In the Name of ALLAH, Ever Beneficent, I infinitely Merciful
Obesity
Pathophysiology & Classification

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Why are we so concerned about obesity?

• Obesity is common
• Obesity is serious
• Obesity is preventable

**Obesity... a rising pandemic**
Topics that I will not cover today......

• Dietary and nutritional recommendations

• Surgical options for weight loss
The Epidemic of Obesity
The Obesity Epidemic

• Most important public health problem

For the first time in human history, in the year 2000 it was estimated that there were more **overweight** than **underweight** people.

Source: Mendex, Monteiro, & Popkin 2005
Prevalence of Obesity

775 million obese people in the World including adult, children, and adolescents.

- 650 million adults are obese
- 125 million children under the age of 5 years are obese

WHO (July 1st, 2017)
National Diabetes Survey Pakistan 2016-2017

Prevalence of Diabetes in Pakistan

26.19% Type 2 Diabetes
7.14% new cases
19.05% known cases

This means on average, 1 in 4 person have type 2 diabetes in Pakistan

Diagnosis on the basis of 2-hours OGTT criteria
National Diabetes Survey Pakistan 2016-2017

Prevalence of Pre-Diabetes in Pakistan

14.47%
Pre-Diabetes

This means on average, 3 in 20 person is at risk of diabetes in Pakistan

Diagnosis on the basis of 2-hours OGTT criteria
According to Asian cutoffs,

- Overweight (BMI ≥ 23) 76.2%
- Obesity (BMI ≥ 25) 62.1%

According to WHO cutoffs,

- Overweight (BMI ≥ 25) 47.5%
- Obesity (BMI ≥ 27) 62.1%

Prevalence of Obesity

62.1%
Diabetes Risk Factors

A study on 15-25 years old adolescents of Hub- Baluchistan

Obesity tripled
10.15% to 27.82%

P<0.001

Smoking
4.06% to 21.3%

P<0.001

Family history of DM doubled
7.61% to 16.52%

P<0.001

Metabolic Syndrome and Childhood Obesity

Proportion of dyslipidaemia and insulin resistance in children according to arm-fat percentage terciles

9.6 million children are OW and obese

A study on 8-10 Year old children of Karachi (Pakistan)

- Overweight: 9.8%
- Obesity: 4.3%
- Poor intake of fruits and vegetables: 80%
- Consumption of aerated sweetened drinks and fast food daily: 40%
The Vicious Cycle Of Childhood Obesity

Healthy Child

Obese Adult
- Coronary Artery Disease
- Diabetes
- Pulmonary disease
- High medical bills
- Mortality

Severely Obese Child
- Extra 20-50 lbs.
- Exercise uncomfortable & painful
- The other kids make fun of me

Mildly Obese Child
- Extra 10 lbs.
- Inhibits Movement
- I'm too tired to climb stairs

Moderately Obese Child
- Exercise
- No Action

Asthma, Diabetes, & Musculoskeletal Disease Prevent Exercise and Bring On Depression & Low Esteem

TELEVISION

Video Games

High Fat Foods
Low and Middle Income Countries

Double Burden of Disease
According to WHO there is a “double burden” of disease

• infectious disease and under-nutrition

• chronic disease related to obesity...especially in urban settings
Why Treat Obesity?

Obesity is more than just a cosmetic problem
OBESITY

center piece of jig-saw puzzle of metabolic syndrome
Pathophysiology of Obesity
What Causes Obesity ???

• Genetic predisposition
• Disruption in energy balance
• Environmental and social factors
Obesity Has Multiple Pathophysiologic Origins

- Epigenetic
- Genetic
- Physiologic
- Behavioral
- Sociocultural
- Environmental

What Causes Obesity ???

Simple equation...when you eat more than you use..it is stored in your body as “fat”.

- Global shift in how we eat
- Western diet of processed food
- Higher sugar, fat and calories in what we eat
- Less nutrients
- Reduced intake of vitamins and minerals
What Causes Obesity ???

Energy Intake

Energy Expenditure

nutritional, activity levels, endocrine, genetic, drugs
Obesity

Weight gain:

Energy In

Energy Out
Physical Activity Patterns & Trends

• Walking has declined significantly

• Activity at work continue to decline

• Activity at home & leisure decline
High-Tech increases Body Weight

Cellular phones and remote controls deprive us from walking!

20 times daily x 20 m = 400 m
Walking distance lost/year
400x365 = 146,000 m

146 km = 25 h of walking

1 h of walking = 113-226 kcal

Energy saved = 2800-6000 kcal

0.4 - 0.8 kg adipose tissue

Rossner, 2002
OBESITY AND GENETICS

How genes contribute to obesity???

One/ more abnormality of pathway regulating feeding center

Abnormality of energy expenditure and fat storage
Lean and Mean Environment Over Thousands of Years

Survival

Selection of Genes

Metabolic Syndrome

Fat and Lenient Environment Over Hundreds of Years
Body-Weight Regulation

Sensory Input

Controller

Leptin

Adipose tissue

Controlled System

Efferent signals

afferent signals
Leptin

- Naturally occurring Protein hormone secreted by adipocytes
- Levels correlate with lipid content of cells
- Leptin acts on the hypothalamus to reduce hunger and to stimulate energy expenditure
Ghrelin

• Hormone secreted in the stomach
• Acts on the hypothalamus to stimulate appetite
• Levels peak just before meals and drop afterward

Regulation of Body Weight

Translation System
Is it the “right” amount?
- Brain

Messenger System
How much fat is stored?
- Peripheral Tissues

Effector System
How to make the correction?
- Energy Balance
Measuring Obesity

Body Mass Index = $\frac{\text{weight (kg)}}{\text{Height (m)}^2}$

- Surrogate marker for body fat content.
- BMI not a direct estimate of adiposity; large muscle mass.
Waist circumference independent of BMI/weight, confers additional health risk with:

- Glucose intolerance/Diabetes Mellitus
- Hypertension
- Dyslipidemia

WC in any weight category confers similar risk

Men = Greater than 40 inches
Women = Greater than 35 inches

Arch Intern Med. 2002;162:2074
Android and Gynoid Fat Distribution

Central obesity (apple-shaped) mainly due to visceral fat

Lower body obesity (pear shaped) mainly due to subcutaneous fat

Android fat distribution (apple-shaped)

Gynoid fat distribution (pear shaped)
**Waist Circumference & BMI**

**And Disease Risk**

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Obesity Class</th>
<th>Men ≤ 102 cm (≤ 40 in)</th>
<th>Women ≤ 88 cm (≤ 35 in)</th>
<th>&gt; 102 cm (&gt; 40 in)</th>
<th>&gt; 88 cm (&gt; 35 in)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5 – 24.9</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0 – 29.9</td>
<td>Increased</td>
<td>High</td>
<td>High</td>
<td>Very High</td>
</tr>
<tr>
<td>Obesity</td>
<td>30.0 – 34.9</td>
<td>I</td>
<td>High</td>
<td>Very High</td>
<td>Very High</td>
</tr>
<tr>
<td></td>
<td>35.0 – 39.9</td>
<td>II</td>
<td>Very High</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extreme Obesity</td>
<td>≥ 40</td>
<td>III</td>
<td>Extremely High</td>
<td>Extremely High</td>
<td></td>
</tr>
</tbody>
</table>

*Disease Risk * Relative to Normal Weight and Waist Circumference

*Disease risk for type 2 diabetes, hypertension, and cardiovascular disease

Adapted from:
Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults
### WHO Asia Pacific Guidelines for Obesity

<table>
<thead>
<tr>
<th>Category</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal Weight</td>
<td>18.5-22.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>≥23</td>
</tr>
<tr>
<td>At risk</td>
<td>23-24.9</td>
</tr>
<tr>
<td>Obesity</td>
<td>≥25</td>
</tr>
</tbody>
</table>


Why is a BMI of 20-25 considered as a reference weight?

This is because the relationship between morbidity and mortality and BMI is minimal at that range.
**Other Markers of Fat**

**Body Fat Percentage:** The percentage of fat in body; people with similar BMI can have different fat percentages.

### Examples of hidden fat

<table>
<thead>
<tr>
<th></th>
<th>CaseA</th>
<th>CaseB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>F</strong></td>
<td>Gender</td>
<td>F</td>
</tr>
<tr>
<td>34</td>
<td>Age</td>
<td>34</td>
</tr>
<tr>
<td>6'7 7/8&quot;</td>
<td>Height</td>
<td>6'7 1/2&quot;</td>
</tr>
<tr>
<td>144.0 lb</td>
<td>Weight</td>
<td>141.0 lb</td>
</tr>
<tr>
<td>22.0 (Normal)</td>
<td>BMI</td>
<td>21.8 (Normal)</td>
</tr>
<tr>
<td>27.2% (Normal)</td>
<td>Body fat percentage</td>
<td>34.5% (High)</td>
</tr>
</tbody>
</table>
Step by Step Approach for Managing Obesity
ALGORITHM COMPONENTS

1. Obesity Screening

2. Diagnosis

3. Treatment: Goals and Considerations

4. Follow-Up
1. Screen positive for overweight or obesity
   **BMI ≥25 kg/m²**
   (≥23 kg/m² in some ethnicities)

2. Presence of weight-related disease or complication that could be improved by weight loss therapy
2. Evaluate Patient

- 1. Medical history
- 2. Physical examination
- 3. Clinical laboratory tests
- 4. Review of systems, emphasizing weight-related complications
- 5. Obesity history: graph weight vs age, lifestyle patterns/preferences, previous interventions
3. Treatment Based on Clinical Judgment

**PRIMARY**
- Healthy meal plan
- Physical activity
- Health education
- Built environment

**SECONDARY**
- Lifestyle/behavioral therapy
- Consider pharmacotherapy if lifestyle alone not effective

**TERTIARY**
- Lifestyle/behavioral therapy
- Consider pharmacotherapy (BMI ≥27)

**TERTIARY**
- Lifestyle/behavioral therapy
- Add pharmacotherapy (BMI ≥27)
- Consider bariatric surgery (BMI ≥35)
Treatment Approach

- Make the diagnosis (and communicate it)
- Assess readiness for change
- Prescribe diet and exercise
- Consider medications and surgery
Treatment Approach (Contd.)

• Initial goal: 10% weight loss
• Rate of weight loss
  • 1 to 2 pounds per week
• Slow weight loss is more stable

• After 6 months, weight loss is more difficult
  • Ghrelin & Leptin are at work!
  • Changes in resting metabolic rate
  • Energy requirements decrease as weight decreases
  • Diet adherence wavers
Physical Activity

Physical activity should be an integral part of weight loss

- Start slowly
- Increase intensity & duration gradually
- Long-term goal
  - 30 to 45 minutes or more of physical activity
  - 5 or more days per week
  - Burn 1000+ calories per week
Recommend Physical Activity

• What does it take to burn 1000 calories per week?

- Running 11 miles
- Walking 12 miles
- Gardening 5 hours
- Cycling 22 miles
Indications for use of obesity drugs

A combined intervention of behavior therapy, dietary changes and increased physical activity should be maintained for at least 6 months before considering pharmacotherapy.
Pharmacotherapy for Weight Loss

• **Adjunct** to diet & physical activity
• BMI $\geq 30$ Or, BMI $\geq 27$ with other risk factors
• Should not be used for cosmetic weight loss
  • Only for risk reduction
• Use only when 6-month trial of diet & physical activity fails to achieve weight loss
CONTRAINDICATIONS OR CAUTIONS TO THE USE OF OBESITY DRUGS

- Pregnancy or lactation
- Unstable cardiac disease
- Uncontrolled hypertension (SBP >180, DBP > 110 mmHg)
- Unstable severe systemic illness
- Unstable psychiatric disorder or history of anorexia
- Other drug therapy, if incompatible (eg MAO inhibitors, migraine drugs, adrenergic agents, arrhythmic potential)
- General anesthesia

NHLBI Obesity Education Initiative, Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults
### Currently Available Agents Indicated for Treatment of Obesity

<table>
<thead>
<tr>
<th>Generic</th>
<th>Usual Dose</th>
<th>Mechanism of Action</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Orlistat</strong></td>
<td>120 mg with each meal</td>
<td>Peripheral: Blocks absorption of about 30% of consumed fat</td>
<td>GI symptoms (oily spotting, flatus with discharge, fecal urgency, oily stools, incontinence)</td>
</tr>
<tr>
<td>Phentermine</td>
<td>15-37.5 mg per day as a single or split dose</td>
<td>Central: Stimulates release of norepinephrine</td>
<td>CNS stimulation, tachycardia, dry mouth, insomnia, palpitations</td>
</tr>
</tbody>
</table>
Newer drugs approved by FDA

- **Lorcaserin- June 2012** (Selectively activates serotonin 2C receptors in brain promotes satiety)

- **Phentermine & Topiramate ER-** July 2012 (mediates release of catecholamine's in hypothalamus reduced appetite)

- **Naltrexone & Bupropion-** Sept 2014 (Effect on 2 separate areas of brain. Exact neurochemical effects not known)
  - Mesolimbic dopamine circuit
  - Exact neurochemical effects not known

- **Liraglutide-** Dec 2014 (Glucagon like peptide 1 receptor agonist.)
Remember There is no miracle drug to tackle obesity overnight.
Future drugs may use new strategies

• Combine drugs that affect appetite and those that affect addiction (or craving)
• Stimulate gut hormones that reduce appetite
• Shrink the blood vessels that feed fat cells in the body, thereby preventing them from growing
• Target genes that affect body weight
• Change *bacteria* in the gut to control weight
Obesity
What needs to be done?

• Low-cost and effective screening strategies
• Massive awareness campaigns
• Population based implementation
• Identification of roles of various stake holders
Focus on children
Role of multiple stakeholders

- Food Industry
- Physician Associations
- Teaching Faculties
- Donors Philantropy
- Pharmaceutical industry
- Public Health Depts
- Public forums PNDS NADEP etc.
- Media

Our responsibility
Few major examples of such collaborations

• Lowest salt in crisps in United Kingdom
• Cycling mandatory over the weekends in Brazil/Argentina
• No soft drinks vending machines in schools in Saudi Arabia
• Scottish pizza developed with minimal entrepreneurship and complete taste
Analysis shows the pizzas, which cost around £3.50, to be healthier than shop-bought salads.
Conclusion

- Diet/lifestyle changes remain the mainstay of the treatment of obesity
- Expect only modest weight loss at best with current drugs
- Be aware of Rx indications and contraindications
- Off label use of non-indicated products is not recommended
- Investigational agents may offer hope for treatment of obesity in the future
Taking Action to Prevent Obesity

Change will come more easily if everyone is involved.
“Enjoy present pleasures in such a way as not to injure future ones.”

~Seneca (4 BC- 65 AD)
Thank You

For Your Kind Attention...!!