

# Positive Findings Of Blood Cultures In Febrile Children Presenting With Thalassemia Major In A Tertiary Care Hospital

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## Author's Contribution

<sup>1,2</sup> Conception of study

<sup>1,2,5</sup> Experimentation/Study Conduction

<sup>1,2,3,4</sup> Analysis/Interpretation/Discussion

<sup>1,2,3,4,5</sup> Manuscript Writing

<sup>6</sup> Critical Review

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## Abstract

**Objective:** To assess the status of bacterial pathogens in thalassemia major patients presenting with fever in a tertiary care hospital.

**Methods:** A retrospective descriptive study was conducted at the thalassemia major clinic at the Children's Hospital, PIMS, Islamabad from November 2020 to October 2021 in which 102 patients of thalassemia major who presented with fever and were suspicious of having septicemia were enrolled. Their demographic characteristics and pathological findings were noted in this study. A standardized approach was followed for blood withdrawal and sample collection required for performing blood cultures. The data were analyzed with SPSS version 21.

**Results:** Females were in the majority. A total of 57 (56.0%) patients had positive blood cultures. The most frequent bacterial pathogen was Klebsiella pneumonia 13 (12.7%), followed by E-coli 11 (10.7%), staphylococcus aureus 7 (6.8%), pseudomonas 8 (7.8%) and streptococcus type pathogens 6 (5.8%).

**Conclusion:** Positive culture findings were high in the thalassemia major patients who presented with fever.

**Keywords:** Pathogens, positivity, thalassemia major, fever, septicemia.

## Introduction

Thalassemia major is an inherited disorder of the blood. Affected children are unable to produce normal blood products due to defective beta chains. About 56000 conceptions worldwide result in thalassemia, and data from the middle east suggests a prevalence of 0.25% to 33% in the under 5 population.<sup>1</sup> Thalassemia major is common in Asian and African populations. Due to constant transfusions at intervals, children often develop iron overload which leads to an increased risk of developing repetitive bacterial infections. Various gram-positive and gram-negative bacterial pathogens have been found responsible for septicemia and compromised condition of thalassemia major patients.<sup>2</sup> The underlying paths for this increased susceptibility to infections in thalassemia major are not well known. Many of the factors that are probably accountable are associated with either the disease (e.g. anemia, reticuloendothelial system dysfunction because of iron and hemolyzed erythroblasts, iron overload, and altered immune response) or the treatment (splenectomy, transfusion-related infections, and iron chelation).<sup>3</sup> Many scientific reports have suggested that infection is common in thalassemia major patients and that more than 10% of these infections were severe.<sup>4, 5</sup> Iron chelation therapy helps in minimizing toxicity in the body and maintains the compromised immune system in proper shape.<sup>6</sup> The sufferings of thalassemia major patients are many folds including regular investigations to check hemoglobin status and blood transfusions, frequent hospital visits, multiple pricks, iron overload, risk of getting transfusion-related infectious diseases like hepatitis B & C and HIV as well as contacting common bacterial pathogens from the hospital environment.<sup>7,8</sup> These risks are routinely faced by thalassemia major patients. We planned this study to quantify the causative bacterial agents causing fever and septicemia in thalassemia major patients with the hope of generating an evidence base that can then be used to address this problem.

## Methodology

This was a retrospective descriptive study conducted at the thalassemia major clinic at the Children's Hospital, PIMS, Islamabad from November 2020 to October 2021 after seeking permission from the ethics review board. A total of 102 thalassemia major

patients who had fever of more than 100°F or higher were included through non-probability, consecutive sampling. Afebrile patients of thalassemia major and febrile patients of other hemolytic anemias were excluded from this study. The demographic characteristics and symptoms were noted on structured proforma. The blood samples for the purpose of culture were obtained from the participants. The 10ml blood sample was drawn by following the standardized approach of blood sampling. Specifically, the approach of venipuncture was used after the sterilization of the skin through an alcohol swab. A tourniquet was used during the process of blood sampling.

The data were analyzed with SPSS version 21. Frequency and percentages were calculated from categorical variables and mean and standard deviation from continuous/numerical variables. The chi-square test was applied while comparing study parameters according to patients' gender.

## Results

A total of 102 cases of thalassemia major were selected in this study. All 100% of children were receiving iron chelation. The average age of patients was  $3.9 \pm 0.9$  years with the majority between 2 and 4 years 66 (64.7%). The female gender was dominant 58 (56.9%). Around half 53 (52.0%) had vomiting and 56 (54.9%) children had irritability as shown in Table 1. Blood culture was positive in 57 (56.0%) patients as shown in Figure I. The most frequent bacterial pathogen was Klebsiella pneumonia 13(12.7%), followed by E-coli 11(10.7%), staphylococcus aureus 7(6.8%), pseudomonas 8(7.8%) and streptococcus type pathogens 6(5.8%).

The other frequent bacterial pathogens found in the study were Staphylococcus epidermidis 4(3.9%) and salmonella typhi 3(2.9% as shown in Table 2.

The bacterial pathogens were analyzed according to age and gender. We noticed older age boys had a greater frequency of staphylococcus aureus whereas younger age groups had a higher frequency of Klebsiella pneumonia, streptococcus, and E coli. However, this difference is not statistically significant ( $P>0.05$ ). Similarly, not statistically significant ( $P>0.05$ ) difference was found in the frequency of pathogens among the two genders. It was witnessed that more females had normal blood culture findings than males (48.2% versus 38.6%) but it was also not statistically

significant ( $P>0.05$ ). Further details can be seen in Table 3.

**Table-1: Demographic and clinical characteristics of patients (n=102)**

	No of cases	%age
<b>Age (years)</b>		
Up to 2	5	4.9%
2.1 to 4	66	64.7%
4.1 to 6	31	30.4%
Mean ± SD	3.9 ± 0.9	
<b>Gender</b>		
Male	44	43.1%
Female	58	56.9%
<b>Fever</b>		
Yes	97	95.1%
No	5	4.9%
<b>Vomiting</b>		
Yes	53	52.0%
No	49	48.0%
<b>Irritability</b>		
Yes	56	54.9%
No	46	45.1%

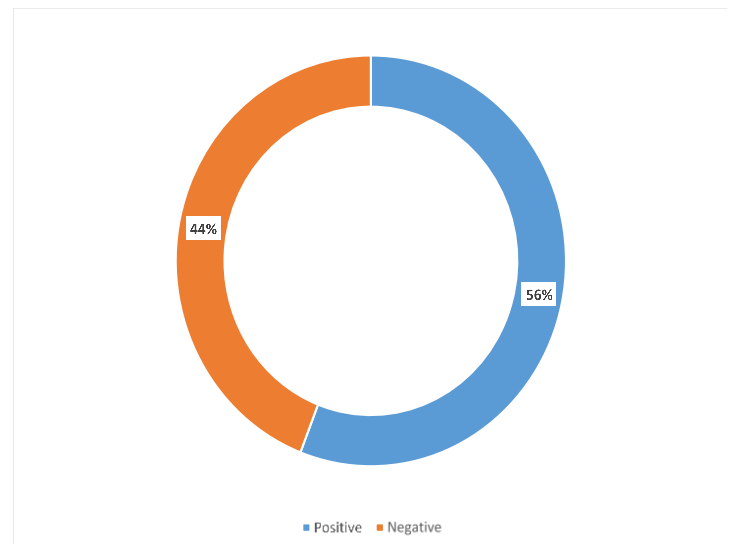
**Table-2 Bacterial pathogens isolated in the study patients (n=102)**

	No of cases	%age
Klebsiella pneumoniae	13	12.7%
E-coli	11	10.7%
Pseudomonas	8	7.8%
Staphylococcus aureus	7	6.8%
Streptococcus	6	5.8%
S. epidermidis	4	3.9%
Salmonella typhi	3	2.9%
Others	5	4.9%
No growth	45	44.1%

**Table-3 Bacterial pathogens according to gender in the study (n=102)**

	Male (n=44)	Female (n=58)	p-value *
Klebsiella pneumoniae	6 (13.6%)	7 (12.1%)	0.81
E-coli	6 (13.6%)	5 (8.6%)	0.41
Pseudomonas	4 (9.0%)	4 (6.8%)	0.72
Staphylococcus aureus	3 (6.8%)	4 (6.8%)	1.0
Streptococcus	3 (6.8%)	3 (5.1%)	1.0
S. epidermidis	3 (6.8%)	1 (1.7%)	0.31
Salmonella typhi	2 (3.4%)	1 (1.7%)	0.57
Others	0 (0.0%)	5 (8.6%)	0.07
Nil	17 (38.6%)	28 (48.2%)	0.33

\* Chi-square test applied. Note: if the value was less than 5 in a 2x2 column, fisher's exact value was quoted



**Figure-1 Frequency of positive culture findings in the study (n=102)**

## Discussion

The mechanisms behind the spread of infections in transfusion-dependent thalassemia major patients are not well known. The current study aimed at finding the pathogenic causes of fever and infections in thalassemia major patients and found a high rate of positive culture findings in more than half of the study cases. The most common pathogens were *Klebsiella pneumoniae*, *E-coli*, *Staphylococcus aureus*, *Pseudomonas*, and *Streptococcus* in this study.

Al Badry BJ et al witnessed bacterial infections in 37.5% of cases with the most common types as streptococcus genus, staphylococcus, proteus, and *E-coli*.<sup>9</sup> Rahav G and Colleagues also noted one-third of a patient had different culture-proven infections, with the most common being staphylococcus aureus, streptococcus, *E-coli*, and *Klebsiella pneumoniae*.<sup>10</sup> Another previous study also highlighted immune response in thalassemia patients specially bactericidal activity.<sup>11</sup> Findings of all these studies are quite lower than those of our study which show very compromised conditions of thalassemia major patients in our study. Frequent visits of thalassemia major patients to hospitals for transfusion and during that period investigations and other inoculations put those at risk of catching hospital-acquired bacterial infections. Moreover, due to low immune status, these children become favorite carriers and hosts for infection spread.<sup>12</sup>

A higher incidence of *Staphylococcus aureus* is possibly related to subcutaneous injections and indwelling intravenous devices for intensive chelation. The major causative organisms in the series from the Far East were Gram-negative bacilli, especially *Klebsiella pneumoniae* which was particularly found in liver abscesses.<sup>13</sup>

In this study, we also assessed the variation of pathogens according to the age and gender of patients. But we could not find any previous evidence pertaining to variations of different bacterial pathogens analyzed in detail according to gender and age.

It is well known that the severe condition of thalassemia major has been associated with increased susceptibility to infections; nonetheless, relevant scientific evidence pertaining to the incidence of infections and the spectrum of causal organisms is limited. Moreover, bacterial infections remained the

main cause of mortality among thalassemia major patients.<sup>14, 15</sup>

Along with low immune and compromised conditions, one of the causes of frequent and recurrent infections in thalassemia major patients can be antimicrobial resistance.<sup>3</sup> In the settings of developing countries like Pakistan, the health infrastructure is not up to mark and here inappropriate prescription and over-the-counter antibiotics is a routine issue that leads to antimicrobial resistance.<sup>16,17</sup>

This study has many advantages; firstly, in terms of rare forms of data pertaining to bacterial pathogens in thalassemia major patients. Secondly, a reasonable number of thalassemia major cases of thalassemia were observed. The limitations were in terms of the outcome of the study cases after catching bacterial pathogens. The information regarding drug susceptibility was also not gathered which could have shown the picture of antimicrobial resistance in thalassemia major patients. Moreover, the long-term effects of bacterial pathogens in those cases who survived were also not observed which could have given an in-depth view of these patients.

## Conclusion

A high proportion of thalassemia major cases (56%) were found with a positive culture test. The most common pathogens were *Klebsiella pneumoniae*, *E-coli*, *Staphylococcus aureus*, *Pseudomonas* and *Streptococcus*. Further large-scale prospective studies with rigorous research procedures are needed, specifically to answer the long terms outcome as well as details of drug susceptibility and final outcomes are mandatory before the generalization of findings of this study.

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