

## Research Article

# Substantiation of Multinational Association for Supportive Care in Cancer (MASCC) Score in Risk Assessment of Febrile Neutropenic Patients in Hematological Disorders: A Regional Study from Pakistan

Qurratul Ain Rizvi<sup>1</sup>, Aisha Jamal<sup>1</sup>, Naveena Fatima<sup>2</sup>, Munira Borhany<sup>1</sup>, Uzma Zaidi<sup>1</sup>, Tahir Sultan Shamsi<sup>1,\*</sup>

<sup>1</sup>Department of Clinical Hematology & BMT, National Institute of Blood Disease & Bone Marrow Transplantation, Karachi, Pakistan.

<sup>2</sup>Department of Research & Development, National Institute of Blood Disease & Bone Marrow Transplantation, Karachi, Pakistan.

**Abstract: Background:** The incidence of neutropenia in hematological malignancies comprises of huge burden of febrile neutropenia. Multinational Association of Supportive Care in Cancer (MASCC) risk index score is the most widely used model for forecast of complications.

**Objective:** The aim of this study was to determine diagnostic accuracy of MASCC scoring system in febrile neutropenia patients suffering from hematological disorders.

**Materials & Methods:** Patients suffering from hematological disorders and presenting with febrile neutropenia were stratified into low and high risk groups according to MASCC score. The standard score range from 0 to 26 points; score of more than or equals to 21 were considered to be low risk and score of less than 21 was high-risk category. As an in-patient at National Institute of Blood Disease & Bone Marrow Transplantation, they were followed over the course of illness for development of any serious medical condition until resolution of febrile neutropenia.

**Results:** Of 217 patients, serious medical conditions were documented in (63%) of individuals among the high-risk group cohort and (13%) developed serious medical conditions in low-risk cohort. Major disease encountered was acute leukemia (69%). Hypotension 14 (22.2%) and hepatic failure 14 (22.2%) were among the two most common variables of established serious medical condition. The overall sensitivity and specificity of MASCC score was 69.8% and 81.8%, with the positive and negative predictive value of 61.1% and 86.8% respectively.

**Conclusion:** The score has been re-validated in this study and determined its significance in ascertainment of high-risk cohort among febrile neutropenic patients in the current era, thereby helping the physicians to tailor the management approach accordingly.

**Keywords:** MASCC, Febrile neutropenia, Leukemia, Hematological disorders, Cytotoxic chemotherapy.

## INTRODUCTION

Febrile episodes in neutropenic patients poses a serious threat to life, and requires prompt actions which include in-patient care, use of broad spectrum antibiotics, early recognition of possible complications and assessment of response to treatment [1]. Patients with Febrile Neutropenia (FN) comprises of diverse group of population with unequivocal risks of developing serious complications, response to antibiotics and therefore mortality. The incidence of neutropenia as a complication of chemotherapy given for hematological malignancies comprises of huge burden of febrile neutropenia. Cytotoxic chemotherapy, both in induction and consolidation phase have profound risk of neutropenia and therefore predisposition to all types of bacterial and fungal infection as time taken for counts recovery is prolonged. The incidence rate per cycle of chemotherapy is about 43% [2]. Increased rates are being observed in patients with major co-morbidities and documented sepsis or infection [3]. In addition to a mortality risk of 1-18%, FN is associated with descent in quality of life, delay in subsequent cycles of chemotherapy,

increment in financial burden. All these factors subsequently lead to a breach in treatment and thereby affecting the overall survival [4]. In addition to FN in hematological malignancies, the propensity to develop infection has posed one of the most fearsome challenges in the clinical management of patients undergoing hematopoietic cell transplantation from the earliest days. Infections remain a major cause of morbidity and mortality in patients undergoing Hematopoietic Stem Cell Transplantation (HSCT). Febrile neutropenia is documented in setting of bone marrow transplant, as patients receive immunoablative and myeloablative conditioning regimen [5, 6]. Therefore there is a need of risk stratification at presentation of patient with FN into low risk and high risk groups on the basis of various parameters that can predict the outcome. Low risk patients defined at initial presentation can be the candidate of oral antibiotic therapy [6, 7]. Various studies have been attempted previously to identify the risk factors and develop predictive models. The validated scoring systems that are being used to determine the risk of medical complications include the Talcott rules, the MASCC score, and the Clinical Index of Stable Febrile Neutropenia (CISNE) score. Currently, MASCC risk index score is the most widely used model for forecast of complications [8-18]. This scoring system has

\*Address correspondence to this author at the Department of Clinical Hematology & BMT, National Institute of Blood Disease & Bone Marrow Transplantation, Karachi, Pakistan.

Email: t.shamsi.62@gmail.com

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been assessed for risk stratification in various studies one of which have a positive predictive value of 93% with sensitivity 65% and specificity of 75% [3]. This study was conducted to determine the significance of MASCC score in our local population so that better prognostic groups can be assigned at the initial presentation of patients and individually tailored patient management approach can be implicated, thereby preventing both over and under treatment.

## MATERIALS AND METHODS

It was a cohort study. Data was collected from all patients suffering from hematological disorders and presenting with febrile neutropenia from Aug 2017 to Aug 2018. The ethics committee of our hospital approved this study (NIB-D/RD-183/29-2017) and consent was taken prior to the enrollment of candidate in study group. Patients developing FN as a complication of drug therapy / infections in beta thalassemia major, neonates, and those with immunodeficiency disorders were excluded from the study. Patients were stratified into low and high risk groups according to MASCC score [19]. The standard score range from 0 to 26 points with score of more than or equals to 21 were considered to be low risk and score of less than 21 were high-risk category. All patients were admitted to the inpatient facility and were managed according to Infectious Diseases Society of America (IDSA) guidelines of management of FN. They were followed for development of any serious medical condition until resolution of febrile neutropenia. FN was defined as a single oral temperature of 38.5°C or more or a temperature of 38.0°C or more that persists for 1 hour in presence of absolute neutrophil count (ANC) of less than 500 cells/mm<sup>3</sup> or a count of less than 1000 cells/mm<sup>3</sup> with a predicted decrease to less than 500 cells/mm<sup>3</sup> [3]. Serious medical complications (SMC) were the group of variables designated to determine the adverse clinical course. The presence of any one of them was to be considered significant. These variables include hypotension, respiratory / renal / hepatic failure, intensive care admission, altered mental status, congestive cardiac failure, and massive bleeding requiring transfusions. Resolution was considered when patient becomes afebrile, clinically stable, and recovery of ANC more than 500 cells/mm<sup>3</sup>. Outcome measures were, resolution of FN without SMC in low risk group (true negative), resolution of FN with SMC in low risk group (false negative), resolution of FN without SMC in high-risk group (false positive), resolution of FN with SMC in high-risk group (true positive). Data was recorded and analyzed by using Microsoft Excel 2010 and SPSS version 23. Frequencies and percentages were calculated for categorical variables, mean and standard deviation were computed for quantitative variables. Sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated by cross tabulation and Chi square test was applied to observe the association. P value ≤0.05 was considered significant.

## RESULTS

Table 1 describes the characteristics of patients. A total of 217 Febrile Neutropenic episodes in hematological disorder patients were studied. One hundred and ten (51%) cases were male and mean age was 38.3 ± 23.2 years. The major disease entity encountered was leukemia (both acute myeloid and lymphoblastic leukemia) constituting 149 cases (69%). Seventy-two (33%) patients were stratified as high risk according to scoring system variables.

**Table 1.** Baseline Characteristics of Patients (n=217).

Characteristics	Frequency (%)
<b>Gender</b>	
Male	110(51)
Female	107(49)
<b>Age (in years)#</b>	
>18	47.9±18.2
<18	8.6±4.7
<b>Risk Groups</b>	
Low Risk	145(67)
High Risk	72(33)
<b>Primary Disease</b>	
Aplastic anemia	11(5)
Acute Lymphoblastic Leukemia	68(31)
Acute Myeloid Leukemia	81(37)
Hodgkin Lymphoma (HL)	9(4)
Non Hodgkin Lymphoma (NHL)	12(6)
Multiple Myeloma	10(5)
Post Bone Marrow Transplant	26(12)
<b>Serious Medical Complications (SMC)</b>	
With SMC	63(29)
Without SMC	154(71)

#: age is presented as mean ± standard deviation.

The associations of age, gender and primary disease with risk groups presented in Table 2. Age was found to be associated with high-risk score (p=0.004) while gender stratification with risk groups was not found statistically significant (p=0.666). Significant population in high-risk cohort was found to be suffering from acute myeloid leukemia (p=0.032). SMC were majorly seen in high-risk category than low risk category and it was found to be statistically significant (p<0.001). A comparison with previous studies in terms of sensitivity and specificity is given in Table 3.

Hypotension 14(22.2%) and hepatic failure 14(22.2%) were found to be the most common SMC in patients Fig. (1).The

overall sensitivity and specificity of MASCC score was found to be 69.8% and 81.8% respectively, along with positive and negative predictive value of 61.1% and 86.8% respectively.

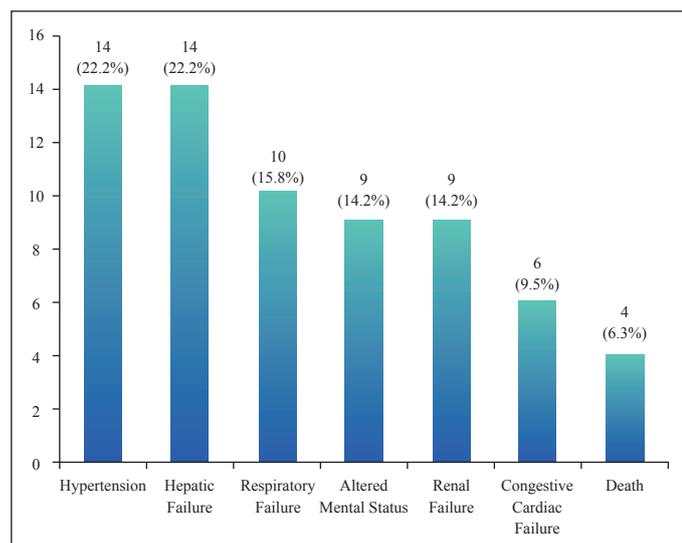
**Table. 2.** Association of Age, Gender, Disease, and SMC with Risk Groups (n=217).

Stratified Variables	Risk Groups		P-Value
	Low	High	
	(≥21)	(<21)	
	n(%)	n(%)	
<b>Age</b>			
< 18 years	44 (30)	9 (13)	**0.004
>18 years	101(70)	63(88)	
<b>Gender</b>			
Male	75(52)	35(49)	0.666
Female	70 (48)	37(51)	
<b>Primary Disease</b>			
Aplastic Anemia	6 (4)	5 (7)	*0.032
Acute Lymphoblastic Leukemia	44 (30)	24(33)	
Acute Myeloid Leukemia	50 (35)	31(43)	
Lymphoma	13 (9)	8(11)	
Multiple Myeloma	7 (5)	3(4)	
Post Bone Marrow Transplant	25 (17)	1(2)	
<b>Serious Medical Complications (SMC)</b>			
With SMC	18 (13)	45(63)	**<0.001
Without SMC	127 (87)	27 (37)	

\*p-value significant at ≤0.05, \*\*p-value significant at p<0.01.

**Table. 3.** Comparison of Sensitivity and Specificity of MASCC Score with Previous Studies.

Author and Year	Sensitivity (%)	Specificity (%)
Klastersky <i>et al.</i> 2000 [19]	71	68
Taj <i>et al.</i> 2017 [20]	65	75
Current study, 2019	69.8	81.8



**Fig. (1).** Frequency of Serious Medical Complications (n=63).

## DISCUSSION

MASCC risk index score is implicated widely as a model for risk stratification of patients presenting with febrile neutropenia. Various studies have been undertaken to determine its significance in prediction of complications. The original validation of MASCC score was done in year 2000 and it identified low- risk group with PPV of 91% [19]. This scoring system has been assessed for risk stratification in further studies. A regional study was conducted in year 2017. This study accurately determined the low risk patients with the PPV documented to be 93% with sensitivity 65% and specificity of 75% [20]. The rationale of this study was to determine the diagnostic accuracy of MASCC score in prediction of serious medical condition. Previous studies have identified the implication of this score in prediction of low risk individuals. We aimed to predict high-risk individuals through identification of variables that may identify the probable grave course of illness. In this study, 63% of individuals develop serious medical

condition in high-risk group category. The incidence of SMC in high-risk category is found to be of significance as expected and thereby determining the accuracy of this score in prediction of high-risk individual. Whereas 13% develop serious medical condition assigned to be in low-risk category. The incidence of SMC tends to be low in low risk group as expected, thereby again determining the accuracy of this score in predicting low risk individuals as well. The major disease entity that we came across was leukemia (both myeloid and lymphoid). The incidence of high-risk groups identified within the leukemia cohort was significant, determining the possible hostile disease. This finding further highlights the need of vigilant monitoring in this cohort of patients. The overall sensitivity, specificity, PPV and NPV determined in our study is concordant with the previous study results as we described in Table 3 [19, 20]. Therefore, the initial stratification of patients at the time of presentation enables the physician to plan the management plan accordingly. Individuals assigned in low risk group may be safely managed to an extent on outpatient basis, depending upon the clinical status. This implies an important aspect of our region, as the factors such as financial and social concerns, that are encountered in the management may be addressed to certain level. Similarly, the patients that are identified as high-risk individuals can be offered an astringent management plan in anticipation of developing serious medical complications. This will eventually leads to the reduction of overall morbidity and mortality associated with febrile neutropenia. Therefore, MASCC risk index is still of significance in individualize the patient management approach.

### LIMITATIONS

It was a single center study and lost to follow ups are the major drawbacks in cohort studies.

### CONCLUSION

Serious medical complications are documented in 63% of individuals in high-risk group cohort. Whereas, 13% of developed serious medical condition in low-risk cohort. The overall sensitivity and specificity of MASCC score are found out to be 69.8% and 81.8% respectively, with the positive and negative predictive value of 61.1% and 86.8%. Therefore these results re validated this scoring system, and determined its significance in ascertainment of risk stratification in current era, helping the physicians to tailor the management approach of FN patients accordingly.

### LIST OF ABBREVIATIONS

MASCC	Multinational Association for Supportive Care in Cancer.
FN	Febrile Neutropenia.
HSCT	Hematopoietic Stem Cell Transplantation.
CISNE	Clinical Index of Stable Febrile Neutropenia.
IDSA	Infectious Diseases Society of America
ANC	Absolute Neutrophil Count.
SMC	Serious Medical Complications.

### AUTHORS' CONTRIBUTION

**Quratul Ain Rizvi** had the main idea of the study, recruited patient, searched the literature and wrote the manuscript. **Aisha Jamal** contributed in acquisition of data, literature search and manuscript writing. **Naveena Fatima** contributed in statistical analysis and interpretation of data. **Munira Borhany** and **Uzma Zaidi** contributed in manuscript writing. **Tahir Sultan Shamsi** critically reviewed and approved the final version of manuscript.

### CONFLICT OF INTEREST

Declared none.

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