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Research Article

Chronic Renal Complications and Their Risks in Thalassemic Patients Receiving Transfusion

Sahin Bayramli [1], Aysu Ismayilova [1], Aygun Suleymanova [1] and Shamsiyya Asgarli [2]

[1] Department of Natural Sciences, School of Innovative Engineering and Natural Sciences, Western Caspian University, Baku, AZ1072, Azerbaijan

[2] Thalassemia Division of the National Center of Hematology and Transfusion, Ministry of Health of the Republic of Azerbaijan

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Abstract

Our study aimed to describe the prevalence, main clinical features, and risk factors for renal and urinary tract complications in patients with thalassemia. This study assessed renal complications and their main clinical features in 177 thalassemic patients evaluated between 2025 and 2026 and compared the results with renal complications observed in sickle cell anemia. This study evaluated 177 patients with thalassemia examined between 2025 and 2026. Findings from renal ultrasonography alongside clinical data regarding age contribution, transfusion therapy, and detected renal pathologies were analyzed. Additionally, the clinical utility of clinical parameters and ultrasound findings in assessing renal function was reviewed. Finally, this study investigated the primary mechanisms of renal damage in thalassemia, highlighting key differences from the renal changes characteristic of sickle cell anemia.

Keywords: thalassemia, renal complications, microlithiasis, chronic transfusion, iron overload, renal function, eGFR, renal ultrasonography.

1. Introduction

Thalassemia is a group of hereditary hematological disorders caused by defects in the synthesis of hemoglobin globin chains. Severe forms of the disease require regular erythrocyte transfusions, which serve as the primary therapeutic approach to extend patients' lifespan. However, long-term transfusion therapy leads to systemic iron overload, resulting in tissue damage and ultimately organ failure. Among the organs affected, the kidneys are particularly vulnerable. Renal complications in thalassemic patients stem from multiple factors, including prolonged anemia, hypoxia, oxidative stress, and iron overload. Chronic anemia can induce renal hemodynamic alterations and early-stage hyperfiltration, whereas long-term disease progression may lead to tubular dysfunction, proteinuria, and other renal manifestations. In addition to iron toxicity, the use of certain iron chelators can also exert nephrotoxic effects.

Evaluating renal status in thalassemic patients relying solely on serum creatinine levels is insufficient. Comprehensive assessment—including estimated glomerular filtration rate (eGFR), urinary albumin and protein levels, calcium, phosphate, uric acid parameters, and renal ultrasonography—enables early detection of subtle renal changes.

Thalassemia patients require long-term blood transfusion therapy. Regular transfusions, along with accompanying

comorbidities, impair renal function. Tissue hypoxia, hemolytic processes, and iron overload play pivotal roles in the deterioration of renal function. Dysfunction of the renal tubules is among the primary drivers of the onset and progression of renal damage. Therefore, regular monitoring of the kidneys, ureters, and urinary bladder is essential in thalassemia patients receiving chelation therapy [1], [2].

Renal injury in thalassemic patients should be evaluated by considering both glomerular and tubular alterations. Chronic anemia in thalassemia leads to reduced oxygen delivery to the kidneys. The resulting hypoxic state negatively impacts renal hemodynamics and the filtration system. Consequently, compensatory hemodynamic adaptations emerge in thalassemic patients, manifesting in early stages as an elevated estimated glomerular filtration rate (eGFR)—a hyperfiltration phenomenon that serves as an early marker for the eventual development of renal failure. When the organism is exposed to prolonged, continuous hypoxic and hemodynamic alterations, progressive damage to the renal parenchyma ensues. Recurrent hemolytic events further exacerbate renal injury. During hemolysis in thalassemic patients, the breakdown of erythrocytes releases toxic cell debris and free hemoglobin, which impairs renal function and induces tissue injury. Furthermore, renal hypoxia adversely affects cellular energy metabolism. Decreased oxygen availability impairs mitochondrial oxygenation, leading to a marked reduction in ATP synthesis. In the setting of ATP depletion, intracellular accumulation of fluid and sodium (Na^+) occurs, ultimately triggering renal cell swelling and tissue damage [2], [3]. Can be expressed as below: Hemolysis – Oxidative stress – Renal cell damage – tubular dysfunction – kidney damage

During hemolysis, reactive oxygen species (ROS) and oxidative stress are generated, which exacerbate renal injury. Hemolysis-induced phosphaturia, hypercalciuria, and other metabolic byproducts directly target and damage the tubular structures. Another critical mechanism contributing to renal damage in thalassemic patients is iron overload. In patients receiving chronic erythrocyte transfusions, systemic iron accumulates and can also enhance intestinal iron absorption. Excess iron heightens oxidative stress, subsequently damaging various tissues, including renal glomeruli and particularly renal tubular structures [3].

Another key mechanism is hypercalciuria. In thalassemia patients, disrupted bone metabolism and altered mineral homeostasis lead to increased urinary calcium (Ca^{2+}) excretion [4], [5], [6].

In chronically transfused patients, hyperoxaluria represents an additional mechanism of renal injury. Increased urinary excretion of oxalate in these patients stimulates the precipitation of calcium oxalate crystals. Furthermore, hyperuricosuria plays a significant role: persistent erythrocyte destruction during hemolysis accelerates purine metabolism, leading to elevated uric acid levels that create a lithogenic environment. Hypocitraturia—a decrease in urinary citrate—further increases the risk of stone formation [5], [7], [8].

Tubular dysfunction is another vital mechanism. Elevated urinary protein and albumin excretion, accompanied by excessive urinary excretion of calcium and phosphate, predominantly signal the onset of proximal renal tubular damage [3], [9].

Additionally, iron chelation therapy can contribute to renal tissue damage. In thalassemic patients, chelation regimens frequently utilize deferasirox-containing agents, which can induce serum creatinine elevation. Deferasirox administration is associated with excessive urinary excretion of phosphate, uric acid, and other solutes, culminating in hypophosphatemia, hyperphosphaturia, and hypercalciuria [10], [11], [12], [13].

2. Materials and Methods

This retrospective observational study used the examination of hospital medical records of 177 patients with thalassemia assessed between August 2025 and August 2026. Data was collected with the permission of the healthcare institution. The study aimed to describe the frequency and distribution of renal and urinary tract abnormalities in patients with thalassemia, with particular emphasis on renal ultrasonographic findings and available clinical characteristics.

Data were retrospectively collected from patients' medical histories, available laboratory analysis results, medical records, and renal and abdominal ultrasonography reports. The extracted information included age, documented

renal abnormalities, and available records on erythrocyte transfusion therapy. Laboratory results were reviewed according to their availability in the medical records; therefore, not all laboratory parameters were necessarily available for every patient.

Renal ultrasonography reports were assessed to identify documented renal and urinary tract abnormalities. The recorded findings included microlithiasis, renal calculi, parenchymal and sinus cysts, increased renal parenchymal echogenicity, and other reported abnormalities. Of the 177 patients enrolled in the study, renal ultrasonographic abnormalities were documented in 137 patients. As more than one abnormality could be present in each patient, the number of recorded findings was not necessarily equivalent to the number of affected patients. The analysis relied on the findings documented in the available ultrasonography reports.

Patients were categorized into five age groups: 0–10 years, 11–18 years, 19–30 years, 31–50 years, and ≥50 years. The distribution of documented renal abnormalities across these age groups was summarized using the available medical records (Table 1) and (Figure 1).

Table 1. Statistics on renal complications.

Age Group	Number of Patients	Number of Pathology-Detected Patients
0-10	30	15
11-18	43	31
19-30	48	41
31-50	38	35
50+	18	15

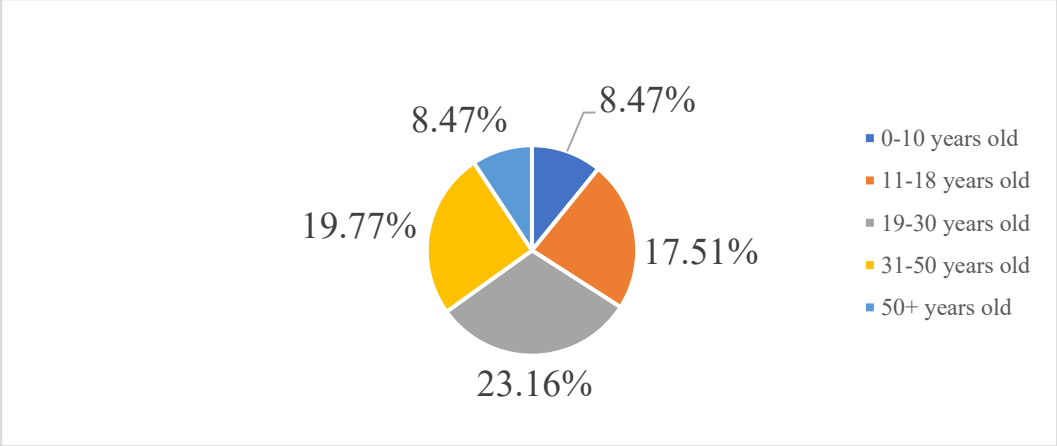


Figure 1. Statistics on renal complications.

The data were evaluated using descriptive statistics. Absolute numbers and percentages were used to summarize patient characteristics, age-group distributions, and renal ultrasonographic findings. No inferential statistical methods were applied, and adjusted estimates of the relationships between potential risk factors and renal abnormalities were not obtained. Estimated glomerular filtration rate (eGFR) was not estimated in this study.

The study was conducted with the permission of the healthcare institution. The use of patient medical records complied with the applicable institutional requirements for privacy and confidentiality and protection of personal information. Details of ethics committee approval, including the committee's name and approval reference, should be reported if applicable and documented.

3. Results

Out of the 177 thalassemic patients evaluated in the study, renal ultrasonographic (USM) abnormalities were detected in 137 individuals. It should be noted that multiple concurrent renal pathologies were identified in several patients. Based on renal ultrasonography findings evaluated between August 2025 and August 2026, microlithiasis (fine urinary crystals) emerged as the most prevalent abnormality among thalassemic patients with identified renal pathologies, affecting 68.93% of the cohort (Figure 2).

In patients receiving chronic blood transfusions, elevated urinary excretion of lithogenic substances creates a favorable biochemical environment for the nucleation and development of renal microcrystals and small calculi. Hypercalciuria and hyperuricosuria play pivotal roles in this process. Furthermore, chronic hemolysis and high erythrocyte turnover accelerate purine catabolism and uric acid excretion, thereby promoting urate crystal formation and facilitating the crystallization of calcium-bearing (Ca2+) salts. Over time, the aggregation and growth of these microcrystals can lead to frank nephrolithiasis, mechanical irritation of the urinary tract mucosa, and occasional hematuria [4], [5], [14].

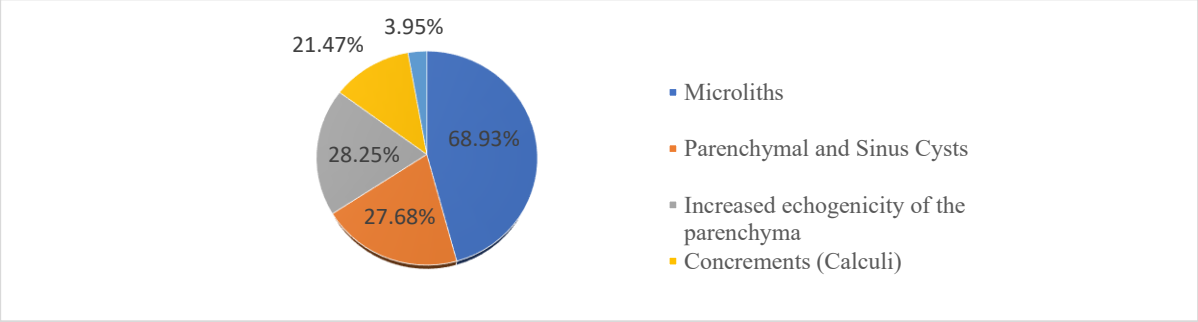


Figure 2. Most common kidney complications

Prolonged transfusion therapy duration in patients receiving long-term blood transfusions is directly correlated with progressive renal dysfunction. Suboptimal adjustment of inter-transfusion intervals induces renal tissue injury through two primary pathophysiological mechanisms [1], [2], [3]:

1) ***Hypoxia and Ischemia:*** Extended intervals between transfusions lead to protracted anemia and tissue hypoxia. The renal cortex and medulla are exquisitely sensitive to oxygen deprivation. Consequently, chronic hypoxia induces glomerular hyperfiltration, tubular atrophy, and interstitial fibrosis [1], [3].

2) ***Iron Overload and Hemosiderosis:*** Excessive iron accumulation in renal tubular epithelial cells drives the generation of free radicals (via Fenton chemistry), causing increased parenchymal echogenicity and cystic parenchymal changes [1], [3], [10].

According to data collected between August 1, 2025, and August 1, 2026, 89 out of 177 thalassemic patients (50.28%) received regular transfusion therapy (Figure 3). Extending transfusion intervals or administering therapy irregularly exacerbates hypoxic injury within the renal parenchyma. Conversely, optimizing transfusion schedules alongside appropriate iron chelation therapy significantly mitigates the risk of developing renal complications. Among the cohort of 177 thalassemic patients evaluated for renal complications, the overall mortality rate was found to be 1.69%.

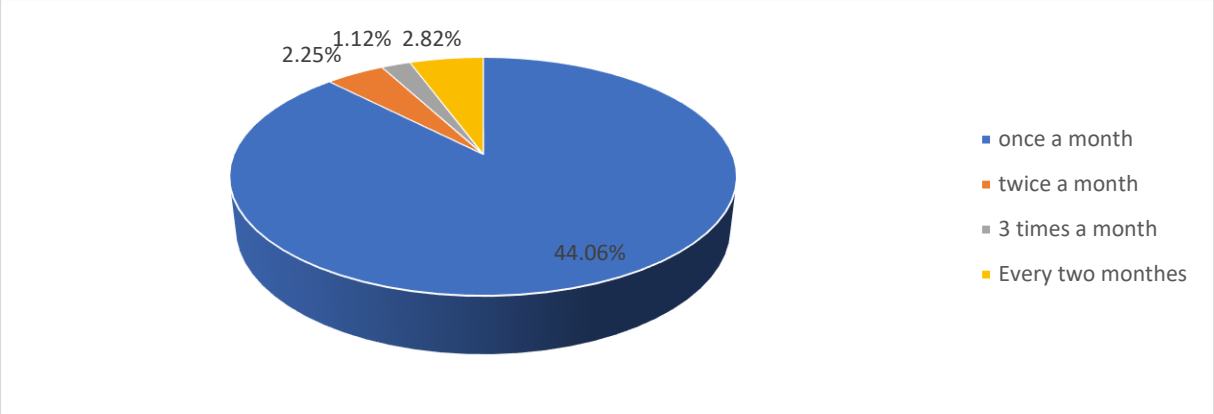


Figure 3. Annual percentage of patients receiving regular transfusion therapy.

Renal complications in patients with sickle cell anemia (SCA) differ significantly from those observed in thalassemic patients due to distinct underlying pathophysiological mechanisms. In SCA, chronic hemolysis coupled with the presence of hemoglobin S (HbS) triggers erythrocyte sickling, particularly within the vasa recta of the renal medulla where localized microvascular occlusion impairs blood flow. The unique microenvironment of the renal medulla—characterized by low oxygen tension, high osmolality, and an acidic pH—provides optimal conditions for HbS polymerization and sickling. Initial renal impairment in SCA typically presents as a loss of urinary concentrating capacity (hyposthenuria) due to ischemic damage within the renal medulla. Concurrently, compensatory glomerular hyperfiltration develops. Persistent hyposthenuria and chronic hyperfiltration accelerate glomerular structural injury, leading to progressive albuminuria and eventually chronic kidney disease (CKD). Moreover, focal ischemic microinfarctions in the medullary pyramids frequently result in renal papillary necrosis and gross or microscopic hematuria. In contrast, renal involvement in \beta-thalassemia is primarily driven by chronic anemia-induced hypoxia, systemic iron overload secondary to regular blood transfusions, tubular dysfunction, and the nephrotoxic effects of certain chelation regimens.

Overall, the cardinal features that distinguish renal involvement in sickle cell anemia from that in beta-thalassemia include medullary vaso-occlusion, early-onset albuminuria, renal papillary necrosis, and hematuria [15], [16]. In patients with chronic anemia, laboratory testing serves as the initial diagnostic step for evaluating renal complications. The primary biomarkers include serum creatinine, urinary albumin, estimated glomerular filtration rate (eGFR), proteinuria, and routine urinalysis. However, serum creatinine alone is insufficient for detecting early hyperfiltration. Comprehensive diagnostic assessment requires adjunctive monitoring of serum calcium (Ca2+), phosphate (P), and uric acid parameters.

In addition to biochemical testing, renal ultrasonography is routinely utilized to identify structural abnormalities such as renal cysts and hydronephrosis. Concurrent evaluation of both laboratory markers and ultrasonographic findings enables early detection of renal parenchyma damage [2], [3], [17], [18]. Continuous erythrocyte transfusion therapy in patients with thalassemia inevitably leads to systemic iron accumulation and severe iron overload. Excess labile iron catalyzes the generation of reactive oxygen species (ROS), triggering reactive oxidative stress that damages renal tissue and other parenchymal organs.

To mitigate iron toxicity, iron chelation therapy is initiated in thalassemic patients. The primary chelation agents utilized in clinical practice include deferasirox, deferiprone, and deferoxamine. By reducing systemic iron burden, chelation therapy partially attenuates iron-induced oxidative tissue damage. However, the use of deferasirox in particular can be associated with adverse renal effects, such as transient or persistent elevations in serum creatinine and proteinuria. Consequently, routine and rigorous monitoring of renal function is mandatory for all patients undergoing iron chelation therapy [1], [3], [10], [11].

4. Conclusion

Analysis of clinical data from 177 patients with \beta-thalassemia major receiving chronic transfusion therapy between 2025 and 2026 demonstrates a high prevalence of renal and urinary tract complications. Ultrasonographic evaluation revealed microlithiasis as the most frequent renal abnormality, accounting for 68.93% of all detected renal pathologies. The prevalence of renal involvement exhibited a clear age-dependent trajectory: 8.47% in the 0–10 age group, increasing to 23.16% in the 19–30 age group, and remaining elevated at 19.77% in the 31–50 age group. These findings highlight that advancing age, disease duration, and cumulative transfusion duration are critical risk factors for the development of renal pathology.

The underlying pathophysiology of renal injury in chronically transfused thalassemic patients is multifactorial, primarily driven by chronic anemia, tissue hypoxia, iron overload, hemolysis-induced oxidative stress, tubular dysfunction, and the nephrotoxic potential of iron chelation therapy. These mechanisms are distinct from those observed in sickle cell anemia (SCA), where renal injury is predominantly characterized by erythrocyte sickling and microvascular vaso-occlusion within the renal medulla, hyposthenuria, hematuria, renal papillary necrosis, and progressive glomerular alterations, including focal segmental glomerulosclerosis (FSGS).

The results of this study emphasize that evaluating renal function in thalassemic patients should not be restricted solely to serum creatinine measurement. A comprehensive diagnostic approach—incorporating estimated glomerular filtration rate (eGFR), urinary albumin-to-protein ratios, urinary calcium, phosphate, and uric acid parameters alongside renal ultrasonography—is essential for clinical management. Early identification of subclinical renal changes and individualization of therapeutic strategies are crucial for preserving long-term renal function. Overall, renal complications in patients with beta-thalassemia represent a distinct entity requiring dedicated clinical surveillance.

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Author Contributions

The sole author is responsible for conceptualizing, collecting, and analyzing data, and writing and editing the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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