Diabetes and the Metabolic Syndrome in the Asian Population

Alka Kanaya, MD
Associate Professor of Medicine, UCSF
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Roadmap

1. Diabetes in Asian Americans
   - Prevalence in the U.S.
   - Risk factors
     - Metabolic syndrome
   - Consequences of diabetes
2. Asian research: MASALA study
   - Follow-up statistics

Asian subgroups in U.S. (% of total Asian population)

Prevalence of Metabolic Disorders and CHD in Asians

Barnes, 2008
Diabetes prevalence

- many small studies of AAPI in select US regions
- very little systematically collected data on DM
- comparisons of disease prevalence and risk factor associations problematic
- Existing data suggest that Filipino, Asian Indians, and NHOPS have high DM prevalence
- sampling strategies should be powered to disaggregate the AAPI data into specific ethnic subgroups

Pathogenesis & Risk Factors

- Complex disorder:
  - Insulin resistance
  - B-cell dysfunction
- GWAS studies: (mostly European)
  - Mostly found genes for β-cell or insulin secretory defects
  - Few genetic clues for insulin resistance
  - No GWAS in Asian populations

Risk Factors for DM

- Overweight
- Metabolic syndrome
- Behavioral
  - Diet
  - Exercise
  - Smoking
- Sociocultural factors
  - “Acculturation”
  - English language proficiency
### Overweight

<table>
<thead>
<tr>
<th></th>
<th>WHO</th>
<th>Asia-Pacific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal wt.</td>
<td>18.5 - 24.9</td>
<td>18.5 - 22.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0 - 29.9</td>
<td>23.0 - 24.9</td>
</tr>
<tr>
<td>Obese</td>
<td>≥30.0</td>
<td>≥25.0</td>
</tr>
</tbody>
</table>

WHO, 2004

### The ‘Metabolic Syndrome’

Also known as:
- Syndrome X
- Insulin Resistance Syndrome
- The Deadly Quartet
- The Dysmetabolic syndrome

### Five Definitions

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HDL</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>TG</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>BP</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Waist</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Other: Insulin</td>
<td>Insulin</td>
<td>Several</td>
<td>Insulin</td>
<td>Ualb</td>
<td></td>
</tr>
</tbody>
</table>

### NCEP criteria

- Fulfill ≥ 3 criteria:
  - Waist: >102 (or 94) cm ♂, >88 cm ♀
  - HDL: <40 men, <50 women (or meds)
  - Triglycerides: ≥ 150 mg/dL (or meds)
  - BP: ≥130/≥85 (or med use)
  - Fasting glucose: ≥100 mg/dL (or meds)

NCEP, Circ, 2005
**IDF criteria**

- Must have central obesity:
  - Waist: >94 cm ♂, >80 cm ♀ (lower for Asians)
- And fulfill ≥ 2 criteria:
  - HDL: <40 ♂ or <50 ♀ (or med use)
  - Triglycerides: ≥ 150 mg/dL (or med use)
  - BP: ≥130/≥85 (or med use)
  - Fasting glucose: ≥100 mg/dL (or diabetes)

Alberti, 2005

**Coexistence of Obesity, Diabetes, and MS**

**Visceral Adiposity**

**Fat Depots:**
- Subcutaneous: 60-70%
- Intra-abdominal: 15-25%
  - Visceral (or intraperitoneal)
  - Retroperitoneal (5%)
- Intramuscular: 5-10%
- Linked with diabetes and atherosclerosis since 1940’s

Després, Quebec
Visceral Fat distribution

Subcutaneous depot can only store a set amount
Excess fat is deposited in visceral depot and inside organs (liver, muscle, pancreas, heart, endothelium)
Recruitment of lipids in non-adipocytes to store fat cause lipotoxicity & lipoapoptosis

Adipose Tissue “Overflow” Hypothesis

Ethnic differences in fat dist.

- Asians and Latinos are more prone to visceral obesity
- A.A. and Whites develop less visceral obesity
  - A.A. have more subcutaneous fat stores than Whites

Why is visceral fat so bad?

Kopelman, 2000
What it secretes...

- Lipoproteins
  - LPL
  - CETP
  - Apo E
  - PLTP
- Complement Factors
  - Adipsin
  - C3
- Growth Factors
  - TGF-β
  - IGF-1
  - VEGF
- Peptides
  - Adiponectin
  - PAI-1
  - Angiotensinogen
  - Agouti
  - Resistin
  - Visfatin
- Cytokines
  - TNFα
  - IL-6

Adipose Tissue

Proposed Mechanism

- Vascular Inflammation
  - IL-6 & TNF-α
- Dyslipidemia
  - FFA
- Reduced Thrombolysis
  - PAI-1
- Hypertension
- Insulin Resistance
- Visceral Adipose tissue
- CVD

Behavioral Risk Factors

- Diet:
  - Western diet associated with ↑ risk
  - Lower risk with Med diet, high fiber
  - Little data on Asian dietary patterns
  - Japanese American data
  - SHAPE study findings

Sociocultural factors

Rosenson, 2005
Limited English proficiency (LEP)

- LEP in California AAPI:
  - 38.0% Asian Americans
  - 13.6% NHOPI
- Little data about Asian LEP and DM prevention and management
- Kaiser study: diabetic Asians with LEP less likely to monitor glucose

Consequences of DM

- Ethnic minority groups (African Americans and Latinos) have higher risk ESRD but lower CVD risk compared to Whites
- "Asians" have been aggregated to show similar findings

Disaggregating Asian subgroups

- We analyzed Kaiser data (DISTANCE)
- 10 year follow-up (1996-2006)
- N=64,211 with diabetes
- Complications: (incidence of...)
  - MI
  - CHF
  - Stroke
  - ESRD
  - Lower extremity amputations (LEA)
  - Retinopathy

Summarizing Outcomes

- Considerable heterogeneity among AAPI subgroups for all outcomes
- Most with lower risk of MI, CHF, CVA than Whites---but not Pacific Islanders and South Asians
- Most with higher risk of ESRD than Whites—but not South Asians
- Most with lower risk of LEA than Whites, Blacks, and Latinos—but not Pacific Islanders
- Need to disaggregate “Asian” data: may shed light into to etiologic differences in disease
Roadmap

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2. Asian research: MASALA study
   - Follow-up statistics

Metabolic syndrome and Atherosclerosis in South Asians Living in America (The MASALA study)

Design

- **MASALA**
  - Population-based
  - Ages 45-84 yrs
  - N = 150
  - One site
  - Prospective cohort
  - Started in 2006

- **MESA**
  - Population-based
  - Ages 45-84 yrs
  - N = 6,500
  - 6 sites (Columbia, Hopkins, NWU, Minnesota, UCLA, Wake Forest)
  - Prospective cohort
  - Started in 2000

Anthropometry

<table>
<thead>
<tr>
<th></th>
<th>Age-adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Indian</td>
</tr>
<tr>
<td>n=150</td>
<td>n=769</td>
</tr>
<tr>
<td>BMI Kg/m²</td>
<td>26±5</td>
</tr>
<tr>
<td>Waist, cm</td>
<td>96±12</td>
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</tbody>
</table>

* p<0.001 in comparison to Indians
### Anthropometry vs. DEXA

<table>
<thead>
<tr>
<th></th>
<th>Overall (n=150)</th>
<th>Men (n=75)</th>
<th>Women (n=75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, kg/m²</td>
<td>26 ± 5</td>
<td>26 ± 4</td>
<td>26 ± 5</td>
</tr>
<tr>
<td>Waist circ., cm</td>
<td>96 ± 12</td>
<td>98 ± 10</td>
<td>94 ± 14</td>
</tr>
<tr>
<td>Total fat mass, kg</td>
<td>24.6 ± 8.1</td>
<td>22.7 ± 7.5</td>
<td>26.4 ± 8.3</td>
</tr>
<tr>
<td>Total fat, %</td>
<td>35.1 ± 8.0</td>
<td>29.5 ± 6.0</td>
<td>40.6 ± 5.5</td>
</tr>
</tbody>
</table>

### Glucose Tolerance

- **Normal**: 34%
- **PreDM**: 37%
- **T2DM**: 29%

### Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Indians (n=150)</th>
<th>White (n=2507)</th>
<th>Black (n=1821)</th>
<th>Latino (n=1429)</th>
<th>Chin. (n=769)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM*</td>
<td>26</td>
<td>7**</td>
<td>19</td>
<td>19</td>
<td>14**</td>
</tr>
<tr>
<td>Pre-DM</td>
<td>25</td>
<td>25</td>
<td>28</td>
<td>30</td>
<td>33</td>
</tr>
<tr>
<td>Normal</td>
<td>48</td>
<td>68</td>
<td>53</td>
<td>51</td>
<td>53</td>
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</tbody>
</table>

*Defined by hypoglycemic med use or FPG ≥126 mg/dl
Pre-DM: fasting glucose 100-125 mg/dl
** p<0.05 compared to Indians

Kanaya, 2009
Higher Diabetes Prevalence

After adjusting for age, sex, education, income, smoking, alcohol, exercise, BMI, waist circ., HTN, HDL, and triglycerides

<table>
<thead>
<tr>
<th></th>
<th>Indians</th>
<th>White</th>
<th>Black</th>
<th>Latino</th>
<th>Chin.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=150</td>
<td>n=2507</td>
<td>n=1821</td>
<td>n=1429</td>
<td>n=769</td>
</tr>
<tr>
<td>25</td>
<td>5**</td>
<td>14*</td>
<td>12**</td>
<td>16*</td>
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</tbody>
</table>

*p<0.05; **p<0.001 in comparison to Indians

Predictors of DM & Pre-DM

Adjusted for sex and age

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>3.31 (1.49-7.33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>4.72 (1.42-14.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>Liver/Spleen atten., HU</td>
<td>0.50 (0.31-0.81)</td>
<td>0.005</td>
</tr>
<tr>
<td>Internal CIMT, per SD</td>
<td>1.92 (1.26-2.94)</td>
<td>0.002</td>
</tr>
<tr>
<td>ALT, per SD</td>
<td>1.81 (1.08-3.06)</td>
<td>0.03</td>
</tr>
<tr>
<td>Traditional beliefs</td>
<td>2.32 (1.03-5.22)</td>
<td>0.03</td>
</tr>
<tr>
<td>Visceral fat area, per SD</td>
<td>1.57 (0.99-2.48)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Diet association with DM

<table>
<thead>
<tr>
<th></th>
<th>Diabetes</th>
<th>No Diabetes</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteins, g/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute</td>
<td>75</td>
<td>68</td>
<td>0.09</td>
</tr>
<tr>
<td>Percent</td>
<td>15.2</td>
<td>14.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Energy-adjusted</td>
<td>74</td>
<td>69</td>
<td>0.07</td>
</tr>
<tr>
<td>Animal</td>
<td>32</td>
<td>29</td>
<td>0.29</td>
</tr>
<tr>
<td>Fish</td>
<td>4</td>
<td>2</td>
<td>0.39</td>
</tr>
<tr>
<td>Vegetable</td>
<td>26</td>
<td>37</td>
<td>0.34</td>
</tr>
<tr>
<td>Carbohydrates, g/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute</td>
<td>276</td>
<td>282</td>
<td>0.75</td>
</tr>
<tr>
<td>Percent</td>
<td>80.6</td>
<td>82.7</td>
<td>0.08</td>
</tr>
<tr>
<td>Energy-adjusted</td>
<td>272</td>
<td>282</td>
<td>0.37</td>
</tr>
<tr>
<td>Fat, g/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute</td>
<td>90</td>
<td>90</td>
<td>0.79</td>
</tr>
<tr>
<td>Percent</td>
<td>28.2</td>
<td>27.9</td>
<td>0.10</td>
</tr>
<tr>
<td>Energy-adjusted</td>
<td>90</td>
<td>90</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Metabolic syndrome

Age adjusted

<table>
<thead>
<tr>
<th></th>
<th>Indians</th>
<th>Chin.</th>
<th>White</th>
<th>Black</th>
<th>Latino</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=150</td>
<td>n=801</td>
<td>n=2608</td>
<td>n=1869</td>
<td>n=1490</td>
</tr>
<tr>
<td></td>
<td>41</td>
<td>26**</td>
<td>30*</td>
<td>36</td>
<td>43</td>
</tr>
</tbody>
</table>

*p<0.05 and **p<0.001 compared to Indians
Second MASALA exam

- 2009-2010
- N=132 (88% follow-up)
- Repeat glucose tolerance test, repeat physical exam, lab tests
- Focus on measures of endothelial function

Planned MASALA expansion

- Funded to increase cohort to n=900 at two sites (UCSF + NWU)
- Timing and measures similar to MESA exam 5
- Data collection to start in 2010...
- Prospective study for CHD events