Global Epidemic and Burden of Diabetes in Asia Pacific

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Past President, Research Society for Study of Diabetes in India (RSSDI)
Past President, All India Association for Advancement of Research in Obesity
Vice President, Association of Physicians of India, Emeritus Editor, JAPI
Scope

• Burden of Diabetes and Prevalence Data in Asia Pacific Regions-

• Characteristics of Risk Factors for type 2 diabetes in Asia and Asian Indians

• Case Study India: Evolution of Phenotype and Genotype

• Preventive Themes for Asian Indians
Samburu Tribe (Kenya):
Prevalence of T2DM
0.1%

White Caucasian:
Prevalence of T2DM
5%

Indo Chinese-Asian:
Prevalence of T2DM
10-20%
The Global Burden

• The number of people with type 2 diabetes is increasing in every country
• 80% of people with diabetes live in low- and middle-income countries
• The greatest number of people with diabetes are between 40 to 59 years of age
• Diabetes caused 4.6 million deaths in 2011
• Diabetes caused at least USD 465 billion dollars in healthcare expenditures in 2011; 11% of total healthcare expenditures in adults (20-79 years)
• 78,000 children develop type 1 diabetes every year
<table>
<thead>
<tr>
<th>REGION</th>
<th>Population 2011</th>
<th>Population 2030</th>
<th>Increase in the no. of diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>387</td>
<td>658</td>
<td>90</td>
</tr>
<tr>
<td>EUR</td>
<td>653</td>
<td>673</td>
<td>22</td>
</tr>
<tr>
<td>MENA</td>
<td>356</td>
<td>539</td>
<td>83</td>
</tr>
<tr>
<td>NAC</td>
<td>322</td>
<td>386</td>
<td>36</td>
</tr>
<tr>
<td>SACA</td>
<td>289</td>
<td>376</td>
<td>59</td>
</tr>
<tr>
<td>SEA</td>
<td>856</td>
<td>1,188</td>
<td>69</td>
</tr>
<tr>
<td>WP</td>
<td>1,544</td>
<td>1,766</td>
<td>42</td>
</tr>
<tr>
<td>World</td>
<td>4,407</td>
<td>5,586</td>
<td>51</td>
</tr>
</tbody>
</table>
Figure 3.0. Percentage of total cases of diabetes (20-79 years) by IDF region, 2011 and 2030
# The Top 10s: (number of people with diabetes)

**Top 10: Countries/territories of number of people with diabetes (20-79 years), 2011 and 2030**

<table>
<thead>
<tr>
<th>COUNTRY/TERRITORY</th>
<th>2011</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>90.0</td>
<td>129.7</td>
</tr>
<tr>
<td>India</td>
<td>61.3</td>
<td>101.2</td>
</tr>
<tr>
<td>United States of America</td>
<td>23.7</td>
<td>29.6</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>12.4</td>
<td>17.9</td>
</tr>
<tr>
<td>Brazil</td>
<td>12.4</td>
<td>16.8</td>
</tr>
<tr>
<td>Japan</td>
<td>10.7</td>
<td>16.4</td>
</tr>
<tr>
<td>Mexico</td>
<td>10.3</td>
<td>14.1</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>8.4</td>
<td>12.4</td>
</tr>
<tr>
<td>Egypt</td>
<td>7.3</td>
<td>11.8</td>
</tr>
<tr>
<td>Indonesia</td>
<td>7.3</td>
<td>11.4</td>
</tr>
<tr>
<td>Pakistan</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*IDF Diabetes Atlas 5th edition, 2011*
• Diabetes burden shifting to developing countries

• India and China will lose national income to the tune of nearly US$900 billion between 2005 and 2015 to diabetes and cardiovascular disease

• IDF predicts that diabetes will cost the world economy US$ 376 billion in 2010 and a 100 billion within a generation

• Asian populations are racially heterogeneous and have differing demographic, cultural and socio economic characteristics
East Asia Western Pacific: No1 Hub

- The world’s most populous region, the Western Pacific has 39 countries and territories with predicted populations for 2011 ranging from 1.3 billion for China to less than 1,500 for the smallest Pacific island nations of Niue and Tokelau. Similarly, the economic profile of countries varies from per capita GDPs of over USD 35,000 for Australia, Hong Kong, Taiwan, and Singapore to less than USD 3,000 for the poorest countries.
Map 3.7. Prevalence (%) estimates of diabetes (20-79 years), 2011, Western Pacific Region

WESTERN PACIFIC REGION AT A GLANCE

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population (millions)</td>
<td>2,217</td>
<td>2,378</td>
</tr>
<tr>
<td>Adult population (20-79 years, millions)</td>
<td>1,544</td>
<td>1,766</td>
</tr>
</tbody>
</table>

DIABETES (20-79 YEARS)

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional prevalence (%)</td>
<td>8.5</td>
<td>10.6</td>
</tr>
<tr>
<td>Comparative prevalence (%)*</td>
<td>8.3</td>
<td>8.5</td>
</tr>
<tr>
<td>Number of people with diabetes (millions)</td>
<td>131.9</td>
<td>187.9</td>
</tr>
</tbody>
</table>

IGT (20-79 YEARS)

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional prevalence (%)</td>
<td>5.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Comparative prevalence (%)*</td>
<td>5.4</td>
<td>5.7</td>
</tr>
<tr>
<td>Number of people with IGT (millions)</td>
<td>84.9</td>
<td>114.1</td>
</tr>
</tbody>
</table>

TYPE 1 DIABETES (0-14 YEARS)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of children with type 1 diabetes (thousands)</td>
<td>30.7</td>
</tr>
<tr>
<td>Number of newly-diagnosed cases per year (thousands)</td>
<td>5.0</td>
</tr>
</tbody>
</table>

DIABETES MORTALITY (20-79 YEARS)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of deaths, men (thousands)</td>
<td>973.1</td>
</tr>
<tr>
<td>Number of deaths, women (thousands)</td>
<td>735.2</td>
</tr>
</tbody>
</table>

HEALTHCARE EXPENDITURES DUE TO DIABETES (20-79 YEARS, USD)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total healthcare expenditures, R-2*, [billions]</td>
<td>72.2</td>
</tr>
</tbody>
</table>

*see Glossary
Mortality: Deaths due to DM highest

- The Western Pacific Region also has the highest number of deaths attributable to diabetes in 2011 of any region with 1.7 million deaths among adults or over 15% of all deaths. China alone had 1.1 million deaths due to diabetes in 2011. Substantially more men (973,000) than women (735,000) died of diabetes in 2011 in the region and 46% of diabetes deaths occurred in those under the age of 60.
Map 3.6. Prevalence* (%) estimates of diabetes (20-79 years), 2011, South-East Asia Region

*comparative prevalence
## Undiagnosed diabetes

**Table 2.3. Undiagnosed diabetes (20-79 years) by region and income group, 2011**

<table>
<thead>
<tr>
<th>REGION</th>
<th>PROPORTION UNDIAGNOSED (%)</th>
<th>CASES (MILLIONS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td></td>
<td>11.6</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>77.9</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>80.0</td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td></td>
<td>19.0</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>29.3</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>35.9</td>
<td></td>
</tr>
<tr>
<td>High-income countries</td>
<td>36.6</td>
<td></td>
</tr>
<tr>
<td>Middle East and North Africa</td>
<td></td>
<td>19.2</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>50.0</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>61.6</td>
<td></td>
</tr>
<tr>
<td>High-income countries</td>
<td>40.7</td>
<td></td>
</tr>
<tr>
<td>North America and Caribbean</td>
<td></td>
<td>11.9</td>
</tr>
<tr>
<td>Low-income countries</td>
<td>29.4</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>41.2</td>
<td></td>
</tr>
<tr>
<td>High-income countries</td>
<td>27.7</td>
<td></td>
</tr>
<tr>
<td>South and Central America</td>
<td></td>
<td>11.2</td>
</tr>
<tr>
<td>South-East Asia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-income countries</td>
<td>48.1</td>
<td></td>
</tr>
<tr>
<td>Middle-income countries</td>
<td>51.1</td>
<td></td>
</tr>
<tr>
<td>Western Pacific</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-income countries</td>
<td></td>
<td>36.2</td>
</tr>
<tr>
<td>Middle-income countries</td>
<td></td>
<td>56.9</td>
</tr>
<tr>
<td>High-income countries</td>
<td></td>
<td>46.7</td>
</tr>
</tbody>
</table>

**Source:** IDF Diabetes Atlas 5th edition, 2011
Asia: Epicenter of “Dual Quake-CVD and DM”:
“The Problems is as Big as Global Warming”

Mark Hanson, Int Soc Dev Origins Dis
“What AIDS was in the last 20 years of the 20th century, diabetes and its consequences will be in the first 20 years of this century”

Paul Zimmet, Time, December 2002
Evolution...

2012 BC...

Used to walk miles to find his food

2012 AD...

Needs to walk miles to digest food
Evolution of Epidemic!! ...

Hunter - Gatherer
Energy Expending

Sedentary
Energy Conserving
Are Races and Geographies Important for Diabetes?

High Prevalance >20%  
- Micronesians  
- Polynesians  
- “Amerinds" as being the "aboriginal Native indian group" of the Americas

High Numbers 10%  
- China  
- India  
- Asia
Race Configuration

- **China** Han Chinese 91.9%, Zhuang, Uygur, Hui, Yi, Tibetan, Miao, Manchu, Mongol, Buyi, Korean, and other nationalities 8.1%

- **India** Indo-Aryan 72%, Dravidian 25%, Mongoloid and other 3%

- **United States** White: 211,460,626 (75.1%); Black: 34,658,190 (12.3%); Asian: 10,242,998 (3.6%); American Indian and Alaska Native: 2,475,956 (0.9%); Native Hawaiian and other Pacific Islander: 398,835 (0.1%); other race: 15,359,073 (5.5%); Hispanic origin: 35,305,818 (12.5%)
Human Migration: Asian Migration in the last 200 years

Mutation rate = 2.2 - 2.9% / Ma
Time estimates are YBP

Wallace DC. 2005.
Global Migration of Asian Indians: 200 years

- Where did Indians migrate?
- Wave 1: Singapore, South and East Africa, Mauritias and Fiji, West Indies (Carribean)
- Wave 2: United Kingdom, Netherlands, Australia, Spain & Indonesia
- Wave 3: North America: United States and Canada
- Wave 4: ROW
Impact of Migration = NCD: CVD/DM

- Within India: Tribal-Village-Small Town-Small Cities-Metros
- Outside India: Asia Africa EU and North America

Migration and its impact on adiposity and type 2 diabetes

Anoop Misra, M.D.\textsuperscript{a,\*}, and Om P. Ganda, M.D.\textsuperscript{b}

\textsuperscript{a} Department of Diabetes and Metabolic Diseases, Fortis Hospital, New Delhi, India
\textsuperscript{b} Joslin Diabetes Center, Boston, Massachusetts, USA

Manuscript received November 16, 2006; accepted June 8, 2007.
### CV Risk Factors in Migrant and Native Siblings

Bhatnagar et al., Lancet, 1995

<table>
<thead>
<tr>
<th>Variables</th>
<th>Punjab (n=65)</th>
<th>W. London (n=118)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>22.9</td>
<td>26.8</td>
</tr>
<tr>
<td>Cholesterol (mmol/L)</td>
<td>4.9</td>
<td>6.5</td>
</tr>
<tr>
<td>Apo B (mg/dL)</td>
<td>62.5</td>
<td>103.6</td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>132</td>
<td>146</td>
</tr>
</tbody>
</table>

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Review

Migration and its impact on adiposity and type 2 diabetes

Anoop Misra, M.D.,*,†, and Om P. Ganda, M.D.

*Department of Diabetes and Metabolic Diseases, Fortis Hospital, New Delhi, India
†Joslin Diabetes Center, Boston, Massachusetts, USA

Manuscript received November 16, 2006; accepted June 8, 2007.
Young, Ambitious and Diabetic:
“Asians are Getting Diabetes Sooner, and Dying Younger”
Margaret Chan, DG, WHO
Characteristics of Risk Factors
in Asian countries...

- Diabetes develops a decade earlier “Young Onset Diabetes”
- Socio-economic transition, modernisation, urbanisation
- Abdominal Obesity
- Higher rates of clustering CV risk factors i.e. metabolic syndrome

Ramachandran et al; Diabetes in Asia, Lancet 2010; 375: 408-18;
Joshi et al; JAPI, Vol 52 May 2004

The per capita expenditure on health care in India is only 6.4% of the average world spending, while India accounts for 23.5% of the world’s disability adjusted life-years lost due to diabetes (DALYs). Due to scant resources and burgeoning...
The average age of onset of diabetes in Asian/Indians is a decade earlier than other races. Many are in late 20s, working in burgeoning new businesses.
Diabetes in India: Case Study

Asian Indian Phenotype Evolution
Genomic Environment and Demographics
INCREASING PREVALENCE OF DIABETES : INDIA

Wild S et al, Diabetes Care, 2004; 27: 1047 – 1053
Diabetes Atlas, International Diabetes Federation, December 2006
Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase I results of the Indian Council of Medical Research–INDia DIABetes (ICMR–INDIAB) study

R. M. Anjana • R. Pradeepa • M. Deepa • M. Datta • V. Sudha • R. Unnikrishnan • A. Bhansali • S. R. Joshi • P. P. Joshi • C. S. Yajnik • V. K. Dhandhania • L. M. Nath • A. K. Das • P. V. Rao • S. V. Madhu • D. K. Shukla • T. Kaur • M. Priya • E. Nirmal • S. J. Parvathi • S. Subhashini • R. Subashini • M. K. Ali • V. Mohan • on behalf of the ICMR–INDIAB Collaborative Study Group

Received: 3 June 2011 / Accepted: 28 July 2011 / Published online: 30 September 2011 © Springer-Verlag 2011
DIABETES IN INDIA (2011)

~ 62.4 million people have diabetes

PRE DIABETES IN INDIA (2011)

~ 77.2 million people have prediabetes
Diabetes in Mumbai: Mini India

- Population: 18 million
- Floating population: 2 million
- Every 8th Mumbaikar Diabetic
- Every 4th will be Diabetic
- Mumbai—All classes affected Urban to slums
- Huge Urban-Rural Divide
- Mini India—Cosmopolitan
- Lifestyle is the primary factor
- Stress and Lack of Physical activity

WIDS, Joshi SR 2004
Screening India’s Twin Epidemic (SITE)

A Cross-sectional study to estimate the prevalence of diagnosed and undiagnosed cases of diabetes and hypertension in outpatient settings in major cities across India

2009-10: OPD setting with General Practitioners

Urban India Disease Distribution: 8 states and 16,000 patients

- Only DM, 2200, 14%
- Only HTN, 3985, 25%
- Twins, 3227, 21%
- None, 6250, 40%

Total 9412 (60%) of 15662 patients were affected with Diabetes, HTN or Both

18.4% (2031) were pre-diabetics

Diabetes 35%
18.4% Pre DM

60.1% (6521) were pre-hypertensive

Diabetes at primary Care

Diabetic patients: associated co-morbid conditions

Overall n = 5427

4528 (97.7%) out of 4634 known DM pts were on Rx#

# Data on file
Categorical summary of Body Mass Index & Waist-hip ratio

Among those visiting the clinics 73% were either overweight or obese and 86% had truncal obesity.

BMI is categorized according to guidelines which were jointly released in November 2008 by Indian health ministry, Diabetes Foundation of India, All-India Institute of Medical Science (AIIMS), Indian Council of Medical Research and National Institute of Nutrition.

WHR was categorized into normal or presence of truncal obesity according to sex-specific norms according to National Cholesterol Education Program:
- Subjects with more than 0.90 for males and more than 0.80 for females in WHR = truncal obesity
- Subjects with less than 0.90 for males and less than 0.80 for females in WHR = normal

More wealth and mechanisation.

Bad Nutrition, unhealthy foods (high sat. fat, trans fats), more eating out

Students under pressure from exams and parents, overeat, skip meals, play less.

More alcohol and smoking

Obesity as a status symbol (“the larger the abdomen, the more the power, money and sexual stamina”)
Is Asian India Phenotype

- Is it Genetic???
- Is it Environmental???

- Do we have Genomic Data from India

- ICMR Advanced Center for Genomics (Dr Mohan’s Center), Chennai
### PC1-K121Q Polymorphism

<table>
<thead>
<tr>
<th>Region</th>
<th>Non-diabetics</th>
<th>Diabetics</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Indians in Chennai</td>
<td>n=456</td>
<td>n=223</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>South Asians in Dallas</td>
<td>n=962</td>
<td>n=121</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Caucasians in Dallas</td>
<td>n=717</td>
<td>n=141</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>

Apolipoprotein C3 gene variants in MS in Asian Indians

- Overall, APOC3 promoter variants were associated with a greater likelihood of MetS compared to wild type [C-482T (OR: 4.3; 95% CI: 2.2, 8.6 [p <0.0001]), T-455C (OR: 3.6; 95% CI: 2.0, 6.7 [p <0.0001])].
Apolipoprotein C3 gene variants in nonalcoholic fatty liver disease

- 95 health Asian Indian men in USA
- 60% increase in the fasting plasma triglyceride concentration, an increase by a factor of approximately two in the plasma triglyceride and retinyl fatty acid ester concentrations after an oral fat-tolerance test, and a 46% reduction in plasma triglyceride clearance. The prevalence of nonalcoholic fatty liver disease was 38% among variant-allele carriers and 0% among wild-type homozygotes
- The polymorphisms C-482T and T-455C in APOC3 are associated with nonalcoholic fatty liver disease and insulin resistance
Beta cell function Genomics:
KCNQ1 Genetic Variations

• East Asians more than Asian Indians
• Chinese, Malays, Asian Indians
• Max in Chinese, Japanese but also in Malays and Asian Indians
• Genomic Variations in East Asians (more beta cell) and Asian Indians (More IR)

• Tan et al, Diabetes 2009;581145-49
Is Indian Society a “Dopaminergic Society ??

- Islet β-cell
  - Impaired Insulin Secretion
  - Decreased Incretin Effect
  - Decreased Glucose Uptake

- Islet α-cell
  - Increased Glucagon Secretion
  - Increased Lipolysis
  - Increased Glucose Reabsorption
  - Increased HGPG
  - Decreased Glucose Uptake

- Neurotransmitter Dysfunction

During the harsh winter months when food availability is LOW, mammalian species in the wild and migratory birds develop an insulin resistant / Glucose intolerant state

1. increased basal lipolytic activity and reduced peripheral glucose utilization
2. Increases hepatic glucose output
3. CNS mediated effects help protecting the brain against glucopenia

Then, during summer…

They revert back to the insulin sensitive, glucose tolerant state
Altered Hypothalamic Function in Response to Glucose Ingestion in Obese Humans

Lower Posterior Hypothalamus

<table>
<thead>
<tr>
<th>Magnitude of Inhibitory Response (%)</th>
<th>Obese</th>
<th>Lean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>8</td>
</tr>
</tbody>
</table>

$P<0.01$

<table>
<thead>
<tr>
<th>Time to Max Inhibitory Response (min)</th>
<th>Obese</th>
<th>Lean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

$P<0.01$

Changes due to D2/D3 receptors

- D$_2$/D$_3$ deficits in obese patients leads to:
  - Less sensitive to reward stimuli.
  - Inability to control food intake.
  - Over consumption of food (hyper phagia).
  - Decreased metabolism in brain involved with inhibitory control.

- **Autonomic dysfunction**
  - Vagally-mediated hyperinsulinaemia
  - Low resting metabolic rate

- Reduced voluntary energy expenditure
- Impaired gut-brain satiety signalling?

*J Addict Med 2009;3: 8–18*
Indians have a high likelihood of abnormal dopamine levels

- Genetic influence
  - making us more prone to develop IR state
- Growing economy and changing lifestyle leading to increased stress
  - Alteration in dopamine level

“Making Asian Indians a Dopaminergic society”

Secular Changes in Environment in Asia

China India

- Food eaten outside of home
- Food availability
- Portion size shifts
- Food marketing
- Transportation
- TV, video, computer work
- Economy and employment shifts
Lifestyle Challenges ...
Lifestyle Challenges ...
CHANGING FACE OF INDIA

Demographic transition
• Epidemiological transition
• Rapid Urbanization
• Industrialization
• Increasing income levels
• Changing lifestyles, values and culture
1961 – IMPORT OF WHEAT FROM US

1960’s & 70’s – “GREEN REVOLUTION”
TODAY INDIA IS SUFFERING FROM A DISEASE CALLED “AFFLUENZA”

THREE MAIN RISK FACTORS
1. Increased calories (glycemic load)
2. ↓ Physical activity
3. Urbanization
Rapid Increase in Portion Sizes

DO NOT UPSIZE !!!
We Need To Minimize
Not Maximize
Refined Grain and Metabolic Syndrome

Refined grain intake (quartiles)

‡ Odds ratios were adjusted for age (5 year category), sex (males / females), smoking (current, past and never smokers), alcohol (current, past and never consumers), BMI (quintiles), Metabolic Equivalent (METS), total energy (kcal), legumes (g/d), visible fats and oils (g/d), dairy products (g/d), sugars (g/d), fruits and vegetables (g/d), tubers (g/d), fishes and sea foods and nuts and oil seeds (g/d).

†P for trend calculated by using the median of each category of intake as a continuous variable in the regression model. The reference category was the lowest quartile.

Radhika G, Sudha V, Mohan V, Metabolism 2009; 58; 675-681
**RISK OF TYPE 2 DM BY DIETARY GLYCEMIC LOAD**

(WHITE RICE INTAKE)

**P for trend <0.001, 95% CI in parentheses**

**Quartiles of glycemic load**

<table>
<thead>
<tr>
<th>Quartile</th>
<th>Glycemic Load</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>(198.7g/d)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2nd</td>
<td>(252.2g/d)</td>
<td>2.69</td>
<td>[1.42-5.09]</td>
</tr>
<tr>
<td>3rd</td>
<td>(307.2g/d)</td>
<td>3.85</td>
<td>[2.08-7.10]</td>
</tr>
<tr>
<td>4th</td>
<td>(413.4g/d)</td>
<td>4.25</td>
<td>[2.3-7.77]</td>
</tr>
</tbody>
</table>

The adjusted model adjusted for age (years in quintiles), sex (males / females), body mass index (continuous), family history of diabetes (3 categories), cigarette smoking [categorized as non-smokers and habitual smokers]; alcohol [never, past and current smoking]; physical activity (Strenuous, no exercise, sedentary), Income in Indian Rupees (<2000, 2000-5000, >5000-10,000, >10,000). *Tests for linear trend were conducted across increasing categories by treating the medians of intake in categories as continuous variable. 95% Confidence interval in parentheses. T2DM, Type 2 Diabetes

INTERACTION OF GLYCEMIC LOAD AND FM HISTORY ON TYPE 2 DIABETES RISK

* Mean glycemic load

The adjusted model adjusted for age (years in quintiles), sex (males / females), body mass index (continuous), family history of diabetes (3 categories), cigarette smoking [categorized as non-smokers and habitual smokers]; alcohol [never, past and current smoking]; physical activity (Strenuous, no exercise, sedentary). Income in Indian Rupees (<2000, 2000-5000, >5000-10,000, >10,000). *Tests for linear trend were conducted across increasing categories by treating the medians of intake in categories as continuous variable. 95% Confidence interval in parentheses. T2DM, Type 2 Diabetes

PHYSICAL ACTIVITY - Enabling Environment

- Crowds - Roads, Work, Home
Major Culprit: TV
“SEDENTARISM”

- Key Risk factor for Diabetes
- Lack of Activity as well as NEAT
- NEAT-Non Exercise Activity Thermogenesis
Basal metabolic rate

Activity thermogenesis

Thermic effect of food

Exercise

Non-exercise Activity Thermogenesis (NEAT)

Kcal/day

Basal metabolic rate
| Occupation-type                                      | NEAT  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Chair-bound</td>
<td>300</td>
</tr>
<tr>
<td>Seated work: no option of moving</td>
<td>700</td>
</tr>
<tr>
<td>Seated work: discretion &amp; requirement to move</td>
<td>1000</td>
</tr>
<tr>
<td>Standing work; e.g. homemaker, shop assistant</td>
<td>1400</td>
</tr>
<tr>
<td>Strenuous work; e.g. agriculture</td>
<td>2300</td>
</tr>
</tbody>
</table>

Data assuming BMR = 1600 kcal/day

Sitting NEAT 300-700
Standing NEAT 1000 to 1400
NEAT = 2000 kcal/day

NEAT = 700 kcal/day
PREVALENCE OF DIABETES IN RELATION TO PHYSICAL ACTIVITY

SYNERGISTIC EFFECT OF HERITABILITY AND PHYSICAL ACTIVITY ON GLUCOSE INTOLERANCE

*Mohan V et al, J Assoc Physicians India, 2003; 51:771-777*

**Chennai Urban Population Study**

<table>
<thead>
<tr>
<th>Family history</th>
<th>Physical activity</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>+ Active</td>
<td>Reference</td>
</tr>
<tr>
<td>Positive</td>
<td>+ Active</td>
<td>2.5 times</td>
</tr>
<tr>
<td></td>
<td>- Active</td>
<td>2.0 times</td>
</tr>
<tr>
<td></td>
<td>+ Sedentary</td>
<td>3.0 times</td>
</tr>
<tr>
<td>Positive</td>
<td>+ Sedentary</td>
<td>3.0 times</td>
</tr>
</tbody>
</table>
Are Asian Indians Different?

- Thin Fat Indians – More Fat
- Thin Fat Indians – Less Muscle
- Sarcopenic and Abdominal Obesity

Is it Genetic???
Is it Environmental???

2 key words: Sedentarnism and Affluenza
# Comparative Body Composition in Asian Indian, African, American and Caucasian Men

<table>
<thead>
<tr>
<th></th>
<th>Asian Indian</th>
<th>African, American</th>
<th>Caucasian</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>20</td>
<td>32</td>
<td>146</td>
</tr>
<tr>
<td>Age (Yr)</td>
<td>27-63</td>
<td>35-64</td>
<td>40-59</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.5±2.5</td>
<td>26.36±2.3</td>
<td>26.4±3.6</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>33±7</td>
<td>26.7±6.3</td>
<td>26.9±4.8</td>
</tr>
<tr>
<td>Body fat / BMI</td>
<td>1.34</td>
<td>1.02</td>
<td>1.01</td>
</tr>
</tbody>
</table>

*Banerjee et al. J Clin Endocrinol Metab 1999; 84: 137-144*
Body Composition of Non-obese Asian Indians: 
Comparisons with African Americans

Banerji et al., J Clin Endocrinol Metab, 1999
Body Mass Index: Inter-ethnic comparison

Asian Indians

RELATIVE ACCUMULATION OF INTRA-ABDOMINAL VS. SUBCUTANEOUS DEPOT ACCORDING TO ETHNICITY

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org
IS IT ONLY BMI CUT OFF WHICH MATTER IN ASIANS?
BMI 23

WHAT ABOUT WAIST CIR ??
BMI: 22.5
WC: 98 cm

BMI: 19.5
WHAT ABOUT BODY FAT COMPOSITION AND ITS METABOLISM?
Body Fat Distribution: MRI Studies
Asian Indians (BMI~23) vs. Caucasians (BMI~24), USA

Fat area on CT

Glucose disposal rates

Raji et al., 2001
### Adipose Tissue Metabolism in Non-diabetic Asian Indians vs. White Caucasians

<table>
<thead>
<tr>
<th>Variables</th>
<th>Asian Indians</th>
<th>Caucasians</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>24 +3</td>
<td>26 +4</td>
</tr>
<tr>
<td>WC</td>
<td>85 +9</td>
<td>89 +11</td>
</tr>
<tr>
<td>Total Body fat</td>
<td>24 + 6</td>
<td>26 +4</td>
</tr>
<tr>
<td>Truncal skinfolds</td>
<td>130 +44</td>
<td>116 +47</td>
</tr>
<tr>
<td>Peripheral SF</td>
<td>70 +31</td>
<td>77 + 39</td>
</tr>
</tbody>
</table>

*Abate et al., JCEM, 2004*
AT Metabolism in Non-diabetic Asian Indians

NEFA (umol/L)  

\[ P < 0.001 \]

Leptin (ng/ml)  

\[ P < 0.003 \]

Abate et al., JCEM, 2004
Mean Adipocyte Size

South Asians: 3491±1393
White Caucasians: 1648±648

Chandalia et al., PlosOne, 2007
Asian Indians are Sarcopenic

- More Fat, Less Muscle
- Less Muscle Mass
- Mitochondrial defects and IR
- Indians and Mitochondria?
Asian Indians have enhanced skeletal muscle mitochondrial capacity to produce ATP in association with severe insulin resistance

- Type 2 diabetes has become a global epidemic, and Asian Indians have a higher susceptibility to diabetes than Europeans. We investigated whether Indians had any metabolic differences compared with Northern European Americans that may render them more susceptible to diabetes.
- Despite being more insulin resistant, diabetic Indians had similar muscle OXPHOS capacity as nondiabetic Indians, demonstrating that diabetes per se does not cause mitochondrial dysfunction. Indians irrespective of their diabetic status had higher OXPHOS capacity than Northern European Americans, although Indians were substantially more insulin resistant, indicating a dissociation between mitochondrial dysfunction and insulin resistance.

Accumulation of ectopic lipid metabolites, activation of the unfolded protein response (UPR) pathway, and innate immune pathways have all been implicated in the pathogenesis of insulin resistance.

Pathways are also closely linked to changes in fatty acid uptake, lipogenesis, and energy expenditure that can impact ectopic lipid deposition.

Cellular changes may converge to promote the accumulation of specific lipid metabolites (diacylglycerols and/or ceramides) in liver and skeletal muscle, a common final pathway leading to impaired insulin signaling and insulin resistance.
Ethnic differences in insulin levels and T2D

Caucasian

Japanese

Adapted from (Botnia Study) *Diabetes* 2000

Adapted from Fukushima *Metabolism* 2003 and *Diabetes Res Clin Pract* 2004

(Age, weight adjusted)
Insulin sensitivity

Postprandial response to 75g carbohydrate meal differs across ethnicities

Change in plasma glucose (mmol/L)

Change in plasma insulin (pmol/L)

Dickinson et al. Hum Nutr Metab 2002;132:2574-9
Insulin Sensitivity in Caucasians and Asian Indian Subjects at Identical Insulin Levels

Raji et al JCEM  Aug 2004;89_3965-72
Asian Indians are More Insulin Resistant than White Caucasians

At comparable values of BMI

At comparable values of BF

Chandalia et al., J Clin Endocrinol Metab, 1999

Raji et al., J Clin Endocrinol Metab, 2001
Glucose Infusion Rates during Hyperinsulinemic Euglycemic Clamp

Punjabi Sikhs vs. Caucasians, UK

Kooner et al., Int J Obesity, 2001
WHY ARE INDIANS MORE PRONE TO TYPE 2 DIABETES AND CAD?

Greater ethnic susceptibility and genetic familial aggregation of type 2 diabetes

- Low birth weight – thin fat Indian
- Inflammatory markers; CRP
- Abdominal obesity and visceral fat
- Levels of adiponectin

Lower age at onset of Type 2 diabetes

- Lower threshold for BMI for diabetes
- Serum insulin levels/insulin resistance

Characteristic dyslipidemia:
- HDL cholesterol
- Triglycerides & small dense LDL

Increased prevalence of type 2 diabetes / premature CVD

SUMMARY OF RISK FACTORS FOR CAD IN INDIANS

Genetic / ethnic susceptibility

- Low HDL, High TC/HDL ratio
- Triglycerides
- Modest elevation of LDL
- CRP
- Fibrinogen
- Platelet activation
- tPA, PAI-1

Low BIRTH WEIGHT

GLUCOSE INTOLERANCE (DM + IGT) / INSULIN RESISTANCE

OBESITY (Central Body)

Lp(a)

Modest elevation of LDL

Low HDL, High TC/HDL ratio

CRP

Fibrinogen

Platelet activation

CAD

GLUCOSE INTOLERANCE (DM + IGT) / INSULIN RESISTANCE

OBESITY (Central Body)

Lp(a)

Modest elevation of LDL

Low HDL, High TC/HDL ratio

CRP

Fibrinogen

Platelet activation

CAD

What are the Guidelines for Physical Activity in Asian Indians?
Effect of supervised progressive resistance-exercise training protocol on insulin sensitivity, glycemia, lipids, and body composition in Asian Indians with type 2 diabetes.

- Moderate-intensity PRT for 3 months resulted in significant improvement in insulin sensitivity, glycemia, lipids, and truncal and peripheral SCAT in patients with type 2 diabetes. Resistance training should be an integral part of exercise regimen in Asian Indians with type 2 diabetes. (Misra A et al. Diabetes Care. 2008 Jul;31(7):1282-7)

- Optimal mix of exercise modalities in the prescription of exercise has not been identified for it benefits to the metabolic, body composition and muscular health markers common in obesity and T2DM.
Guidelines for Physical Activity

• Physical inactivity should be avoided
• Pre-participation medical consultation is recommended for those with chronic conditions and symptoms
• Inactive people should start slow and gradually increase physical activity
• In general a total of 60 mins of physical activity/d (as opposed to 30-45 min/d previously) preferably on all days of the week is recommended everyday: including aerobic activity, work-related activity and muscle strengthening resistance exercises.
Guidelines for Physical Activity

• Work related activity should be encouraged wherever possible.
• Brisk walking is preferred initial mode of exercise and does not require any special training or equipment.
• The physical activity can be accumulated throughout the day in blocks as short as 10 minutes. Physical activity should be increased gradually over period of time.
There is a dose-response relationship between physical activity and health, greater benefit is derived by exceeding minimum recommendations.

For additional and more extensive health benefits, adults can increase their aerobic physical activity to 300 minutes (5 hours) a week of moderate-intensity, or 150 minutes a week of vigorous-intensity aerobic physical activity.
Guidelines for Physical Activity

- Dynamic yoga should be encouraged
- Children should undertake at least 60 min of outdoor physical activity. Screen time (TV / Computers) should be less than 2 hrs a day.

- New Guidelines Published

Leashing The Monster

“Prevention Strategies Should Span The Lifetime”
Tackling the Critical Challenges: It is Time!

“These are the Best of Times, These are the Worst of Times”
Prevention Theme 2011

- “Eat less, Eat on time, Eat right
  Walk More,
- Sleep well
- And Smile”

Joshi SR. RSSDI Theme for Prevention 2011
Eco diseases of Asian Indians: CVD-DM

- Asians Indians- decrease in energy expenditure (and a lower plane of energy throughput), an increase in food energy density (through increased fat and sugary drink intakes), and a decrease in certain health protective foods (lentils, soy, greens) and beverages (tea).

- Sets the stage for 'eco-diseases'. In a population probably genetically programmed (but modifiably) in utero to abdominal obesity, diabetes (type II and gestational) and cardiovascular disease, these conditions may be rapidly acquired on migration, along with certain cancers (breast, colo-rectal and prostate).
A Hidden Curse of Centuries Unfolds Now!

“In Times of Plenty, our Body Engines are Running in Famine Mode”
A Hidden Curse of Centuries Unfolds Now!

• Man had to struggle against harsh climatic conditions for survival.
• It has been observed that people who have been adapted to cold environment for generations demonstrate some resistance to develop diabetes.
• It is hypothesized that presence of thick subcutaneous fat, reactivation of brown adipose tissue in cold environment and effective mitochondrial enzyme systems for heat generation act as adaptive mechanisms for survival in cold environment and retard the development of visceral obesity.
• Mitochondrial defects have been found in patients with DM and NAFLD Changes of nuclear genes which encode mitochondrial enzyme systems involved in thermo genesis could be the cause for development of visceral obesity and DM.
A Hidden Curse of Centuries Unfolds Now!

“In Times of Plenty, our Body Engines are Running in Famine Mode”

Being Active and Eating healthy can only stem the epidemic
Be Strong, Build Muscle and efficient Mitochondria may be necessary too
Acknowledgements

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• Vijay Panikar, Mumbai
2000 B.C.

EVOLUTION...

2000 A.D.

Thank you
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