - 0.26.The correlation of LDH & Hb F is not significance p= 0.55 and the correlation coefficient is R= - 0.062. The correlation of LDH & Retics not significance. p = 0. 3 and the correlation coefficient is, R= 0.106. The correlation of BIT& BID is significance p=0.00 and the correlation coefficient is , R= 0.342 .The correlation of BIT & Hb is not significance p= 0.31 and the correlation coefficient is , R= - 0.106.The correlation of BIT & HbF is not significance p=0.74 and the correlation coefficient is R=, - 0.035.The correlation of BIT & Retics is not significance p=0.75 and the correlation coefficient is R=0.033 .The correlation of BID & Hb is not significance p=0.65 and the correlation coefficient is R= - 0.047.The correlation of BID & HbF is not significance p=0.66 and the correlation coefficient is R= - 0. 046 .The correlation of BID & Retics is significance p= 0.00 and the correlation coefficient is R= 0.307 .The correlation of Hb & HbF is significance p= 0.01 and the correlation coefficient is R = 0.254.The correlation of Hb & Retics is significance p= 0 and the correlation coefficient is R= - 0.28.The correlation of HbF & Retics is not significance p= 0. 12 and the correlation coefficient is R= - 0.15

Bayes Factor Inference on Pairwise Correlation

		SGOT	SGPT	LDH	BIT	BID	Hb	Hb F	RETICS (%)
SGOT	Pearson Correlation	1	0.638	0.32	0.342	0.32	-0.085	-0.041	0.076
	Bayes Factor		0	0.085	0.048	0.094	8.858	11.436	9.444
	N	95	95	95	92	93	95	95	95
SGPT	Pearson Correlation	0.638	1	0.027	0.238	0.421	0.025	0.034	0.09
	Bayes Factor	0		11.92	0.903	0.002	11.98	11.697	8.497
	N	95	95	95	92	93	95	95	95
LDH	Pearson Correlation	0.32	0.027	1	0.208	0.171	-0.266	-0.062	0.106
	Bayes Factor	0.085	11.92		1.709	3.183	0.419	10.346	7.37
	N	95	95	95	92	93	95	95	95
BIT	Pearson Correlation	0.342	0.238	0.208	1	0.342	-0.106	-0.035	0.033

	Bayes Factor	0.048	0.903	1.709		0.053	7.339	11.518	11.56
	N	92	92	92	92	90	92	92	92
BID	Pearson Correlation	0.32	0.421	0.171	0.342	1	-0.047	-0.046	0.307
	Bayes Factor	0.094	0.002	3.183	0.053		11.061	11.108	0.141
	N	93	93	93	90	93	93	93	93
Hb	Pearson Correlation	-0.085	0.025	-0.266	-0.106	-0.047	1	0.254	-0.281
	Bayes Factor	8.858	11.98	0.419	7.339	11.061		0.578	0.276
	N	95	95	95	92	93	95	95	95
Hb F	Pearson Correlation	-0.041	0.034	-0.062	-0.035	-0.046	0.254	1	-0.158
	Bayes Factor	11.436	11.697	10.346	11.518	11.108	0.578		3.841
	N	95	95	95	92	93	95	95	95
RETICS (%)	Pearson Correlation	0.076	0.09	0.106	0.033	0.307	-0.281	-0.158	1
	Bayes Factor	9.444	8.497	7.37	11.56	0.141	0.276	3.841	
	N	95	95	95	92	93	95	95	95

For paediatrics sickle patients, It is evident that LDH has a strong relationship with HbF, Retics (%), and SGPT.LDH experiences a moderate relationship with BID and BIT. LDH shows a high likelihood of no relationship with Hb and SGOT. Similarly, for Hb, there exists a high likelihood of relationship with SGPT, SGOT, BIT and BID. A moderate relationship exists between HbF and Retics (%). This is evident from the data placed in table HbF shows a potential relationship with LDH, SGOT, SGPT and BID. It shows moderate relationship with retics (%) and BIT. It shows a small likelihood of relationship with Hb. This is evident from the data placed in table. Similarly, Retics(%) shows a strong relationship with LDH and BIT. In contrast, it shows a moderate relationship with Hb, HBF, SGOT and SGPT. It shows a smaller likelihood of no relationship with BID. This is evident from the data placed in table. SGOT shows a strong relationship with Hb and HBF. It shows a weaker relationship with retics (%). Table indicates SGOT has no relationship with LDH, SGPT, BIT and BID. SGPT shows a strong relationship with LDH, Hb and HbF. It shows a weaker relationship with retics (%). It shows no relationship with SGOT and BID. BIT shows a strong relationship with Hb and Retics (%), while it shows moderate relationship with LDH and HbF, no relationship with other variables. This is evident from the data placed in table. Lastly, BID shows a strong relationship with Hb and HbF, while, showing a moderate relationship with LDH. It shows no relationship with other variables. The type of relationship, whether directly related, indirectly related, no relation is evident from the Pearson correlation coefficient (r). LDH is inversely proportional to Hb and Hb F but directly proportional to Retics, SGPT, SGOT, BIT and BID.

Hb is inversely proportional to LDH, Retics, SGOT and BIT but directly proportional to HbF, SGPT and BID. HbF is inversely related to LDH, retics, SGOT, SGPT, BID and BIT. And directly proportional to Hb. Retics is inversely proportional to Hb, HbF and directly proportional to LDH, SGOT, SGPT, BIT and BID. SGOT is inversely proportional to Hb and HbF and directly proportional to LDH, Retics (%), SGPT, BID and BIT. SGPT is inversely proportional to HbF and directly proportional to LDH, Hb, Retics (%), SGOT, BID and BIT. BIT is inversely proportional to Hb and HbF but directly proportional to LDH, Retics (%), SGOT, SGPT and BID. BID is inversely proportional to HbF and directly proportional to LDH, Hb, Retics (%), SGPT, SGOT and BIT.

Adult

Paired Samples Test

		Paired Differences									
					95% Confidence Interval of the Difference						
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	t	df	Sig. (2-tailed)	Correlation	Sig.
Pair 1	SGOT - SGPT	16.83084	18.63166	1.91157	13.03538	20.62631	8.805	94	0	0.689	0
Pair 2	SGOT - LDH	-915.624	540.5573	55.46001	-1025.74	-805.507	-16.51	94	0	0.296	0.004
Pair 3	SGOT - BIT	40.63622	23.96166	2.484708	35.70137	45.57106	16.355	92	0	0.289	0.005
Pair 4	SGOT - BID	42.41249	23.50922	2.424791	37.59734	47.22765	17.491	93	0	0.358	0
Pair 5	SGOT - Hb	34.46137	24.59022	2.522903	29.45209	39.47065	13.659	94	0	-0.111	0.282
Pair 6	SGOT - Hb F	27.25611	24.77977	2.54235	22.20821	32.304	10.721	94	0	0.029	0.782
Pair 7	SGOT – RETICS (%)	34.64768	23.85625	2.4476	29.78792	39.50745	14.156	94	0	0.182	0.077
Pair 8	SGPT - LDH	-932.455	544.4429	55.85866	-1043.36	-821.546	-16.693	94	0	0.142	0.169
Pair 9	SGPT - BIT	24.01224	22.95965	2.380805	19.28375	28.74072	10.086	92	0	0.091	0.384
Pair 10	SGPT - BID	26.01547	22.54337	2.325171	21.39814	30.6328	11.189	93	0	0.535	0
Pair 11	SGPT - Hb	17.63053	22.87392	2.346815	12.97087	22.29018	7.513	94	0	0.049	0.635
Pair 12	SGPT - Hb F	10.42526	23.6266	2.42404	5.61228	15.23825	4.301	94	0	-0.001	0.991
Pair 13	SGPT – RETICS (%)	17.81684	21.80692	2.23734	13.37455	22.25914	7.963	94	0	0.311	0.002
Pair 14	LDH - BIT	955.6286	550.6022	57.09479	842.2334	1069.024	16.738	92	0	0.115	0.271
Pair 15	LDH - BID	950.4398	544.2356	56.13362	838.9696	1061.91	16.932	93	0	0.145	0.162
Pair 16	LDH - Hb	950.0855	548.0084	56.22448	838.4505	1061.72	16.898	94	0	-0.348	0.001
Pair 17	LDH - Hb F	942.8802	546.3187	56.05112	831.5894	1054.171	16.822	94	0	0.16	0.122
Pair 18	LDH – RETICS (%)	950.2718	547.2089	56.14245	838.7996	1061.744	16.926	94	0	0.008	0.936
Pair 19	BIT - BID	2.347027	2.006161	0.209157	1.931563	2.762491	11.221	91	0	0.241	0.02
Pair 20	BIT - Hb	-6.17675	3.071501	0.3185	-6.80932	-5.54418	-19.393	92	0	-0.038	0.715
Pair 21	BIT - Hb F	-13.4907	6.331311	0.656526	-14.7946	-12.1868	-20.549	92	0	-0.104	0.32
Pair 22	BIT – RETICS (%)	-5.92191	5.768302	0.598145	-7.10988	-4.73395	-9.9	92	0	0.04	0.707
Pair 23	BID - Hb	-8.48218	2.357069	0.243113	-8.96495	-7.9994	-34.89	93	0	0.043	0.678
Pair 24	BID - Hb F	-15.6269	5.920224	0.610625	-16.8394	-14.4143	-25.592	93	0	0.018	0.867
Pair 25	BID – RETICS (%)	-8.31409	5.256625	0.54218	-9.39075	-7.23743	-15.335	93	0	0.311	0.002
Pair 26	Hb - Hb F	-7.20526	6.010274	0.616641	-8.42962	-5.98091	-11.685	94	0	0.132	0.202
Pair 27	Hb – RETICS (%)	0.186316	6.046286	0.620336	-1.04538	1.418007	0.3	94	0.765	-0.088	0.397
Pair 28	Hb F – RETICS (%)	7.39158	8.04906	0.82582	5.7519	9.03126	8.951	94	0	-0.011	0.912

For Adults

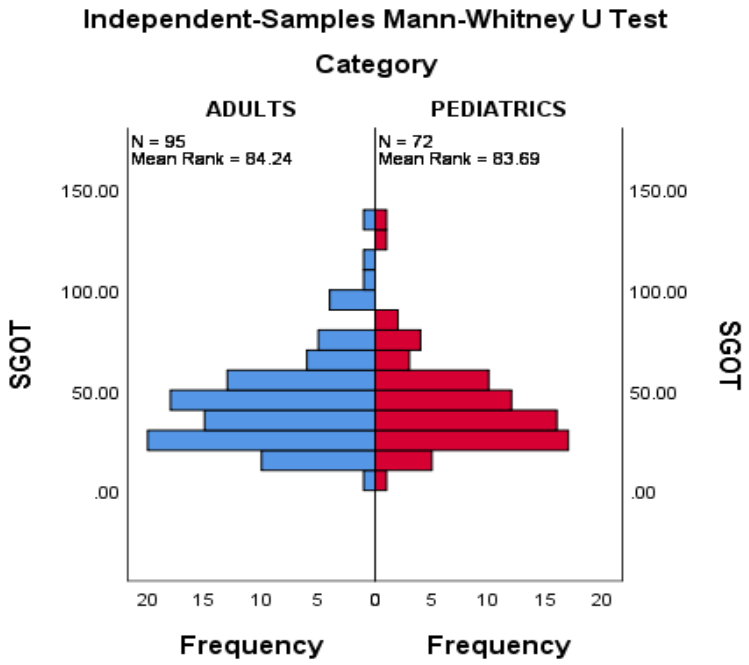
Bayes Factor Inference on Pairwise Correlations									
		SGOT	SGPT	LDH	BIT	BID	Hb	Hb F	RETICS (%)
SGOT	Pearson Correlation	1	0.689	0.296	0.289	0.358	-0.111	0.029	0.182
	Bayes Factor		0	0.183	0.24	0.024	6.938	11.881	2.603
	N	95	95	95	93	94	95	95	95
SGPT	Pearson Correlation	0.689	1	0.142	0.091	0.535	0.049	-0.001	0.311
	Bayes Factor	0		4.809	8.37	0	11.029	12.342	0.114
	N	95	95	95	93	94	95	95	95
LDH	Pearson Correlation	0.296	0.142	1	0.115	0.145	-0.348	0.16	0.008
	Bayes Factor	0.183	4.809		6.683	4.635	0.032	3.753	12.302
	N	95	95	95	93	94	95	95	95
BIT	Pearson Correlation	0.289	0.091	0.115	1	0.241	-0.038	-0.104	0.04
	Bayes Factor	0.24	8.37	6.683		0.835	11.428	7.463	11.382
	N	93	93	93	93	92	93	93	93
BID	Pearson Correlation	0.358	0.535	0.145	0.241	1	0.043	0.018	0.311
	Bayes Factor	0.024	0	4.635	0.835		11.27	12.107	0.121
	N	94	94	94	92	94	94	94	94
Hb	Pearson Correlation	-0.111	0.049	-0.348	-0.038	0.043	1	0.132	-0.088
	Bayes Factor	6.938	11.029	0.032	11.428	11.27		5.484	8.64
	N	95	95	95	93	94	95	95	95
Hb F	Pearson Correlation	0.029	-0.001	0.16	-0.104	0.018	0.132	1	-0.011
	Bayes Factor	11.881	12.342	3.753	7.463	12.107	5.484		12.268
	N	95	95	95	93	94	95	95	95
RETICS (%)	Pearson Correlation	0.182	0.311	0.008	0.04	0.311	-0.088	-0.011	1
	Bayes Factor	2.603	0.114	12.302	11.382	0.121	8.64	12.268	
	N	95	95	95	93	94	95	95	95

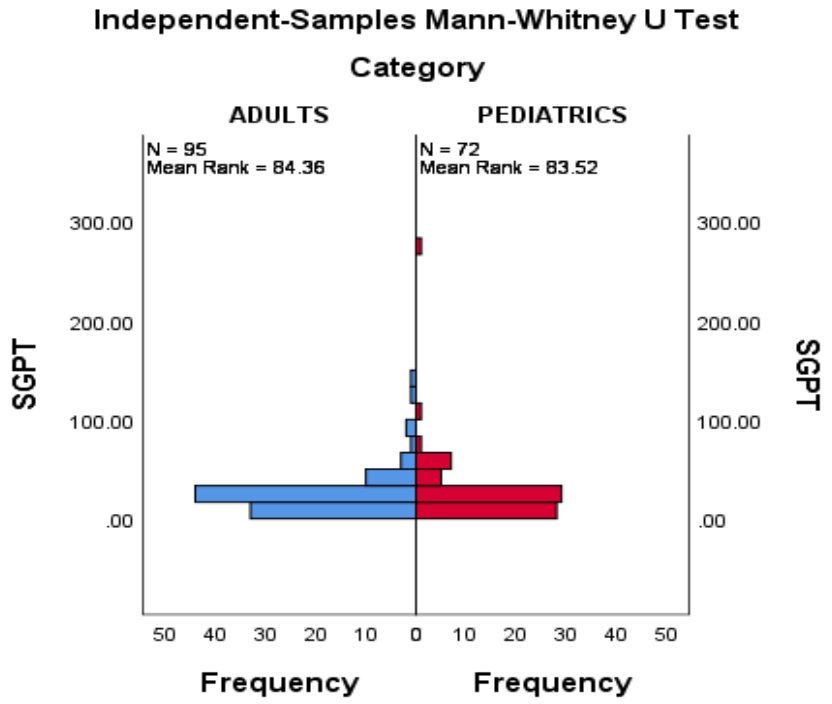
The correlation of SGOT & SGPT is significant, p = 0, correlation coefficient is R=0.689. The correlation of SGOT& LDH is significant, p = 0.004, correlation coefficient is R = 0.296. The correlation of SGOT & BIT is significant, p =0.005, correlation coefficient is R = 0.289. The correlation of SGOT & BID is significant, p = 0, correlation coefficient is R=0.358.The correlation of SGOT & HB is not significant, p=0.282 correlation coefficient is R = -0.111. The correlation of SGOT & HbF is not significant, p=0.782, correlation coefficient is R=0.029. The correlation of SGOT & Retics is not significant, p= 0.077, correlation coefficient is R= 0.182. The correlation of SGPT & LDH is not significant, p=0.169, correlation coefficient is R= 0.142. The correlation of SGPT & BIT is not significant, p=0.384, correlation coefficient is R= 0.091. The correlation of SGPT & BID is significant, p =0, correlation coefficient is R= 0.535. The correlation of SGPT & Hb is not significant, p =0.635, correlation coefficient is R= 0.049. The correlation of SGPT & Retics is not significant, p=0.991, correlation coefficient is R= -0.001. The correlation of SGPT & Retics is significant, p= 0.002, correlation coefficient is R= 0.311. The correlation of LDH & BIT is not significant, p = 0.271, correlation coefficient is R= 0.115. The correlation of LDH & BID is not significant, p = 0.162 correlation coefficient is R= 0.145.The correlation of LDH & Hb is significant, p = 0.001, correlation coefficient is R=-0.348. The correlation of LDH & HbF is not significant, p=0.122, correlation coefficient is R= 0.16.The correlation of LDH& Retics is not significant, p = 0.936, correlation coefficient is R=0.008.The correlation of BIT & BID is significant, p = 0.02, correlation coefficient is R= 0.241.The correlation of BIT& Hb is not significant, p = 0.715, correlation coefficient is R =-0.038 .

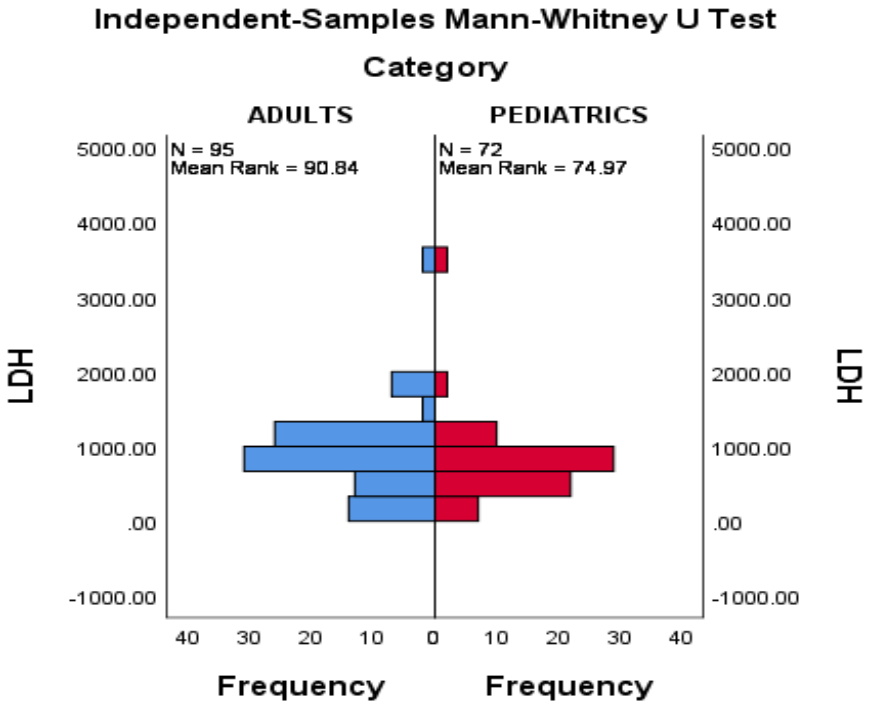
The correlation of BIT & HbF is not significant, p = 0.32, correlation coefficient is R = -0.104.The correlation of BIT & Retics is not significant, p = 0.707, correlation coefficient is R = 0.04**.**The correlation of BID & Hb is not significant, p =0.678 , correlation coefficient is R = 0.043**.**The correlation of BID & HbF is not significant, p =0.867 , correlation coefficient is R = 0.018**.**The correlation of BID & Retics is significant, p =0.002 , correlation coefficient is R = 0.311**.**The correlation of Hb & HbF is not significant, p =0.202 , correlation coefficient is R = 0.132**.**The correlation of HbF & Retics is not significant, p 0.397, correlation coefficient is R = -0.088**.**

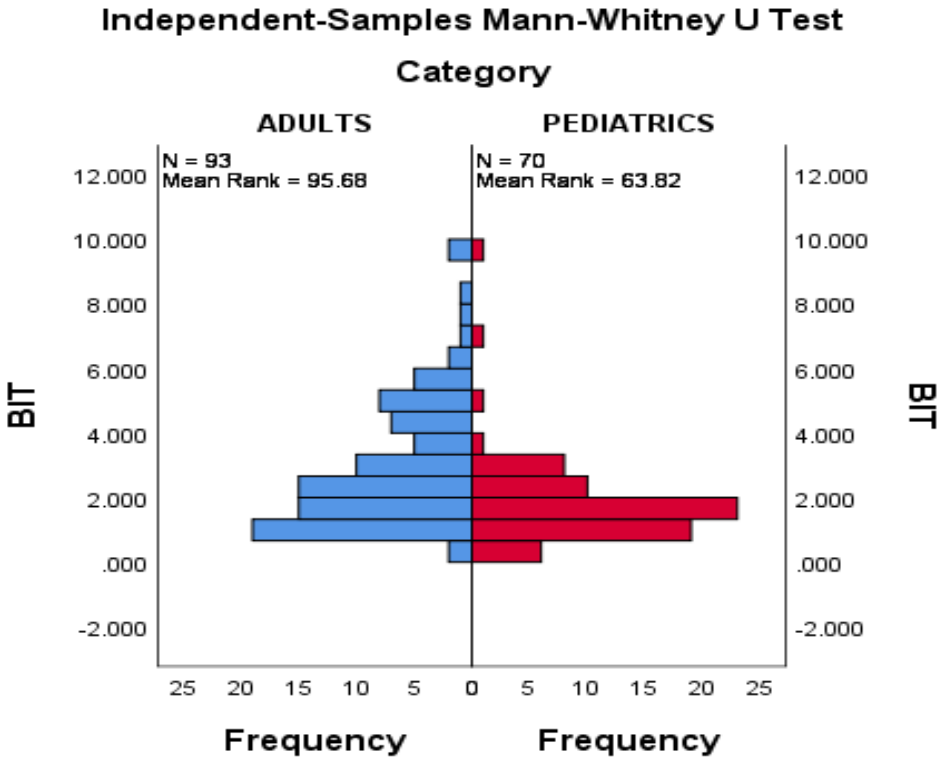
The correlation of HbF & Retics is not significant, p = 0.912, correlation coefficient is R = -0.011.

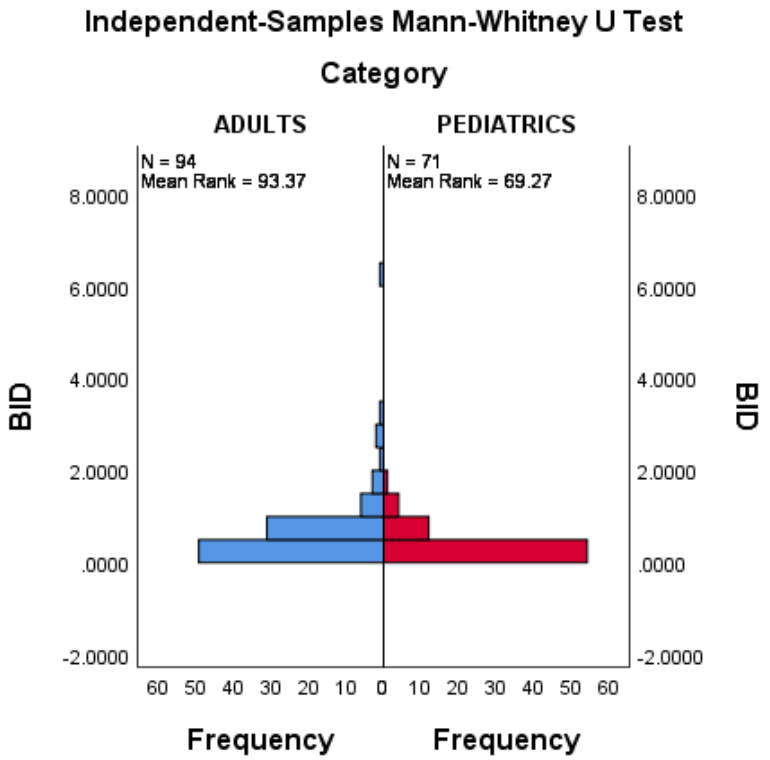
It is evident that LDH has a strong relationship with HbF, Retics (%), and SGPT. LDH experiences a moderate relationship with BID and BIT. LDH shows a high likelihood of no relationship with Hb and SGOT. Similarly, for Hb, there exists a high likelihood of relationship with SGPT, SGOT, BIT and BID. A moderate relationship exists between Hb and HbF, Retics (%). This is evident from the data placed in table 3. HbF shows a potential relationship with LDH, SGOT, SGPT and BID. It shows moderate relationship with retics (%) and BIT. It shows a small likelihood of relationship with Hb. This is evident from the data placed in table 3. Similarly, Retics (%) shows a strong relationship with LDH and BIT. In contrast, it shows a moderate relationship with Hb, HBF, SGOT and SGPT. It shows a smaller likelihood of no relationship with BID. This is evident from the data placed in table 3. SGOT shows a strong relationship with Hb and HBF. It shows a weaker relationship with retics (%). Table 3 indicates SGOT has no relationship with LDH, SGPT, BIT and BID. SGPT shows a strong relationship with LDH, Hb and HbF. It shows a weaker relationship with retics (%). It shows no relationship with SGOT and BID. BIT shows a strong relationship with Hb and Retics (%), while it shows moderate relationship with LDH and HbF, no relationship with other variables. This is evident from the data placed in table 3. Lastly, BID shows a strong relationship with Hb and HbF, while, showing a moderate relationship with LDH. It shows no relationship with other variables. The type of relationship, whether directly related, indirectly related, no relation is evident from the Pearson correlation coefficient (r). LDH is inversely proportional to Hb and Hb F but directly proportional to Retics, SGPT, SGOT, BIT and BID. Hb is inversely proportional to LDH, Retics, SGOT and BIT but directly proportional to HbF, SGPT and BID. HbF is inversely related to LDH, retics, SGOT, SGPT, BID and BIT. And directly proportional to Hb. Retics is inversely proportional to Hb, HbF and directly proportional to LDH, SGOT, SGPT, BIT and BID. SGOT is inversely proportional to Hb and HbF and directly proportional to LDH, Retics (%), SGPT, BID and BIT. SGPT is inversely proportional to HbF and directly proportional to LDH, Hb, Retics (%), SGOT, BID and BIT. BIT is inversely proportional to Hb and HbF but directly proportional to LDH, Retics (%), SGOT, SGPT and BID. BID is inversely proportional to HbF and directly proportional to LDH, Hb, Retics (%), SGPT, SGOT and BIT.

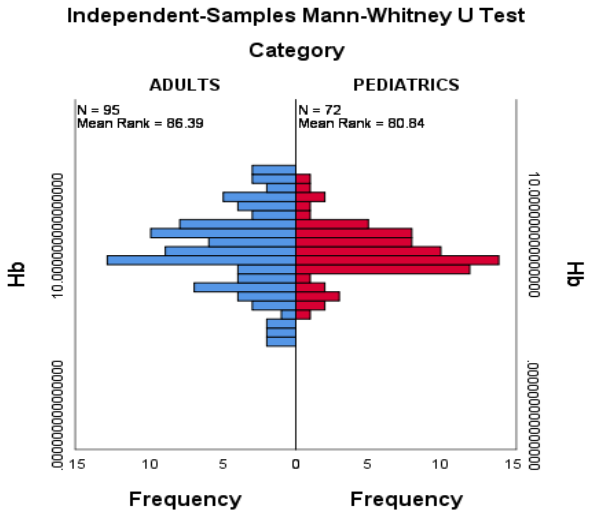


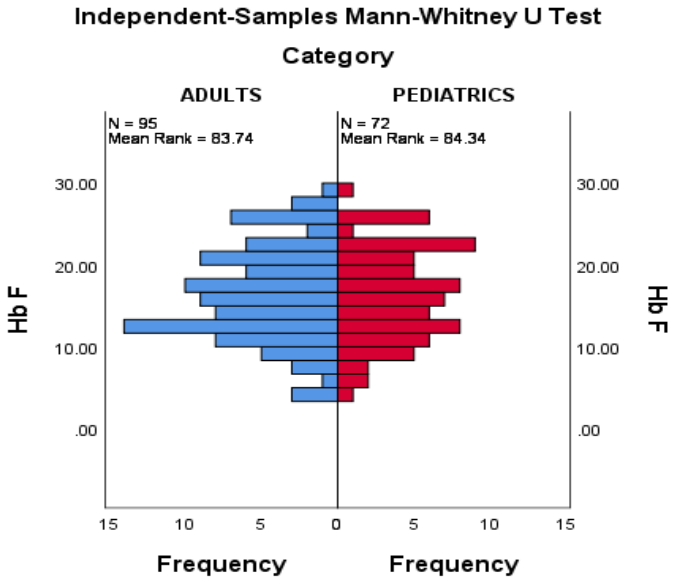

Independent-Samples Mann-Whitney U Test
Category
ADULTS
PEDIATRICS
N = 95
Mean Rank = 84.36
N = 72
Mean Rank = 83.52
SGPT
300.00
200.00
100.00
.00
50 40 30 20 10 0 10 20 30 40 50
Frequency
Frequency

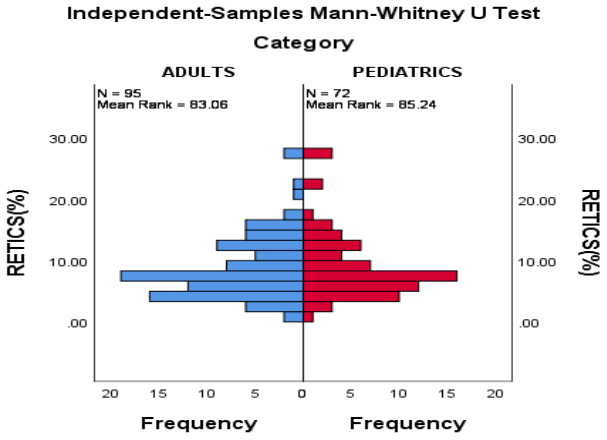

Independent-Samples Mann-Whitney U Test
Category
ADULTS
PEDIATRICS
N = 95
Mean Rank = 90.84
N = 72
Mean Rank = 74.97
LDH
5000.00
4000.00
3000.00
2000.00
1000.00
.00
-1000.00
40 30 20 10 0 10 20 30 40
Frequency
Frequency


Independent-Samples Mann-Whitney U Test
Category
ADULTS
PEDIATRICS
N = 93
Mean Rank = 95.68
N = 70
Mean Rank = 63.82
BIT
BIT
12.000
10.000
8.000
6.000
4.000
2.000
.000
-2.000
25 20 15 10 5 0 5 10 15 20 25
Frequency
Frequency


Independent-Samples Mann-Whitney U Test
Category
ADULTS
PEDIATRICS
N = 94
Mean Rank = 93.37
N = 71
Mean Rank = 69.27
BID
BID
8.0000
6.0000
4.0000
2.0000
.0000
-2.0000
60 50 40 30 20 10 0 10 20 30 40 50 60
Frequency
Frequency


Independent-Samples Mann-Whitney U Test
Category
ADULTS
PEDIATRICS
N = 95
Mean Rank = 86.39
N = 72
Mean Rank = 80.84
Hb
Hb
Frequency
Frequency


Independent-Samples Mann-Whitney U Test
Category
ADULTS
PEDIATRICS
N = 95
Mean Rank = 83.74
N = 72
Mean Rank = 84.34
Hb F
Hb F
Frequency
Frequency


Independent-Samples Mann-Whitney U Test
Category
ADULTS
PEDIATRICS
N = 95
Mean Rank = 83.06
N = 72
Mean Rank = 85.24
RETICS(%)
RETICS(%)
Frequency
Frequency

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of SGOT is the same across categories of Category.	Independent-Samples Mann-Whitney U Test	.942	Retain the null hypothesis.
2	The distribution of SGPT is the same across categories of Category.	Independent-Samples Mann-Whitney U Test	.911	Retain the null hypothesis.
3	The distribution of LDH is the same across categories of Category.	Independent-Samples Mann-Whitney U Test	.036	Reject the null hypothesis.
4	The distribution of BIT is the same across categories of Category.	Independent-Samples Mann-Whitney U Test	.000	Reject the null hypothesis.
5	The distribution of BID is the same across categories of Category.	Independent-Samples Mann-Whitney U Test	.001	Reject the null hypothesis.
6	The distribution of Hb is the same across categories of Category.	Independent-Samples Mann-Whitney U Test	.462	Retain the null hypothesis.
7	The distribution of Hb F is the same across categories of Category.	Independent-Samples Mann-Whitney U Test	.937	Retain the null hypothesis.
8	The distribution of RETIC S(%) is the same across categories of Category.	Independent-Samples Mann-Whitney U Test	.774	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .050.

Discussion

Hb

Many researchers had worked on Odisha sickle patients and have drawn inferences like low Hb in all sickle patients. The mean Hb for male is significantly more than females. The mean Hb for Adults group is higher than paediatrics sickle patients. Adults male show high Hb counts than adults female. Paediatrics female shows high Hb value than paediatrics male group. Low hemoglobin in sickle patients were also studied previously by ,Vidhyanand et al,2017 , ,Tripathi et al, 2018,Sandor et al,2017, ,Samal et al,2019,SATYA, 2019, Verma etal.,2020 , Mohanty et al,2020. The fact that the mean Hb is low in sickle cell disease patients may be related to increased hemolysis and frequently occurring recurrent infections.

HbF

The mean HbF is high in total cases and the mean HbF of females is higher than males. Paediatrics group show high HbF value than adults group. Adults male shows high HbF than adults female. Paediatrics female shows high HbF than paediatrics male. HbF is generally high in sickle patients. All the sickle cases are above the normal range. In the current study, foetal haemoglobin levels were higher in both sexes. Our study is found similar with the data of SATYA, 2019, Mohanty et al,2020 , Verma et al., - 2020. High concentrations of HbF are present in a developing baby. After birth, HbF levels typically reach negligible levels after six months. Especially, In India, sickle cell disorder patients show High levels of hemoglobin F after birth & its high level is maintained in later age also. Alexandra,2019, described Deoxy sickle haemoglobin (HbS) polymerization is inhibited by foetal haemoglobin (HbF), which modifies the sickle cell anaemia phenotype. It has been demonstrated that hydroxyurea combined with recombinant erythropoietin therapy further raises haemoglobin F levels and encourages the growth of F-cells that contain haemoglobin F. A developing foetus needs foetal haemoglobin (HbF), a physiological protein tetramer, to survive in uterus. Because maternal haemoglobin has a relatively lower affinity for oxygen, oxygen can be transferred from maternal to foetal blood effectively. HbF is known to relieve sickle-cell disease symptoms in addition to playing a crucial physiologic role (SCD).

Retics

The mean retics for total cases is high and the mean retics for male is higher than female patients. Paediatrics group shows high retics count than adults group. Adults male and paediatrics male shows high retics than adults female and paediatrics female respectively. Hyperhemolytic crisis may cause high production of reticulocytes, furthermore, Red blood cells are destroyed by this kind of anaemia before they can naturally expire. Our data are comparable to those from Brahme et al. (2016) and Nagose et al. (2018). Young red blood cells called reticulocytes are created in the bone marrow and remain there until they mature into red blood cells and enter the bloodstream. The majority of people have very low numbers because the majority of reticulocytes remain in the bone marrow, and they also have higher reticulocyte counts because, due to anaemia, their bodies must produce more red blood cells, requiring the bone marrow to work harder.

SGOT

The mean SGOT is high in total sickle cases. Males show higher SGOT levels while females shows normal SGOT levels. Adults group shows higher SGOT than paediatrics group. Adults male and paediatrics male shows higher SGOT than adults female and paediatrics female respectively. High SGOT levels is seen may be due to hemolysis. Our study supports the previous studies of Tripathi P et al. 2016, study shows a significant higher values of AST in the SCA patients. Garg D et al. 2018, 74% of the subjects had levels that were above normal, while 26% had levels that were within the acceptable range. Acute intrahepatic cholestasis or the massive buildup of sickle cells in the hepatic sinusoids and stasis, which severely damages hepatocytes and Kupffer cells, are two potential causes of elevated transaminases (AST) levels. Serum enzymes (AST) were significantly higher in the sickle cell population than in the control group, suggesting that hemolysis may be ongoing and continuous. In comparison to controls, Augustina (2016) found that aspartate amino transferase was significantly higher in subjects who had received multiple and infrequent blood transfusions. This slight elevation of the liver function tests could be the result of increased hemolysis and transient red cell aplasia, both of which are common in SCA patients. The activities of liver enzymes have been found to be increased in SCA patient on blood transfusion. Mohanty AP et al, 2020, showed elevated AST levels. Meher et al, 2019.,the SCA cases had significantly higher AST, than that of the controls . Liver enzymes of AST, was elevated during severe VOC as compared to mild VOC. This may be due to hyper hemolysis; there is an increase in liver enzyme activity to neutralizing heme toxicity.

SGPT

The mean SGPT level is lower in total sickle cases and males have higher SGPT levels than females. SGPT of paediatrics group is higher than adults group Male adults exhibit higher SGPT levels than female adults. Male paediatricians have higher SGPT values than female paediatricians. Alanine aminotransferase (ALT), which is released by abnormal liver function, is a helpful test for identifying liver damage. Hemolysis increases ALT levels in SCD as well, or it may be brought on by the enzymes' leakage from the mitochondria and cytoplasm of the liver tissue as a result of hepatic injury, which is common in sickle cell anaemia. (Brahme, 2016) (Nsiah et al., 2011) (Tripathi P et al. in 2016). In 2018, Garg D et al. discussed potential causes of elevated transaminases (ALT) levels, including acute intrahepatic cholestasis, massive sickle cell accumulation in the hepatic sinusoids, and stasis that significantly damages hepatocytes and Kupffer cells. Serum enzymes (ALT) were significantly higher than control levels, suggesting that ongoing hemolysis may be occurring continuously to counteract heme toxicity in the sickle cell population (ASAOLU, 2010). (Meher et al, 2019). In contrast to controls, Augustina in 2016 reported that alanine amino levels were significantly higher in subjects who had received multiple and infrequent blood transfusions. This slight elevation of the liver function tests could be the result of increased hemolysis and transient red cell aplasia, both of which are common in SCA patients.

LDH

Males have higher LDH levels than females, but LDH is higher in sickle cell cases. LDH is higher in the adult group than in the paediatric group. Male adults and paediatric patients exhibit higher LDH levels than female adults and paediatric patients, respectively. No sickle cases were discovered in LDH below the normal range. 2015, Alzahri LDH was discovered to be high. In sickle cell disease patients, serum LDH is currently used as a marker for the risk of vaso-occlusive crisis (VOC) and pain crises. LDH is a recognised biomarker for intravascular hemolysis. Serum LDH is therefore the gold standard. 2019 (Meher et al) (Ehtesham, 2020). LDH might serve as a biomarker for both hemolysis and mortality in sickle cell disease. Serum LDH and plasma haemoglobin released during hemolysis were used by Kato et al. (2013) to investigate whether LDH functions as a mortality biomarker in sickle cell disease. LDH level may be a helpful tool in the diagnosis of painful sickle cell crises. Statistics show that LDH were higher. LDH therefore seems to function as good prognostic markers to evaluate and monitor in sickle cell crises (Verghese, 2019). The aspartate aminotransferase, reticulocyte count, unconjugated bilirubin concentration, serum haptoglobin, and plasma haemoglobin are the other commonly used indicators of intra- or extra-vascular hemolysis. Vaso-occlusion in SCD is pathophysiologically characterised by endothelial activation and secretion of adhesive molecules. . It has been demonstrated that higher LDH activity is correlated with higher levels of active von Willebrand factor, a hyperadhesive molecule best known for mediating platelet adhesion (Chen et al,2011)

Billirubin

The total Billirubin is higher in sickle cell cases while males have higher billirubin levels than females. The Direct billirubin is high in total sickle cases while males shows higher values than females.Totalbillirubin is higher in adults group than paediatrics group. Adults male and paediatrics male shows higher total billirubin than adults female and paediatrics female respectively. Direct billirubin is high in adults group than paediatrics group. Adults male and paediatrics male shows higher direct billirubin than adults female and paediatrics female respectively. This study shows significant higher values of total bilirubin is the possible cause of SCA in patients is increased red blood cell lysis (Tripathi P et al. 2016) (Meheret al, 2019)(Mohanty AP et al, 2020)(ASAOLU, 2010) or may be brought on by the frequent transient red cell aplasia and increased hemolysis that SCA patients experience. (Augustina , 2016).

Conclusion

The present study evaluated the effect of hematobiochemical parameters on the pathophysiology of the sickle cell disease (SCD) cases and maximum hospitalizations were seen in winter seasons due to severe painful crisis and acute anemia. Splenomegaly and hepatomegaly were most common symptoms found in Odisha patients. The clinical symptoms of Odisha sickle cell disease patients reveal microcytic anemia due to iron deficiency and the pathophysiology varies from individual to individual. The changes in LDH and bilirubin go along with the changes in hematological parameters. In this study, serum LDH may be considered as an indicator of the severity of the disease.

Mann-Whitney U Test (MWUT) is used to test the biochemical and haematological parameters change in SCD same across categories of adults and pediatrics or not. MWUT revealed that SGOT,SGPT, Hb, HbF, Retics has similar distribution but, LDH, BIT, BID are not same distribution. Early detection of LDH and Correction of these factors can guarantee improved sickle cell patient outcomes.

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Conflict of Interest –

There is no conflict of Interest.

Ethical Clearance –

This study was approved by institutional Ethical Committee.

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