

Adipocytokines and CHD scores as predicted by various criteria of metabolic syndrome in Type 2 diabetic subjects

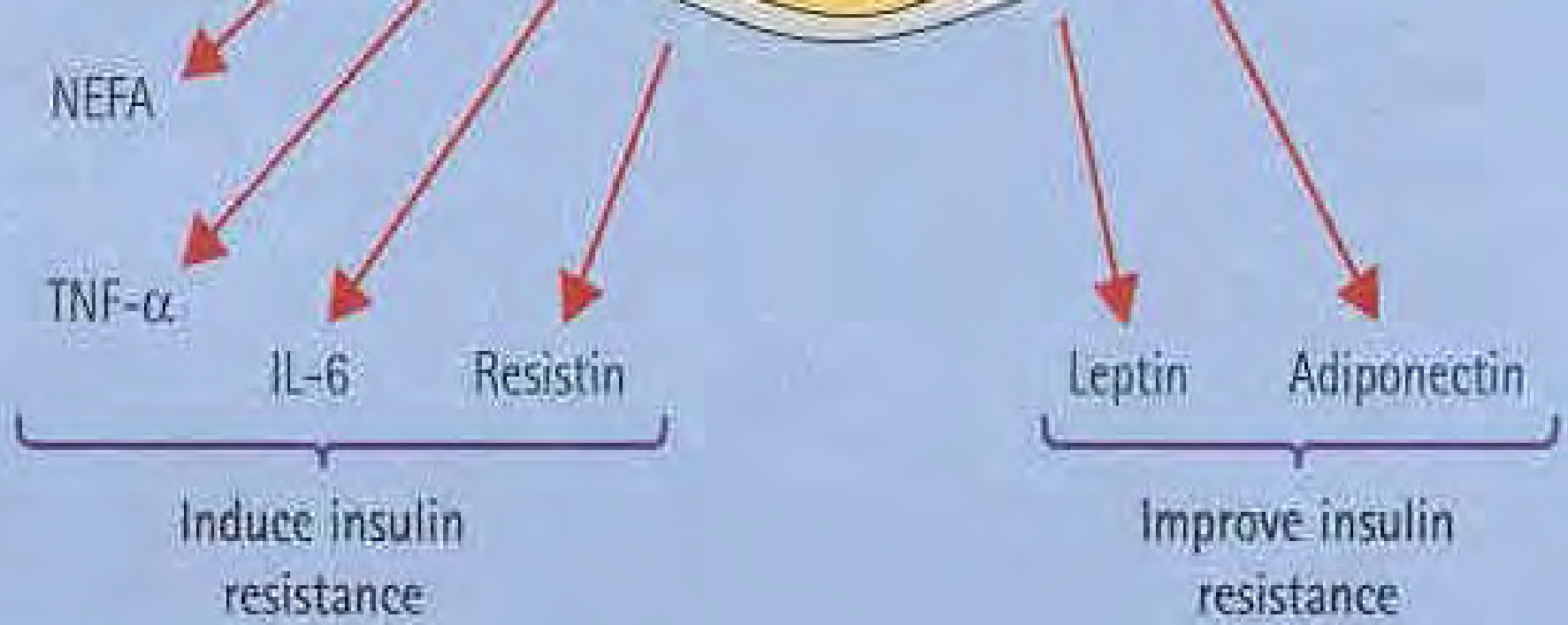
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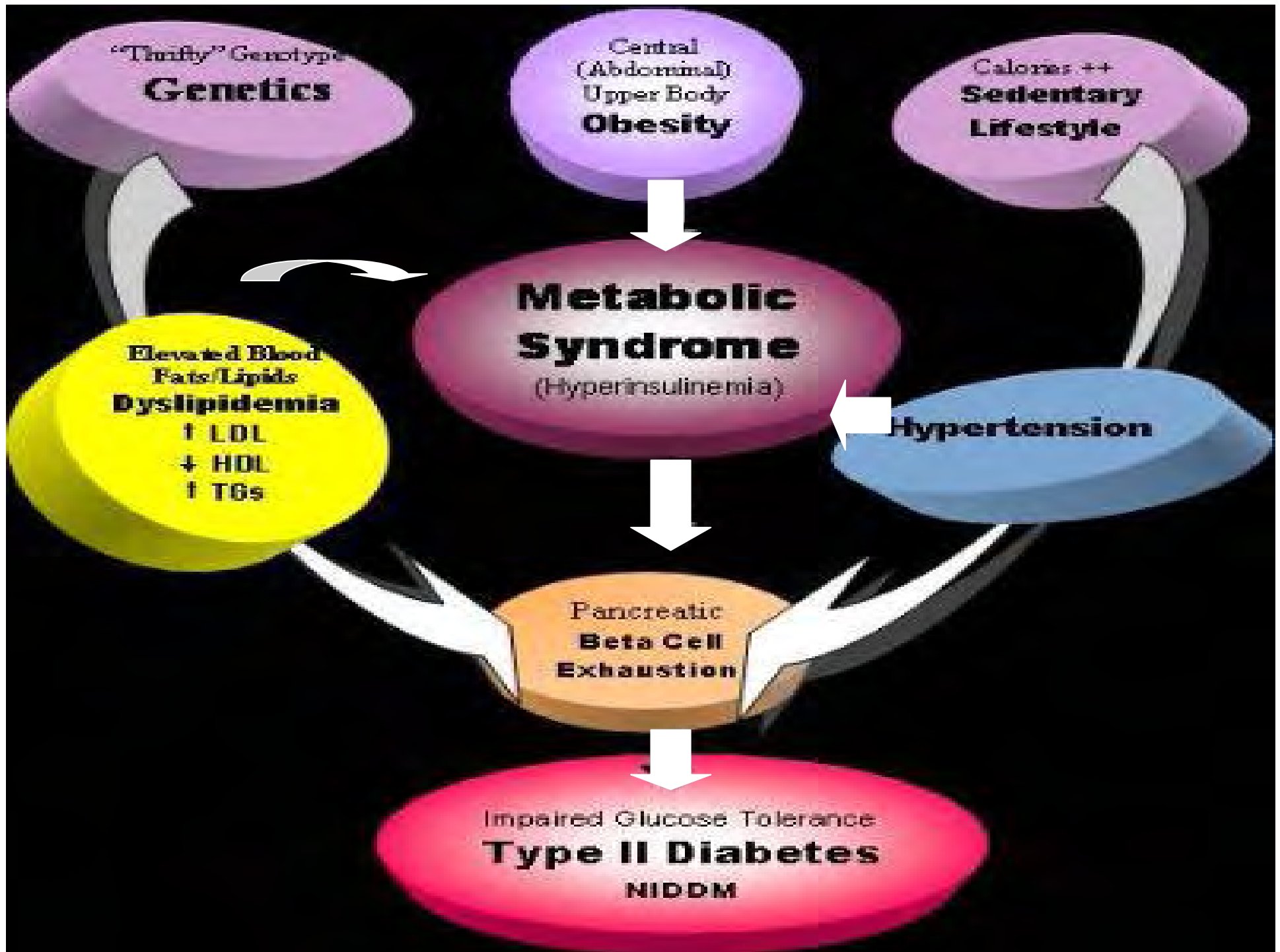
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Adipocyte

The adipocytokines' relative roles in modifying appetite, insulin resistance and atherosclerosis are the subjects of intense research as they may be modifiable causes of morbidity in people with obesity





Significance of Metabolic Syndrome

- Characterized by metabolic and hemodynamic abnormalities which increases risk of cardiovascular disease
- When clustered together, the risk is greatly increased!
- Is considered an independent risk factor for cardiovascular disease
- In diabetics, there is a strong correlation between metabolic syndrome and cardiovascular disease

Commonly used definitions from international health authorities

International Diabetes Federation
(2005)




International Diabetes Federation

National
Cholesterol
Education
Program Adult
Panel Treatment
III (2001)

World
Health
Organization
(1998)

Metabolic Syndrome

**American Heart
Association** 
Learn and Live.



| Risk factors | World Health Organization (1998) | NCEP-ATP III (2001) | IDF (2005) |
|---------------------------------------|---|--|--|
| <i>Waist Circumference/BMI</i> | BMI $\geq 30\text{kg/m}^2$ and/or waist-hip ratio ≥ 0.9 for men and ≥ 0.85 for women | ≥ 102 cm for men and ≥ 88 cm for women | ≥ 94 cm for men and ≥ 80 cm for women |
| <i>Blood Pressure</i> | $\geq 140/90$ mmHg or on medications | $\geq 130/\geq 85$ mmHg | $\geq 130/\geq 85$ mmHg |
| <i>Fasting Plasma Glucose</i> | with diabetes, impaired glucose tolerance or insulin resistance | ≥ 6.1 mmol/L or on medication for diabetes | ≥ 5.6 mmol/L or with pre-existing diabetes |
| <i>Fasting Triglycerides</i> | ≥ 1.7 mmol/L | ≥ 1.7 mmol/L | ≥ 1.7 mmol/L |
| <i>HDL-cholesterol</i> | < 0.91 mmol/L for men and < 1.01 mmol/L for women | < 1.04 mmol/L for men and < 1.3 mmol for women | < 1.04 mmol/L for men and < 1.3 mmol for women |
| <i>Urinary albumin excretion rate</i> | $\geq 20\text{ug/min}$ | none | none |
| Diagnosis | Diabetes, impaired glucose intolerance or insulin resistance plus any two or more risk factors | At least 3 risk factors | Abdominal obesity plus two other factors |

Objective

This prospective and cross-sectional study aims to identify which among the definitions of MS is strongly associated with pathological levels of *leptin, adiponectin, resistin, TNF-a, CRP* and those at risk of *developing coronary events* among type 2 diabetics of Saudi Arabia.

Methodology

- 305 (160 males; 145 females) adult type 2 diabetic Saudis were recruited
- Each participant was screened for the presence of metabolic syndrome based on the three definitions
- Leptin, adiponectin, resistin, tumor necrosis factor- α , and C-reactive protein were analyzed using enzyme-linked immunosorbent assays

Risk Assessment Tool for Estimating 10-year Risk of Developing Hard Coronary Heart Disease

- Based from the “Framingham Heart Study” to estimate 10-year risk for hard coronary heart **disease** outcomes (*Myocardial Infarction and Coronary Death*)
- Risk factors included in the Framingham calculation are:
 - Age
 - Total cholesterol
 - HDL-cholesterol
 - Systolic Blood pressure
 - Treatment for Hypertension
 - History of Smoking



Results

Clinical and metabolic characteristics of male and female diabetic subjects

| Parameter | Males | Females | P-value |
|--------------------------|-------------------|-------------------|---------|
| N (%) | 160 | 145 | |
| Age (years) | 54.8 ± 10.28 | 49.46 ± 8.87 | 0.0001 |
| BMI (kg/m ²) | 28.75 ± 33.20 | 33.20 ± 5.73 | 0.0001 |
| Waist-hip ratio | 1.38 ± 0.36 | 1.08 ± 0.31 | 0.0001 |
| Systolic BP (mmHg) | 115.46 ± 23.16 | 128.27 ± 22.70 | 0.0001 |
| Diastolic BP (mmHg) | 93.96 ± 13.02 | 83.64 ± 14.46 | 0.0001 |
| Glucose (mmol/L) | 8.62 ± 1.13 | 9.89 ± 3.78 | 0.007 |
| Insulin (ng/ml) | 20.33 ± 16.41 | 23.13 ± 28.34 | 0.30 |
| HDL-C (mmol/L) | 1.07 ± 0.69 | 1.40 ± 1.14 | 0.008 |
| LDL-C (mmol/L) | 2.85 ± 0.86 | 2.94 ± 0.86 | 0.43 |
| Triglycerides (mmol/L) | 2.09 ± 1.39 | 2.06 ± 2.15 | 0.90 |
| Total Chol (mmol/L) | 4.84 ± 0.98 | 5.08 ± 1.13 | 0.09 |
| Leptin ng/ml # | 10.12 (0.84-58.1) | 28.85 (4.0-122.0) | 0.0001 |
| Adiponectin ?g/ml # | 11.96 (1.5-110.1) | 11.21 (2.1-41.7) | 0.49 |
| Resistin ng/ml # | 14.46 (5.4-103.9) | 15.65 (5.5-57.0) | 0.23 |
| CRP ?g/ml # | 2.97 (0.04-39.0) | 5.77 (0.07-41.6) | 0.0001 |
| TNF-@ pg/ml | 4.71 ± 2.54 | 4.47 ± 1.96 | 0.53 |

*Data presented as mean (SD) and mean (range) for parameters not normally distributed; significant at p value < 0.05.

Over-all frequency of patients identified to have metabolic syndrome by various definitions with associated etabolic abnormality (% cases)

| N=305 | IDF | NCEP-ATPIII | WHO |
|-------------------------------|------------|--------------------|------------|
| Metabolic syndrome (MS) | 190 (62.3) | 177 (58.0) | 177 (58.0) |
| Hyperleptinemia | 111 (58.4) | 105 (59.3) | 101 (57.1) |
| Hypoadiponectinemia | 36 (18.9) | 33 (18.6) | 32 (18.1) |
| Hyperresistenemia | 15 (7.9) | 15 (8.5) | 13 (7.3) |
| Elevated CRP | 79 (41.6) | 75 (42.4) | 70 (39.5) |
| Cardiovascular risk score >30 | 13 (5.5) | 11 (5.0) | 13 (6.3) |

Odds-ratio (*confidence interval 95%*) of selected adipocytokines, CRP and cardiovascular risk score to various definitions of metabolic syndrome

| Parameter | Males | Females |
|--|------------------|-------------------|
| Hyperleptinemia (> 7 ng/ml in males; > 20 ng/ml in females) | | |
| IDF | 0.78 (0.15-4.13) | 2.09 (0.14-30.71) |
| NCEP-ATPIII | 1.97 (0.51-7.57) | 1.59 (0.11-24.04) |
| WHO | 1.73 (0.49-6.11) | 0.24 (0.04-1.28) |
| Hypoadiponectinemia (< 6 µg/ml) | | |
| IDF | 0.76 (0.07-8.70) | 6.00 (0.47-76.17) |
| NCEP-ATPIII | 2.49 (0.3-21.76) | 0.10 (0.007-1.44) |
| WHO | 0.52 (0.10-2.66) | 1.08 (0.20-5.74) |
| Hyperresistinemia (>22ng/ml) | | |
| IDF | 0.79 (0.22-2.83) | 0.47 (0.18-1.23) |
| NCEP-ATPIII | 1.07 (0.30-3.82) | 0.53 (0.20-1.37) |
| WHO | 1.28 (0.32-5.04) | 0.34(0.12-0.95) |
| C-Reactive Protein (>3 µg/ml) | | |
| IDF | 0.46 (0.06-3.46) | 3.07 (0.21-45.10) |
| NCEP-ATPIII | 1.40 (0.28-7.15) | 1.59 (0.11-24.04) |
| WHO | 2.04 (0.46-9.04) | 0.24 (0.44-1.28) |

Multinomial logistic analysis of CVD risk score versus various definitions

| CVD Risk Score | ? | Odds-Ratio | Confidence Interval | P-Value |
|---------------------------|-------------|-------------|---------------------|-------------|
| > 10 risk score | | | | |
| IDF | 0.65 | 1.92 | 0.55-6.69 | 0.31 |
| NCEP-ATPIII | -0.31 | 0.73 | 0.24-2.22 | 0.58 |
| WHO | 1.82 | 6.15 | 2.64-14.62 | 0.00 |
| >20 risk score | | | | |
| IDF | 0.30 | 1.35 | 0.21-8.81 | 0.75 |
| NCEP-ATPIII | -0.42 | 0.66 | 0.17-2.26 | 0.54 |
| WHO | 2.06 | 7.88 | 1.75-34.93 | 0.01 |
| >30 risk score | | | | |
| IDF | 1.16 | 3.19 | 0.18-56.45 | 0.43 |
| NCEP-ATPIII | -1.43 | 0.24 | 0.05-1.27 | 0.10 |
| WHO | 2.21 | 9.10 | 0.64-129.12 | 0.10 |

What makes the WHO-defined MS the best predictor for greater CVD risk?

- The components of WHO-defined MS are independent risk-factors of CVD already:
 - BP - $\geq 140/90$ mmHg or on medications
 - FPG - with diabetes, impaired glucose tolerance or insulin resistance
 - presence of microalbuminuria



Conclusion

- *Gender differences* exist in assessing risk of various adipocytokine abnormalities in relation to the various criteria.
- This study supports the use of **WHO** definition among Arabs since it gives the highest probability of detecting patients at risk for hard CVD outcomes.

THANK YOU