

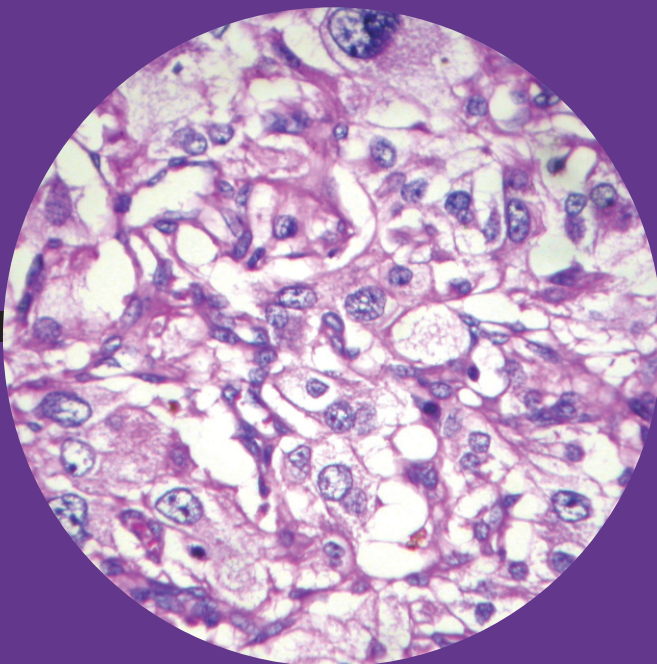


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## Unexpectedly low HbA1c levels in two diabetes patients following dapsone use

Sir,

Glycated hemoglobin (HbA1c) is an important indicator of long term glycemic control in diabetes patients, which reflects the levels of blood glucose to which the erythrocyte has been exposed to during its lifespan (120 days). However, there are a number of clinical situations in which the HbA1c values may be inappropriately high or low for the true level of glycemic control. We report here two patients with type 2 diabetes patient who had inappropriately low HbA1c levels following chronic administration of dapsone.

Patient 1 was a 36-year-old male who presented to us in January 2012 for evaluation and control of diabetes. He was diagnosed to have type 2 diabetes 10 years ago and was initially managed with oral antidiabetic drugs alone. Worsening control of diabetes necessitated the addition of insulin therapy 4 years ago. He was also diagnosed to have lepromatous leprosy an year ago and has been on multidrug therapy, including dapsone, for the same ever since.

On examination, the patient was not pale, cyanosed or icteric. He had thickening of both ulnar nerves, sensory deficit over the ulnar distribution in both hands, early claw hand deformity, and infected bunion over the dorsum of the left hand and an ulcer over the right medial malleolus. His fasting and postprandial blood glucose levels were 167 and 289 mg/dl, respectively. However, his glycated hemoglobin (HbA1c) level, measured by high performance liquid chromatography (HPLC; Biorad Variant, Biorad, Hercules, California, USA), was surprisingly low (4.4%), which remained unaltered (4.5%) on repeat testing on another machine the following day. In view of the discrepancy between the plasma glucose and the HbA1c levels, a serum fructosamine assay was carried out, which revealed poor glycemic control (286  $\mu\text{mol/l}$ ; good control, less than 260  $\mu\text{mol/l}$ ).

In view of the history of chronic dapsone use, the possibility of drug-induced alteration in the HbA1c level was considered and the patient investigated along those lines. Hemogram showed mild anemia (Hb 10.1 g/dl) and an elevated leucocyte count (13,170/ $\text{mm}^3$ ). Serum bilirubin was normal; however, the reticulocyte count (3%; normal -- up to 2%) and lactate dehydrogenase (198; normal up to 190) were found to be elevated, suggesting the presence

of hemolysis. Methemoglobin levels were also found to be elevated (3%; normal, less than 1%), suggesting a possible additional mechanism for the lowering of HbA1c.

Patient 2 was a 65-year-old male who presented to us in January 2012 for evaluation of diabetes. He had type 2 diabetes of six years' duration and was on combination therapy with sulfonylurea and metformin. He had been regularly monitoring his glucose levels at home and the values ranged from 140 to 160 mg/dl in the fasting state to 200 to 220 mg/dl in the postprandial state. Surprisingly, his HbA1c level [(measured by measured by the high performance liquid chromatography (HPLC) method (Biorad Variant, Biorad, Hercules, California)] was found to be exceedingly low (3.8%). The patient denied the occurrence of any hypoglycemic attacks. Serum fructosamine values were at the upper end of normal (260  $\mu\text{mol/l}$ ), corresponding with his home blood glucose monitoring values. Further enquiry revealed that the patient had consulted a dermatologist in August 2010 with complaints of scaly patches over the forearms and legs, and had been put on dapsone (100 mg/day), which he had been continuing ever since. Prior records revealed HbA1c values of 7.5% and 6.8% prior to starting dapsone, which dropped to 4.5% 6 months after initiation of the drug, and to 3.8% at the time of his visit to our center.

The patient did not have any symptoms suggestive of anemia or hemolysis. He was not pale, icteric or cyanosed. His hemoglobin concentration, RBC count, and serum bilirubin were within normal limits. His reticulocyte count was at the upper limit of normal (2%). The methemoglobin level was 0.7%.

Dapsone is a compound used for the treatment of Hansen's disease, in addition to certain dermatological conditions such as dermatitis herpetiformis. Five cases of dapsone-related reduction in HbA1c level have been reported in the literature,<sup>[1-4]</sup> none of which were from India. Dapsone is known to induce hemolysis, which can lower the HbA1c by reducing RBC lifespan. Dapsone may also promote the oxidation of hemoglobin to methemoglobin, thereby interfering with the HPLC assay used to detect HbA1c. Dapsone has also been shown to reduce the lifespan of RBCs independent of its hemolytic effect.

In our first patient, there was evidence of both hemolysis as well as methemoglobinemia, both of which could have contributed to the inappropriately low HbA1c level. The second patient had normal methemoglobin levels, but the reticulocyte count was at the upper limit of normal, suggesting that he had mild subclinical hemolysis. This, associated with the reduction on RBC lifespan induced by the drug, could have led to the drop in HbA1c.

Type 2 diabetes is a common disorder in India and HbA1c assays are widely used to guide treatment. Dapsone use is also not uncommon in India. It is therefore essential that clinicians be aware of the HbA1c lowering effect of dapsone and be cautious while interpreting the HbA1c results of patients who are on this agent.

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