

# Burden of Hemoglobinopathies in West Bengal; the Future Scenario of Care & Control

Prakas Kumar Mandal

## ABSTRACT

As per 2011 census in India, population of West Bengal was 9.13 crore. The state has a relatively higher burden of thalassemia; it was reported that around 6-10% of the population are carriers of the disease. Current effort is to know the actual burden of thalassemia and other hemoglobinopathies in different areas of West Bengal. An electronic search was done on thalassemia and other hemoglobinopathies for published literature in different data bases; all the titles available in 'English' were screened for. There were many publications in both rural and urban population on spectrum and distribution of hemoglobinopathies from different districts of West Bengal; most are based on hospital based studies. In search of the actual burden of the disease, I had chosen mainly community based studies reflecting the rural population and also few hospital based studies with large population. The results from such published reports from different districts were analyzed. Hemoglobinopathies are an important public health problem in multiethnic Bengali population. Adequate care of the affected patients requires proper diagnostic and therapeutic measures. Emphasis on an integrated comprehensive approach with special attention on prevention of hemoglobinopathies is the key to successful implementation of a control programme.

**Keywords:** Hemoglobinopathies, West Bengal, Future Direction

## INTRODUCTION

As per 2011 census in India, population of West Bengal was 9.13 crore, which is around 7.6% of the total population (121.02 crore) of the country.<sup>1</sup> The state has a relatively higher burden of thalassemia; it is estimated that around 6-10% (in absence of proper survey actual level of incidence cannot be correctly guessed) of the population are carriers of the disease and they live normal life without any physical problem arising out of that.<sup>2</sup> Marriage of two such individuals may lead to birth of a thalassaemic child; thalassemia can be eradicated by avoiding marriage between two carriers. The immediate task is to arrange for pre-marriage counseling. Moreover, couples who are at-risk of having children with hemoglobin disorders may voluntarily choose the option of avoiding the birth of an affected child by prenatal diagnosis. Thus, the prenatal women (PNW) are very important target group for carrier screening to prevent the birth of a thalassaemic child. Population in West Bengal is not a homogenous group; different geographic regions of West Bengal have subtle as well as more pronounced variations between each other, showing particularly different socio-cultural aspects. Overall outcome of thalassemia counseling depends on the attributes that include level of education (no education vs.

primary/secondary/higher education), work status (not working and have paid job), place of residence (urban and rural), religion and socio-economic status.<sup>3,4</sup> A national multi-centric Task Force Study of the Indian Council of Medical Research (from 2000 to 2005) for thalassemia screening showed the carrier rate of 3.1% for  $\beta$ -thalassaemia and 4.1% for Hb E from Kolkata, West Bengal.<sup>5</sup> In another city-based study by Mohanty D et al<sup>6</sup>, it has ranged from 4 to 10%; showing significant regional variations. The West Bengal State Thalassemia Control Programme (STCP) involves two nodal centers in Kolkata (Nilratan Sircar Medical College and Institute Of Hematology & Transfusion Medicine) with 34 thalassemia care units (TCUs) in different districts and sub-divisions; 17 TCUs under each nodal center. Awareness, screening and counseling is being done and several reports have been published on the prevalence of  $\beta$  thalassemia, HbE and other hemoglobinopathies in both urban and rural areas. Current effort is to know the burden of thalassemia and other hemoglobinopathies and also the related management issues in different districts of West Bengal.

## METHODS

An electronic search was done on thalassemia and other hemoglobinopathies for published literature in PubMed, Medline, Google scholar, Index Copernicus, Directory of open access journals (DOAJ) and other data bases. The search was focused on 'thalassaemia', 'hemoglobinopathy', 'population screening', 'prenatal diagnosis', 'West Bengal', 'Eastern India'. All the titles and abstracts with full article available till June, 2020 in 'English' were screened for published literature 'on thalassemia and other hemoglobinopathies' from this eastern state (West Bengal) of India (figure 1). There were many publications on large population screening in both rural and urban areas from different districts of West Bengal. Few other studies with small number of cases also found from different private and corporate laboratories mainly based on urban population. To study the burden of thalassemia and other hemoglobinopathies in West Bengal, we reviewed the articles with large number of cases of population screening

Associate Professor, Department of Hematology, NRS Medical College, Kolkata-700014, India.

**Corresponding author:** Dr. Prakas Kumar Mandal, Department of Hematology, NRS Medical College; 138, AJC Bose Road; Kolkata-700014, India

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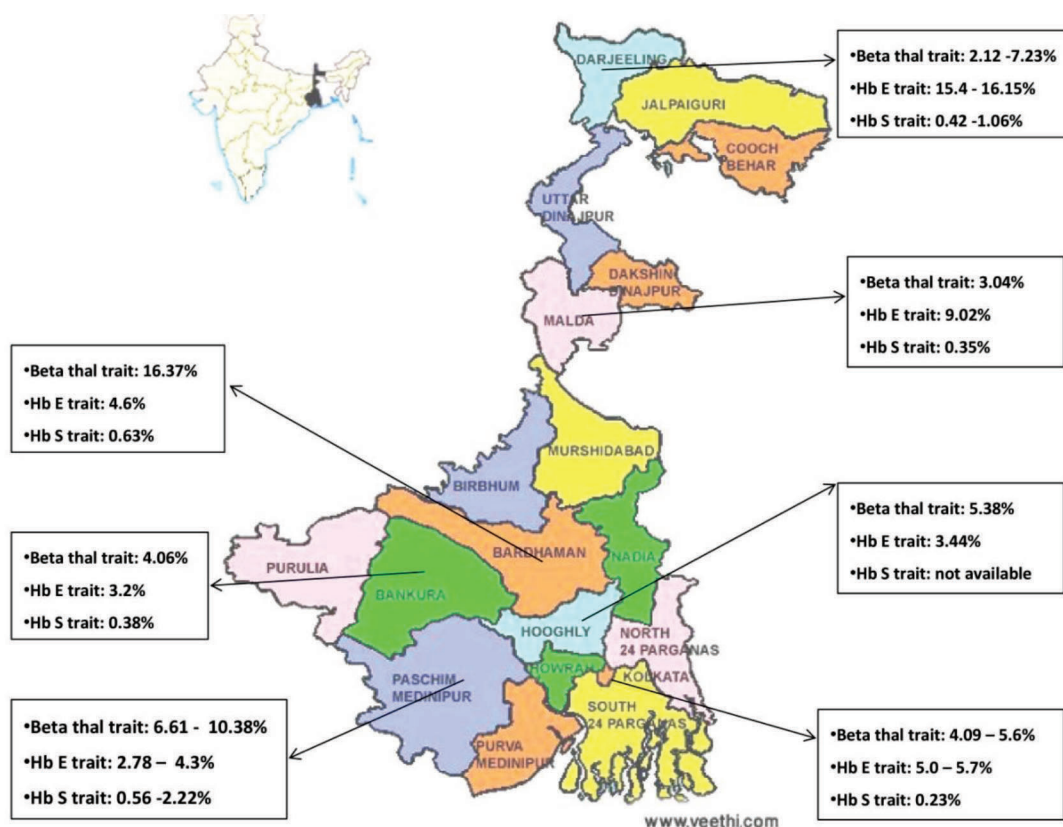
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Name of the study	Study period	Name of the district	Total no. of screening	Abnormal Hb	Beta thalassemia major	Hb E-Beta thalassemia	Hb EF disease	Hb S-Beta thalassemia	Sickle cell disease	Beta thalassemia trait	Hb E trait	Hb D trait	Hb S trait	Hb Lepore trait	HPFH	Others
Goswami BK et al <sup>20</sup>	2010	Six districts of North Bengal	1872	47.5%	0.67%	7.15%	11.9%	1.41%	0.94%	7.23%	16.15%	0.37%	0.42%	0.94%	NA	0.32%
Ghosh N et al <sup>19</sup>	2011	Darjeeling	188 (PNW)	26.6%	NA	0.53%	6.91%	NA	NA	2.12%	15.4%	NA	1.06%	NA	NA	0.53%
Naskar S et al <sup>22</sup>	2012-2013	Malda	5156	12.88%	0.02%	0.62%	1.96%	NA	NA	3.04%	9.02%		0.35%			0.47%
Mondal SK et al <sup>23</sup>	2005-2015	Bankura	119,336	12.17%	1.66%	1.16%	0.34%	0.26%	0.32%	4.60%	3.02%	0.09%	0.38%	0.004%	0.12%	0.21%
Jain BB et al <sup>21</sup>	2006-2009	Burdwan	3823	29.3%	0.03%	3.5%	0.18%	0.30%	0.15%	16.37%	4.60%	0.10%	0.63%	NA	0.21%	3.2%
Bhattacharyya KK et al <sup>27</sup>	2012-2015	Hooghly	21,137	13.1%	0.28%	0.49%	NA	NA	NA	5.38%	3.44%	NA	NA	NA	NA	2.64%
Choudhuri S et al <sup>14</sup>	2009-2012	Kolkata	20,883 (PNW)	10.5%	NA	0.09%	NA	NA	NA	4.09%	5.7%		0.23%	NA	NA	0.36%
Mukhopadhyay D et al <sup>28</sup>	2010-2013	Kolkata	10,407	14.5%	NA	NA	NA	NA	NA	5.6%	5.0%	NA	NA	NA	NA	3.9%
Dolai TK et al <sup>24</sup>	2007-2011	Paschim Medinipore	35413	16.23%	NA	NA	NA	NA	NA	10.38%	4.30%	0.37%	1.12%	NA	NA	0.06%
Mandal PK et al <sup>25</sup>	2010-2013	Paschim Medinipore	50487	11.62%	0.73%	0.42%	0.05%	0.15%	NA	6.61%	2.78%	0.21%	0.56%	NA	0.07%	0.03%
Chattopadhyay P et al <sup>26</sup>	2017-2019	Paschim Medinipore	903 (PNW)	13.68%	NR	0.33%	0.33%	0.11%	0.33%	8.34%	1.56%	0.11%	2.22%	NR	0.33%	0.13%

NA= data not available; HPFH- hereditary persistence of fetal hemoglobin, PNW=prenatal women,

**Table-1:** District wise distribution of hemoglobinopathies in West Bengal



**Figure-1:** Distribution of carrier states of the three common hemoglobinopathies in West Bengal (in cases where more than one study reports available from the same district the results are expressed as range) [map of West Bengal available from- [www.veethi.com](http://www.veethi.com)]

from published literature from different districts that may actually reflect the heterogenous population from different socio-economic status. Besides this, few other available publications on different aspects of thalassemia management are also systematically reviewed here.

## RESULTS

The results from published reports from different districts are presented in table 1. Three most common carrier states revealed in the review had shown wide range of variation among studies from different districts; plotted in figure 1. The detection rate of abnormal hemoglobins in the population ranged from 10.5% in Kolkata to 47.5% in northern districts of West Bengal. Few other studies also found on different aspects of complications of iron to overload and different modalities of thalassemia management available in this part of the country.

## DISCUSSION

By far, the inherited disorders of hemoglobin are the most common monogenic diseases worldwide.<sup>7</sup> Approximately 7% of the world's populations are being carriers of some or other form of hemoglobinopathies, these are one of the major health problems worldwide.<sup>8</sup> During the seven decades since Haldane<sup>9</sup> first proposed the malaria hypothesis, evidence has steadily grown to confirm malaria as primary force behind high frequency of inherited hemoglobin disorders seen in many tropical and sub-tropical countries. The molecular defects that result in the thalassemias are extremely diverse, having arisen separately and been locally amplified, in

multiple populations throughout the malaria-endemic regions of the world.<sup>7</sup> Thalassemia and other hemoglobinopathies is a major public health problem in West Bengal, India. Reports published by Mohanti D et al<sup>5</sup> in 2008 showed carrier rate for b-thalassemia and HbE in West Bengal were 3.1% and 4.1% respectively; very high prevalence (22%) of HbE reported from Kolkata,<sup>10</sup> the capital city of West Bengal. Since the classic description of hemoglobin E in 1954 by Chernoff et al,<sup>11</sup> it has been found to be an important public health problem in the Indian subcontinent and Southeast Asia. The first case of Hb E/b-thalassemia in India was reported by Chatterjea JB et al<sup>12</sup> from Calcutta (now Kolkata). Hb E-beta thalassemia is the predominant symptom producing thalassemia in this part of the country.<sup>13</sup> Most centers in West Bengal reporting the carrier frequencies of b thalassemia, Hb E and other hemoglobinopathies now use CBC and HPLC analysis of hemoglobins.<sup>14</sup> Years back, the Naked Eye Single Tube Red Cell Osmotic Fragility Test [NESTROFT], a rapid screening test was largely being used as a first approach for detection of  $\beta$ -thalassaemia trait.<sup>15</sup> Hemoglobin (cellulose acetate) electrophoresis or isoelectric focusing (IEF) are still performed in many laboratories.<sup>16</sup> With the advent and wide availability of high throughput methods such as cation-exchange high performance liquid chromatography [CE-HPLC] or more recently capillary electrophoresis [CE] are generally employed.<sup>17,18</sup> At present in all TCUs in West Bengal, HPLC [VARIANT-II™ beta short program (Bio-Rad Laboratories, Hercules, CA, USA)] is used for diagnosis of beta thalassemia, HbE, Hb S and also

other hemoglobinopathies. It gives reliable and reproducible results, but it is costlier, needs expertise personnel and well equipped laboratory set up and thus not available for population screening at the remotest village areas. In search of a screening test which is much cheaper, easy to perform, requires less expertise and can be done at the community level (primary health center level also), Mandal PK et al<sup>13</sup> very recently studied Dichlorophenolindolphenol (DCIP) test to detect Hb E; concluded that it is a simple, easy to perform and cost effective method for detecting HbE and can be used in rural areas in a population with high prevalence with access to limited health care facilities.

### **Why it is important to know the burden of thalassemia and haemoglobinopathies in West Bengal?**

The answer lies in deciding whether to provide haemoglobinopathy care only in the urban based areas or whether it should be broad-based across the length and breadth of the state. The detection rate of abnormal hemoglobins in the population ranged from 10.5% to 47.5%.

### **Prevalence of carriers/traits**

As shown in table 1 from studies in different districts of West Bengal, the prevalence of disease burden and heterozygous/carrier states for abnormal hemoglobins are not the same in all areas; even there is gross variations in different published reports from same geographic region (district).

**Beta thalassemia trait** -The beta thalassemia carrier rate ranged from 2.12% to 16.37%. The lowest rate of 2.12% was reported by Ghosh N et al<sup>19</sup> based on a study in a small population of antenatal mothers from rural areas of Darjeeling District. But, another study by Goswami BK et al<sup>20</sup> from North Bengal, comprising of six districts, i.e. Darjeeling, Jalpaiguri, Coochbehar, North Dinajpur, South Dinajpur and Malda had shown a carrier frequency of 7.23% for beta thalassemia trait. The highest reported rate of 16.37% was from Burdwan district by Jain BB et al.<sup>21</sup> Naskar S et al<sup>22</sup> and Mondal SK et al<sup>23</sup> from the districts of Malda and Bankura district reported prevalence of 3.04% and 4.6% respectively. Studies by Dolai TK et al,<sup>24</sup> Mandal PK et al,<sup>25</sup> and Chattopadhyay P et al<sup>26</sup> from PaschimMediniporedistrict, situated in the western part of the state, revealed carrier rate of 10.38%, 6.38% and 8.34% respectively; thus showing a gross difference in these three reports from the same geographic area. Bhattacharyya KK et al<sup>27</sup> from Hooghly district reported an incidence of 5.38%. Whereas studies by Choudhuri S et al<sup>14</sup> and Mukhopadhyay D et al<sup>28</sup> from Kolkata, capital city of West Bengal reported the incidence of beta thalassemia trait of 4.09% and 5.6% respectively. These data overall reflects that the incidence of beta thalassemia trait is much higher in the population from southern and western part of the state in comparison to the northern districts.

**Hb E trait**-The reported incidence of Hb E trait from different districts ranged from 1.56% to 16.15%; the lowest and highest rate was reported by Chattopadhyay P et al<sup>26</sup> and Goswami BK et al<sup>20</sup> from PaschimMedinipore district and the six districts of northBengal respectively. Reports

by Ghosh N et al<sup>19</sup> and Naskar S et al<sup>22</sup> from the districts of Darjeeling and Malda had also shown higher incidence of Hb E trait of 15.4% and 9.02% respectively. In contrast, the incidence was much lower from the districts situated in the southern part of the state as reported by Bhattacharyya KK et al<sup>27</sup>, Mondal SK et al<sup>23</sup> and Chattopadhyay P et al<sup>26</sup> from the districts of Hooghly (3.44%), Bankura (3.02%) and Paschim Medinipore (1.56%) respectively. Thus, the available published data clearly indicates that, incidence of Hb E trait is much higher in northern districts of West Bengal as compared to that from southern and western parts.

**Hb S, Hb D and other rarertraits-** The reported incidence of HbS trait in larger population based studies were high in the districts of Paschim Medinipore (2.22%). Higher incidence (0.37%) of HbD trait reported by Dolai TK et al<sup>24</sup> and Goswami BK et al<sup>20</sup> from the districts of Paschim Medinipore and north Bengal. Hb Lepore trait was found in 0.94% cases in the study from northern districts and highest (0.21%) prevalence of HbFH reported from Burdwan district.<sup>20,21</sup> Among many other rarer variants of hemoglobins, HbQ India, HbJ Meerut, HbJ Bangkok and other rarer entities reported in very small proportions from different studies.

It is now well evident that a study done in urban population (city or district town) differs from the reports done on a rural population or mixed urban/rural population.

### **Burden of homozygous and compound heterozygous states:**

They are mostly diagnosed at the district level and tertiary level hospital/Medical Colleges. Because of availability of screening centers at the community level now, many of them who are showing early symptoms at a very early age group are being detected there. The prevalence of beta thalassemia major ranged from 0.28% to 1.66%; the highest rate was reported from Bankura district.<sup>23</sup> The prevalence of HbEE disease ranges from 0.05% in Paschim Medinipore district to as high as 11.95% from the northern districts of the state.<sup>20,25</sup> The highest (0.94%) prevalence of sickle cell disease was reported by Goswami BK et al<sup>20</sup> from north Bengal. Among the compound heterozygotes, Hb E-Beta thalassemia was more prevalent in this part of the country in comparison to beta thalassemia major; the prevalence rate ranged from 0.09% in Kolkata to as high as 7.15% in north Bengal.<sup>20,28</sup> Hb S-Beta thalassemia, another clinically significant thalassemia was also reported by many of the studies; prevalence ranged from 0.15% in Paschim Medinipore to 1.14% in north Bengal.<sup>20,25</sup> It is obvious from (table 1) that, the different proportions of homozygous and compound heterozygous states corroborated with the prevalence of different traits present in the community. And in another recently published hospital-based study on prevalence of different hematological diseases in a tertiary hematology care center in Kolkata, Jitani et al<sup>29</sup> reported 3868 cases of hemoglobinopathy of which HbE beta thalassemia, beta thalassemia major and Hb EE disease was seen in 34.08%, 18.67% and 7.88% cases respectively. These results are an indication of gross discrepancies in prevalence rate of any



disease between hospital-based and community level studies and imply the importance of studying any disease at the community level with large population that actually reflects the real scenario. There are very occasional published reports on growth, pubertal development and endocrinal function in thalassaemic children. Baul et al<sup>30</sup> studied the relationship between thyroid dysfunction and iron overload in HbE  $\beta$ -thalassaemia and concluded that prevalence of thyroid dysfunction was found to be higher in HbE $\beta$ -thalassaemia patients. Saha R et al<sup>31</sup> studied Bengali Thalassaemic Children on quality of life of in terms of school functioning activity and remarked that the patient's quality of life as well their school functioning activity affected very badly. Activity in school is considered as an important yardstick for their quality of life; they should be properly educated in order to make their social identity and to confront with every situation in life, like ignorance etc.

### Management issues

The management of thalassemia involves a multidisciplinary team approach and preferably be done at a comprehensive thalassemia care center with the backup of a well-equipped blood bank. However, in resource constraints situation all these facilities are not available everywhere; regular blood transfusion is the only choice left to innumerable thalassaemic children. Only selected aspects of the management are discussed below.

- 1. Blood transfusions-** This is the most important component of thalassemia care; in the initial years the major problem was to obtain blood for transfusions.<sup>32</sup> With the active intervention at the Government level in the availability of blood products, this is not a problem now excepting in situations where voluntary blood donations are less due to some or other reasons. Bhattacharya N et al<sup>33</sup> from Kolkata in 2001 reported use of umbilical cord blood to transfuse patients with thalassaemia major, as a rich source of fetal hemoglobin. The two thalassemia nodal centers in Kolkata are now having the facility of extended blood group antigens and also antibody screening.
- 2. Iron chelation therapy-** The idea is to remove the excess iron in the body resulting from repeated blood transfusions and/or excess iron absorption. In the early years deferoxamine injection (DFO) was the only iron chelator available given over many hours using a (very expensive) pump leading to poor compliance in majority cases. Oral iron chelator deferiprone was approved for use in India in 1994 which is known to cause agranulocytosis in many patients and requires frequent monitoring; then came the effective oral alternative Deferasirox. Not much published data available on use and experience of iron chelation therapy in West Bengal. Mandal PK et al<sup>34</sup> in 2014 reported small number of patients on iron chelation therapy; started in 66.67% of patients who were planned for chelation therapy but majority (52.7%) stopped it on their own mostly because of prohibitive cost issue. Baul S et al<sup>30</sup> in 2019 reported a small group of patients with iron overload where 80% of them were on regular iron chelation therapy with Deferasirox. Improvement in care in respect to iron chelation therapy over years made possible because of the free availability of Deferasirox in all the TCUs in West Bengal since last few years (personal communication).
- 3. Modifiers of fetal hemoglobin (HbF)** – Pharmacological agents such as hydroxyurea (HU) have been known to cause induction of foetal haemoglobin and reduce ineffective erythropoiesis.<sup>32</sup> Bohara VV et al<sup>35</sup> from IHTM, Kolkata in their study in Hb E beta thalassemia (phenotypically thalassemia intermedia) patients used HU in the dose of no more than 10 mg/kg/day showed increase in baseline Hb level with subjective improvement in the patients' symptoms with adverse effects such as nausea, abdominal pain that were self limiting and did not require dose interruption or modification. Sen A et al<sup>36</sup> from NRS Medical College & Hospital, Kolkata very recently reported the efficacy and safety of thalidomide in HbE beta thalassemia; patients received Thalidomide 50mg/day orally with definite increase in Hb levels is seen in 3 months among majority (76.9%) of patients. Nag A et al<sup>37</sup> used thalidomide in HU refractory Transfusion-Dependent HbE-Beta thalassemia Patients; 71.4% attained transfusion independence (complete responders), many attended response within 1 month. They didn't report any grade 3/4 toxicities with thalidomide.
- 4. Splenectomy-** Mandal PK et al<sup>34</sup> from Kolkata reported the profile of HbE  $\beta$ -thalassaemia patients after splenectomy. Out of 1380 E $\beta$ -thalassaemia patients, 72 (5.22%) underwent splenectomy; the reported leading cause (51.39%) was mechanical discomfort. Mean transfusion requirement reduced from 18.1 to 7.8 units/year. Ghosal T et al<sup>38</sup> studied platelet aggregation in both splenectomized and non-splenectomized patients; splenectomized patients had higher platelet aggregation than non-splenectomized patients; confirms a role of splenic absence in platelet hyperaggregation.
- 5. Stem cell transplantation** - Hematopoietic stem cell transplantation (HSCT) is the curative therapy in thalassemia. In India, HSCT in thalassemia started at Christian Medical College & Hospital (CMCH), Vellore; has carried out the maximum number of HSCT for thalassaemia in India.<sup>32</sup> At CMCH, Vellore, total 218 patients with thalassemia were treated with allogeneic HSCT from October 1991 to December 2006.<sup>39</sup> Mukhopadhyay A et al<sup>40</sup> from Kolkata reported transplantation in six thalassaemia patients. Very few other private/corporate hospitals in West Bengal are now doing transplantation in thalassemia patients now (personal communication). Till now, no published reports of HSCT in thalassemia in Govt. sector are available.

**Transfusion-Transmissible Infections (TTI):** - Very high frequency of seropositivity for hepatitis B virus (HBV),

hepatitis C virus (HCV) and human immunodeficiency virus (HIV) reported in multi-transfused patients of beta thalassaemia and EB thalassaemia. De M et al<sup>41</sup> from Kolkata in 1990s reported seropositivity for HBV in 22.1% and 13% cases of beta thalassaemia and EB thalassaemia respectively; HIV seropositivity was detected in 0.8% cases. With the introduction of the universal voluntary blood donation programme, routine screening of blood for HBV and HIV by sensitive tests and early immunization against HBV changed the scenario. Mukherjee K et al<sup>42</sup> from Kolkata studied on 207 patients of beta thalassaemia major, had shown seropositivity of HBV and HCV in 3.38% and 24.64% cases respectively. The relatively high percentage of seropositive cases especially for anti-HCV antibodies was higher for cases who had received more transfusions as compared to those who had received lesser units of blood. Biswas A et al<sup>43</sup> from ICMR Virus Unit, Kolkata studied the prevalence of anti-HCV, HBsAg, HIV in 1711 thalassaemia major patients registered with collaborating thalassaemia clinics from different hospitals and NGOs of West Bengal; dominant TTI was HCV with 18.70% prevalence followed by HIV (3.74%) and HBV (3.33%). Bhattacharyya KK et al<sup>44</sup> from Hooghly district had shown HCV positivity in 25% cases; HCV genotype-3 was the major circulating strain (92.59%) followed by genotype-1. In another study from Kolkata by Biswas A et al<sup>45</sup> in multi-transfused  $\beta$ -thalassaemia patients, out of 172 HCV seroreactive individuals, 59.30% were HCV RNA positive (87.65% were infected with HCV genotype-3). The high rate of TTIs leading to the poor prognosis of the affected individuals highlights the need for more stringent screening of blood or blood products before transfusion.

#### **Prevention of thalassaemia: a necessity in West Bengal**

The need for prevention of thalassaemia in West Bengal is obvious due to high frequency of carrier state of different hemoglobinopathies, high fatality of untreated or undertreated cases, high expenses and difficulties in providing optimal care. Prevention, a good public health practice, would help in reducing the burden of the disease. Preventive programmes based on heterozygote detection, counseling and fetal diagnosis have been very effective in reducing birth of symptomatic thalassaemia infants in Sardinia, Cyprus, Greece and Italy.<sup>46</sup> Premarital screening as a preventive strategy has been advocated by investigators and haematologists in India.<sup>47</sup> In population screening, there are a number of options - pregnant women, relatives of the affected, high school or college students, or the community at large. Carrier screening and prenatal diagnosis should receive the highest priority in the future, in order to reduce the birth of affected children. Chattopadhyay S<sup>48</sup> in an attempt to unravel some of the barriers to the prevention campaign pointed out lack of access, low awareness, low-risk perception and poverty as important proximate constraints. Blood is so deeply valued in the Bengali kinship system that this genetic mutation is perceived to be corrupting the blood (rakterdosh); parents are not inclined to test their daughters because of the possibility of not being able to get them married to eligible

suitors. This study has potential applications for public health prevention programs that confront problems of stigma in program acceptability. Biswas B et al<sup>49</sup> studied on family planning practices in couples with children affected by beta thalassaemia major and stressed on parental screening at every given opportunity in easily comprehensible native language regarding the importance of adopting a suitable contraceptive method for either terminating or spacing childbirth.

Another important issue in prevention is the use of the best available technique that should be affordable, applicable, accurate and easily available for mass screening. As of now, there is no doubt about HPLC being the best one in detecting different hemoglobinopathies, but the technique is time consuming, costlier, needs expertization and not very suitable to screen the vast population in West Bengal. The better possible alternative option to screen for carriers at the grass root level will be - NESTROFT<sup>15</sup> to screen for beta thalassaemia trait and DCPIP<sup>13</sup> for Hb E. In doubtful cases, HPLC analysis should be done for further characterization of the abnormal Hb. The other important observation reported by Dolai TK et al<sup>50</sup> from West Bengal reported concomitant Iron deficiency state in 29.67% females and 3.38% males of beta thalassaemia carriers. Presence of concomitant iron deficiency in  $\beta$ -thalassaemia carriers, HbA<sub>2</sub> is decreased that implies the importance of close vigilance in reporting of HPLC especially for beta thalassaemia carrier state.

Cost is a very important issue discussed in planning for treatment and prevention of thalassaemia. Kantharaj A et al<sup>51</sup> from Bengaluru, India has shown a head to head cost comparison of treatment versus prevention of thalassaemia in India. The estimated cost of treatment of thalassaemia is INR 167,750 per year versus one time (antenatal screening by HPLC) investment cost of prevention @ INR 250. There is no such published data from West Bengal, but if we extrapolate the data it will be obvious that prevention is far cheaper than treatment.

#### **Future direction**

Weatherall DJ<sup>52</sup> in the keynote address on 'the challenge of thalassaemia for the developing countries', suggested that more detailed information on frequency and economic data is required to provide evidence for the health burden posed by thalassemiias in the developing world. Although several reports on the prevalence of thalassaemia carriers is available from districts, many of these are hospital-based and thus do not reflect the true burden of the disease in this state as a whole. More emphasis should be laid on population-based screening than screening in hospital settings. Many ethnic groups in remotest villages have not yet been studied; extremely variable prevalence even within small geographic area shows the need for screening at the sub-division, blocks and village level. Moreover, data from many functioning TCU are not published; therefore not available for review. TCU is a state Government endeavor which aids in case and carrier detection through screening programs and comprehensive management of thalassaemia cases. The primary health centers and rural hospitals located in rural areas need additional

strengthening for immediate management of thalassaemias.<sup>53</sup> The National Health Mission, Ministry of Health and Family Welfare, Govt. of India has published in 2016 the guidelines for 'prevention and control of hemoglobinopathies in India' that emphasizes on an integrated comprehensive approach to hemoglobinopathies with special emphasis on prevention and control and is expected to help both the administrators and clinicians in this endeavour.<sup>54</sup>

## CONCLUSION

Joint efforts by the State Government supported by Govt. of India with the help from thalassaemia societies and NGOs as a part of their social responsibilities and strongly backed by political and religious leaders is required for successful implementation of a national control programme.

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