

ER-DOMA - The entangled relationship between diabetes, obesity, metabolic syndrome and aging

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Diabetes, obesity and metabolic syndrome are the essence of metabolic disorders. A whole gamut of research data indicate that they are complexly entangled and bear a close inter-relationship. These disorders are life-style diseases as well, having genesis in modifiable modern dietary habits and technology-driven sedentary living patterns, apart from non-modifiable genetic makeup. They have an important impact on the morbidity and mortality patterns directly and through their effects on individual aging process. The aging population has a higher incidence of diabetes. On the other hand, overweight and obese persons have higher incidence of diabetes. The research has proven that obesity accelerates aging of adipose tissue, which in turn leads to activation of cascade of various metabolic pathways responsible for aging. Diabetes, too, appears to accelerate aging at cellular level through metabolic alterations.

The experiments in normal mice, variously knocked-out-mice and agouti mice have unfolded the understanding of genetic basis and metabolic pathways. In experiments, the agouti mice, which are genetically obese, having high levels of reactive oxygen species (ROS), increased DNA damage and higher expression of inflammatory markers, lacking telomerase develop shorter telomeres during successive generations. These changes are comparable to normal aging mice. Thus, inference from the research indicates that obesity increases the formation of ROS in adipose cells, and shortens telomeres, which in turn, activates the p53 tumor suppressor leading to inflammation manifested by infiltration by macrophages and elevated level of cytokines. This has been shown to lead to insulin resistance, impaired glucose tolerance and diabetes.

Similarly, the histological and physiological changes in aging organs are associated with oxidative stress, genetic instability and disruption of homeostatic pathways. Aging has been linked to telomere shortening due to impaired cellular ability to detoxify ROS, leading to p53 activation. This potentially impairs insulin secretion and sensitivity. There are, thus, similarities in metabolic dysfunction and deregulation in obese states, diabetes and aging. It has been highlighted that diabetes, obesity and aging may share similar mechanisms and metabolic pathways at cellular level.

Whether diabetes-mediated or obesity-mediated aging is reversible? The caloric restriction with adequate nutrition (CRAN) reduces aging in normal population and has a favorable impact on glucose homeostasis. The CRAN, a selective CRAN or a modality having favorable impact on homeostasis, can be an answer for the exacerbated aging in the special conditions like diabetes, obesity and metabolic syndrome.

Biography

Vinod Nikhra, M.D., is Fellow of International Medical Sciences Academy and Fellow of Royal Society of Medicine. He is trained in Internal Medicine, Endocrinology and Clinical Nephrology. He has authored 4 books, which include *The Anti-Obesity Guide* and *Aging slowly, Living longer*, and contributed more than 46 papers in reputed journals and has been an editor for Journal of Association for Health in Middle Aged and a reviewer for International Journal of Obesity (the Nature group) and Family Practice (the Oxford group). He is a senior consultant physician and on teaching faculty at Hindu Rao Hospital, Delhi, India.

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