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Nursing considerations: future of stem cell transplantation in Egypt

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Abstract

Background: The procedure of hematopoietic stem cell transplantation (HSCT) will keep expanding over the next decades. All around the world, although enormous technological advancement and improvement of scientific approaches to fighting all diseases; especially blood diseases as white blood cell (WBC) disorders, the people still sick and they need treatment. In Egypt, stem cells offer exciting promise for future therapies, but significant technical hurdles remain that will only be overcome through years of intensive research. Since hematopoietic stem cell transplantation started, nurses play an important role in this procedure, qualified nurses involved in every step of the stem cell collection process. They prepared with the knowledge and practice about the cord blood gathering and stem cell banking procedure to do; otherwise, nurses acting an accurate group of functions in stem cell banking, from their understanding the structure of the umbilical cord to defining the sites of obtaining stem cells. Specialized nursing care is essential to avoid and manage the predicted and unpredicted complications of hematopoietic stem cell transplantation. Stem cell transplantation needs to the highly qualified nursing team, their care continuing within phases of transplant for both donors and patients. This article will describe the future of stem cell transplantation in Egypt and Arab world, the most important issues and trends related to HSCT, the Benefits of Umbilical Cord Blood Stem Cell Storage in Stem Cell Banking the formal unities and hospitals for HSCT in Egypt and the nurses' role in stem cells transplantation (Pre, During, Post and Discharge) in Egypt.

Key words: stem cells, hematopoietic stem cell transplantation, cord blood banking, nursing role, stem cell phases.

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1. Introduction

Stem cells (SCs) are unspecialized cells that have two essential characteristics: the capability to distinguish into other cells through mitotic cell division and differentiate into a diverse range of specialized cell types and the capability to self-regenerate [1, 2].

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Bone marrow has at least two types of stem cells, hematopoietic stem cells (HSCs) and mesenchymal stem cells or marrow stromal cells (MSCs) [1]. Stem cells have two general kinds of mammalian stem cells are embryonic stem cells that are obtained from the inner cell mass of blastocysts, and mature stem cells that are found in mature tissues [3].

Hematopoietic stem cell transplantation (HSCT) is the transplantation of multipotent hematopoietic stem cells, generally the main its sources are bone marrow, peripheral blood, or umbilical cord blood, according to the donor it classified into three types when the donor is patient's own stem cells which called autologous, or the donor stem cells come called allogeneic; or from an

identical twin called syngeneic [2, 4,5].
It is a medical life-saving treatment for several diseases as haemato-oncological condition, such as leukemia, lymphoma or multiple myeloma and certain inherited metabolic diseases [2, 4, 5]. Moreover, recently some researchers attempt to use hematopoietic stem cell transplantation for the treatment of diabetes, cardiovascular and neuro-generative diseases, but the applications are still undocumented success [6].
Before patient treatment by HSCT need to assess the stage of the disease, type of disease, conditioning regimen, type of transplant, human leukocyte antigen-matched compatibility, the age of the patient and his or her general health and follow up to decide the patient prognosis [7].

2. Indications for stem cell transplantation:

Divide into malignant as acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), Hodgkin lymphoma (HL) (relapsed, refractory), non-Hodgkin lymphoma (NHL) (relapsed, refractory), neuroblastoma, ewing sarcoma, multiple myeloma, myelodysplastic syndromes, gliomas, and other solid tumors; while non-malignant as thalassemia, sickle cell anemia, aplastic anemia, fanconi anemia, malignant infantile osteoporosis, mucopolysaccharidosis, immune deficiency syndromes and autoimmune diseases [8].

3. Historical background:

More than 40,000 stem cell transplants are being performed annually in the world [6]. Egyptian program of hematopoietic stem cell transplant, established in 1989, but it began slow progress, now more transplants performed by peripheral blood than bone marrow [9]. Egyptian Ministry of Health and Population (MOHP) founding a wide policy on CB banking using guiding principle and codes of ethics from the United States and Europe as a template. In 2007 it accepted a National Blood Policy with procedural guidelines for CB collection and storage to be overseen by the country's National Blood Transfusion Standards [10].

In 2011 the MOHP formed the National Stem Cell Committee tasked with creating protocols of stem cell research and therapy and a national stem cell bank, in 2012 a new stem cell research center established at Sheikh Zayed Hospital, otherwise Zewail City of Science and Technology opened a Center for Stem Cell Research and Regenerative Medicine in 2013 [11]. This city is associating with Assiut University to build a public CB bank [12]. Before a CB bank activates in Egypt, it obtains approval from Al-Azhar University, a well-known center for Islamic learning in Cairo. Egypt licenses both private and public banking in the country, extended confident guidelines are achieved to diminish the possibility of marketable manipulation [13]. At Ain Shams University in Cairo; many a clinical trial performed for transplants by autologous CB in neonates [14].

4. Egypt and the Arab world:

Cord blood banking is a public CB bank, which established in five countries; they are Jordan, Saudi Arabia, Egypt, Qatar, and the United Arab Emirates, designated for their diverse CB banking policies and creativities Table1 [15]. It responsible for assessing case studies suggests strong incentives research for increasing the number of CB units that are collected from and available to Arab populations. Furthermore, it concerning awareness and education of the public to correct the deficit in knowledge related to this issue. It mostly financed by the government, generous sources, and income from exporting CB units to transplant centers, Table2, 3 [16, 13].

Table No 1. Relevant demographic, health, and economic indicators of 4 arab countries studied: Jordan, Saudi Arabia, Uae, Egypt [15]

Country	Population	Arab	Fert	GNI	Health $	Hosp Beds	Leukemia	Lymphoma
Jordan	7.93M	98%	3.16	$4.95k	8.4%	1.8	6.1	8.2
Saudi Arabia	27.3M	90%	2.17	$26.2k	3.7%	2.2	3.8	7.9
UAE	5.63M	13%[|]	2.36	$38.6k	3.3%	1.9	3.7	6.7
Egypt	86.9M	99%	2.87	$3.16k	4.9%	1.7	5.9	9.3

Percent of population of Arab ethnicity (Arab), and total fertility rate (Fert)*; economics: gross national income per capita (GNI) [†] and percent of gross domestic product for health expenditures (Health $); and health: hospital bed density[‡] (Hosp beds) and age-standardized incidence rates[§] of leukemia and lymphoma (both Hodgkin and non-Hodgkin).

Table No 2. Current CB banking options in the arab world [16]

CB Bank	Storage Location	Collection Office Location(s)
Baby Cord	USA (Boston), Jordan (Amman)*	Jordan
Biovault Family	UK (Plymouth)	Lebanon, UAE
Cell Safe	Egypt (Cairo)	Egypt
Cells4Life	UK (Burgess Hill, Essex)	Bahrain, Egypt, Jordan, Kuwait, Lebanon, Qatar, Saudi Arabia, UAE
Center for Stem Cell Research & Regenerative Medicine	Egypt (Assiut)*	Egypt
Cryo-Save	UAE (Dubai), Belgium (Niel)	Egypt, Kuwait, Oman, Saudi Arabia, UAE
DCRC†	UAE (Dubai)	UAE
Future Health Biobank	UK (Nottingham), Switzerland (Châtel-StDenis)	Bahrain, Egypt, Jordan, Kuwait, Lebanon, Morocco, Qatar, Saudi Arabia, Syria, UAE
KAIMRC	Saudi Arabia (Riyadh)	Saudi Arabia
KFSH-RC†	Saudi Arabia (Riyadh)	Saudi Arabia
KHCC	Jordan (Amman)*	Jordan
Precious Cells	UK (Middlesex)	Jordan, Lebanon, UAE
Smart Cells	UK (West Drayton)	Egypt, Jordan, Kuwait, Lebanon, Syria, UAE
Sultan Qaboos Univ. Hospital	Oman (Muscat)	Oman
Virgin Health Bank	Qatar (Doha)	Qatar

Priv means private banks, Publ means public banks, as well as Hybr means hybrids,
*Indicates the CB bank storage facility is currently under construction.
†Indicates CB banks that are Provisional Members of the NetCord consortium.

Table No 3. Timeline of major CB banking developments in the arab world [13]

Year	Development
1998	First Cord Blood transplant is done in Arab world
2003	Muslim World League's Jurisprudential Council issues a *fatwa* approving Cord blood transplants and research begun in SA.
2006	UAE: DCRC opens first CB bank in the region, as a public-private hybrid model SA: KFSH-RC opens the Kingdom's first public CB bank UAE: Cryo-Save Arabia, the largest private CB storage facility in the region, opens in Dubai Healthcare City
2007	EG: Guidelines for CB collection and storage process is accepted by National Blood Policy.
2009	QA: Transferring of Virgin Health Bank its headquarters from London to Doha. EG: Cell Safe opens as the country's first private CB bank
2011	QA: Virgin Health Bank is granted the first (and only, to date) license for CB procurement, processing, and storage. SA: KAIMRC opens the country's second public CB bank and creates the Saudi Donor Registry QA: Virgin Health Bank opens storage and processing facility at Qatar Science & Technology Park EG: National Stem Cell Committee is created and tasked with establishing regulations for stem cell
	research and therapy as well as a public CB bank
2012	EG: Stem cell research center opens at Sheikh Zayed Hospital QA: Stem cell research policy is enacted into legislation, allowing research using CB stem cells
2013	EG: Center for Stem Cell Research and Regenerative Medicine opens in Zewail City of Science & Technology
2014	JO: New stem cell research law is passed, including regulations for CB banking
2015	JO: Projected opening of the first in-country private CB storage facility by the company, BabyCord Jordan EG: Projected opening of the country's first public CB bank, located at Assiut University, in partnership with Zewail City of Science & Technology
2016	JO: Projected opening of the country's first public CB bank, located at KHCC

Over the past decade, several Arab countries have had significant activities related to CB banking, starting primarily with Saudi Arabia (SA) and the UAE. More recently, new developments have been centered in Egypt (EG), Qatar (QA), and Jordan (JO).

The formal unities and hospitals for HSCT in Egypt:

Health Organization has recently clarified that stem cells treat 90 Disease and success rate 100%. So The Egyptian Ministry of Health has established two stem cell treatment units, they are at Sheikh Zayed Specialized Hospital in 6th of October City and Ahmed Maher Hospital, they started the treatment protocol by HSCT in 2012. The success rate is more than 90%, especially in liver diseases and complications, and the establishment of clinics for the comparison of cases and determines who needs to cultivate stem cells at Ahmed Maher Teaching Hospital in Cairo [17].

Other hospitals are Hospital 57357, Nasser Institute, Ain Shams Hospital, and Demerdash Hospital. All the stem cells transplantation cases, which performed in Egypt, have all succeeded. Otherwise, the Egyptian armed forces began their interesting to this treatment and attention to the idea came to establish the bank of the armed forces of stem cells at the Al El Galaa Medical Complex in January 2015 and was actually operational May 1, 2015[18, 19].

This project was processed within seven months with all the technology in it. The armed forces goal now is to focus on the national project of the armed forces, which will cover all provinces. There will be a law for stem cell treatment to regulate the treatment under the supervision of the armed forces [20].

Egyptian experts in HSCT:

There are many doctors specialized in field of treatment by HSCT as Dr. Wael Abou El Kheir Mustafa, Professor of Immunology and Microbiology- Ministry of Health, Consultant of Stem Cell Therapy and Director of Stem Cell Unit, Sheikh Zayed Specialist Hospital, Consultant of Stem Cell Therapy at Ahmed Maher Teaching Hospital, and Secretary of the Egyptian Society for Stem Cell Research [17, 21]. Dr. Abdelhamid Abaza, Assistant Minister of Health and Chairman of the National Commission on Stem Cells [22]. Dr. Hisham Issa, Chairman of the Stem Cell Bank [23]. Dr. Sharif Naseh, founder of the first stem cell bank in Egypt. Dr. Hassani Salama, Supervisor of the experiments of stem cell transplantation in the hospital of Qasr al-Aini [24]. Dr. Abdel Hakim Safwat, who has the first founder in the field of stem cells to treat chronic eye disease [25].

Cord blood stem cells vs. bone marrow stem cells:

The first use of Umbilical Cord blood stem cells transplant in 1988 and it used to treat more than 80 diseases. Umbilical cord stem cell storage is a simple non-invasive procedure and is completely harmless to the mother or the baby. While the collection of stem cells from the bone marrow is an invasive procedure and also requires general anesthesia which comes with its own set of inherent risks [13,26].

The benefits of umbilical cord blood stem cell storage in stem cell banking:

Treatment of cancer cells by chemotherapy or radiation have many complications as cell destruction, this destruction not differentiates between the cancer cells and healthy cells; it destroys both cells. Stem cell therapy helps to replicate the healthy cells or the disease/free cells in patients. Umbilical cord blood characterized by rich with stem cells [26]. These cells have the ability to reproduce themselves and also chance into any other type of cells as blood vessels, immune-system cells, bone cartilage, muscle cells, blood cells and nerve cells. So the establishment of Stem Cell Banking is an important to process, wherever cord blood cells are readily used to replenish the immune system after chemotherapy or radiation available any time of need Table4 [27,28].

Table No 4 Comparison between bone marrow or peripheral blood stem cells and cord blood donated for transplantation [27, 28]

Bone Marrow/Peripheral Blood	Cord Blood
Bone marrow donation requires surgery under general anesthesia. Donors may experience temporary discomfort and/or pain. Long-term consequences of growth factors used in peripheral blood stem cell donations are uncertain.	Stem cell obtained from the delivered placenta and umbilical cord, no medical risk to mother or infant
A transplant needs a donation of a quart or more of bone marrow (mixed with blood).	A small volume (sometimes few ounces) can be used for transplantation. The number of cells needed depends on the recipient's weight.
Bone marrow and peripheral blood grafts have large numbers of stem cells. Engraftment of neutrophil is fast.	Cord blood units contain smaller numbers of stem cells. Slower engraftment may lead to a prolonged hospital stay, and in certain cases, to severe complications.
After a formal search is started, it usually takes 2 or more months to transplant, if a donor is available.	When a match is found, it can take only a few days for confirmatory and special testing for shipment to the Transplant Center (less than 24 hours in an emergency).

Bone Marrow/Peripheral Blood	Cord Blood
Potential donors may no longer be available or may have withdrawn consent. The donor must be presented and retested to check the HLA typing and infectious disease results and to ensure that the donor is still willing and able to donate bone marrow. Significant donor attrition.	Once frozen, a cord blood unit is available until used. There is no donor attrition.
The donor may be accessible to give a second transplant or to donate blood for T-cells if needed.	Donor is not existing for a following second donation
Bone marrow is used fresh (shelf-life measured in hours). Peripheral blood stem cells usually stored for short term (days to a few months).	Cord blood units are cry preserved (stored in special freezers). Frozen cord blood has been transplanted successfully after up to 13 years in storage.
Patient must begin conditioning before the bone marrow or peripheral blood harvest. Coordination between donation and transplant is critical and complex.	Cord blood graft can be shipped to the transplant center before the patient enters the hospital and begins conditioning for transplantation. Coordination is simple. Cord blood units are shipped on demand.
Latent viral infection in the donor is common	The incidence of viral infection in the cord blood donor is sporadic.
No risk of transplanting a genetic disease.	There is a small probability that a rare, unrecognized genetic disease affecting the blood or immune system of the baby may be given with the cord blood transplant.
Severe graft vs. host disease (GVHD) is common with mismatched grafts.	GVHD less frequent, usually less severe and easier to treat
In general needs a perfect match between donor and recipient for 8/8 HLA-A, -B, -C and -DRB1 antigens. Additional HLA factors (HLA-DQ and -DP) increasingly used to improve prognosis.	HLA-mismatched cord blood transplants are possible, making it easier to find an appropriate match. Role of HLA-C, -DQ and -DP are not yet known.

5. The nurse's role in stem cell transplantation:

Stem cell transplantation needs to highly qualified nursing team, the nurses' efficient practices influence on the quality of care and the safety of patients, especially in very ill patients. Their care in transplant process introduced to donors, and recipients; and classified into three phases:

Pre-transplant phase; within this phase the nurses play an important role in the informed consent process, supporting the medical staff's explanations; nurses should assess; 1). Patient's current fears and concerns; 2). Barriers to learning; 3). Nutrition assessment; 4). Understanding of the complete transplant procedure and needed time; 5). Existing complications symptoms from previous therapies or disease; 6). Present coping ability; 7). Current pain; 8). The need for blood/ its product transfusion; and 9). Type of appropriate anesthesia for transplant [7, 32].

Teaching the patients about: The nurse assists the patient with his/her decision by explaining 1. The procedure extent time, mobilization, and transplant process; 2. Role of the caregiver; 3. Care coordination; 4. Confirm family/Friend plan for caregiving; 5; Contact referring physician's office to obtain report; 6. Confirm financial clearance; 7. Confirm housing plan [7, 33, 34, 35, and 36].

Carrying out the medical care plan; by maintaining operational information of planned transplant strategy for the patient [7, 33, 34, 35, and 36]**.**

Pre-transplant investigations for donors are; renal function tests; Electrocardiogram; hepatic function tests; complete blood count; chest X-ray and lung function tests; clotting factors, including thrombin and prothrombin; infection and antibody screen; viral hepatitis screen; disease stages status; bone marrow aspiration biopsy; biochemistry; tissue typing and blood grouping and cross-matching [7,33,34, 35,36].

Donors preparation; before blood collecting from suitable donor; they called the ―forgotten patients‖ of transplant the donor undergoing some investigations as CBC-complete blood count, CMP-comprehensive metabolic panel, pregnancy test (if females), bleeding times, ABO blood type and infectious disease tests — human immunodeficiency virus (HIV), cytomegalovirus (CMV), toxoplasmosis, hepatitis, Epstein-Barr virus (EBV), herpes, HTLV I/II, varicella, and syphilis. Furthermore, the donor should take over a 4-day course of Granulocyte-colony stimulating factor (GCSF); which are glycoproteins to stimulate the multiplying of white blood cell [37]. The course of Granulocyte-colony stimulating factor (GCSF) side effect is a minor bone pain as result of the excessive stem cell crowding with newly produced cell [7].

Transplant phase; Once a patient has met initial screening and ready to undergo HCT at a particular center, the nurse's main responsibility recognizes the details of the effective evaluation Figure1[24]. The organization and time need for care during transplant phase are especially critical if the patient has an unrelated donor. The duration of infusion depends up on the type of stem cell transplant. Otherwise, engraftment of the stem cells can take between 14 and 25 days, depending on the type of stem cells used. Early engraftment high risk of infection so it important that; skilled nursing assess, prevent, detect and treat infections. Any delay in infection diagnosing may lead to increased vulnerability to a wide-ranging of potentially life-threatening organisms [35].

The circulating blood has many immature hematopoietic stem cells; that is like to those in the bone marrows are harvested by apheresis from a possible donor. The apheresis process usually takes for 4–6 hours, depending on the donors' total blood volume Figure2,3[25,30]. After that, the collected stem cell is administered intravenously to the recipient patient. The infused hematopoietic stem cells travel from patient peripheral circulation into the recipient's bone marrow, a process recognized as stem cell homing. This permits the bone marrow to get well, multiply and remain to make healthy blood cells [30, 19].

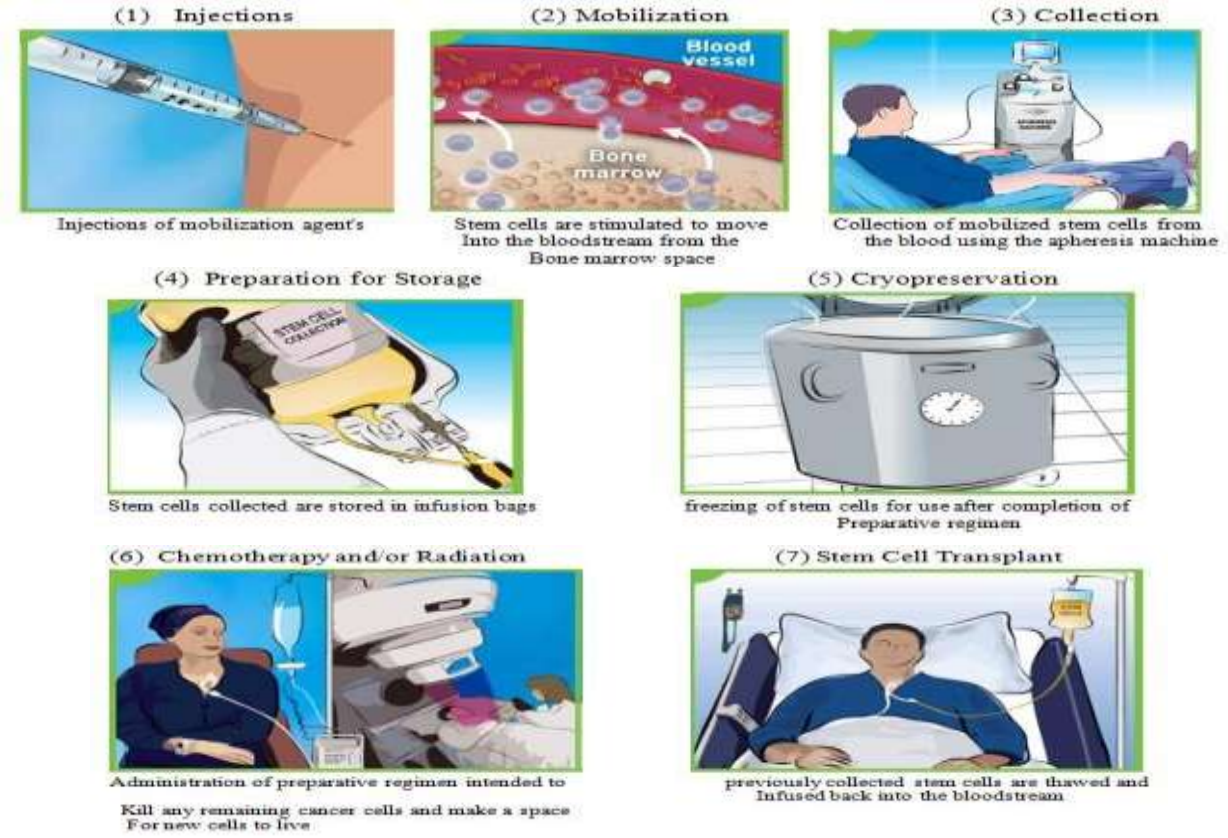

Figure No 1. The stem cell transplant process [24]

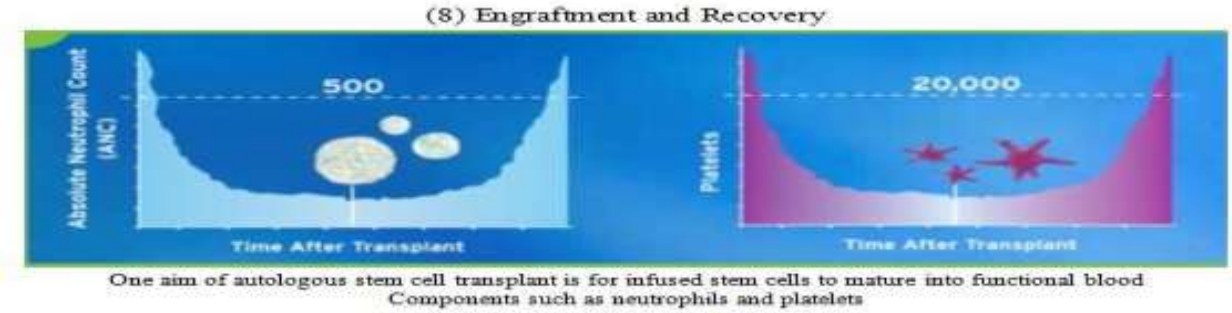

Figure No 2: Apheresis collection [25]

Figure No 3: Example of an apheresis machine [30]

Post-transplant phase; to prevent the infection which leads to the graft failure the nurses should apply protective isolation in most transplant centers, for four to six weeks after transplant; check vital signs; and peripheral oxygen saturation every four hours; the best important sign of infection is elevation in body temperature; additional nurses should observe other signs of chills, rigors. Nurses should daily assessment of any signs of infection in the patient's central venous catheter [7, 19].

In addition, nurses should inquire about and patients' rooms with high efficiency particulate air-filtration systems. This system filters the air, reducing microbes and spores entering the room, avoid visiting, not allowed plants and flowers in the patient's room because of the infection risk; patients wear a mask to decrease the possibility of inhaling aspergillus spores; all staff and visitors must wash their hands and wear a plastic apron before entering the patient's room to reduce the risk of cross-infection [12].

The patient should be well hydrated and intravenous fluids. An accurate fluid chart balance for intake and output chart should be performed. As a result of administration of certain drugs, electrolytes should be monitored. The nurse educates the patient about personal hygiene It is important as frequent proper hand washing, daily shower using disposable, use an individual towel, short clean figure nails, maintain skin clean and dry, oral care and dental checkup are an important part of infection control in transplant patients [7].

Patient pain if present might be managed by medications according to its severity. The patient should have sufficient nutrients. If the patient is not capable to eat, nutritional support may be administered by parenteral nutrition or by enteral feeding using a nasogastric tube [15]. That patient needs to psychological support by spending time with the patient and offering him or her opportunity to talk about anxieties; the nurse's providing information, education and guidance may reduce the undesirable psychological effects of isolation [23].

Discharge checklist for patients after stem cell transplantation:

The nurse should instruct patients about the following:

- Avoid contact with people who have respiratory illnesses.
- Care should be taken when around schoolchildren as there is a risk of exposure to sick children.
- Stop smoking and avoid smoky areas for the first few months following transplantation.
- Avoid public swimming pools in the early weeks of discharge.
- Avoid house cleaning, which will disturb dust.
- Avoid travel for the first six to 12 months. When considering travel, patients should seek advice regarding travel vaccinations, particularly if they are live vaccines.
- It is essential that patients continue to take their medication and attend all follow-up outpatient appointments [7].

6. Complications of HSCT:

HSCT lead to high mortality rate of 38% or higher in the recipient, so its use limits to avoid life-threatening. The most common complications are venous-occlusive disease, mucositis, infections (sepsis), graft-versus-host disease and the development of new malignancies [7].

7. Future of stem cell transplant in Egypt:

Improvement in cure rate than standard approaches, which will become suitable for many older patients with hematological conditions and cancer. Enhanced transplantation procedures across different types of human leukocyte antigen (HLA), minimize and control the complications of transplant. More public awareness about stem cell transplant for increased availability of umbilicus stem cell donor. Activation of nursing care protocol in stem cell process, educational nursing program and establishment of the nursing committee through Ministry of Health and Population**.**

Conclusion

Stem cells are the body's master cells which have the ability to grow into any one of the body's more than 200 cell types. There are different sources of stem cells; as

embryonic stem cells, harvested from umbilical cord blood, another source is adult or mesenchymal stem cells are present in bone marrow, blood, blood vessels, skeletal muscles, skin and the liver. Stem cell transplantation needs to the highly qualified nursing team, their care continuing within phases of transplant for both donors and patients.

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