Diabetes in Asians: Differences in Pathophysiology and Complications

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Outline

- Cases
- The Asian Population
- Epidemiology of Diabetes in Asians
- Pathophysiology of Diabetes in Asians
- Complications of Diabetes in Asians
- Implications for Asians
Let’s start with two cases...

Case 1

- 69 year old Korean female with PMH significant for pre-diabetes presents for pre-diabetes and subclinical hypothyroidism
- Diagnosed with mild diabetes in 2012 – HbA1c 6.5
- Tried metformin which she felt did not work
- Tried glipizide but experienced hypoglycemia

**Presented with HbA1c of 6.1**

- Patient denies diagnosis of gestational diabetes
- Mother with history of diabetes

On exam: BP 106/60, HR 72, Weight 46.8 kg (103 lbs), Height 5’ 2”, **BMI 18.87**
Case 2

- 55 year old **Caucasian** female with PMH significant for hypothyroidism, obesity and depression presents for follow-up of hypothyroidism.

- On exam: BP 119/80, HR 76, Weight 148.7 kg (327 lbs), Height 5’ 11”, **BMI 45.74**

- On labs: **HbA1c 5.5 - Normal**

So how does one explain this discrepancy - thin Asian woman with pre-diabetes and Caucasian woman with morbid obesity with no pre-diabetes / diabetes?
The Asian Population

- **Definition of Asian - person with origins from:**
  - The Far East
  - Southeast Asia
  - The Indian subcontinent

- **In 2012:**
  - Asians – fastest growing racial/ethnic group in the United States
  - Chinese population is the largest followed by Filipinos and Asian Indians
  - Three-fourth of Asian Americans live in 10 states, including California

At-a-Glance: North America and the Caribbean

<table>
<thead>
<tr>
<th>At a glance</th>
<th>2015</th>
<th>2040</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult population (20-79 years)</td>
<td>344 million</td>
<td>413 million</td>
</tr>
<tr>
<td>Diabetes (20-79 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional prevalence</td>
<td>12.9% [10.8-14.5%]</td>
<td>14.7% [11.8-16.7%]</td>
</tr>
<tr>
<td>Age-adjusted comparative prevalence</td>
<td>11.5% [9.5-13.0%]</td>
<td>12.0% [9.5-13.7%]</td>
</tr>
<tr>
<td>Number of people with diabetes</td>
<td>44.3 million</td>
<td>60.5 million</td>
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<tr>
<td></td>
<td>(37.1-49.9 million)</td>
<td>(48.7-69.2 million)</td>
</tr>
<tr>
<td>Number of deaths due to diabetes</td>
<td>324,000</td>
<td>-</td>
</tr>
<tr>
<td>Health expenditure due to diabetes (20-79 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total health expenditure, R=2*, USD</td>
<td>348 billion</td>
<td>390 billion</td>
</tr>
<tr>
<td>Impaired glucose tolerance (20-79 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional prevalence</td>
<td>15.0% [12.8-17.4%]</td>
<td>16.3% [13.9-18.9%]</td>
</tr>
<tr>
<td>Age-adjusted comparative prevalence</td>
<td>13.9% [11.9-16.1%]</td>
<td>13.9% [12.0-16.1%]</td>
</tr>
<tr>
<td>Number of people with impaired glucose tolerance</td>
<td>51.8 million</td>
<td>67.4 million</td>
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<tr>
<td></td>
<td>(44.2-59.7 million)</td>
<td>(57.3-77.9 million)</td>
</tr>
</tbody>
</table>

International Diabetes Federation Atlas. 2015.
## At-a-Glance: Southeast Asia

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2040</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adult population [20-79 years]</strong></td>
<td>926 million</td>
<td>1.31 billion</td>
</tr>
<tr>
<td><strong>Diabetes [20-79 years]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional prevalence</td>
<td>8.5% [6.8-10.8%]</td>
<td>10.7% [8.5-13.7%]</td>
</tr>
<tr>
<td>Age-adjusted comparative prevalence</td>
<td>9.1% [7.3-11.6%]</td>
<td>9.9% [7.9-12.8%]</td>
</tr>
<tr>
<td><strong>Number of people with diabetes</strong></td>
<td>78 million [63-100 million]</td>
<td>140 million [112-180 million]</td>
</tr>
<tr>
<td><strong>Number of deaths due to diabetes</strong></td>
<td>1.2 million</td>
<td>-</td>
</tr>
<tr>
<td><strong>Health expenditure due to diabetes [20-79 years]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total health expenditure, R=2*, USD</td>
<td>7.3 billion</td>
<td>12.9 billion</td>
</tr>
<tr>
<td><strong>Impaired glucose tolerance [20-79 years]</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regional prevalence</td>
<td>4.6% [2.2-6.5%]</td>
<td>5.6% [2.7-7.4%]</td>
</tr>
<tr>
<td>Age-adjusted comparative prevalence</td>
<td>4.7% [2.4-6.7%]</td>
<td>5.4% [2.5-7.2%]</td>
</tr>
<tr>
<td><strong>Number of people with impaired glucose tolerance</strong></td>
<td>42.2 million [20.7-60.2 million]</td>
<td>73.9 million [35.0-96.9 million]</td>
</tr>
</tbody>
</table>

International Diabetes Federation Atlas. 2015.
Number of Adults with Diabetes

### Top ten countries/territories for number of adults with diabetes

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>109.6 million</td>
</tr>
<tr>
<td>India</td>
<td>69.2 million</td>
</tr>
<tr>
<td>United States of America</td>
<td>29.3 million</td>
</tr>
<tr>
<td>Brazil</td>
<td>14.3 million</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>12.1 million</td>
</tr>
<tr>
<td>Mexico</td>
<td>11.5 million</td>
</tr>
<tr>
<td>Indonesia</td>
<td>10.0 million</td>
</tr>
<tr>
<td>Egypt</td>
<td>7.8 million</td>
</tr>
<tr>
<td>Japan</td>
<td>7.2 million</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>7.1 million</td>
</tr>
</tbody>
</table>

- Asia accounts for 60% of the world’s diabetic population

International Diabetes Federation Atlas. 2015.
Diabetes in China

Escalating Diabetes Epidemic in China

Pan et al. Diabetes Care 1994; Gu et al. Diabetologia 2003; Yang et al. NEJM 2010

Crude and adjusted percent of U.S. adults reporting diabetes, Asian populations and whites, 2013-2014 BRFSS

Geiss, ADA 2016
Multivariate adjusted % of U.S. adults reporting diabetes, by BMI, Asian populations and whites, 2013-2014 BRFSS

- Asian Indian
- Chinese
- Filipino
- Japanese
- White

Geiss, ADA 2016
Diabetes Prevalence in California

Figure 1.
Age-adjusted prevalence (in percent) of DM among adults ≥ 18 years old in California, CHIS (California Health Interview Survey) 2009 by ethnicity and gender, p < 0.001 across all ethnic groups among males and females. * p<.05, **p<.01 differences between genders

Why is there such a high prevalence and incidence of diabetes in the Asian population?
Pathophysiology of Diabetes in Asians

- Increased body weight is a risk factor for type 2 diabetes
- Body mass index (BMI) is used in the clinical setting to define overweight and obesity
- Using traditional BMI cutoffs, only 10.8% of Asian Americans meet criteria for obesity vs. 34.9% of all US adults

How can this be explained?

Understanding the Role of Obesity

- Distribution of body fat and differences in body composition play a central role in diabetes risk and development
  - Visceral adipose tissue
  - Ectopic fat – including hepatic fat and pericardial fat
- Asians have a tendency to be “metabolically obese”

Hu F. Diabetes Care, 2011. 34: 1249-1257.
Understanding the Role of Obesity

Significant differences are seen even amongst Asians

Two ongoing studies of community based cohorts:

- **MASALA** – Mediators of Atherosclerosis in South Asians Living in America
- **MESA** – Multi-Ethnic Study of Atherosclerosis (Caucasian, Chinese Americans, Latinos, African Americans)


MASALA vs MESA

- South Asians – higher age-adjusted prevalence of diabetes – 23%
  - Whites – 6%
  - African Americans – 18%
  - Latinos – 17%
  - Chinese Americans – 13%

Adjusted HOMA-IR and HOMA-β in US South Asians compared to other US race/ethnic groups (MASALA and MESA studies)

MASALA vs MESA

MASALA vs MESA

The Effects of Visceral and Ectopic Fat

- Increased insulin resistance
- Increased risk of metabolic syndrome
- Higher levels of inflammatory markers and adipokines (hormones secreted from adipose tissue)
- Higher cardiovascular risk

What about other risk factors?

- The role of urbanization and immigration - Diet
  - Overnutrition
  - Increased intake of animal based foods, energy dense foods, and fast foods
  - Decreased intake of fiber
  - Traditional diets with high glycemic load and foods with high glycemic index

What about other risk factors?

The role of urbanization and immigration – Physical Activity

- Decreased physical activity with increased industrialization and shifting away from agricultural labor

Inherent Risk Factors

- Gene-environment interactions
  - Multiple genetic variants (risk alleles) associated with diabetes
  - Each risk allele increases type 2 diabetes risk by 10-20%
  - Genetic risk factors are amplified by the Westernized diet

Inherent Risk Factors

- **Thrifty genotype hypothesis**
  - Able to store energy during times of food abundance

- **Thrifty phenotype hypothesis**
  - Fetal adaptations to poor intrauterine nutrition in preparation for a life of starvation

Complications from Diabetes

- **Macrovascular disease:**

  - Cardiovascular disease (CVD) / coronary artery disease (CAD) / cerebrovascular disease (CBVD):
    - Decreased risk of CVD in Asians in the US and UK
    - Equal risk of coronary artery disease in Asians in the UK

  - Findings in South Asians
    - CAD and myocardial infarction
    - Cerebrovascular disease
    - Mortality

### Table 1.
Ethnic Group Comparisons: Adjusted HRs of CAD

<table>
<thead>
<tr>
<th>Group (Number With CAD)</th>
<th>HR</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted* HR of various ethnic groups vs. white</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (4,478)</td>
<td>1.0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>African American (2,055)</td>
<td>0.8</td>
<td>0.8–0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hispanic (282)</td>
<td>0.9</td>
<td>0.8–1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>All Asian</td>
<td>1.0</td>
<td>0.9–1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Chinese (262)</td>
<td>0.8</td>
<td>0.7–0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Japanese (95)</td>
<td>0.9</td>
<td>0.7–1.1</td>
<td>0.18</td>
</tr>
<tr>
<td>Filipino (263)</td>
<td>1.2</td>
<td>1.0–1.3</td>
<td>0.02</td>
</tr>
<tr>
<td>Other Asian (24)</td>
<td>0.8</td>
<td>0.5–1.1</td>
<td>0.17</td>
</tr>
<tr>
<td>South Asian† (56)</td>
<td>2.4</td>
<td>1.9–3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Additional models for South Asian people vs. white as referent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age- and sex-adjusted model</td>
<td>2.3</td>
<td>1.7–2.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Added covariates‡</td>
<td>2.3</td>
<td>1.8–3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted* HR of CAD in South Asian people vs. ethnicities other than white as referent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>2.9</td>
<td>2.2–3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.8</td>
<td>2.1–3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Chinese</td>
<td>3.3</td>
<td>1.4–3.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Japanese</td>
<td>3.2</td>
<td>2.3–4.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Filipino</td>
<td>2.3</td>
<td>1.7–3.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other Asian</td>
<td>2.8</td>
<td>2.1–5.6</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; HR = hazard ratio.

Complications from Diabetes

- **Macrovascular disease:**
  - Peripheral artery disease (PAD) / lower extremity amputations (LEA):
    - Decreased risk of LEA in Asians in the US and UK
    - Findings in South Asians

Complications of Diabetes

Microvascular disease

Nephropathy
- In the US and UK, Asians are at higher risk of end-stage renal disease (ESRD)
- South Asians have a higher prevalence of albuminuria and chronic kidney disease (CKD) compared to Whites and Europeans

Neuropathy
- Limited data in Asians
- South Asians have a lower risk of neuropathy compared to Caucasians

Complications of Diabetes

Microvascular disease

Retinopathy

- In the UK, Asians have a lower risk of retinopathy
- Findings of the AdRem (ADVANCE Retinal measurements) study
- South Asians have a higher prevalence of retinopathy compared to Caucasians

Screening Asians for Diabetes

- Diabetes risk is shifted to a lower BMI in Asians due to several risk factors/predisposing factors.
- Asians have a higher risk of complications from diabetes.

Should traditional BMI cutoffs be used to determine which Asian Americans should be screened for diabetes?

Redefining the BMI Cutpoint

Figure 1—Percent distribution of Asian Americans with newly diagnosed type 2 diabetes by BMI.

Redefining the BMI Cutpoint

Based on this data, researchers investigated what would be a more appropriate BMI cutpoint for diabetes screening in Asians.

Using results of hemoglobin A1c and 2-hour oral glucose tolerance test, researchers determined that sensitivity of the screening test is high (84.7%) when using a BMI cutpoint $\geq 23 \text{ kg/m}^2$ for diabetes screening.

ADA Statement

December 2014

ADA lowered BMI cutpoint at which it recommends screening for type 2 diabetes in Asian Americans to 23 kg/m²

Moving Forward…

- Asians should be screened for diabetes at a lower BMI

- Clinical trials have demonstrated that diet and lifestyle modification are very effective in preventing type 2 diabetes in Asian populations

- These findings should be translated into clinical and public health practice – one example:

  https://www.southasianheartcenter.org/

Thank you!
Any questions?