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Impact of consanguineous marriages on thalassemia in Warangal urban and Mahabubabad districts of Telangana state

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Abstract
Hemoglobinopathies includes sickcle cell anemia and thalassemia. Thalassemia is a disorder affecting the structure, function and production of Hb. Mutation in globin genes is the main cause for thalassemia[1]. In the present research work, 275 children, aged 3 - 15 years were evaluated in Warangal Urban district and Mahabubabad district during the period February 2017 to November 2017. The blood samples of 275children were collected for the assessment of thalassemia. Few parameters like age, gender, social status and family history of their parents have been recorded. In the present research study we identified 29 children as thalassemia patients. Out of these 29 thalassemia patients we found 17 children born of consanguineous marriage of their parents. The results represented that one of the main impact factor of thalassemia disorder is consanguineous marriages between their parents. The aim of the present study was to evaluate the prevalence of thalassemia and to assess the effect of consanguineous marriages on the occurrence of thalassemia in Warangal Urban and Mahabubabad districts of Telangana state.

Keywords: hemoglobinopathies, thalassemia, sickcle cell anemia, consanguineous marriages, Warangal urban district and Mahabubabad district

Introduction
Hemoglobinopathies represents a significant national health burden [2]. Major concerned hemoglobinopathic disorders are Sickle cell anemia and Thalassemia. Of the total world thalassemia percentage, 10% thalassemia patients are born in India [3]. Thalassemia is inherited autosomal and causes a serious health problem. Thalassemia is a disease caused by abnormal hemoglobin chain [4].

The thalassemia is classified into α-thalassemia and β-thalassemia [5]. β-thalassemia has three phases, β-thalassemia minor (β-thalassemia trait or Carrier state), β-thalassemia intermedia and β-thalassemia major (Cooley's anemia). B-thalassemia major is severe form of thalassemia**.** In α-thalassemia, production of α -globin chain is affected on Chromosome 16, while in β-thalassemia production of β-globin peptide chain is affected on Chromosome 11 [6]. When parents have no defect in globin genes then there is no chance of being thalassemia in children. If one of the parents is affected or is carrier, then there is a chance of being thalassemia carriers. When both parents are carriers, then 25% children will be normal, 25% will be thalassemic and remaining 50% will be the carriers [7].

In Warangal urban and Mahabubabad districts of Telangana state, different communities are distributed. Several studies on distribution of thalassemia among the various communities are available, but there is no comprehensive data available on the interaction of thalassemia and abnormal hemoglobins [8]. Consanguineous marriages are most common and preferable custom of marriage among different communities. Earlier reports have shown that there is high correlation between consanguineous marriages and inherited congenital malformation [9]. The present study was conducted to identify the most common factor behind thalassemia disorder and also to bring awareness among people to prevent consanguineous marriages.

Materials & Methods
In our study, we screened randomly selected 275 childrens from 2 Mandals (Hanamkonda & Warangal) of Warangal Urban district and 4 Mandals (Gudur, Kesamudram, Mahabuhabad and Kuravi) of Mahabubabad district of Telangana State to assess thalassemia. Few parameters like age, Father Name, gender, social status and family history etc have been taken from these children. Thalassemia can be diagnosed via complete blood count (CBC). 2-3ml of venous blood was collected in centrifuged tubes containing EDTA as anticoagulant. The hemotology analyzer (Sysmex Corporation, Kobe, Japan) was used to determine RBC count, PCV values and Hb percentage. Erythrocytes indices (MCV, MCH & MCHC) were determined from the values of RBC count, Hemoglobin concentration and PCV values. Any increase or decrease in the results may indicate that it requires further evaluation. A low MCV is often the first indication of thalassemia. If the MCV is low and iron deficiency has been ruled out as a cause, then it should be considered as thalassemia. If the MCV less, it would be further screened using Naked Eye Single Tube Red Cell Osmotic Fragility Test (NESTROFT) [10]. The person who shows positive for

NESTROFT would be checked for HbA2 level using HPLC or Hb electrophoresis. Hemoglobin A_2 levels were estimated by elution [11]. The results were analyzed statistically.

Results

In our present research work the hematological investigations revealed that out of 275 children 226 were normal, while 49 children were suspected to have mutant allele for thalassemia. The results demonstrated that the Hb levels, MCH and MCV levels were low in only 49 children when compared with 226 children. These 49 children had RBC count, HB level, PCV value, MCH and MCV levels in between 4.13 ± 1.93 ($\times 10^6$/cmm), 08.05 ± 3.65 (g/dL), 30.85 ± 2.93 (%), 20.13 ± 1.31 (pg) and 69.81 ± 3.86 (fl) respectively. No significant differences were observed in the mean value of MCHC among these 275 children (Table-1).

The blood sample of 49 children who has low hematological parameters can be further screened using NESTROFT method. The back ground information of the thalassemia children such as name, age, gender, native place and family pedigree is summarized. Only 32 blood samples out of 48 gave positive with NESTROFT, while 17 gave negative results (Table -2). Out of these 32 NESTROFT positive blood samples, 29 samples had HbA_2 levels more than 3.5%. The remaining 3 blood samples were false positive since HbA_2 levels were less than 3.5% (Table-3).

Our research work evaluated that out of these 29 thalassemia children, 17 of them (58.62%) were born due to consanguineous marriage (Table -4). The tables 4&5 reported a significant impact of consanguineous marriages on thalassemia disorder.

Discussion

Warangal Urban and Mahabubabad districts are new districts in Telangana state, with different religions which are divided into many castes. Though the rural people constitute a major part of these districts, unfortunately they are highly vulnerable to many heridatory disorders causing high degree of morbidity and mortality. In Warangal Urban and Mahabubabad districts, many diseases are passed on from parents to their children through genes, Thalassemia is one of them. Thalassemia found in all villages of Warangal Urban and Mahabubabad districts. But the prevalence is various from village to village and community to community. In these districts, more consanguineous marriages are taking place but pre marital check up is not under process, which leads to many disorders.

Thalassemia is a common haemoglobinopathy in India as per WHO records [12]. People will not get symptoms of the genetic condition out of one of their genes have mutations [13]. It is a most common blood born single gene disorder which can be transmitted from parents to their children [14]. Thalassemia arises from deletion or mutation in globin genes and it leads to reduction in the production of hemoglobin [15]. Thalassemia patients are not able to make enough hemoglobin which causes anemia [16].

Thalassemia patients suffers from pale skin, headache [17], enlarged liver and spleen [18], Dark urine, Feeling tired, lack of proper growth [19], frequent vulnerability of Jaundice [20], High susceptible to various infections and lack of blood mainly red blood cells which causes high degree of hemolytic anemia [21].

A complete hemogram of an individual will help to detect the β-thalassemia minor, β-thalassemia intermedia and β-thalassemia major. β-thalassemia minor persons look normal, so it is very difficult to detect. But β-thalassemia intermedia and β-thalassemia major can be easily detected and these persons will show some abnormalities. While α -Thalassemia is quite rare in the population, β -Thalassemia prevalence varies 5-15% across India [22].

The prevalence of thalassemia disorder was evaluated by Grow *et al.,* (2014) [2] and Naskar *et al.,* (2015) [23]. Haritha *et al.,* (2012) [8] showed that the thalassemia mutation prevalence among the konda kammaras in vishakapatnam of Andhra Pradesh. Murali *et al.,* (2004) [24] have investigated the prevalence of different mutations in Hyderabad, Nalgonda and Adilabad districts of AndhraPradesh.

During the study period a total 275 children were screened among them 226 were normal, where as 29 children were detected as thalassemia patients. In the present study we found 17 children born of consanguineous marriage out of these 29 thalassemia patients. The tables 4 & 5 demonstrated that the impact of consanguineous marriages on the prevalence of thalassemia. Consanguinity is the main cause to spread the disease [25]. The high mortality rate in developing countries, associated with consanguinity, largely occurs within the first year of birth [26]. Several deaths have also been reported in a proportion of consanguineous families in developing countries [27]. The prevention of thalassemia can be done by increasing the awareness camp, community education and awareness at school level. The prevention and control of thalassemia is more important to reduce the prevalence of this disorder. The main effect of consanguineous marriages is an elevation in the rate for homozygotes in recessive disorders [28, 29].

On the basis of our results, it is highly recommended to prevent the consanguineous marriages. Traditional consanguineous marriages should be avoided. Several studies have also explained about the influence of consanguineous marriages on thalassemia disease. Our results agree with those of Sengupta M. (2007) [30] and Naibkhil & Chitkara (2016) [31], who found that consanguineous marriages play a key role on thalassemia disorder.

Conclusion

Thalassemia is a genetic disorder and it is not easy to control but it can be reduced. A prevention program on thalassemia including health education must be planned and carried out. It is important for couples who are blood relatives and thinking about becoming parents to seek genetic counseling. The prevention of thalassemia disease can be down through discouraging the consanguineous marriages among the people.

Table 1: Various hematological parameters of Warangal Urban and Mahabubabad Districts children (Mean ± SD).

Hematological Parameters	No. of Children	
	226	49
RBC ($\times 10^6$/cmm)	4.55 ± 1.29	4.13 ± 1.93
Hb (g/dL)	13.81 ± 3.77	08.05 ± 3.65
PCV (%)	37.64 ± 1.86	30.85 ± 2.93
MCH (pg)	28.32 ± 4.52	20.13 ± 1.31
MCV (fl)	82.41 ± 4.79	69.81 ± 3.86
MCHC (g/dl)	31.19 ± 2.66	30.25 ± 2.73

Table 2: NESTROFT screening test in 48 children, who has low hematological parameters.

No. of Children	NESTROFT Positive	NESTROFT Negative
49	32	17

Table 3: HbA_2 levels in Warangal Urban & Mahabubabad Districts children.

No. of Children	HbA_2 value range	
	More than 3.5%	Less than 3.5%
32	29	03

Table 4: Effect of Consanguinity on thalassemia Disorder in Warangal Urban and Mahabubabad districts.

Districts	Mandal	Thalassemia Children		Percentage (%)
		Total	Consanguinity	
Warangal Urban	Warangal	8	4	58.62%
	Hanamkonda	5	3	
Mahabubabad	Gudur	9	5	
	Kuravi	2	1	
	Kesamudram	3	2	
	Mahabubabad	2	2	
Total		29	17	

Table 5: Analysis of Mahabubabad and Warangal Urban Districts thalassemia patients.

S. No.	Di	Name	G	AGE In Years	Village/Street	MND	SS	BG	CNG
1	Mahabubabad District	Shiva Charani	F	6	Gundenga	GDR	SC	A^{+Ve}	Yes
2		G. Rajesh	M	12	Ma'Puram	GDR	ST	B^{+Ve}	No
3		G. Prasad	M	11	Ma'Puram	GDR	ST	B^{+Ve}	No
4		Harika	F	13	Bollepallay	GDR	ST	B^{+Ve}	Yes
5		P. Raj Kumar	M	7	Ponagodi	GDR	OBC	B^{+Ve}	Yes
6		M. Yashwanth	M	4	Machala	GDR	ST	A^{+Ve}	No
7		M. Devender	M	12	SureshNagar	GDR	ST	B^{+Ve}	Yes
8		Akshaya	F	4	Guduru	GDR	SC	A^{+Ve}	Yes
9		Varun Akash	M	7	Ap'pally	GDR	SC	O^{+Ve}	No
10		G. Nithin	M	7	Inugurthy	KSM	ST	O^{+Ve}	No
11		Sangam Sidhu	M	12	Kesamdrm	KSM	OBC	A^{+Ve}	Yes
12		G. HariRam	M	12	Dh'tanda	KSM	ST	A^{+Ve}	Yes
13		B. Rishikesh	M	9	Mah'bad	MBD	OBC	A^{+Ve}	Yes
14		Hanumanthu	M	14	Mallela	MBD	ST	A^{+Ve}	Yes
15		P. Blessi	F	13	Kuravi	KRV	SC	O^{+Ve}	Yes
16		J. Tarun Tej	M	9	Nereda	KRV	SC	O^{+Ve}	No
17	Warangal Urban District	Keerthana Sai	M	8	Amb'Street	HNK	SC	AB^{+Ve}	No
18		Imran Ahmed	M	14	L'Singaram	HNK	OC	O^{+Ve}	Yes
19		Tarana Begum	F	14	Gudbandal	HNK	OC	A^{+Ve}	No
20		Hemanthi	F	03	Ash'Colony	HNK	SC	AB^{+Ve}	Yes
21		G. Nandu	M	9	Madikonda	HNK	SC	O^{+Ve}	Yes
22		Md. Asif	M	10	Chintal	WGL	OC	A^{+Ve}	No
23		B. Avinash	M	10	LB Nagar	WGL	SC	O^{+Ve}	No
24		SK. Roshan	M	10	Doc'Colony	WGL	OBC	AB^{+Ve}	No
25		K. Milind	M	7	Ped'gadda	WGL	SC	A^{+Ve}	Yes
26		K. Tirupathi	M	11	Lash'pally	WGL	SC	B^{+Ve}	Yes
27		S. Yuga	M	11	Nallabelli	WGL	OBC	O^{+Ve}	Yes
28		Jiddi Chitti	F	8	Nallabelli	WGL	SC	A^{+Ve}	Yes
29		VenkatRamana	M	13	Nars'peta	WGL	OC	O^{+Ve}	No

Di -District
BG -Blood Group
G –Gender
CNG –Consanguinity

SS –Social Status
BG -Blood Group
WGL -Warangal
HNK -Hanamkonda

GDR -Gudur
KSM -Kesamudram
MBD -Mahabuhabad
KRV -Kuravi

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