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112.THALASSEMIA AND GLOBIN GENE REGULATION

Association of Hemoglobin Levels with Healthcare Resource Utilization and Costs in Non-Transfusion-Dependent α- and β-Thalassemia: A Retrospective Observational Study Using Real-World Data

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Introduction: Alpha (α)- and beta (β)-thalassemia result from reduced synthesis of α- or β-globin, respectively, leading to ineffective erythropoiesis, chronic hemolytic anemia (HA), and related complications. Thalassemia can also be characterized phenotypically as transfusion-dependent thalassemia (TDT) or non-transfusion-dependent thalassemia (NTDT). Decrease in hemoglobin (Hb) has been linked to increased risk of comorbidities and number of comorbidities in NTD β-thalassemia. Healthcare resource utilization (HCRU) has been analyzed in TDT in the US, but there is limited research on the association of Hb levels with HCRU and costs in α- and β-NTDT.

Objective: To assess the association of average Hb levels with HCRU and costs in adult patients with α- and β-NTDT using retrospective claims data.

Methods: This study analyzed data from the Merative ® MarketScan ® Commercial, Medicare, and Lab Results Databases for patients with thalassemia and no evidence of other HAs who were ≥18 years of age on the index date (date of the first observed diagnosis code for α- or β-thalassemia).

Patients were stratified by type of thalassemia (α- or β-thalassemia) and by transfusion dependence (NTDT or TDT). NTDT was defined as <8 transfusions within 12 months of follow-up or with >42 days between any 2 adjacent transfusions. To evaluate if the results in NTDT were driven by patients with β-NTDT, patients with α-NTDT were also analyzed separately.

Hb levels, HCRU (inpatient [IP] admissions, outpatient [OP] visits, and emergency room [ER] visits), and costs were assessed during a variable-length follow-up period (at least 12 months from the index date to end of plan enrollment, end of study, or IP death, whichever occurred first). Available Hb levels were averaged across the follow-up period for each patient. HCRU (number and type of service) and costs (US dollars) were converted to per-patient per-year values. All dollar estimates were inflated to 2020 (using Medical Care Component of Consumer Price Index).

To assess the association of Hb levels with HCRU and cost outcomes, univariate regression analyses with negative binomial models were conducted. Percent changes in cost and incidence rate ratios of HCRU associated with 1 g/dL decrease in Hb level and corresponding 95% confidence intervals and p values (with significance level set to 0.05) were reported.

Results: In the Commercial/Medicare database, 4077 adult patients with thalassemia and a variable length follow-up of at least 12 months were identified (median length of follow-up: 943 days). Of these, 909/4077 (22.3%) had at least 1 Hb value during the follow-up period in the Lab Results database, including 400 patients (44.0%) with α-thalassemia, 509 (56.6%) with β-thalassemia, 898 (98.8%) with NTDT (α or β), and 11 (1.2%) with TDT (α or β). The average Hb value per patient with NTDT (α and β; N=898) was 11.3 g/dL (11.5 g/dL for α-NTDT; N=400). In the NTDT group, 4.1% had at least 1 transfusion in first 12 months of follow up (3.6% had 1-3 transfusions and 0.5% had 4-7).

For all patients with NTDT, with each 1 g/dL decrease in Hb, the number of IP admissions increased by 17%, OP visits by 8%, and ER visits by 11% (all p<0.001). For patients with α-NTDT, with each 1 g/dL decrease in Hb, the number of IP admissions increased by 15%, OP visits by 6%, and ER visits by 16% (all p<0.01; **Table 1**). Regarding costs for all patients with NTDT, with each 1 g/dL decrease in Hb, total healthcare costs increased by 15% (p<0.001), IP costs by 56% (p<0.001), OP costs by 12% (p<0.001), ER costs by 20% (p<0.003), and prescription costs by 12% (p=0.061). For patients with α-NTDT, with each 1 g/dL decrease in Hb, total healthcare costs increased by 14% (p<0.001), IP costs by 47% (p<0.001), OP costs by 10% (p<0.001), ER costs by 30% (p<0.003), and prescription costs by 9% (p=0.322).

It is possible that because of incorrect/incomplete coding, some patients with thalassemia minor may have been included in the analyses, which may account for the higher-than-expected Hb levels in the NTDT cohorts. This may, in turn, underestimate the impact of Hb level on HCRU and costs.
Conclusion: In this study, each 1 g/dL decrease in Hb was associated with significantly higher HCRU and costs. This association was seen in both the NTDT group and α-NTDT subgroup suggesting that both α-NTDT and β-NTDT experience this burden. This analysis indicates that raising Hb levels in patients with both α- and β-NTDT could result in reduced HCRU and costs.

Disclosures Langer: *Agios:* Honoraria, Speakers Bureau. **Rane:** *Agios Pharmaceuticals, Inc.:* Current Employment. **Lombard:** *Agios:* Current Employment, Current equity holder in publicly-traded company. **Gilroy:** *Agios:* Current Employment, Current equity holder in publicly-traded company. **Li:** *Agios Pharmaceuticals, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Zhao:** *Agios Pharmaceuticals, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Lew:** *Agios:* Research Funding. **Davis:** *Agios:* Research Funding; *IBM:* Ended employment in the past 24 months; *Kendryl:* Ended employment in the past 24 months. **Ross:** *Agios:* Research Funding. **Sheth:** *Bristol Myers Squibb/ Celegene:* Consultancy, Other: Travel support, Research Funding; *Fulcrum:* Consultancy; *Bluebird bio:* Consultancy, Other: Travel support; *CRISPR:* Membership on an entity's Board of Directors or advisory committees; *Agios:* Consultancy, Other: Travel support, Research Funding; *Vertex Pharmaceuticals:* Membership on an entity's Board of Directors or advisory committees; *Chiesi:* Consultancy.

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Table 1: The association between hemoglobin level, HCRU, and costs.

	All NTDT (α or β) N=898	α-NTDT Subgroup N=400
HCRU: incidence rate ratio associated with 1 g/dL decrease in average Hb (mean [95% CI])		
IP admissions	1.17 [1.10, 1.24]†	1.15 [1.05, 1.25]*
OP visits	1.08 [1.05, 1.10]†	1.06 [1.02, 1.10]*
ER visits	1.11 [1.05, 1.18]†	1.16 [1.08, 1.26]*
Cost: % change in cost associated with 1 g/dL decrease in average Hb (mean [95% CI])		
Total healthcare costs	15% [10%, 21%]†	14% [7%, 22%]†
IP costs	56% [35%, 81%]†	47% [19%, 82%]†
OP costs	12% [7%, 17%]†	10% [4%, 17%]†
ER costs	20% [7%, 36%]*	30% [9%, 54%]*
Prescription costs	12% [0%, 26%]	9% [−8%, 31%]

*p<0.01; †p<0.001.
α, alpha; β, beta; CI, confidence interval; ER, emergency room; Hb, hemoglobin; HCRU, healthcare resource utilization; ICD, International Classification of Diseases; IP, inpatient; NTDT, non–transfusion-dependent thalassemia; OP, outpatient.
NOTE: ICD9/10 codes were used to identify adult patients (≥18 years) with α- or β-thalassemia if they had ≥2 claims in the OP or IP setting or ≥1 claim in the IP setting from January 1, 2013, to June 30, 2021.
α-Thalassemia ICD codes: Alpha thalassemia major, Hemoglobin H Constant Spring, Hemoglobin H disease, Hydrops fetalis due to alpha thalassemia, Severe alpha thalassemia, Triple gene defect alpha thalassemia.
β-Thalassemia ICD codes: Beta thalassemia major, Cooley's anemia, Homozygous beta thalassemia, Severe beta thalassemia, Thalassemia intermedia, Thalassemia major, Delta-beta thalassemia and Hemoglobin E-beta thalassemia. Index date for thalassemia was defined as the first date of an α- or β-thalassemia diagnosis code.

Figure 1