BioGecko

Vol 12 Issue 02 2023

ISSN NO: 2230-5807

Hemophilia:- To survey the percentage intensity of Haemophilia in Jammu

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Abstract:-

Hemophilia is an inherited bleeding disorder where blood doesn't clotproperly. It is caused when blood does not have enough clotting factor.India lacks a national policy on the prevention and control of genetic disorders. Although the haemoglobinopathies have received some attention, there are scarce data on the epidemiology of other genetic disorders in India. Haemophilia, an inherited single gene disorder with an incidence of 1 per 10,000 births, manifests as spontaneous or trauma-induced haemorrhagic episodes in patients, progressing to chronic disability and premature mortality in untreated patients or patients with sub-optimal treatment. Although the genetic basis of this disorder has been well studied in India, data on the number of patients, trends of the disorder in India, social costs of the condition and opportunities and competencies for offering genetic counselling through a public health programme have not been reported. A clotting factor is a protein in blood that controls bleeding. The primary function of the coagulation system is to maintain the integrity of the endothelium while preserving vasculature patency. The basal state of the coagulation system is nonthrombogenic for 2 main reasons: the coagulation factors circulate in their inactivated forms and the endothelium is nonthrombogenic. Disruption of the endothelium causes exposure of the thrombophilicsubendothelium and initiation of the hemostatic mechanism. In this paper we bring a survey the percentage intensity of haemophilia in jammu.

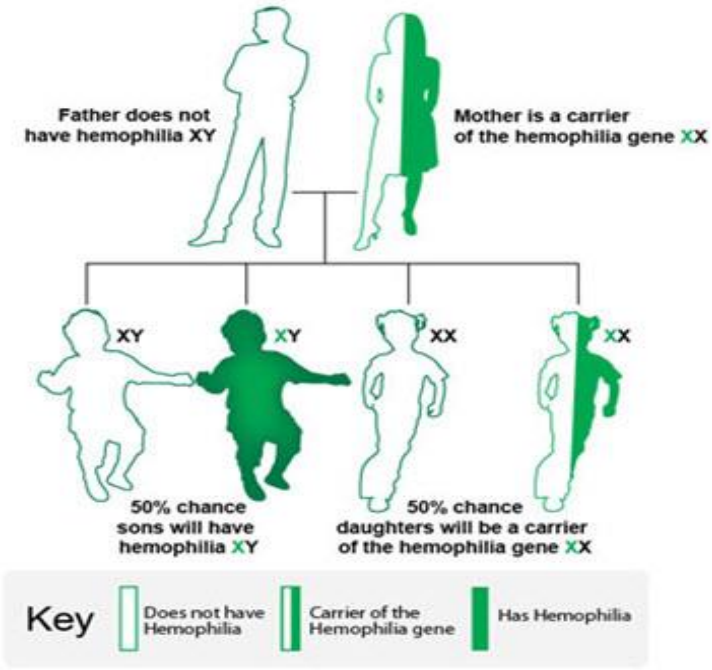
Keywords:-Hemophilia,Epidemiology,clotting factors,Bleeding disorder, Diseases.

Introduction

Genetic disorders are rare conditions that are accorded a low public health priority in India, even though these account for significant suffering of patients and their family members. Hemophilia is usually an inherited bleeding disorder in which the blood does not clot properly. Blood contains many proteins called clotting factors that can help to stop bleeding. People with hemophilia have low levels of either factor VIII (8) or factor IX (9). The severity of hemophilia that a person has to determine by the amount of factor in the blood. The lower the amount of the factor, the more likely it is that bleeding will occur which can lead to serious health problems. In rare cases, a person can develop hemophilia later in life. The majority of cases involve middle-aged or elderly people, or young women who have recently given birth or are in the later stages of pregnancy. This condition often resolves with appropriate treatment. Haemophilia is a serious ailment in which the blood lacks a clotting factor, thus, a cut or even a bruise can be fatal to a homophilic. In Queen Victoria's pedigree, the first instance of haemophilia was in one of her sons. since she passed the mutant allele on to some of her other children (carrier daughter), she must have been a carrier (heterozygous) herself. Scientists think the mutation occurred on an X chromosome in the germ cells of one of her parents. In X-Linked recessive traits, females usually must be homozygous for the recessive allele in order to express the mutant trait. The trait is expressed in males who possess only one copy of the mutant allele on the X chromosome. Therefore, affected males normally transmit the mutant gene to all their daughters but to none of their sons. The instance of father-to-son inheritance of a rare trait in a pedigree trends to rule out X-linked recessive inheritance. Other characteristics of X-linked recessive inheritance are following

1. For X-linked recessive mutant alleles many more males than females should exhibit the trait due to the different number of X chromosome in the two sexes.

2. All sons of an affected (homozygous mutant) mother should show the trait because males receive their only X chromosome from their mothers.
3. The sons of heterozygous (carrier) mothers should show an approximately1:1 ratio of normal individuals to individuals to individuals expressing the trait.



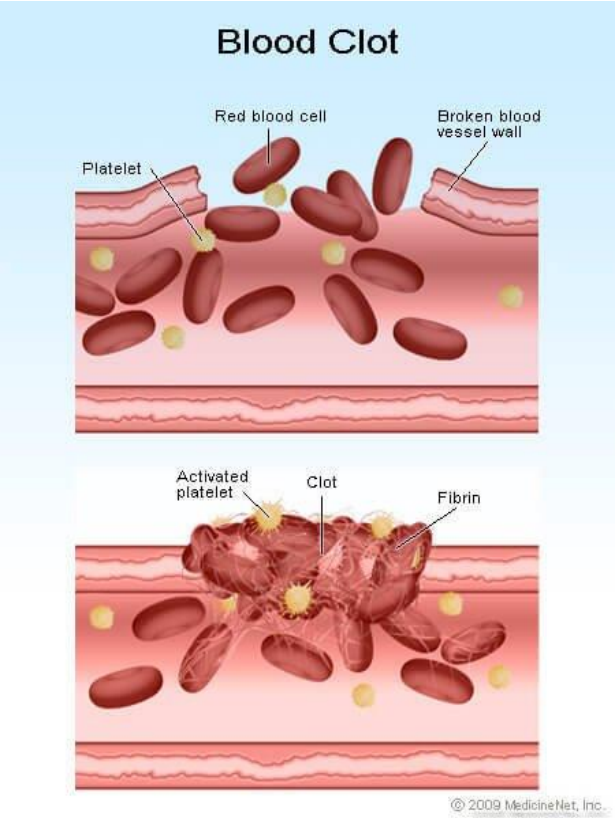
Haemophilia is caused by a mutation or change, in one of the genes, that provides instructions for making the clotting factor proteins needed to form a blood clot. This change or mutation can prevent the clotting protein from working properly or to be missing altogether. These genes are located on the X chromosome. Males have one X and one Y chromosome (XY) and females have two X chromosomes (XX). Males inherit the X chromosome from their mothers and the Y chromosome from their fathers. Females inherit one X chromosome from each parent.In Fig Males have one X and one Y chromosome (XY) and females have two X chromosomes (XX). Males inherit the X chromosome from their mothers and the Y chromosome from their fathers. Females inherit one X chromosome from each parent. The X chromosome contains many genes that are not present on the Y chromosome. This means that males only have one copy of most of the genes on the X chromosome, whereas females have 2 copies. Thus, males can have a disease like hemophilia if they inherit an affected X chromosome that has a mutation in either the factor VIII or factor IX gene. Females can also have hemophilia, but this is much rarer. In such cases both X chromosomes are affected or one is affected and the other is missing or inactive. In these females, bleeding symptoms may be similar to males with hemophilia. A female with one affected X chromosome is a “carrier” of hemophilia. Sometimes a female who is a carrier can have symptoms of hemophilia. In addition, she can pass the affected X chromosome with the clotting factor gene mutation on to her children.Even though hemophilia runs in families, some families have no prior history of family members with hemophilia. Sometimes, there are carrier females in the family, but no affected boys, just by chance. However, about one-third of the time, the baby with hemophilia is the first one in the family to be affected with a mutation in the gene for the clotting factor.

Hemophilia can result in:

- Bleeding within joints that can lead to chronic joint disease and pain
- Bleeding in the head and sometimes in the brain which can cause long term problems, such as seizures and paralysis

- Death can occur if the bleeding cannot be stopped or if it occurs in a vital organ such as the brain.

Hemophilia is not one disease but rather one of a group of inherited bleeding disorders that cause abnormal or exaggerated bleeding and poor blood clotting. The term is most commonly used to refer to two specific conditions known as hemophilia A and hemophilia B, Hemophilia A and B are distinguished by the specific gene that is mutated (altered to become defective) and codes for a defective clotting factor (protein) in each disease. hemophilia C (a deficiency of Factor XI) is encountered, but its effect on clotting is far less pronounced than A or B.Hemophilia A and B are inherited in an X-linked recessive genetic pattern and are therefore much more common in males. This pattern of inheritance means that a given gene on the X chromosome expresses itself only when there is no normal gene present. For example, a boy has only one X chromosome, so a boy with hemophilia has the defective gene on his sole X chromosome (and so is said to be hemizygous for hemophilia). Hemophilia is the most common X-linked genetic disease.Although it is much rarer, a girl can have hemophilia, but she would have to have the defective gene on both of her X chromosomes or have one hemophilia gene plus a lost or defective copy of the second X chromosome that should be carrying the normal genes. If a girl has one copy of the defective gene on one of her X chromosomes and a normal second X chromosome, she does not have hemophilia but is said to be heterozygous for hemophilia (a carrier). Her male children have a 50% chance of inheriting the one mutated X gene and thus have a 50% chance of inheriting hemophilia from their carrier mother.Hemophilia A occurs in about 1 out of every 5000 live male births. Hemophilia A and B occurs in all racial groups. Hemophilia A is about four times more common than B. B occurs in about 1 out of 20- 30,000 live male births.Hemophilia has been called the Royal Disease because Queen Victoria, Queen of England from 1837 to 1901, was a carrier. Her daughters passed the mutated gene on to members of the royal families of Germany, Spain, and Russia. Alexandra, Queen Victoria's granddaughter, who became Tsarina of Russia in the early 20th century when she married Tsar Nicholas II, was a carrier. Their son, the Tsarevich Alexei, suffered from hemophelia.Hemophilia is caused by a genetic mutation. The mutations involve genes that code for proteins that are essential in the blood clotting process. The bleeding symptoms arise because blood clotting is impaired.The process of blood clotting involves a series of complex mechanisms involving 13 different proteins, classically termed factors I through XIII and written with Roman numerals. If the lining of the blood vessels becomes damaged, platelets are recruited to the injured area to form an initial plug. These activated platelets release chemicals that start the clotting cascade, activating the series of 13 proteins known as clotting factors. Ultimately, fibrin is formed, the protein that crosslinks with itself to form a mesh that makes up the final blood clot. The protein involved with hemophilia A is factor VIII (factor 8) and with hemophilia B is factor IX (factor 9).



Hemophilia A is caused by a mutation in the gene for factor VIII, so there is deficiency of this clotting factor. Hemophilia B (also called Christmas disease) results from a deficiency of factor IX due to a mutation in the corresponding gene. A condition referred to as hemophilia C involves a deficiency of clotting factor XI. This condition is much rarer than hemophilia A and B and typically leads to mild symptoms. It is also not inherited in an X-linked manner and affects persons of both sexes. Hemophilia A is more common than hemophilia B. About 80% of people with hemophilia have hemophilia A. Hemophilia B occurs in about 1 out of every 20,000 to 30,000 people. A subgroup of those with hemophilia B has the so-called Leyden phenotype, which is characterized by a severe hemophilia in childhood that improves at puberty. Hemophelia is a serious ailment in which the blood lacks a clotting factor,thus a cut or even a bruise can be fatal to a haemophiliac. In queen Victoria pedigree, the first instance of haemophilia was in one of her sons. since she passed the mutant allele on to some of her other children(carrier daughters), she must have been a carrier (heterozygous) herself. Scientists think the mutation occurred on an X Chromosome in the germ cells of one of her parents. In X-linked recessive traits, females usually must be homozygous for the recessiveallele in order to express the mutant trait. The trait is expressed in males who possess only one copy of the mutant allele on the X chromosomegene to all their daughters but to none of their sons. The instance of father-to-son inheritance of a rare trait in a pedigree tends to rule out X-linked recessive inheritance. Other characteristics of X-linked recessive inheritance are the following

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2. all sons of an affected (Homozygous mutant) mother should show the trait because males receive their only X Chromosome from their mothers.
3. The sons of heterozygous (carrier) mothers should show an approximately 1:1 ratio of normal individuals to individuals expressing the trait.
4. From a mating of a carrier female with a normal male, all daughter will be normal phenotypically.

Clinical Epidemiological characteristics of Haemophilia

1.	Aetiology	Mutation in clotting factor VIII or IX gene, causing haemophilia A and B, respectively. Gene is located on the X chromosome, Xq28 and Xq27.1-q27[22].
2.	Signs and symptoms	Spontaneous bleeding, haematomas, haemarthroses and haematuria, soft tissue bleeds, including life threatening bleeds of the central nervous system. Frequency dependent on residual clotting factor activity, and genotype of patient[23].
3	Complications	Haemarthrosis, transfusion related infections such as HIV and HCV, development of inhibitors[24].
4	Social issues	Poor quality of life[25] due to chronic pain, frequent absenteeism due to bleeding episodes resulting in poor schooling and poor employability, gender related issues due to victimization of mother or maternal guilt, economic consequences due to high cost of treatment product and the need to make out of pocket payments[26].
5	Estimated incidence	Haemophilia A 1 per 5 000 male births[27]. Haemophilia B 1 per 30 000 male births[28].
6	Epidemiology	Haemophilia A is the more common disorder constituting 70 per cent case burden. No ethnic or geographic association has been reported[27].
7	Number of haemophilia A patients in India	11, 586, second highest global burden of patients after USA (13,276)[29]. Extensive underdiagnosis (case detection rate 0.9 per 1,00,000 as compared to 4.3 per 1,00,000 for the USA).
8	Genetics	70 per cent patients report family history and 30 per cent are sporadic cases. If familial, mother is a carrier and has a 50 per cent risk of transmission of the defective gene to son[22].
9	Treatment	Prophylactic infusions of clotting factor concentrate or infusion on demand to stop bleeding. Indian patients usually manage bleeds through basic first aid measure, that is rest, ice application, compression and elevation of affected limb (RICE)[30].
10	Haemophilia care in India	Clotting factor concentrate is imported by the Hemophilia Federation of India (HFI), a patients' organization which has 76 chapters throughout the country[31]. Treatment product is dispensed through these centres, which are also associated with a physician/hospital with specialist services for treating patients with bleeding disorders. A few States and Union Territories (UT) have initiated services for small number of patients through the NRHM flexipool budget. A national haematology programme for haemophilia, thalassaemia and sickle cell anaemia is being piloted in Maharashtra through the NRHM[17].
11	Prevention	Through carrier detection and prenatal diagnosis.

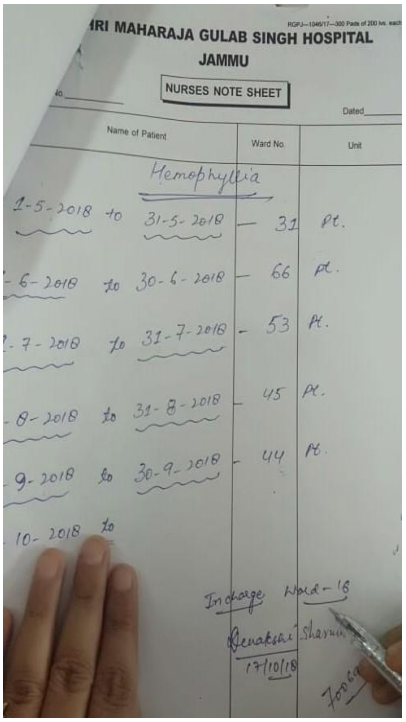
To survey the percentage intensity of haemophilia in jammu

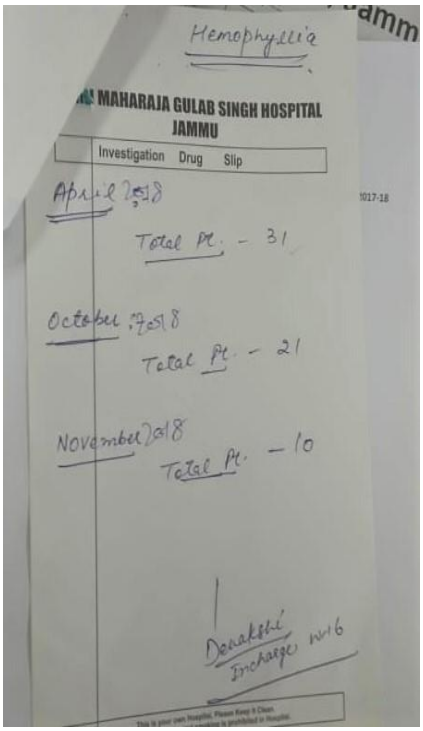
Hemophilia is a group of hereditary genetic disorders that impair the body's ability to control blood clotting or coagulation, which is used to stop bleeding when a blood vessel is broken. As per World Health Organization (WHO), the most common form of male predominant disorder, Haemophilia 'A' occurs in about 1 in 5,000–10,000 male births due to the deficiency of clotting factor VIII, while Haemophilia 'B' that occurs in 1 male birth in 20,000–34,000 male births due to the deficiency of the clotting factor IX.

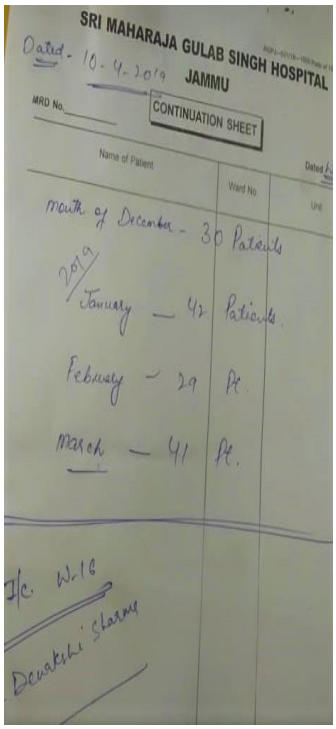
- Dr Mukhtar Ahmed Masoodi, a Haematologist at SKIMS said, "If we apply WHO parameters in J&K, then more than 1000 male are suffering from this disorder, considering the population of the state as 60 Lakh. However, only 258 cases have been registered in the state, 190 in Kashmir and 68 in Jammu.
- Members of the society, Hemophilia patients, their families and friends attended the camp which raised about Hemophilia care through continuous supervision of all the medical and psychosocial aspects of bleeding disorders so that a Hemophilia patient can lead their lives as normal as any one of us.
- Despite improvement in the medical technologies for the treatment of haemophilia, healthexperts believe that nearly 80 per cent of Indians with the serious blood disorder are not diagnosed due to the absence of proper diagnostic facilities in the remote areas.
- According to Haemophilia Foundation of India, the umbrella body for registration of the patient with the disorder, the cause of haemophilia is the inability of the body to produce the anti-haemophilic factor (AHF) in the required quantity.
- There is no known cure for this disorder.If not diagnosed early, the repeated bleeding into joints, bones muscles may lead to synovitis, arthritis and permanent joint deformities.The bleeding itself can lead to wasting and atrophy of muscles.

- Dr Ruby Reshi, head of Pathology department at Government Medical College Jammu in Jammu and Kashmir, said India is fast progressing in the field of haemophilia treatment but the core problem is of diagnosis.

Jammu & Kashmir lacks a policy to tackle haemophilia, a genetic bleeding disorder that affects around 3,000 families in the state.Due to the alleged callous attitude of the government, each year around 1,300 cases remain undiagnosed, said Vijay Kaul, executive director, Society for Haemophilia Care, a Delhi-based non-governmental organisation, in a press conference here today."According to the World Health Organisation (WHO) guidelines, there is a haemophilia patient in every 10,000 population and by that standard Kashmir division, which has 230 registered patients, has missed 1,300 haemophilia cases,"







Conclusion

Hemophilia is a genetic disorder inherited in an Xlinkedfashion. Both diseases cause similar bleedingdiatheses, with the hallmark being hemarthroses.The optimal treatment is recombinant factorreplacement to prevent bleeding; however, thistreatment has many barriers.India with nearly two lakh cases is estimated to have the second highest number of patients with haemophilia, a lifelong bleeding disorder that prevents blood from clotting, doctors said ahead of the World HaemophiliaDay on April 17. The complacency about the low prevalence of genetic disorders in India may have to be revisited. Even at the current rates of case detection, India appears to harbour a large patient burden. The high cost of providing treatment for patients is likely to overwhelm the public health services, suggesting the need for launching a national programme for haemophilia with components of prevention, care and support.

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