wjpmr, 2022, 8(3), 151 – 159.

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

A NARRATIVE REVIEW ON AVASCULAR NECROSIS OF FEMORAL HEAD IN SICKLE CELL PATIENTS IN TRIBAL BELTS OF MAHARASHTRA

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Article Received on 27/12/2021 **Article Revised on 17/01/2022** **Article Accepted on 07/02/2022**

ABSTRACT

Avascular necrosis (AVN), is also known as osteonecrosis. Avascular necrosis is a disease that results from the temporary or permanent loss of blood supply to the bone. When blood supply is cut off, and ischemia of bone tissue has taken place, leading to infarction, ultimately the bone tissue dies and the bone collapses.[1] If avascular necrosis happens near a joint, the joint surface may collapse. More than 20,000 people each year enter hospitals for treatment of osteonecrosis of the hip. In this disease, bilateral involvement is found in many cases. The prevalence of AVN is around 20,000–30.000 new diagnoses per year. This condition may happen in any bone. This can result from trauma such as femoral neck fracture or because of the atraumatic associated etiologies [2] such as excessive alcohol, glucocorticoid use, Sickle Cell anemia, systemic lupus erythematous (SLE), radiation therapy, and coagulopathy. In these conditions there occurs an ischemic consequence because of the compromised blood flow to the femoral head. Most living tissues need oxygen, without which there is inefficient metabolic functioning. Once infarction takes place, oxidative phosphorylation cannot take place and necrosis ensues. AVN is multifactorial but can begin with interruption of blood and oxygen supply to vasculature in and around the bone. It progresses to trabecular thinning (seen in osteoporosis also) and it results in the collapse of the bone. In the case of sickle cell disease, this infarction results from occlusion of the vasculature by red blood cells (RBCs) which have changed their form from biconcave or round to crescent or sickle shape and flow less smoothly in the blood vessels. Their shape allows them to adhere to other RBCs as well as the endothelial walls, worsening vaso-occlusion. This leads to occlusion of bone marrow, ischemia, and progression to AVN. It is common in sickle cell disease. As much as 50% of sickle cell patients can develop AVN by the time they reach the age of 35. However, it is very rare in sickle cell trait (SCT), a much milder form of sickle cell disease in which patients are usually asymptomatic.

KEYWORDS: Avascular necrosis, Sickle cell disease.

INTRODUCTION

Sickle cell hemoglobinopathy is a genetically transmitted multisystem disease that includes a group of disorders that differ in severity of signs and symptoms. The disease is not uniformly seen everywhere but it has some topographical distribution. In India, it is frequently seen in Central India, in and around the vicinity of Nagpur and around the ranges of Satpuda mostly in tribal populations. Despite the fact that Sickle cell hemoglobinopathy is infrequently observed, it has great pathological significance considering the high morbidity and mortality resulting from the disease process. The exact etiopathology at both molecular and genetic levels has been extensively studied thoroughly, yet there is no cure or established treatment regimen that will arrest the disease. The risk of death from complications of Sickle cell disease is highest in children under the age of five years and it is suggested that with early detection and appropriate management the mortality in this age group can be reduced to less than five percent. Different modalities of treatment including bone marrow transplant are still in experimental stages and as of today, we do not have any satisfactory modality available that will be effective in the treatment of this disease and its complications. Hence early diagnosis and efficient medical supervision for recognition of complications remain the gold standard in the management of this inherited disorder. Early diagnosis and appropriate intervention can delay the need for joint replacement. Without treatment, the process is almost always progressive, leading to joint destruction within 5years. Another important aspect as regards the prevention of Sickle cell hemoglobinopathy is genetic hence 1) Premarriage counseling and 2) Prenatal diagnosis in the first trimester for any disability in high-risk couples. 3) Avoiding the consanguineous marriages in the susceptible community. In this autosomal recessive disorder, the incidence can be significantly reduced by using these three gold standards. Skeletal manifestations resulting from this hematological disorder are seen in

patients in all age groups as a result of the disease process, sequelae, and its complications. Observations are based on the Patients studied, followed, and treated at Mahatma Gandhi Institute of Medical Sciences Sewagram, Wardha. Sickling was done by sickling test with sealed moist preparation and diagnosis was confirmed by hemoglobin electrophoresis done with paper electrophoresis as described by Goldberg 1956. Each patient underwent a thorough clinical examination conducted X-ray, M.R.I. were done and subsequently followed. Hence skeletal survey is an important factor in the early detection. Accordingly, apart from Physical Examination, X-rays of the suspected skeletal involvement M.R.I. scan are important landmarks in diagnosing AVN of Femoral Head in sicklers at the earliest amongst the specific community. Promoting awareness regarding Sickle cell disease, its relation with socio-economic status, its presence in certain communities i.e. scheduled castes and tribes, and clues to early diagnosis through mass education and encouraging frequent check-ups, especially in people of the susceptible community will reduce the mortality and morbidity due to Sickle cell disease. Similarly, observations based on personal experience, especially for early detection should assist Orthopedic Surgeons, Radiologists, Pediatricians, and Physicians in the diagnosis and management of patients with Sickle cell hemoglobinopathy. Genetic and marriage counseling still remains the gold standard for prevention and dilution of disease until an effective cure is found.

REVIEW OF LITERATURE

In 1910, J.B. Herrick,[3] a cardiologist from Chicago first reported a case with "peculiar elongated and sickle-shaped red blood corpuscles" in a case of severe anemia. So-called "Herrick anemia". The second and third cases of Sickle cell anemia were reported by Washburn 1911, Cook and Meyer 1915. In 1922 Mason first time used the term "Sickle cell anemia". In 1948, Daland and Castle demonstrated a simple and rapid method for the detection of sickling of red blood cells by the use of reducing agents. Pauling in 1949 found the use of electrophoresis with paper electrophoresis as described by Goldberg in 1956. The erythrocytes from the patient of Sickle cell trait contained approximately 60% normal hemoglobin and 40% abnormal hemoglobin. In Sickle cell anemia patients he found 100% sickle hemoglobins. Ingram 1959 showed the chemical differences in hemoglobin and the patterns of hemoglobin in sickle cell anemia. Ponder in 1948 described the details regarding the pathophysiology of sickling of RBCs. The word 'Crisis' was first used in association with Sickle cell anemia in 1924 by Sydenstricker. However, the accepted definition and classification of the Sickle cell crisis was reported by L.W. Diggs, 1965. Sickle cell disease is an important cause of bone and joint pains and swelling. Skeletal changes in Sickle cell disease were observed as early as 1924 by Graham. Association of skeletal changes with Sickle cell disease was also observed by Caffey 1937, Golding 1959 and Diggs 1965. The effect of Sickle cell disease on the skeletal system during the multiple episodes was reported by Diggs 1965 & Henderson 1946. Etiology Normal Structure of Hemoglobin Hemoglobin is the complex molecule responsible for blood's high solubility for oxygen. Hemoglobin is found in the cytoplasm of red blood cells, erythrocytes, and consists of two pairs of unlike protein subunits, termed goblins, bound into a single molecule. Each globin contains an iron molecule, heme, to which oxygen can bind for transport to the body's tissues. The three dimentional structure is shown in figure1. Through the erythrocyte membrane, Oxygen diffuses and is bound to hemoglobin. Each hemoglobin molecule, with its four globin subunits and corresponding heme rings, can bind a total of four molecules of oxygen. Hemoglobin is commonly abbreviated Hb. Hemoglobin A in adults is abbreviated as HbA consists of two alpha (α) and two beta goblins (β). Fetal hemoglobin, abbreviated HbF, consists of two alpha (α) and two gamma globins (γ). HbF is the primary hemoglobin during the first stages of life.

Hemolytic Anemias

There are multiple genetic conditions known to produce hemolytic anemias. In hemolytic anemias, erythrocytes have shortened survival times and/or experience premature hemolysis. Sickle cell disease is, then, a problem of hemolysis, not of inadequate production. Some of the other conditions that fall into the category of hemolytic anemias are thalassemias, glucose-6-phosphate dehydrogenase (G6PD) deficiency, hereditary spherocytosis, and hemoglobinopathies including sickle cell disease.

Hemoglobinopathies: Sickle Cell Disease

Hemoglobinopathies are a family of hereditary disorders involving structural abnormalities of the hemoglobin molecule.[4] Over 300 hemoglobinopathies have been identified; one of the most notable of these is sickle cell disease, which involves the beta-globin of hemoglobin. Sickle cell disease is the result any of a number of genetic abnormalities that produce aberrant hemoglobin structures, such as hemoglobin S (HbS) and hemoglobin C (HBC). In sickle cell disease, the two alpha globins of hemoglobin are normal, but there are substitutions in the beta chain. In HbS, a substitution of valine for glutamic acid occurs at the sixth amino acid of the beta chain of hemoglobin. In HbC, lysine is substituted for glutamic acid at the sixth amino acid in the beta chain. β-globin is a 145 amino acid sequence. A single substitution mutation in the sequence produces a change in the tertiary structure of the beta-globin such that the oxygen-carryin capacity of HbS and HbC is significantly lower than that of HbA. HbS is the more severe form of the disease.

MATERIAL AND METHODS

This narrative study was conducted after review of different articles related to the Avascular necrosis of femoral head in Sickle cell Anaemia through PUBMED, NCBI, ORTHOBULLETS, JBJS and OCNA.

PATHOPHYSIOLOGY OF SICKLE CELL DISEASE

Protective Effects of HbF

Sickle cell disease involves the β-globins of HbA, so fetal hemoglobin, HbF, is normal. Fetal hemoglobin is not affected by sickle cell disease because it contains two alpha and two gamma globins but no beta-globin. The effects of sickle cell disease are often not noticed until the fifth or sixth month of life after birth because, up to that time, HbF is the primary type of hemoglobin carrying the blood's oxygen. As mentioned, at five or six months after birth, HbF concentrations drop and HbA, which is altered to HbS in sickle cell disease, becomes the predominate type of hemoglobin. HbF actually retards the pathogenic polymerization of HbS in erythrocytes where it is present. Fetal hemoglobin levels tend to drop more slowly with progressing age in HbSS than in HbSC individuals. Hydroxyurea is a common cancer chemotherapeutic agent that increases the amount of HbF found in newly formed erythrocytes, and, as a result, it is commonly used in the treatment of sickle cell disease.

Pathophysiology of Sickling

When oxygen levels drop, HbS tends to polymerize, which brings about a morphological change in the erythrocytes.[5] The erythrocytes containing HbS will distort into elongated sickle shapes. An increase in oxygen levels typically reverses the process, but local cell membrane damage and altered cellular chemistry experienced during repeated sickling episodes eventually result in irreversible sickling of the erythrocytes containing HbS. These sickled erythrocytes can clog arterioles and small vessels due to their altered morphology. These entanglements of the sickled erythrocytes cause localized ischemic events and, being more fragile and of abnormal morphology, the sickled erythrocytes tend to be selected for hemolysis during circulation through the spleen. Increased destruction of erythrocytes in sickle cell disease is associated with hemoglobinemia, bilirubinemia, hemosiderosis, and an increase in urobilinogen in faces and urine. The expected life cycle of the affected erythrocytes is reduced from about 120 days down to about 20 days. The schematic representation of the pathophysiology (in part) of sickle cell anaemia is shown in Fig2.

Avascular Necrosis of Femoral Head

Localized Avascular Necrosis with special focus on femoral head Localized avascular necrosis can occur due to vaso-occlusion by sickled red blood cells.[6] Avascular necrosis can, in some cases, affect heterozygotic subjects (sickle cell trait) as well as homozygous subjects. Avascular necrosis and the resulting inflammatory response is often a painful event that may be anatomically localized or may affect an entire bone. Vaso- occlusion occurs as a microcirculatory event, where local adhesion by "normal" erythrocytes is compounded by less deformable sickled SS erythrocytes to create an obstruction. Some of the conditions that increase the tendency for sickling are hypoxia, hypothermia, and acidosis. Vaso-occlusive events are destructive to many vital organs such as the spleen, kidneys, lungs, heart, and parts of the central nervous system. Subjects with sickle cell disease have increased "fibrous connective tissue and changes in muscle that vary with age and vessel size". In adults, infarcts of the diaphysis often are more commonly manifested as medullary and cortical changes. Sometimes, the medullary narrowing is extensive enough to obliterate the marrow space along a section of the diaphysis, providing an osteosclerotic appearance. A bone in bone appearance may manifest after cortical infarct due to mineralization of the marrow space during the inflammatory response to the infarct. The Diagrammatic representation of avascular necrosis of femoral head is shown in Fig. 3. The head of the femur may undergo avascular necrosis due to sickle cell disease (Figure 3). Osteonecrosis of the femoral head classically develops at an early age. Many subjects are asymptomatic despite permanent morphological alteration of the joints. In rare cases, the deterioration progresses to the point of destructive osteoarthritis and immobility of the joint. In severe cases of avascular necrosis of the femoral head, prosthetic replacement of the joint is "now the most widely practiced therapy," but the procedure is often wrought with complications of sickle cell disease, including high fracture rates of the diaphysis of the femur. Also, the obliteration of the marrow space of the femur from previous necrotic events may create complications because the marrow space has to be bored out to seat the prosthesis on the femur. Infarcts may occur in any part of the neck or the femoral head. Avascular necrosis of juxta-articular bone is associated with degenerative changes in the cartilage and the synovial membrane. Dead bone and granulation tissue grind against the acetabulum. Fragments of necrotic bone, shreds of cartilage, and synovial membrane escape into the joint cavity. The joint space is narrowed, the smooth contour of the synovial surface is replaced by jagged irregularities, and there are secondary hypertrophic arthritic changes. The round head of the femur is squashed or acquires a mushroom shape. In the end stage, the residual capital epiphysis is fused to the pelvis, and the joint is completely ankylosed. Secondary infection may be superimposed at any time, adding insult to injury. Avascular necrosis of the humeral head also occurs, but since the shoulder joint is not weight-bearing, the incidence of collapse or remodeling of the joint is lower following necrosis than in the head of the femur. Infarcts in the cranium may involve a number of clinical manifestations. Infarcts around the orbit will occasionally interfere with the movement of the eye and result in pain and swelling.

Genetics in relation to Sickle Cell

SCD denotes all genotypes[7] containing at least one sickle gene, in which HbS makes up at least half the hemoglobin present. Major sickle genotypes described so far include the following:

- HbSS disease or sickle cell anemia (the most common form) - Homozygote for the S globin with usually a

severe or moderately severe phenotype and with the shortest survival
- HbS/b-0 thalassemia - Double heterozygote for HbS and b-0 thalassemia; clinically indistinguishable from sickle cell anemia (SCA)
- HbS/b+ thalassemia - Mild-to-moderate severity with variability in different ethnicities
- HbSC disease - Double heterozygote for HbS and HbC characterized by moderate clinical severity
- Thalassemia

Rare combinations of HbS with other abnormal hemoglobins such as HbD Los Angeles, G-Philadelphia, HBO Arab, and others Sickle cell trait or the carrier state is the heterozygous form characterized by the presence of around 40% HbS, absence of anemia, inability to concentrate urine (isosthenuria), and hematuria. Under conditions leading to hypoxia, it may become a pathologic risk factor (Maakaron et al., 2020).

DEMOGRAPHY OF AVN IN SSD

Avascular necrosis (AVN) is a debilitating and life-changing complication of sickle cell disease and its prevalence ranges from 3.2% to 26.7% in this group of patients[8,9] (Akinyoola et al., 2007). The prevalence of healthy carriers (sickle cell trait) ranges between 10% and 40% across equatorial Africa and decreases to between 1% and 2% in Northern Africa and less than 1% in Southern Africa (Anie et al., 2010). In West African countries such as Ghana and Nigeria, the frequency of the carrier state is 15-30% while in East African countries such as Uganda and Tanzania, it shows wide variations of up to 45% in some areas (Okpala et al., 2004). In Nigeria, with an estimated carrier prevalence of 24%, 20/1000 births are estimated to be affected by sickle cell disease (SCD) resulting in 150,000 children with SCD born annually in Nigeria. About 300,000 children are born annually worldwide with sickle cell disease with Nigeria accounting for one-third of this population (Iwegbu et al., 1985). About 1.2 million people are affected while India has the highest number of affected people in any one country.

The Tribal Populations of India

India has the largest concentration of tribal populations globally. They are believed to be the early settlers in the country and are considered to be the original inhabitants. According to the Census of India 20115,[10,11,12,13,14,15,16] the total tribal population is about 67.8 million which comes is 8.6 percent of the total population. The States of Madhya Pradesh, Maharashtra, Odessa, Gujarat, Rajasthan, Jharkhand, Chhattisgarh, Andhra Pradesh, West Bengal, and Karnataka account for around 83 percent of the total scheduled tribe population in the country and the majority of these tribal groups live in rural areas. In all, 461 scheduled tribes have been listed6 and they have their own characteristic cultural patterns, languages, and social systems, by and large keeping to themselves. However, Reich et al 7 concluded that "several thousand years ago, the entire subcontinent underwent a period of massive intermarriage, shuffling its population's genetic deck so thoroughly that it left clear traces even in the genomes of today's most isolated tribes". Prevalence of sickle gene in tribal communities in India Sickle hemoglobin in India was by first described by Lehman and Cutbush in 1952 in the tribal populations in the Nilgiri hills in south India similarly Dunlop and Mazumder also reported the presence of sickle hemoglobin in the tea garden workers of Upper Assam who were migrant laborers from tribal groups in Bihar and Odisha. Since then, many population groups have been screened and the sickle cell gene has been shown to be prevalent among three socio-economically disadvantaged ethnic groups, the scheduled tribes, scheduled castes, and other backward classes in India. The prevalence of sickle cell carriers among different tribal groups varies from 1 to 40 per cent in different states of India Kaur et al[17,18,19,20,21,22,23,24] have summarized the distribution of HbS in different tribal groups from individual States is shown in the chart no 1. In a large multicenter study where 15200 individuals from 14 primitive tribes from Maharashtra, Gujarat, Tamil Nadu and Odessa were screened, the HbS allele frequency varied from 0.011 to 0.120. Associated iron deficiency was seen in 26.2 per cent of sickle heterozygotes as well as in 67.7 per cent of sickle homozygotes in this study. Although a large number of tribal groups have been screened for HbS, there are still many gaps in our knowledge about the distribution of the HbS gene in tribal communities in India. Madu et al., (2014) conducted a study to investigate the predictive value of the steady state white cell and platelet count as well as the frequency of bone pain crisis per annum to detect sickle cell patients who will eventually develop avascular necrosis (AVN). In their study of 122 individuals reported that there were 69 males (56.6%) and 53 (43.4%) females, giving a ratio of 1.3:1 is shown in Fig. 4. The patients were aged 6-49 years at presentation of AVN in Sickle cell Anaemia with a mean age of 24.7 ± 7.1 years and median age of 23 years. A total of 58 (47.5%) patients were aged 21-30 years while 37 (30.3%) patients were aged 11-20 years. A total of 23 (18.9%) were aged 31-40 years while two (1.6%) patients each were aged 10 years or below and 41-50 years respectively. The age distribution in patients of of sickle cell anaemia is shown in chart no 2.

The prevalence of AVN was found to be 13.1/1000 amongst sickle cell patients. A total of 23 patients (18.9%) were found to have bone and joint involvement in sickle cell disease in this study. 9 (39.1%) were females while 14 (60.9%) were males. Sixteen patients (13.1%) had AVN of the hip involving 19 hips with 3 patients having bilateral hip involvement. AVN was not noticed in any other joint. Left hip affectation was more common (52.6%) than right hip involvement. The majority (73.7%) of the cases of AVN of the hip were seen in patients aged 21-30 years. Only three cases were noted in patients aged 31-40 years. The rest occurred in patients aged 11-20 years. The mean white cell count was

observed to be 13.5 ± 8.8 × 10 9 /L and the median value was 11.8 × 10 9 /L (n = 101), the mean hematocrit was found to be 22 ± 5.5%, with a median value of 22% (n = 83), and the mean platelet count was 326 ± 145 × 10 9 /L, and the median was 328 × 10 9 /L (n =114).

CLINICAL FEATURES, INVESTIGATION AND TREATMENT FOR AVN

Sickle cell disease (SCD) is an inherited hemoglobinopathy that affects millions of people worldwide. These sickled red cells cause vaso-occlusion, leading to interruption in blood flow ischemia and clinical complications. When the bone is affected, there can be loss of the bony trabeculae subchondral collapse, and joint destruction resulting in avascular necrosis (AVN), often affecting the femoral head. Clinical symptoms of femoral head AVN include pain, gait disturbance, and functional limitations. Earlier natural history studies of femoral head AVN in SCD describe universal progression to chronic skeletal and articular degenerative changes leading to decreased mobility, abnormal gait, and leg length discrepancies.[25,26,27] Deep pain in the groin can be referred to same side knee or buttock is the most common presenting symptom. However, much of these natural history studies were performed prior to widespread hydroxyurea (HU) use or magnetic resonance imaging (MRI) screening, which is able to diagnose the disease at earlier stages.

Classification on the basis of clinical and Radiological Presentation

The French orthopedic surgeon Paul (RP)Ficat (1917-1986) in association with Professor Jacques Arlet[28,29] devised a system of staging idiopathic avascular necrosis of the femoral head in the late 1970s based on two fundamental concepts

- a standard radiograph shows only the shadow of the mineralized portion of a bone
- bone necrosis is the end result of severe and prolonged ischemia

The Ficat and Arlet classification use a combination of plain radiographs, MRI, and clinical features to stage avascular necrosis of the femoral head.

Classification

Stage 0 -plain radiograph: normal
-MRI: normal
-clinical symptoms: nil

Stage I -plain radiograph: normal or minor osteopenia
-MRI: edema
-bone scan: increased uptake
-clinical symptoms: pain typically in the groin

Stage II -plain radiograph: mixed osteopenia and/or sclerosis s and/or subchondral cyst, without any subchondral lucency
-MRI: geographic defect
-bone scan: increased uptake
-clinical symptoms: pain and stiffness

Stage III -plain radiograph: crescent sign and eventual cortical collapse
-MRI: same as plain radiograph
-clinical symptoms: pain and stiffness +/- radiation to knee and limp

Stage IV -plain radiograph: end-stage with evidence of secondary degenerative change
-MRI: same as plain radiograph
-clinical symptoms: pain and limp

Treatment modalities of AVN in Sickle Cell Disease Conservative modalities

AVN therapies include observation, physical therapy (PT), core decompression, and in severe late stages, total hip arthroplasty. The extensive review of the literature signified that, at present, the gold standard treatment modality for femoral head osteonecrosis is unclear. The effect of different non-surgical treatment modalities[30,31,32] such as pharmacological agents (bisphosphonate, anticoagulant, vasodilator, lipid-lowering drugs, etc.), restricted weight-bearing, and biophysical modalities (extracorporeal shock waves and pulsed electromagnetic fields), still need further investigation as there is limited information available in the literature.

Surgical Modalities

Before the head collapse in the early stages of the disease, in young patients in SCA patients, the main goal of the treatment is to alleviate the pain and preserve mobile joint Head preservation is done by core decompression with or without the use of bone grafting[33,34] which has been a predominant modality for approximately three decades Core decompression (CD) was introduced by Ficat and Arlet based on the principle of decreasing intramedullary pressure to allow an increase of blood perfusion to the femoral head Once the head collapses in stage III, the preferred available option is hip replacement by arthroplasty. Surgical management depends greatly on patient factors and the AVN stage, which influence the decision to either replace or preserve the hip. Mont et al. (1995) reported a review study that showed AVN hips treated non-operatively had a success rate of only 23% compared with CD, which showed more promising results systematic review reported a 63.5% clinical success rate of CD with or without bone grafting. In a recent review article, the authors summarized that CD achieves better outcomes when performed in the early disease stages, regardless of associated risk factors. In some studies, the pain was assessed using a visual analog pain scale before and after the surgery to measure its effect on pain. The results indicated a dramatic improvement in patients' pain scores following CD. In patients with the collapse of the head of the femur I stage IV, Total Hip Arthroplasty is the only modality of treatment that remains. But in younger patients, Non-Weight Bearing Ambulation could be taken into consideration. Gene therapy and Stem cell therapy

are newer modalities of treatment for AVN in Sickle cell anemia.

Total hip arthroplasty

Total hip arthroplasty (THA) in sickle cell disease patients can be a challenging procedure. This systematic review evaluated the revision rate, functional outcomes and complications of THA in sicklers. A systematic search was conducted according to the PRISMA guidelines, using four search engines from inception to May 2019.[35] Fifteen studies with 971 THAs were included. There were 437 cemented and 520 uncemented THAs. There were 164 revision THAs (16.8%); 52 uncemented and 105 cemented THAs. Forty-two infections were recorded; 16 infections for cemented and 23 for uncemented THAs. Fifty-seven cups, 26 stems, eight cup/stem with aseptic loosening that were more frequently cemented were reported. The 28 unspecified aseptic loosening cases were more frequently uncemented THAs. All studies demonstrated the functional improvement of patients. There were 109 medical complications (14.3%). Sickle cell crises (SSC) and transfusion reactions were most usually recorded. Forty-six intraoperative complications (4.7%) were reported; 18 femoral fractures, four acetabular and 18 femoral perforations. Seventeen femoral fractures occurred during uncemented THA. THA in SCD is still related to a high risk of complications. The outcomes in properly selected sicklers have been improved. Perioperative adequate hydration, warming, oxygen supply and transfusion protocols are mandated to prevent SCC and transfusion reactions. The surgeon must be prepared to deal with a high rate of intraoperative fractures and have different implant options readily available. No definite conclusion can be made regarding the best fixation mode. Cemented implants demonstrated a higher revision rate and uncemented implants a higher risk for intraoperative complications.

Newer consepts

Gene Therapy-Sickle cell disease encompasses a group of genetic disorders characterized by the presence of at least one hemoglobin S (Hb S) allele, and a second abnormal allele that could allow abnormal haemoglobin polymerisation leading to a symptomatic disorder. Autosomal recessive disorders (such as sickle cell disease) are good candidates for gene therapy because a normal phenotype can be restored in diseased cells with only a single normal copy of the mutant gene.[36]

Elucidation of its molecular basis prompted numerous biochemical and genetic studies that have contributed to a better understanding of its pathophysiology. Unfortunately, the translation of such knowledge into developing treatments has been disproportionately slow and elusive. In the last 10 years, discovery of *BCL11A*, a major γ- globin gene repressor, has led to a better understanding of the switch from fetal to adult hemoglobin and a resurgence of efforts on exploring pharmacological and genetic/genomic approaches for reactivating fetal hemoglobin as possible therapeutic options.

Allogenic Stem cell Therapy- Some children with the disease have been successfully treated with blood stem cell, or bone marrow, transplants.[37] This approach, though, was thought to be too toxic for use in adults. High doses of chemotherapy are used to destroy all of a child's bone marrow, which is then replaced with marrow from a donor. Stem cell recipients typically need to take immunosuppressants for months to a few years. These medications can cause serious side effects. IN earlier studies, transplant recipients were found to have a mix of their own and the donor's cells in their blood. Despite the mix, sickle cell disease was reversed.

FIGURES AND CHARTS

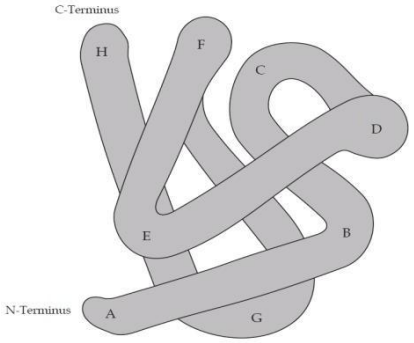

Figure 1. The three-dimensional (tertiary) structure of a b-globin subunit.

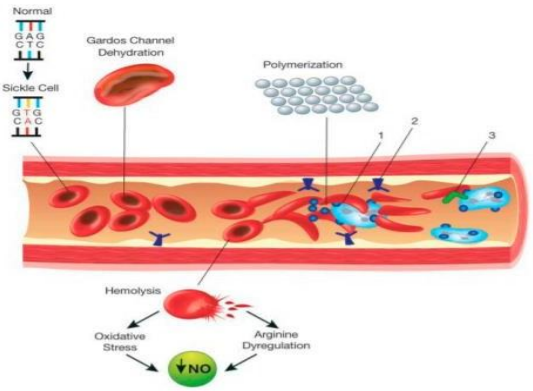

Figure 2: Schematic representation of the pathophysiology (in part) of sickle cell anaemia.

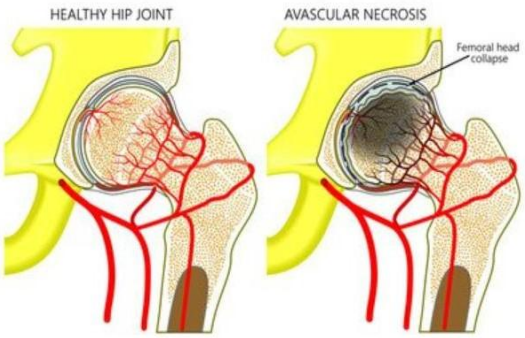

Figure 3: Diagrammatic representation of avascular necrosis of femoral head.

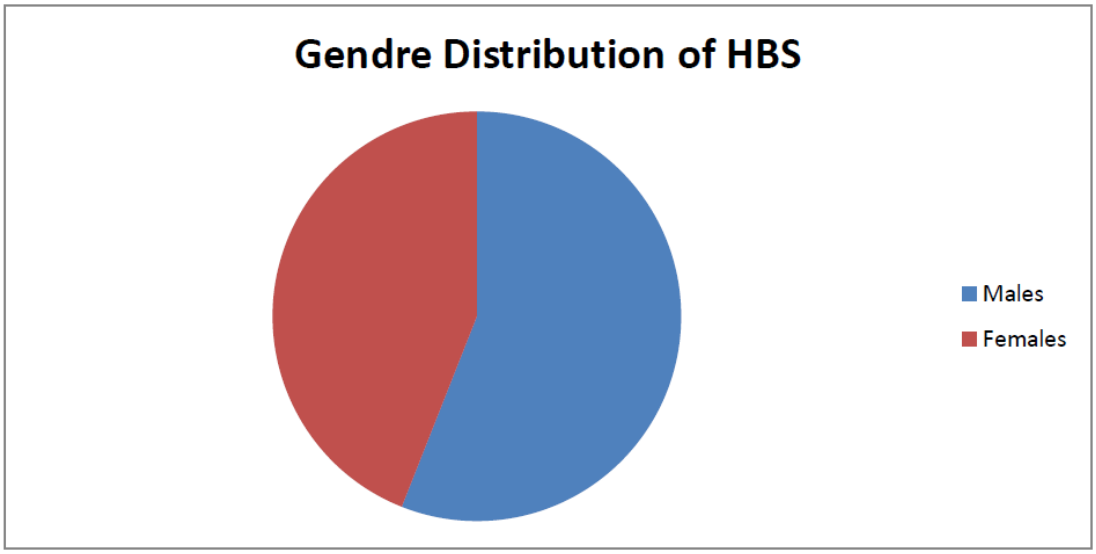

Fig. 4: Gendre Distribution of HBS.

Chart no. 1: The distribution of HbS in different tribal groups from individual States.

SR. NO	State	Region/District	Tribes	Prevalence of HBS in %
1	Madhya Pradesh	27 of the 45 districts	Gonds *and* Bhils	10 to 33
2	Maharashtra	Gadchiroli, Chandrapur, Nagpur, Bandar, Yoetmal and Nandurbar	Bhils, Madias, Pawaras, Par dhans *and* Otkars.	20 to 35%
3	Gujrat	22 districts South Of Gujrat	Chaudry, Gamit, Rohit, Vasava *and* Kukana Dhodia, Dubla, Gamit, *and* Naika	13 to 31%
4	Kerala	Wayanad		18.2 to 34.1%

Chart 2: Age group of presentation in Sickle Cell Anaemia.

AGE GROUP	PERCENTAGE
0-10	1.6
11-20	30.3
21-30	47.5
31-40	18.9
41-50	1.6

CONCLUSION AND RECOMMONDATIONS

Different modalities of treatment are still in experimental stages and as of today, we do not have any satisfactory modality available that will be effective in the treatment of this disease and its complications. Hence early diagnosis, efficient medical supervision for recognition of complications, and appropriate intervention can delay the need for joint replacement, and hence these remain the gold standard in the management of this inherited disorder. Without treatment, the process is almost always progressive, leading to joint destruction within 5years. Another important aspect as regards the prevention of Sickle cell hemoglobinopathy is genetic, hence following are the gold standard in prevention as this is an autosomal recessive disorder and the incidence can be significantly reduced.

1) Premarriage counseling and
2) Prenatal diagnosis in the first trimester for any disability in high-risk couples.
3) Avoiding the consanguineous marriages in the susceptible community.

ACKNOWLEDGEMENTS

We would like to thank all colleagues for helping us during the current study. The special thanks for Dr. Pramod sir, Dr, Kiran sir, Dr Aniket, Dr.Atul and Dr.Mayur.

REFFERENCES

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