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Assessment of factors affecting health related quality of life in Thalassemic children in Assam, India

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Abstract
Introduction
Inherited haemoglobin disorders (sickle-cell disorders and thalassaemias) were originally characteristic of the tropics and subtropics but are now becoming common worldwide due to migration. Haemoglobinopathies are the commonest hereditary disorders in India and pose a major health problem. The data on the prevalence of β-thalassemias and other haemoglobinopathies in different caste/ethnic groups of India is scarce.
Materials & Method
Chi square, Independent t test and one way ANOVA was used for continuous variables. Principal components analysis (PCA) for evaluation of relationship based on available data of the present study and other region. Pearson Correlation coefficient test was assessed to evaluate the relationship in all domains and age at diagnosis. PedsQL 4.0 Generic core scales was used to access the Quality of Life of Thalassemic and Healthy children.
Result
A total of 50 children Thalassemic condition and 50 health children were included in the study with median age at diagnosis was 3 year. It was found that children diagnosed with Thalassemic condition had statistically significantly lower ($p<0.0001$), Emotional Functioning ($p<0.0001$), Social Functioning ($p<0.0001$), school functioning ($p<0.0001$) and Psychological health ($p<0.00001$) compared to healthy Children.
Discussion
From the study a statistically significant difference in score of health well being was observed between Healthy Children and the Children diagnosed with Thalassemic condition. Emotional and Social Functioning were found to be most affected in Thalassemic children. There is a significant gradual increase in mean score with age at diagnosis.
Conclusion
Significantly lower health well being score was observed in Thalassemic children in comparison to Normal healthy children (Control).

Keyword:- *Burden, α halassemia, β thalassemia, Community control, Challenges*

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I. Introduction

The Thalassemia syndromes are a heterogeneous group of Mendelian disorder characterized by lack or decreased synthesis of either α or β globin chains of haemoglobin. It results in ineffective erythropoietin as well as lysis of mature red cells in spleen [1-2]. Every year about 300,000 infants worldwide are born with Thalassemia syndrome and most children with thalassaemia are born in low-income countries [3-4]. Three percent (3%) of world population carries genes of β thalassemia and α-Thalassemia affects 5% of the world's population [5-6]. Thalassemia both β and α are more prevalent in populations of Southeast Asia, Central Africa, and the Middle East [7-10]. Ten percent of the total world thalassemics are born in India every year [11] and In India over 20 million people have thalassemia gene. The prevalence of the gene varies between 3 to18% in north and 1 to 3% in south with certain communities like sindhis, kutchis, lohanas, bhanushalis, Punjabis, mahars, agris, gouds, etc. showing a high prevalence [12]. In India, the treatment and awareness of thalassemia is limited even in the medical profession it is evident that the diagnosis of thalassemia is often delayed and is only possible at Major institutions.
Health Related Quality of Life (HRQoL) is generally conceptualized as a multidimensional construct referring to patients' perceptions of the impact of disease and treatment on their physical, psychological and social functioning and well-being. It is important to understand more about quality of life in paediatric population to evaluate and improve the care patients receive.

The aim of this study is to assess the Health Related Quality of Life (measured using PedsQL Generic Core Scales) of Thalassemic children and compare with normal healthy children.

II. Material & Method

Statistical analysis

Health Related Quality of Life score for each parameter and overall scores were presented in terms of means and standard deviations. Chi square test was used to evaluate association between categorical variables intergroup comparison and Independent t test and one way ANOVA was used for continuous variables. Principal components analysis (PCA) for evaluation of relationship based on available data of the present study and other region as compared to other geographical regions a correlation coefficient matrix of genomic abundance data was generated for extraction of principal components. Varimax rotated first two principal components were used to make a scatter plot. Geographical areas with similar genomic patterns tended to be together in the reduced multivariate data space without loss of information due dimensionality reduction. Pearson Correlation coefficient test was assessed to evaluate the relationship in all domains and age at diagnosis. A p value <0.05 was considered as statistically significant at 95% confidence interval. Data were analyzed using SPSS and GraphPad – Prism 5, software's.

The study was carried out to assess the Health Related Quality of Life of Thalassemic children using PedsQL 4.0 Generic core scales and to compare the Health Related Quality of Life of Thalassemic children with that of Normal healthy children (Control).

III. Result

A total of 50 children Thalassemic condition and 50 health children were included in the study (Table 1). The study was conducted in the Department of Pediatrics, Assam Medical College and Hospital, Dibrugarh, during the period of May 2015- June 2016. The median age at diagnosis was 3 year for the Thalassemic patients.

There is a significant difference in mean Health Related Quality of Life score (HRQoL) score of health well being was observed between Healthy Children and the Children diagnosed with Thalassemic condition. From the study (Table 2, Figure 1)) it was found that healthy children had statistically significantly higher physical health summery mean score (82.19±6.384) as compared to those children diagnosed with Thalassemic condition (62.23±9.426), $t = 12.399$, $p < 0.0001$. The average Emotional Functioning Score was found to be 41.06 points higher in Healthy Children (83.9±6.723) compared to Thalassemic Children (42.84±12.507), $t=20.449$, $p<0.0001$. In the study it was observed that the difference in mean score towards the Social Functioning among Healthy Children (82.6±6.794) and Thalassemic Children (42.38±10.486) was highly significant, $t=22.761$, $p<0.0001$. Statistically significant difference in mean score also observed for school functioning score among Thalassemic Children (57.5±11.704) and Healthy Children (81.2±5.764), $t=12.845$, $p<0.0001$. Psychological health mean summery score among Thalassemic Children was observed as 47.57±8.198 and among Healthy Children it was 82.57±5.03, $t=25.727$, $p<0.0001$. As is evident, in all domains of HRQoL are significantly lower in Thalassemic children in comparison to Normal healthy children (Control). However, Emotional Functioning and Social Functioning were the domains of HRQoL which were found to be most affected in Thalassemic children. There is no significant difference in mean HRQoL score was observed among male and female Thalassemic children.

There was a statistically significant difference in mean score of Physical Health Summary was observed among the Thalassemic children patients with respect to father's educational status as determined by one-way ANOVA ($F = 5.475$, $p = 0.003$). The mean score for physical health was found as increased among Thalassemic children with respect to Fathers years of schooling improved, $p=0.003$. There is no statistically significant difference in mean score was observed among other domain, however there is an improvement in score was observed as for higher education level of attainment by their father (Table 3).

Age at diagnosis was not found significantly different among the parameters under study, although it was observed that the mean score was higher among those who diagnosed at older age. The mean physical score for >4 years group was observed as 64.42±8.486 compared to 61.79±9.973 those who diagnosed at 2-4 years of age and 60.71±9.706 for those who diagnosed at <2 years of age, $p=0.568$. Emotional ($p=0.624$), Social ($p=0.821$), School functioning ($P=0.166$) and Psychological ($P=0.577$) was not also found as statistically significant when compared between the age at diagnosis group. The Emotional Functioning score across all age groups was found to be much lesser than the Other Functioning scores. Thus, it can be concluded that the Emotional Functioning is a more severely affected domain in comparison to Other Functioning in Thalassemic children irrespective of age.

A gradual increase in the domains scores was seen with the decrease in frequency of transfusion, it was observed that those who need to transfuse their blood monthly have a low mean score in all categories under study. A significant difference in emotional ($p=0.002$), Social ($p=0.033$) and psychological ($p<0.0001$) score was observed among the time to blood transfusion groups. A non significant increase in mean physical score was observed as the duration in blood transfusion increases, the physical mean score for those who did transfusion monthly is 61.13±7.936 compared to 62.41±10.549 for those who needs to do transfusion Once in 2 months and 70.31±14.768 for Quarterly group, $p=0.168$. Hence, it can be concluded that children who received more frequent transfusions have impaired functioning scores in all domains.

Figure 2 showing Scatter plots correlation between Health Related Quality of Life (HRQoL) scores and age at diagnosis. From the figure 2 it was seen that there is a gradual increase in physical ($r=0.128$), emotional ($r=0.191$), School Functioning ($r=0.081$) and psychological ($r=0.144$) score with respect to age at diagnosis. A significant decrease in no of required blood transfusion was observed as the age at diagnosis increases ($r= -0.340$). The result of PCA based data all domains data is sown in Figure 3. Clustering of the geographical areas on the basis of similarity in the pattern of the physical, emotional, social and school functioning score from India and around the clearly indicates that the health well being of Dibrugarh India do not resemble with countries Malaysia, Thailand, Jordan, Hong Kong, Middle East and United Kingdom.

In category wise domain analysis of physical, emotional, social and school functioning the mean score is lower than many other parts of the world (Table 4). Physical functioning for Thalassemic children of this study Dibrugarh, India (62.2±9.43) was found out to be significantly lower than countries Thailand (78.2±14.8), Malaysia (69.1±16.4), Middle East (68.4±27.2), Hong Kong (66.7±16.0), United Kingdom (66.5±21.8) while it was found higher than Jordan (54.2±15.1). In comparison of emotional functioning it is observed that in the present study Dibrugarh India (42.84±12.51), had significantly lower mean emotional functioning score than other countries, Middle East has the highest (76.9±24.6) mean score followed by Thailand (75.9±16.6), United Kingdom (73.6±22.7), Malaysia (68.1±17.2), Jordan (62.4±23.3) and Hong Kong (60.8±17.1). Social Functioning was found to be lowest in our study Dibrugarh, India (42.38±10.49) in comparison to Thailand (83.7±14.7), Hong Kong (82.5±17.7), United Kingdom (77.6±19.9), Middle East (76.4±20.6), Malaysia (74.3±18.7) and Jordan (73.3±20.9). Social functioning score of this study Dibrugarh, India (57.5±11.7) found to be higher than Jordan (46.7±21.1) while found lower than countries like Hong Kong (75.4±19.5), Middle East (69.4±21.4), Thailand (67.9±15.9), United Kingdom (60.9±27.5) and Malaysia (60.1±16.4).

IV. Discussion

Thalassemia is a chronic hereditary disease in which patients present with anemia during their first two year of life, requiring regular red blood cell (RBC) transfusions [13]. The presence of a chronic disease like thalassemia places tremendous psychosocial burden on the patient and the family. In developing countries like India, the main cause of death from thalassemia is non-compliance with the treatment due to psychosocial factors [14]. Thalassemia challenges the individual at the physical, emotional, cognitive levels and disrupts the quality of life [15].

There is no sex preponderance was seen in many studies, however, a slight male preponderance can be found [16-17], 56% (28/50) of the cases included in this study are males [16-17]. Thalassemia found as equally influence the mean HRQoL score of male and female (Table 2). Parental education holds significance in the management of Thalassemic children as it is important that the parents to be aware of the disease and the need treatment procedures [18]. The current study also focused on the educational status of the parents, 52.0% (26/50) fathers were found as completed 5-10 years of Education whereas 28% were studied up-to Graduate & Above. A significant difference in mean physical health score among father educational status, p=0.003. In this study it was documented that parents' literacy is associated with higher HRQoL scores, a gradual increase in the domains scores was seen for higher educational status of father.

In our study it is found as Thalassemia is more prevalent among low income group, Majority (52.0%) of the families included in this study had a monthly income of less than Rs. 10000 (INR). A study done on eastern India also shows similar result of high Thalassemic prevalence among low socio income group [19]. Majority of the Thalassemic children included in this study were diagnosed between the ages of 2 years- 4 years with the median age of diagnosis being 3 years. In the study conducted by Caocci et al the median age at diagnosis was found as low as 8 months [17].

Conventional treatment of patients suffering from β thalassemia is regular blood transfusion support from early childhood [20]. In the present study it was observed that larger number of patients included in this study received regular transfusions i.e. 64.0% of all the children diagnosed with Thalassemic require monthly blood transfusion followed by 28% once in 2 months and 8% quarterly; compared to other studies [21-22]; which one of the factor influencing domain scores and low score for all domain was observed among those who needs to transfuse their blood regularly compare to those who did once in 2 months and quarterly.

Age at diagnosis is found to be influence the HRQoL score [23-24], There is a significant relationship between age at diagnosis and HRQol was observed. Increased age at diagnosis showing that there is a gradual increase in physical (r=0.128), emotional (r=0.191), School Functioning (r=0.081) and psychological (r=0.144) score with whereas significant decline in blood transfusion was observed with increasing age (r= -0.340). The result of PCA based on the physical, emotional, social and school functioning score data shows that the health well being of Dibrugarh India don't resemble with parts of the world. In category wise analysis the mean HRQoL score in all domains found to be lower compared too many other parts of the globe. This might be linked to the age at diagnosis, parental educational staus and family income also. Thalassemia is a major health problem that disturbs the lifestyle of the affected patient [25].

In India, stem cell transplantation is not an option for most patients. Supportive treatments, such as blood transfusions and iron chelation are used. Although optimal medical management has reduced the difficulties faced by thalassemics, the psychosocial problems faced by them are now of primary importance. In developing countries like India, the main cause of death from thalassemia is non-compliance with the treatment due to psychosocial factors. A viable option for control is to promote education and awareness programs, Strengthening screening in all the states so that the right burden can be assessed and develop sufficient facilities for genetic counseling and pre-natal diagnosis in the public sector.

V. Conclusion

In the present study, all domains of HRQoL are significantly lower in Thalassemic children in comparison to Normal healthy children (Control), further multicentre study studies desired to explore the same with a special emphasis on evaluation of the emotional and social impact of the disease on children. Exploration of the predictors of psychological problems and HRQoL might improve the quality of interventions and thus better address the needs of these children and their families.

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Figure

IGURE 1 Showing Health Related Quality of Life (HRQoL) mean score s in Thalassemic Children and Healthy Children comparision

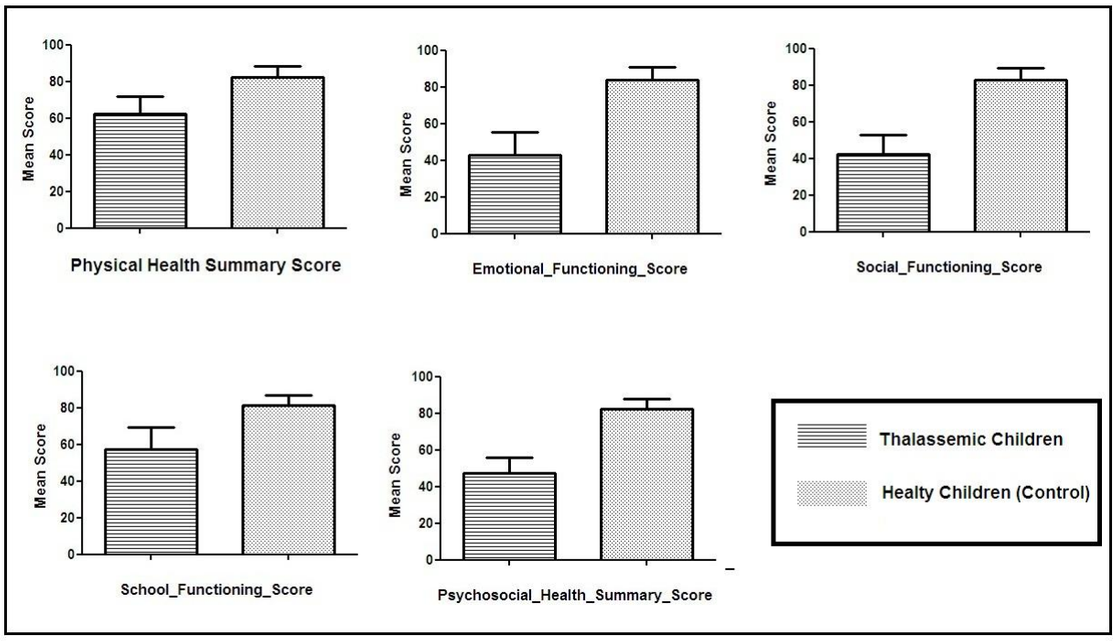

Figure 2 Scatter plots showing the correlation between mean Health Related Quality of Life (HRQoL) scores, No Of Blood transfusion with Age at Diagnosis

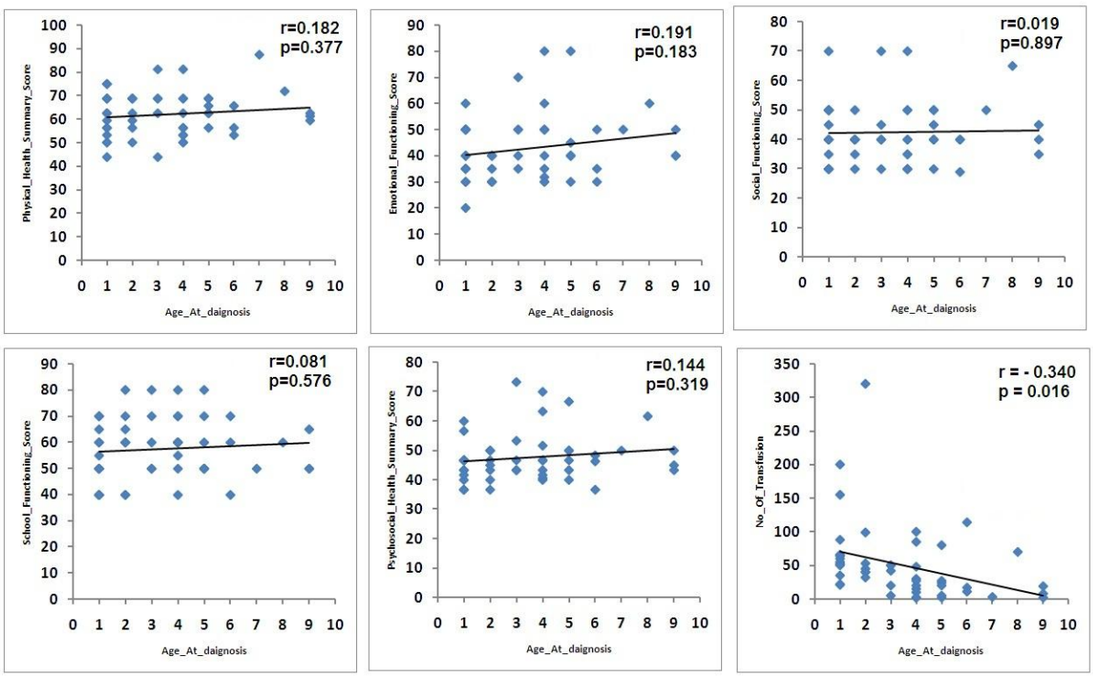

Figure 3 Showing Principal Component Analysis of Health Related Quality of Life (HRQoL) Data

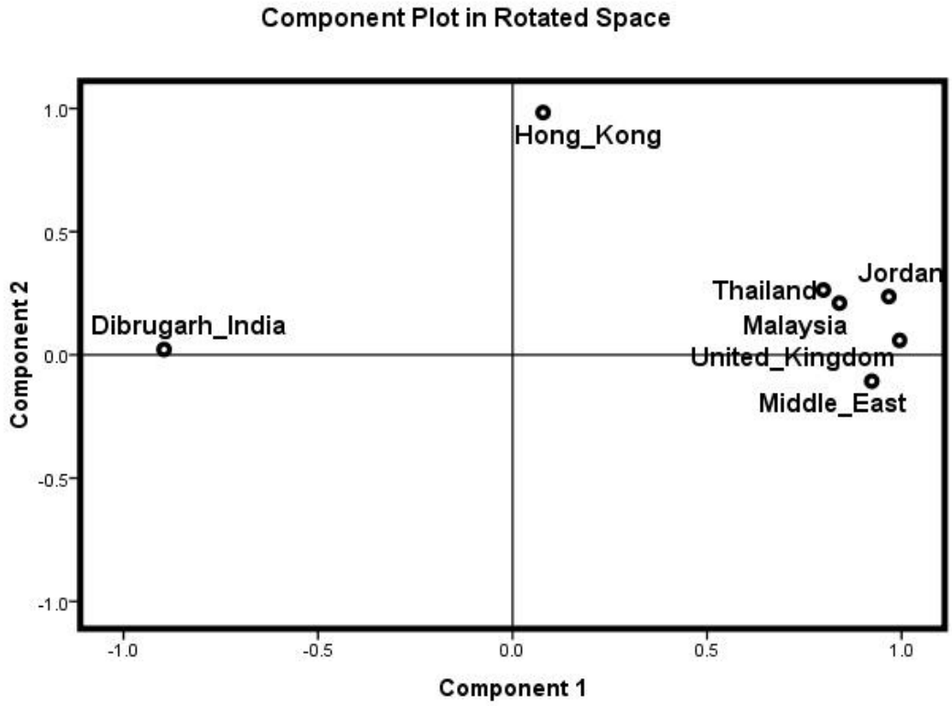

Table 1 Showing demographic characteristics association of Health children and Thalassemic_Children

Category	Total Particiapnts	Healthy_Children_Control	Thalassemic_Children	Total	Chi Value	Sig.
		50 (50.0%)	50 (50.0%)	100 (100.0%)		
Father_Education	Illiterate	4(8%)	7(14%)	11(11%)	6.407	0.171
	Less than 5 Years of Education	3(6%)	0(0%)	3(3%)		
	Completed 5-10 Years of Education	19(38%)	26(52%)	45(45%)		
	Completed 12 Years of Education	6(12%)	3(6%)	9(9%)		
	Graduate & Above (15+ Years of Education)	18(36%)	14(28%)	32(32%)		
Mother_Education	Illiterate	5(10%)	8(16%)	13(13%)	2.866	0.581
	Less than 5 Years of Education	5(10%)	2(4%)	7(7%)		
	Completed 5-10 Years of Education	21(42%)	25(50%)	46(46%)		
	Completed 12 Years of Education	8(16%)	7(14%)	15(15%)		
	Graduate & Above (15+ Years of Education)	11(22%)	8(16%)	19(19%)		
Income	<5000	2(4%)	6(12%)	8(8%)	6.043	0.11
	INR 5000-10000	27(54%)	20(40%)	47(47%)		
	INR 10001-15000	14(28%)	10(20%)	24(24%)		
	INR 15000+	7(14%)	14(28%)	21(21%)		
Age_On_diagnosis	<2 years		14(28%)	14(28%)		0.278
	2-4 Years		22(44%)	22(44%)		
	>4 Years		14(28%)	14(28%)		
Transfusion	Monthly		32(64%)	32(64%)		<0.0001
	Once in 2 months		14(28%)	14(28%)		
	Quarterly		4(8%)	4(8%)		
Sibling_Affected	No		41(87.2%)	41(87.2%)		<0.0001
	Yes		6(12.8%)	6(12.8%)		

Table 2. Health Related Quality of Life (HRQoL) mean score s in Thalassemic Children and Healthy Children comparision

	Thalassemic Children (n=50)	Healthy Children Control (n=50)	Sig. (2-tailed)
PhysicalHealth_Summary_Score	62.23±9.426	82.19±6.384	<0.0001
Emotional_Functioning_Score	42.84±12.507	83.9±6.723	<0.0001
Social_Functioning_Score	42.38±10.486	82.6±6.794	<0.0001
School_Functioning_Score	57.5±11.704	81.2±5.764	<0.0001
Psychosocial_Health_Summary_Score	47.57±8.198	82.57±5.03	<0.0001
Health Related Quality of Life (HRQoL) scores in child patients and comparisons within the patients' group (Male and Female)			
	Male	Female	Sig. (2-tailed)
PhysicalHealth_Summary_Score	60.22±8.784	64.77±9.795	0.090
Emotional_Functioning_Score	42.03±10.932	43.86±14.469	0.612
Social_Functioning_Score	41.25±11.517	43.82±9.064	0.396
School_Functioning_Score	55.89±12.327	59.55±10.791	0.278
Psychosocial_Health_Summary_Score	46.39±9.08	49.08±6.824	0.254

Table 3 Association of Father Educational status, Family Income, Age at diagnosis and Blood Trnsfusion frequency of Thalassemic Children with Health well being Scores

	PhysicalHealth_Summary_Score	Emotional_Functioning_Score	Social_Functioning_Score	School_Functioning_Score	Psychosocial_Health_Summary_Score
Father Educational Status					
Illiterate	55.8±8.156	33.57±4.756	39.29±7.319	48.57±6.268	40.48±2.838
Completed 5-10 Years of Education	59.93±8.605	42.38±12.034	42.65±9.029	59.23±10.459	48.09±5.967
Completed 12 Years of Education	72.92±7.217	46.67±20.817	46.67±20.817	56.67±20.817	50±20.273
Graduate & Above (15+ Years of Education)	67.41±8.104	47.5±12.672	42.5±12.519	58.93±13.035	49.64±9.18
F	5.475	2.182	0.362	1.691	2.346
Sig	0.003	0.103	0.781	0.182	0.085
Family Income					
<5000	53.64±7.241	37.5±9.874	38.17±5.492	55±10	43.56±5.062
INR 5000-10000	60.25±9.342	40.25±12.083	43.25±9.358	56.75±12.802	46.75±7.344
INR 10001-15000	66.56±9.552	46±14.103	38±8.882	56.5±8.835	46.83±6.208
INR 15000+	65.63±7.556	46.56±12.451	46.07±13.471	60.36±13.077	51±10.789
F	3.829	1.299	1.583	0.406	1.424
Sig	0.016	0.286	0.206	0.75	0.248
Age at Diagnosis					
<2 years	60.71±9.706	40.36±10.645	43.57±10.995	52.86±10.869	45.6±6.524
2-4 Years	61.79±9.973	43.04±13.521	41.36±11.253	60.45±12.239	48.28±9.424
>4 Years	64.42±8.486	45±13.009	42.79±9.25	57.5±10.875	48.43±7.837
F	0.573	0.477	0.198	1.866	0.556
Sig	0.568	0.624	0.821	0.166	0.577

Blood Transfusion Status					
Monthly	61.13±7.936	40.06±9.011	41.88±10.06	55.62±11.412	45.85±5.969
Once in 2 months	62.41±10.549	43.57±13.788	39.93±5.69	58.21±10.85	47.24±7.123
Quarterly	70.31±14.768	62.5±17.078	55±19.149	70±11.547	62.5±13.438
F	1.741	7.22	3.679	2.932	10.061
Sig	0.186	0.002	0.033	0.063	0.000
Sibling Affected					
Sibling Affected	63.8±9.297	43.46±13.301	43.29±11.159	56.71±12.279	47.82±8.935
Sibling Not Affected	55.52±8.058	42.5±8.803	37.33±5.538	58.33±8.165	46.06±4.031
t	2.064	0.17	1.276	-0.313	0.473
sig	0.045	0.866	0.208	0.756	0.638

Table 4 Shows the comparison of the findings of this study with the other previously conducted studies

Study	Country (n)	Physical Functioning	Emotional Functioning	Social Functioning	School Functioning
Ismail *et al*, (2006)	Malaysia (n=78)	69.1±16.4	68.1±17.2	74.3±18.7	60.1±16.4
Cheuk *et al*. (2008)	Hong Kong (n=25)	66.7±16.0	60.8±17.1	82.5±17.7	75.4±19.5
Clarke *et al*. (2009)	United Kingdom (n=22)	66.5±21.8	73.6±22.7	77.6±19.9	60.9±27.5
ThavorncharoensaP*et al*. (2010)	Thailand (n=315)	78.2±14.8	75.9±16.6	83.7±14.7	67.9±15.9
Gharaibeh*et al*. (2011)	Jordan (n=128)	54.2±15.1	62.4±23.3	73.3±20.9	46.7±21.1
Caocci *et al*(2012)	Middle East (n=60)	68.4±27.2	76.9±24.6	76.4±20.6	69.4±21.4
Present Study, (2016)	Dibrugarh, India (n=50)	62.22±9.43	42.84±12.51	42.38±10.49	57.5±11.7

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