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Pharmacotherapy type 2 Diabetes Mellitus

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I. INTRODUCTION:-

Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic disorders in which there are **high blood sugar** levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger.[2] If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycaemic state, or death.[3] Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes.

Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced.[8] There are three main types of diabetes mellitus.

Type 1 DM results from the pancreas's failure to produce enough insulin.This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes".The cause is unknown.

Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop.[9] This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes" .The most common cause is excessive body weight and insufficient exercise.

Gestational diabetes is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels.

Prevention and treatment involve maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. Control of blood pressure and maintaining proper foot care are important for people with the disease. Type 1 DM must be managed with insulin injections. Type 2 DM may be treated with medications with or without insulin. Insulin and some oral medications can cause low blood sugar. Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 DM. Gestational diabetes usually resolves after the birth of the baby.

As of 2015, an estimated 415 million people had diabetes worldwide, with type 2 DM making up about 90% of the cases. This represents 8.3% of the adult population, with equal rates in both women and men. As of 2014, trends suggested the rate would continue to rise. Diabetes at least doubles a person's risk of early death. From 2012 to 2015, approximately 1.5 to 5.0 million deaths each year resulted from diabetes. The global economic cost of diabetes in 2014 was estimated to be US$612 billion. In the United States, diabetes cost $245 billion in 2012.

The **classic symptoms** of untreated diabetes are weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 DM, while they usually develop much more slowly and may be subtle or absent in type 2 DM.

Several other signs and symptoms can mark the onset of diabetes although they are not specific to the disease. In addition to the known ones above, they include blurry

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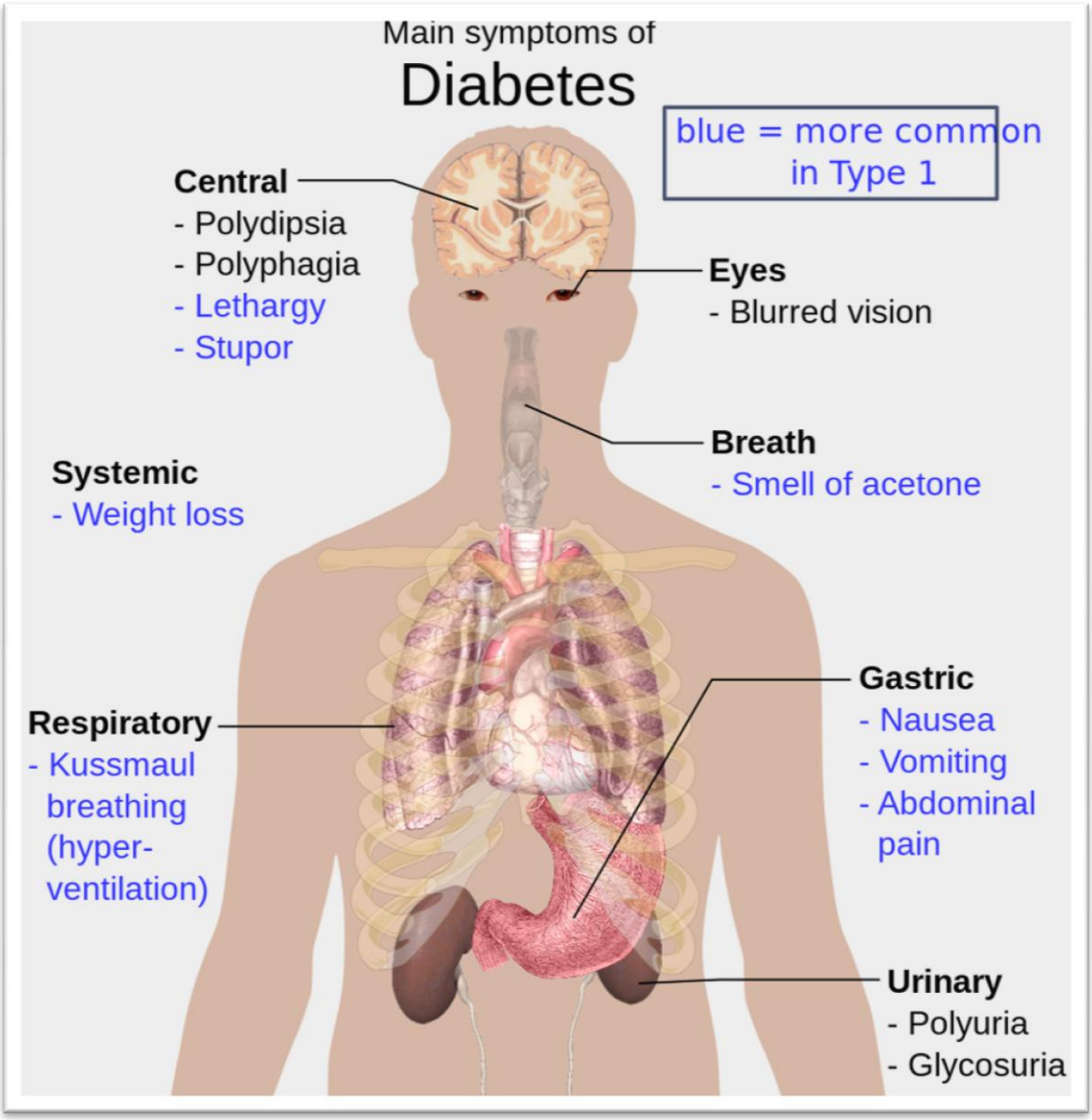

vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermatomes.

II. CASE STUDY:-

A 45 year old woman visited her physician with complaints of increased appetite and thirst with higher frequency of urination. She also had the symptoms of diminished or impalpable pulses in the feet, besides gangrene of the feet. Her fasting blood glucose level was 160 mg/dl, with no presence of glucose or ketone bodies in urine. Her laboratory finding on the oral glucose tolerance test are as follows.

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	FASTING	AFTER 2HRS
BLOOD GLUCOSE	**155**	**205**
NORMAL REFRENCE	**<110**	**<140**
URINE GLUCOSE	**-VE**	**+VE**
KETONE BODIES	**-VE**	**-VE**

A 30 year oldmale had the complaints of increased frequency of urination and urinary tract infection. On routine examination, his urine was found to contain glucose and ketone bodies. He had a random blood glucose concentration 190 mg/dl. His laboratory data on OGTT are given below.Metformin is prescribed. But not get much glucose tolerance happened in patient.

	FASTING	AFTER 2HRS
BLOOD GLUCOSE	**150**	**240**
NORMAL REFRENCE	**<110**	**<140**
URINE GLUCOSE	**-VE**	**+VE**
KETONE BODIES	**-VE**	**-VE**

A 60 year old diabetic woman who had been on insulin for past 5 years visited her physician for a routine check up. She informed that she was scrupulously following the dietary advise and had never missed her insulin injection. The following are the laboratory data of this woman.

PARAMETER	SUBJECT	REFRENCE RANGE
HbA1c	9%	3-5%
BLOOD GULCOSE FASTING	100mg/dl	70-110mg/dl
BLOOD GLUCOSE POST PRANDIAL & BLOOD UREA	140-160mg/dl & 25mg/dl	160mg/dl & 15-40mg/dl

A 25 year old healthy pregnant woman on routine examination was found to contain glucose in her urine. Her random blood glucose was 150 mg/dl. She recalled that before pregnancy her random blood glucose was <110 mg /dl and never she had a glucose excreted into urine. Her mother was a diabetic patient. During her next visit a month later, her fasting and post prandial glucose were respectively 130mg/dl and 180 mg/dl with traces of glucose in urine.

A 78 year old woman was found by a neighbour in drowsy and unwell. She had an upper respiratory tract infection several weeks previously and had been very slow to recover from this. She had een thirsty over period.The only past history was diabetes mellitus and it was controlled by diet.On examination she was dehydrated but her breath did not smell of ketones. What is your diagnose ??

-:PICO:-

	PATIENT	INTERVENTION	COMPARISON	OUTCOME
CASE 1	Increased appetite and thirst with high urination and impalpable pulse	Give antibiotics with hypoglycemic drug metformin 1mg BD and do exercise	After Tx patient blood glucose level decrease	Decrease the blood glucose level and controlled micturition and frequency of urination
CASE 2	Increase the frequency of urination and UTI	Give oral antibiotic and hypoglycemic drug Liragliptine and do exercise	Before Tx patient was tolerated for metformin After Tx of DPP4(-) well controlled glucose	Decrease the blood glucose level and controlled thirst. Effective in DM type 2
CASE 3	Insulin therapy for last 5 years &	Give hypoglycemic drug Pramlinitide	Before Tx patient got insulin monotherapy	Decreased blood glucose level in blood

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	Increase level of glucose in blood	subcutaneous injection	but not controlled After Tx with Amylin analogue controlled glucose level	effective in DM type 2
CASE 4	Past history of diabetes and Glucose in urine	Give oral hypoglycemic drug	After Tx pt. glucose level is in controlled	Decreased blood glucose level in patient and also in urine
CASE 5	Past history of diabetes mellitus and very dehydrated with no smell of ketones and respiratory tract infection	Replacement of fluid and electrolyte losses and insulin use for glucose restoration via injections and antibiotics	Before Tx patient was supposed to b go into diabetic coma After Tx patient blood glucose level was in controlled and decrease ketone bodies level in blood	Reduced dehydration and feel well and controlled glucose level

III. RESEARCH DESIGN & LEVEL OF EVIDENCE

CASE STUDY 1 :- CASE CONTROL STUDY (LEVEL 3)
CASE STUDY2:-CASE SERIES (LEVEL 4)
CASE STUDY 3:-RCT (LEVEL 1)
CASE STUDY 4:-META ANALYSIS OF LEVEL 3 SUDIES (LEVEL 3)
CASE STUDY 5:-CASE REPORT (LEVEL 5)

-:SEARCHING METHODS:-

SEARCH ENGINE USED :- GOOGLE
DATABASES SEACHED:-PubMED
SEARCH FILTER USED:-UNFILTERED

IV. -:CONCLUSION:-

TYPE 2 DM IS A METABOLIC DISORDER THAT CAN BE PREVENTED THROUGH LIFESTYLE MODIFICATION, DIET CONTROL AND CONTROL OF OVER WEIGHT AND OBESITY. EDUCATION OF POPULACE IS STILL KEY TO THE CONTROL OF THIS EMERGINF EPIDEMIC. NOVEL DRUGS ARE BEING DEVELPOED, YET NO CURE IS AVAILABLE IN SIGHT FOR THE DISEASE, DESPITE NEW INSIGHT INTO THE PATHOPHYSIOLOGY OF THE DISEASE. MANAGEMENT SHOULD BE TAILORED TO IMPROVE THE QUALITY OF THE LIFE OF INDIVIDUALS WITH TYPE 2 DM.

DIABETES MELITUS TYPE 2 MAY CAUSE DIABETIC NEUROPATHY. IT IS A CLINICAL SYNDROME CHARACTERIZED BY PERSISTENT ALBUMINURIA THAT IS CONFIRMED ON THAT AT LEAST 2 OCCASION 2-6 MONTHS APART A RESTLESSNESS DECLINE IN THE GLOMERULA FILTRATION RATE AND ELEVATED ARTERIAL BLOOD PRESSURE. DIABETIC NEPHROPATHY IS LEADING CAUSE OF CHRONIC RENAL FAILURE.

DIABETES MAY LEADS TO END STAGE RENAL FAILURE. MICRO ALBUMINURIA MAY OCCUR. THIS PHASE INDICATES INCIPIENT DIABETIC NEPHROPATHY AND CALLS FOR AGGRESSIVE MANAGEMENT AT WHICH STAGE THE DISEASE MAY BE POTENTIALLY REVERSIBLE.

THE PRESET STUDY SUPPORTS THE HYPOTHESIS THAT UPREGULATION OF MCP-1 GENE EXPRESSION BY PERSISTENT HYPERGLYCEMIA IN TYPE 1 DIABETES PATIENT RESULT IN THE RECRUITMENT OF MONOCYTESS INTO THE KIDNEY, POSSIBLY CONTRIBUTING TO THE DEVELOPMENT OF DIABETIC NEPHROPATHY. MOREOVER THESE RESULT SUGGEST THAT THE CAUSATIVE ROLE OF POOR GLYCEMIC CONTROL IN DIABETIC NEPHROPATHY IS MEDIATED BY INCREASED OXIDATIVE STRESS.

THESE FINDINGS ARE POTENTIALLY IMPORTANT FROM A FUNDAMENTAL STAND POINT BECAUSE THEY INDICATES A PATHGENIC ROLE OF MCP-1 IN THE EVOLUTION OF DIABETES MELLITUS COMPLICATIONS. FROM A PRACTICAL PRESPECTIVE THESE RESULTS RAISE THE POSSIBILITY THAT VIT E MAY PROVIDE A NOVEL FORM OF THERAPY FOR PREVENTION OF MICROVASCULAR COMPLICATIONS.

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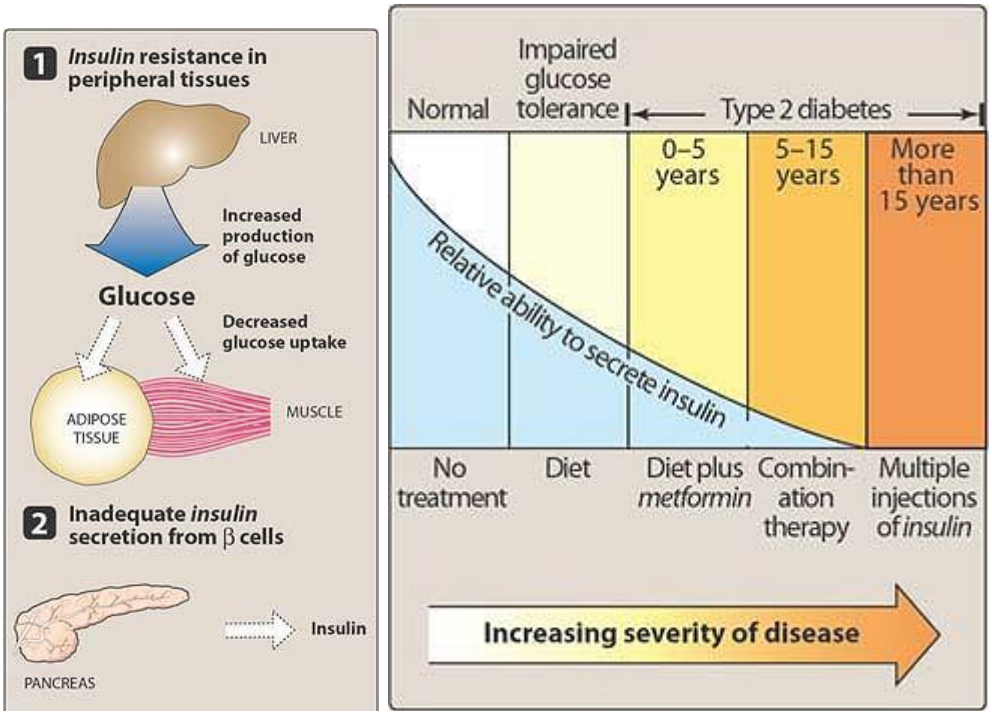
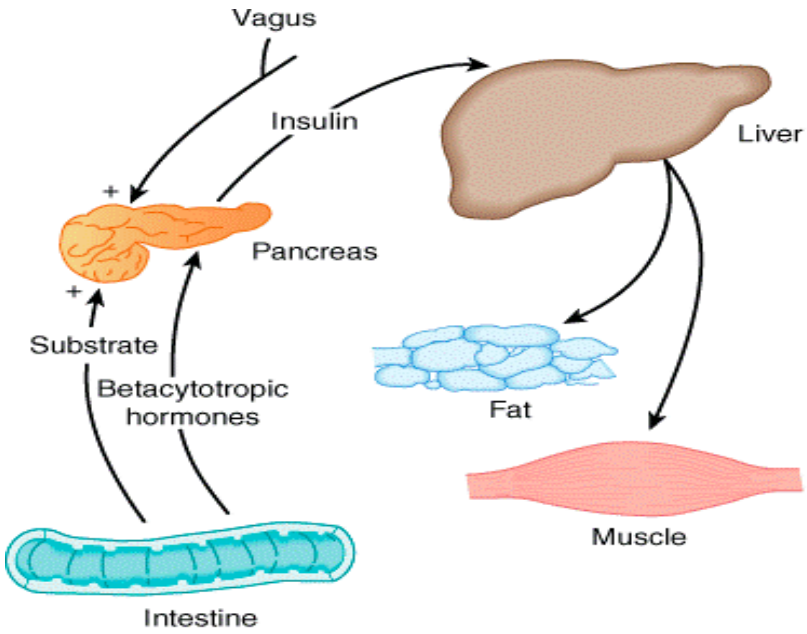
OBESITY AND SECONDARY LIFE SYLE CHANGE WERE FOUND TO BE ASSOCIATED WITH TYPE 2 DM. THERE WAS SIGNFICANT POSITIVE CORRELATION BETWEEN FASTING BLOOD GLUCOSE, HbA1c AND C PEPTIDE STATUS OF TYPE 2 DM. ABNORMALITIES IN LIPID PROFILE WAS FOUND TO BE ASSOCIATED WITH ALL THE TYPES OF DM. PROPER INTERVENTION PROVED TO BE EFFECTIVE IN CONTROLLING ALL TYPES OF DM AND ASSOCIATED MICROVASCULAR AND MACROVASCULAR COMPLICATIONS.

A SIGNIFICANT POSITIVE CORRELATION WAS OBSERVED BETWEEN APOLIPOPROTEIN-A1 AND HDL-C WELL AS BETWEEN APOLIPOPROTEIN-B AND LDL-C. THE LEVELS OF CRP WERE FOUND TO BE INCREASED IN DIABETIC PATIENTS WITH HEART DISEASES. INCIDENCE OF HEART DISEASE AMONG THE DM IN PRESENT STUDY WAS FOUND TO BE ASSOCIATED WITH EACH OF THE LIPID PARAMETERS NAMELY TOTAL CHOLESTEROL, TGS AND LDL AND HDL. AND ALSO INCREASE IN HB LEVEL WAS OBSERVED IN ALL THE TYPES OF DIABETES AFTER INTERVENTIONS.





Source: Katzung BG, Masters SB, Trevor AJ: *Basic & Clinical Pharmacology, 11th Edition:* http://www.accessmedicine.com

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