Pathophysiology Of Cystic Fibrosis

Introduction:

Cystic fibrosis is a serious inherited condition that mainly causes damage to the Respiratory and Digestive system from a young age.

And with the time The lungs and respiratory damage will increase and may eventually stop working properly, and this is one pf the main cause of limiting average of life for cystic fibrosis patients, which is between (40-50) years.

Cystic fibrosis disease can be real life-threatening And it has mortality rate about (1-2%) Per year overall, and this chronic disease currently has no cure we just can reduce a symptoms by taking a specific treatment .

Although people with the condition requires daily care, and they can still do a relatively normal life and work.

The first description of this disease was made in (1983) by the pathologist [Dorothy Andersen], and Cystic fibrosis is the most common lethal genetic disease in the Caucasian population, and about (1400) Cases are diagnosed In each year in the United States

Outlines:

And in this report, we will explain the pathophysiology of CF and the organs that are involved or affected by this disease, and the fertility of the cystic fibrosis patients, and explaining the inheritance patterns and the pharmacological treatment used for this genetic disease.

Detail:

Cystic fibrosis is a multi-system that results mainly from abnormal I am transporter across epithelium cells on this caused by mutation of special gene which is (CFTR) gene.

(CFTR) gene

Cystic fibrosis transmembrane conductance regulator (CFTR) is located on the long arm of chromosome seven and codes for (CFTR) protein in epithelial cell of respiratory tract on gastrointestinal tract and sweat gland.

This protein is a1480 amino acid protein and a six-helix transmembrane domain, and when correctly folded it transported to the plasma membrane as a chloride channel.

Chloride channel

Chloride channels are one of the channels of the plasma membrane that are functionally and

structurally diverse group of anion secretion, channel involved in the process including the regulation of activity of neurons, skeletal, cardiac, and smooth muscle cells, and the acidification of internal and external environment of the cells, and regulation of transporting salts in epithelial cells by transporting chloride ion from the inside the cells to the extracellular fluid.

Pathophysiology of cystic fibrosis

Cystic fibrosis results from a mutation in the (CFTR) gene, [Mutation]: is a structural gene change that can cause a disease or a birth defect. Till now more than 500 types of mutation in the (CFTR) gene have been reported, the commonest one is a deletion of three basic pairs in exon 10, and the corresponding protein lacks the amino acid phenylalanine at position 508 (delta F508).cAnd this mutation causes a defect in the (CFTR) protein and often affect the three-dimensional structure of the protein and prevent (CFTR) from reaching the membrane, and that leads to a chloride channel absence in the epithelial cells plasma membrane, and this causes dysfunction of the salt and water transport and balance, by decreasing chloride secretion and increasing sodium absorption,(sodium absorption is combined with decreasing chloride section) and at the same time water content of the extracellular fluid will be absorbed into the cells (when sodium moves, water follows it), and this will dehydrate extracellular fluid and produce a thick sticky mucous that has a variety of negative effects in various organs.

Systems and organs involved in Cystic Fibrosis

Respiratory system:

The respiratory system is divided into the upper respiratory and lower respiratory part the upper part including nasal passage and sinuses , and lower part consist of lungs, trachea , bronchi , and bronchial tube , and alveoli . And Respiratory organs can be affected in patients with cystic fibrosis.

Lungs' airways normally have a thin layer of mucus that catches dust and bacteria and are moved by hair-like cells (cilia) to the large passage where they can be coughed out. But people with cystic Fibrosis have restricted lung function, due to the thickening of the walls of the airways and clogging the air passages by the thick sticky mucous and this leads to chronic obstructive pulmonary disease (COPD) and causes difficulty in breathing and bronchitis. And at the same time, cilia can not move the thick mucous that caught bacteria and bacterias remain in the air passages and produce a perfect environment for harmful bacteria, and this leads to lung infections, and the most common bacteria associated with cystic fibrosis lung infection is Pseudomonas.

And also the lining of the nose also can be affected , by growing a small non-cancerous called Nasal polyps , that cause a difficulty in breathing.

Digestive system:

The digestive system or gastrointestinal tract consists of many organs that digest and absorb food, people with cystic fibrosis have impaired digestive organs that can not function normally,

of them :

- Pancreas: Pancreas is a digestive organ that creates important enzymes and releases them to the small intestinal to break down fats proteins and carbohydrates in your foods and that is important for releasing the nutrients that your body needs, but cystic fibrosis patients have a thick mucous that blocks pancreatic ducts and fail to produce adequate bicarbonate ion and water in nearly all patients, and in-adequate digestive in most, giving rise to pancreatic insufficiency, that leads to a problem in digestion and malabsorption of important nutrients [fat, soluble vitamins such as (A, E,&K), protein] and leads to malnutrition and unwanted weight loss, and problems in pancreases can also cause cystic fibrosis diabetes.
- Liver: The liver is one of the digestive organs and is a large organ that locates on the right-hand side of the belly, that has many functions in the body including (protein and glycogen, cholesterol, and triglycerides synthesis, and making blood clotting factor, and biles production), but if people with cystic fibrosis blocked by the mucous, liver will get inflamed and sever scarring (cirrhosis) may occur.
- Small intestine: small intestine is part of the intestines organ, and most of the absorption of nutrients and minerals occurs there, and it lines between the stomach and large intestine, and it receives bile and pancreatic enzymes through the pancreatic duct that help in digestion, but the lining of the small intestine in cystic fibrosis patient can erode, because of breaking down the high acidic food that comes from the stomach.
- Large intestine: large intestine is part of the intestines organ, and it’s the final secretion of the digestive system, and it’s larger and thicker than the small intestine .and performs absorption of water and vitamins while converting digestive food into feces, but the thick secretions of people with cystic fibrosis can make face very thick and cause blockage, and in some cases, the intestine may also start to fold in on itself (intussusception).

Sweat glands :

Sweat glands are a type of exocrine gland, which produce and secrete substances by way of a duct onto an epithelial surface, and they are tubular structures that their main function is regulating body temperature by secreting water to the skin surface where heat is lost by evaporation. And they are controlled by the sympathetic nervous system. In people with cystic fibrosis, their body salts are lost in sweat and reabsorbed by the sweat duct, and this reabsorption process is markedly abnormal in people with cystic fibrosis, and cells of the sweat duct may defect.

Reproductive system :

The reproductive system is one of the main systems in the body and its main function is producing offspring and regulating some of the hormones in the body, but reproductive organs can be affected by the thick sticky mucous that is produced in people with cystic fibrosis, the thick mucous may block the ducts in reproductive organs and my lead to fertility problems.

Fertility of cystic fibrosis patient

Fertility is a capacity to produce offspring, and any problems in reproductive system my cause infertility which is the failure to achieve a clinical pregnancy after 12 months or more of regular

unprotected sexual intercourse.

95% of men with cystic fibrosis are infertile because of the blockage or absence of the sperm canal, known as the congenital bilateral absence of the vas deference that connects the epididymis to the ejaculatory ducts, because of this sperm can not inter and change to the semen, so they can not reach female reproductive organ and fertilize an egg through intercourse.

20% of women with cystic fibrosis are infertile, most of the women with cystic fibrosis have no difficulties in getting pregnant, but some of them because of having a thicker cervical mucus causing difficulty for sperm to penetrate the cervix, and this will increase the amount if the time that women with cystic fibrosis need to get pregnant.

Inheritance patterns of Cystic Fibrosis

Cystic fibrosis is an example of a genetic autosomal recessive disease. So that means people should have a mutation in both copies of the (CFTR) gene that they receive from the parents, to have cystic fibrosis, but if the person has a mutation only in one copy of the (CFTR) gene and the other copy is normal (she/he) does not have cystic fibrosis, (she/he) is just a cystic fibrosis carrier. people with cystic fibrosis can pass copies of their mutated (CFTR) gene to their children.

If a cystic fibrosis patient has a child with a cystic fibrosis carrier, the chances are:

- 50% chance for a child to have cystic fibrosis.
- 50% chance for a child to be a carrier of cystic fibrosis.

If a cystic fibrosis patient has a child with a healthy person, the chance is :

- 100% child to be a carrier of cystic fibrosis.

And also cystic fibrosis carrier can pass their copy of mutated (CFTR) gene to their children, and if the cystic fibrosis carrier has a child with another carrier of cystic fibrosis, the chances are:

- 25% chance for a child to have cystic fibrosis.
- 25% chance for a child to be healthy.
- 50% chance for a child to be a carrier of cystic fibrosis.

Pharmacological treatment of cystic fibrosis

There is no cure for patients with cystic fibrosis, but the treatments can reduce the complication and difficulty of the symptoms and provide a better quality of life for the patients. Close monitoring and regular treatment for the patient can slow the progression of cystic fibrosis , and give a patient more and better life expectancy, and the treatments contain taking medication or having a surgical procedures or having a regular home care. And here we will talk about the

medicines and drugs that we use as a type of treatment:

Antibiotics can be used to reduce lungs infection, and prevent the lungs from future infections. Antibiotics can be liquid or tablets, or capsules and these antibiotics can be taken by the mouth or can be injected into the blood vessels or can be injected into a muscle or inhaled, and also antibiotics classified by the type of bacteria that they affect and the mechanisms of their works. Example of these antibiotics that are suitable for cystic fibrosis patient are (Penicillins, Amino glycosides, Cephalosporins, Vancomycin and Sulfonamides).

We also have Mucus thinning medication that thins the sticky mucous that helps to be coughed out and this can reduce difficulty in breathing. Both Hypertonic saline and Recombinant human DNase reduce the viscosity of the mucous and increase lung function and decrease lung damage.

And anti-inflammatory drugs are useful for cystic fibrosis patient because it reduces pain and high body temperature of the patient, such as (Ibuprofen, and Indomethacin).

Bronchodilators are a type of drug that is used to relax the muscles of the airways, (Albuterol, Ventolin, Combivent) are used for treating cystic fibrosis patients.

And because of the effect of cystic fibrosis on the gastrointestinal tract, digestion and nutrients absorption function may be affected, and this may lead to impaired growth, and for this, patients can take Oral pancreatic enzymes and Fat-soluble vitamins for compensation of these damages.

Conclusions:

The main conclusion that we can have for this disease is that (CFTR) loses its function as a chloride channel, and I noticed that this is the main cause of the cystic fibrosis phenotype. And when (CFTR) gene mutated leads to a well-defined set of symptoms , and cystic fibrosis like any other disease has its pathophysiology that explains how this disease occurs and how many organs and systems are affected. And because CF is a genetic disease sometimes families ask about the inheritance pattern of cystic fibrosis one of the most sensitive things about cystic fibrosis is that it affects the fertility of the patients, but fortunately, there are technical procedures for this problem. And for treatments I believe that the researches can discover a better drugs for this disease, and I think genes therapy is a good option for treating cystic fibrosis disease since the gene mutation is the main cause of the disease.