



Frequency of Urinary Tract Infection among Febrile Pediatric Thalassemic Patients in Babylon Hereditary Blood Disease Center in Babylon Governorate / Iraq

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Abstract

Background: *There is an increased risk of infections in patients with thalassemia compared to general population including urinary tract infections (UTI). The susceptibility to infections in thalassemia arises from iron overload, transfusion therapy, splenectomy, zinc deficiency & disease itself. all these changes inherent to the pathological process which can interfere with the immune systems*

Aims of study: *The study was carried out to determine the frequency of urinary tract infection among thalassemic patients, its correlation to risk factors including vaccination, splenectomy, iron overload, Hb level and to determine microorganism causing urinary tract infection among thalassemic patients and control group .*

Methods: *A case control study was carried out at the Babylon hereditary blood disease center in Babylon Maternity and Children Teaching Hospital in Hilla / Iraq from March to October 2018 among 100 febrile thalassemic patients as patients group , comparison to 100 febrile non thalassemic patients as control group with age ranging between 6 months -15 years. Urine exam & culture, serum ferritin, Hb, C-reactive protein, ESR were sent for all patients.*

Results: *The current study has revealed that 14 % of thalassemic patients developed UTI, in comparison to 5% in non thalassaemic patients .The infection is more among those with low Hb, incomplete vaccination, splenectomized patients but has no relation to gender & type of thalassemia and E. coli was the commonest microorganism among both group.*

Conclusion: *This study revealed that the frequency of UTI among febrile thalassemic patients is 14 %, its increased among splenectomized patients, incomplete vaccination and iron overload.*

Keywords: *thalassemia , urinary tract infection, splenectomy, Immune system, iron overload, vaccination.*

Introduction

Thalassemia is a heterogeneous group of heritable Hypochromic anemia of various degrees of severity, resulting from genetic defects include total or partial deletions of globin chain genes and

nucleotide substitutions, deletions or insertions that result in decreasing or total suppression of hemoglobin polypeptide chain.⁽¹⁾

Thalassemia is characterized by abnormal hemoglobin synthesis, which results in decreased

oxygen delivery to the tissues and to improve the oxygen-carrying capacity of the blood. Patients who receive regular transfusions may result in iron overload in various organs including heart, liver and endocrine organs. ^(2,3,4,5)

The susceptibility to infections in thalassemia arises from iron overload, transfusion therapy, splenectomy, zinc deficiency & disease itself. All these changes inherent to the pathological process which can interfere with the immune systems. ^(6,7,8)

One of the first lines of defense against bacterial infection is the withholding of nutrients to prevent bacterial outgrowth in a process termed nutritional immunity (the most significant form of nutritional immunity is the sequestration of nutrient iron). ⁽⁹⁾

Bacteria can acquire iron from transferrin and lactoferrin.

The excess iron increases the virulence of numerous pathogens and in iron overload state.

The effect of excess iron on immunological functions include Suppression of monocyte-macrophage system, changes in subpopulations of T-lymphocytes, increasing CD8 and suppression of CD4, increased secretion of immunoglobulins and inhibiting the function of the complement system, impaired neutrophil function, impaired monocyte/macrophage activity against pathogens and decreased natural killer cells activity. ^(10,11,12)

The patients after splenectomy, the immune system is modified, Expressed in quantitative changes of lymphocytes without any functional disorders. ⁽¹³⁾

Splenectomized patients have a significant infection risk, because the spleen is the largest accumulation of lymphoid tissue in the body including splenic macrophages that attack encapsulated organisms (in the absence of spleen, the ability to fight off these pathogens is severely diminished), spleen is also a major site of early immunoglobulin M production, which is important in the acute clearance of pathogens from the bloodstream. ⁽¹⁴⁾

Efficient phagocytosis depends on splenic macrophages and on the production of many substances (opsonins, properdin, tuftsin) which

are reduced in splenectomized patients, however encapsulated pathogens (Streptococcus pneumoniae, Haemophilus influenza type B, Escherichia coli, Neisseria meningitidis) are the most fearsome. ⁽¹⁵⁾

In zinc deficiency, the Zinc is an immunoregulator and low level of zinc in thalassemic patients associated with changes in lymphocyte subpopulations which is adjusted after zinc administration. ⁽¹⁶⁾

Repeated transfusions lead to a continuous alloantigen stimulation & disruption of the immune balance in thalassemic patients. ⁽¹⁵⁾

Aims of study

The study was carried out to:

1. Determine the frequency of UTI among thalassemic patients and Its correlation to risk factors include vaccination, splenectomy, iron overload and Hb level.
2. Determine microorganism causing UTI among thalassemi patients and control group.

Patients and Methods

A case control study was carried out at the Babylon hereditary blood disease center at Babylon maternity and children hospital From March to October 2018 and the study included 100 febrile thalassemic patients as patients group with age ranged from 6 month to 15 years and mean age 6 ± 2.4 years, classified into (44) males and (56) females, compared to 100 non thalassemic patients as control group, classified in to (43) males and (57) females with mean age of 7 ± 1.2 years, consulted pediatric clinic or attended the emergency unit in the hospital.

Inclusion criteria includes B⁻ thalassemic patients (B thalassemia major, intermedia, minor and sickle cell thalassemia) with fever of more than 37.4°C , their age ranged between 6 months and 15 years, no history of antibiotic use in the preceding 3 days, no malnourished children or any conditions that increased the risk of UTI as vesico

urethral reflux (VUR), obstructive uropathy, diabetes mellitus (DM) and uncircumcised child.

The physical examination was initially directed at measuring the axillary temperature for those of less than 6 years with added 0.5⁰C and measured orally to those above 6 years, then complete examination was done including chest, abdomen, tonsils, meningeal signs and skin examination.

Clinical diagnosis of UTI was made to those with abdominal pain, dysuria, frequency, renal angle tenderness and supra pubic tenderness.

Examination for any signs & symptoms of respiratory distress and Chest X ray (CXR) for those with suspected of pneumonia.

A through history and examination with investigations were done to prove or exclude other diagnosis including hepatitis, measles, mumps, otitis media and others.

All patients (patients and control group) sent for general urine exam (GUE) & urine culture collected either through midstream urine in sterile universal container in toilet trained patients or through urine bag in infant to those who are not toilet trained(methods of supra pubic aspiration or urinary catheter used are refused by parents).

Samples collected after cleaning the genital area with soap and water or povidone iodine then rinsing the area with water.

The samples examined within 15 minute of collection and pyuria was considered as positive if pus cell of more than 5 cell/m³ and Pure colony count of $\geq 10^5$ /ml is considered positive culture.

Blood was aspirated and sent for ferritin, Hb, WBC (white blood cell), CRP, ESR. Ferritin was not repeated to those patients measured within last 3 month prior to presentation, while in other patients, it was sent after stabilization of condition (not during the febrile illness).

A value of more than 1000 ng/ml is considered a state of iron overload.

Hb was classified as low if less than 8.5gm/dl (normal if more than 8.5gm/dl) in low transfusion regimen (in our patients, we used low transfusion regime).

Statistical analysis

Data was collected and included in a data based system and analyzed by statistical package of social sciences (SPSS version24). discrete variables presented as number and percentage, were analyzed using chi square like comparison between patients and control in presence of urinary tracts infection , continuous variables presented as mean & significance was set at the $P \leq 0.05$ level in all analyses.

Ethical Issue: informed consent was obtained from patient or patients accompany.

The results

In this study, it includes 100 febrile thalassemic patients classified into 44 males and 56 females with mean age of 6 \pm 2.4 years compared to 100 non thalassemia, classified into 43 males and 57 females with mean age 7 \pm 1.2 years .

Table 1: Frequency of UTI among patients and control group :

Group	Urinary tracts infection		Total	p. value
	+ve cases	-ve cases		
Thalassemic patients	14 (14 %)	86 (86 %)	100	0.04
Control group	5(5%)	95(95%)	100	

There is statistically significant increased in the frequency of UTI in thalassemic patients (14%), compared to control group (5%) with P. value <0.05 .

Table 2: Causes of fever among patients and control group:

Causes of fever	Thalassemic patients	Control group
	No.	No.
<i>Pneumonia</i>	25	14
<i>Tonsillitis</i>	15	16
<i>UTI</i>	14	5
<i>PUO</i>	13	12
<i>AGE</i>	9	8
<i>Typhoid fever</i>	5	12
<i>Otitis media</i>	4	6
<i>Abscess</i>	4	1
<i>Hepatitis</i>	4	6
<i>Measles</i>	3	5
<i>Cholecystitis</i>	2	0
<i>Cellulitis</i>	1	0
<i>Mump`s</i>	1	4
<i>Kala azar</i>	0	4
<i>Meningitis</i>	0	5
<i>Septicemia</i>	0	2

Pneumonia is the commonest disease occurring in both thalassemia and control group .

Table 3: Risk factors causing UTI among thalassemic patients.

Risk factor	UTI +ve	%	Total No.	P. value
Iron overload	11	16.9 %	65	0.3
Without iron overload	3	8.5%	35	
Splenectomised	10	37%	27	0.002
Not splenectomised	4	5.4%	73	
Vaccination				
Incomplete	9	27.2 %	33	0.01
Complete	5	7.4%	67	
HB < 8.5	10	16.3%	61	0.5
Hb > 8.5	4	10.2%	39	

There is a statistically significant increased in risk of infection among splenectomised & incomplete vaccination

Table 4 : Distribution of cases according to age and sex in both groups

Age	Patients UTI		Total	p-value
	Male	Female		
Patients group				
< 2 years	1	0	1	0.7
≥ 2-10 years	4	9	13	
≥ 10-15 years	0	0	0	
Total	5	9	14	
Control group				
< 2 years	1	0	1	0.4
≥ 2-10 years	0	4	4	
≥ 10-15 years	0	0	0	
Total	1	4	5	

No statistical significant of UTI among males and females in both groups

Table 5: Distribution of cases according to the type of thalassemia:

Type of thalassemia	UTI +ve	Total	%	P.value
Major	11	74	14.8%	0.2
Intermedia	2	15	13.3%	0.3
Minor	1	10	10 %	0.5
Sickle thalassemia.	0	1	0	
Total	14	100		

No statistical significance in distribution of cases according to the type of thalassemia.

Table 6: Microorganism causing UTI among patients & control groups:

Microorganism	UTI				P-value
	Thalassemia	%	Control	%	
E. coli	11	78.5 %	4	80 %	0.5
Klebsiela	2	14.2 %	1	20 %	0.6
pseudomonus	1	7.1%	0		0.5
Total	14		5		

E. coli is the commonest organism in both groups

Table 7: Signs, symptoms and investigations of UTI in patients and control group.

Factors		Patients group (14 positive patients)	Control group (5 positive patients)
symptoms	Abdominal pain	9	3
	Dysuria	8	2
	Frequency	6	2
	Hematuria	5	1
	Dribbling	6	1
Signs	Tenderness	7	2
	Abdominal mass	0	1
investigation	Hb < 8.5 gm/dl	10	1
	WBC > 11000	2	1
	ESR > 40	0	0
	CRP +ve	3	1
		0	0
	GUE < 5 cell	1	0
	> 5 cells	13	5
Serum ferritin	< 1000 ng/ml	3	5
	≥ 1000-< 2500 ng/ml	3	0
	≥ 2500 ng/ml	8	0

The abdominal pain is commonest symptoms among both groups and UTI commonly occurred to those patients with Hb of less than 8gm/dl.

Discussion

The result of the current study shows that 14 % of patients group have UTI, in comparison to only 5% in control group and is statistically significant (P value < 0.05).

The mechanism for increasing susceptibility to infection are related to anemia , iron overload, altered immune response & splenectomy.

This result is higher than the result done by Galia Rahav⁽¹⁷⁾ shows only 7 % , this difference could be explained by different methods of doing urine culture including urine bag, midstream urine &

supra pubic aspiration with variable sensitivity and specificity.

Urine bag and midstream urine are methods used in this study resulting in false positive result, in comparison to supra pubic aspiration which used in Galia Rahav⁽¹⁷⁾ which associated with high sensitivity and specificity.

Urinary tract infection is forming the 3rd important cause in febrile thalassemic patients after pneumonia & tonsillitis which account 25% ,16 % respectively.

A distinct increased in UTI following splenectomy & incomplete vaccination, in splenectomized patients, there was 37 % (10/27 patients) associated with infection, in comparison to 5.4 % (4/73 patients) in non splenectomized patients.

This may be related to spleen importance for the immunological surveillance and reservoir of immune competent lymphocyte,⁽¹⁵⁾ also the antibody response to antigen is impaired , in addition to inefficient phagocytosis (which depend on splenic macrophages & production of many substance like (opsonin , properdin and tuftsin)are reduced & impaired chemotaxis.⁽¹⁸⁾

Most of the vaccine that is used for thalassmic patients given against S. pneumonia, N. meningitides & H. influenza, but in the current study, there is increased risk for E. coli among both groups which may be explained by small sample size of the patients and high predilection of E. coli infection into urinary tract.

Urinary tract infection increased in patients with iron overload (its increased with increased level of iron overload) and statistically is insignificant, but its percentage is 16.9% (11/65 patients), in comparison to 8.5% (3/35 patients) in non iron overload as iron overload may be related to alteration of chemotactic phagocyte properties of neutrophil resulting in reduction their ability to kill invading pathogen, also the saturated transferrin allow the labile iron to be available for bacteria.⁽¹⁹⁾

The level of Hb and gender are not associated with risk of UTI, even those patients with low

Hb (< 8.5 gm / dl) associated with 16.3 %, compared to 10.2 % in those patients with Hb level (>8.5 gm /dl).

The frequency of UTI increased in first 10 years of age, especially between 2-10 years which explained by incomplete vaccine & poor hygiene.

Urinary tract infection occurs more in females patients in both groups, attributed to the short female urethra with its close proximity to anal canal allowing easier contamination and ascending of infection.

Generally, there was high incidence of UTI among patients with B- thalassemia major, compared to B-thalassemia intermedia, minor and sickle cell thalassemia as risk factor for infection occur more in B-thalassemia major like iron overload, splenectomy & allogenic blood transfusion, while in the current study there was no significant difference among all patients with different types of thalassemia which may be explained by small sample size.

Escherichia coli is the commonest microorganism in our study as it is able to attach the bladder wall and produced biofilm that resist the body immune response⁽²⁰⁾.

The abdominal pain & dysuria are the concurrent symptoms in all patients, while tenderness occur in 50 % and no cases of abdominal mass.

This indicate that signs and symptoms of UTI were not specific.

The investigation like WBC, ESR, CRP, are negative in patients with UTI, while pyuria occur in most cases of UTI.

Conclusion

- 1) The current study revealed that the frequency of UTI among febrile thalassemic patients is 14 %, and its increased with splenectomy, incomplete vaccination and in cases of iron overload.
- 2) Abdominal pain and dysuria are the commonest symptoms, while the pyuria occur in 92 % of all cases

Recommendations

- 1) Urinary tract infection is common in febrile thalassaemic patients, therefore routine screening is recommended during febrile illness.
- 2) Encouragement of giving vaccine to all thalassaemic patients according to the national program & additional vaccine including E coli vaccine has shown promise in preventing UTI.
- 3) Splenectomy shouldn't be done unless strictly indicated.
- 4) Advise the family to maintain pre transfusion Hb above 8.5 gm /dl with adequate chelation therapy.

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