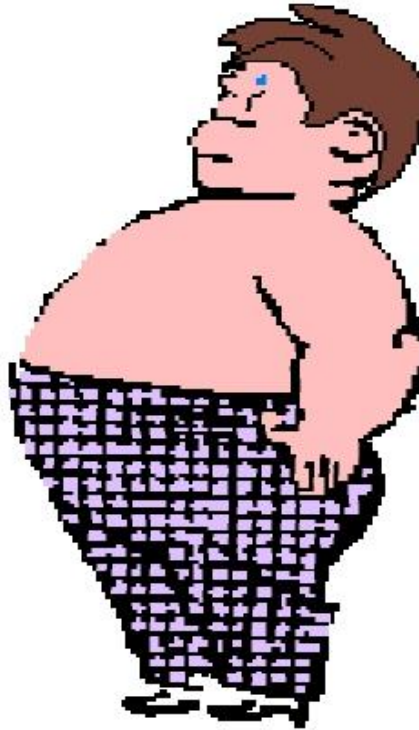


Type 2 DM in Children & Adolescents



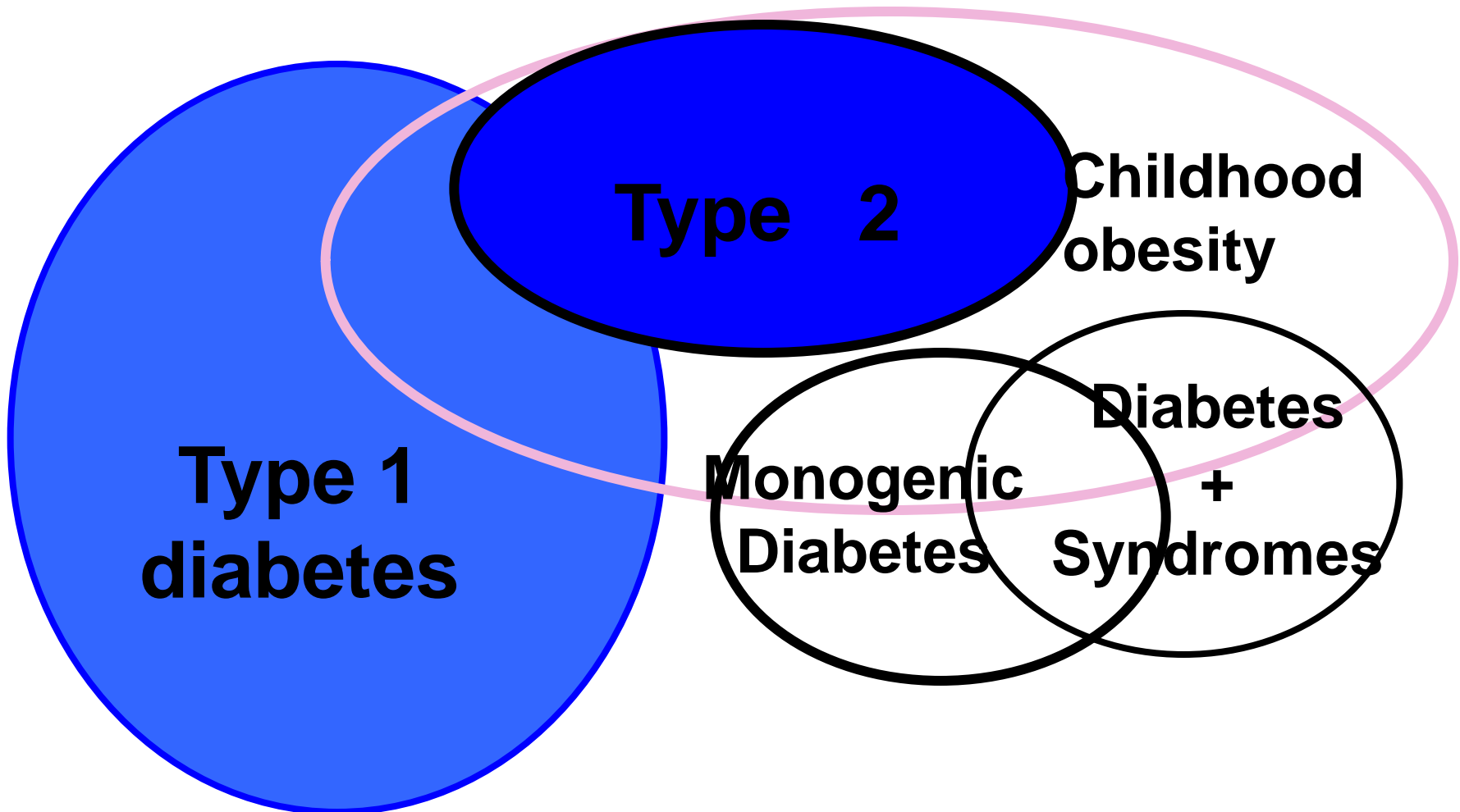
Prof. Abdulmoein Al-Agha, FRCPCH(UK)

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Outline

- Introduction on type 2 DM in children
- Escalating rates of pediatric obesity with increasing prevalence of type 2 DM
- Pathophysiology
- Clinical presentations
- Screening
- Prevention & therapy (few lines)
- Our local study on children and adolescents with obesity at KAUH- Jeddah, KSA

Paediatric Diabetes



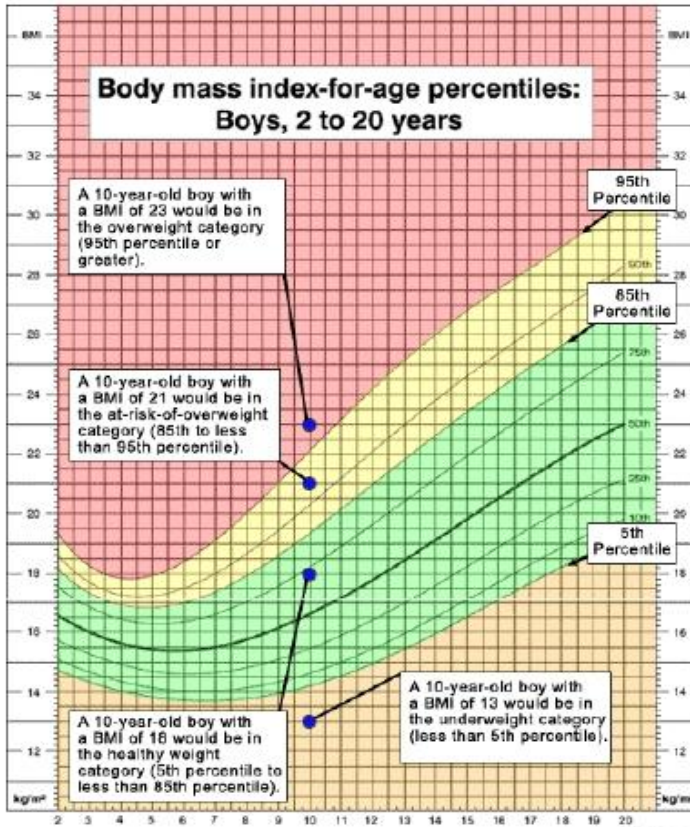
Introduction

- With the escalating rates of obesity, type 2 diabetes is increasing, not only in adults but also in youth
- In the SEARCH for Diabetes in Youth study, it is estimated that the number of adolescents per year diagnosed with type 2 diabetes is ~3,700 and still increasing!!!!
 - *Endocrinol Metab* 2009;94:2215–2220
 - *Epidemiology of type 2 diabetes in children and adolescents. Endocr Res* 2008;33:35–58

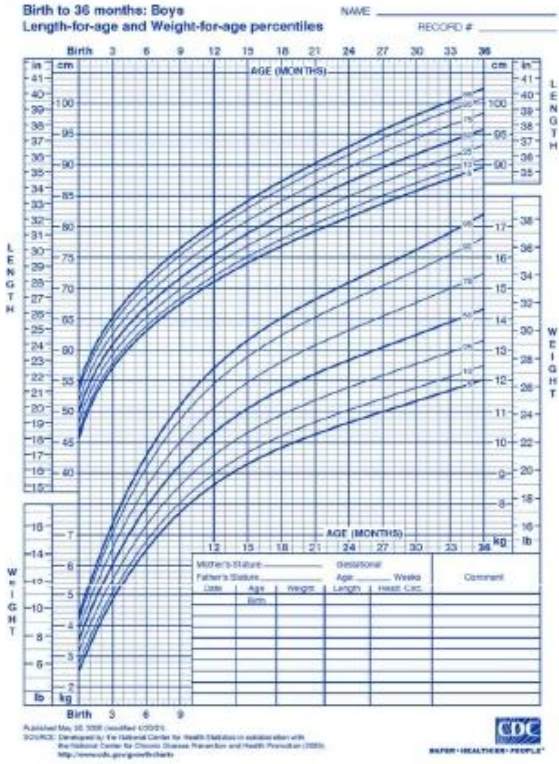


Establish diagnosis: BMI

- $BMI = \text{weight (kg)} / [\text{height (M)}]^2$
- Correlates well with direct measures of adiposity
- Overweight child: BMI $>$ 85th and $<$ 95th percentile
- Obese child: BMI $>$ 95th percentile
- If child $<$ 3 years old, use weight for height charts



- underweight, less than the 5th percentile
- healthy weight, 5th percentile up to 85th percentile
- at risk of overweight, 85th to less than the 95th percentile
- overweight > 95th percentile



www.cdc.gov/growthcharts/

Rising Rate of Childhood
Overweight is **ALARMING!**

Approximately 1 of every 4 children in the United States is considered overweight



Farina



Mickey



Joe

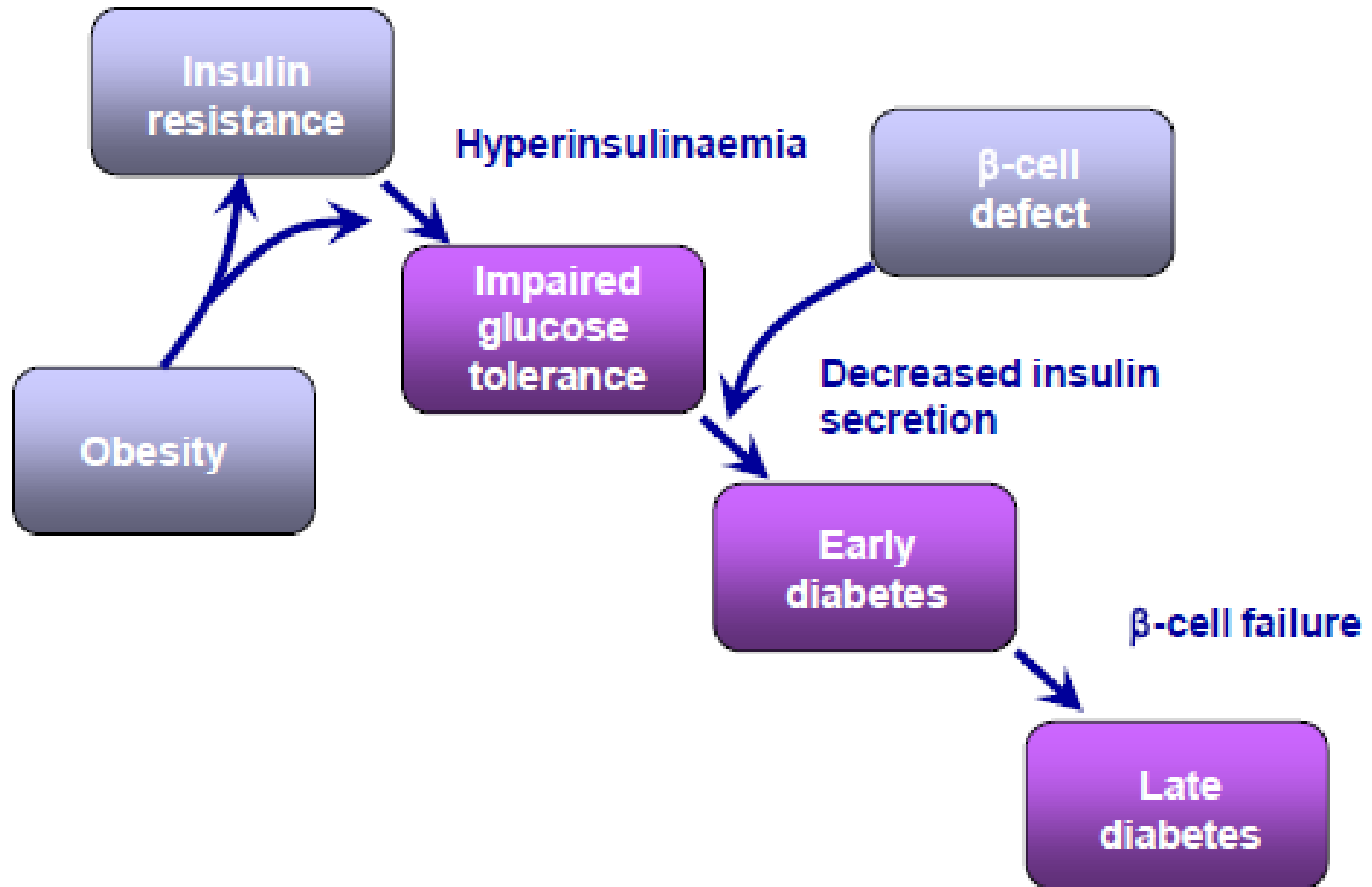
Prevalence of overweight & obesity in Saudi children & adolescents

- Mohammad I. El Mouzan,^a Peter J. Foster,^b Abdullah S. Al Herbish,^a Abdullah A. Al Salloum,^a Ahmad A. Al Omer,^c Mansour M. Qurachi,^d and Tatjana Kecojevic^b

- ***Ann Saudi Med.* 2010 May-Jun; 30(3): 203-208**

- The national sample size, in Saudi reference was 19 317 healthy children & adolescents from 5 - 18 years of age
- The prevalence of **overweight 23.1%**, **obesity 9.3%** & **severe obesity 2%**, in all age groups

Underlying causes of type 2 diabetes



Obesity is a major factor for insulin resistance



Acanthosis nigricans



Genetics & Environment for type 2 DM

“Genetics = the Loaded
Gun; the Environment
pulls the trigger” Pamela Peeke,
MD, U of Maryland



Ethnicity of Children with Newly Diagnosed T2DM

Ethnicity	# newly diagnosed (%)	% of population diagnosed age <10 years
Total (%)	227 (100%)	8%
Aboriginal	100 (44.1%)	11%
Caucasian	57 (25%)	8.8%
African / Caribbean	23 (10.1%)	4.3%
Asian	23 (10.1%)	8.7%
Mixed ethnicity	14 (6.2%)	--
Hispanic	4 (1.8%)	--
Middle Eastern	1 (0.4%)	--

Screening

- Risk factors for childhood type 2 diabetes include:
 - T2DM in a first- or second-degree relative
 - High risk ethnic or racial group
 - Obesity
 - Impaired glucose tolerance (IGT)
 - Polycystic ovary syndrome (PCOS)
 - Exposure to diabetes in utero
 - Acanthosis nigricans
 - Hypertension and Dyslipidemia
 - Nonalcoholic fatty liver disease (NAFLD)
 - Use of atypical antipsychotic medications

Screening and Diagnosis

Recommended
screening test

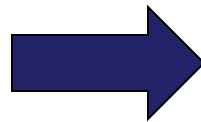


Fasting plasma
glucose (FPG)

BMI $\geq 99^{\text{th}}$ %ile

and/or

Multiple risk factors



Oral glucose tolerance
test (OGTT)

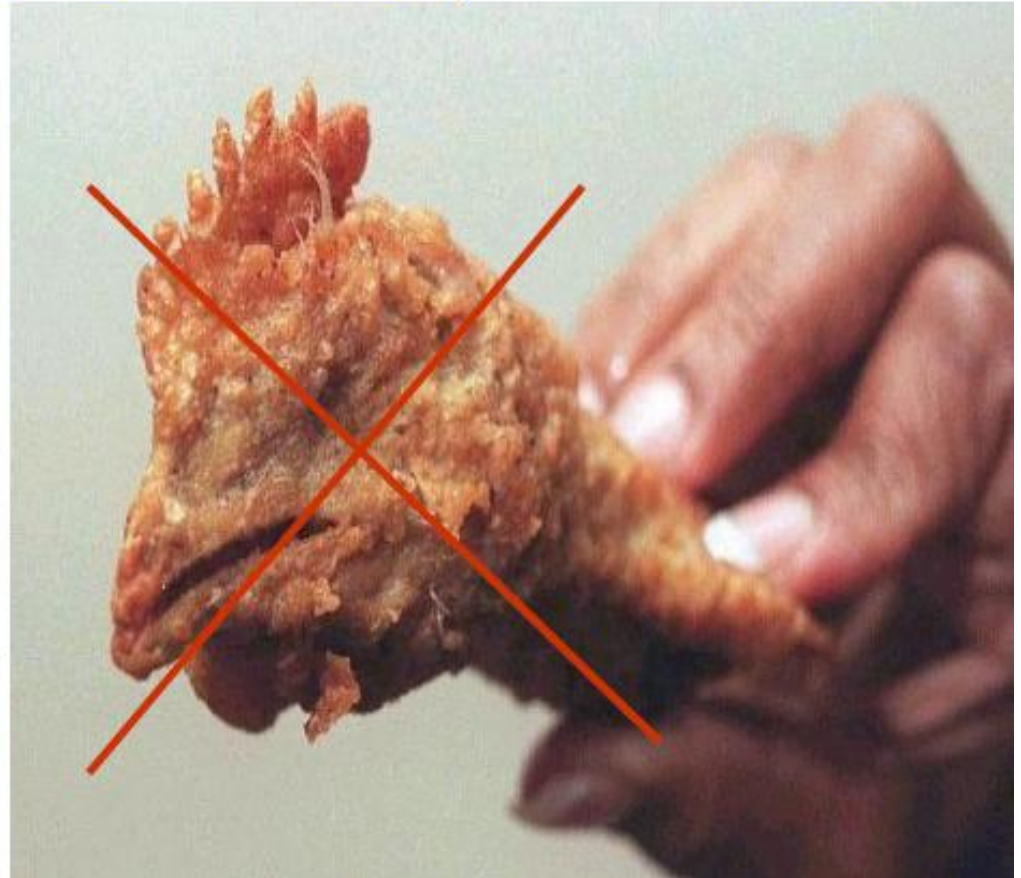
Diagnostic criteria for above same as for adults

Clinical Presentations

- Youth with type 2 diabetes at an average age of 13.5 years (at midpuberty) present a physiologic state characterized by temporary insulin resistance
- The clinical presentation is a wide spectrum:
 - from asymptomatic (obese at-risk youth diagnosed during screening for type 2 diabetes)
 - To more typical presentation of polyuria and/or polydipsia (with or without weight loss), blurry vision, monilial vaginitis in females, etc.,
 - to critically ill individuals presenting with diabetic ketoacidosis (DKA) /hyperglycemic hyperosmolar nonketotic (HHNK) state

Prevention of obesity

قال صلى الله عليه وسلم (ما ملأ آدمي وعاء شرا من بطنه، بحسب ابن آدم لقيمات يقمن صلبه، فان كان لا بد فاعلا فثلث لطعامه وثلث لشرابه وثلث لنفسه). رواه أحمد والترمذي



Prevention

- Breastfeeding beneficial in reducing risk
- Obesity is a major modifiable risk factor
- Family-based lifestyle interventions with a behavioral component aimed at changes in diet and physical activity patterns have been shown to result in significant weight reduction in children and adolescents

Preventing Obesity in Young Children



Strategies for Promoting Healthy Eating, Exercise and Parent Involvement

Super Sized Fast Food

1610 Calories
63 gm fat



Life Style Modifications



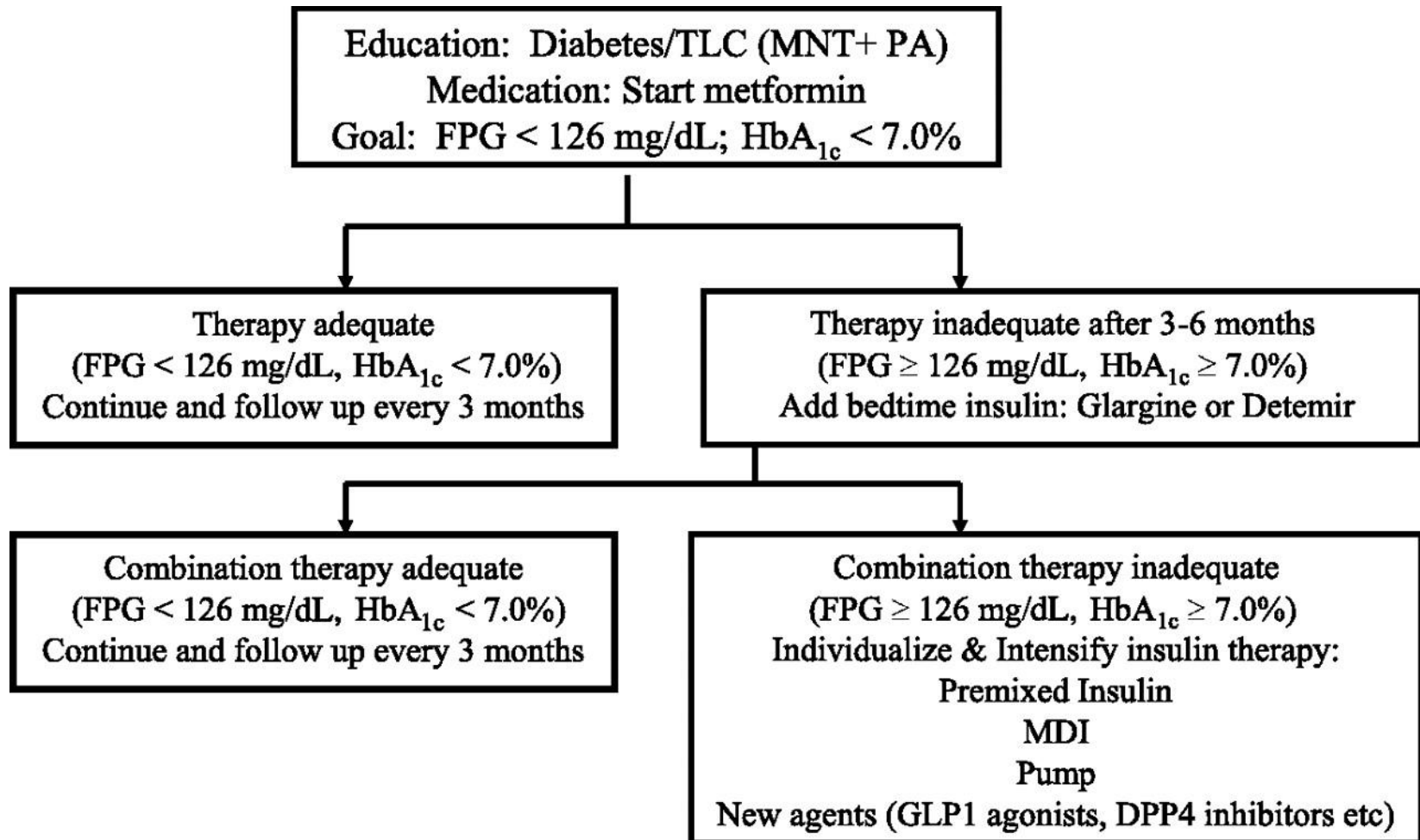
Physical Activity

- Increased activity not only increases calorie use but also appears to decrease appetite
- In children younger than 2 yr of age ,AAP recommends avoiding TV computers
- children 2-18yr of age should have < 2hr/day of “screen time” (TV, video games, computer) and TV should be removed from children bedrooms

How can insulin resistance be managed?

- Improve insulin resistance through:
 - Diet
 - Exercise
 - Pharmacological intervention with agents that target insulin resistance

Treatment algorithm for type 2 diabetes in adolescents.



Flint A , and Arslanian S Dia Care 2011;34:S177-S183

Bariatric surgery

- Roux-en-Y gastric bypass (RYGB) is a surgical technique promoted as a safe and effective option for adolescent weight loss
- Currently, eligibility criteria for adolescents include a BMI >35 kg/m² if a serious comorbidity (such as type 2 diabetes) is also present, Tanner stage IV or V, and skeletal maturity

**Prevalence of Hyperinsulinism, Type 2 D M
& Metabolic Syndrome among Saudi
Overweight & Obese Pediatric Patients at
King Abdul-Aziz University, Jeddah, Saudi
Arabia**

**Al-Agha A, Ochiltree A, Shata N,
Minerva Pediatr. 2012 Dec;
64(6):623-31.**

Background

- Obesity and overweight among children and adolescents is increasing at an alarming rate, which lead to the increase in the incidence of their related co-morbidities, renders the child prone to insulin resistance, dyslipidemia, type 2 diabetes mellitus (T2DM) and ultimately metabolic syndrome (MS)

Objectives of study

- 1) To evaluate the prevalence of Hyperinsulinism among overweight & obese pediatric patients
- 2) The prevalence of T2DM among those with Hyperinsulinism
- 3) The prevalence of metabolic syndrome and its components among (T2DM) pediatric patients visiting Pediatric Endocrinology clinic at KAUH

Methodology

- A retrospective cross-sectional study conducted on overweight and obese pediatric patients attending the pediatrics diabetes clinic at King Abdul-Aziz University Hospital, Jeddah, Saudi Arabia, from 2006 to 2010
- 387 patients (ages from 2 to 18 years)
- Those with hyperinsulinism underwent further investigations to assess the prevalence (T2DM) and the prevalence of (MS) among (T2DM) patients

Definitions used in the study

- Overweight and obesity for children and adolescents were defined as \geq 85th and 95th percentile of BMI, respectively, plotted on the CDC BMI charts

Definitions used in the study

- Weight and height measurements at King Abdul-Aziz University Hospital are taken according to the CDC guidelines and are measured in kilograms and centimeters, respectively
- Weight and waist circumference measurements were taken with cloth
- Waist circumference was measured in centimeters

Definitions used in our study

- Hypertension in children and adolescents was defined as systolic blood pressure and/or diastolic blood pressure \geq 95th percentile, plotted on the CDC age-gender specific blood pressure charts and measured on \geq 3 separate occasions
- Dyslipidemia was defined as the presence of any of the following:
 - Cholesterol $>$ 5.2 mmol/L,
 - Triglycerides $>$ 2.3 mmol/L,
 - Low density lipoprotein (LDL) $>$ 3.57 mmol/L
 - High density lipoprotein (HDL) $<$ 0.9 mmol/L

Definitions used in this study

- The diagnosis of (PCOS) was established via using the Rotterdam consensus on diagnostic criteria for PCOS
- The revised 2003 criteria were:
 - Oligo- and/or anovulation
 - Clinical and/or biochemical signs of hyperandrogenism
 - Polycystic ovaries, by pelvic ultrasound (specifically looking for the presence of 12 or more follicles in each ovary measuring 2 ± 9 mm in diameter, and/or increased ovarian volume (>10 ml)
- The presence of **two out of three** criteria confirmed the diagnosis of PCOS
- The LH to FSH ratio was also calculated, a ratio greater than 1:1 was considered elevated

Definitions used in study

- The diagnosis of (T2DM) was established via fasting serum glucose ≥ 7 mmol/L.
- Random or two-hour postprandial serum glucose ≥ 11.1 mmol/L with classic symptoms of hyperglycemia and HbA1c $\geq 6.5\%$
- Hyperinsulinism was established by elevated serum levels of insulin > 17 mIU/L (3 - 17 mIU/L) & C- peptide > 1.47 nmol/L (0.37 - 1.47 nmol/L)
- Serum uric acid > 428 μ mol/L was considered elevated (155 - 428 μ mol/L).
- Acanthosis nigricans (AN) was diagnosed clinically

Definitions used in study

Metabolic syndrome (MS)

- Was defined by de Ferranti et al, as the presence of three of the following:
 - fasting serum glucose ≥ 6.1 mmol/L,
 - waist circumference $>$ 75th percentile for age and sex
 - systolic and/or diastolic blood pressure $>$ 90th %ile plotted on pediatric charts
 - triglycerides ≥ 1.1 mmol/L,
 - high density lipoprotein HDL-C < 1.3 mmol/L

Statistical analysis

- The data was gathered on a datasheet from the university hospital database and patients clinical charts.
- All laboratory information was taken from the university hospital centralized laboratory phoenix database system.
- Tables were exported to the SPSS (version 16) and Epi info (version 3.5.1) software, where the data was analyzed and the formation of tables commenced.
- Analysis of quantitative data was done via the two-sample t-test.
- The level of significance was expressed as P-value; $P > 0.05$ = non-significant (NS), $P < 0.05$ = significant (S), and $P < 0.001$ = highly Significant (HS)

Results

- Out of 387 patients (ages from 2 to 18 years) 44.7% patients had hyperinsulinemia & 20.23% of them had (T2DM)
- Mean & SD for serum insulins were 30.04 \pm 12.7 mIU/L in pre-pubertal children & 46.15 \pm 22.1 mIU/L in pubertal adolescents (P = 0.0136)

Results

- The overall prevalence of (MS) among (T2DM) pediatric patients was 14.29%.
- Only 1 of those with (MS) was pre-pubertal.
- The prevalence of each of the diagnostic components were:
 - 31.43% had elevated fasting serum glucose,
 - 23% had a waist circumference > 95th percentile,
 - 28.57% had high triglyceride levels,
 - 22.86% had low levels of HDL
 - 14% had high blood pressure (11 % for SBP and 3% for DBP)
 - 2.86% had Hyperurecemia

Results

- In our cohort, the overall prevalence of dyslipidemia was 28.57%.
 - 25.71 % had elevated triglycerides
 - 2.86% had elevated LDL
 - 8.5% had low levels of HDL
 - 20% had elevated serum total cholesterol

Results

- The prevalence of (PCOS) in our cohort was 21.74%.
- All pubertal females with (PCOS) had a BMI > 85th percentile, 40% had a BMI > 95th percentile,
 - All complained of menstrual irregularities, 60% had (MS) and 80% had (AN), all had serum DHEAS > 95th age-gender specific percentile and all showed multiple ovarian cysts by pelvic ultrasound.
- All pubertal females with (PCOS) had an LH / FSH ratio of > 1:1.

Discussion

- In our cohort, the prevalence of secondary hyperinsulinism (44.7%) was lower than what was reported by a study conducted in San Diego, California (51.9%) and higher than another study in London (40%)

Discussion

- The prevalence of (T2DM) in our population (20.3%) was within the American Diabetes Association (ADA) issued consensus statement regarding the prevalence of (T2DM) in children and adolescents.
- The ADA stated that (T2DM) now accounts for as many as 8 to 46% of new cases of pediatric diabetes

Discussion

- Dyslipidemia within our cohort (28.57%), which almost near to what other studies have reported, range of dyslipidemia (30% to 55%)
- We reported the prevalence of hypertension within our cohort as 34.29%, two other studies in London and Turkey reported a lower prevalence (32% and 22%, respectively)

Discussion

- The overall prevalence of (MS) in our cohort was within the prevalence range used by the WHO which is (4.5% to 38.7%).
- In our cohort (14.29%) was higher than a study in the USA reported (10%), and less than what studies in Turkey, Spain and Bolivia have reported (27.2%, 18.6% and 36%, respectively)

Discussion

- We also reported that the prevalence of (MS) was higher among females with (T2DM) than males, other studies reported a higher prevalence among males, and some reported no difference in the prevalence with respect to gender
- Furthermore, the prevalence of (MS) was greater among pubertal children and adolescents than pre-pubertal children in our cohort

Conclusions

- Obesity and its co-morbidities were prevalent among Saudi pediatric patients.
- We recommend preventing excessive weight gain through the promotion of a healthy lifestyle, family educational seminars and the reinforcement of indoor exercises.

Our conclusions

- **We believe this is due to** lack of family education seminars and the abundance of fast food establishments accessible to our youth are the most salient of reasons
- As many studies have proven, parents have an integral role in the management of childhood obesity
- We recommend the promotion of family education seminars in Saudi Arabia, mainly to increase the awareness of obesity and its co-morbidities and the reinforcement of a healthier diet, primarily one with high fiber, low sodium, simple carbohydrates and saturated fats content.

Conclusions

- Saudi Arabia has a desert landscape with a harsh climate, such conditions discourage children and adolescents from outdoor activities, mainly exercises and sports
- In order to overcome such issues, we recommend the promotion of indoor exercises for at least 30 minutes per day and to limit television usage hours to a maximum of 2 hours per day.



References

- Kiess W, Galler A, Reich A, [Müller G](#), [Kapellen T](#), [Deutscher J](#), et al. Clinical aspects of obesity in childhood and adolescence. *Obes Rev* 2001;2:29–36.
- Berenson GS. Obesity—a critical issue in preventive cardiology: the Bogalusa Heart Study. *Prev Cardiol* 2005;8:234–41.
- Verhulst SL, Schrauwen N, Haentjens D, [Rooman RP](#), [Van Gaal L](#), [De Backer WA](#), et al. Sleep-disordered breathing and the metabolic syndrome in overweight and obese children and adolescents. *J Pediatr* 2007;150:608–12.
- Glaser NS. Non-insulin-dependent diabetes mellitus in childhood and adolescence. *Pediatr Clin North Am* 1997;44:307–37.
- Pinhas-Hamiel O, Dolan LM, Daniels SR, Standiford D, Khoury PR, Zeitler P. Increased incidence of non-insulin-dependent diabetes mellitus among adolescents. *J Pediatr* 1996;128:608–15.

References

- Reich A, Müller G, Gelbrich G, Deutscher K, Gödicke R, Kiess W. Obesity and blood pressure results from the examination of 2365 schoolchildren in Germany. *Int J Obes Relat Metab Disord* 2003;27:1459–64.
- Cruz ML, Weigensberg MJ, Huang TT, Ball G, Shaibi GQ, Goran MI. The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. *J Clin Endocrinol Metab* 2004;89:108–13.
- Goodman E, Daniels SR, Morrison JA, Huang B, Dolan LM. Contrasting prevalence of and demographic disparities in the World Health Organization and National Cholesterol Education Program Adult Treatment Panel III definitions of metabolic syndrome among adolescents. *J Pediatr* 2004;145:445–51.
- Molnar D. The prevalence of the metabolic syndrome and type 2 diabetes mellitus in children and adolescents. *Int J Obes Relat Metab Disord* 2004; 28:S70–S74.
- Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, Yeckel CW, et al. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med* 2004;350:2362–74.

References

- de Ferranti SD, Gauvreau K, Ludwig DS, Newfeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the third national health and nutrition examination survey. *Circulation* 2004; 110: 2494–7.
- Kuczumarski RJ, Ogden CL, Grummer-Strawn LM, Flegal KM, Guo SS, Wei R, et al. CDC growth charts: United States. *Adv Data* 2000;314:1–27.
- Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod* 2004;19:41–7.
- Rosenbloom AL. Age-related plasma insulin response to glucose ingestion in children and adolescents. *IRCS Metab Nutr: Pediatr* 1974;2:1210.
- Schwimmer JB, Burwinkle TM, Varni JW. Health-related quality of life of severely obese children and adolescents. *JAMA* 2003;289:1813–9.
- Viner RM, Segal TY, Lichtarowicz-Krynska E, Hindmarsh P. Prevalence of the insulin resistance syndrome in obesity. *Arch Dis Child* 2005;90:10–4.

References

- American Diabetes Association. Type 2 diabetes in children and adolescents. *Pediatrics* 2000;105:671–80.
- [Likitmaskul S, Kiattisathavee P, Chaichanwatanakul K, Punnakanta L, Angsusingha K, Tuchinda C.](#) Increasing prevalence of type 2 diabetes mellitus in Thai children and adolescents associated with increasing prevalence of obesity. *J Pediatr Endocrinol Metab* 2003;16:71–7.
- Wabitsch M, Hauner H, Hertrampf M, [Muche R, Hay B, Mayer H, et al.](#) Type II diabetes mellitus and impaired glucose regulation in Caucasian children and adolescents with obesity living in Germany. *Int J Obes Relat Metab Disord* 2004;28:307–13.

Thank you