Diabetes mellitus

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It is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia due to defective insulin secretion or defective insulin action or both.
It is the commonest metabolic disease in man.

Type1 diabetes mellitus (T1DM)
Insulin dependent diabetes mellitus (IDDM) also known as Juvenile onset DM.
It is the commonest type in childhood. It occurs due to defective insulin secretion as a result of B-cell destruction in the pancreas(immune-mediated) usually leading to an absolute insulin deficiency.

Type 11 diabetes mellitus(T11DM)
Non-insulin dependent diabetes mellitus(NIDDM), formerly known as Adult-onset diabetes, maturity-onset diabetes(MOD).
It occurs as a result of insulin resistance with relative insulin deficiency.

Maturity –onset diabetes of the young(MODY)
Abnormal carbohydrate tolerance may also occurs in children who have a strong family history of diabetes type 11 in a pattern suggestive of dominant inheritance and require treatment with insulin.

Other types:
Secondary diabetes ;
Examples ; diabetes secondary to exocrine pancreatic diseases e.g. cystic fibrosis ,
diabetes secondary to endocrine diseases other than pancreatic diseases e.g.
Cushing syndrome .
Ingestion of certain drugs or posions.
Certain genetic syndromes; Turner's syndrome, Prader-Willi syndrome, Down syndrome.

Type 1 IDDM (T1DM)

Epidemiology;
The prevalence of T1DM among school-aged children in USA is about 1.9/1000. The frequency is highly correlated with increasing age. Males and females are equally affected and there is no apparent correlation with socioeconomic status.
Peak of presentation occurs in two age groups; at 5-7years of age and at puberty, 1st peak corresponds to the time of increased exposure to infectious agents, while the 2nd peak is correspond to the pubertal growth spurt induced by gonadal steroids which may antagonize insulin action and to the emotional stresses of puberty. Seasonal variation; more frequency appears in autumn and winter months.

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Etiology ;
There is no clear pattern of inheritance.
Family history is present in 10% of cases.
Considerable evidences now support an autoimmune basis for development of T1DM, autoimmune destruction of pancreatic islets. As there is islet cells antibodies(ICA), increased prevalence of TIDM among persons with Addison disease, Hashimoto thyroditis and perncious anemia. T1DM frequently associated with certain histocompatibility antigens HLA particularly HLA-B8 -DR3 -B/W15 and –DR4.
Epidemics of mumps, rubbela and coxsakie viral infections have been associated with subsequent increase in incidence of T1DM.
Stress and exposure to certain chemical toxins have been implicated for development of T1DM.

Pathogenesis;
In T1DM insulin serum level may be even zero, the pathogenesis includes destruction of 90% of the B-cell in the pancreas. Insulin is anabolic hormone which lead to an increase in the uptake of glucose by the liver cells and muscles, increase synthesis of lipids and proteins. So decrease insulin leads to decrease uptake of glucose and leads to hyperglycemia and also break down of lipids and proteins leads to ketone bodies formation, thus chronic hyperglycemia more than 180mg/dl leads to glucosuria which leads to polyurea and polydypsia and muscle wasting and dehydration, ketoacidosis leads to hyperventilation with lethargy and sometimes coma and death ensue in few months.

Clinical manifestations;
The natural history includes 4 distinct stages: (1) preclinical β-cell autoimmunity with progressive defect of insulin secretion, (2) onset of clinical diabetes, (3) transient remission "honeymoon period," and (4) established diabetes associated with acute and chronic complications and decreased life expectancy.
Early presentation; acute onset duration varies but it often less than one month these include ; polyurea , polydypsia, weight loss, polyphagia, nocturia, secondary enuresis which means enuresis in a previously toilet-trained child, pyogenic infections of the skin and monilial vaginitis in teenage girl.
Late presentation; ketoacidosis may be responsible for initial presentation of many diabetic patients, history of polyurea , polydypsia, nausea, vomiting, lethargy, poor concentration(defective school performance), abdominal pain with or without acute abdomin, hyperventilation with fruity odor, drowsiness from disorientation to coma and signs of dehydration.

Diagnosis;
Depends on clinical and laboratory findings;
random blood sugar more than 200mg/dl is diagnostic, urine test glucosuria.
Differential diagnosis;
Urinary tract infection here there is frequency not polyuria.
Compulsive water drinking, pneumonia, meningitis, acute abdomen , salisylate poisoning and renal glucosuria.

Managements; include

1. start treatment i.e. insulin replacement.
2. monitoring and follow up
3. education (diet and exercise)
4. psychological
5. management of complications

Insulin replacement;

If the child is in good condition and there is no vomiting nor dehydration with good tolerance to food and blood glucose level 250-400mg/dl start insulin .

Insulin of three types ; short acting and medium acting and long acting.

Short acting ; onset (20-30minutes) , peak action in 2hrs-4hrs or 8hrs , duration (6-8hrs) with average dose 1unit/kg/24hrs divided into 3times a day before each meal to prevents hypoglycemia.

Medium acting ; onset (1-4hrs) , peak action(4-12hrs) , duration of action 16-18hrs , so it is given once dialy.

Regimen treatment;

Two doses regimen ; is the most popular for school-aged children , the procedure is to start with short acting insulin in the first 1-2days 1unit / kg /24hrs, to be given 3times / day before meals and then check up if the codition is ok move to the combination of short acting and medium acting insulin.

The dose is regulated as 1unit /kg/24hrs , 2/3 of the dose is given in the morning before breakfast and the remaining 1/3 of the dose is given before the dinner at evening.

Multiple doses regimen; it is composed of multiple injections of short acting insulin before meals in addition to long or medium acting insulin injection given at bed time.

Long acting insulin; onset (4-6hrs), peak action (8-20hrs) , duration(24-36hrs), the advantages of this type is the more flexibility in timing meals and is good for individuals with variable day to day activities , while it's disadvantage is difficult compliance, it is more suitable for adolescents than young children.

Family education ;

you should explain to the family , the nature of the diabetes mellitus, the control of the disease and it's complications .

Insulin administration; learn them how to give insulin dose, time , site of injection.

Adjustment of the dose according to the level of blood sugar, illness, exercise and hypoglycemic episodes.

Learn them how to do urine and blood testing.

Diet ; there should be no much restriction of diet because the child is in a period of growth , so you should stress on regular meals and not miss any meal especially supper because it may lead to hypoglycemia. You must link the diet with exercise , encourage small frequent meals 3 main meals and 3 snacks. 50-60% of calories from carbohydrate, encourage to take high fiber containing food, vegetables fruits and restrict highly refined sugar.

Hypoglycemia ;

In children ; fasting plasma glucose level below 50mg/dl is hypoglycemic.
Symptoms and signs ; sweating, pallor, fatigue, hunger, tachycardia and nervousness.
Central nervous system dysfunction is manifested by headache, irritability, alteration in behavior, drowsiness, mental confusion, psychotic behavior seizures and coma.
Hypoglycemia in diabetic children occurs due to ;

1. inadequate carbohydrate intake.
2. excessive exercise in relation to insulin intake.
3. defective counter-regulatory response; abnormal glycogen response to fall in serum glucose with abnormality in catecholamine response.

Treatment of hypoglycemia ;
If **mild** to **moderate**; administer sugar drink or glucose tablets 5-15gm, while if **sever** and consciousness is impaired ; give glucose IV 10-30% 200-500mg/kg or glucagon 0.5mg.
Remission phase ; after diagnosis of TIDM the child may get better with a period of 2-3months due to endogenous insulin, so he need less insulin and he may have hypoglycemia(honey-moon period). Some people use herbs during this period thinking that the child is cured but actually it is the remission period then after they bring the child with ketoacidosis.
Exercise ; there is no form of exercise should be forbidden to the diabetic child, regular exercise tend to improve glucoregulation by increase insulin recepters, through increase utilization of glucose by the muscles. In poorly controlled patients vigorous exercise may cause ketoacidosis due to exercised induced increase in the counter-regulatory hormones.

Aim of controlling T1DM;

1. achieve normal life style i.e. should remain in school.
2. prevent complications.
3. normal physical and mental development and education.
4. relieve symptoms of hyperglycemia e.g. nocturia
5. avoid hypoglycemia by fixed regular meals.

Assessment and maintenance of control (follow up)
After hospitalization the patient should be followed by diabetic clinic weekly then every 2weeks, and then monthly, looking for the following;

1. the general well being of the child, his general condition, his activities, school attendance, night mares, and nocturia.
2. satisfactory linear growth and weight gain.
3. home blood sugar monitoring, it should be between 90-180mg/dl and urine test for ketones.
4. measurement of the level of glycosylated hemoglobin which is good indicator for long term glycemic control, it is resulting from non-enzymatic reaction between glucose and hemoglobin (Hb_{A1c}), (normally 5% of adult Hb is glycosylated) , it reflects the average blood glucose level in the last 2months , it should be measured every 3months, and it should not be more than 7% (good control), but in case of poor control it may reach 12%.
5. complete physical examination ; at least once/ year about pubertal stage, thyroid goiter, other auto-immune diseases e.g. chronic lymphocytic thyroiditis associated with celiac disease (6% of T1DM children have celiac disease).
6. absence of nocturia indicate good control.

7. evaluation for the presence of diabetic complication e.g. ophthalmological examination (after 6years) to look for microangiopathy in the retina. Evaluation of reflexes and sensation , evaluation of renal system for persistant proteinurea and albuminurea, for hypertension and peripheral pulses, macroangiopathy, and tendon reflexes for peripheral neuropathy, look for skin ulceration, flexion deformities, the collagen is affected, the skin become adhere to bone , joint is not affected, controlling retinopathy by laser if indicated to avoid blindness.

Complication of childhood diabetes;

Acute complications;

1. hypoglycemia.
2. ketoacidosis
3. injection site problems : lipohypertrophy due to insulin injection, lipoatrophy due to Ag-Ab reaction
4. skin lession :the site of injection has suspitability for infection as canidiasis ,pustules , thick skin side effect of insulin treatment as necrobiosis , lipodiabetoconum
5. hepatomegaly : fluctuation between hypo & hyper glycemia in poorly controlled T1DM patient lead to glycogen deposits in the liver leading to hepatomegaly
6. joint contracture : finger flexion deformity with adherent skin
7. impaired vision : as result of transient change in osmotic pressure of the lens leading to early blindness.
8. growth failure : occur in poorly controlled diabetic , with association to hypothyrodism.

Long term complication of IDDM

1. diabetic retinopathy : simple or proliferative
2. diabetic neuropathy : tingling and numbness with loss of sensation of pain in the calf , so check reflex & sensation especially postural sensation
3. diabetic nephropathy : check the blood pressure and for protienurea
4. arterial diseases : cardiac diseases perphral arterial disease
5. diabetic autonomic neuropathy : as attacks of postural hypotension and nocturnal diarrhea

<u>These complications depend on :</u>
Duration (not occur before 5 years)
Controlling of diabetes
Genetic predisposition

Brittle diabetes ; implies that the control of blood sugar fluctuates wildly and rapidly despite frequent adjustment of the dose of insulin.
Somogyi phenomenon ; hypoglycemia begetting hyperglycemia is believed to be due to outpouring of counter-regulatory hormones in response to insulin induced hypoglycemia. Hypoglycemic episode manifested as late nocturnal or early morning sweating, night terrors and headache alternating rapidly within 4-5hrs with ketosis hyperglycemia and glcosuria.
Dawn phenonmen; in which early morning elevation of blood glucose level occur between 5-9 a.m. without preceding hypoglycemia.

Diabetic ketoacidosis

It occurs in ; (causes)
1. established case of diabetes, but miss insulin injection for 2-3days.
2. with sever stress condition ; trauma, vomiting, infection, and psychological condition.
3. it may be the initial presentation of the diabetes mellitus.

Pathophysiology ; it is due to increase catabolism with low level of insulin.
Clinical picture ; Symptoms ; polyurea, thirst, weight loss, nausea, vomiting, abdominal pain and blurred vision. Signs ; dehydration, hypotension, tachycardia, hyperventilation, smell of acetone, hypothermia, confusion, drowsiness and coma.
Biochemical finding ; diabetic ketoacidosis ; exist when there is ; hyperglycemia i.e. blood glucose level 300mg/dl and above, hyperketonemia and ketonurea, acidosis PH is less than 7.2. Bicarbonate less than 15mEq/L , Pottasium total level is depleted but normal serum level.

Management;
Should look for precipitating factor e.g. miss insulin injection, infection screen should be done, do biochemical tests. The aim is to correct dehydration and maintain electrolyte balance.
Treatment ;
Nothing by mouth , start IVF assume 10% dehydration , calculate the deficit ;
deficit = (body weight in gm x 10%) x100. replace the deficit within 24hrs not more than 40% fluid deficit in the first 6hrs.
Calculate the maintenance ; maintenance = 1500 x surface area (m^2)
Total requirement for 24hrs = (deficit + maintenance), must be given in the 36-48hrs not more than 4 liters in 24hrs. Use normal saline as initial fluid infusion. Change to 4.3% dextrose 1/5 normal saline when blood sugar below 300mg/dl , reduce IVF accordingly till oral fluids are commenced.
Insulin ; use soluble insulin , give 0.1U/kg or 0.2U/kg 2hrly until blood glucose level below 300mg/dl , then change to 6hrly sliding scale giving insulin according to blood sugar and ketones +sugar in urine.

Blood glucose Mg/dl	Urine glucose Gm/100ml	Ketoneuria	Insulin U/kg
>350	5	+	0.5
250-350	5	-	0.4
	2	+	0.4
170-250	2	-	0.3
	1	+	0.3
90-170	1	-	0.2
<90	0-0.5	-	0.1

Bicarbonate is not to be used unless the PH is 7.1 or less.
1-2 mmol/kg should be infused over 2hrs .
Ensure urine output , to give potassium KCL 10mEq/500ml of fluid.
Remember severely ill patient do not require more rapid metabolic correction.

Complications of DKA;
1. Immediately after treatment cerebral odema occur with rapid correction
2. cerebral thrombosis due to dehydration
3. respiratory distress & circulatory failure due to dehydration .