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On Exploration of Challenges for Bone-marrow Transplant and Bone Marrow Donation in India and Exploring the Hierarchical Inter-relationships amongst them

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ABSTRACT

Bone marrow transplant has undoubtedly transformed the landscape of blood cancer treatment, offering hope to patients facing life-threatening diseases. While challenges like donor availability and cost persist, ongoing research and technological advancements are paving the way for improved outcomes and increased accessibility. Further, it has become quite important to unravel the complexities and the art of bone marrow transplant, it is as well important to prioritize access to patients, complications must get reduced and treatment calls refined better. Present research article tires to explore the area of bone marrow transplant and bone marrow donation [through registries] and further establish mathematical hierarchical inter-relationships amongst them using Interpretive Structural Modeling Methodology [ISM].

Keywords: Bone marrow transplant registries, ISM methodology, Hierarchical inter-relationships

Bone marrow transplant, also known as hematopoietic stem cell transplant, have been a lifeline for thousands of blood cancer patients worldwide [Bladé J. *et al.* (1998); Pavletic *et al.* (2005); Alijurf *et al.* 2019]. These life-saving procedure involves replacing damaged or malfunctioning bone marrow with healthy stem cells to restore the patient's ability to produce healthy blood cells. To improve outcomes and accessibility for all patients. Bone marrow is a spongy tissue found inside the bones that plays a crucial role in the production of blood cells, including red blood cells, white blood cells, and platelets. Bone marrow transplant involves the infusion of healthy stem cells, typically obtained from a compatible donor, into the patient's bloodstream. These stem cells then migrate to the bone marrow and begin to produce healthy blood cells, effectively replacing the cancerous or dysfunctional cells. This procedure can be a curative option for many blood cancer patients, offering the hope of remission or a complete cure.

India staggers with a significantly lesser number of bone marrow donors and stooping bone marrow donation rates, despite increasing demand for bone marrow transplants in the country. While about only 2,000 stem cell transplants take place in India every year, around 80,000 to 1,00,000 annual transplants are required to tackle the large burden of blood cancers and fatal blood disorders. However, it is very hard to find a matching donor. India has only about 4 lakh donors registered on the bone marrow registry [Dedhia and Parekh (2014)] and the chances of finding a donor match are as low as 10% to 15% compared to the West where the chances of matching are as high as 60% to 70%. This crisis can be attributed to a large number of challenges, starting from a complete lack of awareness about the

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procedure to dearth of well-equipped bone marrow donation centers in the country.

Present research work tries to explore the hierarchical inter-relationships amongst the challenges faced by bone marrow transplant in India through ISM methodology. Section 2 presents the challenges in bone marrow transplant

Challenges in bone marrow transplant and Donation

1. Challenges in bone marrow transplant

[Dedhia and Parekh (2014); web ref : carehospitals.com; indiatimes.com 2023; Alijurf *et al.* (2019)]

While bone marrow transplant has undoubtedly revolutionized the treatment of blood cancers, they come with their own set of challenges and limitations that the medical community must address.

1.1 Donor Availability [DA]: Finding a suitable donor remains a significant hurdle for many patients. Compatibility is often determined by matching specific hla alleles, and not all patients have a compatible family member or unrelated donor readily available.

1.2 Pre-transplant Conditioning [PTC]: Preparing the patient's body for a transplant often requires high-dose chemotherapy or radiation therapy to eliminate cancer cells and create space in the bone marrow for the donor cells. This process can be physically and emotionally taxing for patients.

1.3 Infections and Complications [I&C]: The period following a bone marrow transplant is marked by heightened vulnerability to infections and other complications. Patients must be closely monitored and receive supportive care to mitigate these risks.

1.4 Cost and Access [C&A]: The cost of bone marrow transplant can be prohibitively high, making them inaccessible to many patients, particularly in countries without universal healthcare coverage. Access to these life-saving procedure remains a significant concern.

2. The challenges faced by bone marrow donation in India [web ref: healthcareradius.in, Alijurf *et al.* (2019)]

2.1 Inadequate donation centers and lack of funds for function of registry [IDC]: Not many hospitals in the country have the infrastructure to support bone marrow donation in large numbers. There are inadequate donation centers. There are lack of funds for function of registry.

2.2 Inadequate funding [IF]: The problem of funding is mostly due to the registries being not financially supported by the state or central government of India. The funding for the few existing registries comes from the private organization and not many people help in fundraising for managing the registries.

2.3 Lack of awareness [LOA]: Unawareness largely makes people reluctant to come forward and register for donating bone marrow. Creating sufficient awareness can bust several myths related to bone marrow transplants and help people make informed decisions about becoming donors. Bone marrow or stem cell donation is the only organ donation where the donor saves lives without any loss for themselves as the stem cells almost immediately regenerate.

2.4 Lack of matching donors [LMD]: Availability of adequate matching donors can help reducing the cost of procuring matched stem cells from abroad can be saved. Despite having a unique gene pool due to a variety of ethnicity, culture, language, marriages within communities and migration waves, it is very difficult to find a matched unrelated donor. That is mostly because of a very less number of willing donors registering for donating stem cells in comparison to the western countries. An increasing number of donor drives and awareness programs need to be conducted to encourage more donor registry in the country. India, for example, has a large, non-homogeneous population with >300 distinct ethnic groups and 438 languages. In India, there are five organizations listing donors for international recipients.

2.5 Increased donor dropout rates [IDDR]: It is important to check the rising donor dropout rates at various stages of the procedure and the inability to control this dropout rate has always remained as a serious challenge in the country.

2.6 Inadequate donation centers [IDC]: Not many hospitals in the country have the infrastructure to support bone marrow donation in large numbers. Also, the medical fraternity does not have adequate number of doctors with expertise in the area of bone marrow transplant.

2.7. Complicated in house built programs [CIHBP]: Information technology (IT) is necessary to run donor searches, to analyze HLA-haplotype frequencies and to predict the chances of finding a donor for each patient, who usually desperately needs a transplant in the shortest possible time-frame. Historically, large international registries developed their own software with their internal IT staff and/or external software companies and some may have used blood bank software as their starting point. These in-house built programs are typically complex and tightly tailored to the local needs. They are not available commercially and thus not available for emerging registries.

2.8. Utilization of artificial intelligence [UAI]: Artificial intelligence (AI) particularly with machine learning (ML) technology is revolutionizing the field of HCT in the selection of donors, and predicting outcomes after allo-HCT and even in GVHD. The use of AI for donor–recipient pair matching in unrelated donor registries has been evaluated by multiple investigators and some have proven to increase accuracy of predictions for matching as well as for outcomes.

3. ISM Methodology

Interpretive Structural Modeling (ISM) is an interactive learning process in which a set of unique, interrelated variables are structured into a comprehensive model presented as a hierarchy graph. The method is interpretive in that the group's judgement decide whether and how items are related.

The various steps involved in ISM are *Identification of elements* which are relevant to the decision maker's problems and issues. Thereafter, e*stablishing the contextual relationship* between elements with respect to which pairs of elements will be examine. Thereafter, d*eveloping a self-interaction matrix (SSIM*): This matrix gives the pairwise relationship between two variables i.e. *i and j.* It establishes relationship of "Lead to" between criteria. It uses the four symbols *viz.* V , A X and O for the type of relation that exists between two sub-variables under consideration. Using SSIM matrix, initial reachability matrix can be formed, it has all values in binary form. Decision maker must check for rule of transitivity.

Level Partition and Canonical Matrix: From the reachability matrix, the reachability set and antecedent set for each criterion is found (Warfield, 1974). The element for which the reachability and intersection sets are the same is the top-level element. The whole process of partitioning is based on establishing the precedence relationships and arranging the elements in a topological order. After that, we are classifying variables based on *relative driving power and dependence power into* various categories like autonomous, dependent, driver and linkage. Finally, d*evelopment of Diagraph/ ISM from the canonical matrix form.*

4. Case example

Eight major challenges discussed above in section 2 *viz*. Inadequate donation centers [IDC]; Inadequate funding [IF]; Lack of awareness [LOA]; Lack of matching donors [LMD]; Increased donor dropout rates [IDDR]; Inadequate donation centers [IDC]; Complicated in house built programs [CIHBP];Poor utilization of artificial intelligence [PUAI]are studied with the help of ISM methodology for the possible hierarchical interrelationships amongst them.

Explanation: Complicated in-house built in programs. These in-house built programs are typically complex and tightly tailored to the local needs. They are not available commercially and thus not available for emerging registries and which is why it is quite possible that the country may not have accurate / correct data for bone marrow transplant / donation registries and may, therefore, show inaccurate number when explored. Similarly, because of a very less number of willing donors registering for donating stem cells in comparison to the western countries, sometimes even if they donate, they want to be disclosed or explored which is another possibility that we may have incorrect data of bone marrow transplant /donation. Inadequate funding could be a result of inadequate donation center and vice versa because there is not so much hype / advertising / awareness that one should allocate a significant amount of funds towards such cause. Inadequate medical staff and /or doctors is also a result of inadequate funding , and increased donor dropout rates .

Like ways, another factors could also be related based on V, A, X, O relationship.

Note: *Kindly note that the SSIM is created form author's point of view which is subject to location, country and its requirements. This may subject to change.*

4.1 Structural Self – Interaction Matrix [SSIM]

This matrix gives the pair-wise relationship between two variables i.e. *i and j* based on VAXO. SSIM has been presented below in Fig. 1.

Fig. 1: SSIM matrix for pair wise relationship amongst challenges faced by organic textile industry in India

Sl. No.	Barriers	1 IDC	2 IF	3 LOA	4 LMD	5 IDDR	6 IDC	7 CIHBP	8 PUAI
1	IDC		A	A	V	V	V	V	V
2	IF			A	A	A	A	A	A
3	LOA				V	V	V	V	V
4	LMD					A	A	A	A
5	IDDR						A	A	A
6	IDC							V	A
7	CIHBP								V
8	PUAI								

4.2 Initial reachability matrix [IRM]

The SSIM has been converted in to a binary matrix called the initial reachability matrix shown in Fig. 2 by substituting V, A, X, O by 1 or 0 as per the case. After incorporating the transitivity, the final reachability matrix is shown below in the Fig. 3.

Fig. 2: IRM matrix for pair wise relationship amongst challenges faced by bone-marrow donation in India

Sl. No.	Barriers	1 IDC	2 IF	3 LOA	4 LMD	5 IDDR	6 IDC	7 CIHBP	8 PUAI
1	IDC		0	0	1	1	1	1	1
2	IF	1		0	0	0	0	0	0
3	LOA	1	1		1	1	1	1	1
4	LMD	0	1	0		0	0	0	0
5	IDDR	0	1	0	1		0	0	0
6	IDC	0	1	0	1	1		0	0
7	CIHBP	0	1	0	1	1	0		1
8	PUAI	0	1	0	1	1	0	0	

4.3. Final reachability matrix [FRM]

Final Reachability Matrix (FRM), representing in Table, is constructed by finding transitivity in the matrix, which is an indirect relation between factors. If transitivity is found in the matrix, the final transitivity matrix value is put as 1*. After removing the transitivity, final reachability matrix is obtained along with the driving power as well as dependence power.

Fig. 3: FRM matrix for pair wise relationship amongst challenges faced by bone marrow donation in India

Sl. No.	Barriers	1 IDC	2 IF	3 LOA	4 LMD	5 IDDR	6 IDC	7 CIHBP	8 PUAI	D.P
1	IDC		0	0	1	1	1	1	1	6
2	IF	1		0	0	0	0	0	0	2
3	LOA	1	1		1	1	1	1	1	8
4	LMD	0	1	0		0	0	0	0	2
5	IDDR	0	1	0	1		0	0	0	3
6	IDC	0	1	0	1	1		0	0	4
7	CIHBP	0	1	0	1	1	0		1	5
8	PUAI	0	1	0	1	1	0	0		4
		3	7	1	7	6	2	3	4	

Possible sequence : 2, 4 → 5 → 8 → 1, 7, 6 → 3

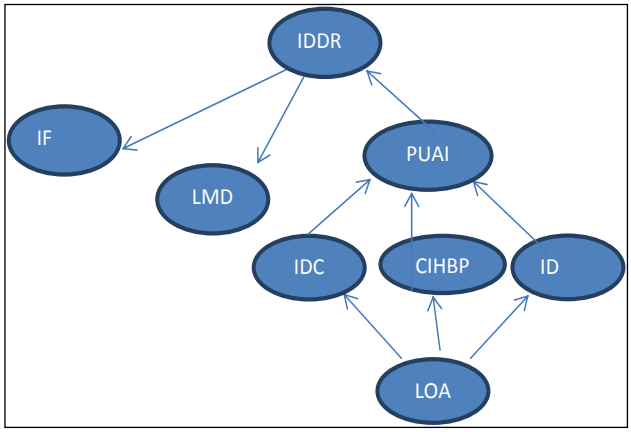
4.4 Level Partition matrices

Table 1: Iterations

Reachability set	Antecedent set	Intersection set	Iteration	Element at iteration
2, 4	1,2,3,4,5, 6,7,8	2, 4	I	2 , 4
2,4,5	1,3,5,6, 7,8	5	II	5
2,4,5,8	1,3,6, 7,8	8	III	8
2,4,5,1, 6, 7,8	1,3,6,7	7,1,6	IV	7,1,6
1,2,3,4,5, 6,7,8	3	3	V	3

Possible sequence : 2,4 → 5 → 8 → 1,7, 6 → 3

5. ISM Diagraph



CONCLUSION

The present research highlights the hierarchical inter-relationships amongst the various challenges faced by bone marrow transplant and bone marrow donation in India with the help of Interpretive Structural Modeling Methodology.

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