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CHILDHOOD OBESITY CAN LEAD TO TYPE 2 DIABETES AND HIGH CHOLESTEROL IN ADOLESCENTS

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ABSTRACT
Childhood obesity is the most prevalent nutritional disorder among children and adolescents worldwide. Approximately 43 million individuals are obese, 21-24% children and adolescents are overweight and 16-18% of individuals has abdominal obesity. Obesity increases the risk of diabetes type 2 and high cholesterol in children and adults. It predisposes the individual to insulin resistance and type 2 diabetes, hypertension, hyperlipidemia, liver and kidney diseases and causes reproductive dysfunction in adults. Factors, such as eating habits, genetics, environment, metabolism and lifestyle play an important role in the development of obesity. Over 90% of obesity cases are idiopathic and less than 10% are associated with genetic and hormonal causes. Obesity occurs when the body consumes more calories than it burns, through overeating and under exercising. The symptoms of obesity include breathing disorders, sleep apnea, chronic obstructive pulmonary disease, certain types of cancer such as prostate, bowel, breast and uterine, coronary heart disease, diabetes (type 2 in children), depression, liver and gallbladder problems, gastro-esophageal reflux disease, high blood pressure, high cholesterol, stroke and joint diseases such as osteoarthritis, pain in knees and lower back. Environmental, behavioral such as consumption of foods, genetic and family factors contribute to pediatric obesity. Obesity can be countered through lower calorie consumption, weight loss and diet programs, as well as increased physical activity. A number of endogenous molecules, leptin, are known to affect body weight. These molecules serve as potential targets for the pharmacological manipulation of obesity. Sibutramine and orlistat are primarily used for the treatment of adult obesity, which produces modest weight loss. For children and obese adolescents, metformin is used in the case of insulin resistance and hyper-insulinemia. Bariatric surgery is performed for the treatment of severe childhood obesity. The causes, symptoms, prevention and treatment of pediatric obesity and how it causes diabetes type 2 and high cholesterol are described in the present review.

KEY WORDS: Childhood, Obesity, Type 2 Diabetes, Cholesterol, Adolescents.

INTRODUCTION
OBESITY
A medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health. People are generally considered obese when their body mass index (BMI), a measurement obtained by dividing a person's weight by the square of the person's height, is over 30 kg/m^2, with the range 25–30 kg/m^2 defined as overweight[7]. Obesity increases the likelihood of various diseases and conditions, particularly cardiovascular diseases, type 2 diabetes, obstructive sleep apnea, certain types of cancer, osteoarthritis and depression.Obesity is most commonly caused by a combination of excessive food intake, lack of physical activity, and genetic susceptibility[7].A few cases are caused primarily by genes, endocrine disorders, medications or mental disorders [8].Obesity is mostly preventable through a combination of social changes and personal choices.Changes to diet and exercising are the main treatments. Diet quality can be improved by reducing the consumption of energy-dense foods, such as those high in fat and sugars, and by increasing the intake of dietary fiber[7].

DIABETES
Diabetes means a disease in which the body's ability to produce or respond to the hormone insulin is impaired, resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood.Insulin is a peptide hormone produced by beta cells of the pancreatic islets, and it is considered to be the main anabolic hormone of the body [1].It regulates the metabolism of

carbohydrates, fats and protein by promoting the absorption of, especially, glucose from the blood into fat, liver and skeletal muscle cells [2]. In these tissues the absorbed glucose is converted into either glycogen via glycogenesis or fats (triglycerides) via lipogenesis, or, in the case of the liver, into both. Glucose production (and excretion into the blood) by the liver is strongly inhibited by high concentrations of insulin in the blood[3].

Diabetes mellitus: - Diabetes mellitus is derived from:
- The Greek word *diabetes* meaning siphon - to pass through.
- The Latin word *mellitus* meaning honeyed or sweet.

This is because in diabetes excess sugar is found in blood as well as the urine[6].It is a metabolic disorder characterized by hyperglycemia, glycosuria, hyperlipidemia, negative nitrogen balance[4]. High glucose level is because the body produces inadequate insulin or the body cells do not respond properly to the insulin produced by the body[5].

TYPES OF DIABETES MELLITUS
1) Type 1 Diabetes (Insulin-dependent diabetes mellitus / juvenile or early onset diabetes mellitus)
In this type of diabetes, the body does not produce enough insulin, that is, the person's pancreas stop producing insulin.it is caused by the immune system destroying the cells in the pancreas that make insulin. It is an autoimmune disease. The antibodies that destroy beta cells are detectable in blood. Type 1 diabetes usually develops before a person is 40-years-old i.e., in early adulthood or teenage. Patients with type 1 diabetes will need to take insulin injections for the rest of their life. Type 1 diabetes can develop quickly, over weeks or even days[4,5].

2) Type 2 Diabetes (Non-Insulin-dependent diabetes mellitus / maturity onset diabetes mellitus)
In Type 2 Diabetes, the body produces enough insulin but cannot use it properly or the cells in the body display insulin resistance.There are no loss or moderate reduction in beta cell mass. Some people may be able to control their type 2 diabetes symptoms by losing weight, following a healthy diet, doing plenty of exercise, and monitoring their blood glucose levels.Type 2 diabetes may develop gradually [4,5].

3) Gestational Diabetes
This type affects females during pregnancy. Some women have very high levels of glucose in their blood, and their bodies are unable to produce enough insulin to transport all of the glucose into their cells, resulting in progressively rising levels of glucose.The majority of gestational diabetes patients can control their diabetes with exercise and diet. Between10% to 20% of them will need to take some kind of blood-glucose-controlling medications. Undiagnosed or uncontrolled gestational diabetes can raise the risk of complications during childbirth.This may or not disappear after delivery[5].

SIGNS AND SYMPTOMS OF DIABETES
- Increased frequency of urination, especially at night.
- Frequently feeling thirsty.
- Weakness and fatigue.
- Unexplained loss of weight.
- Genital itching or thrush.
- Blurred vision.
- Increase in healing time of cuts and wounds.

BLOOD GLUCOSE CHART

Mg/DL	Fasting	After Eating	2-3 hours After Eating
Normal	80-100	170-200	120-140
Impaired Glucose	101-125	190-230	140-160
Diabetic	126+	220-300	200 plus

CHOLESTEROL
Cholesterol is derived from
- the ancient Greek word *chole-(bile)* and
- The word *stereos* (solid).

Followed by the chemical suffix-*ol* for an alcohol, is an organic molecule.It is a sterol (or modified steroid), a type of lipid molecule, and is biosynthesized by all animal cells, because it is an essential structural component of all animal cell membranes; essential to maintain both membrane structural integrity and fluidity[9].

Cholesterol is a type of fat (lipid) in our blood. Our cells need cholesterol, and our body makes all it needs. But it is also get from the food that we eat. If too much cholesterol is there it starts to build up in arteries (Arteries are the blood vessels that carry blood away from the heart). This is called hardening of the arteries,

or atherosclerosis. It is the starting of some heart and blood flow problems. The buildup can narrow the arteries and make it harder for blood to flow through them and also leads to dangerous blood clots and inflammation that can cause heart attacks and strokes[10].

Different types of cholesterol are

- LDL (Low Density Lipoprotein) is the **"bad" cholesterol**. Because it takes cholesterol to the arteries, where it may collect in artery walls. Too much cholesterol in arteries may lead to a buildup of plaque known as atherosclerosis. This can increase the risk of blood clots in arteries. If a blood clot breaks away and blocks an artery in heart or brain, it may have a stroke or heart attack. So it can raise risk of heart disease, heart attack, and stroke. Plaque

buildup may also reduce blood flow and oxygen to major organs. Oxygen deprivation to organs or arteries may lead to kidney disease or peripheral arterial disease, in addition to a heart attack or stroke.

- HDL (Low Density Lipoprotein) is the **"good" cholesterol**. Because it transports cholesterol to liver for expelling from the body. HDL helps rid the body's excess cholesterol. So it's less likely to end up in arteries and is linked to a lower risk of heart disease, heart attack, and stroke[10,11].

Total cholesterol is the sum of blood's cholesterol content including HDL, LDL and very low density lipoprotein.

NORMAL RANGE

National Cholesterol Education Program Cholesterol Guidelines	Desirable	Borderline High	High
Total Cholesterol	Less than 200	200 – 239	240 and higher
LDL Cholesterol (the "bad" cholesterol)	Less than 130	130 – 159	160 and higher
HDL Cholesterol (the "good" cholesterol)	50 and higher	40 – 49	Less than 40
Triglycerides	Less than 200	200 – 399	400 and higher

OBESITY IN CHILDREN AND ADOLESCENTS
The incidence of overweight and obesity among children has increased dramatically in recent decades, with about one-third of children in the U.S. currently being either overweight or obese. Being overweight in early childhood increases risk for later obesity. There is also increasing incidence of type 2 diabetes (T2D) among youth in recent years, with obesity and family history of T2D generally present. Lower income and ethnic minority status are associated with both obesity and T2D in youth. Most youth with T2D do not achieve optimal glycemic control, and are at high risk for later health complications. Obesity and T2D represent significant public health issues with potentially great personal and societal cost[12].

OBESITY DEFINITION
Obesity is typically defined as having an excess of body weight caused by a chronic caloric imbalance with more calories being consumed than expended each day. Body mass index, or BMI, is a measure used to classify children as overweight or obese[12].

EPIDEMIOLOGY
Recent estimates from the National Health and Nutrition Examination Survey indicate that:

o Approximately one-third of children in the United States are overweight or obese, with approximately 17% meeting criteria for obesity.

o Worldwide, approximately 43 million preschool-aged children have been estimated to be overweight and obese, and 92 million are considered to be at risk of overweight.

o Children from African American and Hispanic cultures are at an increased risk for being overweight or obese.

o A recent national longitudinal study in the US indicated that 12.4% of children in kindergarten were obese and another 14.9% overweight; overweight 5-year-olds were four times more likely than normal weight children to become obese later in childhood at age 14, and among children who later became obese, half were overweight at baseline and three-quarters were above the 75th %ile for BMI[12].

COMORBIDITIES
Children who are obese are at a significantly elevated risk for adverse health outcomes including both medical and psychological problems. The most common medical co-morbidities associated with obesity include metabolic risk factors for T2D including high blood pressure, high cholesterol, impaired glucose tolerance, and metabolic

syndrome. Orthopedic problems, sleep apnea, asthma, dental problems, and fatty liver disease are also common comorbidities of obese children and adolescents [12].

BODY MASS INDEX
The BMI is defined as the body mass divided by the square of the body height, and is universally expressed in units of kg/m^2, resulting from BMI is proportional to the mass and inversely proportional to the square of the height. Mass in kilograms and height in meters[13]. The formula is:

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

| BMI of less than 18.5 **Underweight** |
| BMI of 18.5 - 25 **Healthy weight** |
| BMI of 25 - 30 **Overweight** |
| BMI of over 30 **Heavily overweight** |

CAUSES OF CHILDHOOD OBESITY
Pediatric or childhood obesity is the most prevalent nutritional disorder among children and adolescent's worldwide. Obesity occurs when the body consumes more calories than it burns through overeating and under-exercising. Childhood obesity is caused by excessive food consumption and drinking of high-calorie sweetened beverages, no exercise or physical activity, as well as genetic factors. Consumption of fatty foods and a high sugar diet, as well as tobacco smoking, and no exercise qualify as the main reasons for obesity among children and adults. The body weight is regulated by various physiological mechanisms that maintain the balance between energy intake and energy expenditure. These regulatory systems under normal conditions.Therefore, factors that can raise energy intake or decrease energy expenditure cause obesity in the long term. Genetic factors have a significant impact on individual predisposition, but other factors of behavior and environment may also play a role in childhood obesity[14].

TREATMENT OPTIONS FOR CHILDHOOD OBESITY
There are currently three main treatment modalities for childhood obesity: lifestyle modifications (which aim to induce negative energy balance through diet, exercise, counseling, or combinations of these), medications, and bariatric surgery.

- **Lifestyle modifications**
Lifestyle modifications include exercise, diet, counseling, and combinations of these.
- **Exercise**: Obesity has a complex development, involving environmental, physiologic, and genetic factors, the basic cause of this condition is an imbalance between energy intake and energy expenditure. Physical activity is the only modifiable component of the energy expenditure portion of the energy balance equation. Consequently, increasing physical activity has the potential to improve weight loss and maintenance.

- **Diet**: While dietary modification is needed to reduce caloric intake, specific changes in diet composition and content are controversial.Low-fat diets (18–40% caloric intake from fat) used alone, can result in modest reduction in body weight.Low-fat diets can improve weight loss.

- **Counseling**: Behavior modification targeting the obese child and the family is integral to weight management, but few data exist on counseling as the sole treatment modality. Counseling provides awareness among the parents and children about the harmful effects of obesity related diseases.

- **Combination of diet, exercise, and/or counseling**: Combinations of diet, exercise and counseling are generally thought to be more effective for pediatric weight management than each component alone[24].

✛ Anti - obesity drugs
Mechanism of action
Current and potential anti-obesity drugs may operate through one or more of the following mechanisms:

- Catecholamine releasing agents such as amphetamine, phentermine, and related substituted amphetamines (e.g., bupropion) which act as appetite suppressants are the main tools used for the treatment of obesity.
- Increase of the body's metabolism.
- Interference with the body's ability to absorb specific nutrients in food. For example, Orlistat (also known as Xenical and Alli) blocks fat breakdown and thereby prevents fat absorption.
  The OTC fiber supplements glucomannan and guar gum have been used for the purpose of inhibiting digestion and lowering caloric absorption.

❖ Orlistat
It interferes with intestinal fat absorption. Its primary function is preventing the absorption of fats from the human diet by acting as a lipase inhibitor, thereby reducing caloric intake. Orlistat acts by decreasing hydrolysis of ingested triglycerides and reducing gastrointestinal absorption of fat by approximately 30% via inhibition of intestinal lipases. Owing to its negligible absorption in the small intestine, orlistat is regarded as safe; however, unabsorbed fat excreted in feces can cause transient diarrhea, abdominal discomfort, and flatulence.

❖ Sibutramine
It is a central serotonin and norepinephrine reuptake inhibitor used for treatment of obesity in adolescents aged 16 years or older. It is an anorectic agent. Used to produce appetite suppression for the purpose of attaining weight loss in the treatment of patients with obesity [24,25].

PATHOPHYSIOLOGY OF OBESITY TO DIABETES TYPE 2
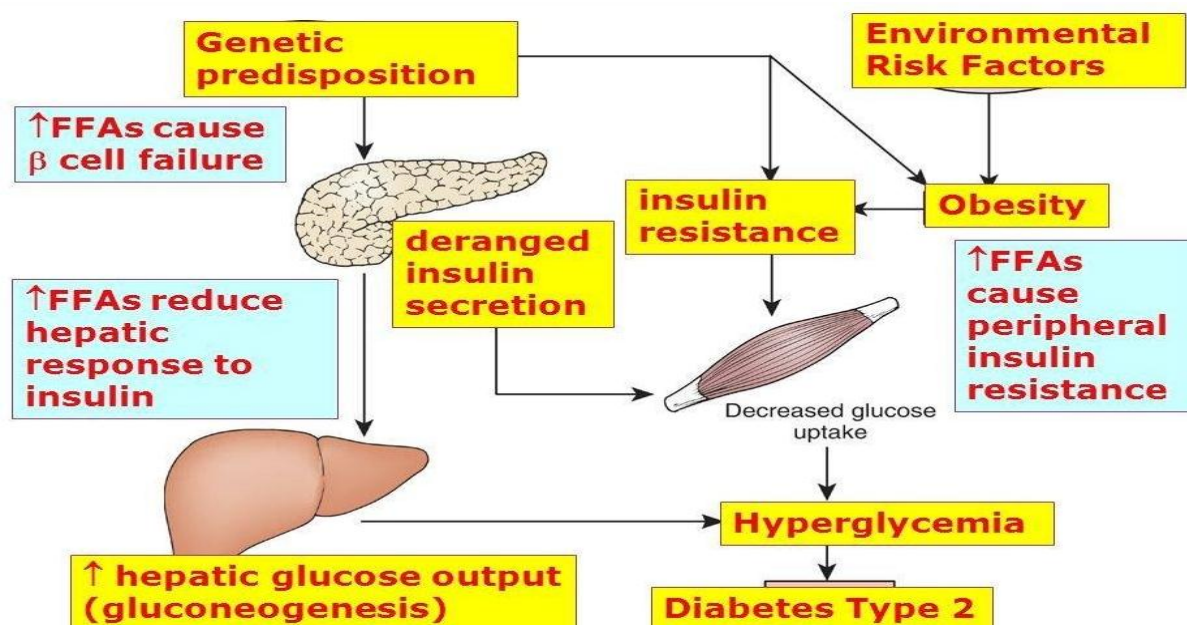
FACTORS OF OBESITY LEADING TO TYPE 2 DIABETES
A number of factors contribute to pediatric or childhood obesity. These can be divided into

- Genetic Factors.
- Behavioral Factors.
- Environmental factors.
- Biological Factors.

▪ GENETIC FACTOR
Genetic factors stem from the genes of parents, frequently leading to children becoming overweight. These are unable to change. Parental obesity is a risk factor. Sometimes obese parents produce obese children.it influence body size and shape, body fat distribution and metabolic rate. Genetic contribution to obesity is estimated at 25 -40 %[14].

▪ BEHAVIOURAL FACTOR
Behavioral factors include food consumption and drinking of high-calorie sugar-sweetened beverages that are of low nutritional value, which are readily available for children. Lack of physical activity also contributes to obesity. It is able to change by proper diet, exercise, education[14].

▪ ENVIRONMENT FACTOR
It includes ready availability of palatable energy dense food and sedentary life styles like watching TV for a long time, spending a large amount of time using technology such as cell phones, television, computers or video games without any other physical activity. Consuming some drugs, endocrine disorders, hypothalamic injury also included. These can be able to change by some extend[14].

▪ BIOLOGICAL FACTOR

It includes gender, age. In case of gender women carry more fat, but men carry more fat around the stomach.so there are more prone to the risk. With age the maintenance of body weight is more difficult[14].

IMPACT OF CHILDHOOD OBESITY ON T2DM

Obesity now affects 15% of children and adolescents in the United States. BMI in childhood changes substantially with age and is not applicable when defining childhood obesity. In the United States, the 85th and 95th percentiles of body mass index for age and sex based on nationally representative survey data have been recommended as cut off points to identify overweight and obesity. T2DM in children and adolescents is an important public health problem directly related to the epidemic of childhood obesity. The increasing rates of youth T2DM parallel the escalating rates of obesity, which is the major risk factor affecting insulin sensitivity. Altered glucose metabolism, manifested as impaired glucose tolerance (IGT), appears early in obese children and adolescents. Obese young people with IGT are characterized by marked peripheral insulin resistance and a relative beta-cell failure. The prevalence of the metabolic syndrome is considerable among obese adolescents and the diseases that are associated with obesity in children include T2DM, hypertension, hyperlipidemia, gallbladder disease, nonalcoholic to hepatitis, sleep apnea, and orthopedic complications[15].

OBESITY'S ROLE IN THE DEVELOPMENT OF TYPE 2 DIABETES
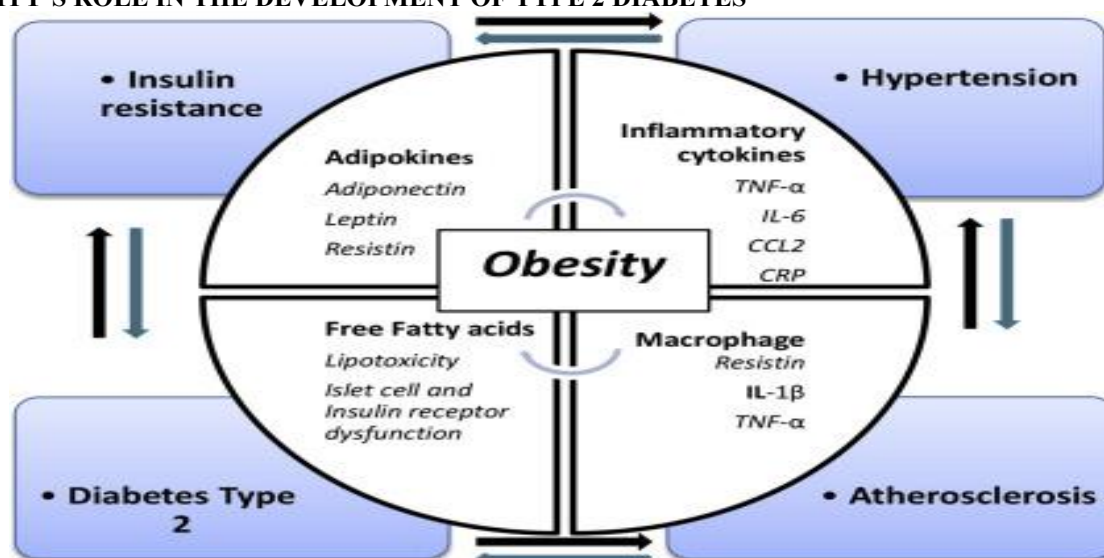
➢ INSULIN RESISTANCE

Insulin resistance is defined as a failure of target organs to respond normally to the action insulin. It is a condition in which cells, particularly those of muscle, fat, and liver tissue, display resistance to insulin by failing to take up and utilize glucose for energy and metabolism. Insulin resistance is the major factor in the development of type 2 diabetes.The majority of the people with type 2 DM have multiple genetic defects. Insulin resistance is usually be related with substances secreted by adipocytes ("adipokines" including leptin, adiponectin, tumor necrosis factor alpha, and resistin).with increasing degree of obesity, insulin resistance increases in those with a family history of type 2 diabetes [15].

Three distinct mechanisms have been proposed to link obesity to insulin resistance and predispose to type 2 diabetes:

1) Increased production of adipokines/cytokines, including tumor necrosis factor-a, resistin, and retinol binding protein 4, that contribute to insulin resistance as well as reduced levels of adiponectin.

2) Ectopic fat deposition, particularly in the liver and perhaps also in skeletal muscle.
3) Mitochondrial dysfunction, evident by decreased mitochondrial mass and/or function mitochondrial dysfunction could be one of many important underlying defects linking obesity to diabetes, both by decreasing insulin sensitivity and by compromising b-cell function[16].

Hypothesis: How Obesity Causes Insulin Resistance
✓ The Adipokine Hypothesis
Obesity leads to an alteration in the profile of hormones secreted by adipose tissue (adipokines). In the obese state, adipose tissue secretes proportionally more adipokines that cause insulin resistance and fewer that promote insulin sensitivity.

✓ The Inflammation Hypothesis
Obesity is associated with an increase in adipocyte secretion of chemokines, which promote macrophage infiltration. In addition to increased macrophage infiltration, obesity is also associated with increased macrophage activation. Activated macrophages produce

cytokines that can negatively impact insulin sensitivity[17].

Thus the development of insulin resistance is an important component in the development of type 2 diabetes. The connection is also seen in the fact that weight-loss can improve control or cure type 2 diabetes. In addition to the degree of obesity, where the excess body fat is deposited is important in determining the risk of type 2 diabetes. The degree of insulin resistance and the incidence of type 2 diabetes are highest in a person with an "apple" shape. These persons carry the majority of their excess body weight around their abdomen. In contrast, the "pear" shaped person carries most of their weight in the hips and thighs and this is not as likely to be associated with insulin resistance[18].
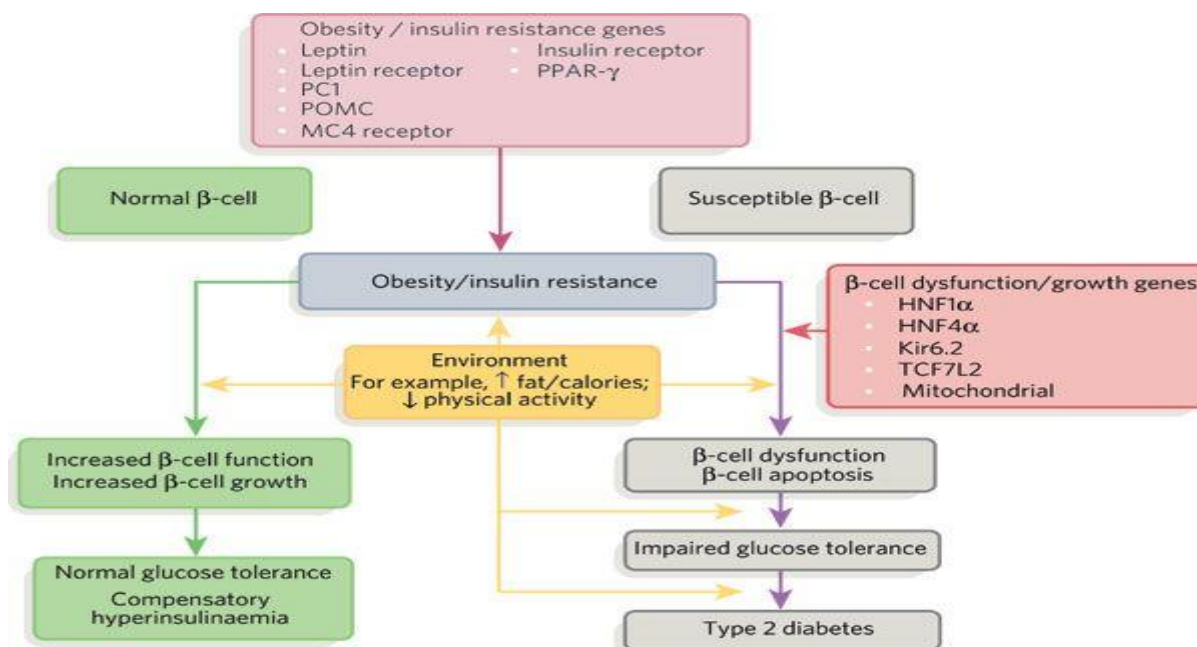
Role of Adipokines

The **adipokines**, or adipocytokines (Greek adipo-, fat; cytos-, cell; and -kinos, movement) are cytokines (cell signaling proteins) secreted by adipose tissue. The first **adipokine** to be discovered was leptin in 1944.
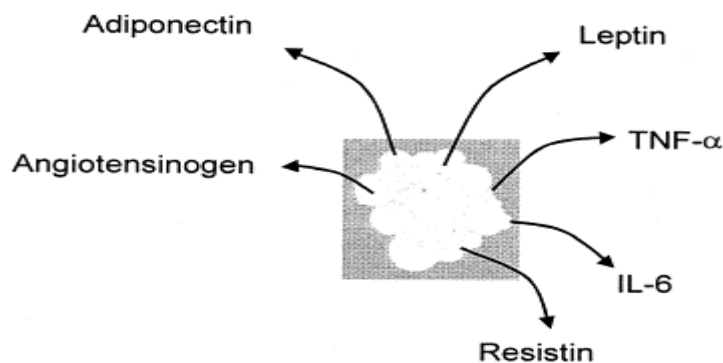
o **Leptin**
Leptin is secreted by adipocyte and its secretion depends upon adipocyte mass. It gives information about the quantity of stored fat to hypothalamus. Leptin deficiency and leptin resistance are associated with obesity and insulin resistance[15].

o **Adiponectin**
Adiponectin is a protein hormone that modulates a number of metabolic processes, including glucose regulation and fatty acid oxidation. Adiponectin is exclusively secreted from adipose tissue (and also from the placenta in pregnancy) into the bloodstream and is very abundant in plasma relative to many hormones[19].

Adiponectin is secreted from an adipocytes tissue, reduces the levels of blood free fatty acids and has been associated with improved lipid profiles, better glycemic control, and reduced inflammation in diabetic patients. Adiponectin is having inhibitory effect on insulin resistance and hence deficiency of Adiponectin is having stimulatory effect on insulin resistance and causes development of type 2 diabetes. Apart from these visfatin and vaspin also having an inhibitory effect on insulin resistance[19].

o **Tumor necrosis factor-alpha**
TNF-alpha (TNFa) from adipose tissue may play a major role in stimulating the insulin resistance. FFA in obesity, that leads to fatty acid toxicity are responsible for increased expression of TNFa in obesity. This is due to because of a fatty acid-binding protein in adipocytes, aP2, which provides the link by which FFA in obesity leads to increased expression of TNFa in obesity. There is a strong correlation between the degree of obesity, hyper-insulinemia, and TNFa mRNA in adipose tissue. Plasma TNFa levels were positively correlated with increased insulin resistance[15].

Role of Chemokine molecules
The chemokine molecule CXCL5 (CXC ligand 5) are present at high levels in the macrophage fraction of white adipose tissue. When it binds to the chemokine receptor CXCR2, it reduces insulin-stimulated glucose uptake in muscle and has a vital role of CXCL5 in developing insulin resistance.

o **Plasminogen activator inhibitor**
Plasminogen activator inhibitor 1, an inhibitor of fibrinolysis, is another protein secreted from adipocytes. High levels of plasminogen activator inhibitor 1 are a prior indicator of onset of diabetes. Other adipocytokines, including adiponectin, tumor necrosis factor alpha, and leptin, are not independently prior predict of diabetes.

o **Resistin**
Resistin stimulates the insulin resistance and decreases glucose uptake and utilization by the adipocytes. Thus, resistin may be a hormone that links obesity and leads to development of type 2 diabetes.

o **Interleukin-1 beta**
Another cytokine, interleukin-1 beta, an inhibitor of glucose-induced insulin secretion undergo increased synthesis by the islets of the beta cells under situations of high glucose levels. Chronic exposure to hyperglycemia leads to high levels of interleukin-1-beta within the islet destroys beta cell function[15].

**FACTORS AFFECTING ON INSULIN RESISTANCE**
Adipokines such as Adiponectin, visfatin, and vaspin are having an inhibitory effect on insulin resistance, whereas adipokines such as leptin, IL-6, TNF-alpha, resistin and all these factors are involved in stimulating the insulin resistance, which plays a major role in the development of type 2 diabetes mellitus[15].
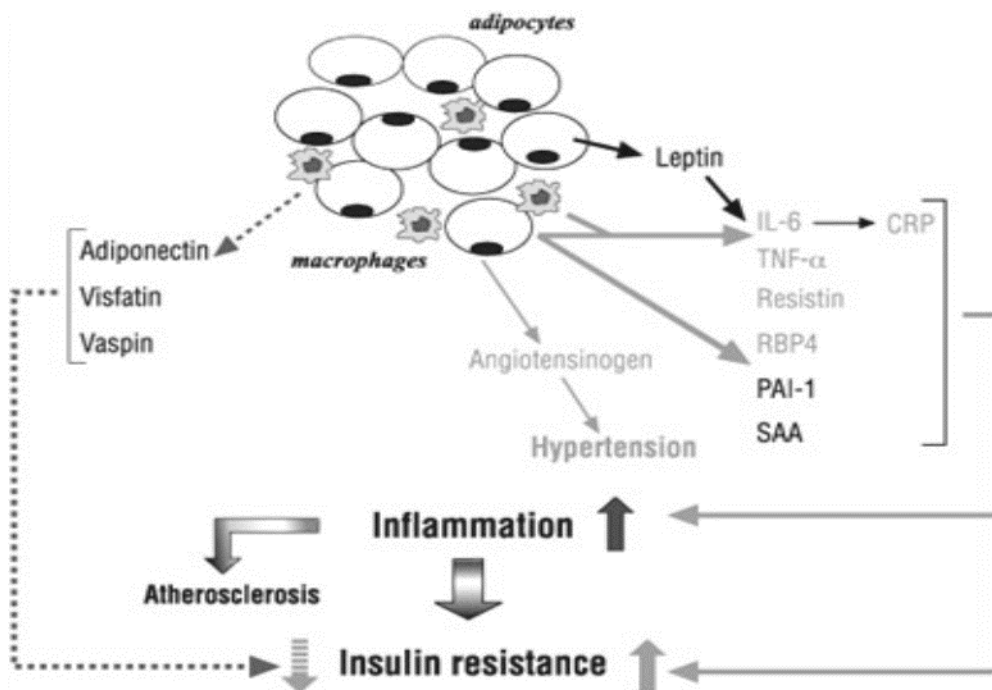
FREE FATTY ACIDS
Usually in obesity persons, plasma FFA levels are high. Sudden increased levels of FFA is a major risk factor for type 2 diabetes may inhibit insulin secretion and can inhibit insulin-stimulated glucose uptake and utilization by the cells in patients with type 2 diabetes. Increased plasma FFA in obese persons may inhibit insulin secretion and blocks glucose supply in patients' with Type 2 diabetes. Increased plasma FFA in obese persons also causes the cytokine damage, a substance derived from adipose tissue, that leads damage of cytokine-induced organs[15].
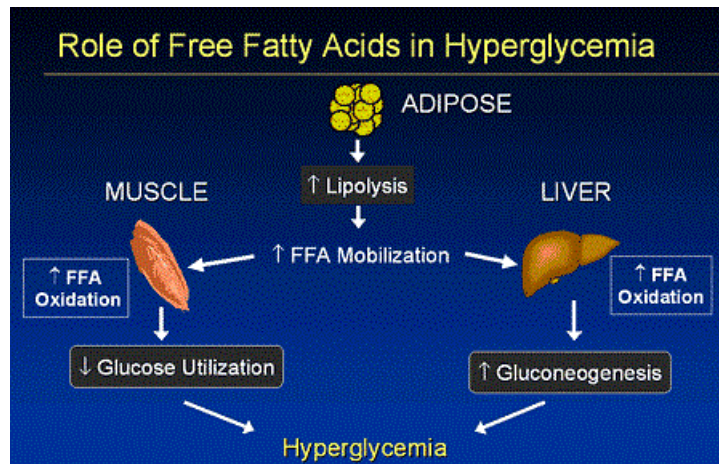
CHILDHOOD OBESITY LEADS TO TYPE 2 DIABETES MELLITUS
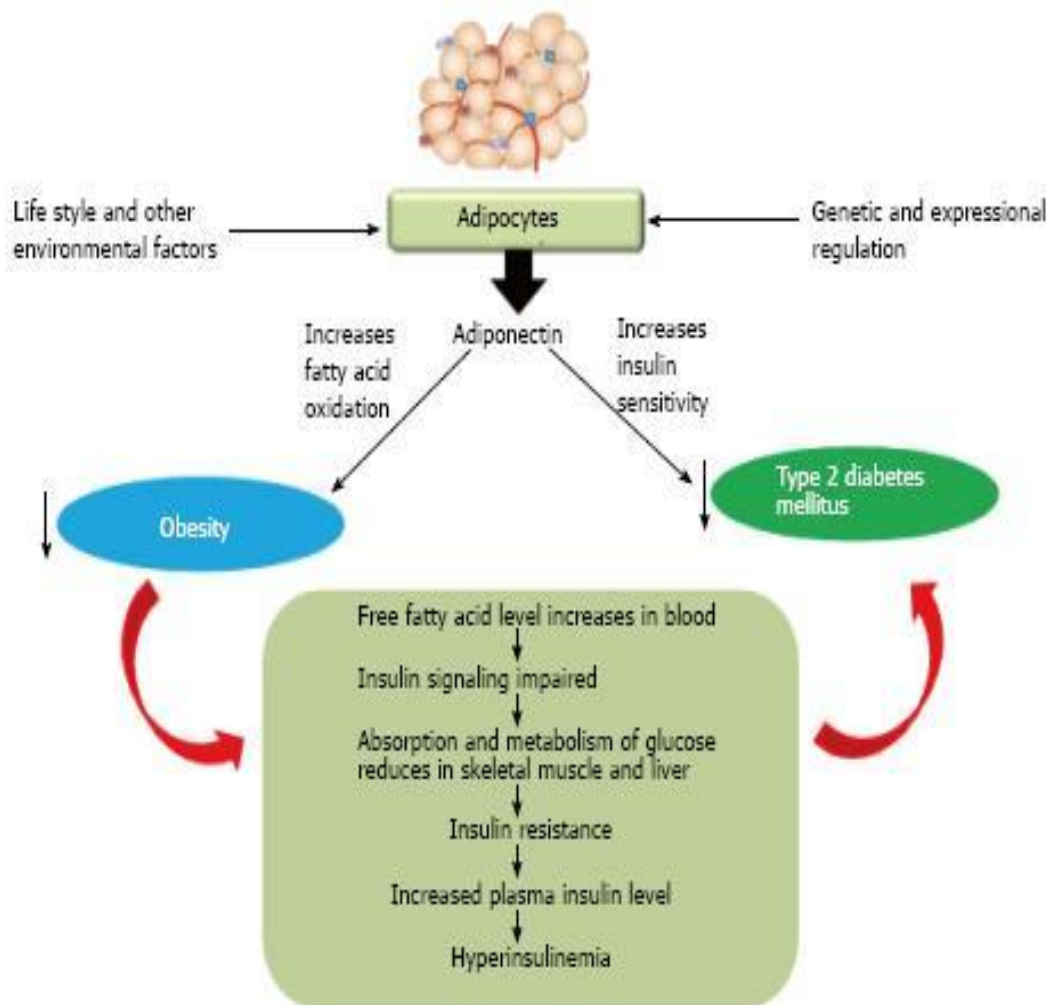
TREATMENT
Management of type 2 diabetes includes
- Healthy eating
- Regular exercise
- Possibly, diabetes medication or insulin therapy
- Blood sugar monitoring

These steps will helps to keep blood sugar level closer to normal, which can delay or prevent complications.

- **HEALTHY EATING**

It's important to include in diet with high-fiber, low-fat foods like fruits, vegetables, whole grains. Also need to eat fewer animal products, refined carbohydrates and sweets. Low glycemic index foods also may be helpful.

The glycemic index is a measure of how quickly a food causes a rise in your blood sugar. Foods with a high glycemic index raise your blood sugar quickly. Low glycemic index foods may help to achieve a more stable blood sugar. Foods with a low glycemic index typically are foods that are higher in fiber.

- **PHYSICAL ACTIVITY**

Everyone needs regular aerobic exercise, and people who have type 2 diabetes are no exception. Aim for at least 30 minutes of aerobic exercise five days of the week. Stretching and strength training exercises are important, too. A combination of exercises — aerobic exercises, such as walking or dancing on most days, combined with resistance training, such as weightlifting or yoga twice a week — often helps control blood sugar more effectively than either type of exercise alone.

Physical activity lowers blood sugar. Check blood sugar level before any activity. There is a need to eat a snack before exercising to help prevent low blood sugar if we take diabetes medications that lower your blood sugar.It lowers blood sugar and helps cells use insulin.It also helps muscles use glucose. It is essential to check blood sugar before and after exercise.

- **MONITORING BLOOD SUGAR**

Depending on treatment plan, it is essential to check and record blood sugar level every now and then or, if we are on insulin therapy, multiple times a day. Careful monitoring is the only way to make sure that blood sugar level remains within target range.

Sometimes, blood sugar levels can be unpredictable. With help from diabetes treatment team or doctors learn how blood sugar level changes in response to food, exercise, alcohol, illness and medication[20,21].

DIABETES MEDICATIONS AND INSULIN THERAPY

Some people who have type 2 diabetes can achieve their target blood sugar levels with diet and exercise alone, but many also need diabetes medications or insulin therapy. The decision about which medications are best depends on many factors, including your blood sugar level and any other health problems. Doctor might even combine drugs from different classes to help to control blood sugar in several different ways.

Examples of possible treatments for type 2 diabetes include:

- **Metformin (Glucophage, Glumetza, others)**

Generally, metformin is the first medication prescribed for type 2 diabetes. It works by improving the sensitivity of body tissues to insulin so that body uses insulin more effectively. Metformin also lowers glucose production in the liver. Metformin may not lower blood sugar enough on its own. Your doctor will also recommend lifestyle changes, such as losing weight and becoming more active.

Side Effects: Nausea and diarrhoea. These side effects usually go away as our body gets used to the medicine. If metformin and lifestyles changes aren't enough to control your blood sugar level, other oral or injected medications can be added.

- **Sulfonylureas**

These medications help your body secrete more insulin. Examples: Glyburide (DiaBeta, Glynase), glipizide (Glucotrol) and glimepiride (Amaryl). Possible side effects include low blood sugar and weight gain.

- **Meglitinides**

These medications work like sulfonylureas by stimulating the pancreas to secrete more insulin, but they're faster acting, and the duration of their effect in the body is shorter. They also have a risk of causing low blood sugar, but this risk is lower than with sulfonylureas.Weight gain is a possibility with this class of medications as well.
Examples: Repaglinide (Prandin) and Nateglinide (Starlix).

- **Thiazolidinediones**

Like metformin, these medications make the body's tissues more sensitive to insulin. This class of medications has been linked to weight gain and other more-serious side effects, such as an increased risk of heart failure and fractures. Because of these risks, these medications generally aren't a first-choice treatment.

Examples: Rosiglitazone (Avandia) and pioglitazone (Actos).

- **DPP-4 inhibitors**

These medications help reduce blood sugar levels, but tend to have a modest effect. They don't cause weight gain.
Examples: Sitagliptin (Januvia), Saxagliptin (Onglyza) and Linagliptin (Tradjenta).

- **GLP-1 receptor agonists**

These medications slow digestion and help lower blood sugar levels, though not as much as sulfonylureas. Their use is often associated with some weight loss. This class of medications isn't recommended for use by itself.

Examples: Exenatide (Byetta) and liraglutide (Victoza). Possible side effects include nausea and an increased risk of pancreatitis.

- **SGLT2 inhibitors**

These are the newest diabetes drugs on the market. They work by preventing the kidneys from reabsorbing sugar into the blood. Instead, the sugar is excreted in the urine.

Examples: Canagliflozin (Invokana) and Dapagliflozin (Farxiga). Side effects may include yeast infections and urinary tract infections, increased urination and hypotension.

o   **Insulin therapy**
Some people who have type 2 diabetes need insulin therapy as well. Today insulin is often prescribed sooner because of its benefits. Because normal digestion interferes with insulin taken by mouth, insulin must be injected. Depending on needs, doctor may prescribe a mixture of insulin types to use throughout the day and night. Often, people with type 2 diabetes start insulin use with one long-acting shot at night.

Insulin injections involve using a fine needle and syringe or an insulin pen injector, a device that looks similar to an ink pen, except the cartridge is filled with insulin.

There are many types of insulin, and they each work in a different way. They are
>Insulin glulisine (Apidra)   >Insulin lispro (Humalog)
>Insulin aspart (Novolog)   >Insulin glargine (Lantus)
>Insulin detemir (Levemir)   >Insulin isophane (Humulin N,Novolin N)
Together with a doctor advice decide which medication is best after considering many factors, including costs and other aspects of health.

•   **Bariatric surgery**
If a person have type 2 diabetes and body mass index (BMI) is greater than 35, he may be a candidate for weight-loss surgery (bariatric surgery). Blood sugar levels return to normal in 55 to 95 percent of people with diabetes, depending on the procedure performed. Surgeries that bypass a portion of the small intestine have more of an effect on blood sugar levels than do other weight-loss surgeries. Drawbacks to the surgery include its high cost, and there are risks involved, including a risk of death. Additionally, drastic lifestyle

changes are required and long-term complications may include nutritional deficiencies and osteoporosis[13].

OBESITY LEADS TO HIGH CHOLESTEROL LEVEL
•   **Hypercholesterolemia**, also called **high cholesterol**, is the presence of high levels of cholesterol in the blood.

Cholesterol is a fat-like substance found in the bloodstream as well as in body organs and nerve fibres. It is used to produce cell membrane, vitamin D, hormones, bile acids etc. Most body cholesterol is made by the liver from a wide variety of foods, especially from saturated fats. A diet high in saturated fat, low in unsaturated fat, heredity and some metabolic conditions such as diabetes, determine an individual's level of LDL or 'bad' cholesterol.
High cholesterol is a condition in which three important fats found in bloodstream go out of balance:
•   levels of LDL cholesterol, also called "bad cholesterol," are too high.
•   Levels of triglycerides are too high.
•   Levels of HDL cholesterol, also called "good cholesterol," are too low [22].
75% of the cholesterol is made by the liver.
25% of the cholesterol is found in brain.
25% comes from the food we eat.

Obesity is a risk factor for high cholesterol
Obesity people often have too much cholesterol in their blood. In obesity, triglycerides and LDL or "bad"—cholesterol tends to be high. HDL or "good" cholesterol is too low. This increases risk of heart disease, heart attack, and stroke. Body weight has a direct association with cardiovascular risk factors, including high cholesterol. This means that as weight increases, LDL cholesterol and triglycerides also increases [21].

PATHOPHYSIOLOGY OF OBESITY TO HYPERCHOLESTEROLEMIA
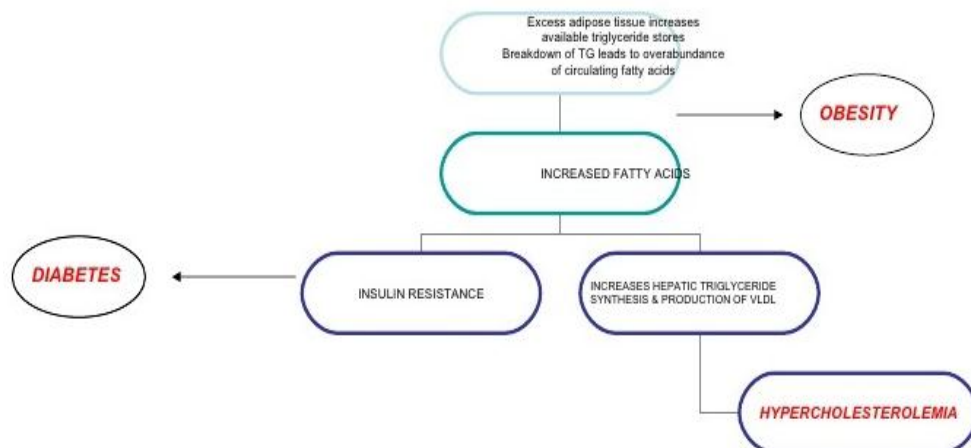
OBESITY CAN CHANGE THE WAY OUR BODY HANDLES CHOLESTEROL

Obesity blunts our response to changes in the type of fats we eat. Obesity increases the amount of LDL cholesterol that liver makes. It also decreases clearance of LDL cholesterol from blood. A few ways this happens is that?

- Our body's normal process that adjusts LDL production and clearance based on the fats that consume doesn't work. That's why changing your diet has little effect on its own.
- Inflammation throughout the body is a common complication of obesity. This constant inflammation decreases our body's response to changes in dietary fat intake.
- Insulin resistance is also common in obesity. It causes changes in the enzymes your body needs to handle cholesterol normally [21].

EFFECT OF OBESITY ON HIGH-DENSITY LIPOPROTEIN METABOLISM

The concentration of HDL-cholesterol is adversely altered in obesity, with HDL-cholesterol levels associated with both the degree and distribution of obesity. More specifically, intra-abdominal visceral fat deposition is an important negative correlate of HDL-cholesterol. The specific sub fractions of HDL that are altered in obese states include the HDL2, apolipoprotein A-I, and pre-beta1 sub fractions. Decreased HDL levels in obesity have been attributed to both an enhancement in the uptake of HDL2 by adipocytes and an increase in the catabolism of apolipoprotein A-I on HDL particles. In addition, there is a decrease in the conversion of the pre-beta1 sub fraction, the initial acceptor of cholesterol from peripheral cells, to pre-beta2 particles. Conversely, as a means of reversing the decrease in HDL levels in obesity, sustained weight loss is an effective method. More specifically, weight loss achieved through exercise is more effective at raising HDL levels than dieting. Exercise mediates positive effects on HDL levels at least partly through changes in enzymes of HDL metabolism. Increased lipid transfer to HDL by lipoprotein lipase and reduced HDL clearance by hepatic triglyceride lipase as a result of endurance training are two important mechanisms for increases in HDL observed from exercise [20].

CAUSES OF HIGH BLOOD CHOLESTEROL

Many factors can affect the cholesterol levels in blood. We can control some factors, but not others.

Factors that Can Control
Diet

Three nutrients in your diet make LDL levels rise:
•Saturated fat, a type of fat found mostly in foods that come from animals.
•Trans fat, found mostly in foods made with hydrogenated oils and fats such as stick margarine, crackers, and French fries; and
•Cholesterol, which comes only from animal products.

Diets with too much saturated fat, Trans fat, and cholesterol are the main cause for high levels of blood cholesterol.

Cholesterol is found in foods that come from animal sources, such as egg yolks, meat, and cheese. Some foods have fats that raise our cholesterol level.

Saturated fat raises your low-density lipoprotein (LDL) cholesterol level more than anything else in our diet. Saturated fat is found in some meats, dairy products, chocolate, baked goods, and deep-fried and processed foods.

Tran's fatty acids (Tran's fats) raise your LDL cholesterol and lower your high-density lipoprotein (HDL) cholesterol. Tran's fats are made when hydrogen is added to vegetable oil to harden it. Tran's fats are found in some fried and processed foods.

Limiting foods with cholesterol, saturated fat, and trans fats can help to control your cholesterol levels.

Physical Activity

Lack of physical activity can lead to weight gain. Being overweight tends to raise your LDL level, lower your HDL level, and increase your total cholesterol level. (Total cholesterol is a measure of the total amount of cholesterol in your blood, including LDL and HDL.)Routine physical activity can help you lose weight and lower your LDL cholesterol. Being physically active also can help to raise your HDL cholesterol level.

Over Weight

Excess weight tends to increase your LDL level. Also, it typically raises triglycerides, a fatty substance in the blood and in food, and lowers HDL. Losing the extra pounds may help lower your LDL and triglycerides, while raising your HDL.

Factors You Can't Control
Heredity

The amount of LDL cholesterol our body makes and how fast it is removed from our body is determined partly by genes. However, very few people are stuck with high cholesterol just by heredity and everyone can take action to lower their cholesterol. Furthermore, even if high cholesterol does not run in your family, it can still develop it. High cholesterol is a common condition among persons, even young persons, and even those with no family history of it.High blood cholesterol can run in families. An inherited condition called familial hypercholesterolemia causes very high LDL cholesterol. ("Inherited" means the condition is passed from parents to children through genes.) This condition begins at birth.

Age and Sex

Blood cholesterol begins to rise around age 20 and continues to go up until about age 60 or 65. Before age 50, men's total cholesterol levels tend to be higher than

those of women of the same age but after age 50, the opposite happens. That's because with menopause, women's LDL levels often rise. Starting at puberty, men often have lower levels of HDL cholesterol than women. As women and men age, their LDL cholesterol levels often rise. Before age 55, women usually have lower LDL cholesterol levels than men. After age 55, women can have higher LDL levels than men[23,24].

DIAGNOSIS OF HYPERCHOLESTEROLEMIA

High blood cholesterol is diagnosed by checking the cholesterol levels in blood. A blood test called a lipoprotein panel can measure cholesterol levels. Before the test, person has to fast (not eat or drink anything but water) for 9 to 12 hours. The lipoprotein panel will information about:

- Total cholesterol: Total cholesterol is a measure of the total amount of cholesterol in blood, including low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol.
- LDL cholesterol: LDL, or "bad," cholesterol is the main source of cholesterol buildup and blockages in the arteries.
- HDL cholesterol: HDL, or "good," cholesterol helps remove cholesterol from arteries.
- Triglycerides: Triglycerides are a type of fat found in your blood. A high level of triglycerides in the blood may raise the risk of coronary heart disease, especially in women. Testing for total and HDL cholesterol does not require fasting. If total cholesterol is 200 mg/dL or more, or if HDL cholesterol is less than 40 mg/dL, doctor will likely recommend that we have a lipoprotein panel. (Cholesterol is measured as milligrams (mg) of cholesterol per deciliter (dL) of blood.) The tables below show total, LDL, and HDL cholesterol levels and their corresponding categories.

Total Cholesterol Level	Total Cholesterol Category
Less than 200 mg/Dl	Desirable
200–239 mg/Dl	Borderline high
240 mg/dL and higher	High
LDL Cholesterol Level	**LDL Cholesterol Category**
Less than 100 mg/dL	Optimal
100–129 mg/dL	Near optimal/above optimal
130–159 mg/dL	Borderline high
160–189 mg/dL	High
190 mg/dL and higher	Very high
HDL Cholesterol Level	**HDL Cholesterol Category**
Less than 40 mg/Dl	A major risk factor for heart disease
40–59 mg/Dl	The higher, the better
60 mg/dL and higher	Considered protective against heart disease

TREATMENT

If high cholesterol level is because of obesity then the first choice of treatment is by

➢ Therapeutic Lifestyle Changes or TLC

TLC (therapeutic lifestyle changes) is a set of tools we can use to get results. This help to make the lifestyle changes that will lower blood cholesterol and reduce other diseases and risk for heart disease. It explains how to follow the TLC diet (low in saturated fat, Trans fat, and dietary cholesterol), increase physical activity, and manage weight for people whose cholesterol level is above their goal.

TLC Program has three parts:
■ Diet
• Decrease saturated fat, transfat, and cholesterol.
• Add plant stanols and sterols and increase soluble fiber.
■ Physical activity

■ Weight management

A lot of benefit can obtained from the TLC. Here are some estimates of how much can lower LDL cholesterol by following various steps. The estimates are what expected based on research is. The more you do with the TLC, the lower your LDL will go.

TLC DIET

In TLC diet, we need to make dietary changes and to become physically active.

- With the TLC diet, less than 7 percent of our daily calories should come from saturated fat. This kind of fat is found in some meats, dairy products, and chocolate, baked goods, and deep-fried and processed foods.
- No more than 25 to 35 percent of our daily calories should come from all fats, including saturated, Trans, monounsaturated, and polyunsaturated fats.

- Also should have less than 200 mg a day of cholesterol. The amounts of cholesterol and the types of fat in prepared foods can be found on the foods' Nutrition Facts labels.
- Diet options used for more LDL lowering
• 2 grams per day of plant stanols or sterols.
• 10–25 grams per day of soluble fiber.
- Only enough calories to reach or maintain a healthy weight.
- In addition, you should get at least 30 minutes of a moderate intensity physical activity, such as brisk walking, on most, and preferably all, days of the week.

Foods high in soluble fiber also are part of the TLC diet. They help prevent the digestive tract from absorbing cholesterol. These foods include:

- Whole-grain cereals such as oatmeal and oat bran
- Fruits such as apples, bananas, oranges, pears, and prunes
- Legumes such as kidney beans, lentils, chick peas, black-eyed peas, and lima beans

A diet rich in fruits and vegetables can increase important cholesterol-lowering compounds in diet. These compounds, called plant stanols or sterols, work like soluble fiber.

A healthy diet also includes some types of fish, such as salmon, tuna (canned or fresh), and mackerel. These fish are a good source of omega-3 fatty acids. These acids may help protect the heart from blood clots and inflammation and reduce the risk of heart attack.

Also should try to limit the amount of sodium (salt) that we eat. This means choosing low-salt and "no added salt" foods.

Try to limit drinks with alcohol. Too much alcohol will raise our blood pressure and triglyceride level. (Triglycerides are a type of fat found in the blood.) Alcohol also adds extra calories, which will cause weight gain [8].

Weight management
If overweight or obese, losing weight can help lower LDL cholesterol. Maintaining a healthy weight is especially important if having a condition called metabolic syndrome. The five metabolic risk factors are a large waistline (abdominal obesity), a high triglyceride level, a low HDL cholesterol level, high blood pressure, and high blood sugar. Metabolic syndrome is diagnosed if any have at least three of these metabolic risk factors.

Physical Activity
Routine physical activity can lower LDL cholesterol and triglycerides and raise our HDL cholesterol level.

People gain health benefits from as little as 60 minutes of moderate-intensity aerobic activity per week. The more active we are, the more we will benefit

Cholesterol-Lowering Drugs
Many people are able to lower their LDL enough with TLC alone. If LDL needs to be more lowering, it may have to take a cholesterol-lowering drug in addition to TLC. However, by staying on the TLC, drug at the lowest possible dose is needed. So don't give up our healthy lifestyle changes.

There are various types of drugs used to lower LDL, and they work in different ways. And if have any side effects from a medicine, tell doctor as soon as possible. The amount or type of drug can be changed to reduce or stop bad side effects. If one drug does not lower your LDL enough, it may be given a second medication to go with it.

The major types of cholesterol-lowering drugs are
● Statins: lovastatin, pravastatin, simvastatin, fluvastatin, atorvastatin, and rosuvastatin. Statins stop an enzyme that controls the rate at which the body produces cholesterol.They lower LDL levels more than other types of drugs—about 20–55 percent—and also moderately lower triglycerides and raise HDL.
● Ezetimibe: This drug reduces the amount of cholesterol absorbed by the body. Ezetimibe can be combined with a statin to get more lowering of LDL. Ezetimibe lowers LDL by about 18–25 percent.
● Bile acid resins. These bind with cholesterol-containing bile acids in the intestines and are then eliminated from the body in the stool. They lower LDL cholesterol by about 15–30 percent.
● Nicotinic acid—also called niacin. This is a water-soluble B vitamin that should be taken only under physician supervision. It improves all lipoproteins—total cholesterol, LDL, triglycerides, and HDL—when taken in doses well above the vitamin requirement. LDL levels are usually reduced by about 5–15 percent, and up to 25 percent in some patients.
● Fibrates. They mostly lower triglycerides and, to a lesserdegree, raise HDL levels. Fibrates are less effective in lowering LDL level[23,24].

DISCUSSION
Childhood interventions and prevention of obesity is a necessary factor which requires reformation on a global aspect. Today Obesity is a leading factor of unstable economy and increased in the health care cost. Proper education regarding nutrition, promoting health life styles and knowledge regarding food should be propagated globally. Restrictions should be placed on the junk foods, ads shown on the television, otherwise which leads to increase in the consumption of this food in teenage, children and adults. Promoting health lifestyle should be a global goal and should be promoted through workshops, onsite seminars, pre-natal education, live media, school sites, brochures and by health care professionals. By educating children about their food habits by implementing nutritional programs at schools and promoting the benefits of healthier foods to parents are strategies to create awareness about the risks of

childhood obesity. The prevalence of childhood obesity can be decreased or prevented with the induction of changes in health behavior.

For our daily body activities we need energy that comes from the food that we eat. More activities and exercise burn more calories that we get from food. But when our food calories exceed the body need, they will be stored in the body as fat.

Fighting obesity is an important aspect of being able to cure disease naturally. The less we eat and fewer calories we eat, the more weight we will loss. Increased weight gain and decreased physical activity are the common environmental risk factors for development of Type 2 diabetes. So excess weight is an established risk factor for type 2 diabetes. So obesity is also associated with an increase in mortality and a considerable reduction in life expectancy.

CONCLUSION
This project reviews the complex relationship between type 2 diabetes and high cholesterol with obesity. Obesity stands out as a risk factor for Type 2 DM & high cholesterol. Thus obesity may be a precursor for Type 2 DM, following insulin resistance and high cholesterol.

The modern sedentary life and caloric abundance has created new physiological conditions capable of changing the level of expression of a number of genes involved in fuel metabolism and body weight regulation. Obesity induces insulin resistance Increased weight gain and decreased physical activity are the common environmental risk factors for development of Type 2 diabetes.

So most important environmental risk factors in most patients who develop type 2 diabetes and high cholesterol were high caloric intake, decreased physical activity and sometimes family history and stronger multiple genetic predisposition.

For treatment and prevention of Type 2 DM and high cholesterol, reduction of obesity is a key goal all over the world. Regular physical activity can help you manage your weight and, in that way, help lower your LDL. It also can help raise HDL and lower triglycerides, improve the fitness of our heart and lungs, and lower blood pressure. And it can reduce our risk for developing diabetes the main treatment of both conditions is reduced caloric intake and increased physical activity. Newly diagnosed cases of Type 2 DM and obesity are always treated in this way.

Visceral obesity plays an important role in the development of diabetes by mobilizing free fatty acids and causing cholesterol by increasing the LDL level, triglycerides etc. Preventing and treating obesity will help in the prevention and treatment of diabetes and reducing the cholesterol level to normal. Promoting a

healthy lifestyle in children and adolescents will put them on a path that will decrease their risk of diabetes, its complications and other diseases. Helping adults at high risk for diabetes to change their diet and life prevent them from developing diabetes and its consequences style.

Making lifestyle changes is never easy. But by adopting the proper management, treatment including proper diet with high nutrition status, regular exercise and keeping the key goal in mind we can achieve a healthy body and prevent them from other diseases.so a healthy, prosper, society can develop.

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