433 Teams

MEDICINE

15 | Type 1 Diabetes Mellitus

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Objectives:

1. Describe the overview of type 1 diabetes and its epidemiology

2. Define the Etiology and pathophysiology

3. Know the Diagnosis and clinical presentation

4. Know the Acute and chronic complications

5. Manage the patients

Type 1 Diabetes Mellitus

<u>Introduction</u>:

- It accounts 5% of all diabetic patients.

- The danger of diabetes that it is not only the disease but it is also an inviter for other   co morbidities.

- the prevalence of type 1 DM is 30 children in each 100000 in KSA

- One third of the patients in any clinic are diabetic.

- There are 5 characteristic features for DM1:(young -thin –Acute onset -DKA –sever insulin reduction)

- Nowadays also children might have DM2 because of obesity so, combination of all the 5 feature is diagnostic.

- This is characterized by a severe deficiency of insulin.
  Patients require insulin to live.

- The onset is typically in youth (before age 20), but can occur at any age.

- Not related to obesity.

Figure 1: The HLA region on chromosome 6 (from Mehers and Gillespie 2008). The T1D associated haplotypes are DRB1*03-DQB1*02 and DRB1*04-DQB1*0302

- T1DM is a t-cell mediated autoimmune disease that involves destruction of Beta cells resulting in absolute insulin deficiency.

- Overt Type 1 DM does not appear until about 90% of β cells are destroyed.

- It develops in genetically susceptible individuals who are exposed to an environmental factor that triggers the autoimmune response:

  ➢ **Genetic predisposition:** chromosome 6 short arm (HLA-DQ/DR), Concordance rate between identical twins is 50%
  ➢ **Environmental predisposition**

Clinical presentation:

- Cardinal symptoms are (polyphagia, polydipsia , polyuria and weight loss).
- Symptoms often develop quickly over days to weeks.
- Sometimes appear after an illness.
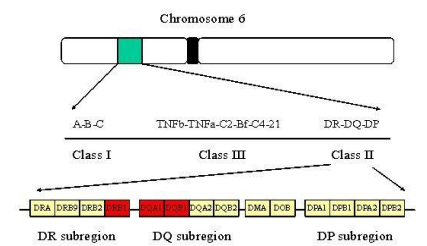- Patients often present with acute DKA(Diabetic Ketoacidosis).

TABLE 4-5 Symptoms of Diabetes Mellitus	
Symptom	**Cause**
Polyuria	Glucose in renal tubule causes osmotic retention of water, causing a diuresis
Polydipsia	A physiologic response to diuresis to maintain plasma volume
Fatigue	Mechanism unknown, but probably due to increased glucose in plasma
Weight loss	Due to loss of anabolic effects of insulin
Blurred vision	Swelling of lens due to osmosis (caused by increased glucose)
Fungal infections	Fungal infections of mouth and vagina common—*Candida albicans* thrives under increased glucose conditions
Numbness, tingling of hands and feet	Neuropathy Mononeuropathy: due to microscopic vasculitis leading to axonal ischemia Polyneuropathy: etiology is probably multifactorial

Pathogenesis:

-The human leukocyte antigen (HLA) haplotype DR3 AND /OR DR4 in chromosome 6 short arm are associated in increase susceptibility to type 1 DM

-islet cell antibody (ICA) is the result of having the gene and that will lead to destruction of the B cell by the antibody.

- Some people might have the gene and the antibody but the disease is not present because there are other factor contribute in development of the disease

That why **they don't test the people genetically** because it does not worth it. We should wait until the disease is developed.

Triggering factors for DM1:

environmental: virus : if a kid had an infection with mumps virus or coxaci B virus this will trigger for b lymphocytes to produce antibodies so when the m-RNA is reading to produce antibodies against the virus it will also stimulate the lower segment to produce antibodies so produces ICA .

Another new antibody is called insulin autoantibody or antigen (receptor) so if a child was having the three his chances of having dm1 is 70% if 2 genes 40% if 1 the 10%

There is an acute inflammation so the antibodies will attack the beta cells.

Diagnostic Tests

Diabetes is defined/diagnosed as:

-Two fasting blood glucose measurements greater than 126 mg/dL.

-Single glucose level above 200mg/dL with above symptoms.

-Increased glucose level on oral glucose tolerance testing.

-Hemoglobin A1c >6.5% is a diagnostic criterion and is the best test to follow response to therapy over the last several months.

TABLE 4-4 Diagnostic Criteria for Diabetes Mellitus

Glucose Test	Impaired Glucose Tolerance (mg/dL)	Diabetes Mellitus (mg/dL)
Random plasma	—	>200 with diabetic symptoms
Fasting	110–126	>126 on two occasions
2-hr postprandial	140–200	>200
Hemoglobin A1c (%)	5.7–6.4	>6.5

Note:

-For diagnosis:

Specific test : is for diagnosis ,when it is **positive** that means the disease is present   When it is **negative** that means you might be normal

Good in rolling in the disease

Sensitive test: for screening , when it is **positive** that mean you might have the disease

 When it is **negative** that mean for sure you are normal

Good in rolling out the disease

The test	Specificity	Sensitivity
Fasting blood sugar	+	
Random blood sugar		+
OGTT	+	+

 HbA1c: is for DM2 because it needs time for the glycation to happen in the body protein and DM1 is acute process.

Management
-Insulin is the main treatment.
Method of administration:
* Self-administered by SC injection in abdomen, buttocks, arm,leg.

* Given intravenously for emergency ketoacidosis.
 Regimens:
• Most type I diabetic patients require 0.5 to 1.0 unit/kg per day to achieve acceptable glycemic control.
• Start with a conservative dose and adjust the regimen according to the patient's glucose levels.
• Many different regimens exist, and every patient has unique needs

Intensive insulin therapy:
* Long-acting insulin: is given once daily in the evening.
 Regular insulin: is given 30 to 45 minutes before each meal, and should be adjusted according to pre-prandial home glucose measurements.

- These more aggressive therapies have been shown to significantly decrease the incidence of diabetes complications such as retinopathy and microalbuminuria when compared to prior regimens. All attempts should be made to get patients on more aggressive treatment protocols.

- With intensive insulin therapy, the risk for hypoglycemia is a serious concern.

- Alternatively, a continuous SC infusion of insulin can be given via an insulin pump. Pre-prandial boluses are given in addition to the basal infusion.

If the patient is unable/unwilling to carry out an intensive insulin program:

- Give 70/30 units before breakfast and before the evening meal for basal coverage.
- Give a short acting insulin (regular) for prandial control if necessary.
- Adjust doses according to fasting and 4 PM glucose determinations.

Inpatient management of diabetic patients (sliding scale)
- An insulin sliding scale (SSI) of regular insulin doses given according to bed- side finger-stick glucose determinations is helpful in controlling blood glucose levels in the hospital setting.
- In general, SSI should be used in addition to a regimen of intermediate-acting insulin. If given alone, hyperglycemia usually results.
- Monitor blood glucose four times per day: before meals and at bedtime.
- If the home insulin dose is unclear, or if the patient anticipates greater requirements of insulin due to an illness, use the following approach to adjust appropriate insulin doses:
  1-Take the total number of units of regular insulin that the patient required in 1 day (while on the sliding scale).
  2-Add two-thirds of this to the pre breakfast dose and one-third before dinner. It should be given as 70/30 (i.e., 70% NPH/30% regular).

Modifying insulin doses

- Physical activity—depending on the intensity of the activity, decrease insulin dosage 1 to 2 units per 20 to 30 minutes of activity.
- During illness, administer all of the routine insulin. Many episodes of DKA occur during episodes of illness.
- Stress and changes in diet require dosing adjustments.
- Patients undergoing surgery should get one-third to one-half of the usual   daily insulin requirement that day, with frequent monitoring and adjustments as necessary.

NOTE:

Beta cells transplant: it is very effective way of treatment and can cure patient but it has some problems:
            -for each patient we need pancreas of 2 brain dead body
            -the transplant will start to dysfunction after 5 years
            -the patient need to be on immunosuppressant
Stem cells : is not effective yet because they cannot control the production of insulin

Pharmacokinetics of Insulin Formulations			
Insulin formulation	**Onset**	**Peak action**	**Duration**
Lispro, aspart, and glulisine	5–15 minutes	1 hour	3–4 hours
Regular	30–60 minutes	2 hours	6–8 hours
NPH	2–4 hours	6–7 hours	10–20 hours
Glargine	1–2 hours	1–2 hours	24 hours

CLINICAL PEARL 4-11

Monitoring Glucose Levels in DM

- HbA_{1c} gives an estimate of the degree of glucose control over 2 to 3 months.
- The American Diabetes Association recommends a treatment goal of HbA_{1c} <7.0%. In general, HbA_{1c} >10% is poor control, 8.5% to 10% is fair control, 7.0% to 8.5% is good control, and <7.0% is ideal.
- The American Diabetes Association recommends keeping fasting blood glucose level <130 mg/dL and peak postprandial blood glucose <180 mg/dL.

Diabetic ketoacidosis

Patients present with :

Hyperventilation   • possibly altered mental status   • metabolic acidosis with an increased anion gap.

• Hyperkalemia in blood but decreased total body potassium because of urinary spillage.

Increased anion gap on blood testing   • Serum is positive for ketones   • nonspecific abdominal pain

-There is no prevention of DM1

-Mortality : is due to the complication of the disease .

-hypoglycemia is not a strong

mortality factor

QUESTIONS

1Among female children and adolescents, the first sign of type 1 diabetes may be:

a.   Rapid weight gain
b.   Constipation
c.   Genital candidiasis
d.   Insomnia

2. Blood sugar is well controlled when Hemoglobin A1C is:

a.   Below 7%
b.   Between 12%-15%
c.   Less than 180 mg/dL
d.   Between 90 and 130 mg/dL

3. Which of the following regimens offers the best blood glucose control for persons with type 1 diabetes?

a.   A single anti-diabetes drugs
b.   Once daily insulin injections
c.   A combination of oral anti-diabetic medications
d.   Three or four injections per day of different types of insulin

Answers

1. C: The signs and symptoms that suggest type 1 diabetes include excessive thirst, hunger, urination, weight loss, fatigue, irritability, blurred vision, and infection with candida albicans (also known as yeast infections).

2. A: A1c measures the percentage of hemoglobin that is glycated and determines average blood glucose during the two to three months prior to testing. Used as a diagnostic tool, A1C levels of 6.5% or higher on two tests indicate diabetes. A1C of 6% to 6.5% is considered prediabetes.

3. D: Because persons with type 1 diabetes do not produce insulin, they require insulin and cannot be treated with oral anti-diabetic drugs. Several injections of insulin per day, calibrated to respond to measured blood glucose levels, offer the best blood glucose control and may prevent or postpone the retinal, renal, and neurological complications of diabete

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