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Thyroid Function Test In Sickle-Cell Disease

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Abstract
Objective: *This cross-sectional study aimed to evaluate the thyroid function (triiodothyronine [T3], thyroxine [T4], and thyroid-stimulating hormone [TSH] levels) in patients with sickle-cell disease (SCD).*
Methods: *This cross-sectional observational study was conducted at BRLSABVM Medical college,Rajnandgaon(Chhattisgarh).Patients included from Medicine and Paediatrics Department. Sixty-eight patients with SCD were enrolled for assessing their thyroid function. The reference ranges for serum T4 (4.5–12 µg/dL), serum T3 (60–200 ng/dL), and TSH (0.3–5.5 uIU/mL) were defined to evaluate the thyroid function.*
Results: *The average TSH, mean T4 level, and mean T3 level among the patients were 4.02, 4.67, and 74.15, respectively. The incidence rates of hypothyroidism and euthyroid status were 23.5% and 76.5%, respectively. While 9.59 g/dL was the mean hemoglobin level, 11–16 g/dL was observed in 42.6% of patients compared to <11 g/dL in 57.4% of patients. Patients within the age group of 14-25 years had a higher incidence of hypothyroidism (62.5%). The differences in hypothyroidism between males and females were statistically insignificant (68.8% vs. 31.2%, p = 0.11).*
Conclusion: *Patients with SCD had clinically significant reductions in T3 and T4 levels. In addition, higher levels of TSH and reductions in endogenous T3/T4 levels were observed in male patients. Overall, SCD was associated with a higher incidence of hypothyroidism.*
Keywords: *Sickle-cell anemia, Sickle-cell disease, Hypothyroidism, Thyroid function test.*

INTRODUCTION

Hemoglobinopathies are diseases that affect how hemoglobin works, is made, and is built [1]. When a glutamate is replaced by a valine at the sixth position, it causes a point mutation in the beta globulin gene, which leads to a hereditary structural problem with hemoglobin. The first disease related to abnormal hemoglobin was found in Chicago by James Herrick in 1910 [2]; this condition was later called sickle cell anemia in 1922 [3]. The complications of sickle cell disease (SCD) include long-term damage to organs, organ failure, both acute and chronic anemia, blockage of small blood vessels, breakdown of red blood cells, and problems with hemoglobin production [4]. When hemoglobin sickles, it can't carry as much oxygen, which leads to anemia, hemolytic crises, and damage to organs. People with SCD are at a high risk of death, have more years lost to disability due to organ problems, and live shorter lives [5]. Those with the HbSS form of hemoglobin are especially likely to have SCD [6]. This condition is most common in the Indo-Arabian region and sub-Saharan Africa [7]. In India, SCD was first described by Dunlop and Mujumdar, but its frequency was first recorded in 1967 by Raman et al. in Western Odisha [8]. Sickling happens at birth in low numbers, but it increases over several months [9]. Vaso-occlusive crises happen when there is a lot of HbS in the blood. In Africa, infants and children with homozygous SCD often die early [10]. But people with the same condition in other parts of the world can live between 35 to 66 years. Studies show that the rate of SCD is similar in men and women [11]. Globin is a protein about 64,000 Da in size and makes up most of hemoglobin [12]. It also combines with heme, which is part of each of the two globin chains. Hemoglobin's structure comes from a complex arrangement of alpha, beta, and delta chains. Two alpha chains and two beta chains form HbA, while the combination of alpha and beta chains makes up HbA2 [13]. The complications of SCD include blood vessel blockage, infections, anemia, and hemolysis [14]. Infections in SCD patients raise the risk of other health issues and death. However, the main cause of death in older SCD patients is stroke and acute chest syndrome [15]. The symptoms of SCD include a steady state, acute crisis, and long-term problems. The steady state is linked to gallstones, enlarged spleen, and jaundice.

The way the disease SCD shows itself includes three main phases: steady state, acute crisis, and long-term complications. During the steady state, people may have gallstones, an enlarged spleen, yellowing of the skin (jaundice), and slow growth [16]. In an acute crisis, there is a higher chance of sudden kidney failure and reduced spleen function. Serious complications during this time can include liver problems like

blockage of bile flow and trapping of red blood cells in the liver [17]. Over time, SCD can lead to long-term issues such as kidney disease, high blood pressure in the lungs, strokes, and loss of vision [18].
It is important to check how the thyroid works in people with SCD to better understand the risk of both sudden and long-term health problems.
Recent studies have found a strong link between SCD and higher levels of free T4, which can affect the heart and increase the risk of sudden heart-related death [19]. This may be because the heart muscle cells in SCD do not function normally due to changes in thyroid hormone levels. However, current research does not offer clear guidelines to measure the risk of other health problems that come with SCD. This study was done to address this by looking at the thyroid function in people who have SCD.

METHODS

Study design This cross-sectional observational study was conducted at BRLSABVM Medical college, Rajnandgaon(Chhattisgarh) .The investigation was performed in the sickle cell clinic, Medical and Pediatrics ward and outpatient department (OPD) .The study population was comprised patients with SCD (n=68) who received treatment .

Inclusion and exclusion criteria

Patients with a definitive SCD diagnosis were included in this study. The diagnostic confirmation was done by high-performance liquid chromatography, hemoglobin electrophoresis, and sickling test. However, patients with sickle cell trait, sickle beta thalassemia, sickle cell-hemoglobin C, diabetes mellitus, hypertension, and chronic kidney disease were excluded from this study.

Data and sample collection The data collection sources included the patient's detailed clinical history, clinical examination findings, bed head tickets, sickling slide test, hemoglobin electrophoresis results, high-performance liquid chromatography outcomes, and radioimmunoassay for thyroidstimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3) levels. This study enrolled 68 patients who fulfilled the eligibility parameter. The clinical variables were analyzed after collecting 5 mL of the patient's blood through venous access. Total T4, total T3, and TSH levels were calculated after serum separation. The reference ranges for serum T4 (4.5–12 µg/dL), serum T3 (60–200 ng/dL), and TSH (0.3–5.5 uIU/mL) were defined to evaluate the thyroid function.

Data analysis The statistical analysis of the patient data was performed by IBM SPSS27 version. The means, standard deviations, and percentages of T3, T4, and the TSH were calculated for examining the thyroid function [20].

RESULTS

This study included 68 patients with SCD; of them, 51.5% (n=35) were males and 48.5% (n=33) were females. The mean age of the patients with SCD was 24.38 years (standard deviation: 6.82). Patients between the age group of 45–60 years were 1.5% of the total study population. In addition, 4.4% of patients were in the age range of 35–45 years, and 29.4% of them were in the age group of 25–35 years. However, most of the patients (64.7%) belonged to the age group of 14–25 years. The laboratory assessments and clinical examinations aimed to determine the overall health status of the study participants. Table 1 describes the overall clinical signs of patients with SCD. While hypotension was recorded in 29.4% of patients, normal systolic blood pressure was observed in 70.6% of patients. Of note, no patient had abnormal diastolic blood pressure. Most patients (92.6%) had a normal heart rate, whereas tachycardia was reported in 7.4% of the participants. Normal respiratory rate was reported in 60.3% of patients with SCD, whereas tachypnea was observed in 39.7% of participants. Almost 7.4% of patients had <95% of oxygen saturation level. Table 2 demonstrates the hematological profile of patients with SCD. The blood glucose levels of most patients (98.5%) were reportedly normal; however, a random blood sugar of >150 g/dL was observed in one patient. While 9.59 g/dL was the mean hemoglobin level, 11–16 g/dL was observed in 42.6% of patients compared to <11 g/dL in 57.4% of patients. Overall, 7.4 of patients had <1.5 lac platelet count,

DISCUSSION

While most (76.5%) of the patients had normal thyroid function, 23.5% were found to have hypothyroidism. People aged between 14 and 25 years had a higher chance of having hypothyroidism (62.5%). The difference in hypothyroidism rates between males and females was not statistically significant (68.8% vs. 31.2%, p=0.11).

The results of this study agree with the findings of Soliman et al., who described the connection between central or primary hypothyroidism and sickle cell disease (SCD), considering the severity of anemia and the age of patients [21].

Additionally, poor chelation is seen in patients with high ferritin levels [22]. El-Alfy et al. found that patients with SCD had higher pulsatility and resistance in their thyroid blood flow, along with a smaller thyroid size [23]. Özen et al. reported a significant decrease in endocrine functions among SCD patients [24]. It is important to identify all possible causes of hypothyroidism in SCD to understand how it affects endocrine problems. Phillips Jr et al. found that hypothyroidism can happen in SCD patients who get many blood transfusions, which may affect endocrine function [25]. A recent study shows a possible link between thyroid disease and pulmonary arterial hypertension [26]. This suggests that checking blood pressure in the lungs for SCD patients could help in better diagnosis.

As SCD progresses, the function of the blood vessels gets worse, leading to a smaller thyroid size [23].

Studies show that 10% and 12% of SCD patients have subclinical and primary hypothyroidism, respectively [27]. Thyroid function tests show similar results across all genotypes of SCD patients [28]. Research indicates that SCD patients who have viral hepatitis C have a significant decrease in thyroid size [29]. However, there is no clear link between iron overload (measured by liver iron and ferritin levels) and thyroid blood flow changes [23]. Still, issues with blood vessels and tiny blood flow in the thyroid may hurt its function in SCD patients.

The mixed results from thyroid function tests in SCD patients show the need for better diagnostic tests to improve patient outcomes.

It is important to check if other health problems affect the thyroid function in SCD patients. Also, high thyroid-stimulating hormone (TSH) levels and lower levels of endogenous T3 are linked to the SS genotype in male SCD patients [30].

In addition, SCD may be linked to high levels of the TSH-releasing hormone, causing TSH to build up abnormally, which can lead to thyroid problems [19]. Recent studies have found that people with high iron deposits in their bodies often have thyroid issues, suggesting that damage to cells from too much iron in the blood might affect thyroid function in SCD patients [21]. However, most people with SCD do not experience issues with their pituitary-thyroid system [31]. Also, the abnormal levels of T3 and T4 in SCD show that the thyroid-binding proteins in the blood are not working as they should [32]. These findings highlight the importance of checking thyroid function in SCD patients to understand their overall health.

This cross-sectional study was performed on 68 patients with SCD, including 48.5% of females and 51.5% of males, respectively. The overall results indicated the mean values of T4 (4.67±0.86/range: 2.08–5.93), T3 (74.15/range: 2.08–5.93), and TSH (4.02±2.33/range: 2.01–11.96).

The inconsistent findings of the thyroid function test in SCD cases indicate the need for further diagnostic assessments for improving clinical outcomes. It is important to rule out the possible impact of comorbidities on the thyroid function of patients with SCD. Clinically significant elevation in the TSH and reduction in endogenous T3 levels in SCD cases also correlate with the SS genotype of the male patients [30]. In addition, SCD is possibly associated with high levels of the TSH-releasing hormone, resulting in abnormal accumulation of TSH, which eventually leads to thyroid dysfunction [19]. Findings from recent studies indicate abnormal thyroid function in patients with high iron deposits, which indicates the possible impact of cellular damage due to transfusional hemosiderosis on the thyroid function of patients with SCD [21]. However, most patients with SCD do not develop pituitarythyroid axis abnormality [31]. In addition, the abnormal levels of T3 and T4 in SCD indicate inconsistencies in the thyroid-binding levels of the globulin [32]. These outcomes substantiate the requirement of the thyroid function test in SCD to determine the clinical outcomes.

CONCLUSION

This study looked at the results of thyroid function tests in people with sickle cell disease (SCD).The findings showed that T3 and T4 levels were significantly lower in these patients, which is linked to the disease's condition. Male patients had higher TSH levels and lower amounts of naturally produced T3 and T4. Also, there was a higher rate of hypothyroidism in SCD patients. Since current research hasn't explained the causes of thyroid issues in SCD, future studies should look into these results to better understand how hypothyroidism develops and what health problems it might cause in people with SCD.

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