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Editorial

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Adrenal Insufficiency in Patients with Beta-Thalassemia Major in the Southeast of Iran

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Letter to Editor

Beta-thalassemia is a hereditary blood disorder in which the synthesis of the hemoglobin beta chain is halted or severely diminished, chiefly due to genetic mutations. Today, the province of Sistan and Baluchistan has the highest disease prevalence in southeast Iran, with about 3,000 thalassemia patients[1]. Adrenal dysfunction has been reported to arise in patients with beta-thalassemia major due to iron deposition in adrenal glands [2]. We aimed to determine the prevalence of adrenal insufficiency in children with β-thalassemia major who had been referred to Ali Asghar Hospital, Zahedan. The Local Ethics committee of Zahedan University of Medical Sciences approved the study's design (IR.ZAUMS.REC.1396.239).

Fifty patients (33 females and 17 males, mean age: 22.34 ± 5.60 years) diagnosed with beta-thalassemia major were selected for the purpose of this study. Before the scheduled blood transfusion at 8 a.m., 5 mL of blood was collected from each patient. Upon completing blood transfusion, the patients were intravenously injected with 250 µg of cosyntropin to stimulate cortisol release. Then, two consecutive series of blood samples were collected 30 and 60 minutes after the injection. The samples were sent to the hospital laboratory to evaluate total and post-stimulation serum cortisol levels.

As shown in Table 1, 30 minutes after the administration of cosyntropin, 100% of patients had experienced a significant rise in their basal cortisol level, and either had normal or higher than normal level of cortisol in their blood ($p < 0.001$). However, 60 minutes after the injection of cosyntropin, 100% of patients had cortisol level above the normal range ($p < 0.001$). Besides, of the 18 patients aged 18 and below, only 3 subjects (16.66%) had insufficient basal cortisol level, whereas 15 (83.83%) had normal basal cortisol level ($p < 0.001$). We found that 60 minutes after the cosyntropin injection, all patients in both age groups had cortisol level above the normal range ($p < 0.001$). The resulting increase in the serum cortisol level of patients (n=5) with subnormal baseline cortisol 30 minutes after stimulation with

cosyntropin indicated secondary adrenal insufficiency in these patients.

Table 1: Distribution of gender groups at cortisol levels at different times after injection in patients with thalassemia major

Time after injection	Cortisol level	Patients, n (%)			P
		Male	Female	Total	
8 a.m. (baseline)	Insufficient	2(4)	3(6)	5(10)	<0.001
	Normal	15(30)	30(60)	45(90)	
	Total	17(34)	33(66)	50(100)	
30 minutes	Insufficient	0(0)	0(0)	0(0)	<0.001
	Normal	17(34)	33(66)	50(100)	
	Total	17(34)	33(66)	50(100)	
60 minutes	Insufficient	0(0)	0(0)	0(0)	<0.001
	Normal	17(34)	33(66)	50(100)	
	Total	17(34)	33(66)	50(100)	

The results of this study favored the sensitivity of the low-dose ACTH stimulation test in the examination of the hypothalamic-pituitary-adrenal axis in patients with secondary adrenal insufficiency over the high-dose test. It concluded that in patients with a normal baseline cortisol level, the low-dose test could efficiently detect hidden secondary adrenal insufficiency [3].

In 2017, 726 thalassemia patients aged between 2.5 and 80 years were registered at 12 thalassemic centers in 9 various countries. Of whom, 522 patients were registered from Qatar, Iran, Oman, Cyprus, and Jordan. In their population, the most common complications were osteopenia and osteoporosis (22.3%), hypogonadism (10.1%), and primary hypothyroidism (5.5%). In the subpopulation multivariate analysis, older age was found to be a risk factor for osteoporosis (Odds ratio: 7.870, 95 percent confidence interval (CI): 4.729-13.099, P 0.001), hypogonadism (Odds ratio: 6.310, 95 percent confidence interval (CI): 2.944-13.521, P 0.001), and non-insulin-dependent diabetes mellitus (NIDDM). These findings suggest the relatively high prevalence of endocrine complications in beta-thalassemia patients [4].

Another study in 2015 sought to evaluate possible endocrine disorders in 150 patients with beta-thalassemia major aged 15 to 22 years. The results of this study revealed the prevalence of primary hypothyroidism (6%), hypoparathyroidism (3.7%), type 1 diabetes (3.7%), and adrenal insufficiency (only one patient) in this population[5]. Our study, however, only investigated the presence of adrenal insufficiency among a specifically selected population of beta-thalassemia major patients and revealed a 10 percent prevalence of endocrine disorder.

This study had limitations. First, the sample size was small. Second, as the half-life of cortisol is twice as long as this duration, it would be helpful if this study also considered the individual differences in the clearance of cortisol from the bloodstream. Since stress, body mass index, corticosteroid-binding globulin, and hypothalamic-pituitary-adrenal axis can affect the adrenal response to cosyntropin, these factors should be taken into account in the future studies.

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