

## World Pediatrics-2020: Endothelial disorders in children with diabetic nephropathy - Miguel Maluf - National O.O. Bogomolets Medical University

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Endothelial dysfunction comprises a number of functional alterations in the vascular endothelium that are associated with diabetes and cardiovascular disease, including changes in vasoregulation, enhanced generation of reactive oxygen intermediates, inflammatory activation, and altered barrier function. Hyperglycemia is a characteristic feature of type 1 and type 2 diabetes and plays a pivotal role in diabetes-associated microvascular complications. Although hyperglycemia also contributes to the occurrence and progression of macro vascular disease (the major cause of death in type 2 diabetes), other factors such as dyslipidemia, hyperinsulinemia, and adipose-tissue-derived factors play a more dominant role. A mutual interaction between these factors and endothelial dysfunction occurs during the progression of the disease. We pay special attention to the possible involvement of endoplasmic reticulum stress (ER stress) and the role of obesity and adipose-derived adipokines as contributors to endothelial dysfunction in type 2 diabetes. The close interaction of adipocytes of perivascular adipose tissue with arteries and arterioles facilitates the exposure of their endothelial cells to adipokines, particularly if inflammation activates the adipose tissue and thus affects vasoregulation and capillary recruitment in skeletal muscle. Hence, an initial dysfunction of endothelial cells underlies metabolic and vascular alterations that contribute to the development of type 2 diabetes.

Diabetes mellitus is a common metabolic disease with a high and growing prevalence affecting 4% of the population and, worldwide, 171 million people in 2000 and an expected 366 million in 2030. Type 1 diabetes is characterized by an absolute deficiency of insulin attributable to pancreatic insufficiency. In contrast, type 2 diabetes is characterized mainly by insulin resistance, viz., a reduced response of glucose uptake rate during insulin exposure, and therefore represents a relative deficiency of insulin in spite of high plasma levels of insulin.

Because of the progressive dysfunction of the pancreatic  $\beta$ -cells, this eventually can also lead, in type 2 diabetes, to an absolute deficiency of insulin for tissue cells. Endothelial dysfunction comprises a number of functional alterations in the vascular endothelium, such as impaired vasodilation, angiogenesis and barrier function, inflammatory activation, and increased plasma levels of endothelial products, all of which are generally associated with cardiovascular disease. Endothelial dysfunction in type 1 diabetes is probably the consequence of the metabolic changes related to diabetes, in particular hyperglycemia. With age, a number of microvascular complications develop in type 1 diabetes patients, in particular retinopathy, nephropathy, and the diabetic foot. In contrast, the relationship between endothelial dysfunction and diabetes is much more complex in type 2 diabetes and saddles patients with a heavy burden, particularly with respect to cardiovascular disease. In type 2 diabetes, a common cause may underlie both endothelial dysfunction and the development of hyperglycemia, whereas other factors such as dyslipidemia additionally contribute to both. Endothelial dysfunction may thus play a primary role in the development of the vascular complications of type 2 diabetes, complications that are aggravated by hyperglycemia, but that are not primarily dependent on the development of hyperglycemia.

In the present survey, we discuss the nature of endothelial dysfunction in type 1 and 2 diabetes and the way that it relates to these conditions. After discussing the effects of hyperglycemia on endothelial functioning, we will turn to the way that, in type 2 diabetes, obesity and fat-derived adipokines act locally on arteries and arterioles and can contribute to insulin resistance and reduced glucose uptake in muscle. Further insights into the interrelationship between endothelial/vascular (dys) functioning, type 1 and 2 diabetes, and obesity may help to improve further the treatment of these epidemically increasing metabolic disorders.