Fragile X Syndrome

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Abstract
Fragile X syndrome is of rising maternal public health concern. Fragile x syndrome is an inherited form of learning disability which was discovered in the late 1970s. It was discovered by cytogenetic detection of an associated fragile site on the X chromosome. Fragile x syndrome makes clinical diagnosis difficult as it is associated with subtle physical features and few medical problems. There is no known cure, and treatment plans consisting of behavioral interventions are the most effective for living with fragile x syndrome. Future better future treatment care plans, there needs to be in-depth research surrounding the social determinants of health factors, which can affect a person who has fragile x syndrome. As well as how having fragile x syndrome makes one more vulnerable to other chronic illnesses.

Background:
Fragile X syndrome is one of the most commonly known inherited causes of intellectual disabilities. Both males and females who have fragile x syndrome exhibit a wide range of intellectual ability and may have various degrees of behavioral, emotional, social, and learning difficulties. “In 1991, the gene responsible for FXS was identified on the X chromosome and named fragile x mental retardation 1 (FMR1 gene)” (3).

By definition, Fragile X syndrome is a genetic disorder, which means there are changes to the genes in a person. Fragile X syndrome is caused by a change in the fragile x mental retardation 1 (FMR1) gene. Fragile X syndrome and fragile x syndrome-associated disorders are caused by a trinucleotide repeat (CGG) expansion mutation, which occurs in the promoter region (exon 1) of FMR1. “Affected individuals with the full FXS mutation have > 200 repeats. When the full mutation is present, FMR1 methylation occurs during gestation, which causes silencing of gene transcription” (3). “The FMR1 gene usually makes a protein called fragile x mental retardation protein (FMRP)” (3). Fragile x mental retardation protein (FMRP) is needed for there to be healthy brain development. People who have Fragile X syndrome are missing this necessary protein for proper brain development. Other people who have fragile x-associated disorders have changes in their FMR1 gene but make some protein for brain development. Fragile X syndrome affects both females and males. It is seen that females have milder symptoms when compared to males. “The exact number of people who have FXS is unknown, but it has been estimated that about 1.4 per 10,000 males and 0.9 per 10,000 females have FXS” (1). It affects almost twice as many males as it does females. However, it is shown that four times as many females appear to be carriers of the altered gene when compared to males. “1:250 females and 1:1000 males” (1). Most males who are diagnosed with fragile x syndrome have an intellectual disability. It is seen that a small number of males have less impaired function due to methylation patterns or mosaicism. “In females, FMRP levels depend on the X activation ratio or the percent of cells expressing the normal allele on the active X chromosome resulting in a range of normal intellectual ability to moderate intellectual disability” (1). Fragile X Syndrome has also been found in many major ethnic groups and races.

Scientists over the past two decades have made significant advancements in identifying and describing cellular, genetic, and molecular underpinnings of Fragile X Syndrome. These significant advancements help to make there be a more precise diagnosis of the condition. The current challenge at hand is to move from focusing on accurate diagnosis and make sure there is public health action in regards to Fragile X Syndrome. To ensure there is appropriate public health action taken it is required there be a better understanding of the natural history of Fragile X syndrome, clear description on how the complex conditions can affect the individual diagnosed and their families, and the identification of studied interventions and treatments which will lead to better health outcomes. Learning about the lifespan of those infected by Fragile X syndrome from a clinical aspect, family aspect, caretaker aspect, it will help as we design both treatments and services to provide the best optimal care.
Signs & Symptoms

There are various signs to look out for to see if one may have Fragile X Syndrome. For a young child, one can start to notice if the child has developmental delays such as not walking, not sitting, or talking around the age of other children the same age would. Another sign to look out for is learning disabilities, new ways of thinking, or one cannot look for social and behavioral problems as well. These signs include the child not making eye contact, having trouble paying attention, having anxiety, acting and speaking without thinking, headbanging, etc. “Fragile x syndrome is characterized by moderate intellectual disability in affected males and mild intellectual disability in affected females” (5). It is seen that males who have fragile x syndrome have some degree of the intellectual disability, which can range from mild to severe. It is seen that females who have fragile X syndrome can have normal intelligence and some degree of intellectual ability. “The physical features in affected males are varied and may not be obvious. An example of this is that the physical features affected include a large head, long face, protruding ears, prominent forehead, and chin, loose joints, low muscle tone, flat feet, poor ear infection, heart problems, and crossed eyes (strabismus). Autism spectrum disorders can also occur and is frequently seen in people with fragile x syndrome. The autistic behaviors which could be displayed include hand flapping, poor eye contact, or self-stimulating behaviors. Early motor and language delays can be present and become more apparent over time.

Screening, Testing, and Diagnosis

There are several approaches to screen prenatally based screening programs for several genetic conditions in newborns, preconception, and in prenatal settings. Specific criteria, such as those developed by the World Health Organization, are available to provide guidance on the suitability of screening (4).

Early diagnosis starts when a child is young. The diagnosis of fragile x syndrome when the young child is approximately three years old of age. The child should show signs of delayed or should be concerned about his or her development. The child should be referred to a pediatrician or a qualified health professional for an early checkup (4). Early intervention starts when a child is young. The diagnosis of fragile x syndrome is not always easy for the family to accept. The diagnosis is often delayed or not made at all. For the best optimal treatment plan for people who have fragile x syndrome, the child should be diagnosed as early as possible. Fragile x males rarely have children” (4). If a pre-mutation is identified in a woman, she will be offered DNA and amniocentesis testing to determine the fragile x genotype of the fetal cells. There is no effective treatment for the mental retardation associated with fragile x syndrome, but prenatal screenings for the disorder allow the parents to have the option of selective termination of affected fetuses. This would be an act of secondary prevention. Treatment methods that have been described include behavior therapy, which involves the help with identifying fetuses that transitioned to the full mutation “Prenatal screening would be restricted to pregnant women, because normal transmitting males do not give rise to offspring with the fragile X phenotype and because full mutation fragile x males rarely have children” (4). If a pre-mutation is identified in a woman, she will be offered DNA and amniocentesis testing to determine the fragile x genotype of the fetal cells. There is no effective treatment for the mental retardation associated with fragile x syndrome, but prenatal screenings for the disorder allow the parents to have the option of selective termination of affected fetuses. This would be an act of secondary prevention. The identification and treatment of fragile x syndrome are of high public health importance. The information presented provides an understanding of fragile x syndrome as well as screening protocols and its lack of inefficient treatment options. There is a wealth of information and research did in regards to fragile x syndrome, but much work is needed to support affected individuals and families fully. There are areas in which we have a wealth of data and areas in which we are lacking. Medical care for fragile x syndrome includes regular physical exams and appointments, mental health services, and behavioral health services (8).

To test for fragile x syndrome, DNA has to be taken by conducting a blood test. A doctor or genetic counselor can discuss the benefits and risks of this test. If the test results come back positive, a further genetic test is needed. This test is called the fragile x syndrome test. The test is done on a blood sample and can take several weeks to be completed. If the test results are negative, it means that the person does not have fragile x syndrome. If the test results are positive, it means that the person has fragile x syndrome. This test can be used to confirm the diagnosis, to help with planning for the future, and to provide genetic counseling for parents and other family members.

The identification and treatment of fragile x syndrome are of high public health importance. The information presented provides an understanding of fragile x syndrome as well as screening protocols and its lack of inefficient treatment options. There is a wealth of information and research did in regards to fragile x syndrome, but much work is needed to support affected individuals and families fully. There are areas in which we have a wealth of data and areas in which we are lacking. Medical care for fragile x syndrome includes regular physical exams and appointments, mental health services, and behavioral health services (8).

Currently, there is no successful treatment available for fragile x syndrome. Treatment services can help those infected with fragile x syndrome learn essential skills. These services can include a range of options, such as education, physical therapy, occupational therapy, and speech therapy. The services are designed to help individuals with fragile x syndrome live fulfilling lives and contribute to their communities (8).

The medical problems and physical features associated with fragile x syndrome are already well documented. What is lacking is the public health issues that are related to fragile x syndrome. These public health issues that have little research include dietary issues, obesity, sleep disorders, cardiovascular disease, and mental health conditions. The treatment options for fragile x syndrome include medication, therapy, and other interventions. The types of medication used to treat fragile x syndrome include antidepressants, antipsychotics, and mood stabilizers (8).

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