Comorbidity Index in Predicting Toxicity and Mortality Risk among patient Undergoing Hematopoietic Stem Cell Transplantation

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Abstract

Abstract: Despite current improvement in supportive care, mortality after hematopoietic stem cell transplantation remains high. Caring for patients undergoing hematopoietic stem cell transplantation is one of the most challenging in nursing subspecialities. **Aim:** Assess comorbidity index in predicting toxicity and mortality risk among patient undergoing hematopoietic stem cell transplantation through: assess comorbidities of patient's pre-hematopoietic stem cell transplantation, assess toxicity and mortality risk post hematopoietic stem cell transplantation & assess the relation of pre-transplantation comorbidity scores and post transplantation-related toxicity and mortality in patients undergoing hematopoietic stem cell Transplantation. **Study design:** A descriptive retrospective design was utilized to conduct this study. **Subject:** A purposive sample of (44) patients undergoing allogeneic hematopoietic stem cell transplantation was recruited in this study. **Setting**: This study conducted at The Bone Marrow Transplantation Unit in Nasser institute for research and treatment. **Tools:** Tool I. Patient structured interview questionnaire, Tools II. The hematopoietic stem cell transplantation specific-comorbidity index (HCT-CI) & Tools III Seattle Criteria for Organ Toxicity after Bone Marrow Transplantation. **Results:** The study revealed that there was a positive correlation between comorbidity, organ toxicity and total mortality post bone marrow transplantation with p value 0.01. **Conclusion:** Comorbidity index is an important tool to predict toxicity and mortality rate among patient undergoing hematopoietic stem cell transplantation as there was a positive correlation between patient's comorbidity (obesity, cerebrovascular disease, cardiac disease, infection, renal disease, prior malignancy, hepatic disease and psychiatric disorder) and total toxicity and mortality post bone marrow transplantation. **Recommendations:** Apply Comorbidity Index in predicting toxicity and mortality risk among patient undergoing Hematopoietic Stem Cell Transplantation.

Key words: Comorbidity Index, Hematopoietic Stem Cell Transplantation

Introduction

Malignant diseases are becoming increasingly common in the population possibly because of enhanced life expectancy. Among various malignancies, acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) account for most hematological malignancies in elderly patients **(Chien, et al., 2021).**

Hematopoietic cell transplant (HCT) provides a potentially life-prolonging or curative option for many patients with hematologic malignancies, and with greater experience and improved supportive care, physicians are increasingly referring older adults for this procedure. The Center for International Blood and Marrow Transplant Research has recorded a significant increase in the number of older adults undergoing autologous (auto-HCT) or allogeneic transplant **(Rodrigues, 2020).**

Candidates for allogeneic hematopoietic stem cell transplantation (HSCT) are evaluated along two axes: risk for relapse and for non-relapse mortality (NRM). Systems standardizing the various features of transplantation, such as categories of conditioning intensity, disease risk, comorbidity burden, serve as tools for both analysis and clinical decision making **(Fein, et al., 2018).**

Individual comorbidities have distinct contributions to non-relapse mortality (NRM) following allogeneic hematopoietic cell transplantation (allo-HCT). the Simplified Comorbidity Index, are highly predictive of non-relapse mortality (NRM) (**Shouval et al., 2021).**

The role of comorbidity in transplantation was codified by **Sorror et al. (2005)** with the introduction of the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) over a decade ago. As the past 15 years have seen meaningful changes in transplantation practice, supportive care and overall outcomes, so, this thesis was done to evaluate whether the impact of individual comorbidities composing the score, as well as others, had evolved alongside. Furthermore, given the differing mechanisms and toxicity profiles of the conditioning agents **(Fein, et al., 2018).**

Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI) has been validated in both prospective and retrospective studies and is therefore the score most frequently used in everyday practice **(Carré, et al., 2020).**

The nurse plays an important role for patients undergoing hematopoietic stem cell transplantation (HSCT). Nursing responsibilities of patient undergoing HSCT include assessment, teaching, care coordination, and carrying out the medical care plan at each phase **(Thakar, et al., 2019).**

Aim of the study:

The study was conducted to fulfill the following aim: Assess comorbidity index in predicting toxicity and mortality risk among patient undergoing hematopoietic stem cell transplantation through:

1. Assess comorbidities of patient's pre-hematopoietic stem cell transplantation.
2. Assess toxicity and mortality risk post hematopoietic stem cell transplantation.
3. Assess the relation of pre-transplantation comorbidity scores and post transplantation-related toxicity and mortality in patients undergoing hematopoietic stem cell Transplantation.

Research questions:

Does the comorbidity index predict toxicity and mortality risk among patient undergoing hematopoietic stem cell transplantation?

Subject and Methods

Research Design:

A descriptive retrospective design was utilized to conduct this study.

Subject: A purposive sample of (44) patients undergoing allogeneic hematopoietic stem cell transplantation was recruited in this study. The sample was calculated by power and sample size calculation Pass II program and assuming AUC (Area under curve) for hematopoietic stem cell transplantation specific-comorbidity index (HCT-CI) Score for prediction of toxicity = 0.80, 50% of patients suffered from toxicity, and the ratio of 201 patients who admitted to The Bone Marrow Transplantation Unit in Nasser institute for research and treatment at 2019. According to the statistical department which affiliated to the setting with the following criteria, the required sample size of 44 patients was needed, setting power at 80% and alpha-error at 0.05.

Inclusion criteria

1. An adult patient over 18 years old, from both genders.
2. Patients who undergoing first allogeneic hematopoietic stem cell transplantation for a nonmalignant or malignant origin.
3. Patients who have single or multiple organ comorbidities

Setting: This study conducted at The Bone Marrow Transplantation Unit in Nasser institute for research and treatment.

Tools applied:

Data were extracted from the medical records as well as laboratory values at the time of transplant. They were retrospectively analyzed. The data were collected through the following three tools:

I. Patient structured interview questionnaire:

This tool was developed by the researcher based on review of relevant recent related literature **(Asslan et al., 2019, Zawam, Salama, Alsirafy, Bishr, 2019, Sorror et al., 2015, Chemnitz et al., 2014)** and it includes three parts:

- Part 1: It includes demographic characteristics of patient's personal data as (age, gender, level of education, occupation, residence).
- Part 2: It used to assess patient medical data pre hematopoietic stem cell transplantation, that included patient diagnosis, date of admission, date of transplantation, stem cell source, HLA typing, type of conditioning regimen, baseline

vital signs such as (blood pressure, heart rate, respiratory rate and temperature), and investigations of pre transplantation period.

- Part 3: It includes Patient clinical data post hematopoietic cell transplantation (physiological parameter and investigation of post transplantation period).

II. The hematopoietic stem cell transplantation specific-comorbidity index (HCT-CI):

This tool hematopoietic cell transplantation-specific comorbidity index (HCT-CI) was adopted from **(Sorror, 2005)**. It tool used to assess pre-allogenic transplantation comorbidities and to predict probability of post-transplant mortality. The index has been shown sensitively capture the prevalence and magnitude of severity of various organ impairments before HCT and to provide valuable prognostic information for both overall survival (OS) and non-relapse mortality (NRM) after hematopoietic stem cell transplantation thereby representing a helpful instrument in patient counseling.

The HCT-CI consists of different categories of organ dysfunction includes cardiac, bowel disease, diabetes, cerebrovascular disease, psychiatric disturbance, hepatic, renal, obesity, infection, rheumatologic, peptic ulcer, pulmonary and prior malignancy.

Scoring system:

Hematopoietic cell transplantation-specific comorbidity index (HCT-CI) classifies patients into three risk groups: A score of 0 indicates low risk, a score of 1-2 degree indicates intermediate risk and any score ≥3 indicates a high risk.

III. Seattle Criteria for Organ Toxicity after Bone Marrow Transplantation

This tool was adopted from **(Bearman, 1988),** used to assess the toxicity grading of eight organs post bone marrow transplantation. It includes (heart, bladder, kidneys, lungs, liver, mucosa, central nervous system, and gut).

Scoring system:

Each organ dysfunction was assessed by the researcher according a set of criteria for being low or high toxicity. It was graded using an empirically designed system to assess toxicity in eight organs which assigns of 0 to 4 grades for each of eight organ system. Toxicity was assessed and graded on days 0, 7, 14 post transplantation, it was categorized as low if total sum of toxicity grades for eight organ systems was 0 up to 2 and high if the total sum was greater than 2.

Validity and reliability: Testing validity of the research tools were reviewed by a panel of experts; from critical care nursing staff at faculty of nursing -Ain Shams University to ascertain that the tools face and content matching with the research aim. No modifications were done. Testing reliability of proposed tools was done statistically by alpha Cronbach test for the following:

- Structured interview questionnaire = 0.812 good reliability.

Pilot study: A pilot study was conducted on 10% of total study subjects (4 patients) in order to test applicability of tools and clarity of designed questionnaire. Patients who participated in the pilot study were included in the main study subject; no modifications were done.

Protection of Human Rights: Ethical approval was obtained from Scientific Ethical Committee of the faculty of nursing of Ain Shams University before starting the study. Approval was obtained from the director of the hematopoietic stem cell transplantation unit in Nasser Institute for research and treatment for chart reviews medical records as well as laboratory values at the time of transplant and post transplantation.; the data is anonymous, and used for research purposes only.

Field work:

Assessment phase:

Extensive reviewing of recent related literature and theoretical knowledge of various aspects of the study using books, articles, internet, periodicals and magazines was done to develop data collection tools.

Implementation phase:

Data collection for the studied patients with hematopoietic stem cell transplantation started from January to December 2021. The researcher visited the study setting 2 days each week during Monday and Tuesday from 8.5 am to 2 pm. Data collection done by reviewing patients' files and charts from Nasser institute data center.

The tools for data collection were filled in by the researcher. The patients' files were screened for eligibility. The patient's name, age, sex, diagnosis, length of stay, date of diagnosis, type of conditioning regimen, stem cell source, lab investigations, the presence of comorbidities and

vital signs were all obtained from the file which took 15-20 minutes for every patient.

The pre-transplantation assessment of comorbidity was done according to the criteria of the HCT-CI, clinical data collected by screening the medical records as well as all laboratory values and relevant investigations that were performed within the routine workup for transplant. Comorbidities of each patient were scored according to the HCT-CI scoring system on the worksheet took 20-30 minutes to fill the index for every individual patient. The final score obtained for each patient was then correlated with the post transplantation assessment of toxicities captured by Seattle Criteria toxicity scoring system that were assessed at day 0, 7 and 14 from transplantation which took 20-30 minutes to be filled for each patient.

Statistical analysis: The collected data were organized, tabulated, analyzed and presented in number, percentage, tables and figures as required using appropriate statistical tests to test significant of the result. The data were collected and coded. Then, presented using descriptive statistics in the form of frequencies and percentages for qualitative variables, and mean and standard deviation for quantitative variables. The statistical analysis was done using Logistic regression mode, Multiple Linear regression model, Correlation.

Results

Table 1 showed that the mean age of the studied patients was **39.09±5.46.** 61.4 % were males.

Table 2 presented that 45.5 of the studied patients had acute myeloid leukemia. 50 % of the studied patients had the disease more than 12 months ago. 52.3% of the studied patients had advanced phase of disease. 81.8 % of them received stem cells from peripheral blood, 100% of the studied patients had HLA type from Matched related donor. 77.3 had Myeloablative conditioning regimen and 79.5 stayed in hospital more than 35 days.

As for body mass index, **Table (3)** illustrated that, 45.5 % of the studied patient's height ranged from 160 – 170 cm and 43.2 % weighted 90 - 110 kg. The calculated body mass index was 29.5% for obesity grade II and grade III of the studied patients.

Regarding comorbidity index of the studied patients, **Table 4** showed that that 43.2% and 43.2% of the studied patients had a comorbidity of mild hepatic disorder and obesity respectively. And 27.3%, 11.4% and 9.1% of the studied patients had suspected or proven infection requiring treatment, diabetes, cardiac comorbidity respectively.

Figure 1 showed that, 47.7 % of the studied patients had an Intermediate toxicity and mortality risk (Non relapse mortality 21%).

Table (5) reflected that 13.6 %, 18.2%, 15.9% of patients suffered from hepatic toxicity grade 1 in day 0, day 7 and day 14 respectively. 36.4 % and 27.3 % of patients suffered from stomatitis in day 7 grade II and grade 1 respectively. 18.2 % suffered from GIT toxicity grade 1 in day 7 and 18.2 % in day 14. 18.2% of patients suffered from pulmonary toxicity in day 14. 13.6% suffered from stomatitis grade III in day 14.

Regarding the total organ toxicity for the studied patients **Figure (2)** showed that 84 % of the studied patients had a high toxicity score.

By testing mortality rate for patients with Hematopoietic stem cell transplantation, **Figure (3)** shows that 9.1 % of the studied patients died post bone marrow transplantation.

Table (6) shows statistically significant correlation between mortality and obesity, cerebrovascular disease, cardiac disease, infection, renal disease, prior malignancy, hepatic disease and psychiatric disorder with odd ratio 11.42, 10.33, 7.85, 5.75, 3.95, 3.92, 2.40, 2.10 respectively at p value <0.05.

Table (7) stated high significant through F test value was 14.887 with p value 0.000**. Total toxicity score, Phases of underlying disease (Advanced), type of conditioning regimen and BMI had high frequency positive effect on HCT-CI score at p value <0.01**. While Length of stay >21 days and age had slight positive effect on HCT-CI score with p value <0.05.

Table (8) showed a highly significance correlation between comorbidity and Cardiac toxicity, Renal toxicity, Hepatic toxicity, CNS toxicity, Stomatitis and GI toxicity at p <0.01**. and also has a slight significance correlation with Bladder toxicity, Pulmonary toxicity at p <0.01* post bone marrow transplantation.

Table (9) showed that there is a positive Correlation between comorbidity and total mortality post bone marrow transplantation with p value 0.01**. Also, there is a positive correlation between total organ toxicity and total mortality post bone marrow transplantation with p value 0.01**.

Table (1): Distribution of the studied patients according to their demographic characteristics (n=44)

Demographic characteristics	N	%
Age (years)		
20-<40	25	56.8
40-<60	17	38.6
≥ 60	2	4.6
Mean± SD 39.09±5.46		
Sex		
Male	27	61.4
Female	17	38.6

Table (2): Distribution of the studied patients according to their clinical data (n=44)

Clinical data	N	%
Patient diagnosis		
AML	20	45.5
ALL	15	34.1
SAA	2	4.5
MF	3	6.8
Mastocytosis	1	2.3
MPAL	1	2.3
MDS	2	4.5
Duration		
1 - <6 months	4	9.1
6 – <12 months	18	40.9
≥12 months	22	50
Phases of underlying disease		
Early	21	47.7
Advanced	23	52.3
Stem cell source		
Bone marrow	8	18.2
Peripheral blood	36	81.8
Umbilical cord blood	0	0
HLA type		
Matched related donor.	44	100
Matched un-related donor.	0	0
Haploidentical.	0	0
Type of conditioning regimen		
Myeloablative.	34	77.3
Non-Myeloablative.	0	0
Reduced Intensity Conditioning	10	22.7
Length of stay		
≤ 21 days	9	20.5
>21 days	35	79.5

Table (3): Distribution of the studied patients according to their anthropometric measures (n=44)

Items	N	%
Patients' height:		
150 - <160	9	20.4
160 - 170	20	45.5
>170	15	34.1
Patients' weight:		
70 - <90	8	18.2
90 - 110	19	43.2
>110	17	38.6
BMI		
Normal	12	27.3
Overweight	11	25
Obesity grade I	8	18.2
Obesity grade II	7	15.9
Obesity grade III	6	13.6

Table (4): Distribution of the studied patients according to their Hematopoietic cell transplantation comorbidity index (HCT-CI) (n=44)

Comorbidities	N	%
Cardiac		
Atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias requiring treatment	**2**	4.5
Coronary artery disease requiring treatment, congestive heart failure, myocardial infarction, or EF of ≤ 50%	**2**	4.5
Heart valve disease: except asymptomatic mitral valve prolapse	**4**	9.1
Bowel disease		
Crohn's disease or ulcerative colitis requiring treatment	**0**	0
Diabetes		
Requiring treatment with insulin or oral hypoglycemic, but not controlled with diet alone	**5**	11.4
Cerebrovascular disease		
Transient ischemic attacks or cerebrovascular accident	**2**	4.5
Psychiatric disturbance		
Depression/anxiety requiring psychiatric consult or treatment	**3**	6.8
Hepatic		
Mild	**19**	43.2
Moderate to severe	**1**	2.3
Renal		
Moderate to severe	**3**	6.8
Obesity		
Patients with a BMI of >35 for adults	**19**	43.2
Infection		
Suspected or proven infection requiring treatment	**12**	27.3
Rheumatologic		
Rheumatologic disorder requiring treatment at any time	**0**	0
Peptic ulcer		
Requiring treatment	**0**	0
Pulmonary		
Moderate	**2**	4.5
Severe	**0**	0
Prior malignancy		
Treated at any time point in the patient's history, excluding non - melanoma skin cancer. Exclude malignancies of same lineage as current malignancy requiring transplant	**3**	6.8

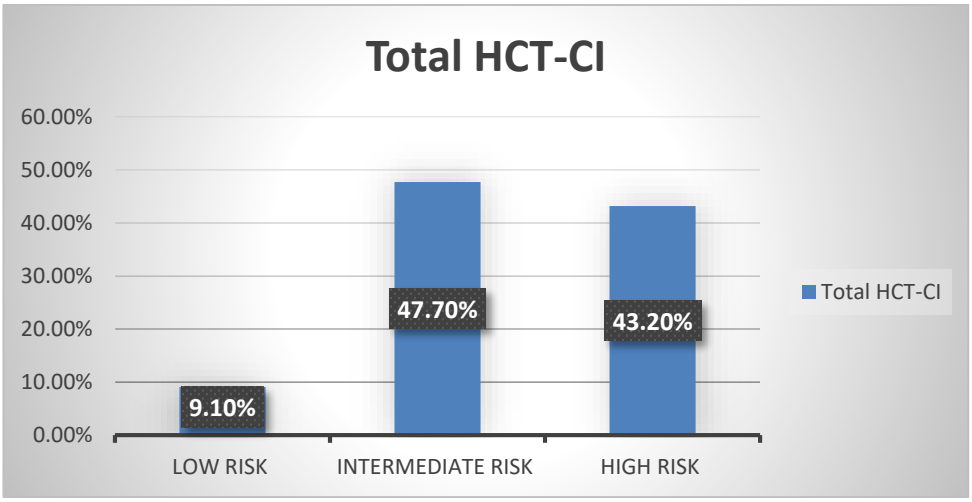

Figure (1): Percentage distribution of the studied patients according to their total Hematopoietic cell transplantation comorbidity index (HCT-CI) (n=44).

Table (5): Distribution of the studied patients according to their organ toxicity post bone marrow transplantation (n=44)

Comorbidities	Day 0		Day 7		Day 14	
	N	%	N	%	N	%
Cardiac						
Grade I	0	0	2	4.5	0	0
Grade II	0	0	0	0	3	6.8
Grade III	0	0	0	0	0	0
Bladder toxicity						
Grade I	0	0	1	2.3	0	0
Grade II	0	0	0	0	0	0
Grade III	0	0	0	0	0	0
Renal toxicity						
Grade I	1	2.3	4	9.1	2	4.5
Grade II	0	0	0	0	0	0
Grade III	0	0	0	0	0	0
Pulmonary toxicity						
Grade I	2	4.5	5	11.4	8	18.2
Grade II	0	0	0	0	0	0
Grade III	0	0	0	0	0	0
Hepatic toxicity						
Grade I	6	13.6	8	18.2	7	15.9
Grade II	0	0	2	4.5	2	4.5
Grade III	0	0	0	0	0	0
CNS toxicity						
Grade I	1	2.3	2	4.5	2	4.5
Grade II	0	0	1	2.3	0	0
Grade III	0	0	0	0	1	2.3
Stomatitis						
Grade I	1	2.3	12	27.3	0	0
Grade II	0	0	16	36.4	4	9.1
Grade III	0	0	2	4.5	6	13.6
GI toxicity						
Grade I	3	6.8	8	18.2	8	18.2
Grade II	0	0	2	4.5	1	2.3
Grade III	0	0	1	2.3	0	0

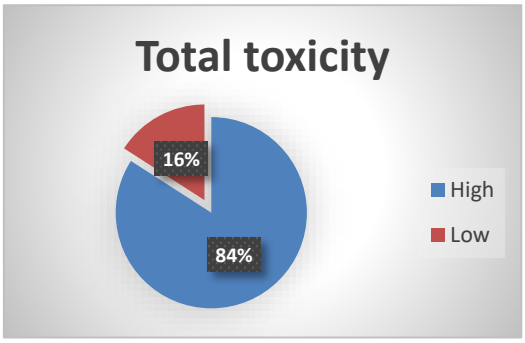

Figure (2): percentage distribution of the studied patients according to their total organ toxicity post bone marrow transplantation (n=44).

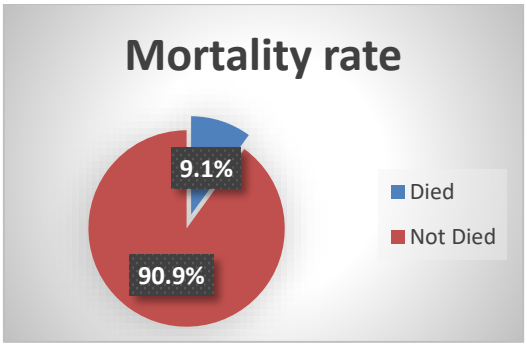

Figure (3): percentage distribution of the studied patients according to their mortality rate post bone marrow transplantation (n=44).

Table (6): Relation between Predisposing risk factors for HCT-CI and mortality rate among study patients (n=44)

Predisposing risk factors	Odds Ratio	(95% Confidence Interval)		P. value
		lower	upper	
Cardiac disease	**7.85**	4.2	9.12	**.000****
Cerebrovascular disease	**10.33**	3.6	12.08	**.000****
Prior malignancy	3.92	1.12	6.24	**.003****
Hepatic disease	2.40	1.99	6.700	**.005****
Infection	**5.57**	1.35	7.58	**.000****
Psychiatric disorder	2.10	1.03	3.809	**.007****
Renal disease	3.95	1.23	4.71	**.031***
Obesity	**11.42**	4.82	13.09	**.000****

Table (7): Relation between HCT-CI score and mast related items

	Unstandardized Coefficients		standardized Coefficients	T	P. value
	B		Beta		
• **Length of stay >21 days**	.217		.153	2.706	**.022***
• **Advanced disease**	.345		.267	6.557	**.002****
• **BMI**	.477		.401	9.510	**.000****
• **Type of conditioning regimen**	.319		.278	5.908	**.005****
• **Age**	.241		.198	2.968	**.034***
ANOVA					
Model	**R2**		**F**	**P. value**	
Regression	0.49		14.887	**.000****	

Table (8): Correlation between hematopoietic cell transplantation comorbidity index HCT-CI and organ toxicity post bone marrow transplantation

Organ toxicity post bone marrow transplantation	Hematopoietic cell transplantation comorbidity index (HCT-CI)
Cardiac	r. 0.799 p <0.01******
Bladder toxicity	r. 0.211 p <0.05*
Renal toxicity	r. 0.631 p <0.01******
Pulmonary toxicity	r. 0.226 p <0.05*
Hepatic toxicity	r. 0.701 p <0.01******
CNS toxicity	r. 0.522 p <0.01******
Stomatitis	r. 0.603 p <0.01******
GI toxicity	r. 0.499 p <0.01******

Table (9): Correlation between hematopoietic cell transplantation comorbidity index, total organ toxicity and total mortality after bone marrow transplantation

	Hematopoietic cell transplantation comorbidity index (HCT-CI)
Total organ toxicity	r. 0.599 p <0.01**
Total mortality	r. 0.610 p <0.01**

Discussion

Concerning demographic characteristics of the studied patients, the result revealed that; about more than half of studied patients' age was range from (20 - 40) years with mean age 39.09±5.46.

This finding was in agreement with **El Afifi et al. (2016)** in their study entitled "Effect of comorbidities on hematopoietic stem cell transplantation outcome in adult patients with different hematologic diseases: a single-center experience in Egypt" who studied the same range of age group (median age of 27 years), also these finding supported by **Törlén (2017)** "Impact of Pre-transplantation Indices in Hematopoietic Stem Cell Transplantation: Knowledge of Center-Specific Outcome Data Is Pivotal before Making Index-Based Decisions" with median age 49 years old.

On the other hand, this finding was incongruent with the study done by **Carre et al. (2019)** titled about "Role of Age and Hematopoietic Cell Transplantation-Specific Comorbidity Index in Myelodysplastic Patients Undergoing an Allotransplant: A Retrospective Study from the Chronic Malignancies Working Party of the European Group for Blood and Marrow Transplantation" found that nearly one third of of 1245 patients had median age 59 years at transplantation.

Regarding gender, the study result revealed that more than half of the studied patients were males. This result supported by **Carre et al. (2019)** who found that more than half of the studied patients were males.

Regarding diagnosis the present study revealed that more than two fifth of the studied patients had acute myeloid leukemia (AML) This is certainly because it is the commonest type of leukemia in adults and the 6th highest cause of cancer-related death in males worldwide. This result supported by **Passweg et al. (2019)** in their study titled "The EBMT activity survey report 2017: a focus on allogeneic HCT for nonmalignant indications and on the use of non-HCT cell therapies" who found that about half of candidates had AML.

These results are inconsistent with **Berro et al. (2017)** who found in the study titled "Hematopoietic Cell Transplantation–Specific Comorbidity Index Predicts Morbidity and Mortality in Autologous Stem Cell Transplantation" that about half of the studied sample had Multiple myeloma.

Regarding the duration of the underlying disease, half of the studied patients were diagnosed before the procedure of HSCT for more than 12 months. This duration may be consumed in the management trials of therapy other than HSCT or trial to achieve complete remission before proceeding to the procedure. this result is consistent with **Halaburda et al. (2020)** who found that time from diagnosis to transplantation were 17 months. And on the other hand, this result was incongruent with **Salvatore et al. (2018)** who found in their study that Interval from diagnosis to allo-HSCT was 5 months ranged from 1-18 months.

Regarding phase of the underlying disease, the present study revealed that more than half of the studied patient had an advanced phase of disease which is related with poor overall survival. This is because the present study includes patients with comorbidities that influence the general patient status and delay the decision of transplantation. These data are in the same line with **Törlén et al. (2017)** who found that more than half of the studied patients were in the second complete remission.

Regarding the source of stem cells, the current study stated that the majority of the studied sample received peripheral blood stem cells. This may be due to that PBSCs are more easily and comfortable, without a general anesthetic. These data came in the same line

with **Belete et al. (2017)** who found that nearly all included patients (97%) receive peripheral blood stem cells.

Regarding HLA type, the current study presented that all study sample receive stem cells from matched related donor. This is because the policy of the institution where the study performed stated that all patients undergoing BMT should have matched related donor before performing any transplantation related procedures.

Regarding Type of conditioning regimen, the current study presented that more than three quarters of the participated patients had a Myeloablative conditioning regimen. The new researches revealed that no specific or single conditioning intensity can be outlined to be followed in certain circumstances including comorbid receiver. This reading is consistent with **Halaburda et al. (2020)** in their study titled "Allogeneic stem cell transplantation in second complete remission for core binding factor acute myeloid leukemia: a study from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation" showing that more than two third of the participated patients received MAC. Also study for **Lussana et al. (2016)** where the majority (83.3%) of the sample had MAC. But this result is contradicted with **Østgård et al. (2018)** who found more than two third of the study received Non Myeloablative Conditioning regimen.

As regard to the length of stay (LOS), this study showed that more than three quarters of the study sample stayed at hospital for more than 21 days. This logic finding state the complexity of the management of patients who had chronic illness and undergoing a massive course of treatment including conditioning regimen with either type or phases of severe marrow ablation. These finding came in the same line with finding of **(Hershenfeld et al., 2020 who stated** the mean length of hospital stay was 33.6 days. Also, this finding congruent with finding by **Godara et al. (2021)** who found that the Median LOS was 25.8 days for allo-HSCT.

Regarding anthropometric data, it was found that about half of the studied patients height ranged 160 – 170 cm and more than two fifth of the studied patients weighted 90 – 110 kg. Near one third of the studied patients had obesity grade II and grade III which both considered a comorbidity. This high percentage reflect a great effect on post transplantation toxicity in this study. This result not similar with the result of **Zawam, et al., (2019)** who found that about two fifth of their study patients had a normal BMI.

Regarding comorbidities, hepatic and obesity were most commonly comorbidities within the studied patients. More than two fifth of the studied patients had mild Hepatic comorbidity. This high percentage of hepatic comorbidity is due to high prevalence of hepatitis C virus (HCV) which is the most common cause of liver cirrhosis in Egypt. 15% of the population is seropositive for Hepatitis C virus (HCV). The incidence rate of HCV is 2.4 per 1000 person-year. Similar results were reported in study by **El Afifi et al. (2016)** which was conducted at the Bone Marrow Transplantation Unit, Ain Shams University, that Hepatic comorbidity was the most common observed association in their study group. **Chemnitz et al., (2015)** also approved the high distribution of hepatic comorbidity in their study population.

The other comorbid with a high percentage were obesity which assumed more than two fifth of the studied patients. This is due to the prevalence and burden of obesity in Egyptian population, the estimated annual deaths due to obesity in 2020 was about 115 thousand (19.08% of the total estimated deaths). According to "100 million health" survey, which was conducted in Egypt in 2019 and screened 49.7 million adult Egyptians (≥18 years old), there was about two fifth (39.8%) of adult Egyptians suffered from obesity as stated by **Aboulghate et al. (2021).** The study by **Doney, et al., (2018)** came in contradictory with current study reading as obesity was represented only with ten percent of the total study group. This contradiction may be resulted from the differentiation in the society culture and life style.

Other comorbid also came on the top is a suspected or proven infection that consumed more than quarter of the studied patients. The common infections were HCV, CMV and rarely Toxoplasmosis. This reading came in the same line with study for **Miller et al., (2017)** who

found that two fifth of his study population had infection. This agreement is logically interpreted by the presence of low immunity state, so we can find that infectious diseases are a frequent complication in HSCT patients, resulting in a more prolonged hospitalization and increased morbidity, mortality, and cost.

Diabetes mellitus also took the fourth place on the distribution of comorbidity in pre hematopoietic bone marrow transplantation assessment accounting for more than 10% of studied subjects. It may be due to the prevalence of diabetes mellitus in Egyptian population which was about 16.6 % in 2011- the single year for which the data is available. This is divergent by **Chemnitz et al., (2015)** who reported that diabetes mellitus was infrequent and not associated with a significant impact on OS in their study.

Regarding the total comorbidity score, according to Hematopoietic cell transplantation comorbidity index (HCT-CI), near half of the studied patients had an Intermediate toxicity and mortality risk and more than two fifth had a high risk. This result is in an agreement with study titled "The Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) Predicts Outcomes in Patients with Acute Myeloid Leukemia and Myelodysplastic Syndromes Receiving CD34+ Selected Grafts for Allogeneic Hematopoietic Cell Transplantation" **by Barba et al., (2016)** who found that about one third of the studied patients (31%) had a score of 1-2 (intermediate risk) and near half (47%) had a score ≥ 3 (high risk). Also, **Chemnitz et al., (2014)** in their study titled "Pretransplant Comorbidities Maintain Their Impact on Allogeneic Stem Cell Transplantation Outcome 5 Years Posttransplant: A Retrospective Study in a Single German Institution" showed that about half of the study group had an intermediate toxicity and mortality risk.

On other hand a study by **Carre et al., (2020)** titled "Role of Age and Hematopoietic Cell Transplantation-Specific Comorbidity Index in Myelodysplastic Patients Undergoing an Allotransplant: A Retrospective Study from the Chronic Malignancies Working Party of the European Group for Blood and Marrow Transplantation" who found that more than two fifth of their study population had a low toxic mortality risk.

Regarding total organ toxicity post bone marrow transplantation, the current study showed that the majority (84 %) of the studied patients had a high toxicity score. This finding is logically matched with the HSCT-CI scores which predict the majority of the studied patient with either intermediate or at high risk of toxicity and mortality.

Conclusion

Comorbidity index is an important tool to predict toxicity and mortality rate among patient undergoing hematopoietic stem cell transplantation as there was a positive correlation between patient's comorbidity (obesity, cerebrovascular disease, cardiac disease, infection, renal disease, prior malignancy, hepatic disease and psychiatric disorder) and total toxicity and mortality post bone marrow transplantation.

Recommendation

- Further studies are recommended to assess Comorbidity Index in Predicting Toxicity and Mortality Risk among patient Undergoing Hematopoietic Stem Cell Transplantation
- Apply Comorbidity Index in predicting toxicity and mortality risk among patient undergoing Hematopoietic Stem Cell Transplantation.

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