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Ageing and Insulin: Inter Alia Diabetes, Obesity and Fitness Concerns

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Abstract: This article argues the essence of insulin sensitivity versus secretion including insulin resistance in the clinical strategy for the treatment, lifestyle changes, prompt interventions and control of diabetes. Progressive decline of glucose tolerance as advanced age occurs has been associated with the pathogenesis of type 2 diabetes due to peripheral insulin resistance and impaired β cell function. In elderly persons, insulin secretion is deranged concomitantly with decreased insulin clearance rate and augmented circulating proinsulin level that ostensibly explicates age-related hyperglycemia. Insulin is associated with numerous pathophysiological processes exhibited during brain function in learning and memory, as well as the regulation of ageing, metabolic syndrome, obesity, diabetes and cardiovascular diseases in Man. Elevated chronic peripheral insulin, decreased insulin action and brain insulin contents are pathognomonic of the insulin resistance syndrome. All these are associated through specific mechanisms in the pathophysiology of ageing and insulin in concert with risk factors and the concomitant complications. Ostensibly, progressive excess insulin induces synchronous elevated levels of oxidative stress and inflammatory impacts which exacerbate or are exacerbated by advancing age, culminating as inimical consequences to healthy lifestyles, longevity or extended lifespan. Therapeutics and other healthcare measures may be beneficial in order to prevent, mitigate or amend insulin aberrations in the elderly and during the ageing process. The mainstay in managing an elderly patient with perturbed insulin action, is control of therapeutic application, as it can reverse acute terminal states. Treatment necessitates stringent and thorough expertise, knowledge and skills for optimum provision and effective cerebral, cardiovascular and skeletal protection for a healthier lifespan and longevity. This article will be of immense contribution in the understanding of the prevention, control and treatment of insulin resistance, metabolic syndrome, diabetes, obesity, cardiovascular and neurological disorders during ageing.

Keywords: Hypertension, cardiovascular diseases, neurodegenerative disorders, insulin resistance and sensitivity.

Review Paper

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INTRODUCTION

This study contributes to the understanding of the aetiology, prevention, treatment and control of insulin resistance and sensitivity, metabolic syndrome, diabetes, obesity, cardiovascular and neurological disorders, especially in the elderly. Modifications or alterations associated with ageing include decreased glucose tolerance due to increased insulin resistance from receptor and/or post-receptor derangements and diminished pancreatic islet B-cell sensitivity to glucose [1]. Insulin has effects on ageing and lifespan, and provides a mechanism in gene manipulations for prolonged lives and healthier lifestyles, and as preserved insulin sensitivity associated with longevity. Insulin function is dependent on mechanisms which are determinants of its circulating levels, secretion, clearance and sensitivity in its target tissues. Ageing enhances deranging impacts on these processes which debilitate insulin functionality, resulting in augmented risk for morbidity, untoward sequelae and mortality [1]. Certain models of impaired insulin signaling are associated with prolonged longevity or resistance to life-threatening factors, such as oxidative stress [1, 3]. Insulin and insulin signaling are associated with successful ageing and longevity. This entry enunciates the importance of insulin sensitivity versus secretion as being critical to the clinical strategy in the treatment, lifestyle changes, early interventions and control of type 2 diabetes [1-5]. Calorie restriction enhances lifespan in numerous species [3]. Diet manipulation that affects the glucose-insulin system ostensibly benefits lifespan and diminishes the incidence of ageing-related chronic

diseases. During ageing, augmented circulating abundance of glucose and other reducing sugars secondary to age-triggered insulin resistance nonenzymatically reacts with proteins and nucleic acids to debilitate tissue elasticity. Adequate control of factors associated with risks for obesity, diabetes, cardiovascular disease, and other insulin and ageing complications can be retarded during ageing for optimum longevity and lifespan [5-7].

Mechanism and characterization of insulin and ageing

As ageing progresses, the hormone, insulin is the major substance that potentiates glucose uptake from the blood stream by cells. There is evidence that calorie restriction enhances longer lifespan [1-5]. Also, controlled famine [1-3] can considerably sustain mammalian lifespan; and lean mammals are less vulnerable to old age disorders as obese ones [1, 4]. The mechanisms have not been clearly elucidated, though.

It has been reported that chemical messages from an insulin-like hormone are decreased inside fat cells; while lifespan is enhanced [1, 4]. The investigation also highlights the role of insulin in regulation of its synthesis. The inhibition of insulin action within specific cells allows the entire body to maintain a prolonged health, with concomitant retardation of ageing. These result when there is decrement in insulin-like signaling with resultant extension of life expectancy, or if either the insulin-like receptor (InR) or its receptor substrate undergoes mutation, or there is ablation of insulin-producing cells [1, 2]. Although, it is not definite when insulin effects ageing, insulin independently achieves this effect, regulates its own production, and directly regulates tissue ageing. Thus, low insulin concentrations promote stronger and healthier cells for the prevention of infections and age-related disorders [5, 6].

The regulation of ageing is an intricately complex physiological mechanism inculcating secretion of hormones, nutritional inputs, and regulation of metabolism. The characterization of ageing is intermittent dissipation of physiological functionality with resultant enhanced susceptibility to mortality. The progressive debilitative process is evident and manifests in all living organisms, and constitutes the prime risk factor for aberrant disorders, such as obesity, diabetes, neurodegenerative and cardiovascular diseases.

A vast majority of age-related diseases have been linked with the derangement of insulin action. Insulin and IGF1 receptors mediate their effects inter alia on regulating cell proliferation, differentiation [7], metabolism and growth [6]. Insulin action is dependent on mechanisms which are determinants of its circulatory levels, secretion, clearance and sensitivity in target tissues. Ageing has debilitating impact on these mechanisms which derange insulin action leading to elevated risk in morbidity and mortality. The improvement of insulin action is a pertinent trajectory for healthier and longer life span [7] and life expectancy.

Insulin resistance is untoward biologic response in the stimulation of insulin to target tissues vis-a-vis adipose tissue, liver and muscle. Insulin resistance deranges glucose discharge, with resultant compensatory elevated formation of beta-cell insulin and hyperinsulinaemia. The metabolic repercussions of insulin resistance are liable to result in dyslipidemia, endothelial dysfunction, increased inflammatory markers, hyperglycemia, hypertension, hyperuricaemia, prothrombic condition and visceral adiposity. The elucidation of the aetiology and features of insulin resistance as well as the activity of the multidimensional professional healthcare team are pertinent in its management and prognosis [1, 4-8]. These suggest that insulin resistance and hyperinsulinemia are aetiologically correlated with the aforementioned cluster ingredients which are defined as the insulin resistance syndrome, syndrome X, or the metabolic syndrome [8]. Elderly persons present greater glucose intolerant and insulin-resistant stances. There is extant polemic as to whether this decrement in functionality is an invariable resultant impact of biological ageing or due to environmental or lifestyle factors, such as augmented obesity, a deranged configuration of fat dissemination, or physical inactivity or deficient exercise evidenced in ageing [8]. It has been shown that these alterable environmental or lifestyle variables culminate in enhanced insulin resistance and hyperinsulinaemia, and constitute risk factors for development of metabolic syndrome disorders. Reversal of these untoward states in elderly individuals exhibited improved insulin sensitivity, and glucose tolerance. Conversely, insulin secretion, ostensibly declined with age following adjustments for disparities in adiposity, fat distribution, and physical activity [8] or exercise. Despite improvements in lifestyle or other environmental influences, these may contribute to the glucose intolerance evidenced in much older persons [8]. Age-related augmentation in glucose levels is suggested to be associated with aberrant insulin secretion; with sex difference detected with respect to the effect of aging on insulin resistance [9].

An investigation in disparate states of glucose homeostasis in elderly patients as compared to healthy young subjects and young patients with type 2 diabetes intravenous glucose tolerance test suggested that insulin resistance was characteristic of conventional ageing trajectory, with senility as a consequential or invariable risk factor for glucose intolerance and metabolic syndrome with its consequential complications [10]. Insulin secretion and insulin clearance as well as insulin and target tissue interactions were impaired in elderly patients. These functionalities are intermediate between healthy and type 2 diabetic subjects, with predilection

of the elderly general population for the risk of deranged glucose tolerance or diabetes with its concomitant vascular sequelae.

Obesity, skeletal muscle and impaired bone regulation

As a model for accelerated ageing, obesity is associated with peripheral insulin resistance, depleted adiponectin abundance, and augmented chronic inflammation [11]. Ageing, obesity, and insulin resistance derange bone regulation, leading to imbalance in bone homeostasis and disorder. The conventional debilitative process associated with aging, such as augmented adipogenicity, menopause, andropause and changes in the fate of the mesenchymal stem cell fate. These are potential aetiologies of diminished bone density, with consequential osteoporosis, a critical risk factor of bone fracture in the elderly. Functional restrictions of the aging musculoskeletal system result in limited or restrained physical activity and adverse adipogenicity. Obesity in advanced age results in rapid, aggravated and untoward sequelae, such as impaired health, deteriorated bone health, diminished bone formation, enhanced bone resorption, augmented adipose tissue deposition, deranged bone morphology, and bone fragility as well as challenges, issues and opportunities in bone remodeling. The ensuing mechanistic insights per bone homeostasis and interventions for the prognosis of bone quality in aged and obese persons are pertinent measures. Characteristic presentation of skeletal ageing with concomitant diminished regulators of bone remodeling dispose to age-related bone dissipation. Obese-insulin resistance leads to untoward impacts in bone remodeling for aged inpatients. Synergistic impacts of obesity and ageing results in adverse rapid bone dissipation. In the aged-obese individual, decrement in BAT, Thy-1 and DOCK7 are aetiologic agents of skeletal tissue derangement, requiring prompt and optimum interventions for good prognosis [11]. The prime objective is to enhance and consolidate modifications of lifestyles in these patients. Dietary intervention must incorporate holistic calorie restriction and decrement in high glycaemic index carbohydrates. Physical activity or exercise enhances calorie dissipation and insulin sensitivity in muscle tissue.

Age increase is directly proportional to the risk of developing type 2 diabetes; and associated with senile skeletal muscle dysfunctionality. As skeletal muscle ages, mitochondrial deterioration, intramyocellular lipid accumulation, elevated inflammation, oxidative stress, altered activity of insulin sensitivity regulatory enzymes, endoplasmic reticulum stress, diminished autophagy, sarcopenia and over-activated renin-angiotensin system may be enacted [12]. These modifications may tantamount to defective skeletal muscle insulin sensitivity and elevated risk for insulin resistance and type 2 diabetes as skeletal muscle ages. Explicating the process in the enhanced risk of insulin resistance in the ageing of skeletal muscle provides an encompassing understanding for the high incidence of type 2 diabetes in elderly persons, and implement modalities in the prevention, treatment [12] and management of type 2 diabetes [13-15] in elderly individuals.

Glucose tolerance diminishes intermittently with age, and is characterized by high prevalence of type 2 diabetes and postchallenge hyperglycemia in the older population. In humans, age-associated glucose intolerance correlates with insulin resistance, but circulating insulin concentrations mimic those of younger individuals. In certain presentations of hyperglycemic challenge, insulin is lower in older people, and may be due to β-cell dysfunction. With insulin sensitivity being controlled for, insulin secretory deficit were inevitably detected in ageing [16]. Superimposed on this is the decrement of β-cell sensitivity to increase in hormones with increasing age. In the presence of untoward β-cell compensation to age-related insulin resistance, older individuals may be susceptible to postchallenge hyperglycemia and type 2 diabetes. A proper understanding of the metabolic modifications correlated with ageing, provides the latitude for the development of interventions in prevention and therapeutics, especially in a high risk population for glucose intolerance. The interaction of diverse variables associated with ageing, such as augmented adiposity, diminished physical activity or exercise, therapeutics, syndemics, comorbidities and insulin secretory derangement associated with ageing, ostensibly contribute to modifications in glucose tolerance [16].

Mitochondrial effects

Mitochondrial defect inevitably signifies cellular ageing [3, 17, 18]. Mitophagy is a critical mitochondrial quality control mechanism that eliminates dysfunctional mitochondria and aids in cell survival. Insulin-like growth factor 1 (IGF-1) promotes survival of smooth muscle cells (SMCs), but its potential effect on cellular aging is elusive. An antiageing effect was suggested on detection that IGF-1 diminished cell senescence, inhibited DNA telomere shortening, augmented mitochondrial membrane potential, activated cytochrome C oxidase, and minimized mitochondrial DNA derangement in sustained cultured (aged) aortic SMC. IGF-1 enhanced mitophagy in aged cells, and it was associated with mitigated expression of cyclin- dependent kinase inhibitors p16 and p21 and augmented levels of Nrf2 and Sirt3 [19], biogenesis in regulators of mitophagy and mitochondria. SiRNA-induced suppression of either Nrf2 or Sirt3 obliterated IGF-1-induced upregulation of mitophagy. Thus, indicating that the Nrf2/Sirt3 pathway was necessary for the impact of IGF-1 on mitophagy. PINK1 is a prime mitophagy regulator. The silencing of PINK1 suppressed mitophagy and inhibited IGF-1-induced antiageing impacts in aged SMC, as expected

with the pertinent function of mitophagy on the impact of IGF-1 in cellular ageing. IGF-1 inhibited cellular ageing via Nrf2/Sirt3-dependent mitophagy activation [19]. Thus, the findings suggest that IGF-1 signaling activation is a viable potential approach for mitophagy activation and retardation of cellular ageing. Insulin-like growth factor 1 (IGF-1) is an endocrine and autocrine/paracrine growth factor expressed by a vast majority of cells, such as vascular SMC; and has crucial impacts on cell growth, differentiation, and migration. Numerous data indicate that IGF-1 [19, 20] sustains mitochondrial functionalities in vitro and in vivo; with cancer cell viability dependent on the stimulation of IGF-1 for mitochondrial biogenesis and mitophagy. A therapeutic potential is essential for IGF-1 in mitophagy stimulation and resultant retardation of cellular ageing.

It is suggested from studies of genetic and metabolic features associated with healthy longevity and old age survival that the conserved ancient IIS pathway has a factor in human longevity [21]. Expansive research indicts insulin and insulin signaling in good prognosis for ageing and longevity. Studies of insulin and insulin receptors exposed the physiological insulin relevance to the brain. Pathways which influence responses of an organism to modifications in its environment are involved in the genetic regulation of lifespan among disparate species. An established prime pathway via genetic analysis is insulin/insulin-like growth factor-1(IGF-1) signaling (IIS) [22, 23]. Insulin/IGF-1-like ligands signal via insulin and IGF-1 receptors. In mammals, insulin/IGF-1 signaling is associated with ageing, lifespan, and longevity [24]. Even though, insulin and IGF-1 function substantially through defined receptors, there exists an expansive overlap and interaction in downstream signaling cascades with resultant problems to estrange impacts of insulin signaling from impacts of IGF-1 signaling. The phenotype of healthy longevity is sustenance of insulin sensitivity [25], as depicted in familial human longevity and the elderly. Insulin has effects in all the functionalities of human physiology, such as regulation of peripheral glucose homeostasis, crucial contributory neuromodulator to neurobiological processes, undergirds behavioural, cellular, biochemical, and molecular functionalities. Research has depicted the role of type 2 diabetes in premature ageing syndrome, and the elevated incidence of insulin resistance with age [2, 17, 18].

Neurodegenerative disorders and tumours

There is expansive empirical evidence that growth hormone and IGF-1 are pertinent for normal development of the bodies and brains of mammals. IGF-1 permeates the blood-brain barrier, and there is extant scientific interest in age-related decrements of serum growth hormones and IGF-1 as mechanisms in effecting cognitive functionality in elderly persons [26]. Humans and other mammals exhibit elevated levels of IRs in several brain regions and nuclei, but it is uncertain whether insulin production occurs in the brain. The pathophysiological process of insulin in the brain regarding ageing and longevity are not yet clear. In direct proportionality to global ageing, there is unprecedented acceleration in the prevalence of obesity, metabolic syndrome, type 2 diabetes, and neurodegenerative diseases [2, 3, 13-18, 27]. Insulin resistance is not an uncommon comorbid presentation in these varied aberrations with cardiovascular disorders [3, 28]. It is pertinent to understand insulin action for healthy longevity in relation to age-related diseases, perturbations of glucose metabolism, retarded and premature ageing [29]. It is suggested that hyperglycemia and hyperinsulinaemia are crucial both in ageing and cancer development. The life elongation impact due to calorie restriction relates to IGF-1 decrement. It is suggested that antidiabetic biguanides are pertinent for both life span prolongation and cancer prevention [30].

Type 2 diabetes and cardiovascular impacts

It is established that ageing correlates with an elevated incidence of hypertension, type 2 diabetes, and coronary heart disease. Speculations are rife as to the underlying common process [8] in the aetiology of these disorders as to manifest in syndemics [27], comorbidity [28], or frequent clustering of these disorders in the same person [8]. Evidence depicts that insulin resistance and/or hyperinsulinaemia correlate with glucose intolerance, dyslipidaemia presenting as elevated plasma triglyceride and decreased high-density lipoprotein-cholesterol concentrations, and higher systolic and diastolic blood pressure levels.

Insulin resistance in type 2 diabetes and obesity constitutes a major risk factor for cardiovascular anomaly. Insulin forms a crucial therapeutic component for blood glucose management in diabetes. Insulin may be critical for normal cardiovascular function, and it's deficit depicted in insulin resistance culminates in cardiovascular impairment and disorder. Insulin is a prime ingredient of glucose-insulin-potassium cocktail with crucial protective influence through phosphatidyl 3'-kinase-protein kinase-protein B-endothelial nitric oxide synthase, PI 3K-Akt-eNOS dependent signalling process in combination with its metabolic modulation that conversation it with effective organ protector as applicable in numerous clinical interventions in health and disease [31-33].

Hypertestosteronamia may be involved in states of insulin in resistant pathogenesis and androgen replacement therapy, thereby rendering importance to glycaemic control and cardiovascular risk, as particularly evident in diabetic male subjects [34, 35].

Methods in the investigation of ageing on insulin

Insulin resistance is a condition whereby a defined concentration of insulin presents a diminished biological impact. Also, insulin resistance has been

permissively related as the requirement of the minimum of 200 units of insulin daily for the attainment of glycaemic control and prevention of ketosis. The insulin resistance syndromes present expansive clinical spectra inculcating the metabolic syndrome, diabetes, obesity glucose intolerance, and a dire insulin-resistant state [36]. A vast majority of these disorders are associated with diverse metabolic, endocrine, and genetic states. Furthermore, these syndromes may be associated with certain immunologic disorders, and depict unique phenotypic features. The metabolic syndrome, an insulin- resistance condition known as syndrome X or the dysmetabolic syndrome is of immense public health and clinical significance. Patients presenting with diabetes, obesity and high blood pressure have untoward responses to insulin [37, 38], and may develop with ageing. Insulin resistance fosters diabetes pathophysiology and constitutes a hallmark of obesity, metabolic syndrome, and numerous cardiovascular disorders [39-41]. Thus, the abundance of insulin sensitivity and/or resistance is of immense significance in basic science, clinical practice and epidemiological instances. The methods employed in the determination of insulin sensitivity incorporate hyperinsulinaemic-euglycaemic and hyperglycaemic clamps as well as intravenous glucose tolerance tests [42]. Numerous hormones and regulatory factors impact on insulin action with possible contributary influences in insulin resistance exhibited in obesity. Furthermore, abnormal free fatty acid metabolism is essentially involved in insulin resistance and the aberrant carbohydrate metabolism depicted in obese or diabetic individuals. Thus, the underlying mechanisms involved in the aetiology of insulin resistance are multidimensional and incorporate the insulin signaling pathway. Ageing is associated with augmented bodyweight and fat mass [43, 44]. Abdominal fat is not merely related to hyperinsulinaemia, but visceral adiposity correlates with, and is directly proportional to insulin resistance. As obesity is an inducer for diabetes associated insulin resistance, obese individuals present higher concentrations of non-esterified fatty acids, glycerol, hormones, and pro-inflammatory cytokines which may contribute to the aetiopathogenesis of insulin resistance when discharged by adipose tissue [45]. The modifications or alterations in body composition due to ageing by diet and exercise/training may retard the onset of insulin resistance. Weight dissipation, aerobic and resistive exercise training lead to excoriation of total body and abdominal fat [46, 47]. Bodyweight excoriation enhances insulin sensitivity with improvement in glucose tolerance. Moreover, the insulin resistance exhibited in aged individuals are modifiable via physical training or exercise. Significant improvements have been detected in glucose metabolism due to physical training or exercise in middle-aged and elderly persons. The successes in insulin sensitivity with resistive training are directly proportional to improvements in aerobic exercise. Improvements in glucose metabolism following bodyweight dissipation and exercise/training may be attributable to alterations in body composition and decrement in total and central body fat. Additional alterations in skeletal muscle [30], blood flow and certain mechanisms possibly interact in the modification of insulin resistance with exercise training. Lifestyle changes, bodyweight excoriation and physical activity are functional and beneficial health provisions [40, 41] for the enhancement of insulin sensitivity and prevention of glucose intolerance and type 2 diabetes during ageing.

Therapeutic interventions and other healthcare measures

There is progressive derangement in β-cell function in type 2 diabetes irrespective of the type of treatment. Persistence hyperglycemia causes progressive decline of β-cell functionality with resultant β-cell exhaustion and culminating in β-cell excoriation and dysfunctionality. Type 1 diabetes constitutes an autoimmune state with a remarkable inherited stance, and an increasing global incidence. Approximately 25% of these cases are diagnosed in early adulthood and into advanced age [43]. The improvements in care and decline in mortality rate have been attributed to the increase of elderly persons presenting with type 1 diabetes. There is a paucity of clinical trials in persons older than 70 years of age having type 1diabetes with comorbidities, dependency and frailty. Type 1 diabetes management and the therapeutic objectives must be personalized according to the health status and life expectancy of the patient. With regard to healthier elderly patients, insulin treatment regimens inculcating multiple insulin injections or insulin pump therapy on a daily basis which approximate normal physiological insulin secretion ought to be employed in order to achieve lower glycaemic goals, with concomitant reduction in hypoglycemic risk, and frequent glucose monitoring with preferential application of continuous glucose monitoring systems [47, 48]. It is appreciable to apply less stringent glycaemic targets and insulin regimens in frail persons with poor prognosis or health. Ageing disorders, such as poor cognition, hearing and vision as well as depression, chronic pain and defective mobility may impede intricate insulin regimens. In such instances, the prime therapeutic objective would be ameliorating the acute hyperglycemia impacts, mitigating hypoglycemic risk, and optimizing quality of life [48]. Newfangled insulin preparations and advanced technology in insulin delivery and monitoring of blood glucose have contributed to augmented management of type 1 diabetes in all age groups.

Insulin resistance is a common characteristic of ageing, accompanied with loss of gonadal function in female persons due to decreased plasma estrogen abundance. Diverse aetiologies have been attributed for this insulin resistance, such as alterations in steps of the insulin pathway [49]. Findings indicate that 17β-estradiol treatment can ameliorate the deranging impact

of ageing on insulin sensitivity, in the minimum, at the plasma membrane level localized Glut4; with further research methodology required to elucidate it [49].

DISCUSSION

The ageing process and ageing have been associated with deranged insulin sensitivity and elevated type 2 diabetes prevalence with evidence that ageing deranges insulin sensitivity independently of modified body composition in humans. It is suggested that genetic factors contribute in age-related metabolic dysfunction [50]. The processes of obesity- and ageing-associated insulin resistance are ostensibly disparate, with therapeutic challenges and opportunities for type 2 diabetes in the ageing population. There is an ardent need for caregivers to motivate patients for achievement of recommended treatment goals [51] and targets in order to prioritize interventions and programmes for the improvement of care in insulin-ageing complications.

Insulin resistance is the hallmark of several ageing-related disorders and morbidities. Insulin is not merely the aetiology of belly fat but superimposes on the risk of cardiovascular disorders. In the elderly population, insulin resistance progressively increases with age leading to elevated type 2 diabetes incidence [52]. Alterations in body composition and insulin resistance correlate with dysregulation of physiological pathways with resultant obesity and diabetes [53], premature senescence, and cardiovascular disease risks [2, 9, 10, 54]. Insulin secretion ostensibly decreases with age even after adjusting for disparities in adiposity, fat dissemination, and physical activity [8]. This suggestively contributes to glucose intolerance in the elderly, despite improved lifestyles. There is associated ageing with hyperinsulinemia, but findings are contradictory between modified insulin clearance and insulin secretion. Elevated insulin secretion is the aetiology of physiological hyperinsulinaemia in ageing, and not decrement in insulin clearance.

Progressive dissipation of physiological functionality with resultant augmented susceptibility to mortality [7] and morbidity is pathognomonic of ageing. With the advent of ageing, peripheral insulin resistance is progressively enhanced, with concomitant compensatory chronic increases in circulating insulin concentrations. The impact of ageing on insulin secretion suggests that relative insulin secretory derangements are directly proportional to progressive increasing age [7]. Neurological [55], diabetes and obesity impairments [56] in the elderly have their aetiologies via a constellation of environmental and genetic variables or gene-environment interactions [2] which are superimposed on conventional age-related alterations [17, 18].

Apparently, insulin resistance with ageing correlates substantially to lifestyle, for instance, impoverished diet and nutrition, as well as diminished capacity to exercise or physical activity. It is pertinent to control biomarker risk factors [51] in patients with age-related disorders and their complications to meet therapeutic targets {14, 15, 56, 57]; and for the elderly not to shirk responsibility in order to attain prolonged and healthier lifestyle and lifespan. The shift in age distribution in the elderly and progressive ageing evident in a vast majority of populations have been directly proportional to worldwide epidemic of obesity and its associated metabolic aberrations, such as, type 2 diabetes. Adipose tissue (AT) impairment is broadly depicted as pathognomonic of the ageing process with resultant systemic metabolic modifications. These are exhibited as insulin resistance, ectopic lipid accumulation and chronic inflammation which are indicted for augmented risk of obesity and type 2 diabetes onset correlated to ageing. Conversely, obesity and type 2 diabetes, pathognomonic of AT derangement, depict several similar physiologic features as ageing, such as elevated burden of senescent cells and epigenetic modifications. In perspective, these chronic metabolic aberrations may connote a condition of accelerated or premature ageing [39-41, 58-62]. Progressively, chronic insulin resistance may result in prediabetes and culminate in type 2 diabetes due to lack of treatment or persistent incurability [63].

CONCLUSION

This article argues the clinical strategies and mechanisms in the prevention, treatment and control of insulin impairment, metabolic syndrome and other associated disorders in the ageing process. The hormone, insulin impacts on ageing and lifespan, with provision of mechanisms for the manipulation of genes for longevity ad healthier lifestyles. Sustained insulin sensitivity is associated with longevity, and insulin resistance predicts age-related disease occurrence, such as hypertension, coronary heart disease, stroke, cancer as well as brain functionality in learning and memory, regulation of ageing, metabolic syndrome, obesity and diabetes. Ageing progressively debilitates insulin function with resultant risk for morbidity, complications and mortality.

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