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Beta Thalassemia Major Bone Marrow Transplant

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Abstract— Bone Marrow Transplant is the only possible cure till now for the genetic disorder thalassemia. Thalassemia Major can be managed by regular blood transfusions and iron chelation, but the quality of life is still poor and individuals suffering from this blood disorder are at risk of infections and other complications of iron overload which ultimately reduces the chances of survival. This article deals with the in-depth knowledge about the process of BMT for a person suffering from beta thalassemia major complication.

***Index Terms*— Bone marrow, Mutation, Sepsis, GVHD, Iron overload.**

1. Introduction

Beta Thalassemia Major, known as Cooley's Anaemia is a serious genetic blood disorder as a result of mutations in the HBB gene which is essential for producing the beta globin chains associated to haemoglobin. These mutations significantly halt beta globin production, impairing the formation of normal adult haemoglobin (HbA) in red blood cells. Consequently, individuals with this condition experience severe anaemia and require ongoing medical intervention throughout their lives. Genetically in this type of thalassemia there is an autosomal recessive inheritance pattern. In Beta Thalassemia Major, the lack of functional beta-globin chains results in the production of abnormal haemoglobin's, such as HBF and HbA2, and causes red blood cells abnormalities in shape.

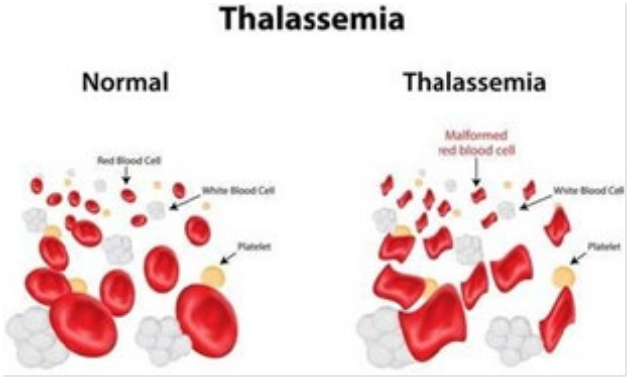

Fig. 1.

A. *Beta Thalassemia Major (Cooley's Anaemia)*

Severe mutations in both genes cause significant anaemia. This form necessitates regular blood transfusions and other medical interventions to manage symptoms and complications.

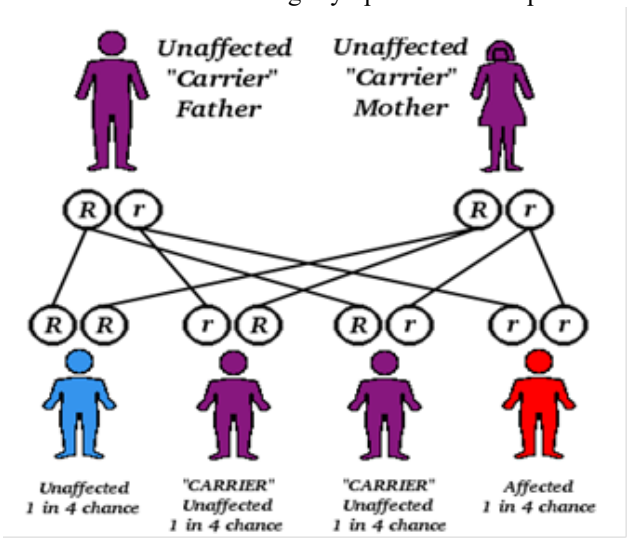

Fig. 2.

2. Mutations in Beta Thalassemia Major

A. *Point Mutations*

1) *Nonsense Mutations*

- *Codon 39 (C>T)*: Leads to the premature introduction of a stop codon.
- *Codon 17 (A>T)*: Results in a non-functional beta-globin protein.

2) *Splice Site Mutations*

- *IVS I-110 (G>A)*: Disrupts splicing in intron 1.
- *IVS II-654*: Reducing beta-globin production.
- *IVS I-5 (G>C)*: Significant mutation near the splice site.

3) *Promoter Region Mutations*

- *-28 (A>G)*: Reduces transcription efficiency by altering the promoter region.

B. *Frameshift Mutations*

- *Codon 6 (-A)*: A single nucleotide deletion at codon 6, causing a frameshift.
- *Codons 8/9 (+G)*: A nucleotide insertion between codons 8 and 9, disrupting the reading frame.

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C. Large Deletions

- *619 bp Deletion*: A deletion spanning 619 base pairs in the beta-globin gene cluster.
- *δβ-Thalassemia Deletions*: Extensive deletions affecting both the delta (δ) and beta (β) globin genes.

D. Rare Mutations

- *Codon 15 (TGG>TGA)*: Converts a tryptophan codon into a stop codon, prematurely terminating protein synthesis.
- *Cap Site (+1 A>C)*: Impairs transcription initiation by altering the cap site.

E. Regional Variations in Mutations

- *Mediterranean regions*: Common mutations include IVS-I-110 (G>A) and Codon 39 (C>T).
- *South Asia*: Frequently observed mutations are IVS-I-5 (G>C) and Codon 15 (G>A).

F. Southeast Asia

Large deletions and frameshift mutations are more prevalent.

3. Bone Marrow Transplant

A BMT or Hematopoietic stem cell transplant is a potential curative treatment for beta-thalassemia major, a severe form of thalassemia. This procedure aims to replace the existing cells in the patient's bone marrow with healthy cells from a donor allowing the production of functional red blood cells that can carry oxygen effectively throughout the body. The success of BMT largely depends on finding a donor generally sibling whose Human Leukocyte Antigen (HLA) type matches with the patient's cell. Siblings or close relatives are often preferred donors due to close genetic match. However, unrelated donors with a suitable HLA match may also be considered. A sibling match reduces the risk of complications where the donor's immune cells may attack the patient's tissues. Pre transplant process require patient to undergoes conditioning therapy, which typically involves chemotherapy. This preparatory step serves two main purposes which is Destroying the malfunctioning bone marrow to make room for the new stem cells & suppressing the immune system to lower the chances of rejecting the donor cells. Following conditioning, healthy stem cells are collected from the donor's marrow or peripheral blood or umbilical cord blood and infused into the patient through an intravenous (IV) line. These stem cells travel to the patient's bone marrow where they start making new healthy red blood cells, white blood cells, and platelets. The process of engraftment when the donor stem cells start functioning and producing new cells usually takes a few weeks. During this critical phase, patients are closely monitored for infections and other complications, as their immune system is significantly weakened. After the transplant, medications are prescribed to prevent issues such as infections and GVHD. Long-term follow-up care, including regular blood tests and doctor visits, is essential to ensure the success of the procedure and the proper functioning of the transplanted bone marrow. The outcomes of BMT for beta-thalassemia major are more favourable in younger patients and when the donor is an HLA-matched sibling. In such cases, cure rates can reach up to 80%. However, success is not guaranteed, as complications can arise during or after the transplant phase. The use of unrelated or partially matched donors lowers the success rates and increases the risk of adverse effects.

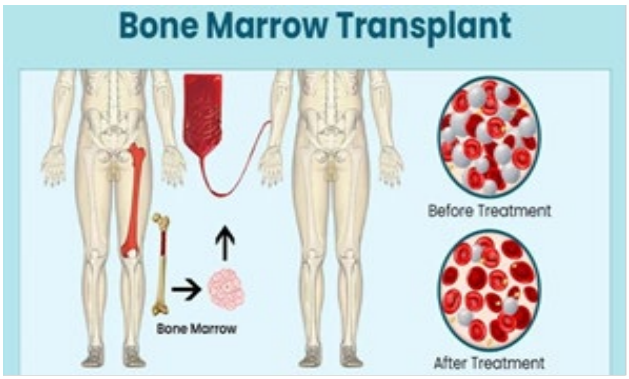

Fig. 3.

4. Pre-Steps for BMT

Bone marrow transplant (BMT) is a highly intricate procedure that requires patients to fulfill several criteria to enhance the likelihood of success, particularly for conditions like beta-thalassemia major. The process begins with a thorough medical evaluation and a physical examination and extensive blood tests. These assessments ensure the patient's organs are functioning adequately and help identify any underlying issues, such as infections or complications commonly associated with beta-thalassemia major. A critical step is pre-transplant conditioning, which involves the use of chemotherapy, and in some cases, low-dose radiation therapy. This treatment helps eradicate the damaged bone marrow, suppress the immune system to reduce the risk of transplant rejection, and create space for healthy stem cells to engraft and proliferate. For individuals with beta-thalassemia major, conditioning regimens may be tailored to address specific complications of the disease, such as iron overload or organ dysfunction. Equally important is ensuring psychological and emotional preparedness. Counseling sessions are essential to help the patient, and their family understand the procedure, the recovery process, and the challenges they may face. Mental health evaluations are conducted to ensure the patient can cope with the stress of the treatment and recovery period. Finding a compatible donor is another critical aspect. Human leukocyte antigen (HLA) typing is performed to identify a donor with a matching tissue type. Ideally, this would be a sibling or unrelated individual with a high degree of compatibility. In cases where a matched donor is unavailable, alternative strategies, such as haploidentical transplants or cord blood transplants, may be considered. Effective infection control is vital since patients with beta-thalassemia major are already vulnerable to infections due to frequent transfusions and iron overload. Screening for active infections is mandatory, and any infections must be treated before the procedure. Dental evaluations are conducted to address oral health issues, and

immunizations may need to be updated to reduce the risk of preventable diseases during the immunocompromised state post-transplant. Comprehensive organ function assessments are also necessary, focusing on the heart, liver, kidneys, and lungs, as beta-thalassemia major can lead to complications like cardiomyopathy or liver damage from iron overload. Maintaining proper nutrition and physical health is critical for recovery. Patients are encouraged to follow a nutritious diet and address any deficiencies through supplements, especially since beta-thalassemia major can lead to anemia and other nutrient imbalances. Additionally, financial and logistical planning is crucial. Patients and their families must understand the costs involved, arrange insurance or funding, and organize the logistics for frequent follow-ups and medications post-transplant. Lastly, informed consent is required, with the patient and their family made fully aware of the potential risks, including GVHD, infections, bleeding, and possible organ complications. A reliable caregiver should be identified to provide emotional and practical support during the recovery period. Before a BMT patients must undergo a comprehensive series of tests to check readiness for the procedure. These assessments are critical for evaluating overall health, detecting potential complications, and determining donor compatibility. The process starts with detailed blood tests. A complete blood count evaluates red and white blood cells, hemoglobin levels, and platelets, providing insight into the patient's overall blood health. Specific tests, such as serum ferritin and transferrin saturation, are performed to assess iron overload, a common issue in beta-thalassemia major due to frequent blood transfusions. Liver and kidney function tests, including bilirubin, ALT, AST, creatinine, and blood urea nitrogen (BUN), evaluate how well these vital organs are functioning, especially given the strain from iron overload. Infection screenings for hepatitis-B/C, HIV and cytomegalovirus (CMV) are critical as infections must be treated or managed before proceeding. Additionally, a coagulation profile checks the blood's clotting ability to reduce bleeding risks during or after the transplant. Heart and lung evaluations are also crucial. An electrocardiogram (ECG) assesses heart rhythm for abnormalities, while an echocardiogram examines heart function and structure to detect conditions like cardiomyopathy, which can result from iron accumulation. Pulmonary function tests (PFTs) evaluate lung capacity and efficiency, ensuring the respiratory system can withstand the demands of conditioning and recovery. Imaging studies, such as chest X-rays, help detect lung infections or abnormalities. Advanced imaging like MRI or CT scans is often used to assess organ health, particularly the liver, heart, and endocrine glands, which may be affected by iron overload. A bone marrow biopsy and aspiration may also be performed to evaluate marrow function and confirm the need for a transplant. A pivotal component of preparation is human leukocyte antigen (HLA) typing, which determines compatibility between the patient and potential donors. This test identifies proteins, or antigens, on white blood cells that influence immune responses. A close matched donor reduces the risk of complications like transplant rejection GVHD. HLA typing involves analyzing a blood or cheek swab sample in a laboratory to identify critical HLA markers. A sibling is often the best potential donor, with a 25% chance of being fully HLA-compatible. If no sibling match is found, unrelated donors or alternative options like haploidentical transplants or cord blood transplants are explored. Additional evaluations include a dental examination to address any oral infections or issues that could worsen during the period of immunosuppression. Psychological assessments ensure that both the patient and their caregivers are mentally prepared to deal with the physical and emotional challenges of the procedure and recovery.

5. Lucarelli System

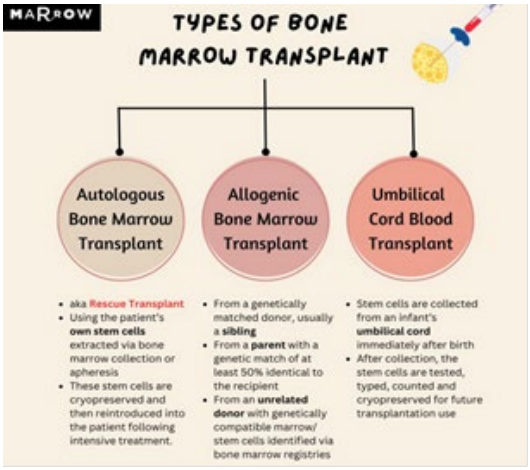

Fig. 4.

The Lucarelli classification is a system designed to evaluate the severity of beta thalassemia major which is a hereditary blood disorder caused by reduced or absent production of beta-globin chains in haemoglobin. This condition leads to severe anaemia, resulting in complications such as ineffective red blood cell production (erythropoiesis), excessive iron absorption, and iron overload. Without appropriate treatment, iron buildup may cause serious organ damage. This classification divides beta thalassemia major into three categories based on disease progression and related complications. In Class I (Mild), symptoms are less severe, and anaemia can be managed with regular blood transfusions. Iron overload at this stage is mild to moderate, as assessed by diagnostic tools like liver iron concentration (LIC). In Class II (Moderate), the condition worsens, presenting with more pronounced symptoms such as persistent fatigue, growth delays, and skeletal deformities. At this stage, iron overload begins to cause damage to organs, particularly the liver, necessitating more intensive treatment. Class III (Severe) is marked by advanced complications, including significant organ damage due to liver fibrosis or cirrhosis, heart issues, and endocrine dysfunctions like diabetes or hormonal imbalances, all caused by extensive iron deposition. Clinicians use a variety of diagnostic tools to determine the severity of beta thalassemia major. These include serum ferritin measurements and MRI T2 imaging to evaluate iron levels in critical organs, as well as genetic testing to detect mutations in the gene responsible for the disorder. Bone marrow analysis may also be used to study

the efficiency of red blood cell production. The Lucarelli classification is integral in guiding the treatment and management of beta thalassemia major. Standard treatment involves routine blood transfusions to address anaemia and chelation therapy to remove excess iron. In severe cases, HSCT may offer a potential cure. Lifelong monitoring is essential to manage complications such as liver disease, cardiac dysfunction, or hormonal disorders. By categorizing the severity of the condition, this classification system allows the medical providers to develop personalized treatment plans that improve both the quality of life and long-term outcomes for individuals with beta thalassemia major.

6. The Complete Procedure of Bone Marrow Transplant

BMT is the only definitive treatment for beta-thalassemia major, an inherited blood disorder caused by faulty haemoglobin production. This procedure involves replacing the affected individual's diseased cells with cells from a donor, preferably a sibling with a closely matched human leukocyte antigen (HLA). The process follows several critical steps to improve the chances of success. Before undergoing the transplant, the patient undergoes a series of medical evaluations, including blood tests, imaging scans, and bone marrow assessments, to determine their overall health and organ function. A suitable donor is identified through HLA matching, as a close genetic match minimizes complications and reduces the risk of transplant rejection. If a fully matched sibling is unavailable, alternative options include unrelated matched donors or partially matched (haploidentical) donors. Once a donor is selected, the patient proceeds with conditioning therapy, which involves chemotherapy, and in some cases, radiation therapy. This phase is crucial as it destroys the defective bone marrow, clears room for the new stem cells, weakens the immune system to prevent rejection, and reduces the likelihood of disease recurrence. Common chemotherapy drugs such as busulfan and cyclophosphamide are used to eliminate abnormal bone marrow cells while minimizing toxicity. The next step involves collecting stem cells from the donor, which can be done in different ways. If bone marrow extraction is chosen, the donor undergoes a procedure under anaesthesia, where stem cells are withdrawn from the hip bone using a needle. Peripheral blood stem cells can be collected after the donor receives injections of drug G-CSF to increase the number of cells in circulation. These cells are then collected by apheresis. In some cases, umbilical cord blood from a newborn sibling can also serve as a valuable stem cell source. Once collected, the donor's stem cells are injected into the recipient's bloodstream through a central venous catheter, much like a blood transfusion. Over the next few weeks, these cells migrate to the bone marrow. This crucial stage, known as engraftment, typically takes two to four weeks. Following the transplant, the patient is kept in a controlled, sterile environment to reduce infection risks, as their immune system remains significantly weakened. Supportive care, including blood transfusions, antibiotics and immunosuppressive drugs, is provided to aid recovery and prevent GVHD. The initial 100 days post-transplant are particularly critical, requiring close medical supervision. If engraftment is successful, the patient gradually starts producing normal haemoglobin, potentially removing the need for lifelong blood transfusions. However, complete immune system recovery may take up to a year.

7. Medications Bone Marrow Transplant

This process typically includes chemotherapy drugs such as Busulfan which clears out the marrow to create space for new donor cells, and Cyclophosphamide, which helps in immunosuppression to prevent graft rejection. Fludarabine is also used to lower immune response, reducing the risk of transplant failure, while Melphalan is sometimes included to further destroy thalassemic bone marrow.

Anti-thymocyte globulin (ATG) is commonly used to suppress T-cells and lower GVHD risk, while Alemtuzumab (Cam path) serves as an alternative option for immune suppression.

Mesna is given to protect the bladder from the toxic effects of Cyclophosphamide, preventing hemorrhagic cystitis. Additionally, hydration and electrolyte management play a crucial role in flushing out chemotherapy related toxins and safeguarding kidney function.

Immunosuppressive medications like Cyclosporine are essential in reducing GVHD risk, along with Methotrexate, which is administered in low doses to further lower this risk. Some patients may receive Mycophenolate mofetil (MMF) as alternative immunosuppressant, while others may require Tacrolimus in place of Cyclosporine.

A combination of antibiotics (such as Ciprofloxacin or Cefepime) is used to combat bacterial infections, while antifungal medications (like Fluconazole or Voriconazole) protect against fungal infections. Additionally, antiviral drugs such as Acyclovir and Ganciclovir help prevent viral reactivations, particularly cytomegalovirus (CMV).

8. Monitoring of the Patient Undergoing BMT

Monitoring a patient undergoing bone marrow transplantation (BMT) is a highly intricate and essential process aimed at ensuring the success of the procedure while minimizing complications. Since BMT serves as a curative therapy by replacing defective stem cells with healthy donor-derived cells, continuous evaluation at various stages is necessary. The monitoring process is categorized into four primary phases: pre-transplant, conditioning, post-transplant, and long-term follow-up to ensure a smooth recovery. Before undergoing BMT, a comprehensive evaluation is performed to assess the patient's overall health and ensure they are suitable candidates for transplantation. A complete blood count (CBC) is conducted to determine the severity of anaemia and track blood cell levels. Additionally, liver and kidney function tests are performed to evaluate organ health. Since individuals with beta thalassemia major frequently experience iron overload due to repeated blood transfusions, ferritin level assessment and cardiac MRI (T2 MRI) are crucial to monitor iron deposition, particularly in the heart. HLA typing is also essential to find a compatible donor, either from a sibling or an unrelated match.

Since chronic anaemia and excessive iron accumulation can lead to cardiac complications, patients undergo ECG and echocardiography to assess heart function. Furthermore, pulmonary function tests (PFTs) are conducted to evaluate lung health. Before initiating immunosuppressive therapy, infectious disease screening (CMV, EBV, hepatitis B/C, and HIV) is performed to rule out active infections. Considering the physical and emotional challenges associated with BMT, nutritional and psychological assessments are carried out to prepare the patient for treatment.

During the conditioning regimen, the patient is given high-dose chemotherapy to eliminate diseased marrow cells and suppress the immune system to prevent graft rejection. Throughout this phase, continuous monitoring of signs such as body temperature, heart rate, blood pressure/infection and oxygen saturation is crucial. Daily CBCs help track declining blood counts, while liver and kidney function tests assess chemotherapy-induced toxicity. Chemotherapy can cause electrolyte imbalances. Another major side effect of chemotherapy is mucositis, a condition that leads to painful sores in the mouth and gastrointestinal tract. Regular oral examinations help in early detection and management. Since the immune system is significantly weakened during this stage, fever monitoring and blood cultures are essential to identify potential infections promptly. The post-transplant phase is critical, requiring constant observation to ensure proper engraftment and detect potential complications. During the first 30 days, the primary goal is to monitor for engraftment which is indicated by an ANC >500 for three consecutive days. Daily CBCs help track hematopoietic recovery, while organ function tests assess any toxicity-related complications. Since beta thalassemia patients are at higher risk of liver damage due to iron overload, liver function tests (bilirubin, ALT, AST) are closely monitored to identify signs of Veno-occlusive disease (VOD), a serious condition affecting the liver. Additionally, electrolyte monitoring continues due to the persistent effects of chemotherapy. Another major risk during this period is GVHD in which the transplanted cells attack the recipient's tissues. Symptoms such as skin rashes, liver dysfunction, and gastrointestinal issues are closely monitored. Since viral reactivation is a concern, weekly CMV and EBV PCR tests are conducted. Pain management and symptom relief measures are also implemented to ease the discomfort associated with the recovery process.

Between 30- and 100-days post-transplant, additional assessments are performed to evaluate long-term engraftment success. A marrow biopsy is conducted to confirm the presence and activity of transplanted cells, while chimerism testing determines the percentage of donor-derived cells in the bloodstream, serving as an important marker of transplant success. Immunosuppressive therapy monitoring is crucial to prevent both GVHD and graft rejection. If any lung-related complications arise, pulmonary function tests are repeated. Since infections remain a significant risk, opportunistic infections such as fungal pneumonia and cytomegalovirus reactivation are actively monitored.

9. Possible Risks Pre/Post BMT

A. Mucositis

Mucositis is a common complication in individuals undergoing bone marrow transplants (BMT), particularly those with thalassemia. The preparatory process for BMT often includes intensive chemotherapy and, in some cases, radiation therapy. While these treatments are essential for eliminating the existing bone marrow, they also harm rapidly dividing cells, especially in the mucosal linings of the mouth and digestive tract. This damage leads to mucositis, which manifests as painful inflammation and ulceration. Following transplantation, mucositis can significantly affect a patient's ability to eat and drink, making proper nutrition challenging. The associated pain can be severe, necessitating medical interventions such as analgesics, infection management, and therapies to promote tissue recovery. In extreme cases, when oral intake becomes impossible, intravenous nutrition may be required. Preventive and mitigating measures include maintaining proper oral hygiene, using specialized mouth rinses, and employing cryotherapy to minimize the severity of the condition.

B. Veno Occlusive Disease (VOD)

Also called sinusoidal obstructive syndrome (SOS), is a severe liver disorder that often develops following high-dose chemotherapy part of the bone marrow transplantation. This condition arises when the small veins in the liver blocked due to endothelial cell damage, leading to restricted blood flow and liver swelling. VOD is commonly linked to treatments for diseases such as leukaemia and thalassemia. Typical symptoms include jaundice (yellowing of the skin and eyes), liver enlargement accompanied by pain (hepatomegaly), fluid accumulation in the abdomen (ascites) causing weight gain due to fluid retention. Blood tests frequently reveal elevated bilirubin levels and irregular liver enzyme readings, indicating liver damage. Diagnostic imaging, such as ultrasound, can assist in identifying liver swelling and circulatory issues. Management primarily involves supportive care, including fluid balance regulation and pain control.

C. SEPSIS

Sepsis is a medical condition that occur when the body immune system respond to an infection which cause inflammation led to tissue damage, organ failure, and eventual death. It can be caused by bacterial, viral, fungal, or parasitic infections including gram positive and gram-negative bacteria impacting stomach lining, kidney injury and lungs. The excessive inflammatory reaction can impair blood circulation, affecting various organs. Key symptoms of sepsis include fever, an increased heart rate, confusion, and low blood pressure. If not promptly treated, it can progress to severe sepsis, where vital organs such as the kidneys, liver, or lungs begin to fail. In extreme cases, sepsis can advance to septic shock causing drop in blood pressure, significantly increasing the risk of death. Diagnosis generally involves blood tests to detect infections and assess organ function, along with imaging techniques to identify the infection source. Treatment requires urgent medical intervention, including antibiotics, intravenous fluids, and, in

Table 1

Stem Cell Collections	Stem cell from Bone Marrow	Peripheral Blood Stem Cells	Cells from Umbilical Cord
Procedure	This need stem cells collected from related or Unrelated donor who is HLA type matched (10/10 or 12/12) near sibling is best. Procedure Involve High dose chemotherapy to destroy exiting marrow cells. Once Engraftment happens around 15 to 21 days for RBC, WBC, Neutrophils and platelets to appear, patient is being monitored for any complications like GVHD, sepsis which may change outcome.	Mobilize stem cell in peripheral blood and collected for infusion. Process remains the same as mentioned in Bone marrow. Engraftment is fast in this case.	Stem cells which were collected and preserved during birth can be used for such disease where related sibling is not available. Engraftment remains slow but GVHD risk is not that much due to self-stored cells.
Associated Risks (Class 1,2,3)	There might be low T-cells and GVHD risk high. Risk of Sepsis is very high during phase of immunosuppression by chemotherapy drugs. Sepsis may cause life risk.	Risks are same as Bone Marrow. but we get high T-cells. HLA compatibility is must. There is sever Sepsis risks due to compromised immune system and may cause life risk.	Risk of infection to recipient.
Conditioning Regimen	1. Busulphan/Cyclophosphamide 2. Triosulphan/Thiotepa/Fludarabine In all Cases High Risk and SEPSIS and eventual death during the treatment.	Same as Bone marrow	Same as Bone marrow.

some cases, vasopressors to maintain stable blood pressure. Patients with severe sepsis may need additional support, such as oxygen therapy or dialysis, depending on the severity of organ impairment. Rapid detection and immediate treatment are essential to managing sepsis effectively, as it can escalate quickly and result in life-threatening complications.

D. Graft Versus Host Disease (GVHD)

Graft-versus-host disease (GVHD) is a potential threat following stem cell transplant where the transplanted immune cells mistakenly attack the host tissues, identifying them as foreign. This condition typically arises due to incomplete compatibility between the donor and recipient, even when they are closely matched. GVHD acute/chronic may develop within the first 100 days post-transplant, affect the skin, liver and gastrointestinal system. Symptoms include skin rashes, jaundice, and diarrhea. In contrast, chronic GVHD may impact multiple organs, leading to complications such as skin thickening, dry eyes, and lung dysfunction. The main cause of GVHD is the immune response of the donor cells against the recipient's tissues causing inflammation and tissue damage. Treatment mainly involves immunosuppressive medications, such as corticosteroids, to control the immune response, alongside newer targeted therapies. Preventive strategies, including careful donor-recipient matching and prophylactic drug administration play a vital role in reducing the likelihood of GVHD.

E. Intravascular Coagulation

This is a serious complication that can occur during or post bone marrow transplant (BMT) for thalassemia. It is characterized by widespread abnormal blood clotting, which simultaneously leads to excessive clot formation and an increased risk of bleeding. Several factors can trigger DIC in BMT patients, including chemotherapy-related tissue damage, infections, liver dysfunction—commonly associated with thalassemia. The formation of small clots within blood vessels can impair blood circulation to vital organs, while the depletion of clotting factors results in uncontrolled bleeding. Symptoms may include excessive bruising, severe bleeding, and organ dysfunction. Diagnosis is confirmed through blood tests, and treatment primarily involves addressing the underlying cause, restoring clotting factors, and managing bleeding.

F. Neutropenic Enterocolitis

Neutropenic enterocolitis is a severe complication reported during the treatment primarily due to the effects of chemotherapy or radiation used in preparation for the procedure. These treatments lead to neutropenia, a significant drop in neutrophil levels, which compromises the immune system. As a result, the intestinal lining becomes more vulnerable to infections, causing inflammation in the small intestine and colon with symptoms abdominal pain, fever, bloating, and diarrhea. If not treated promptly, the infection can spread into the bloodstream, triggering sepsis—a life-threatening condition characterized by widespread inflammation and potential organ failure.

10. Conclusion

As of today, Bone marrow transplant helps in achieving thalassemia free status but need fully matched HLA donor preferable sibling. This treatment result in stem cell engraftment. Only Drawback is lack of donor, GVHD, Sepsis but can be considered as one of the viable options.

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