

production. HMW oligomer may be protective with inhibition of NF κ B, whereas the low and medium subforms are associated with nephropathy. Altered glycosylation of lysine leading to changed adiponectin function has been postulated as another mechanism.

Has adiponectin come of age as a routine test or as a predictor of obesity, T2DM, T1DM or even development of microangiopathy or comorbidities? Not yet. There are simpler and better clinical methods now. To some extent it may have role in adult T2DM. Its utility in T1DM, especially children, is far from clear.

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Thalassemia: Cardiac Iron and Chelators

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Iron overload in thalassemia is a serious and potentially fatal condition as excess iron is toxic to tissues and organs, particularly the liver and the heart. The serum ferritin level is useful in assessing iron balance trends, but does not accurately predict quantitative iron stores. Measurement of the iron level by liver biopsy is the standard method for accurately determining the iron store. A ferritometer and specialized MRI software are emerging alternatives for liver biopsies. Although quantitative liver iron measurement accurately guides the use of iron chelators, it may not reflect cumulative changes in cardiac iron. Thalassemics may have cardiac iron overload even at the time of a safe liver iron measurement [1].

Cardiac damage caused by iron overload is the main cause of death in thalassemia. An increased risk of iron-induced cardiac disease is observed with liver iron concentration (LIC) values above 15mg of iron per gram of dry weight of liver, and in patients with serum ferritin values above 2500 microgram/liter. The rate of iron loading depends mainly on the rate of blood

transfusions, which causes a net iron deposition in the body, of about 15-20 mg/day. In practice, the goal of chelation therapy is to achieve an iron balance by accessing two iron pools, namely intracellular labile iron pool (LIP) and iron from red cell catabolism [2].

After the introduction of deferoxamine in 1963, several efforts were made to synthesize orally active iron chelators. Following the screening of more than 700 chelators from various chemical classes, deferasirox emerged as a highly selective chelator for iron with high oral potency and tolerability. Deferasirox mobilizes iron stores by binding selectively to the ferric form of iron and enters most of the cells to reach the major intracellular sites of iron accumulation. For myocardial iron, deferasirox has the ability to enter myocardial cells and chelate iron from these cells. It was also observed from myocyte cultures that it rapidly gains entry in the myocytes and binds to labile intracellular iron, leading to decreased free radical production.

In recent years, clinical trials have been conducted to evaluate the effect of deferasirox on myocardial iron and

the left ventricular ejection fraction (LVEF). Of the 23 patients who received deferasirox 10-30 mg/kg/day, for 13.1 (± 0.78) months; the mean myocardial T2* measurement was inversely related to myocardial iron content. Deferasirox treatment led to significant reductions in mean serum ferritin concentrations and LICs, while no changes in LVEF were noted [3]. Study conducted by Pathare, *et al.* [4] monitored cardiac siderosis using T2 MRI in 19 heavily iron overloaded patients with β -thalassemia major receiving iron chelation therapy with deferasirox over an 18 months period. Deferasirox therapy significantly improved mean cardiac T2 from a baseline of 17.2 (10.8) to 21.5 (12.8) ms. A concomitant reduction in median serum ferritin, and mean LIC was also noted. Improvements were seen in patients with various degrees of cardiac siderosis, including myocardial iron in those patients with a baseline cardiac T2 of <10ms, indicative of high cardiac iron burden [4].

Studies on long term use, dose, efficacy and safety profile of deferasirox have concluded that deferasirox in doses of 20-30 mg/kg/day could effectively reduce iron burden [5]. Further, efficacy of available chelators on myocardial iron and biventricular function by quantitative MRI in 550 thalasseemics concluded that oral deferasirox has better global systolic ventricular function compared to oral deferiprone and subcutaneous desferoxamine [6].

In the background of such global studies, this prospective, open label, single arm study on 30 patients by Merchant, *et al.* [7] reported good safety profile of deferasirox, and showed that it effectively chelates myocardial iron, more efficacious in moderate to severe cardiac iron overload. In addition, there was a significant decrease in serum ferritin in those patients with cardiac T2* <10 ms and between 10-20 ms. Similar cardiac findings have also been reported by other researchers

[4]. Although the sample size is small, this study adds that for Indian population, deferasirox is a safe and efficacious iron chelator without any significant adverse effect even with doses of >30 mg/kg/day. Thus, the data shows promising results of deferasirox on cardiac iron and quantifies myocardial iron by non-invasive method. Presently, many thalassemia centers monitor cardiac iron with T2 weighted MRI imaging, but routine application of this technology has not been implemented across all centers.

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Public Health Significance of Shigellosis

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Shigellosis is an important intestinal infection of public health concern, accounting for 140 million cases globally per year and 60 000 deaths annually of which 60% occur in children below 5 years of age [1]. The disease can occur as

sporadic, epidemic and pandemic forms. The disease has a short incubation period. In 1969-1970, an epidemic of shigellosis caused by multi-drug resistant *S.dysenteriae* type 1 occurred in Central America and rapidly spread to different parts of Africa and Asia. The epidemic was seen