# Unreliable HbA1c in Hemolytic Anemia: A Case of Hereditary Spherocytosis

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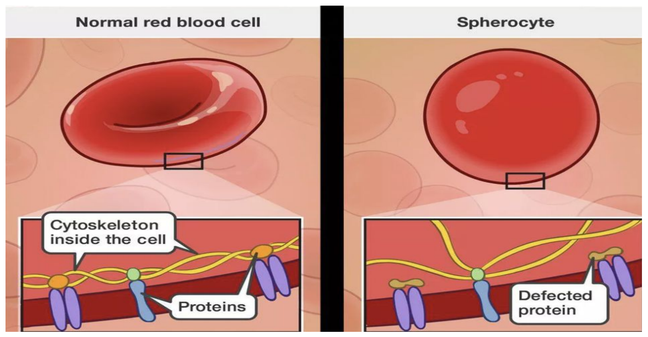
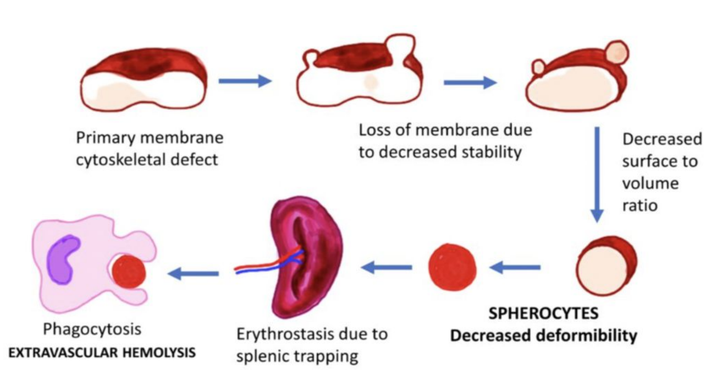
## Introduction

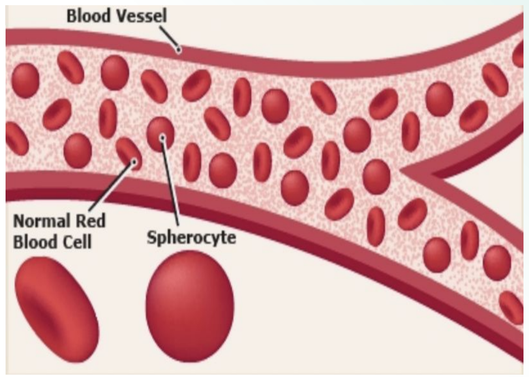
Hemoglobin A1c (HbA1c) is a cornerstone in diagnosing and monitoring diabetes mellitus, reflecting average blood glucose over approximately three months. However, its accuracy relies on normal red blood cell (RBC) lifespan. In conditions such as hereditary spherocytosis (HS), a hemolytic anemia characterized by membrane protein defects and reduced RBC survival, HbA1c may be misleadingly low. HS is an inherited hemolytic anemia characterized by defects in RBC membrane proteins, leading to spherical-shaped erythrocytes with increased fragility and shortened lifespan. However, HbA1c accuracy is contingent upon normal RBC lifespan. In HS, accelerated erythrocyte turnover leads to inaccurate readings of long-term glycation, potentially resulting in falsely low HbA1c values despite hyperglycemia.




## Case Presentation

We report the case of a 46-year-old female with HS who presented with anemia, classic hyperglycemic symptoms, decreased HbA1c, and elevated fasting glucose levels. Despite repeated fasting blood glucose readings >180 mg/dL, her HbA1c remained at 4.2%. Further evaluation confirmed increased reticulocyte count and evidence of chronic hemolysis. Given the discordance between glycemic measures and HbA1c, alternative markers including fructosamine and home sugar monitoring, were utilized to assess glycemic control more accurately.




## Potential Therapeutic Application

Numerous cases have been reported in which falsely low HbA1c levels were caused by drug-induced hemolysis [1,2]. To more accurately monitor blood glucose levels in patients with hemolytic conditions, we recommend the use of fructosamine testing, continuous glucose monitoring, or daily at home glucose measurements. Fructosamine provides a reliable short-term indicator of glycemic control and is unaffected by hemolytic disorders or other red blood cell abnormalities [3,4,5]. In contrast, these same hemolytic conditions can significantly distort HbA1c levels. Despite being inexpensive and clinically useful, fructosamine remains underutilized [3]. Fructosamine has proven effective in monitoring glycemic control in patients with sickle cell disease and beta-thalassemia [6]. Therefore, we recommend a routine fructosamine level be considered in all patients with red blood cell disorders or when discrepancies exist between glucose measurements and HbA1c values.

## Conclusion

This case highlights the diagnostic limitations of HbA1c in patients with shortened RBC lifespan due to HS. Clinicians should consider hemolytic disorders in the differential when HbA1c values do not correlate with clinical or biochemical findings. In such cases, alternative glycemic markers such as fructosamine levels and continuous glucose monitoring should be considered to ensure accurate diagnosis and management.

## References

1. Pant, V., Shrestha, A., Pyakurel, D., Gautam, K., & Pradhan, S. (2021). In-House Algorithm for Reporting Discrepant HbA1c Result and Troubleshooting a Case of False Low HbA1c. EJIFCC, 32(3), 377–384.
2. Pant V. (2022). HbA1c Below the Reportable Range. Laboratory medicine, 53(2), e44–e47. https://doi.org/10.1093/labmed/lmab082
3. Youssef, D., El Abbassi, A., Jordan, R. M., & Peiris, A. N. (2008). Fructosamine--an underutilized tool in diabetes management: case report and literature review. Tennessee medicine: journal of the Tennessee Medical Association, 101(11), 31–33.
4. John, J., Sakarde, A., Chafle, J., Amle, D., Jose, J., Sakhare, V., & Rathod, B. D. (2023). An Assessment of the Utility of Serum Fructosamine in the Diagnosis and Monitoring of Diabetes Mellitus. Cureus, 15(1), e33549. https://doi.org/10.7759/cureus.33549
5. Kang, D. S., Park, J., Kim, J. K., & Yu, J. (2015). Clinical usefulness of the measurement of serum fructosamine in childhood diabetes mellitus. Annals of pediatric endocrinology & metabolism, 20(1), 21–26. https://doi.org/10.6065/apem.2015.20.1.21
6. Kosecki, S. M., Rodgers, P. T., & Adams, M. B. (2005). Glycemic monitoring in diabetics with sickle cell plus beta-thalassemia hemoglobinopathy. The Annals of Pharmacotherapy, 39(9), 1557–1560. https://doi.org/10.1345/aph.1G010

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