

Retrospective review of Infections in Children with β -Thalassemia

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Abstract

Background: The immune system aberrations perceived in thalassemic children are both qualitative and quantitative, concerning many components of immune system; infections are a common complication and they can be fatal.

Objective: To study the thalassemic children for bacterial infection.

Patients and Methods: This is a retrospective cohort study, it was carried out in Al-Batool Teaching Hospital from June - Dec 2017. Criteria for susceptibility of immune-compromised children for bacterial infection were used for thalassemia major and intermedia children with review of patients records and patients/ parents dialogue. Statistical analysis was done by statistical analysis of social sciences (SPSS 22), P-value was set at (0.05) level. A total number of 188 thalassemia children were involved in this study.

Results: Five (2.7%) children were documented as having a clinically important bacterial infection giving an incidence of 0.23 infections per 100 children/ years, four infections were developed in non- splenectomized children giving a rate of (3%). Two bacterial sepsis and two children suffered from draining otitis media, whereas after splenectomy, only one child developed bacterial pneumonia (1.9%).

Conclusion: Only few bacterial infections were developed in studied thalassemic children during the last 12 years. None of them fulfill the immunocompromised criteria.

Keywords: Bacterial infection, Immunity, Thalassemia.

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Introduction

Thalassemias are a group of illnesses, recessively inherited, characterized by nonexistence or reduced production of α or β polypeptide chains that creates the normal adult hemoglobin molecule [1]. Affected

children might be having many sequelae such as heart failure, infections and hepatic disorders, with a higher mortality rate [2]. Infections are a common complication of thalassemia, and they can be lethal. The

mortality rate and morbidity of each infection display incongruity through the world owing to epidemiology of the infection and socioeconomic circumstances for each case [3]. In Taiwan, infection was reported as the most common cause of death [4]. There is a diversity of causes of infection in thalassemia, comprising repeated blood transfusion, iron overload, splenectomy, iron chelating treatment, reduced zinc level, and functional deviation of immune system [2]. The immune system anomalies in thalassemia children to date are both qualitative and quantitative [5-8], furthermore, lessened immunoglobulin secretion has been associated with raised level of IgA, IgG, and IgM. [5,9,10] Many deviations of T- lymphocyte subsets were observed, [5,7,11-13].

Bacterial infections are well recognized sequelae of immune system derangement, [14]. Beta- thalassemia children might have had recurrent attacks of mild and severe infections. like gingivitis, cutaneous abscess, upper respiratory tract infection, and acute gastroenteritis, whereas severe infections included, pneumonia, urinary tract infection, salmonellosis, septicemia, and biliary tract infection [15].

The aim of this study was to evaluate the thalassemia children who were treated for bacterial infections as a consequences of immune system abnormalities.

Patients and Methods

A cohort retrospective study, piloted at Thalassemia Center at Al-Batool Teaching Hospital, Diyala, Iraq from June - Dec 2017.

Thalassemia major and intermediate children were studied and documented for earlier hospital admissions ,for bacterial infections owing to certain criteria declared later on, together with parents/ patients interview for likely outpatients management for bacterial infections documented bacterial soft tissue infections. A questionnaires were arranged involving the following criteria for possibility of immune system derangement: 1) Two or more systemic or serious bacterial infections (e.g., meningitis osteomyelitis, or sepsis); 2) Three or more serious respiratory or documented bacterial soft tissue infections (e.g., lymphadenitis, draining otitis media, or cellulitis,) within 1 yr.; 3) Infections occurring at unusual sites (e.g., liver or brain abscess); 4) Infections with unusual pathogens (e.g., Nocardia, Serratia marcescens, Burkholderia cepacia, or Aspergillus,); and 5) .

Infections with common childhood pathogens but of unusual severity. The enrolled children were classified into surgically splenectomized and non-splenectomized to study the effect of splenectomy.

Statistical analysis

The association between variables were done by means of Statistical Package of Social Sciences (SPSS) v. 22, Chi- square was used and P-value was significant < (0.05).

Results

A total number of 188 thalassemia patients were included in the study, thalassemia major children were 132 (70%) and intermedia 56

(30%), school aged encompassed most of the children (p value=.000) and it was the commonest group for both sexes. Boys was

the major gender for all age groups, it encompassed more than 56% of the whole studied children.

Table (1): A cohort features regarding age & gender

Age	Male Number &percentage	Female Number &percentage	Total number& Percentage (%)
6 months– 6 years	30 (15.9%)	24 (12.8%)	54 (28.7%)
> 6years - 18years	52 (27.7%)	39 (20.7%)	91 (48.4%) **
>18years	25 (13.3%)	18 (9.6%)	43 (22.9%)
Total	107 (56.9%)	81 (43.1%)	188 (100%)

*p-value=.000, highly significant

Within this study, 5 (2.7%) children were having a clinically important bacterial infection; thus over a retrospective of 12 years ,bacterial infection paralleling to an incidence of 0.23 infections per 100 patient years. These infections were dispersed into 5 children, 4 infections were settled in non-splenectomized children to provide a rate of (3%): 2 bacterial sepsis and 2 patients had

draining otitis media, whereas after splenectomy (which was carried out for 54 children, 28.7%), only one child develop bacterial pneumonia (1.9%). None of these infection was fulfilling the criteria of troubled immunity which was stated below. The detail of infection in splenectemised and nonsplenectemised children were shown in Table (2).

Table (2): Distribution of infections sites among thalassemic children with and without splenectomy

Type of infection	Non- splenectomized children		Splenectomized children	
	Positive No. (%)	Negative No. (%)	Positive No. (%)	Negative No. (%)
Systemic bacterial infection				
- Sepsis	2 (1.5)	132 (98.5)	0	54 (100)
- Meningitis	0	134 (100)	0	54 (100)
- osteomyelitis	0	134 (100)	0	54 (100)
Serious respiratory/ soft tissue infections:				
- Pneumonia	0	134 (100)	1 (2)	53 (98)
- Lymphadenitis	0	134 (100)	0	54 (100)
- Draining otitis media	2 (1.5)	132 (98.5)	0	54 (100)
- Cellulitis	0	134 (100)	0	54 (100)
Infections at unusual sites:				
- liver	0	134 (100)	0	54 (100)
- brain abscess	0	134 (100)	0	54 (100)
Infections with unusual pathogens:(e.g., <i>Aspergillus</i>)	0	134 (100)	0	54 (100)
Infections of common pathogens with unusual severity	0	134 (100)	0	54 (100)
Total Number (%)	134 (71.3)		54 (28.7)	

Discussion

There were plentiful studies achieved to evaluate the likely alterations of the immune system in thalassemia in view of humoral and cellular immunity and the consequences were varied, Teny et al.[16] reported that there were important alterations on immune response among thalassemia major. The bacterial infections in this cohort study was five episodes only, which amounts 0.23 attack per 100 child per year, this proportion was far less than that found in other cohorts was 2.6 and 1.6 attacks per 100 child per year.[17,18] This disparities may be linked to demographic/ geographical dissimilarities, in addition to the restricted period of the study matched to other studies, Rahav et al[17] informed a substantial increasing of the infection rate over time, especially after 15 years, which is lengthier than period since establishing of thalassemia center in our locality. Sepsis was one of the substantial severe bacterial infection in this study (n=2, 40%), earlier studies [18,19] found less occurrence of septicemia (14-25%) because of variety of infections like liver abscess which was not seen in this study. Pneumonia comprised 20% of infections within the study, this was nearly consistent with previous studies 26% and 21.4% [17,19]. Draining otitis media constitutes a significant bacterial infections in this study (n=2, 40%), while in other studies it was absent [17,19], this may be due to diverse microorganism or its behavior due to geographic dissimilarities. None of the above mentioned infections was

recurrent or having unusual severity to complete the defined criteria of recurrent bacterial infection of immune deficiency and no any child developed cellulitis, lymphadenitis, unfamiliar site of infection like liver and brain abscess, infection by unusual pathogen or severe infection by a common pathogen. On the other hand, many other bacterial infections were recorded in other studies and not experienced by our children like soft-tissue infection, liver abscess, osteomyelitis, enteritis, pulmonary, renal or abdominal abscesses, or gum abscess, retropharynx or buttocks, and fever of unknown origin. [17,18] . Four of the 5 documented infection were developed in non- splenectomized children, which give a rate of (3%) of infection, in splenectomized child, only one infectious attack (pneumonia) was itemized, (1.9%), this was inconsistent with other studies [15,17,20] where they found that the infection rate of thalassemia is augmented by splenectomy (14.7%, 10.2% and 13% respectively). Children in this study were fully vaccinated, but this discrepancy is possibly due to limited information and short period of the study, anyhow, several other factors may affect the incidence of bacterial infection in thalassemic children like, repeated blood transfusion, low level of zinc, iron overload, and iron chelating therapy. All these might interrelate to give the unpredicted results. This study has many limitations, firstly, the project was retrospective with lack of cultural isolation for etiologic bacteria, secondly, the

short period of treatment for the cohort at the center was not likely to give adequate power for the outcome to match with other studies. These difficulties can be overcome by extended prospective study with demonstration of the infectious pathogens.

Conclusions

Only few bacterial infections were developed in included thalassaemic children during the last 12 years and none of them fulfill immunocompromised criteria. On contrary to other studies, most infections occurred in non splenectomized children.

Recommendation

Extensive, and prospective study for incidence of bacterial infection is suggested, beside re-screening of thalassaemic children for immune system abnormalities with re-evaluation of many other studies for vulnerability to infection.

References

[1]Higgs DR, Thein SL, Woods WG. The molecular pathology of the thalassaemias. In: Weatherall DJ, Clegg B, (eds). The thalassaemia syndrome. 4th ed. Blackwell Science, 2008; p.133-91.

[2]Farmakis D, Giakoumis A, Polymeropoulos E, Aessopos A. Pathogenetic aspects of immune deficiency associated with β -thalassaemia. *Med Sci Monit.*, 2003; 9(1): 19–22.

[3]Bianca Maria Ricerca, Arturo Di Girolamo, Deborah Rund. Infections in Thalassaemia and Hemoglobinopathies: Focus on Therapy-Related Complications. *Mediterr J Hematol Infect Dis.*, 2009; 1(1): e2009028.

[4]Chern JP, Su S, Lin KH, Chang SH, Lu MY, Jou ST, et al. Survival, mortality, and complications in patients with beta-thalassemia major in northern Taiwan. *Pediatr Blood Cancer.*, 2007; 48(5): 550-4.

[5]Dwyer J, Wood C, McNamara J, Williams A, Andiman W, Rink L, et al. Abnormalities in the immune system of children with beta-thalassemia major. *Clin Exp Immunol.*, 1987; 68(3): 621-9.

[6]Dua D, Choudhury M, Prakash K. Altered T and B lymphocytes in multitrans fused patients of thalassemia major. *Indian Pediatr.*, 1993; 30: 893-6.

[7]Sen L, Goicoa MA, Nualart PJ, Ballart IJ, Palacios F, Diez RA, Estévez ME. Immunologic studies in thalassemia major. *Medicina (B Aires).*, 1989; 49(2): 131- 4.

[8]Speer CP, Gahr M, Schuff-Werner P, Schroter W. Immunologic evaluation of children with homozygous beta-thalassemia treated with desferrioxamine. *Acta Haematol.*, 1990; 83: 76-81.

[9] Sinniah D, Yadav M. Elevated IgG and decreased complement component C3 and factor B in Bthalassaemia major. *Acta Paediatr Scand.*, 1981; 70: 547- 50.

[10]Quintiliani L, Mastro Monaco A, Giuliani E, Buzzonetti A, Sisti P, Guglielmetti M, et al. Immune profile alterations in thalassaemic patients. *Boll Ist Sieroter Milan.*, 1983; 62(6): 524-30.

[11]Khalifa AS, Maged Z, Khalil R, Sabri F, Hassan O, el- Alfy M. T-cell functions in infants and children with beta-thalassemia. *Acta Haematol.*, 1988; 79(3): 153-6.

- [12]Ezer U, Gulderen F, Culha VK, Akgül N. Gürbüz O. Immunological status of thalassemia syndrome. *Pediatr Hematol Oncol.*, 2002; 19(1): 51-8.
- [13]Umiel T, Friedman E, Luria D, Cohen IJ, Kaplinsky H, Netzer L, et al. Impaired immune regulation in children and adolescents with hemophilia and thalassemia in Israel. *Am J Pediatr Hematol Oncol.* 1984; 6(4): 371-8.
- [14] Rebecca H. Buckley. : Evaluation of the Immune System. In: Robert M. Kliegman, Bonita Stanton, Joseph St. Geme, Nina Felice Schor, Richard. Behrman (ed). *Nelson textbook of paediatrics*, 2011, 19th edition. Elsevier - Health Sciences Division, Saunders; P. 680-683.
- [15]Wanachiwanawin W. :Infections in E-beta thalassemia. *J Pediatr Hematol Oncol.*, 2000; 22(6): 581-7.
- [16]Teny T. Sari, Djajadiman Gatot, Arwin A.P. Akib, Saptawati Bardosono, Sri R.S. Hadinegoro, Alida R. Harahap, et al. Immune Response of Thalassemia Major Patients in Indonesia with and without Splenectomy. *Acta Med Indones-Indones J Intern Med.*, 2014; 46(3): 217-25.
- [17]G. Rahav, V. Volach, M. Shapiro, D. Rund, E.A. Rachmilewitz, A. Goldfarb. Severe infections in thalassaemic patients: prevalence and predisposing factors. *Br J Haematol.*, 2006; 133: 667-74.
- [18] S.C. Wang, K.H. Lin, J.P. Chern, M.Y. Lu, S.T. Jou, D.T. Lin, et al. Severe bacterial infection in transfusion-dependent patients with thalassemia major. *Clin Infect Dis.*, 2003; 37: 984-988.
- [19]Alvin R.Yapp. Robert Lindeman. Nicole Gilroy. Zhanhai Gao. C. RainaMacIntyre. Infection outcomes in splenectomized patients with hemoglobinopathies in Australia. *International Journal of Infectious Diseases*, 2009; 13(6): 696-700.
- [20]Sakran W, Levin C, Kenes Y, Colodner R, Koren A. Clinical spectrum of serious bacterial infections among splenectomized patients with hemoglobinopathies in Israel: a 37-year follow-up study. *Infection*, 2012; 40(1): 35-9.