Thalassemia

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1 Thalassemia is caused by hundreds of inherited hemoglobin gene mutations, and presentations range from asymptomatic to transfusion dependent

The prevalence of thalassemia in the Canadian population is not known but is likely increasing owing to immigration patterns.[1] Individuals from sub-Saharan Africa, Southeast Asia, Mediterranean countries, the Middle East and the Indian subcontinent are at particular risk, with prevalence ranging from less than 1% to 40% in some ethnic populations.[1] Ethnicity should not preclude screening when there is clinical suspicion.[2,3]

2 Thalassemia should be suspected in people with unexplained microcytosis, with or without anemia

The guideline from The Canadian Haemoglobinopathy Association recommends that people with unexplained microcytosis, in the absence of iron deficiency, should be screened with complete blood count, electrophoresis and high-performance liquid chromatography testing.[2] Hemoglobin electrophoresis alone cannot rule out thalassemia. Elevated hemoglobin A_2, with or without fetal hemoglobin elevation, is generally diagnostic of β-thalassemia trait and does not require genetic confirmation. Diagnosis of α-thalassemia always requires genetic analysis, as results of hemoglobinopathy investigations are generally normal.[2,4] Genetic testing is recommended for suspected carriers before conception and in people with clinical manifestations of thalassemia.

3 Intestinal iron absorption is enhanced in thalassemia

People with thalassemia should not receive supplemental iron unless they have documented iron deficiency.[5] Iron overload should be suspected in patients with serum ferritin over 300 μg/L, and these patients should be referred to a hematologist for consideration of magnetic resonance imaging (MRI) and chelation or phlebotomy.[5]

4 Thalassemia can affect diabetes monitoring

Owing to reduced red cell lifespan and abnormal glycation of hemoglobin A, hemoglobin A_{1c} testing may be unreliable in people with thalassemia and is not recommended, regardless of the severity of thalassemia.[6] People with thalassemia are at increased risk of diabetes mellitus from iron overload, regardless of whether they are receiving transfusions, and especially as they age.[5] Fasting or oral glucose tolerance tests are preferred for monitoring.[2]

5 People with symptomatic thalassemia should be referred for specialized care

Multidisciplinary thalassemia clinics manage issues including transfusion, iron overload monitoring with MRI, iron chelation, organ complications, bone marrow transplantation and clinical trials.[1] The Canadian Haemoglobinopathy Association provides a list of provincial specialist centres and a consensus statement on thalassemia care at www.canhaem.org.

References

1. Sayani FA, Kwiatkowski JL. Increasing prevalence of thalassemia in America: implications for primary care. *Ann Med* 2015;47:592-604.
2. Belletrutti M, Bolster L, Corriveau-Bourque C, et al. Consensus statement of clinical care of patients with thalassemia in Canada, 2nd ed. In: Ezzat H, editor. The Canadian Haemoglobinopathy Association; 2017. Available: www.canhaem.org/wp-content/uploads/2018/10/consensus-statment-Thalassemia-Final.pdf (accessed 2019 Nov. 25).
3. Viprakasit V, Ekwattanakit S. Clinical classification, screening and diagnosis of thalassemia. *Hematol Oncol Clin North Am* 2018;32:193-211.
4. Wilson RD, De Bie I, Armour C, et al. Joint SOGC-CCMG opinion for reproductive genetic carrier screening: an update for all Canadian providers of maternity and reproductive healthcare in the era of direct-to-consumer testing. *J Obstet Gynaecol Can* 2016;38:742-62.e3
5. Taher A, Vichinsky E, Musallam K, et al. Guidelines for the management of non-transfusion dependent thalasseami. 2nd ed. Nicosia (Cyprus): Thalassemia International Society; 2017. Available: www.thalassemia.org/boduw/wp-content/uploads/2011/09/Guidelines-for-Mgmt-of-NTDT-TIF-2017.pdf (accessed 2020 Mar. 3).
6. De Sanctis V, Soliman AT, Elsedfy H, et al. Growth and endocrine disorders in thalassemia: The international network on endocrine complications in thalassemia (I-CET) position statement and guidelines. *Indian J Endocrinol Metab* 2013;17:8-18.

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