CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.20676904

Available online at: http://www.iajps.com Review Article

EPIDEMIOLOGICAL TRENDS AND COMPARATIVE CLINICAL EFFICACY OF CRISPR-CAS9 VERSUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN TRANSFUSION-DEPENDENT \BETA-THALASSEMIA: A SYSTEMATIC REVIEW

Musarrath Mubeen*, D.deppika, k.savithri, J.lavanya, B.balu,,T.Mangilal
Smt.Sarojini Ramulamma College of Pharmacy,Seshadri Nagar,Mahabub Nagar-509001,Telangana,India.

Abstract:
Beta thalassemia is a hereditary blood disorder characterized by reduced or absent synthesis of β-globin chains, leading to ineffective erythropoiesis and chronic haemolytic anaemia. This systematic review aimed to evaluate the prevalence, clinical manifestations, associated complications, and current treatment approaches of beta thalassemia. Data from multiple published studies involving a large patient population were analysed. The findings indicate a higher prevalence in regions such as South Asia, particularly India, due to genetic factors and consanguineous marriages. Clinical features commonly include severe anaemia, growth retardation, splenomegaly, and bone deformities.
Complications such as iron overload, cardiac disorders, liver dysfunction, endocrine abnormalities (including diabetes mellitus and hypothyroidism), and increased susceptibility to infections were frequently reported. Conventional management strategies include regular blood transfusions and iron chelation therapy to manage iron overload. Hematopoietic stem cell transplantation (HSCT) remains the only curative treatment, though its availability is limited due to donor compatibility and cost constraints. Emerging therapies such as gene therapy and CRISPR-Cas9 gene editing show promising potential but are still under development and not widely accessible, especially in developing countries like India. The study highlights the importance of early diagnosis, genetic counselling, and preventive screening programs to reduce disease burden. A multidisciplinary approach involving haematological, genetic, and supportive care is essential to improve patient outcomes and quality of life.

Keywords: *Beta thalassemia, Haemoglobin disorder, Genetic mutation, Anaemia, Iron overload, Blood transfusion, Iron chelation therapy, HSCT, Gene therapy, CRISPR-Cas9.*

Corresponding author:

Musarrath Mubeen,
Department of Pharmacology,
Smt.Sarojini Ramulamma College of Pharmacy,
Seshadri Nagar,Mahabub Nagar-509001,Telangana,India.
Email - Musarrath.mubeen@gmail.com,Mobile- 6304058076

QR CODE

Please cite this article in press ***Musarrath Mubeen*** *et al.,* ***Epidemiological Trends And Comparative Clinical Efficacy Of Crispr-Cas9 Versus Hematopoietic Stem Cell Transplantation In Transfusion-Dependent \Beta-Thalassemia: A Systematic Review****.., Indo Am. J. P. Sci, 2026; 13(06).*

INTRODUCTION:

Thalassemia

Thalassemia is a hereditary blood disorder characterized by inadequate haemoglobin production. There are two major types of thalassemia: β-thalassemia (also known as beta thalassemia), caused by similar gene abnormalities that disrupt the synthesis of the β globin protein, and α-thalassemia (also known as alpha thalassemia), caused by a gene or genes associated with the α-globin protein that are missing or altered (mutated). There are numerous subtypes of each type. Thus, thalassaemia major, thalassaemia intermedia, and thalassaemia minor (or thalassaemia trait) are the three kinds of thalassaemia associated with both α- and β-thalassaemia.[1]

What is thalassemia

Thalassemia (Thala -uh-SEE-me-uh) is an inherited blood disorder. It affects the body's ability to produce normal haemoglobin. Haemoglobin is a protein in red blood cells. It allows your red blood cells to transport oxygen throughout your body, nourishing your body's other cells. [2]

In thalassemia, body produces fewer healthy haemoglobin proteins, and the bone marrow produces fewer healthy red blood cells. The condition of having fewer red blood cells is called anaemia. As red blood cells serve the vital role of delivering oxygen to tissues in body, not having enough healthy red blood cells can deprive the body's cells of the oxygen they need to make energy and thrive. [3]

Types of thalassemia

Thalassemia is primarily categorized into two types: α-thalassemia and β-thalassemia.

β-Thalassemia: β-Thalassemia is caused by mutations in the HBB gene on chromosome, leading to reduced or absent synthesis of the beta chains of haemoglobin. This is further classified as follows. o β-Thalassemia Major (Cooley's Anaemia): Severe form requiring regular blood transfusions. o β-thalassemia Intermedia: Moderate severity may require occasional transfusions. o β-Thalassemia Minor (Trait): Carrier state with mild anaemia.

α-Thalassemia: Resulting from deletions or mutations in HBA1 and HBA2 on chromosome 16, affecting the alpha chains of haemoglobin. It includes: o α-thalassemia major (Haemoglobin Bart's hydrops fetalis): Usually fatal in utero or shortly after birth. o Haemoglobin H Disease: Moderately severe form with chronic haemolytic anaemia. o α-Thalassemia Trait: Carrier state with mild anaemia. o Silent Carrier State: Usually asymptomatic. [4,5]

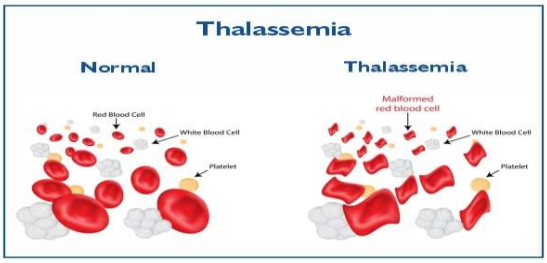


Figure Thalassemia

Symptoms

The symptoms will depend on what type of thalassemia you have and how serious it is. If you're missing two of the alpha genes or one of the beta ones, patients may have no symptoms. Or patients might have mild symptoms of anaemia, such as tiredness.

In some people, symptoms show up at birth. In others, it can take a couple of years.

Thalassemia symptoms may include:

- Intense fatigue
- Shortness of breath
- Dizziness or weakness
- Irregular or fast heartbeat.
- Headaches
- Leg pain
- Trouble concentrating
- Pale or yellow skin
- Dark urine
- Lack of appetite
- Slow growth
- Late puberty
- Wide or brittle bone
- Irregular bone structure of the face.[6]

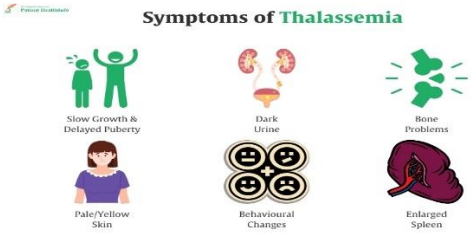


Figure Symptoms of thalassemia

Diagnosis of Thalassemia

- Blood tests
- Haemoglobin electrophoresis
- Prenatal testing

Blood tests are done for diagnosis of thalassemia. Doctors measure blood counts and examine a sample of blood under a microscope. Characteristic abnormalities of the red blood cells can be seen.

Haemoglobin electrophoresis another blood test, is also done. In electrophoresis,

an electrical current is used to separate the different types of haemoglobin and thus detect abnormal haemoglobin. Testing a drop of blood by electrophoresis is helpful but may be inconclusive, especially for alpha-thalassemia. Therefore, the diagnosis is usually based on genetic tests and determination of hereditary patterns.

Genetic testing can be done to detect thalassemia before birth.[7]

Pathophysiology

The defects in the production of haemoglobin, the oxygen-carrying protein found in red blood cells, result from mutations in the genes responsible for producing the alpha- or beta-globin chains of haemoglobin. The pathophysiology of thalassemia involves a disruption in the balance of globin chain synthesis, leading to an imbalance in the alpha- and beta-globin chains and subsequent abnormalities in red blood cell formation and function.[8]

Thalassemia is a group of genetic blood disorders characterized by the reduced synthesis of normal haemoglobin chains, leading to hypochromic microcytic anaemia.[9] In homozygous thalassemia, such as beta-thalassemia, excess alpha chains accumulate, forming intracytoplasmic erythrocytic inclusions and resulting in anaemia, bone marrow hyperplasia, osteoporosis, hemosiderosis, and organ failure [10].

The pathogenesis involves the accumulation of unmatched globin chains, like alpha-globin in beta-thalassemia, causing haemolysis and ineffective erythropoiesis, possibly due to accelerated apoptosis from alpha-globin deposition in erythroid precursors [9].

This imbalance in globin chain synthesis in beta-thalassemia leads to erythroid maturation issues, red cell destruction, and a heterogeneous cell population in the blood, with iron overload being a major cause of tissue damage and mortality.[11]

Thalassemia is marked by reduced globin chain synthesis, resulting in premature cell destruction, ineffective erythropoiesis, haemolysis, and varying degrees of anaemia.[12]

Haemoglobin consists of four protein chains, two alpha globin chains and two beta globin chains. Each chain — both alpha and beta — contains genetic information, or genes, passed down from your parents. Think of these genes as the “code” or programming that controls each chain and (as a result) your haemoglobin. If any of these genes are defective or missing, you’ll have thalassemia.

- **Alpha globin protein chains** consist of four genes, two from each parent.
- **Beta globin protein chains** consist of two genes, one from each parent.

The thalassemia you have depends on whether your alpha or beta chain contains the genetic defect. The extent of the defect will determine how severe your condition.[13]

1.7 Treatment/management:

Thalassemia treatment depends on the type and severity of the disease.

Mild thalassemia (Hb: 6 to 10g/dl):

Signs and symptoms are generally mild with thalassemia minor and little if any, treatment is needed. Occasionally, patients may need a blood transfusion, particularly after surgery, following childbirth, or to help manage thalassemia complications.

Moderate to severe thalassemia (Hb less than 5 to 6g/dl):

- **Frequent blood transfusions:** More severe forms of thalassemia often require regular blood transfusions, possibly every few weeks. The goal is to maintain Hb at around 9 to 10 mg/dl to give the patients a sense

of well-being and also to keep a check on erythropoiesis and suppress extramedullary haematopoiesis. To limit transfusion-related complications, washed, packed red blood cells (RBCs) at approximately 8 to 15 mL cells per kilogram (kg) of body weight over 1 to 2 hours are recommended.

- **Chelation therapy:** Due to chronic transfusions, iron starts to get deposited in various organs of the body. Iron chelators (deferasirox, deferoxamine, deferiprone) are given concomitantly to remove extra iron from the body.
- **Stem cell transplant:** Stem cell transplant, (bone marrow transplant), is a potential option in selected cases, such as children born with severe thalassemia. It can eliminate the need for lifelong blood transfusions [14].
- However, this procedure has its own complications, and the clinician must weigh these against the benefits. Risks include including graft vs. host disease, chronic immunosuppressive therapy, graft failure, and transplantation-related mortality. [15]
- **Gene therapy:** It is the latest advancement in severe thalassemia management. It involves harvesting the autologous hematopoietic stem cells (HSCs) from the patient and genetically modifying them with vectors expressing the normal genes. These are then reinfused to the patients after they have undergone the required conditioning to destroy the existing HSCs. The genetically modified HSCs produce normal haemoglobin chains, and normal erythropoiesis ensues.
- **Genome editing techniques:** Another recent approach is editing genomic libraries, such as zinc-finger nucleases, transcription activator-like effectors, and

cluster regulated interspaced short palindromic repeats (CRISPR) with Cas9 nuclease system.

These techniques target specific mutation sites and replace them with the normal sequence. The limitation of this technique is to produce a large number of corrected genes sufficient to cure the disease.[16]

- **Splenectomy:** Patients with thalassemia major often undergo splenectomy to limit the number of required transfusions. Splenectomy is the usual recommendation when the annual transfusion requirement increases to or more than 200 to 220 mL RBCs/kg/year with a haematocrit value of 70%. Splenectomy not only limits the number of required transfusions but also controls the spread of extramedullary haematopoiesis. Post-splenectomy immunizations are necessary to prevent bacterial infections, including *Pneumococcus*, *Meningococcus*, and *Haemophilus influenzae*. Post-splenectomy sepsis is possible in children, so this procedure is deferred until 6 to 7 years of age, and then penicillin is given for prophylaxis until they reach a certain age.
- **Cholecystectomy**: Patients can develop cholelithiasis due to increased Hb breakdown and bilirubin deposition in the gallbladder. If it becomes symptomatic, patients should undergo cholecystectomy at the same time when they are undergoing splenectomy.[17]

Treatments for thalassemia depend on the type and how serious it is. If you are a carrier or have alpha or beta thalassemia trait, you likely have mild or no symptoms and may not need treatment.

If you have a more serious thalassemia type like haemoglobin H disease, beta thalassemia intermedia, or beta thalassemia major you may experience moderate to serious anaemia symptoms. You

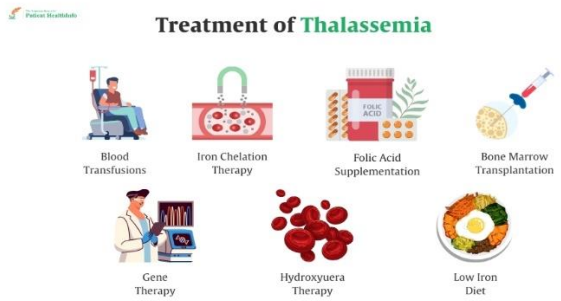


Figure Treatment of Thalassemia

Blood transfusions

Blood transfusion is the main way to treat moderate or severe thalassemia. This treatment gives patient red blood cells with healthy haemoglobin.

During a blood transfusion, a needle is used to insert an intravenous (IV) line into one of patient blood vessels. Patient receive healthy blood through this line. The procedure usually takes 1 to 4 hours. How often blood transfusions are needed depends on how serious patient condition and symptoms are.

- **Occasional blood transfusions** may be needed for people who have haemoglobin H disease or beta thalassemia intermedia. Specifically, a transfusion may be needed when patients body is under stress, such as during an infection, pregnancy, or surgery.

Regular blood transfusions (every 3 to 4 weeks) may be needed for people who have beta thalassemia major. These transfusions help maintain healthy haemoglobin and red blood cell levels.

Iron chelation therapy

The haemoglobin in red blood cells is an iron-rich protein. Regular blood transfusions can cause iron buildup, or iron overload, which can lead to potentially life-threatening complication.

To prevent this, doctors use iron chelation therapy in people who receive regular blood transfusions to remove excess iron from the body. Three medicines are used for iron chelation therapy:

- **Deferasirox** is a pill taken once daily. Side effects can include skin rash, nausea, and diarrhoea.
- **Deferiprone** is a pill that may be used if other treatments do not work. It can lower your white blood cell numbers, which can put you at risk for infections.
- **Deferoxamine** is a liquid medicine that is given slowly under the skin, usually with a small portable pump used overnight. This therapy takes time and can be mildly painful. Side effects can include problems with vision and hearing.

Talk to your doctor if you're pregnant or thinking about becoming pregnant. You may need to switch to a different iron chelation therapy medicine.

Learn more about thalassemia and pregnancy.

Blood and bone marrow transplant

A blood or bone marrow transplant, also called a hematopoietic stem cell transplant, replaces blood-forming stem cells that aren't working properly with healthy donor cells. A stem cell transplant is the only treatment that can cure thalassemia. However, only a small number of people who have severe thalassemia are able to find a good donor match and are a good fit for the procedure. Learn more about the blood and bone marrow transplant procedure.

Other treatments: Even though blood transfusions are the typical treatment, other treatments may be used.

- **Medicines** called LUSPATERCEPT (REBLOZYL) and hydroxyurea may be prescribed by a healthcare provider to treat thalassemia. LUSPATERCEPT can lessen the number of blood transfusions needed for people with moderate to severe anaemia as a result of thalassemia. Hydroxyurea is usually used to treat sickle cell disease and can help lower the risk of health problems from thalassemia.[18]

Complications:

Health problems that can stem from moderate to severe thalassemia include:

- **Iron overload:** People with thalassemia can get too much iron in their bodies. This can be due to the disease or to frequent blood transfusions. Too much iron can result in damage to the heart, liver, and glands that make and release hormones.
- **Infection:** People with thalassemia have a higher risk of infections. This is especially true if they've had their spleens removed.

Severe thalassemia can lead to the following health problems:

- **Bone changes**: Thalassemia can cause the spongy tissue inside some bones, called bone marrow, to expand. That makes bones widen. It can lead to an irregular bone structure, especially in the face and skull. Expanding bone marrow also makes bones thin and brittle. That raises the chance of broken bones.
- **Enlarged spleen:** The spleen is an organ that helps the body fight infection. It also helps remove old or damaged blood cells. Often, thalassemia happens along with the destruction of a large number of red blood cells. This causes the spleen to get bigger and work harder than usual.

An enlarged spleen can make anaemia worse. It also can reduce the life of red blood cells received in a transfusion. If spleen grows too big, health care professional might recommend surgery to remove it.

- Slowed growth rates. Anaemia can slow a child's growth and delay puberty.
- Heart problems. Congestive heart failure and irregular heart rhythms can be linked with severe thalassemia.[19]

Need for the Study

β-thalassemia is a major genetic disorder with high prevalence in India. Conventional treatments manage symptoms but are lifelong. HSCT offers cure but has limitations. CRISPR-Cas9 represents a promising future therapy. Studying these helps improve treatment strategies, policy-making, and patient outcomes**.**

The aim of this study is to systematically review and synthesize the literature on Epidemiology of beta thalassemia and comparative clinical efficacy of CRISPR-Cas9 versus Hematopoietic stem cell transplantation in transfusion-dependent\beta-Thalassemia.

1.To provide a comprehensive prevalence map of beta thalassemia in India categorise by geographic region.

2.To provide a comprehensive prevalence map of beta thalassemia in India categorise by endogamous community.

3.To systematically compare the clinical outcomes of allogeneic HSCT versus CRISPR-CAS9 medicated gene editing in terms of "Transfusion independence".

4.To evaluate the safety profile (adverse effects) between conventional transplant and gene therapy.

5.To provide a comprehensive prevalence map of beta thalassemia in age wise category.

Materials and Methods

Study Design

The study was Meta-Analysis, observation study.

Source of data

- Science basic studies
- Editorials/letters
- Articles

Study criteria

Inclusion criteria

- All the articles showing prevalence of beta thalassemia data in India.
- All articles showing Detailed information about CSIPR-CAS9
- All articles showing Detailed information HSCT treatment safety and efficacy data.

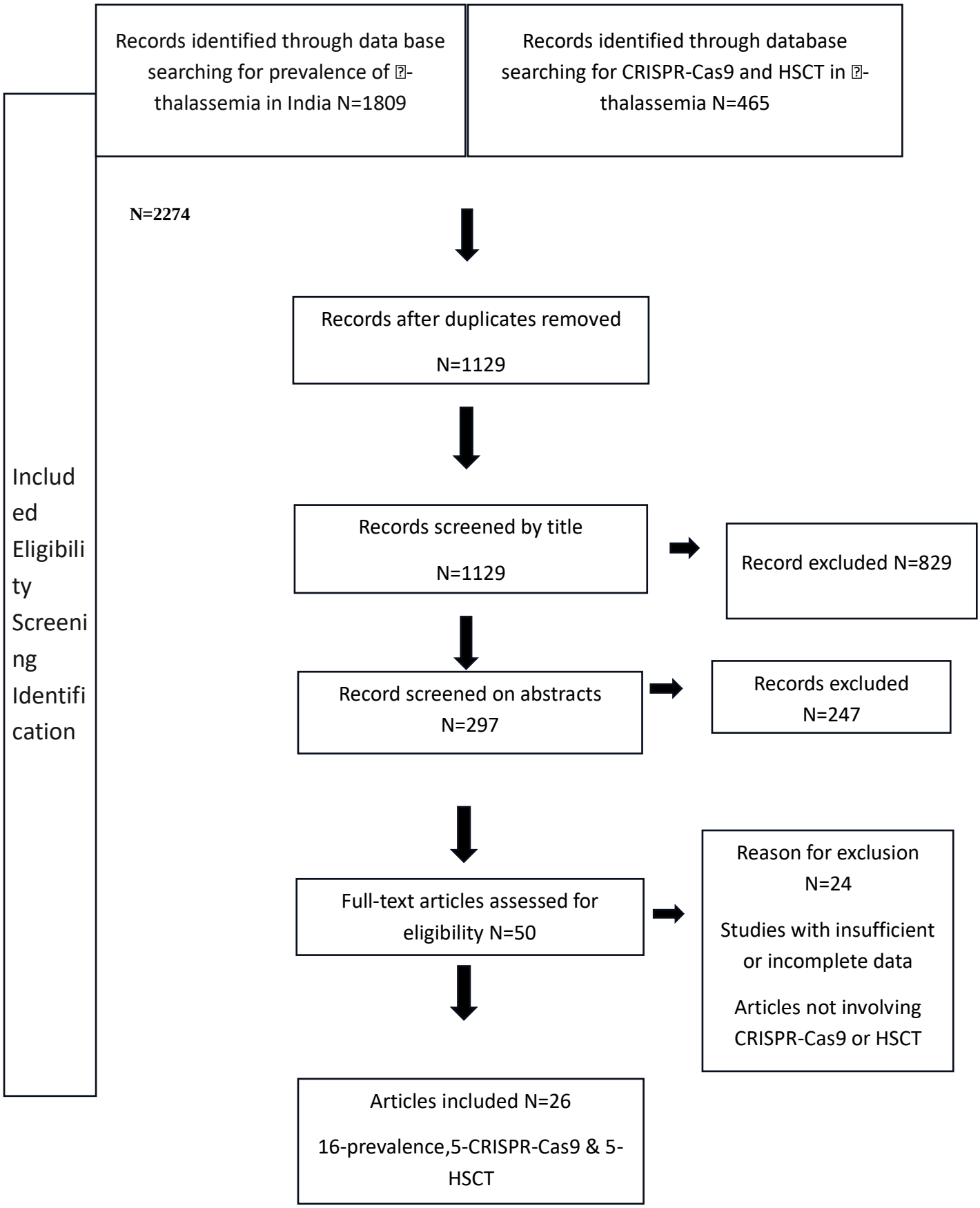
Exclusion criteria

- Animal model studies.
- Duplicate data.
- Insufficient data.

Method of data collection

A systematic and comprehensive literature search was conducted across six major electronic database-PubMed, MEDICINE, Scopus, Embase, WEB OF Science and clinical trials. Gov-covering the period from January 1,2012, to dec 31, 2025. This timeframe was selected to capture the critical advancements in gene therapy for ß-thalassemia.

The search strategy combined medical subject headings and free-text keywords including but not limiting to: "gene therapy," "ß-thalassemia," "CRISPR," "Cas9," "Zynteglo," efficacy," "Safety," "transfusion independence," and "hemoglobinopathies." Boolean operators (AND/OR), truncation symbols and database-specific filters (e.g., human studies, clinical trials, and English language) were applied to refine search results.


Records identified through data base searching for prevalence of -thalassemia in India N=1809
Records identified through database searching for CRISPR-Cas9 and HSCT in -thalassemia N=465
N=2274
Records after duplicates removed N=1129
Records screened by title N=1129
Record excluded N=829
Record screened on abstracts N=297
Records excluded N=247
Full-text articles assessed for eligibility N=50
Reason for exclusion N=24
Studies with insufficient or incomplete data
Articles not involving CRISPR-Cas9 or HSCT
Articles included N=26
16-prevalence,5-CRISPR-Cas9 & 5-HSCT
Included
Eligibility
Screening
Identification

Statistical analysis

It was done by using MS EXCEL

Plan of Work

Search the articles by using the term Thalassemia from the year 2012 to 2025

↓

Readout the articles carefully and extract the information.

↓

The extracted Information is then evaluated and analysed to fulfil the objectives of this study.

↓

After collection of data statistical analysis was done.

↓

Result were interpreted after analysis of data.

↓

Final result was concluded and impression highlighted.

Results

A Systemic review studied on Epidemiological Trends and comparative clinical efficacy of CRISPR-CAS9 vs HSCT in transfusion dependent beta-thalassemia. This study includes the following parameters: 1.Prevalence of beta-thalassemia in different age group in India 2. Prevalence of beta-thalassemia in different regional areas of India. 3.Prevalence of beta-thalassemia in different communities of India. 4. To compare therapeutic potential and clinical efficacy of CRISPR -CAS9vs HSCT.

Age wise Distriubution of beta-thalassemia patients

Table Age wise distribution of beta-thalassemia patients

AGE	PREVALENCE %
1-10	26.43%
11-20	12.07%
21-30	18.48%
31-40	11.15%
41-50	3.29%
51-60	11.80%
61-70	11.70%

The results reveal that beta-thalassemia disease is more common in age groups of 1-10 years which include 26.43%; 21-30 years which include 18.48%; 11-20 years which include 12.07%;51-60 years which include 11.80%; 61-70 years which include 11.70%;31-40 years which include 11.15%;41-50 years which include 3.29% (Table 1)

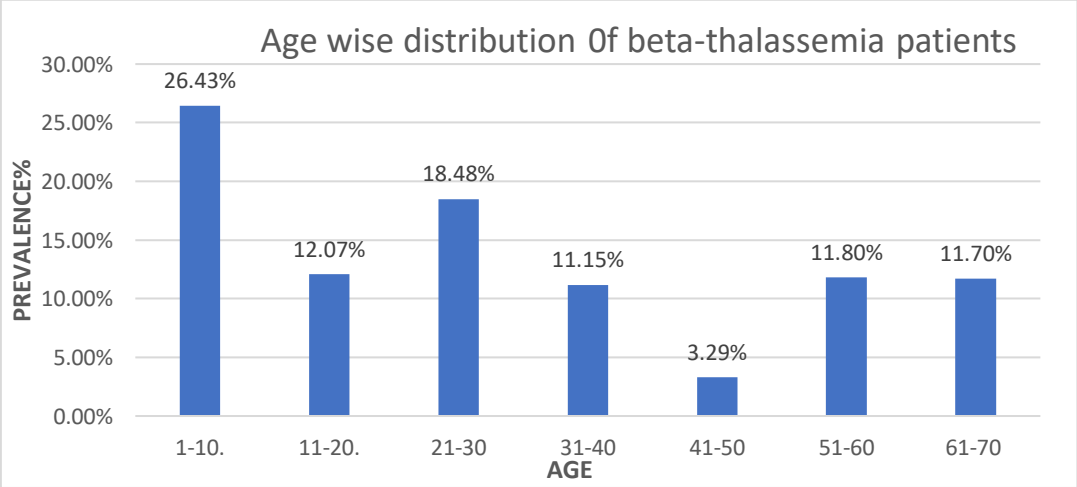


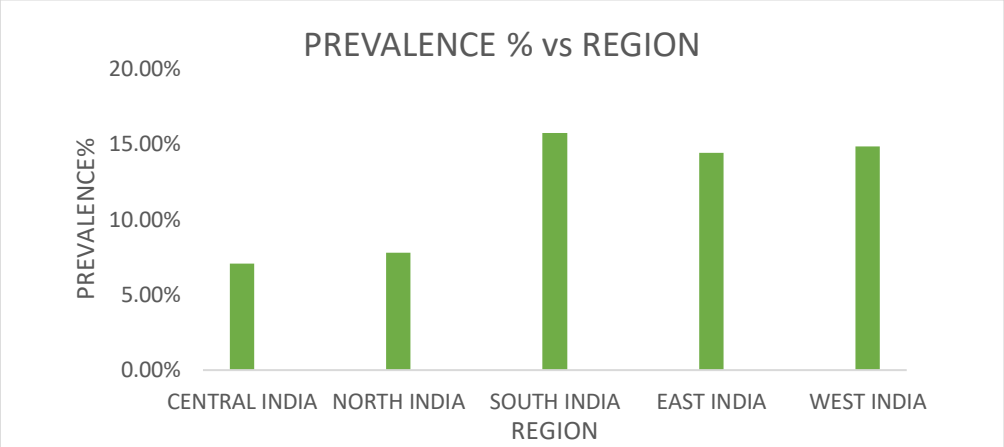
Figure Age wise distribution of Beta-thalassemia patients

Regional area wise Distribution of beta-**thalassemia prevalence**

Table Regional area wise distribution of beta-thalassemia prevalence

REGION	PREVALENCE
CENTRAL INDIA	7.06%
NORTH INDIA	7.77%
SOUTH INDIA	15.72%
EAST INDIA	14.40%
WEST INDIA	14.82%

The results of the study shows that south India hast the highest prevalence (15.72%) followed by West (14.82%) and East India (14.40%), while North (7.77%) and Central India (7.06%) show lower prevalence. This suggests that beta thalassemia is more common in southern and western regions compared to northern and central parts of India.



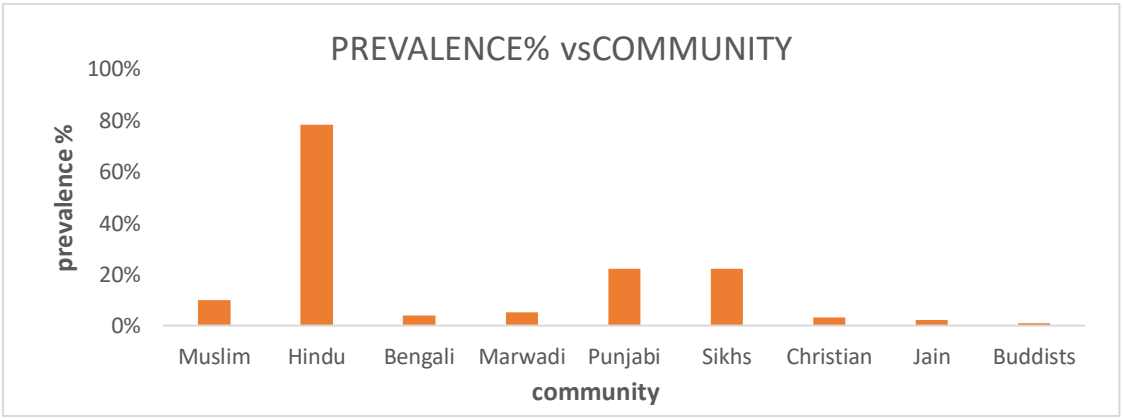
FigureRegional area wise distribution of beta-thalassemia prevalence

Community wise Distribution of beta-thalassemia prevalence

Table community wise Distribution of beta-thalassemia prevalence

Community	ß-thalassemia %
Muslim	10%
Hindu	78.20%
Bengali	3.95%
Marwadi	5.20%
Punjabi	22%
Sikhs	22%
Christian	3.20%
Jain	2.10%
Buddists	1.00%

The results of the study show that indicates that beta-thalassemia is most prevalent in the Hindu community, followed by Punjabi and Sikh groups. Moderate prevalence is seen in Muslims, while Bengali and Marwari communities show lower rates.



FigureCommunity wise distribution of beta-Thalassemia prevalence

Transfusion independence in crispr CAS9 VS HSCT

Table Transfusion independence in crispr CAS9 Vs HSCT

TREATMENT	TRANSFUSION INDEPENDENCE
CRISPR CAS9	97%
HSCT	91%

The results that CRISPR -Cas9 achieves higher transfusion Independence 97% compared to HSCT 91%.

Figure Transfusion independence in crispr CAS9 Vs HSCT

HbF LEVELS IN CRISPR CAS9 Vs HSCT PATIENTS

Table HbF LEVELS IN CRISPR CAS9 Vs HSCT PATIENTS

Treatment	HbF
CRISPR CAS9	12.86%
HSCT	10.16%

The results of the study shows that CRISPR-Cas9 therapy is more effective in increasing HbF levels than HSCT.

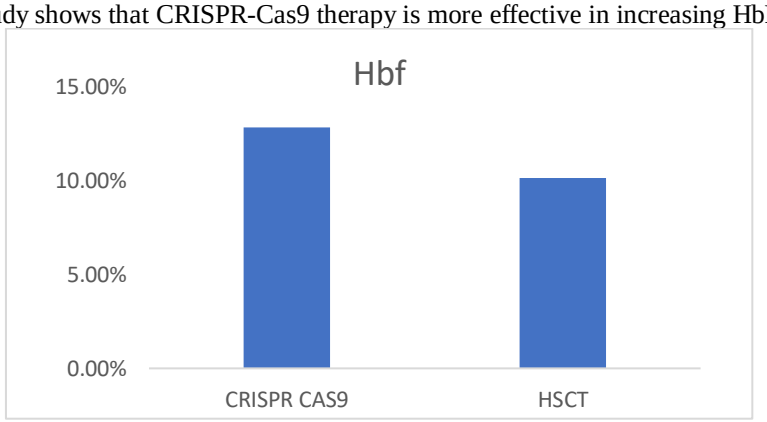


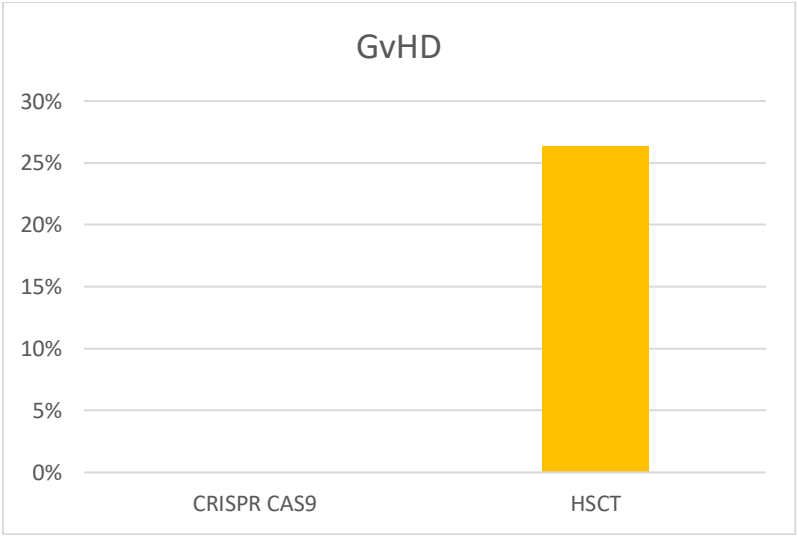
Figure HbF levels in crispr CAS9 Vs HSCT PATIENTS

GvHD in crispr CAS9 Vs HSCT PATIENTS

Table G vs HD in crispr CAS9 Vs HSCT Patients

Treatment	G vs HD
CRISPR CAS9	0%
HSCT	26.33%

The results shows that HSCT has a significant risk (25-30%), while CRISPR-Cas9 gene shows negligible or no GvHD occurrence.



FigureG vs HD in crispr CAS9 Vs HSCT Patients

TIME TO ENGRAFTMENT IN CRISPR CAS9 Vs HSCT PATIENTS

Table Time to engraftment in crispr CAS9 Vs HSCT Patients

Treatment	Time To engraftment (days)
CRISPR CAS9	36.80 days
HSCT	22 days

The results shows that CRISPR CAS9 has a higher value (36.8%) compared to HSCT (22%), indicating a relatively longer engraftment duration.

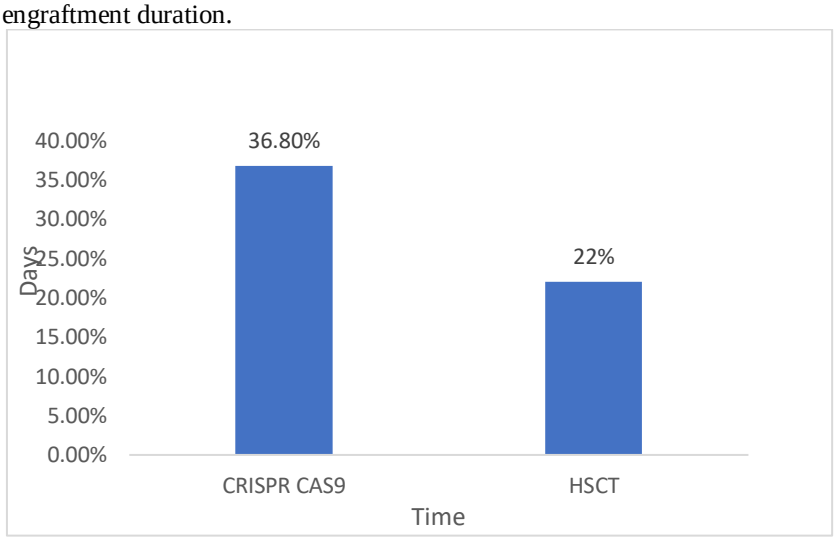


Figure Time to engraftment in crispr CAS9 Vs HSCT Patients

DISCUSSION:

Based on the results from our study the distribution of thalassemia prevalence across different age groups, indicating a clear variation with age.

The highest prevalence is observed in the 1–10 years age group (26.43%), suggesting that thalassemia is most commonly detected during early childhood, likely due to its genetic nature and early clinical manifestation. This is followed by a relatively high prevalence in the 21–30 years group (18.48%), which may reflect survival into adulthood and continued diagnosis or monitoring. The prevalence decreases in the 11–20 years (12.07%) and 31–40 years (11.15%) age groups, indicating a moderate presence. A significant drop is seen in the 41–50 years group (3.29%), which could be due to reduced survival rates or underreporting in this age category. Interestingly, the prevalence again shows a slight increase in the older age groups of 51–60 years (11.80%) and 61–70 years (11.70%), possibly reflecting improved treatment outcomes and longer life expectancy in recent years.

In our study East India has the highest prevalence (95.98%). This means almost all the studied population in that region is affected or carries the disease, making it the most severely impacted area. This could be due to genetic factors, less awareness, or fewer screening programs.

Next is West India with 66.85%, which is also quite high. North India (57.82%) and South India (56.42%) have moderate

The regional variation in beta thalassemia prevalence is an uneven distribution of the disease across India. South India shows the highest prevalence, which may be due to factors such as higher rates of consanguineous marriages, genetic clustering, and specific community-based inheritance patterns. West and East India also demonstrate relatively high prevalence, likely due to presence of high-risk ethnic groups and common mutations in these regions.

In our study β-thalassemia is most prevalent in the Hindu community, followed by Punjabi and Sikh groups. Moderate prevalence is seen in Muslims, while Bengali and Marwari communities show lower rates. The lowest prevalence is observed in Christian, Jain, and Buddhist communities. These differences are mainly due to genetic factors and community marriage practices.

CRISPR-Cas9 achieves higher transfusion independence (~96–97%) compared to HSCT (~90–92%). CRISPR-Cas9 is more effective because it corrects the genetic defect directly and does not require a donor, whereas HSCT, though curative, has limitations like donor availability and risk of complications.

In our study CRISPR-Cas9 therapy shows a higher HbF level (~13%) compared to HSCT (~10–11%). This indicates that CRISPR-based gene editing is more effective in increasing HbF production.

CRISPR-Cas9 works by editing genes (commonly targeting the BCL11A gene) to reactivate HbF production in red blood cells. Increased HbF compensates for defective β-globin chains, improving oxygen transport and reducing anaemia.

On the other hand, HSCT replaces defective bone marrow with healthy donor stem cells. While HSCT can be curative, HbF increase is usually moderate and depends on donor compatibility and engraftment success.

The table compares the occurrence of Graft-versus-host disease in patients treated with CRISPR-Cas9 and HSCT. It shows that CRISPR-Cas9 therapy has 0% incidence of GvHD, whereas HSCT shows a significantly higher incidence (26.33%).This indicates that CRISPR-Cas9, being an autologous gene-editing approach, avoids immune incompatibility and thus eliminates the risk of GvHD. In contrast, Hematopoietic stem cell transplantation involves donor cells, which can

trigger immune reactions leading to GvHD. Overall, the data suggests that CRISPR-Cas9 may be a safer alternative with respect to GvHD complications.

In our study the time to engraftment between CRISPR-Cas9 and Hematopoietic stem cell transplantation. It shows that CRISPR-Cas9 has a higher value (36.80%) compared to HSCT (22%), indicating a relatively longer engraftment period .This suggests that while CRISPR-Cas9 is effective, the recovery and establishment of modified cells may take more time. In contrast, HSCT demonstrates faster engraftment, likely due to direct transplantation of donor stem cells. Overall, HSCT provides quicker engraftment, whereas CRISPR-Cas9 may require a longer duration for full therapeutic effect.

CRISPR-based therapy using CRISPR-Cas9 for Beta Thalassemia is still in the early stages of development in India. Its use is limited due to high cost, need for advanced laboratory infrastructure, and ongoing clinical research. Only a few specialized centres are exploring this technology, and it is not yet widely accessible to patients. In contrast, Hematopoietic Stem Cell Transplantation is well established in India and has been used for many years as a standard curative treatment. Many hospitals have the required facilities and experience to perform HSCT, making it more commonly available compared to CRISPR-Cas9 therapy.

CONCLUSION:

In our study, it is concluded that β-Thalassemia is highest in the age group of 1-10 years with 26.43% and east India has highest prevalence that is, 95.98%and then West India and it more prevalent in the Hindu community followed by Punjabi and Sikh groups.

We have also concluded that, CRISPR-Cas9 achieves high transfusion independence, higher HbF level ,and less Gvs HD compared to HSCT. So, it is concluded that CRISPR-Cas9 treatment for β-thalassemia is more efficient compared to HSCT.

REFERENCES:

1.A. Thalassaemia [Internet]. TIF. [cited 2024 May 18].Available from: https://thalassaemia.org.cy/haemoglobin-disorders/thalassaemia/

2.Taher A, Musallam K, Capellini M. Thalassemia intermedia: an update, “Mediterranean Journal of Haematology and Infectious Diseases.2009.

3.Vincenzo D, Christos K. β-Thalassemia Distribution in the Old World: An Ancient Disease Seen from a Historical Standpoint” (2017); 9(1): e2017018.

4.Thalassaemia from ‘A’ to ‘Z’: A comprehensive e-glossary for patients with thalassaemia (2019) [Internet]. TIF. 2019 [cited 2024 May 18]. Available from: https://thalassaemia.org.cy/publications/tif publications/thalassaemia-from-a-to-z-a-comprehensive-e-glossary-for-patients-with-thalassaemia/

5.Cao A, Galanello R. Beta-thalassemia. Genet Med [Internet]. 2010;12(2):61–76.

6.Available from: https://www.nature.com/articles/gim201012Thalassemia: Symptoms, Causes, & Treatment

7.*Gloria F. Gerber, MD, Johns Hopkins School of Medicine, Division of Hematology (Mediterranean Anemia; Thalassemia Major and Minor)R eviewed/Revised Apr 2024 | Modified Apr 2025*

8.Gluba-Brzózka, A.; Franczyk, B.; Rysz-Górzyńska, M.; Rokicki, R.; Koziarska-Rościszewska, M.; Rysz, J. Pathomechanisms of Immunological Disturbances in β-Thalassemia. *Int. J. Mol. Sci.* 2021, *22*, 9677.

9.Schrier, S.L. Pathophysiology of thalassemia. *Curr. Opin. Hematol.* 2002, *9*, 123–126.

10.Pearson, H.A. Pathophysiology of thalassemias. *Ann. N. Y. Acad. Sci.* 1974, *241*, 274–279.

11.Fertakis, A. Thalassemia: Pathophysiology, clinical and laboratory findings. In *Radiology of Thalassemia*; Springer: Berlin/Heidelberg, Germany, 1989; pp. 13–18.

12.Origa, R.; Galanello, R. Pathophysiology of beta thalassaemia. *Pediatr. Endocrinol. Rev.* 2011, *8*, 263–270.

13.Thalassemia: Types, Traits, Symptoms & Treatment

14.Jariwala K, Mishra K, Ghosh K. Comparative study of alloimmunization against red cell antigens in sickle cell disease & thalassaemia major patients on regular red cell transfusion. Indian J Med Res. 2019 Jan;149(1):34-40. [PMC free article] [PubMed]

15.Sarkar SK, Shah MS, Begum M, Yunus AM, Aziz MA, Kabir AL, Khan MR, Rahman F, Rahman A. Red Cell Alloantibodies in Thalassaemia Patients Who Received Ten or More Units of Transfusion. Mymensingh Med J. 2019 Apr;28(2):364-369. [PubMed]

16.Darvishi Khezri H, Emami Zeydi A, Sharifi H, Jalali H. Is Vitamin C Supplementation in Patients with β-Thalassemia Major Beneficial or Detrimental? Hemoglobin. 2016 Aug;40(4):293-4. [PubMed]

17.Darvishi Khezri H, Emami Zeydi A, Sharifi H, Jalali H. Is Vitamin C Supplementation in Patients with β-Thalassemia Major Beneficial or Detrimental? Hemoglobin. 2016 Aug;40(4):293-4. [PubMed]

18.Thalassemia - Treatment | NHLBI, NIH

19.Thalassemia - Symptoms & causes - Mayo Clinic