GENETIC BEHAVIOUR, DISABILITY CAUSED DUE TO BLOOD DISORDER HAEMOPHILIA, THALASSEMIA, SICKLE CELL DISEASE

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ABSTRACT

BACKGROUND

Thalassemia are inherited blood disorders characterized by abnormal haemoglobin production (Low red blood cells) it is a genetic disorder inherited from a person's parents.[1]

In 2013, thalassemia occurs in about to 280 million people, with about 4,39,000 having severe disease. Male and female similar have rates of deaths. In 2015 it results in 16,800 deaths down from 1990 - 36000 deaths those you are minor degrees of thalassemia. Similar to those with sickly cell trait, have some production against malaria, explaining why they are more common in reasons of the world were malaria exists. Sickle cell anaemia is an inherited form of anaemia- a condition in which there are not enough healthy red blood cells to carry adequate oxygen in body, it becomes rigid, sticky and are shape like sickle or crescent moon. The cells struck in small blood vessel, which slow or block blood flow and oxygen to our parts of body. There is no cured for most people with sickle cells anaemia, but treatments can relive pain and help prevent problems associated with the disease.[2] The purpose of this study is to improve efficiency, improve health care delivery, improve quality assistance/quality improvement.

KEYWORDS

Inheritance of Anaemia, Crises, Frequent Infection, Genetic Counsellor, Splenomegaly, Broken Bole, Haemoglobin, Chelating Therapy, Cardiac Issues.

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BACKGROUND

Figure 1. Human Blood

Haemophilia

According to the world federation of haemophilia (WFH), about one in 10,000 people are born with disease. According to the National Heart, Lung and Blood Institute (NHLBI), eight out of 10 people with haemophilia have haemophilia A. Haemophilia is an inherited genetic condition. It is known as coagulation cascade.[3]

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Haemophilia is an inherited bleeding disorder in which a person lacks or has low levels of certain proteins called "clotting factors" and the blood doesn't clot property as a result. This leads to excessive bleeding. There are 13 types of clotting factors, and these work with platelets to help the blood clot. Platelets are small blood cells that form in your bone marrow.

Types of Haemophilia

Haemophilia A, B, C
Haemophilia A: Caused by a deficiency in Factor VIII.
Haemophilia B: Factor IX (Christmas Disease)
Haemophilia C: Factor XI

Figure 2

Acquired haemophilia. Immune system forms antibodies that attack factors VIII or IX. This condition is not curable it develops after birth.

Symptoms of Haemophilia

Blood in urine, stool, Deep bruise, Gums, Nosebleeds, Pain in the joints, Irritability etc.

Signs of Haemophilia

Headache, Vomiting, leg pain, double vision, sleepiness etc.

Complications

Joint damages, deep internal bleeding in brain and infection.

Treatment

Haemophilia A prescription hormones, injection, desmopressin, haemophilia B in fused blood with donor clot factor recombination, coagulant factors.

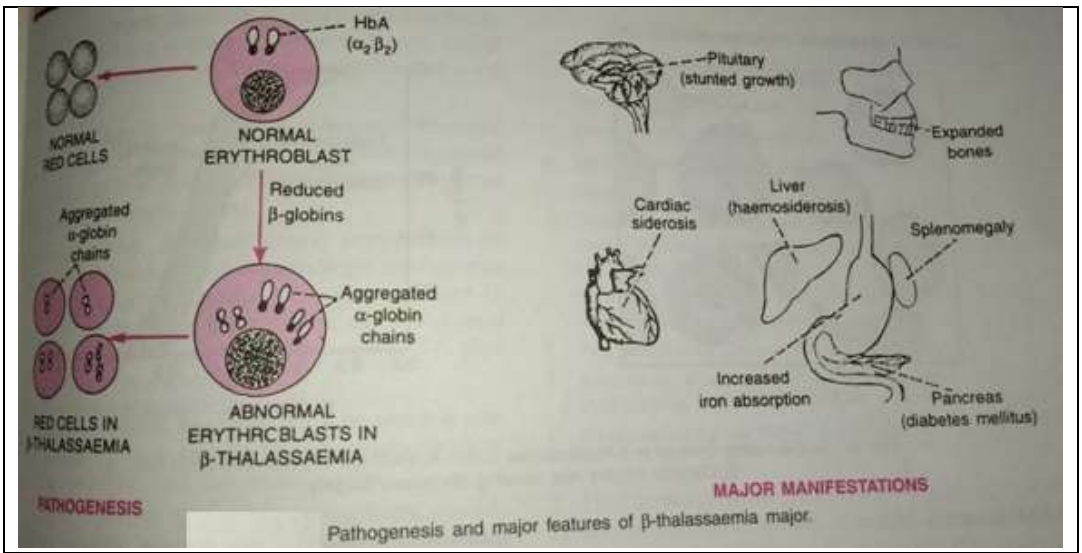

Figure 3

Haemophilia C Plasma Infusion

Thalassaemia (Cooley's anaemia) a hereditary blood disease, widespread in the Mediterranean countries, Asia, and Africa in which there is an abnormality in the protein part of the haemoglobin molecule. The affected red cells cannot function normally; leading to anaemia other symptoms include enlargement of the spleen and abnormalities of the bone marrow. Individuals inheriting the defective gene from both parents are severely affected (Thalassaemia major), but dose inheriting it from only one parent are usually symptom free. Patients with the major disease are treated with repeated blood transfusions or bone marrow transplantation. The disease can be detected by prenatal diagnosis.[4]

Type α- Thalassemia	HB	HB Electrophoresis	Clinical Syndrom
1. Hydrops Fetalis	3-10 g/dl	HB Barts (1%) (100%)	Fatal in Ulterior in Early Infancy
2. HB H disease	2-12 g/dl	Hbf (10%)	Haemolytic Anaemia
3.·- Thalassemia Trait	10-14 g/dl	Normal	Microcytic Hypochromic Blood Picture but No Anaemia
Type ß- Thalassemia			
1. ß- Thalassemia Major	<5 g/dL	HBA (0.50%)	Severe congenital haemolytic anaemia, requires blood transfusions
2. ß- Thalassemia Intermedia	5-10 g/dL	Variable	Severe anaemia, but regular blood trans not required
3. ß- Thalassaemia Minor	10-12 g/dL	Hb	

Table 1. Classification of Thalassemia

Thalassemia

Figure 4

In 1932 First Case was noted. The word thalassemia derived from Greek.

Thalass = Sea, Emia = blood.

Celebrating World Thalassemia Day on 8th of May was established by the World Health Organization in order to raise the public awareness about this disease, prevention measures and measures to avoid its transmission.

According to the statistics, around 19% of the total population is the carrier of Thalassemia gene in the Saudi Arabia Kingdom. Thus, world thalassemia day is celebrated

there as a big event by organizing variety of preventive programs to increase awareness and reduce spread of this genetic disease. This event celebration promotes and encourages the common public for the pre-marriage test to reduce the genetic problems among families.

Around 3.4% of the people are carrier of the thalassemia and around 7000 to 10,000 children are born with thalassemia per year in India. It can be of any type such as alpha thalassemia, beta thalassemia, delta thalassemia and combination of other haemoglobinopathies (haemoglobin C, D, E and S).

Mild thalassemia sometimes does not show any symptoms thus can be undiagnosed until blood test (complete blood count, CBC test). It can be treated through the blood transfusion, B group Thalassemia vitamins supplements, Iron chelation therapy and Blood and bone marrow stem cell transplantation to maintain the normal level of haemoglobin and healthy RBCs.

Since, it is an inheritable disease so cannot be prevented completely however, it can be lessened through the prenatal tests which helps in the early detection and cure before the child birth. It is requested to all the carriers of thalassemia gene to meet a genetic counselor as soon as possible to get proper treatment before being a parent of child or prevent the gene to get inherited to their child.

Sickle-Cell Disease (Drepanocytosis)

A hereditary blood disease that mainly affects people of African ancestry but also occurs in the Mediterranean region and reaches high frequencies in parts of Saudi Arabia and India. It occurs when the sickle-cell gene has been inherited from both parents and is characterized by the production of an abnormal type of haemoglobin -sickle-cell haemoglobin (Hbs) which precipitates in the red cells when the blood is deprived of oxygen, forming crystals that distort the cells into the characteristic sickle shape: this process is known as sickling. An excess of sickle cells in the circulation results in blockage of small blood vessels, producing episodes of severe pain (a sickle-cell crisis). Sickle cells are rapidly removed from the circulation, leading to anaemia and jaundice. There is no satisfactory treatment; the highest mortality is in childhood, but some patients may live to an age of 60-70 years.

The carrier condition (sickle-cell trait) occurs when the defective gene is inherited from only one parent. It generally causes no symptoms but confers some protection from malaria, which accounts for the high frequency of the gene in malarias areas. U a general anesthetic is to be given to a patient with this condition, the anesthetist should be alerted.

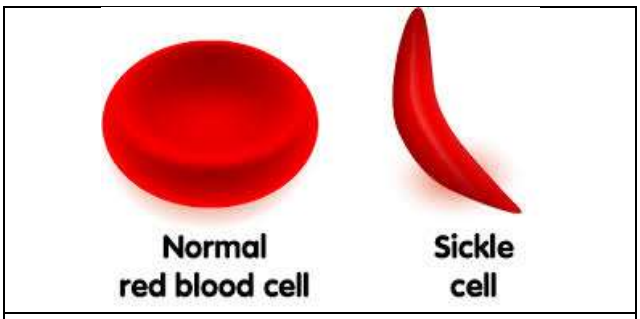

Figure 5

June 19 is World Sickle Cell Day.

In 2008, June 19 was officially designated as World Sickle Cell Awareness Day.

The international awareness day is observed annually in an attempt to increase public knowledge and an understanding of sickle cell disease, while educating those who may not know enough about the struggles experienced by patients and their families and caregivers. Sickle cell disease patients have red blood cells that are hard, sticky and C-shaped (like the farm tool, a "sickle), and the potentially-fatal rare genetic condition affects an estimated 95,000 Americans – both adults and children. The misshapen sickle cells clog smaller blood vessels, result in excruciating pain and put patients at an increased risk for infection acute chest syndrome and stroke.

Sickle cell disease has been a focus for Rare Disease Report throughout the years, and the resources below are sure to be helpful to patients, caregivers and advocates.

At the 58th Annual American Society of Hematology (ASH) Meeting & Exposition in December, Rare Disease Report met with Kevin Kuo, MD of the University of Toronto to discuss transitioning teens with sickle cell disease into adulthood.

The abnormal haemoglobin results in lower concentration of oxygen. Consequence red blood cells become sickle shaped and may rupture, causing hemolytic anaemia. The two conditions are compared in Table 1.

Occurrence	It is seen in a heterozygote with one normal and one abnormal gene	It is seen in a homozygote with both abnormal genes
Amount of Abnormal Haemoglobin	30%	100%
Severity	Less severe (Directed only by fatal examination of blood)	Fatal

Table 2. Comparison of Sickle Cell Trait and Sickle Cell Anaemia

Every April 17 World Haemophilia Day is recognised worldwide to increase awareness of haemophilia and other inherited bleeding disorders. This is a critical effort since with

increased awareness comes better diagnosis and access to care for the millions who remain without treatment.

Share your personal experiences and knowledge with one another. HFA will be celebrating peer support and bleeding disorders awareness on World Haemophilia Day by launching a series of new personal stories.

Thal-as-mia a heterogenic nous group of hereditary hemolytic anaemias marked by a decreased rate of synthesis of one or more haemoglobin polypeptide chains, classified according to the chain involved {α, ß,}; the two major categories are α-and ß- thalassemia.

α- thalassemia that caused by diminished synthesis of alpha chains of haemoglobin. The homozygous form is incompatible with life, the stillborn infant displaying severe hydrops fetalis. The heterozygous form may be asymptomatic or marked by mild anaemia.

ß- Thalassemia that caused by diminished synthesis of beta chains of haemoglobin. The homozygous form is called t. major and major, the homozygous form of ß - thalassemia, in which haemoglobin A is completely absent. It appears in the newborn period and is marked by Hemolytic, Hypochromic, Microcytic anaemia. Hepatosplenomegaly, Skeletal deformation, Mongoloid Facies, and cardiac enlargement.

Thalassemia minor, the heterozygous form of ß-thalassemia, usually asymptomatic, although there is sometimes mild anaemia.

Sickle cell-Thalassemia a hereditary anaemia involving simultaneous hetero zygosity for haemoglobin s and thalassemia.

DISCUSSION

- Genetics is a rapidly expanding field of the medical science. All components of the human body are influenced by the genes, so knowing the basic concepts of human genetics are essential in the diagnosis, management and prevention of the various disorders. Every person related to medical field needs to know the fundamental aspects of the genetics.
- Man's most precious treasure is his genetics heritage which guides the health and proper development of future generation. The term genetics was coined by Bateson in 19.06. it has been derived from the Greek word 'gene' (gene= 'to become' or to 'grow into')

Why to Study Genetics

- It helps us to understand how normal variations between individuals are brought about.
- Knowledge of genetics is helpful in understanding the causation of diseases.
- A detailed study of the subject is important for understanding of disease process, prognosis and its effective management at the molecular level. Fig. no. 6. (Gregor Mendel) Father of Genetics.

Figure 6. Gregor Mendel

- Means of prevention of genetic disorders through genetic counselling and antenatal diagnosis
- Genetics serves to solve even legal problems. Legal cases like disputed parentage and investigation of crimes may be sorted out by an analysis of blood groups.

Father of Genetics

- DNA fingerprinting or other inherited characteristics
- It is a branch of science which deals with the application of principles of heredity for the improvement of mankind.
- Gregor Mendel (1822-1884) an Austrian monk considered as "Father of Genetics"

Children with congenital asplenia or splenectomy (Functional Asplenia) or sickle cell disease should receive H1b as well as Pneumococcal vaccine.

Factors Responsible for Chromosomal Aberrations

- Ionizing radiation
- Viruses
- Chemical carcinogens
- Late maternal or paternal age
- Nondisjunction

Structural Abnormalities

- Deletion
- Ring chromosome
- Duplication
- Translocation
- Insertion
- Isochromosome
- Inversion

Disorders Affecting Autosomes

- Cri du chat syndrome – 5p
- Down's syndrome – Trisomy 21
- Patau's syndrome – Trisomy 13
- Edward Syndrome – Trisomy 18
- Philadelphia chromosome – t (22q-; 9q+)

Functions

- Genes maintain the specificity of an individual
- Genes play vital role in the transmission of characters from parents to off springs
- Genes are very important for synthesis of various proteins and enzymes of the cell.
- Eugenics refers to improvement of the genetic stock of the race. Eugenic aspects of services to the mother include prevention of births of children with serious genetic disease, e.g., Down's syndrome, muscular dystrophies, haemophilia etc. this may be achieved

through nonterminal or terminal methods of contraception or through medical termination of pregnancy screaming and abortion

- In the initial phase the main focus will be upon prevention and control of alcohol related problems. Later on addictions, juvenile delinquency and acute adjustment problems will be brought into the ambit. Community leaders and PHC medical officers would be actively involved in this activity.
- Management: -
  1. Avoid routine use of Iron
  2. Blood transfusion prolong life only
  3. Iron over load – chelation therapy
  4. Medication: Deferoxamine, deferiprone. Deferasirox these drugs improve life.
  5. Bone marrow transplantation (BMT)
  6. Society and culture participation
  7. Umbilical cord was saved transplantation
  8. Genetic counselling
  9. Prenatal diagnosis
     - Non-invasive
       - Ultrasound
       - Fetal echocardiograms
       - Computerized tomography (CT) and magnetic resonance imaging.
     - Invasive
       - Serum alpha fetoprotein(AFP)
       - Amniocentesis
       - Chorionic villous sampling
       - Fetal blood sampling
       - Fetoscopy
     - Elimination in diet
       - Phenylalanine in Phenylketonuria
       - Reduction of diet with high cholesterol in familial hypercholesterolemia
       - Carbohydrate in galactosemia
     - Supplementation in diet: Vitamin c supplementation in deficiency of vitamin c Synthesis
     - Replacement Therapy
       - Patients of haemophilia can be helped by administering ant haemophilic globulin
       - Replacement of Vitamin D in vitamin D resistant rickets
       - Thyroxin in congenital hypothyroidism
     - Surgical procedures:
       - Spina bifida can be corrected by surgical methods
       - Colectomy can be done in polyposis coli
       - Organ replacement includes kidney transplant in adult polycystic disease
     - Gene therapy
       - Replacement of a mutant gene causing the disease with a healthy functioning
       - Introducing of a new gene into the body which helps to fight disease.
       - Inactivation of the mutant gene, responsible for abnormal functioning.

Figure 7

CONCLUSION

MPWs

- Early recognition of all severe mental disorders and epilepsy in the community
- Referral of the identified patients to the primary health centers
- Regular follow up of such patients in the community, with feedback to the doctors at the PHC
- Education and motivation of the patient, s family members and neighbours to look after the patient humanely
- Management of psychiatric emergencies, e. g, acute excitement, when no doctor is available.

MOs

- Diagnosis and management of severe mental disorder, both acute and chronic
- Referral of difficult cases for specialist opinion to district hospital and receiving them back for further follow—up
- Supervision and guidance of multipurpose workers.

Budget

- The planning commission allocated Rs. 1.00 crore for implementing the program during the 7th plan NIMHANS, Bangalore, has been entrusted the job for preparing the necessary manuals related to the program.

Figure 8

Haemophilia either of two hereditary disorders in which the blood clots very slowly, due to deficiency of either of two coagulation factors; haemophilia A, due to deficiency of Factor VIII (antihaemophilic factor); or haemophilia B, due to deficiency of Factor IX (Christmas factor). The patient

may experience prolonged bleeding following any injury or wound, and in severe cases there is spontaneous bleeding into muscles and joints. Bleeding in Haemophilia may be treated by recombinant – DNA- derived factor VIII or plasma factor VIII concentrate. Alternatively, concentrated preparations of factor VIII or factor IX, obtained by freezing fresh plasma, may be administered (see Cryoprecipitate). Haemophilia is controlled by a sex-linked gene, which means that it is almost exclusively restricted to males; women can carry the gene and pass it on to their sons – without being affected themselves. The genes encoding factors VIII and IX have been used in gene therapy trials for haemophilia-haemophiliac n.

Genotype	Clinical Diagnosis	Hb A	Hb S	Hb A2	Hb F
AA	Normal	97-99%	0	1-2%	<1%
AS	Sickle Trait	60%	40%	1-2%	<1%
SS	Sickle Cell Anaemia	0	86-98%	1-3%	5-15%
S β+ Thalassemia	Sickle β Thalassemia	0	70-80%	3-5%	10-20%
Sb+ Thalassemia	Sickle β Thalassemia	10-20%	60-75%	3-5%	10-20%
AS, α Thalassemia	Sickle Trait	70-75%	25-30%	1-2%	<1 %

Table 3

Prevention

- The initial page, the main focus will be upon prevention and control of alcohol related problems. Later acute adjustment problems will be brought into the ambit. Community leaders and PHC medical officers would be actively involved in this activity.
- Awareness campaigns
- Chelating therapy
- Perinatal diagnosis
- Launching a serious of new personal stories
- International awareness day is observed annually in all over attempt to increase public knowledge understand the problem
- Struggles experience by patient and their family and care givers and advocates
- Sickle cell anaemia Day is 19th June
- Thalassemia Day 8th April[6]
- Haemophilia Day 17th April
- CBC (Complete blood count) tests all the people throughout the world on the above days. Like Saudi Arabia Kingdom.
- Without blood test do not marry, not to give child birth
- Pre-marriage test to reduce genetic problems of families.
- Light it up day = in Australia and around world will support the world blood disease days by change their lighting red on those days. It shows support on night.[7]
- Prevent disease to spread in the community, society, state, country finally world.
- Genetic council genetic testing as soon as to get proper treatment[8]

Recent Advances in Genetics[9]:

Applications of genomic library

- Determining the complete genome sequence of a given organism
- Helps to understand the molecular basis various diseases
- Human proteins like insulin and growth hormone can be produced
- Study of genetic mutations in cancer tissues.

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