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Adiposopathy- Altered Physiology of Visceral Adipose Tissue

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The burden of obesity and associated disorders is ever-increasing in modern lifestyle. Obesity is strongly associated with increase in all-cause mortality. Obesity results from chronic positive energy balance. Excess fat is stored in two compartments: subcutaneous and visceral. Of these, major chunk of fat 80% is deposited subcutaneously while a smaller percentage as visceral fat depot. Continued accumulation of adipose tissue leads to initially hypertrophy and later visceral accumulation. In the initial stages of development of obesity, subcutaneous adipose tissue acts like a sink, protecting the organs from excess of FFAs and triglycerides but when the stress of excess caloric intake overrides the capacity of subcutaneous fat, visceral fat depot starts expanding.[1]

It is now well-established fact that visceral adipose tissue is biologically more active than subcutaneous one expressing a wide range of adipokines both pro and anti-inflammatory. Contrary to old belief, adipose tissue is a complex, highly secretory endocrine organ capable of physiological modulation of signals that regulate appetite, energy expenditure, insulin sensitivity, endocrine and reproductive functions, bone metabolism, inflammation and immunity.[1]

Most important and well-established indicator to define obesity is Body Mass Index (BMI) which fails to diagnose visceral obesity. Amongst obese individuals there is a subgroup of metabolically normal overweight and obese, while visceral adiposity can be seen in normal weight individuals. In first case, inspite of large amount of adipose tissue deposition, the individual is not suffering from metabolic diseases like diabetes, hypertension, CAD etc. thus apparently protected while in another case despite of normal weight as per BMI, the patient suffers from metabolic derangements. What is evident from recent research is that mere deposition of fat is not sufficient in development of metabolic derangements but the abnormal functioning of adipose tissue is responsible for these consequences.[2]

Adiposopathy is a disease characterized by pathologically functioning adipose tissue that is promoted by positive caloric balance and sedentary lifestyle in genetically and environmentally susceptible patients and is manifested by adipocyte hypertrophy, visceral adiposity and/or ectopic fat deposition, which physiologically results in adverse endocrine and immune consequences leading to metabolic disease. Even racial susceptibility to CAD and Diabetes is attributed to increased expression of leptin, CRP, free fatty acids(pro-inflammatory) and reduced expression of adiponectin which is anti-inflammatory.[2]

Visceral adipose tissue that surrounds visceral organs like epicardial fat, omental fat becomes pro-inflammatory in functioning. The bulk of the immune response appears to be largely macrophage driven, primarily by pro-inflammatory M1 phenotype cells in animal models.[3] More conversion of M2(anti-inflammatory) macrophages to M1(pro-inflammatory) is reported in visceral adipose tissue. A wide array of pro-inflammatory markers released from adipose tissue, particularly visceral adipose tissue is reported (Table 1).

Table 1: List of adipokines released from visceral adipose tissue[3]

Sr No	Adipokines	Sr No	Adipokines
1	Adiponectin	16	Omentin
2	Angiopoietin-like 2 (ANGPTL-2)	17	Plasminogen activator inhibitor-1 (PAI-1)
3	Angiopoietin-like 4 (ANGPTL-4)	18	Prostaglandins
4	Angiotensinogen	19	P-selectin
5	Apelin	20	Rentionol binding protein 4 (RBP-4)
6	C-reactive protein (CRP)	21	Resistin
7	Chemokine (C-C motif) ligand-5 (CCL-5)	22	Serum amyloid A (SAA)
8	Free fatty acids (FFA)	23	Toll-like receptor-4 (TLR-4)
9	Intercellular adhesion molecule-1 (ICAM-1)	24	Tumor necrosis factor-alpha (TNF-α)
10	Interleukin-18 (IL-18)	25	Vascular cell adhesion molecule-1 (VCAM-1)
11	Interleukin-6 (IL-6)	26	Vascular endothelial growth factor-A (VEGF-A)
12	Leptin	27	Vascular endothelial growth factor- $A_{165}b$ (VEGF-$A_{165}b$)

13	Matrix metalloproteinase	28	Visfatin
14	Monocyte chemotactic protein-1 (MCP-1)	29	Wnt5a
15	Nuclear factor kappa B (NFκB)		

Finally, metabolic disruption and development of metabolic disordersis a result of altered biological signaling between adipose tissue and adjacent adipocytes, as well as impaired 'crosstalk' of adipose tissue with the nervous system, immune system, skeletal muscle, cardiovascular system, liver, gastrointestinal system, adrenal cortex and thyroid, contributing to pathogenic endocrinologic and immune responses.(3)

Thus, in future therapies aiming at mere reduction in adipose tissue may not be sufficient but focus should be on normalizing altered physiological functioning of adipose tissue.

References

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