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Study on the Correlation of "Obesity" and Autoimmune Diseases: Diabetes as An Autoimmune Disease

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Abstract

"Obesity" and related "insulin resistance" pre-dispose persons developing diseases as metabolic chronic, inclusive of T2DM. Despite such problems have an effect on a vast share of the global populace; the underlying pathways of sickness continue to be understood poorly. Improved factor-α of tumor necrosis invention in "AT"is as an "obesity"-related "insulin resistance"inducer signed a brand-new technology of expertise which a sub-clinical procedure of anti-inflammatory triggers the "insulin resistance" and metabolic disease that proceeds kind 2 diabetes. Field advances recognized adaptive and innate immune reaction components as main roles in regulating these anti-inflammatory methods. As specificity ofantigen is an adaptive response immunity indicator, its position in controlling the continual inflammation which associated with"obesity" and T2DM begs the query of it or not "insulin resistance" and T2DMofadditives as an autoimmune. Onsuch perception, we studied the correlation among "obesity" and autoimmunity in diabetes patients.

Key words: autoimmune diseases- "obesity"-T2DM- inflammation- "insulin resistance".

Introduction

Epidemic as"obesity"signifies a main21st century health matter. Disease prevalence has considerablyaugmentedworldwide for last decades, includecountries of low-income. Furthermore, it was reported that pediatric "obesity"considerablyelevates "obesity"risk and complications of cardiovascular throughoutadulthood and childhood. The constantly increasing in prevalence of "obesity" may be attributed to lifestyle habits changes, i.e., junk food assumption and behavior as sedentary. Furthermore, genetic circumstantialhas a functionviaenergy spending affecting and intake offood. The excessing fat existing in obese persons resulting in "AT"as hypertrophic white with a followingdisorder in activity of adipocytes metabolic. "AT" in some obese cases how activity as pro-inflammatory and linkedtocomorbidities of"obesity"-related in children and adults (1). Activeadipocytes dischargenumerouscytokines and hormones mentioned to as adipokines whichemployfunctions being immunologicaland metabolic, where they canmodifycell activity asacquired and innate immune. Besides, they canpromotesignals of pro-inflammatory causing chronic inflammation systemicof small-grade. Besides,many reports confirm evidence of association between immune diseasesand"obesity", i.e.,atopy,cancerand autoimmunity. Thus, the changedadipokines secretion form in "obesity" is regardedas link between comorbidities as immunological and metabolic and"obesity".Obesity and overweight prevalence worldwide wasdoubled overever since 1980 to degreewhichapproximately a 3rdof population of world is classified now as obese or overweight. "Obesity"harmfully affects in USA, wasassessedwherecosts of health sufferedviaonly obese person was USA $1901/year in 2014, and extrapolated to USA $149.4 billion at national level. The total cost in Europe, being indirect and direct due toobesity and overweight of equivalence to GDP 0.47–0.61%. WHdescribesobesity and overweight as unusual or accumulation ofexcessive fat which displaysheathrisk (2). "The body mass index" measured via dividing BW(Kg)/ height^2(m), is metric being simple utilized to designate overall fatness

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of body. For adults, existing guidelines from WHO and Centers ofUS for ControllingDisease and Prevention (CDC) describerange of normal BMI =18.5 to 24.9, while a $BMI \geq 25\ kg/m^2$ = overweight, and a $BMI \geq 30\ kg/m^2$ is categorizedbeing obese, with extreme"obesity" distinctbeing $BMI \geq 40\ kg/m^2$. In spite ofsuchdefinition of relatively simplistic, "obesity" is disease of multifactorial which resulting from chronic positive energy balance, e.g.,if intake of dietary energy more than energy spending. Energy as excess is transformed to triglyceride that is saved in depots of"AT" whichsize enlarging, thusenlargeing fat of body and leading to weight gaining. Food globalizationsystems which yields more affordable and processed food and promoting overconsumption aspassive from energy-dense, poor nutrient beverages and foods was recognized as a main"obesity" epidemic driver; even though a decline in activities as physicalowed to lifestyles modernization isalso likely involved."Obesity"maytake place at any time of life. Studies previous evaluating styles in "obesity"observed the prevalence has augmented in all ages of children and adults, geographical locality indiscriminate, socioeconomic or ethnicity status. In countries of low-income, "obesity"in general is further prevalent among adults of middle-aged from environments of urban and wealthy (particularly women); while, in countries of high-income, it influences all ages and both sexes, while theprevalence is disproportionately larger among groups being disadvantaged (3).

Inflammation and "obesity"

Clinical reports noticed a noteworthy relationship between inflammations as chronic low-grade of serum markers and related comorbidities of"obesity" in adolescent and children. CRPserum levels directly associateto"insulin resistance" and cIMT in adolescents and children ofobesity and overweight. Furthermore, it wasstated that WBC count is foretelling of elevated ventricular hypertrophy and cIMT in obese adolescents and children. Furthermore, losing weight following lifestyle trial intervention was operational in declining insulin resistance and markers of serum inflammatory in obese adolescents and children. Inflammation considered as a mechanism which involvingcellular and non-cellular mediator's series involving in response to infections, damage oftissue, death ofcellular, and cancer. "Obesity" is go along withinflammation as sterile low-gradechronic in "AT"whichwas no-damage linkedof tissueor infection (4). Also, such process is mentioned as Meta inflammation or metabolic inflammation. Metainflammation is player being active in related comorbidities obesity development, as related inflammation obesity mayharmother organs function. Immune responsing ofAT is intermediateviaresident "ICs" "AT"i.e.,mast cells, macrophages, B and T lymphocytes and neutrophils which are the 2nd more denoted cellular kind, following adipocytes. Pathways trigger At inflammations are not clear entirely. Nevertheless, "AT"hypertrophy and hyperplasia taking place in obese personsmight employ significant function. Actually, adipocyte size increase causeshypoxia,oxidative stressOSas intracellular and pro-inflammatory molecules release. Nevertheless, various studies proved that metabolically obese adolescents being unhealthy have a tendency being slighter"adipose cells" that permits for a lesser capacity of saving and supportan additional pronounced free FAflux (5). Activation of inflammasome in sub-cutaneous "AT" SAT was accompanying with reformed distribution of abdominal fat. Activation of inflammasome chronic harms the SAT capability of storage causing a lipid over spillingat visceral "AT" (VAT). Free fatty acids FAexcess gives phenotypeas unfavorable metabolic possiblyviaactivation of macrophage in "AT". Actually, free FAdirectly activates"ICs" and inducingpro-inflammatory mediator's secretion viawork together with "toll-like receptors" TLRs. In VAT, adipocytes are developingphenotype as dysfunctional brandedvialesser"adipose cells" and adhesion molecules expression for macrophages/monocytes.

Macrophages in immune response

"Macrophages considered as mostlycommunaltype ofimmune cellIC in "AT". Number of macrophages has been relatedtosize of adipocytes and severity of obesity. ATs of minorquantity macrophages (ATMs) derive from maturation of pre-adipocyte, whereas the mainstreamarises from circulation as systemic. ATas hypertrophic is promotingmigration of infiltration and macrophage throughchemokines secretion.

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Numerous chemokines are involving in such pathway. Monocyte-chemoattracting protein 1/chemokine C–C motif receptor 2 (MCP1/CCR2) isjoiningreceptor CCR2 macrophage causing infiltration. Furthermore, "obesity"is alteringmacrophages distribution and phenotype. Macrophages might be discreted in 2 subsets based onantigen of membrane and secretion of cytokine: typicallytype of activated M1 and alternative M2. Type of M1 employs anantibacterial and pro-inflammatory function; it is expressinginflammatory mediator's receptor i.e.,colony-stimulating factor of granulocyte-macrophage (GM-CSF), lipopolysaccharides (LPS)and IFN-γ (6). On the contrary, phenotype ofM2 is encouragedviamolecules as anti-inflammatory, namely, IL-10, IL-13, IL-4, and (M-CSF), and showsfunctions of anti-parasitic and anti-inflammatory. Differentmacrophages polarization in human "AT" is affectedviaprominenceof nutrition. In personsof normal weight, the eosinophils prevalence, T"natural killer" and NK –lymphocytes arepolarization promoting toward type ofM2. "These macrophages, in a favorable environment, exert homeostatic actions, regulating cellular proliferation, extracellular matrix deposition, and removing cellular debris in stromal matrix". In obese persons, OS, debris of necrotic cell, and free FAoverload cause a polarization in the direction ofphenotype of M1. Contrasting to M1and M2, macrophages are not migrating in matrix of stroma; they creating aggregates surrounding adipocytes as necrotic, in a usualstructure as crown-like. In humans, the M1 macrophages number correlates directly with inflammation being systemic, "insulin resistance", T2DM, and disease of fatty liver (7).

Cells of lymphocytes and "obesity"

ATis the2nd largest subset IC is denotedvia T-lymphocytes. T-cells aredistributed in CD8+ and CD4+ based onantigens surface. CytokineCD4+secretion arrangementpermitsmoreclassification in Th2 (IL-4, IL-5, and IL-13), Th1 (INF-γ), Th17 (IL-17, IL-21, and IL-22)", and Treg (IL-10 and factor of transforming growth B).CD8+ iscells being cytotoxic which are secretinggranzymes,perforins, and a range of "cytokines" that other mediatingICsactivation. In adipose dysfunctional tissue, sub-population pattern ofT-lymphocyte is polarizing toward activity as pro-inflammatory. Thus, Th1, Th17, and CD8+ are further represented in comparison to anti-inflammatory Th2 and Treg (8).

"ICs" and "obesity"

Mast, neutrophils, and dendritic cells establish a small ICsfraction in AT. However, they havesignificantfunction in process ofamplifying inflammation throughpro-inflammatory mediator's secretion. The eosinophilsnumber instead, is declined. They are promotingmacrophagedifferentiation ofM2 and Th2 and suppresingstimuli of inflammation(9).

Adipokines and "obesity"

In former decades, ATnumber derived cytokines have been considered, as adipokines. In addition to adipocytes, the ATvascular-stromal component harmonizes with secretion of cytokine in dependent adiposity fashion. Adipokines have a vital function not just in homeostasis of energy but also in reaction as immune and inflammatory, mostlyinflammation promoting (10).

Leptin and "obesity"

Leptin was first described in model as murine. It is codedviagenes of human homologous *LEP* and murine *ob*. Models of human and animals presented leptin action inhibition resulting in insulin resistance and assumption of food. Secretion of leptin is correlated positively with mass of AT; thus, obese persons display high levels of leptin plasmatic. However, obese persons are developing leptin resistance along declined sensitivity to stimulus as orexinergic hormone. Leptin has activities being pleiotropic. The chieffunction is food assumption suppression throughhypothalamic nuclei inhibitionwhich stimulates stimulation and hunger of those which promoting satiety (11). Leptin function loss is accompanying with insulin resistance, hyperphagiaand weight rapid gain.Furthermore, leptin effects development of pubertal and displays activity of

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immunomodulatory. Actually, numerous types of ICs express receptor of leptin (LEPR). In neutrophils, leptin is activating signals asanti-apoptotic, causing survival of cell. Furthermore, it is inducing activation of neutrophil in chemotaxis, infiltration of tissue, and O_2 radicals' release terms. Likewise, basophils and eosinophils express LEPR on surface of cell. Regarding neutrophils, leptin behaves as cytokine of persistence for such cells and stimulating infiltration of tissue and releasing of molecules aspro-inflammatory. Furthermore, leptin is vital for a roleof macrophage/monocyte. In experimental *LepR*models, knocking-out mice diminished macrophages activity killing and phagocytosis wasstated. Moreover, leptin prove enhancingsurvival of macrophage and monocyte, migration, pro-inflammatory "cytokines"releasing (namely, TNF-αandIL-6), and surface markers expression (CD69, CD39, CD25, IL-1Rαand CD71,). Also, leptin is stimulatingNK cell cytotoxicity and proliferation and establishescytokine survival for cells of dendritic. Regardingresponse asadaptive immune, hormone is inhibitingapoptosis of T-lymphocyte, promotingresponse ofTh1, suppressingactivity ofTh2, and enhancingproduction of INF-γ and IL-2. Furthermore, it is sustainingfunction of Th17 as pro-inflammatory and activity of B-lymphocyte. Generally, leptin showsactivity as pro-inflammatory, interacting with immune system adaptive and innate. Suchinformationhighlights the vital leptin function in comorbidities pathogenesis obesity, in chronic inflammationand metabolic derangement terms (12).

Tumor necrosis alpha and "obesity"

"TNF-α has a dominantfunction in numerous autoimmune and inflammatory diseases pathogenesis. Cells of macrophage/monocyte are in charge for the chiefserum TNF-α fraction.Furthermore, cytokine levels correlate positively with insulin resistance and measures of adiposity. TNF-α is inhibitingPPAR-γ peroxisome proliferator-activated receptor-gamma expression. PPAR-γ employsactivity duringanti-inflammatory, declining secretion pro-of cytokine beinginflammatory in macrophages of human. Besides, it is interfering with insulin IRS-1 receptor phosphorylation, causing"insulin resistance". Furthermore, treatment of TNF-α antagonist in personsinfluencedviadiseases as autoimmune improvingsensitivity toinsulin. Nevertheless, such observationswaslong-established in obesityinsulinmodels of resistance (13).

Interleukin 6 and "obesity"

IL-6 is considered as mostlysignificantcytokines as pro-inflammatory.Around$^1/_3$ of total IL-6 descendscirculating levels from adipocytes. IL-6 directly stimulates active phase proteins secretion i.e.,fibrinogen and CRP. WCchiefly isassociatING with plasma levels of CRP and IL-6, highlighting the visceral adiposity vital functionin inflammation. Furthermore, it is promotingmolecules of adhesion expression on cells of endothelial for leucocytes, increasinginflammation and vascular damage (14).

Resistin and "obesity"

Resistin is chieflyproducedviamacrophages and monocytes and a small fraction of adipocytes-deriving. It is connectedto"insulin resistance" as is inhibiting insulin receptor signaling throughcytokine signaling-3 suppression (SOCS-3). Subsequently, it mayaffect plasmatic levels of glucose and sensitivity of insulin. Furthermore, it is stimulatingTNF-α and IL-6 release from counteracts and neutrophils adiponectin activity of anti-inflammatory on cells as endothelial (15).

Adiponectin and "obesity"

"AT"is releasing a small adipokines amount with activity an as anti-inflammatory where adiponectin is characterized as the best. Adiponectin is stimulatingoxidation offatty acid and uptake of glucose in liver and skeletal muscle, therefore improvesensitivity of insulin. In macrophages, signal of adiponectin is promotingpolarization of M2 phenotype, TNF-α secretion reduction of, and scavenger enhancement activity. Furthermore, it is stimulatinganti-inflammatory IL-10release. Cytokinesof pro-inflammatory (TNF-α andIL-

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6), OS, and adipocyte hypoxia declinee secretion of adiponectin. Actually, studies have described that levels of hormone are correlated inversely with levels of CRP plasma. Additionally, "obesity" is accompanying with minorlevels of adiponectin and cardiovascular diseases elevated risk. Likewise, to adiponectin, proteins as C1q/TNF-related (CTRPs) are promotingpathway of anti-inflammatory (16). Certain CTRPs are expressing in "AT", i.e.,CTRP6, CTRP3, CTRP12and CTRP9 and inhibit pro-inflammatory activity of macrophage. Additionally, omentin-1 is produced from VAT and declines vascular inhibition inflammation throughexpression endothelial molecules adhesion. Thus, secretion array of adipokine from "AT"employs a vitalfunctionforassociationamongresponse of immune as altered and"obesity", causing inflammation being systemic and reducingtolerance ofimmunity(17).

Protein 4Retinol-binding (RBP-4)and "obesity"

RBP-4 considered as adipokine is involving in insulin resistancepathogenesis. In specific, it declines sensitivity of insulin, declining IRS-1 insulin-prompted phosphorylation. Hepatocytes are the chiefsource of RBP-4, whereasmacrophages and visceral adipocytes are secreting a slightportion. Nevertheless, RBP-4 is produced in manner being dependent VAT to mass, beingproposed as visceral adiposity marker and low-grade inflammation beingchronic. Variation of adipokines as pro-inflammatory weredesignatednamely; angiopoietin-like protein 2 (ANGPTL2), visfatin, CC-chemokine ligand 2 (CCL2), lipocalin, and CXC-motif chemokine ligand 5 (CXCL5).Nevertheless, their function in Metainflammation was not understood entirely(18).

Autoimmunity and "obesity"

Immunological adipose tissue AT function characterization has proposed a probablerelation between autoimmune diseasesand"obesity". Autoimmunity is influenced strongly via genetic background; nevertheless, factors of environmentare vital in immune response beginning. Numerousstudies as observational have stated the link between autoimmune diseasesandobesity; namely, psoriasis, multiple sclerosis, autoimmune thyroiditis, rheumatic arthritis, T1DM, systemic lupus erythematosus, and diseases of inflammatory bowel (19). Nevertheless, information for age of pediatric isscant. Studies as longitudinal have stated that adolescents and obese children showdeveloping multiple sclerosis of2-fold higher risk in maturity; such risksaregreater in femalesin comparison to males and elevates in persons ofgenetic pre-disposing background (HLA DRB1*15). Numerous potential basictrailsweresuggested: deficiency ofvit. D, macrophages M1/M2 phenotypes imbalance, elevated leptinlevels, and minimized levels of adiponectin. Regarding rheumatoid arthritis, obese personsexists as 20% RA greater risk in longitudinalstudies. Moreover, severity of RA and responsiveness of treatment is influenced negatively via adiposity, for instance obese persons are greaterdisposed to disease developing being severe with remissiondeclining and great rate of comorbidities. "Adipokines are involving in joint damage; they are stimulatingpro-inflammatory secretion of "cytokines" and metalloproteinases from synovial fibroblasts and chondrocytes. On the contrary, no firm confirmation is offered to approve the hypothesized association between pathogenesis of systemic lupus erythematosus and"obesity", whereas it has been stated that "obesity"upsurgesactivity of disease. Additional firm confirmation approves that psoriasisand"obesity"isassociated, while the pathogenic under-pinnings of such association are debatablestill. Persons with psoriatic arthritis and psoriasis likely to gain weight due tolifestyle being sedentary; "obesity"deterioratesseverity of disease and comorbidities risk (20). Moreover, loss of weight is improving disease control and treatment responding. Numeroustrailsmotivatesuch observation. Firstly, altered adipokines' milieu describedvia TNF-α, IL-6prevalence and leptin promotingactivation of IC, migration, and proliferation. Additionally, Treg cells reduction with a co-ncurrent Th17 increase has been relatedto autoimmunity. Also, nutrients have a function, as diet of western with contentsof highsugar and fat causingdysbiosis of intestinal and imbalance of Th17/Treg (21).

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In addition, “AT” is involvingaromatizationin peripheral androgens/estrogens, and such mightsignify a ways viathatextra adiposity may pre-dispose to autoimmunity. Actually, women are extrainfluenced viadiseases as autoimmune in compairson to males. Suchremark may be associated to the sexual hormones impact on tolerance ofimmunity. Excitingly, femalesdisplayupperlevels ofleptin plasma in comparisonto males. “It is recognized that dehydroepiandrosterone (DHEA) and estrogens are the chief females' vulnerability mediators to diseases as autoimmune. Such hormones are promotingrelease of immunoglobulin, stimulatingresponses of adaptive immunity, and induction of pro-inflammatory secretion “cytokines”.Regarding RA, adipokines considered to beplayersof dominance in such scenario”. Resistin plasmalevelsand leptin are increased in psoriasispersons. Additionally, experiment*in vitro* presented that leptin is stimulating cytokine releasing in keratinocytes of human (22). Opposing results have been formedregarding adiponectin role in severity and pathogenesis of psoriasis. It might be concluded, extra studies are required to approve and explore the pathwaysas pathophysiological impling the potential associationamongobesity and autoimmunity.

“Obesity” related diseases

“Confirmationproposes that “obesity” and inflammation related may be at any ratepartlyof responsibility ofsuch process. Documents of (NHANES III) wasstatedaffirmativerelationshipamongatopy rates and BMI. However, obese persons do not display a noteworthyserum atopy a marker increase i.e.,levels ofIgE plasma and count of eosinophils (23)“Moreover, proofregardingprobablerelation between other allergic diseasesand“obesity”, that is to say, atopic dermatitis and allergic rhinitis, is scarce. Thus, such field requires to be investigated further deeply. On the contrary, numerousdocuments are obtainableregardingassociation between obesity and asthma in children and adults. Epidemiological studies being cross-sectional have stated that obese children are ofteninfluenced via asthma”. Additionally, a metanalysis include6 perspective establishedstudieswhere children beingobese display a 2-fold greaterasthmarisk in comparison to normal weight children. Additionally, children being obese normallydisplayan extra severe phenotype of asthma which has a tendency to be pharmacologic therapies resistance with recurrent exacerbations (24). However, obese children do not displayexpiratory inflammatory markers levels elevation i.e., exhaled (eNO). “Numerous underlying trails have been suggested for asthmaobesityrelated. In specific, truncal adiposity excess causes a mechanical overloading to respiratory muscles. Such results in declined functional residual capabilitydeclinedvolume as residual and volume of expiratory reserve. Suchreduction in volume exposes obese children to forced expiratory volume impairment in 1 s and forced cruicialcapability ratio (FEV1/FVC)”. Moreover,the mechanical overloading, metabolic disorder mayof a function in asthmaobesityassociated. Insulin resistance and dyslipidemiahave been relatedtoratio of anlessened FEV1/FVC. Insulin considered as stimulus being trophic for cells of small smooth muscle airway (25). It is stimulating laminin makingviapathway of phospho-inositide-3 kinase/Akt (PI3K/AKT), resulting inhypertrophyof muscle. Moreover, it is enhancinghyper-responsiveness of airway throughinnervation of parasympatheticstimulation. Such pathwaysare promotingobstruction of airway throughout physical exercise and respiratory effort perception throughout inspiration. Besides, 3inflammation of chronic low-grade taking place in “obesity”hassignificantfunction. In children being obese, imbalance between phenotype of Th1/Th2 toward reaction of Th1 has been correlated to decline ratio of FEV1/FVC. “Similarly, macrophage pro-inflammatory M1 type induces airway obstruction. Finally, derangement of adipokines' milieu has a role in adult asthma. In particular, leptin serum levels are inversely correlated with pulmonary volumes and FEV1/FVC ratio, while it increases bronchial hyper-responsiveness”. Nevertheless, mostly available proof is according to studies as cross-sectional, and such renders it not easy to understand completely underlying obesity-related asthma pathways(26).

Cancer and “obesity”

Former studies have exposed that status of nutrition influences immuno-competence, as both functions of over-weight influence immune system and under-nutrition. Studies as epidemiological stated that

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personsof“obesity” are in upper riskof infectious disease, complications of disease-associated infectious, and cancer. Regarding cancer, it has been assessed that up to 50% of cancer type’svariety, that is to say, breast, colon, endometrial, prostate,and livermay be caused by“obesity” in adults. Moreover, a growing evidence body proposes that pediatric “obesity” mayelevatecancer risk existence in adulthood”. Regardingautoimmunity and atopy, extrainterplay complex pathways in carcinogenesisobesityrelated (27). The systemic inflammation ofchronic low-grade has been documented as cytokines and carcinogenesis trigger employ a vitalfunction in suchprocess. IL-1β and IL-6 are promotingsurvival and proliferation ofcell. Furthermore, TNF-α is able toelevatedamage ofDNA and proliferation ofcell over pathway of NF-KB with anti-apoptotic upregulation proteins. Besides, IL-6 is inducing genestranscription involving in invasiveness, angiogenesis, and metastasis via activation of STAT3. Likewise, leptin is activatingpathway of STAT3, enhancing cell angiogenesis and proliferation. On the contrary, adiponectin haveactivitiesasanti-tumorigenic and anti-inflammatory via activation of AMPK (AMP-activated protein kinase) and mTORC1inhibition alongothers mediators being tumorigenic. Thus, hypertrophic as dysfunctional “AT”is secreting a higher relative number of mediators as carcinogenic over molecules as anti-tumorigenic. In contrast, “obesity” is relatedtodiminishsurveillance being immune as proposed by elevated infection risk and lower immunization response (28). “Obese persons have a reduced number of ‘NK’, dendritic, and CD8+ cells that mediate cytotoxic functions. In addition, researchers observed that ‘NK’ cells from obese humans secrete lower amounts of INF-γ”. It wasassumed that overloading offree FAis inducing a modification in metabolism of NK cell to β-oxidationof lipidfrom glycolysis, thereforedisruptingcellfunctionandhomeostasis. Suchundeviatingdeclind immune surveillance concern is invasiveness and growth oftumor (29).

“Obesity” and diabetes diseases types

T2DM is disease asmulti-layer and multi-factorial, branded by an altered glucose, proteins and fat metabolism. Hyperglycemia considered aschief commonlydefining characterof T2DMand clustersof patients are recognizablebased oninsulin resistancespecific “IR”combination and relative or absolute shortageof insulin, a mixturewhich resulting intrajectories as clinic being complex underlying imbalancesofearly metabolic development and following complications as cardiovascular (30). T2DMand the complications stayas mainmortality and morbidity causes in western world.Although it is well recognized that T1DM resulting from destruction of β cell cell-mediated autoimmune pancreatic, T2DMhas been considered historically asdisease beingmetabolic, and determinants of metabolic are identified traditionally as main pathogenetic elements. Recently, research has begun to concentrate on inflammation of low-grade (LGI) as a pervasive T2DMfeature, associatedwithdisease progression and development alongcomplications as genesis. Obesity aging and are 2basic risk factors forT2DMdeveloping both known for promotingsystemic chronic and tissue inflammation, frequentlymentioned as meta inflammation and inflammation, respectively. Many publications exhibit that inflammation is not aabsolute bystander but it hascruicialfunction in all main T2DM disease features progression such asβ cell, IR inability or failure coping with elevated insulin request, and destabilization and development of atherosclerotic plaque (31). A putative inflammatory plethora pathways and sources have been suggestedfor explaining suchproof. “Discoveries being seminal and studies majority have mostlyconcentrated on innate immune system cells and recent documents also recommend the acquireddirect immunity involvement. In specific, autoimmunity, a multi-factorial progressionwell-recognizedviaself-tolerance loss and chronic TandB cells excess reactivity, has begun to be known as T1DM and T2DMoverlapping mark. Likewise, dysregulation as metabolic and components as autoimmune are generatingcycle being vicious.The cytokinesincreased productions symbolizing the chronic state of inflammatory in T1DM concurring for destroying pancreatic β cells, and such inflammation-induced damage for tissuecausing“self” antigens release which promoting autoimmune activation. Sequentially, autoimmunity more dam ages secretion of insulin in β cells and promoting hyperglycemia (32).

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T2DM and "obesity"

Circulating auto-antibodies presence in diabetes mellitus as non-insulin-dependent was 1st recognizedover the lastforty years. "Nowadays, the presence of these autoantibodies characterizes a condition referred to as latent autoimmune diabetes of the adults LADA". In such patients, GADA, ICA, ZnT8A and IA-2A are frequently detectedas auto-antibodies.

During diagnosis, patients of LADA do not typicallyrequireinsulin as exogenous and they seem to be affected clinically via"T2D", whereas big% will require it within a few years, display a greatlyβ cell function quickerdropin comparison to patients of "T2D", probably due to ongoing destruction of immune-mediated β cell. Remarkably, studiesdisplayedthat patient of 94% with ICA and patient of 84% with GADA needed therapy of insulin by 6 years, comparing with patient of 14% with no antibodies. A slight study directly has correlated the occurrence of islet auto-antibodies with considerablyminorresponse as acute insulin if compared to group as auto-antibody-negative;whilenoticed identical peripheral 'IR', offeringevidence being compelling that the profound insulin secretion impairment is determined plausibly via the pancreatic β cells immune-mediated injury (34).

''Type 1 diabetes'' and "obesity" (T1D)

Even thoughlegallycategorized as "T1D" for the classicoccurrence of auto-antibodies, patients of LADA show numerous clinical characters which are combination between pathologies of "T1D" and "T2D"(35). Birthweight results as low being factorof risk for equal strength LADA as for "T2D"is proposingetiology of LADA including factors concerning"T2D". Moreover, LADA is related to factors well recognizedfor promoting"T2D", i.e.,physical inactivity, overweight, smoking, and intake of sweetened beverage, proposing LADA mightpartly be avoidable over the same modifications of lifestyle as "T2D" (36). In specific, the LADA risk in respect to overweight/"obesity" was considered in 2 large population-based documents from studiesofNorwegian HUNTandSwedish case-control, whereresultsbacking the hypothesis which, eventhough in the autoimmunity occurrence, factors related to IR, i.e.,extreme weight, mightstimulateLADAonset. LADA metabolomics, patients of "T1D" and "T2D"were unsuccessful to detect a profile of exclusive metabolite for any typesof diabetes. As a substitute, the metabolome diverse along a C-peptide-driven continuum from "T1D" to "T2D", with LADA being as intermediate and metabolically patients nearer to "T1D"display a quickerdevelopment to therapy of insulin than these nearer to "T2D" (37). In contrast, a study analyzing adults of4,374 as cohort with diagnosed freshly diabetes confirmed that status of GADA and C-peptide fasting, while not age at onset, can define diabetic patients groups with differences in clinically relevant in glycemic control and risk of cardio-metabolic, proposing that limits between "T1D" and LADA might be fewer discrete than supposed. Also, studies asparallel confirmed that LADA is relatedto lesser microvascular complications prevalence, mortality being lesser, and lessercardiovascular events risk in comparison to"T2D". LADA risk is increased substantially with "T1D" disease family history but also, albeit considerably less so, of "T2D" disease" (38). The 1st LADA genome-wide relationships studyexposed how the leading genetic signals were shared mainly with "T1D", even thoughaffirmative genetic genome-wide associations were also recorded with "T2D". Investigatorsrecognized a originalsignalbeing independent at the known locus"T1D"protectinggene of (PFKFB3). Suchgene expresses in code insulin signaling and glycolysis regulator and hence it wasreported formerly as a conceivable candidatebiologically in "T2D" diabetes. Also,PFKFB3 result in a decline in glucose consumptionof T cell and survival that in turn harms the immune response in auto-immune circumstancesrequiring additional studies to concludeifsuch genetic factor is actuallycharacterof distinguishing between childhood-onset and adult autoimmune diabetes (39).

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Study on diabetes diseases incidence with correlation to "obesity"

A study survey test was occurred on 60 persons (cases), who visited one of the privateSpecialized Center for Diabetes and Endocrinology, Thi-Qar Iraq, with n = (60), at several different ages, the study recorded and calculated(BMI) of every oneand the every one diabetes diseases typesincidence suffering, the study cases blood glucose levels weremeasured three times in fasting and post prandial.

Results

The study survey of 60 patients from different ages and different BMI as a refer for body weight and "obesity" relativity for blood glucose level estimation, in one of private Specialized Center for Diabetes and Endocrinology recorded that, the diabetes incidence type 1 elevates with BMI increase and somehow as wellalong age increase for kids and teens (table 1), in contrast, the incidence % of '' T2DM'' significantly increased alongBMI increase, in addition to age increase in elder patients (table 2).

Table 1: The correlation between different body mass index (BMI) and diabetes disease incidence at different ages (1-30)years

	Diabetes disease incidence %					
BMI	**18.1**	**22.3**	**25.5**	**27.3**	**29**	**31.3**
1- 5 year	1%	3%	3%	17%	33.30%	34%
10- 15 year	2%	4.20%	5%	12%	26.30%	34.70%
15-30 year	5%	11.70%	20.30%	13.80%	30.10%	37.20%

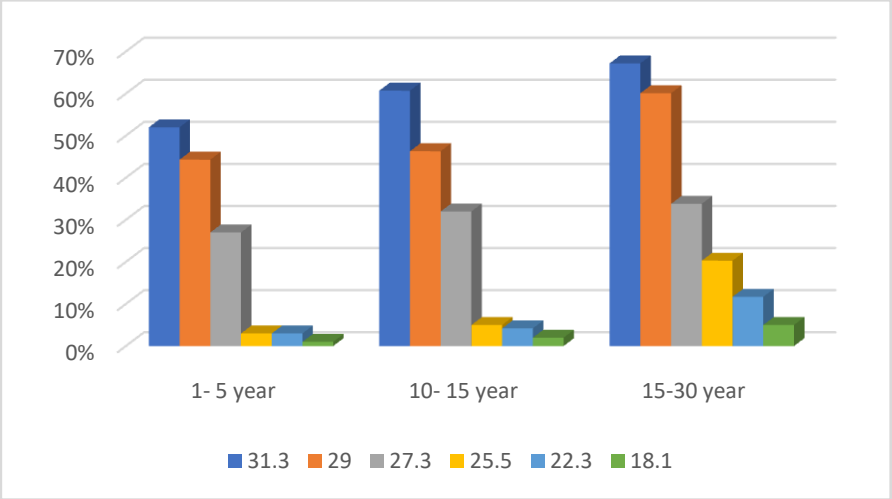

Figure 1: The correlation between different body mass index (BMI) and diabetes disease incidence at different ages (1-30)years

Table 2: The correlation between different body mass index (BMI) and diabetes disease incidence at different ages (35-55) years

	Diabetes disease incidence %					
BMI	**18.1**	**22.3**	**25.5**	**27.3**	**29**	**31.3**
35-40 years	0%	2%	3%	19.70%	27.20%	44%
45-50 years	0%	2.60%	3.40%	30.80%	39.50%	47.60%
50-55 years	1%	3.20%	3.70%	45%	53%	71%

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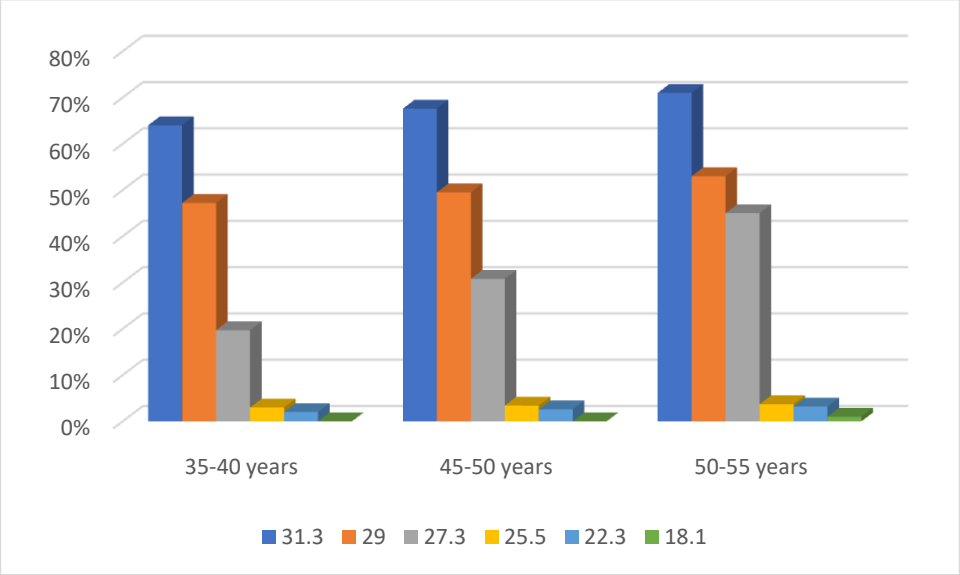

Figure 2: The correlation between different body mass index (BMI) and diabetes disease incidence at different ages (35-55) years

Discussion

In the study for recording the correlation of "obesity" and autoimmune disease (Diabetes Miletus), as an example for autoimmune diseases, '' type 1 diabetes'' is one of autoimmune diseases that isn't significantly correlated with "obesity" obviously, on the other hand '' type 2 diabetes'' had significant correlation with the "obesity" and overweight patients with old ages. As T2MDis brandedvia progressive chronic status, inflammation oflow-grade (LGI) whichjoins the whole disease trajectory, from its inception to development of complication (40, 41)."Collectingproof is revealing a long inflammatory responses "triggers", list possible several of them are encouraged via un-healthy adoptions oflifestyle and age advancing. "Patients of diabetic display an altered ICsnumber and function of both immunity innate and acquired (42). Auto-antibodies as reactive against antigens islet might be detected in a patient'ssub-population, whereasdata emerging are suggesting also altered specific T lymphocyte populations function, include T regulatory (Treg) cells". Suchremarksled to the hypothesis that mounting part of inflammatory response in "T2D" is reasoned to autoimmune phenomenon(43).

Conclusion

Prolonged inflammation that resulted from "AT" and cells in obese patients, is the main reason for many autoimmune cases and related diseases such as ''type 2 diabetes''that had significant correlation with overweight and "obesity".

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