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Study of Prevalence and Risk Factors of Nocturnal Enuresis in Children with Thalassemia Major

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ABSTRACT

Background: Patients with thalassemia major face an extra challenge in the form of nocturnal enuresis.

Objective: To evaluate and assess the prevalence and risk factors of nocturnal enuresis in thalassemia major patients.

Patients and Methods: Data of this cross-sectional study was gathered from the clinical records in the out-persistent facility of Pediatric Hematology and Oncology Unit, Zagazig clinics. The study recruited 132 children aging 6-18 years. They were submitted to careful history taking including (age, sex, place, protocol of therapy, duration of follow up), thorough clinical examination and laboratory tests included: CBC and reticulocyte count, bilirubin (direct – indirect), hemoglobin electrophoresis test, liver function tests, kidney function tests, random blood sugar, urine analysis, bacterial count in urine and paired serum and urine osmolality.

Results: There was statistically significant relation between the age, family history, splenectomy and nocturnal enuresis. There was statistically significant relation between decreasing nocturnal enuresis and regularity of blood transfusion. The ferritin levels were statistically lower in patients with nocturnal enuresis than those without nocturnal enuresis. A statistically significant negative correlation was found between urine osmolality and ferritin levels in patients with nocturnal enuresis.

Conclusion: Family background of enuresis and family and social issues have a significant job in the predominance of bedwetting among thalassemia major patients. The predominance of nighttime enuresis in patients with thalassemia significantly declines with expanding age and customary blood transfusion. The rate of bedwetting increments in thalassemia major patients with iron and hemoglobin inadequacy.

Keywords: Nocturnal Enuresis, Thalassemia Major, Children.

INTRODUCTION

Beta-thalassemia is widely spread in the Mediterranean, Middle-East, Transcaucasus, Central Asia, Indian subcontinent, and Far East **(1).**

Beta thalassemia is collection of inherited blood disturbances distinguished by abnormality in the hemoglobin beta chains synthesis, which leads to mutable phenotypes extended from intense anemia to clinically asymptomatic persons. The average number of people experiencing symptoms in a year is about 1 in 100,000 in the world **(2)**.

There are three main forms of thalassemia: thalassemia major, thalassemia intermedia and thalassemia minor. Persons with thalassemia major suffers from intense anemia within the first two years of life, and they need to regular blood transfusions **(2)**. People who do not receive treatment or do not have regular blood transfusions suffer from growth retardation and skeletal deformities, jaundice, hepatosplenomegaly, leg ulcers, and masses of extramedullary hematopoiesis **(3).**

Nocturnal enuresis is involuntary urination that happens at night while sleeping, after the age when a person should be able to control his or her bladder. A child under 5 years old is not considered enuretic. In order to consider a child at the age of 5-6 years suffering from involuntary urination, he must have two or more episodes of bedwetting per month. While from the age of 6 or more, he has one or more per month **(4).**

Genetic predisposition has a major role in the occurrence of urination in children. There is a study found that if both parents had urination when they were young, their children will suffer from involuntary urination by 77%, and this percentage drops to 43% if one of the parents only has involuntary urination, and decreases to 15% if the parents were not affected by urination when they were young **(3).**

We aimed at this work to evaluate and assess the prevalence and risk factors of nocturnal enuresis in thalassemia major patients.

PATIENTS AND METHODS

Data of this cross-sectional study were gathered from the clinical records in the out-persistent facility of Pediatric Hematology and Oncology Unit, Zagazig clinics. The study recruited 132 children in aging 6-18 years.

Incorporation measures:

- Children with thalassemia major between 6 to 18 years of age.
- Both genders were included

Avoidance measures:

- Thalassemic patients with renal illness.
- Thalassemic patients with diuretic drug ingestion.
- Thalassemic patients with diabetes mellitus.
- Thalassemic patients with diabetes insipidus.

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All cases have been surveyed by:

- Detail history from all patients and their folks were taken including beginning of voiding control, day as well as night wet, history of persistent disease (diabetes mellitus, cardiovascular breakdown, renal disappointment), diuretic drug ingestion, family ancestry of enuresis.
- Careful clinical assessment.
- Laboratory tests: The aftereffects of the accompanying investigations were got from documents of the cases in outpatient facility of Hematology and Oncology Unit, pediatric division, Zagazig College Medical Clinic.
- CBC and reticulocyte check.
- Bilirubin (direct – roundabout).
- Hemoglobin electrophoresis test.
- Liver capacity tests.
- Kidney work tests.
- Random glucose.
- Abdominal ultrasound.

Tests were taken from the cases; they were put away in a refrigerator and were taken to the lab to do the accompanying breaks down:

- Paired serum and pee osmolality.
- Urine examination.
- Bacterial include in pee.

Serum osmolality:

The patient had to give some information about two things:

- All the supplements and medications he was taking.
- A little blood sample was collected from a vein in the patient's arm to determine whether or not he was consuming an excessive amount of water.

Pee osmolality test:

Planning for the pee osmolality test:

The patient had to maintain a healthy diet in the days leading up to the test. Sometimes, the patient was told to avoid drinking for 12 to 14 hours before the exam.

Due to the potential for interactions between some medications and the results of a urine osmolality test (especially dextran and sucrose), we needed to know everything he was taking.

The methodology:

The test calls for a 100% accurate catch-and-pee procedure. If the patient was a woman, she had also to clean her urethra and labia. If the patient was a man, he had to wash the hair from the top of his penis. At that point, the patient urgently urinated in the restroom. Quickly the urine flow was halted and the sterile cup was placed. The patients had to begin urinating again, filling the cup halfway. The coordinated sealing of the cup was an attempt to preserve its value.

Test:

The pee test was by the same token

1) An arbitrary example.
2) Urine test 24 hours.

The examples were gathered into perfect, sterile pee holders.

Osmolality was estimated in the pee utilizing a procedure called osmometer.

This procedure was utilized twoly.

1-Freezing point: It is the most generally utilized technique, acquired based on the estimation of the temperature at which the pee test freezes.

2-Pressure of vanishing:

It is acquired dependent on the temperature and weight at which the pee test vanishes, and calculation of osmolality in the pee by rehashed is viewed as mistaken because of the best particles of waste discharged in the pee, the most significant of which is creatinine, as there are huge amounts in the pee that can influence the outcomes.

The osmolality of urine is measured in mOsm/kg (milliosmoles per kilogramme of water). Typically, results fall between 500 and 850 mOsm/kg, however they can fluctuate slightly.

Ethical approval:

The Zagazig Medical Ethics Committee of the Zagazig Faculty of Medicine gave its approval to this study. Written informed permission was acquired from the parents before their children participate in the study, after being told about the study's goals, methodology, and any applicable objectives. The Helsinki Declaration was followed throughout the study's conduct.

Statistical Analysis:

Data were collected, tabulated, and analysed using IBM Corp. Released 2015. IBM SPSS Statistics 23 for Windows Edition. New York State, Armonk; IBM Corp. Quantitative data was characterised by means, standard deviations, and medians (ranges), whereas qualitative data was characterised by numbers and percentage. When comparing two sets of data that follow the same normal distribution, the t test was employed. In order to compare two groups whose data were abnormally distributed, the Mann-Whitney U test was performed. Chi-square test was used to compare two proportions or other categorical variables. $P<0.05$ was considered significant.

RESULTS

This table shows that the age of the contemplated cases went from 6 to 18 years with mean 10.93 years age and 42.4% were from 6 to 9 years of age. As to 53.8% were guys.

Table (1): Demographic information of the considered gathering

Variable	(n=132)	
Age: (year)		
Mean ± SD	10.93 ± 4.23	
Median	10	
Range	6 - 18	
Variable	**No**	**%**
Age group:		
6– 9 years	56	42.4
10- 14 years	41	31.1
15 – 18 years	35	26.5
Sex:		
Male	71	53.8
Female	61	46.2

This table shows that 43.2% of the contemplated cases had +ve family background of NE and 39.4% had day by day social and family issues. 12.1% of patients were splenectomized, 14.4% of patients were received blood transfusion sporadically and 17.4% didn't take iron chelation routinely

Table (2): Family and present history among the contemplated gathering

Variable	(n=132)	
	No	**%**
Family history of nocturnal enuresis:		
No	75	56.8
Yes	57	43.2
Daily social and family problems:		
No	80	60.6
Yes	52	39.4
Splenectomy:		
No	116	87.9
Yes	16	12.1
Blood transfusion:		
Regular	113	85.6
Irregular	19	14.4
Iron chelation:		
Regular	109	82.6
Irregular	23	17.4

This table shows that 40.9% of the contemplated cases had nighttime enuresis.

Table (3): Frequency of nighttime enuresis among the contemplated gathering

Variable	(n=132)	
	No	**%**
Nocturnal enuresis		
No	78	59.1
Yes	54	40.9

This table shows that there was factual importance decline in mean age among cases who had nighttime enuresis contrasted with cases that hadn't and increment in recurrence of nighttime enuresis among cases from 6 to 9 years of age contrasted with other age gatherings. No distinction was found between them in sex circulation.

Table (4): Relation between nighttime enuresis and age variable among the examined gathering

Variable	No NE (n=78)		NE (n=54)		MW	P
Age: (years)					**5.29**	**<0.001 ****
Mean ± SD	12.58 ± 4.07		8.56 ± 3.23			
Median	13		8			
Range	6 - 18		6 - 18			
Variable	**N**	**%**	**N**	**%**	**χ^2**	**P**
Age group:					**28.12**	**<0.001 ****
6 – 9 (n=56)	20	35.7	36	64.3		
10 – 14 (n=41)	26	63.4	15	36.6		
15 – 18 (n=35)	32	91.4	3	8.6		
Sex:						
Male (n=71)	42	59.2	29	40.8	0.01	0.99
Female (n=61)	36	59	25	41		

**: Highly significant

This table shows that there was measurable noteworthiness increments in recurrence of nighttime enuresis among cases had +ve family background of NE, had social and family issues and cases had unpredictable blood transfusion. Likewise, there was a factual hugeness increment in recurrence of not having NE among cases had done splenectomy.

Table (5): Relation between nighttime enuresis and segment information among the examined gathering

Variable	No NE (n=78)		NE (n=54)		χ^2	P
	N	%	N	%		
Family history of nocturnal enuresis:						
No (n=75)	56	74.7	19	25.3	**17.43**	**<0.001 ****
Yes (n=57)	22	38.6	35	61.4		
Social and family problems:						
No (n=80)	60	75	20	25	21.26	**<0.001 ****
Yes (n=52)	18	34.6	34	65.4		
Splenectomy:						
No (n=116)	64	55.2	52	44.8	**6.08**	**0.01***
Yes (n=16)	14	87.5	2	12.5		
Blood transfusion:						
Regular (n=113)	71	62.8	42	37.2	**4.55**	**0.03***
Irregular (n=19)	7	36.8	12	63.2		
Iron chelation:						
Regular (n=109)	64	58.7	45	41.3	0.04	0.85
Irregular (n=23)	14	60.9	9	39.1		

*: Significant, **: Highly significant

This table shows that there was factual hugeness diminishes in mean ferritin, ALT, Hb and HTC and among cases had nighttime enuresis contrasted with cases hadn't.

Table (6): Relation between nighttime enuresis and research facility discoveries among the contemplated gathering

Variable	No NE (n=78)	NE (n=54)	Test	P
Ferritin: (ng/ml)			**MW**	
Median	1750.5	1190.5	**2.22**	**0.03***
Range	363 - 4470	285 - 3290		
ALT: (IU/L)			**t**	
Mean ± SD	41.13 ± 10.04	27.91 ± 6.25	**8.59**	**<0.001 ****
Creatinine: (mg/dl)			t	
Mean ± SD	0.72 ± 0.17	0.72 ± 0.18	0.08	1.0
Albumin: (mg/dl)			t	
Mean ± SD	4.41 ± 0.49	4.45 ± 0.50	0.47	0.64
Hb: (gm/dl)			**t**	
Mean ± SD	8.78 ± 0.97	8.22 ± 1.01	**3.24**	**0.002 ****
HTC: (%)			**t**	
Mean ± SD	27.17 ± 2.22	26.28 ± 2.06	**2.34**	**0.02***
WBCs: ($x10^3/mm^3$)			**MW**	
Mean ± SD	11.85 ± 2.94	12.21 ± 2.99	**2.03**	**0.08**
Platelets: (x103/mm3)			t	
Mean ± SD	270.26 ± 49.80	275.67 ± 50.06	0.61	0.54

Median and range: Non-parametric test.
*: Significant, **: Highly significant

This table shows that there was factual hugeness negative connection between pee osmolality and ferritin among NE cases.

Table (7): Correlation among pee and serum osmolality and research center discoveries among NE cases

Variable		Urine osmolality (n=54)	Serum osmolality (n=54)
Ferritin (ng/ml)	**r**	**-0.29**	0.06
	P	**0.04***	0.64 NS
ALT (IU/l)	**r**	0.04	0.05
	P	0.78 NS	0.72 NS
Creatinine (mg/dl)	**r**	0.13	0.12
	P	0.36 NS	0.37 NS
Albumin (mg/dl)	**r**	-0.19	0.04
	P	0.16 NS	0.76 NS
Hb (gm/dl)	**r**	0.07	0.02
	P	0.62 NS	0.88 NS
HTC (%)	**r**	0.12	0.04
	P	0.40 NS	0.76 NS
WBCs ($x10^3/mm^3$)	**r**	0.04	0.01
	P	0.77 NS	0.95 NS
Platelets ($x10^3/mm^3$)	**r**	-0.01	-0.22
	P	0.96 NS	0.10 NS

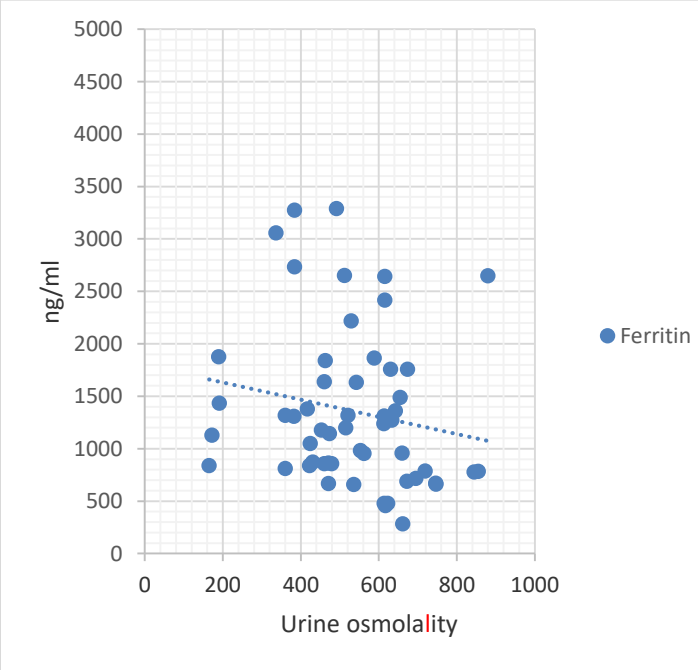

Figure (1): Correlation between pee osmolality and ferritin among NE cases.

DISCUSSION

Thalassemia is an inherited form of anemia caused by hemoglobin manufacturing deficiencies. B-thalassemia, characterized by a shortage of B-globin chains, is fatal and has devastating long-term effects on many systems in the body [(5)].

Bedwetting, also known as nocturnal enuresis, is the most frequent form of urine incontinence in children. The youngster and their family's mental health suffers greatly as a result. The inability to control urination during sleep in otherwise toilet-trained children is known as enuresis nocturna. Primary if no previous attempt at continence has been successful, secondary after 6 months of dry nights [(6)].

This study is a cross sectional study included 132 patients aged 6-18 years old with thalassemia major from the outpatient clinic of Hematology and Oncology Unit, Pediatric Department, Zagazig University Hospital.

We aimed to evaluate and assess the prevalence and risk factors of nocturnal enuresis in children. Males constituted 53.8%of patients and females were 46.2%. Our patients were divided according to the age into three groups from 6-9 years old, from 10-14 years old and 15 to 18 years old. 43.2% of our cases had a family history of nocturnal enuresis, 39.4% had daily social and family problems, 12.1% had a history of splenectomy, 14.4% had a history of irregular blood transfusion and 17.4% were irregular in taking of the iron chelation.

In the present study, (40.9%) of studied patients had nocturnal enuresis and we found the mean values of serum osmolality levels 276.83±5.20 (mOsm/kg) while urine osmolality values were 531.85 ± 162.35 (mOsm /kg) in patients with nocturnal enuresis and 48.1% of patients with enuresis had not bacterial growth.

In our study, there was statistically significant relation between the age and nocturnal enuresis, where the frequency of enuresis is more among the patients from (6-9) years. This came in agreement with **Ekinci *et al.*** [(7)] who found the prevalence of enuresis is higher in younger thalassemic patients. Also, this is compatible with **Mahmoodzadeh *et al.*** [(8)] as the frequency of bedwetting episodes tends to diminish steadily with age, as they discovered.

In our study, there was no statistically significant difference in prevalence of nocturnal enuresis in both sexes. This is compatible with **Mahmoodzadeh *et al.*** [(8)]. But this result is inconsistent with **Saleh and Al-Saffar** [(9)], where they found males were significantly more enuretic than females.

In our study there was statistically significant relation between family history and nocturnal enuresis, where the occurrence of enuresis was more in patients with family history when compared with those without. This is compatible with **Von Gontard *et al.*** [(10)], where he revealed strong correlations between parents' enuresis and their children's bedwetting.

In this study, there was statistically significant relation between increasing the frequency of nocturnal enuresis and family and social problems. This is compatible with **Coppola *et al.*** [(11)] who discovered a correlation between nocturnal enuresis and family difficulties. Also, **Ekinci *et al.*** [(7)] discovered that patients who have everyday social and familial problems are more likely to have recurrent cases of nocturnal enuresis.

The existence of frequent bedwetting, in addition to waking patients and cleaning their clothes or bed linens, is an extra strain for families caring for thalassemic patients because of their severe dependence on them. When incontinence persists into adulthood, it can cause stress on relationships because loved ones may experience conflicting emotions about being a social or emotional burden. They may avoid directly criticizing patients, yet they may act passively aggressively toward their work. All of these things might cause friction in the home [(7)].

In this study, there was statistically significant relation between decreasing nocturnal enuresis and regularity of blood transfusion, while there was no statistically significant relation between regularity and irregularity of compliance of iron chelation therapy. Also, there was statistically significant relation between nocturnal enuresis and splenectomy, severity of enuresis was substantially correlated with sleep apnea, suggesting a link between sleep disorders and hyperplasia of lymphoid organs [(12)].

In our study, there was statistically significant relation between decreasing of hemoglobin and nocturnal enuresis. This is compatible with **Ponticelli *et al.*** [(13)]. Enuresis rates in patients with thalassemia major may have been influenced by the kidney characteristics in relation to anemia levels. Evidence suggests that chronic anemia in thalassemic patients has a role in the development of nephropathy.

Another study by **Ekinci *et al.*** [(7)] attributed the correlation between stress and illness progression to chance or to individual differences in patients' levels of stress.

In our study there was no statistically significant difference in serum creatinine, albumin, WBCs, and platelets levels of thalassemia patients with or without enuresis. Interestingly, the ALT and HTC levels of thalassemia major patients without enuresis were found to be higher than that of those with enuresis. This is compatible with **Ekinci *et al.*** [(7)]. However, this observation seems fortuitous, and its significance may be attributed entirely to the limited size of the sample used.

The ferritin levels were statistically lower in patients with nocturnal enuresis than those without nocturnal enuresis. This is in contrast to **Albayrak *et al.*** [(14)] when they discovered that the nocturnal enuresis group had a greater blood ferritin value than the control group.

CONCLUSION

The predominance of nighttime enuresis in patients with thalassemia significantly declines with expanding age. Family background of enuresis and family and social issues have a significant job in the predominance of bedwetting among thalassemia significant patients. The pervasiveness of nighttime enuresis in thalassemia major patients is diminished with customary blood transfusion. The rate of bedwetting increments in thalassemia significant patients with iron and hemoglobin inadequacy.

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REFERENCES

1. **Cao A, Galanello R (2010):** Beta-thalassemia. Genetics in Medicine, 12(2): 61-76.
2. **Galanello R, Origa R (2010):** Beta-thalassemia. Orphanet Journal of Rare Diseases, 5(1): 11-15.
3. **Chatterjee R, Bajoria R (2010):** Critical appraisal of growth retardation and pubertal disturbances in thalassemia. Ann N Y Acad Sci., 1202:100–14.
4. **Thiedke C (2003):** Nocturnal enuresis. American Family Physician, 67(7): 1499-1506.
5. **Rund D, Rachmilewitz E (2005):** β-Thalassemia. New England Journal of Medicine, 353(11): 1135-1146.
6. **Arda E, Cakiroglu B, Thomas D (2016):** Primary nocturnal enuresis: a review. Nephro-urology monthly, 8(4): e35809. doi: 10.5812/numonthly.35809
7. **Ekinci O, Celik T, Ünal Ş *et al.* (2013):** Nocturnal enuresis in sickle cell disease and thalassemia major: associated factors in a clinical sample. International Journal of Hematology, 98(4): 430-436.
8. **Mahmoodzadeh H, Amestejani M, Karamyar M *et al.* (2013):** Prevalence of nocturnal enuresis in school aged children: the role of personal and parents related socio-economic and educational factors. Iranian Journal of Pediatrics, 23(1): 59-63.
9. **Saleh A, Al-Saffar A (2015):** Nocturnal enuresis and its relation to child's behavior in a sample of children from Baghdad, Iraq. Iraqi Journal of Medical Sciences, 13(1): 7-13.
10. **Von Gontard A**, **Schaumburg H, Hollmann E *et al.* (2001):** The genetics of enuresis: a review. J Urol., 166 (6): 2438–2443.
11. **Coppola G, Costantini A, Gaita M *et al.* (2011):** Psychological correlates of enuresis: a case-control study on an Italian sample. Pediatr Nephrol., 26:1829–36.
12. **Esezobor C, Akintan P, Nwaogazie U *et al.* (2018):** Enuresis in children and adolescents with sickle cell anaemia is more frequent and substantially different from the general population. PloS One, 13(8): e0201860. doi: 10.1371/journal.pone.0201860
13. **Ponticelli C, Musallam K, Cianciulli P *et al.* (2010):** Renal complications in transfusion-dependent beta thalassaemia. Blood Rev., 24:239–44.
14. **Albayrak S, Zengin K, Tanik S *et al.* (2015):** Vitamin B12, folate and iron levels in primary nocturnal enuresis. Pakistan Journal of Medical Sciences, 31(1): 87-90.