

## Re: Ambulatory Blood Pressure Monitoring for Children With Beta-Thalassemia Major: a Preliminary

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Dear Editor,

We read with interest the article by Tabatabaei and colleagues in the past issue of *the Iranian Journal of Kidney Diseases*.<sup>1</sup> Thalassemia is one of the most common hemoglobinopathies in the world, and cardiovascular complication is a major cause of mortality and morbidity in this disease.<sup>2</sup> In hemolytic diseases, such as sickle cell trait and thalassemia, there is systemic vasculopathy.<sup>2</sup> Many investigations have revealed change of elastic properties of great arteries in patients with  $\beta$ -thalassemia major.<sup>3</sup> Gedikli and colleagues, in a case-control study,<sup>3</sup> showed that  $\beta$ -thalassemia major patients compared with healthy control subjects had significantly increased aortic diameters, lower mean aortic strain and distensibility that is associated with ferritin level. They also had higher mean aortic stiffness index related to platelet count.<sup>3</sup> Abdominal aorta stiffness is also detected in  $\beta$ -thalassemia major and it is correlated with left ventricular mass indexes.<sup>4</sup>

The pseudoxanthoma elasticum-like syndrome is reported in  $\beta$ -thalassemia major patients with higher prevalence than in general population. This finding is evidence of elastic tissue injury in these subjects.<sup>5</sup>

In  $\beta$ -thalassemia major, endothelial dysfunction is one of the fundamental pathophysiologic mechanisms that play a role in progression of cardiovascular involvements. Many studies showed there is an endothelial dysfunction in different vascular beds in these patients. Gullu found that diastolic peak flow velocity of the left anterior descending coronary artery was significantly higher in the  $\beta$ -thalassemia major group at baseline, however, coronary flow reserve, (reflecting of microvascular function, is impaired and is significantly lower than control group.<sup>6</sup> He reported that carotid intima media thickness, evidence of early stage of atherosclerosis, is higher in  $\beta$ -thalassemia major group than controls.<sup>6</sup>

Patients with  $\beta$ -thalassemia major showed an impairment of hyperemic response of brachioradial artery whereas glyceryl trinitrate-mediated dilation was preserved. They had greater carotid artery stiffness and brachioradial artery pulse wave velocity. These changes may reduce mechanical efficiency of the heart.<sup>7</sup>

Molecular mechanisms of endothelial dysfunction recently are investigated. Alteration of nitric oxide synthesis and consumption is one of the most important hypotheses.<sup>8</sup> During hemolysis packaged hemoglobin released from red blood cell into plasma and it rapidly reacts with nitric oxide. This provoke consumption of nitric oxide and reduction of concentration of this important vasoactive component.<sup>8</sup> Inflammation is another cause of endothelial dysfunction, levels of serum interleukin-6, vascular cell adhesion molecule 1, and intercellular adhesion molecule 1 can be increased in patients with  $\beta$ -thalassemia major.<sup>8</sup>

Oxidant biomarkers are increased in patients with hemolytic anemia. Upregulation of antioxidant gene in response to oxidative stress even in young patients is reported.<sup>9</sup>

The hypercoagulable state is beside play roles in endothelial dysfunction and others vasculopathy phenomena in hemolytic conditions. The microparticles originating mainly from activated platelets and erythrocytes may provoke this condition.<sup>10</sup> The platelet and erythrocyte-derived microparticles are increased in sickle cell disease patients. Their levels are significantly associated with sickling crisis, pulmonary hypertension, as well as severity of hemolysis, fibrinolysis, and iron overload. Moreover, D-dimer and von Willebrand factor antigen levels are elevated in sickle cell disease compared with controls.<sup>10</sup> Likewise in people with essential hypertension, high levels of microparticles are detected that may contribute to the generation and perpetuation of a thrombotic state.<sup>11</sup>

Autonomic dysfunction and subclinical type of this abnormality are reported in  $\beta$ -thalassemia major patients.<sup>12</sup> Heart rate variability, a marker of cardiac autonomic balance, is depressed in  $\beta$ -thalassemia major patients and it is significantly correlated with hemoglobin level.<sup>13</sup>

Conventional atherosclerosis risk factors are changed, but extent and aspect of changes are anomalous. Some studies showed that  $\beta$ -thalassemia major patients have lower total cholesterol and high-density lipoprotein cholesterol and higher fraction of low-density lipoprotein cholesterol to high-density lipoprotein cholesterol in compared with control group. Moreover, some polyunsaturated fatty acids are decreased in  $\beta$ -thalassemia major subjects. These alternations may be due to hepatic damage and anemia or change of lipid oxidation.<sup>14-16</sup> Noteworthy in beta-thalassemia intermedia patients, total cholesterol, high-density and low-density lipoprotein cholesterol are lower compared with  $\beta$ -thalassemia major patients and normal population.<sup>17</sup>

Blood pressure alteration is another interesting issue that is recently attracting attention. Some researchers showed that mean blood pressure, diastolic blood pressure and systolic blood pressure are lower in compared with normal population.<sup>18</sup> Hypertensive individuals with beta thalassemia trait have better ambulatory blood pressure profile compared to nonanemic and anemic hypertensives patients.<sup>19</sup>

In the study by Tabatabaie and coworkers, a relatively high prevalence of elevated blood pressure (16.7%) and no dipper statuses (56.7%) were reported in  $\beta$ -thalassemia major patients.<sup>1</sup> These findings may be consequent to arterial stiffness, endothelial dysfunction, and autonomic neural dysfunction. Further case-control studies with long-term follow-up are required for evaluation of frequency and importance of blood pressure in  $\beta$ -thalassemia major individuals.

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