

Methods: In STEP 1, 1961 adults aged ≥ 18 years with body mass index (BMI) ≥ 27 kg/m² with ≥ 1 weight-related comorbidity or BMI ≥ 30 kg/m², without diabetes, were randomized to s.c. semaglutide 2.4 mg once-weekly or matched placebo (2:1) for 68 weeks, plus lifestyle intervention. Participants with BMI ≤ 40 kg/m² from 9 sites were eligible for the substudy. Total fat mass, total lean body mass and regional visceral fat mass were measured using DEXA at screening and week 68; visceral fat mass was calculated in the L4 region (both males/females), android region (males), or gynoid region (females), depending on site scanner methodology. Proportions of total fat and lean body mass are shown relative to total body mass; proportion of visceral fat mass is expressed relative to region assessed.

Results: This analysis included 140 participants (semaglutide n=95; placebo n=45) (mean weight 98.4 kg, BMI 34.8 kg/m²; 76% female). Baseline body composition was similar in those receiving semaglutide and placebo (total fat mass proportion: 43.4% vs 44.6%; regional visceral fat mass proportion: 33.8% vs 36.3%; total lean body mass proportion: 53.9% vs 52.7%; respectively). Percentage change in body weight from baseline to week 68 was -15.0% with semaglutide vs -3.6% with placebo. This resulted in reductions from baseline with semaglutide in total fat mass (-19.3%) and regional visceral fat mass (-27.4%), leading to 3.5%-point and 2.0%-point reductions in the proportions of total fat mass and visceral fat mass, respectively. Total lean body mass decreased from baseline (-9.7%); however, the proportion relative to total body mass increased by 3.0%-points. An increasing improvement in lean body mass:fat mass ratio was seen with semaglutide with increasing weight loss from baseline to week 68 (continuous data). Overall, the ratio increased from baseline (1.34 [95% CI: 1.22, 1.47]) to week 68 by 0.23 [0.14, 0.32], with greater improvement in those with $\geq 15\%$ weight loss (n=44; 0.41 [0.28, 0.53]) vs $< 15\%$ weight loss (n=39; 0.03 [-0.05, 0.12]) (observed, dichotomized data; no imputation for missing data). There were no major changes in body composition with placebo from baseline to week 68.

Conclusion: In adults with overweight/obesity, semaglutide 2.4 mg was associated with reduced total fat mass and regional visceral fat mass, and an increased proportion of lean body mass. Greater weight loss was associated with greater improvement in body composition (lean body mass:fat mass ratio).

Adipose Tissue, Appetite, and Obesity INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Incidence of Insulin Resistance in Obese Adolescent of Type-2 Diabetes Mellitus Patients

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Background: Insulin resistance is a reduced response of tissue to insulin-mediated action on cells. It may be due to many reasons, including the surplus of adipose tissue, which cause a resistance of insulin. **Aims and Objectives:** To find the incidence of insulin resistance in obese adolescent of type-2 diabetes mellitus patients.

Material and Methods: The study involved 50 adolescents aged 14–20 years old. Adolescents with BMI > 26.0 Kg/m² were included in the study. Levels of fasting blood sugar, Hb A1c and serum insulin were estimated. The index of Homeostatic model assessment for insulin resistance or HOMA-IR was calculated. The cut-off value of HOMA-IR was > 3.16 for both genders.

Results: It was observed that the values of BMI and level of fasting blood sugar of first degree relatives of diabetics was significantly higher as compared to their controls. Levels of both blood HbA1c and serum insulin were increased but significant difference was observed only in case of serum insulin when compared with their controls.

Conclusion: Obesity in adolescents of first degree relatives of diabetics shows a major reason of insulin resistance. The incidence of insulin resistance in obese adolescents signals a perturbing trend for the burden of type 2 diabetes in our country.

Adipose Tissue, Appetite, and Obesity INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Insulin Resistance Moderates the Association Between BMI and Metabolic Syndrome Severity in Women 4–10 Years After Pregnancy, Independent of Gestational Diabetes Status

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Objective: Obesity and gestational diabetes mellitus (GDM) increase the risk for metabolic syndrome (MetS). Insulin resistance (IR) is associated with obesity, contributes to risk for GDM, and persists after pregnancy even when glucose tolerance returns. Further, IR may enhance the risk of MetS associated with obesity and GDM. The purpose of this study was to test the hypothesis that IR moderates the relationship between BMI and MetS severity 4–10 years after pregnancy, independent of prior GDM, such that the positive association between BMI and MetS severity is stronger among women with greater IR. **Methods:** This hypothesis was tested in a secondary analysis of data collected from women enrolled in a study of the intergenerational transmission of obesity, 4–10 years after the index pregnancy. Recruitment in the parent study was stratified to include women with normal weight without GDM (NW), overweight or obesity without GDM (OwOB), and women with GDM during the index pregnancy. Standard clinical procedures were used to measure height, weight, waist circumference and blood pressure, and a fasting blood draw was obtained with which to measure glucose, insulin, triglycerides, and HDL-cholesterol. MetS was evaluated as

a continuous outcome, reflecting severity, using the method of Gurka and DeBoer.¹ IR was calculated with the homeostatic model assessment (HOMA-IR) and modeled as a continuous variable. An OLS regression model predicting MetS as a function of HOMA-IR, BMI, and their interaction, along with key covariates was used to test whether HOMA-IR moderates the relationship between BMI and MetS severity, independent of GDM. **Results:** The association between BMI and MetS severity was significantly modified by HOMA-IR ($b=0.008$, $p<0.001$), independent of GDM status during pregnancy, such that the positive association between BMI and MetS severity was stronger among individuals with higher HOMA-IR. For example, among women with HOMA-IR values 1-standard deviation below the mean, the estimated association between BMI and MetS severity was ($b=0.0394$, $p<0.001$); however, among women with a HOMA-IR value 1-standard deviation above the mean, the association between BMI and MetS severity was ($b=0.0745$, $p<0.001$). **Conclusion:** IR after pregnancy was a significant moderator of the association between BMI and MetS severity. Future studies should explore whether interventions to improve IR can reduce MetS severity independent of BMI and prior GDM.

References: 1.Gurka MJ, Lilly CL, Oliver MN, DeBoer MD. An examination of sex and racial/ethnic differences in the metabolic syndrome among adults: a confirmatory factor analysis and a resulting continuous severity score. *Metabolism*. 2014;63(2):218–225.

Adipose Tissue, Appetite, and Obesity INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Insulin Resistance Shows Stronger Correlation With Ectopic Liver Fat Instead of Visceral Fat in Asian Indians

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Introduction: Insulin resistance (IR) is associated with abdominal obesity. Asian Indians have higher insulin resistance at lower abdominal obesity levels as compared to the western population. However, the relative association of various compartments of abdominal fat, i.e., Subcutaneous Fat (SCAT), Visceral fat (VAT), and ectopic Liver Fat, is not very clear. Our study's objective was to look for the association of abdominal fat composition in Asian Indians with IR level and gender and diabetes status. **Methodology:** Our study is an analytical cross-sectional study conducted from 2018–2020 at SMS Hospital located in northwest India. 91 subjects were studied during the study period and underwent MRI for SCAT, VAT, and Liver fat estimation. We divided subjects into tertile groups, based on HOMA-IR levels, and statistical analysis for SCAT, VAT, and Lipid fat in each tertile and as a whole group carried out. Similarly, we analysed data in male and female and

diabetic and non-diabetic groups, as tertiles and as a whole. **Results:** Of the recruited subjects 49 were diabetics (M: F=23:26) and 42 were non-diabetic (M: F=12:30). In the overall group, HOMA-IR has a weak positive association with VAT and Liver Fat and a weak negative association with SCAT ($R=0.28, 0.38$ and -0.11 , respectively). From tertile1 to tertile3, there was a consistent increase in VAT and Liver fat (119.3, 121.1, 156.6 cm² and 8.18, 10.02, 10.89% respectively), so that R value increases from -0.24 to 0.21 for VAT and -0.195 to 0.58 for Liver Fat. On the other hand, the SCAT levels were not different and correlation with IR declined from -0.299 to -0.39 . On Sex wise analysis negative correlation of SCAT with IR become substantial from tertile1 to tertile3 in both males and females but strong correlation was seen in females (-0.189 to -0.515) though amount of SCAT was not different among tertiles. Both VAT and Liver Fat increased with tertile1 to tertile3; IR was very strongly correlated with Liver Fat in both the sexes at higher tertiles (0.91 for males and 0.71 for females). In the diabetic group, liver fat was significantly associated with IR at higher tertile ($R=0.9$). The SCAT was negatively associated with IR, and a further decline in correlation coefficient with each tertile, became significant at 3rd tertile (-0.41) with a weak correlation of IR with VAT. These relations have similar SCAT and Liver fat trends but a strong correlation not seen in the non-diabetic group. **Conclusion:** Insulin resistance strongly correlated with ectopic liver fat in Asian Indians including diabetics with no gender disparity which became significant at higher tertile. As compared to ectopic liver fat, VAT has only a minor role in development of IR. SCAT has a protective role against IR in both diabetics and non-diabetics.

Adipose Tissue, Appetite, and Obesity INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Is Insulin Resistance at Baseline a Predictor of Weight Loss After Bariatric Surgery?

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Background: Obesity is a multifactorial disease that is strongly associated to other metabolic disorders, such as insulin resistance and type 2 diabetes. Bariatric surgery is nowadays considered the most effective treatment of morbid obesity. The role of insulin resistance (IR) in weight loss after bariatric surgery is highly unknown.

Aim: To evaluate the association between Insulin Resistance (IR) and percentage of excess weight loss (EWL%) one, two, three and four years after bariatric surgery in patients with morbid obesity. **Methods:** Retrospective longitudinal study in patients with morbid obesity followed in our centre between January 2010 and July 2018 were included.