Cystic Fibrosis

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Overview / Introduction

Cystic Fibrosis (CF) is a genetic disease inherited from the faulty eugenic of both the parents. Individuals having a defective genetic profile from a single parent do not contribute to the life-threatening effect of a chronic disorder, cystic fibrosis (Aziz et al., 2015). The demographic analysis states that about 35,000 adults in the United States are surviving with CF, and 10 million people are the carriers of the defective gene from a single parent, which they are not aware of as it is not problematic. Advancement in healthcare, better prognosis, and treatment regimen facilitates the possibility of surviving longer with CF (Cutting, 2015). Cystic fibrosis transmembrane regulator (CFTR) is a cell protein to manage the outflow of water and salts in the body, which is impaired with CF. As the management of the flow of salt and water is altered, a thick mucus is developed to damage pulmonary, cardiac, digestive, and reproductive health. Also, CF is related to losing excessive salts during sweating, which could lead to electrolyte imbalances and hypotension (Aziz et al., 2015).

Pathophysiology of the genetic disease

The mutations of CFTR genetic coding of the couple result in abnormalities of cyclic adenosine monophosphate (cAMP). CFTR works as a chloride transport channel on mucosal regions of the body cells, which is managed by cAMP (Ong et al., 2017). Epithelial cells do not favor mutation and increase the risk of abnormalities and defective framework. The mutation causes reduced ability to synthesize CFTR, defective production of CFTR, abnormal chloride channel, alteration in genetic coding or reduced transcription, and reduced ability of mucosal cell surfaces to work as a channel carrier (Egan et al., 2016). The mutational genotype has a low shrill to predict the influence of the disease. The performance of CFTR is related to chloride transport, and abnormal CFTR protein results in unmanaged electrolytic balance. This caused reduced hydration and

production of thick and viscous mucus encouraging bacterial growth, severe infections, pulmonary inflammation, pancreatic abnormalities, gastrointestinal disorder, cholelithiasis, and hepatic cirrhosis (Ong et al., 2017).

The probability of risk of an offspring to develop cystic fibrosis could be represented by the visual framework or a Punnett Square.

	C	c
C	CC	Cc
c	Cc	cc

This is the Punnett square representation of cystic fibrosis in which the allele ‘C’ includes for normal offspring, ‘c’ represents mutational phenotype. In this framework, each child would have a 25% risk of developing CF, 25% normal with no risk, and 50% chances of being a carrier of CF (Ong et al., 2017). Pedigree analysis is the method of determining the risk of CF profile in the offsprings based on Mendelian law of inheritance to exactly analyze the pattern of a recessive trait or genetic carriers from one generation to another.

Background (Literature Review)

A cohort analysis of 59 CF carriers was matched with the related subjects, and 57 out of 59 were found with higher odd ratios with increased prevalence rates of bacterial infections, chronic pancreatitis, and male infertility (Nelson et al., 2016). Both carriers and subjects are more prone to experience these conditions affecting various organs of the body in comparison to controls. Carriers have reduced anion channel capacity, and Shah et al. demonstrated that the difference between CF values and controls is mediated by sweat glands (Shah et al., 2016). The carriers

contain the secretion of β-adrenergic agonists to stimulate epithelial cells with mucosal layers (surface). Also, the carriers contain pilocarpine-stimulated chlorine secretory concentrations to differentiate between the control and CF groups. β-adrenergic agonist and pilocarpine stimulate the sweat gland duct to increase the risk of organ damage. These genetic abnormalities of the sweat gland enhance the risk of fluid and electrolyte imbalances with increased consequences of severe dehydration (Shah et al., 2016). The demographics of epithelia through the basolateral entrance or airways shows controlled bicarbonate secretion and are less responsive in causing thick mucus, whereas reduced bicarbonate secretion leads to acidic airway which are potential factors of developing the pulmonary disorder in people with CF, and increased risk of developing the disease in carrier genotype (Cutting, 2015). Abnormal CFTR function is associated with secretion of chlorine and bicarbonate anions, but additional analysis is yet to be done for the relevant profile of these anions with organ failure.

The CF carriers are genetically modified to contain the abnormal coding for developing CF in their children. Also, they are at higher risk of developing pancreatitis, loss of fertility, and gastrointestinal cancer. Early detection of CF-related carriers may assist researchers and physicians in achieving therapeutic outcomes and preventive measures with serious genetic disease (Cook et al., 2016). Known CF carriers should be encouraged to learn the strategies for risk mitigation, such as lifestyle modification, improved social habits, and intervention of early screening to diminish the risk of mutation-induced carcinogenesis.

CFTR controls transmembrane transportation functionality, and abnormal functions may cause thick mucus with respiratory and gastrointestinal illnesses. CFTR dysfunctionality or autosomal mutational coding could be diagnosed by screening sequential parental testing during gestation or before conception as the disease is the abnormality of genetic mutation (Aziz et al., 2015). The

limitations of prenatal parental testing include personal perspectives to avoid abortion or other issues, economic factors, reduced confidentiality, and time are taken to conduct a series of tests. However, molecular screening tests should be prioritized to prevent newborns from the adverse outcome of pulmonary disease, CF. Moreover, the ACMG Standards and Guidelines for Clinical Genetics Laboratories and multiple other research centers in the United States recommend prenatal screening and neonatal screening of cystic fibrosis in the population of higher risk (Aziz et al., 2015).

Mechanism

When both the parents survive the genetically induced disease, cystic fibrosis, the risk of having an offspring with the same disorder is higher. The risk prevails in every one child out of four having one of the parents with a CF carrier. Malfunctioning of the CFTR gene is related to the genetic mutation to build up thick mucus with frequent lung infections, pulmonary edema, and gastrointestinal disorders (Farrell et al., 2017). There are 23 pairs of chromosomes in a person, and alteration in chromosome 7 causes cystic fibrosis. Abnormalities in chromosome 7 disrupt the functionality of CFTR with the increased secretion of epithelial chlorine and bicarbonates to cause trouble in relieving the sticky mucus. The bacterial infection damages pulmonary and pancreatic functions with enhanced fatality (Egan et al., 2016).

Risk and Barrier of Diagnostic Testing

The common barrier of diagnostic testing with CF is psychosocial challenges, and positive screening results in newborns are linked with emotional biases. Providers also find challenges with reduced training and less confidence while testing for CF positive. The other challenges that interfere with the health outcome of a child are poor eating habits, low weight gain, failure of

healthy dietary intervention, struggling meal hours, and poor behavioral approaches that may reduce the cognitive ability and academic performance (Rowe et al., 2016). Also, integration of frequent hospitalizations, multiple therapies (regular use of nebulizers and inhalers) to manage respiratory illness, and other CF-induced complications may impact the physical and mental health of parents. The CF Foundation (CFF) has confirmed the patients of CF and their families with a detrimental quality of life with increased stress, anxiety, and healthcare charges (Farell et al., 2017). CF is a pediatric genetic chronic illness, and a mixed-method exploratory analysis demonstrated that the influence of families is less with the CF-related children, including involvement of them in the mealtime, and other regular tasks, which require the involvement of each family members. The structured criteria encourage less interaction with the child, and the environment has numerous negative effects on the growth of a child. Newborn screening is expensive, and the consequences with positive results are costlier, which includes the major barrier in a testing (Rowe et al., 2016).

Cultural, Ethical, Legal, and Socioeconomic Factors

The most common factors include physical, accessible, decisional, and health privacy. According to the healthcare guidelines, the electronic confidentiality or leaking of important information is highly restricted unless the patient authorizes to share the personal information with others. The intervention of electronic health records increases the risk of leaking private information due to the controversies and discrepancies related to the tool. Moreover, the hacking of sensitive data is another technological issue (Aziz et al., 2015). Discrimination is another issue related to the legal and social unacceptance of the patients of CF. Genetic testing is linked with genetic discrimination to result in unemployment, mental illness, mortgages with increased mortality, and morbidity among the specific population. Personalized medications impact a patient-provider relationship,

and the physicians lack training and time in providing sequential genome testings in the clinical settings, and they find it time-consuming to explain these effects to the patients, which includes as a legal and ethical concern in healthcare (Rowe et al., 2016). The liability of increased harmful incidences with complicated screening, surgery, and transplantation ranks as the prioritized factors with a higher possibility of performing malpractices during the genomic screening of the patients. Other issues are costs, accessibility, and input-output disparities in healthcare technologies (Egan et al., 2016).

Impact of Genetic testing

Carrier testing and screening is an effective method of preventing adverse consequences of cystic fibrosis in the people. The method is advantageous in reducing the cases of CF, but it is equally challenging. The CF-carrier positive patients would be administered for the termination of pregnancy as it is better to opt for abortion rather than conceiving a defective fetus. The situation raises various moral and ethical questions, and a study confirmed that most of the parents after a desire to have a baby after termination, which could increase the risk of couple disputes and domestic violence (Cousar et al., 2017). Being a positive carrier could enhance the feeling of guilt, and raise the issues of psychological incidences, such as stress, anxiety, depression, humiliation, hallucination, and suicidal ideation. Also, spouse and family blame prevents the parents from preceding the screening process (Farell et al., 2017). The statistical representation reveals that episodes of screening tests for risk assessment prevent the couples due to unavailability and higher costs. Most of the families do not want to increase their financial burden with the carrier screening among Caucasians. The failure of successful pregnancy could increase the chances of social exclusion, lost connectivity, and poor communication with families and society. The psychological

impact of genetic testing could be life-threatening, which may result in cognitive failure, lost responsiveness, reduced participation in activities, and functional impairment (Aziz et al., 2015).

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