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Original Research Article.

Changes in Quality of Life in Multiple Myeloma Patients During Treatment a Multicenter Three-Month Follow-Up Study

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ABSTRACT

Introduction: Multiple myeloma (MM) patients report more symptoms resulting in reduced health-related quality of life (HRQoL). Because survival is improving in MM patients there is an increased need for focus on HRQoL. The aim of this study was to assess the changes in QoL in MM patient receiving treatment.

Method: A prospective observational study was carried out Department of Haematology, BSMMU and DMCH Dhaka. A total of 35 multiple myeloma patients, meeting inclusion and exclusion criteria was enrolled in the study. MM patients' age, sex, disease duration and drug history were obtained from hospital files. Health Related Quality of Life HRQoL was assessed using the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life questionnaire (QLQ-C30) and the Quality of Life Multiple Myeloma module (QLQ-MY20). Patients completed the questionnaires baseline; at the end of 01 month and at the end of 03 months of treatment. Results were transformed into scales ranging from 0 to 100 for QLQ-MY20 and QLQ-C30.

Result: Among 35 multiple myeloma patients in this study mean score of EORTC QLQ-C30 in baseline (at one month) and follow up (at three months), found mean change of functional scale (9.5 and 18.0 respectively) was significantly improved. There was significant reduction of mean change of symptom scale at one month (-16.4) and three months (-28.3). Mean changes of global health status/QoL was 1.5 at one month and 11.4 at three months. Mean scores of the EORTC QLQ-MY20 domains at baseline and follow up found disease symptoms was improved but not statistically significant ($p>0.05$) when compared with baseline. There was a steady increased in future perspective score at one and three months (mean changes were -21.4 and 24.4 respectively). Comparison between EORTC QLQ-MY20 domains in bortezomib and non-bortezomib based chemotherapy. Disease symptom score gradually decreased in bortezomib arm. No significant difference of side effect of treatment domain was observed in both groups. Future perspective scores no significant improvement was observed in both groups. Almost three fourth (74.3%) patients were alive, 5(14.3%) were death and 4(11.4%) were lost follow up.

Keywords: Multiple Myeloma (MM), Quality of Life (QoL), European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) Quality of Life Multiple Myeloma Module (EORTC QLQ-MY20).

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INTRODUCTION

Multiple Myeloma (MM) is a bone marrow based multifocal neoplastic proliferation of plasma cells, usually associated with an M (monoclonal) protein in serum and/or urine and evidence of organ damage related to the plasma cell neoplasm[1] (Swerdlow et al. 2017). Despite significant advances in treatment, MM remains incurable disease in which patients often have pronounced symptoms and substantially reduced health related quality of life[2] (Johnsen et al. 2009). Common symptoms of Multiple myeloma are fatigue from anaemia and bone pain due to skeletal involvement, 70% of patients have lytic bone lesions, with or without osteoporosis and 20% of patients have renal insufficiency. Impaired immune function is also an important characteristic of the disease that leads to severe infection[3] (Hoffbrand and Moss 2015).

Multiple myeloma is the second most prevalent blood cancer (15%) after Non-hodgkins lymphoma and represents approximately 1% of all cancer and 20% of deaths from haematological malignancies[4] (Kyle et al. 2003). The median age at diagnosis is approximately 65-70 years. Only 15% and 2% of the patients are younger than 50 and 40 years, respectively[3] (Hoffbrand and Moss 2015). The choice of first-line treatment depends on a combination of factors. The aim of treatment of these patients is to achieve the maximum durable response with minimum treatment-related toxicity. There is no simple answer to the of the best treatment options. The best choice for each patient depends upon individual factors such as age, stage, genetic features, renal status, co-morbidities and personal preference.

Malphalan and Prednisolone (MP) has been the gold standard for over 40 years; however, the scenario has changed with the introduction of novel agents such as Thalidomide, Bortezomib, Lenalidomide etc. For patients with renal insufficiency, previous history or risk of deep venous thrombosis BMP (Bortezomib, Melphalan, Prednisolone) could the preferable option. The most frequent toxicities of Bortezomib include fatigue, gastrointestinal symptoms, cyclical thrombocytopenia and particularly peripheral neuropathy. In patients with pre-existing peripheral neuropathy Len-MP (Lenalidomide, Melphalan, Prednisolone) or Len-dex (Linalidomide, Dexamethasone) should be the choice. Oral treatment (MPT or Len-dex) would be preferable for patients living long distances from hospital. If cost is an issue MPT or Cyclo-TD (Cyclophosphamide, Thalidomide, Dexamethasone) are the cheapest options[3] (Hoffbrand and Moss 2015).

The median survival of MM patients older than 65 years of age is 2-3 years and it is 5-6 years for patients less than 65 years[5] (Bladd and Rosinol 2008). Novel therapies led to improvement in survival. Due to the increased life expectancy of the general population and the improved survival arising from better antimyeloma drugs, the number of MM patients will increase substantially worldwide in the future. The significant challenge of current myeloma management is matching the progress made in improved survival through disease control while optimizing quality of life with effective supportive care from initial diagnosis to end-of-life care.

WHO defines health as "A state of complete physical, mental, and social well-being not merely the absence of disease." The measurement of health and the effects of health care must include not only an indication of changes in the frequency and severity of diseases but also an estimation of well-being and this can be assessed by measuring the improvement in the QoL related to health care. HRQoL can be defined as self-perceived aspects of wellbeing that are related to or affected by the presence of a disease or treatment[6] (Ebrahim, 1995). A multidimensional HRQoL instrument will defined as any quality of life instrument assessing two or more of the three core domains described by the World Health Association: physical, social, and psychological wellbeing[7] (WHOQOL Group 1995). The main purpose for all clinicians is to improve the quality of the patient's life and to avoid iatrogenic harm. It is not enough to make vague, subjective judgments about QoL when treating a patient. Making specific, objective assessments about QoL using validated tools and instruments is needed. The assessment of QoL is an essential element of health-care evaluation and helps in taking suitable measures to increase the QoL of MM patients. There are different HRQOL instruments applied for evaluating myeloma patient. European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) is the most frequently used instrument for measuring patient-reported HRQoL in MM[8] (Wisloff et al 1996). EORTC-QLQ-C30 has gained recognition by different cultures in different countries and used to assess various cancer patients. EORTC-QLQ-Myeloma 20 (EORTCQLQ- MY20) has been designed as a supplement to EORTC-QLQ-C30; and it provides more detailed analysis of MM patients. The reliability and validity of QLQ-MY 20 in MM have been published[9] (Cocks et al 2007). The concepts of QoL and quality adjusted life years in chronic diseases are still emerging concepts in Bangladesh. The main objectives will be to assess the QOL in MM patients receiving chemotherapy with reference to their physical, psychological and social health dimensions.

OBJECTIVES

General

To assess the changes in QoL in MM patient receiving treatment.

Specific

- Assessment of participants QoL before or initial stage of treatment to evaluate the impact of symptomatic myeloma on QoL.
- To measure QoL after 01 month of treatment different chemotherapy.
- To measure QoL after o3 month of treatment with different chemotherapy.
- To compare the changes in QoL at baseline, 01 month and 03 month.
- To compare the differences in QoL according to chemotherapy protocol.

MATERIALS AND METHODS

Study Design: This was a prospective observational study.

Place of Study: The study was carried out in the Department of Haematology, BSMMU and DMCH.

Study Period: September 2016 to September 2017.

Study Population: Multiple Myeloma patients who was attended OPD & IPD, Dept. of Haematology, BSMMU, DMCH, Dhaka**.**

Patient Selection: All patients with multiple myeloma attended in OPD and IPD of haematology department of said department came for treatment meeting inclusion criteria was enrolled after written consent.

SELECTION CRITERIA

Inclusion Criteria

1. Adult patients of either sex.
2. Diagnosed as a case of Multiple myeloma.
3. Well known about their disease.
4. Able to give written and explained consent.
5. Patients planned to receive chemotherapy.
6. Able to understand questionnaire and communicate well.

Exclusion Criteria

1. Patients refusing to participate or those unable to comprehend for other reasons.
2. Suffering from other malignancy.
3. Difficulty in communicating.

Research Equipments

- Pre formed structured data collection sheet. (Appendix –I)
- EORTC QLQ – C30 (Appendix -I)
- EORTC QLQ MY20 (Appendix -I)

Study Procedure

Multiple Myeloma patients who were attended OPD & IPD, Department of Haematology, BSMMU, DMCH, Dhaka, meeting inclusion and exclusion criteria of enrolled patients of multiple myeloma was included. Patients were recruited into the study between September 2016 to September 2017. Institutional ethical committee consent was obtained; MM patients were given information about the study and all gave written informed consent to participate. MM patients' age, sex, disease duration and drug history were obtained from hospital files. Potential protocols were reviewed and chosen to provide a sample with a wide range of treatments and disease characteristics for the purpose of study. Newly diagnosed MM patients going to start therapy within a few days or within 01 week of starting treatment.

HRQoL Assessments

HRQoL was evaluated with the myeloma-specific QLQ-MY20 questionnaire as well as with the general oncology - related QLQC30. These questionnaires were administered in paper format at the hospital. Patients completed the questionnaires at several time points: baseline; at the end of 01 month and at the end of 03 months of treatment.

QLQ-MY20, and QLQ-C30 domains were scored in accordance with their published guidelines (Appendix- I). Results were transformed into scales ranging from 0 to 100 for QLQ-MY20 and QLQ-C30. For the functional scales (Global Health Status and Physical Functioning), higher scores indicate better HRQoL, whereas for the symptom scales (Fatigue, Pain, Disease Symptoms, and Side Effects of Treatment), lower scores indicate a better health state. High score for Disease symptoms and Side Effects of Treatment domain of MY-20 represents a high level of symptomatology or problems, whereas a high score for future Perspective and Body Image represents better outcomes.

Data Collection Procedure

Patient selected as mentioned inclusion and exclusion criteria, after selection completion clinical history and available investigation report were noted in pre-formed structure data collection sheet.

Data Analysis

The data collected was edited by the principle investigator on the same day of collection. Data obtained was recorded then entered into the computer using microsoft excel and analysed with SPSS version 23.0 software package with the help of a statistician. Categorical variables were summarized as proportions, while means, median and standard deviations will used for continuous variables. All scores were transformed into a linear score from 0-100. In order to compare categoric data, chi-square test was used and to compare continuous variables, paired and unpaired t-test was used. In order to determine independent factors which influenced global QoL, linear regression analysis was performed. In the regression analysis 95% CI and OR and p-value was used to determine the factors that was associated with QoL.

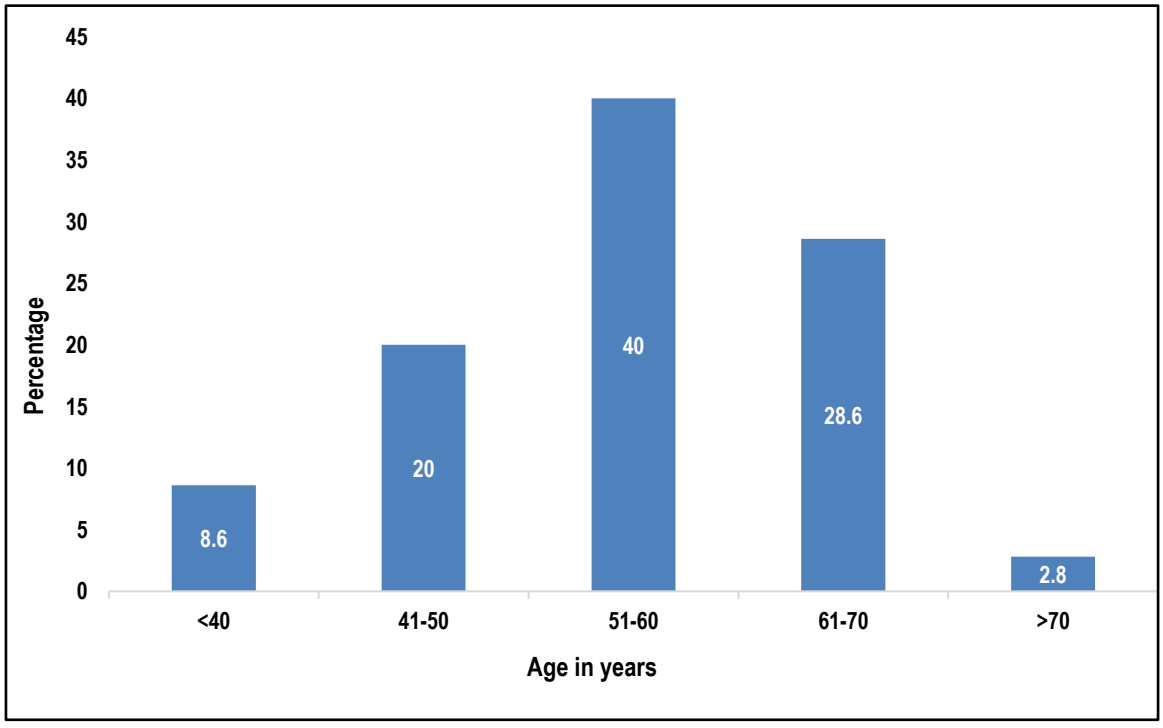

Figure 1: Bar diagram showing age distribution of the patients.

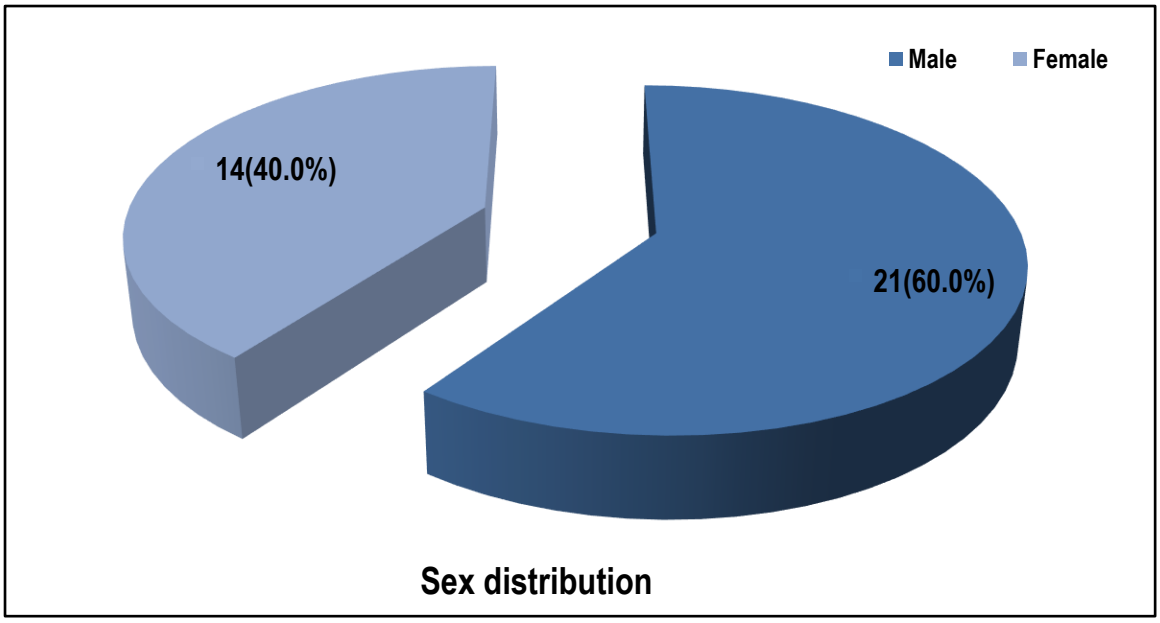

Figure 2: Pie chart showing gender distribution of the patients

Table I: Distribution of the study patients according to chemotherapy regimen (n=35)

Chemotherapy protocol	Number of patients	Percentage
Bortezomib (VRD, VCD, VTD, VD)	24	68.6
Non bortezomib (TD, CTD, RD, MPT)	11	31.4

RESULTS

This observational cross-sectional study was carried out with the aim to assess the changes in QoL in multiple myeloma patients receiving treatment in the department of Haematology, BSMMU and, DMCH, Dhaka between September 2016 to September 2017. During the study period of total 35 patients were enrolled for the study.

Fig: 1 Bar diagram shows distribution of patients with Multiple Myeloma according to age. Maximum 14(40.0%) patients were in age group 51-60 years. The median age was found 60.0 years with ranging from 30 to 73 years.

Fig: 2 Pie chart shows distribution of the study patients according to gender. Male was found 21(60.0%) and female was 14(40.0%). Male: female ratio was 1.5:1.

Table I shows majority 24(68.6%) patients received bortezomib based chemotherapy, 11(31.4%) received non bortezomib based chemotherapy.

Table II: Mean scores of the EORTC QLQ-C30 domains at baseline and follow up

EORTC QLQ-C30 scale	Mean	±SD	Mean Difference	OR*	95% CI Lower-upper	P-value
Function scale						
Baseline	34.8	±19.4				
One month	44.3	±19.3	9.5	0.54	0.23-1.86	0.015[s]
Three months	52.8	±22.4	18.0	0.15	0.01-1.63	0.013[s]
Symptom scales/ items						
Baseline	66.4	±17.9				
One month	50.0	±23.4	-16.4	0.29	0.01-1.58	0.006[s]
Three months	28.4	±19.0	-28.3	0.61	0.09-1.25	0.001[s]
Global health status/QoL						
Baseline	72.1	±21.3				
One month	73.6	±16.9	1.5	0.38	0.01-0.85	0.596[ns]
Three months	83.5	±13.4	11.4	0.39	0.01-1.04	0.004[s]

Note: At one month, three patients drop out due to lost follow up and two patients drop out due to death.
At three month, four patients drop out due to lost follow up and five patients drop out due to death;
s=significant, ns= not significant; P value reached from paired t-test;
*OR and 95% CI was used linear regression

Table III: Mean scores of the EORTC QLQ-MY20 domains at baseline and follow up

EORTC QLQ-MY20 scale	Mean	±SD	Mean Difference	OR*	95% CI Lower-upper	P-value
Disease symptom						
Baseline	51.6	±21.6				
One month	45.5	±22.0	-6.1	0.46	0.14-0.79	0.109[ns]
Three months	42.4	±20.4	-9.2	0.35	0.01-0.78	0.070[ns]
Side effects of treatment						
Baseline	26.8	±11.4				
One month	27.8	±13.0	1.0	0.46	0.23-0.69	0.170[ns]
Three months	24.6	±15.0	-2.2	0.78	0.14-0.95	0.699[ns]
Body image						
Baseline	14.3	±3.3				
One month	57.1	±21.0	42.8	1.10	0.78-1.42	0.129[ns]
Three months	76.0	±40.3	61.7	1.13	0.58-1.68	0.001[s]
Future perspective						
Baseline	41.2	±13.7				
One month	62.6	±20.0	21.4	0.42	0.15-1.99	0.001[s]
Three months	65.6	±18.8	24.4	0.18	0.05-1.53	0.001[s]

Note: At one month, three patient's dropout due to lost follow up and two patients dropout due to death.
At three-month, four patient's dropout due to lost follow up and five patients dropout due to death;
s=significant, ns= not significant; P value reached from paired t-test;
*OR and 95% CI was used linear regression

Table IV: Mean scores of the EORTC QLQ-C30 domains in bortezomib based chemotherapy (n=24)

EORTC QLQ-C30 scale	Mean	±SD	Mean Difference	OR*	95% CI Lower-upper	P-value
Function scale						
Baseline	34.6	±19.5				
One month	46.6	±18.7	12.0	0.63	0.21-1.03	0.008[s]
Three months	57.9	±20.7	23.3	0.35	0.01-0.50	0.006[s]
Symptom scales/ items						
Baseline	68.7	±19.1				
One month	51.1	±26.5	-17.6	0.74	0.17-0.93	0.031[s]
Three months	29.6	±19.8	-39.1	0.33	0.21-0.64	0.001[s]
Global health status/QoL						
Baseline	70.2	±21.9				
One month	70.7	±18.2	0.5	0.22	0.03-0.80	0.890[ns]
Three months	81.7	±14.1	11.5	0.19	0.06-0.99	0.032[s]

Note: At one month, two patients dropout due to lost follow up and one patient dropout due to death.
At three-month, two patients dropout due to lost follow up and three patients dropout due to death;
s=significant, ns= not significant; P value reached from paired t-test;
*OR and 95% CI was used linear regression

Table II shows mean score of EORTC QLQ-C30 in baseline and follow up. It was observed that at baseline there was high symptom scale and reduced functional scale. At one month (OR= 0.54; 95% CI 0.23 to 1.86%) and three month (OR= 0.15; 95% CI 0.01 to 1.63%) functional scale was significantly improved when compared with baseline. Mean changes of functional scale were found 9.5 at one month and 18.0 at three months. There was significant reduction of symptom scale at one and three months. Mean changes of symptoms scales/items were -16.4 and -28.3 at one and three months respectively. No significant improved of global health status/QoL was noticed at one month but at three months follow up it was improved significantly. Mean changes of global health status/QoL was 1.5 at one month and 11.4 at three months.

Table III shows mean scores of the EORTC QLQ-MY20 domains at baseline and follow up, it was observed that at one month and three-month disease symptoms was improved but not statistically significant (p>0.05) when compared with baseline. Mean changes of disease symptom were -6.1 at one month and -9.2 at three months. Side effect of treatment scale was unaltered throughout the assessment period. Mean changes of side effects of treatment scale were 1.0 at one month and -2.2 at three months. Mean changes of body image were 42.8 at one month and 61.7 at three months. There was a steady increased in future perspective at one and three months. Mean changes of future perspective were -21.4 at one month and 24.4 at three months.

Table IV shows mean score of EORTC QLQ-C30 domains in bortezomib based chemotherapy, it was observed that at one month and three-month functional scale was significantly improved when compared with baseline. Reduced score of symptom scale represent reduced level of problems. Significant reduction of symptom scales observed at one and three months. Although QoL was unaltered at one month, it was significantly improved at three months when compared with baseline.

Table V shows mean score of EORTC QLQ-C30 domains in non-bortezomib based chemotherapy, it was observed that score of functional scale was not significantly changed over the assessment period. But symptom scales were greatly reduced at one and three months when compared with baseline. Global health status dimensions did not change during first follow up but significant improvement was observed at three months.

Table VI shows mean scores of the EORTC QLQ-MY20 domains in bortezomib chemotherapy, it was observed that disease symptom gradually improved over period (mean changes was -4.5 at one month and -11.4 at three month) and it was statistically significant when compared with baseline. Body image is a single item scale and improved significantly over time. Future perspective also improved (at one month mean difference 18.1, OR 0.48 and at three month OR 0.67, mean change 26). There was no significant side effect of treatment was observed during first three month of treatment. At one month and three months mean difference 0.2 and -5.6, OR 0.42, 0.12 respectively.

Table VII shows mean scores of the EORTC QLQ-MY20 domains in non-bortezomib based chemotherapy. Mean difference of side effects of treatment score was gradually increased (2.5 at one month and 6.9 at three month) but not statistically significant. Body image dimension was also improved at one month and three months but statistically non-significant. Future perspective was significantly improved at one month (mean difference 29, OR 0.11, 95% CI 0.75 to 1.91) but further deteriorate at three months (mean change 19.3) though statistically non -significant (P value 0.185).

Table VIII shows comparison between EORTC QLQ-C30 domains in bortezomib and non-bortezomib based chemotherapy. Initial symptom burden was similar in both groups. Significant symptom relief was achieved in both group but the differences was not statistically significant. Functional scale progressively improved in bortezomib group, but in non-bortezomib group no significant improvement was noticed during the peri-treatment period. Significant differences of functional scale between groups was shown at three-month follow-up (P value 0.055). Global health status/QoL appeared to be unaltered at one month in both group but improved at three months. There was no statistically significant difference was observed in both arms.

Table IX shows comparison between EORTC QLQ-MY20 domains in bortezomib and non-bortezomib based chemotherapy. Disease symptom score gradually decreased in bortezomib arm and significant improvement was observed. In non-bortezomib arm though symptoms reduced initially at one month it was further increased at three months. No significant difference of side effect of treatment domain was observed in both group but increased score in non-bortezomib domain reflect increased side effect of treatment.

Body image score was very low at baseline (mean 4.2±17.7) in bortezomib group and 36.4±17.7 in non-bortezomib group. Mean difference was significant. Gradually, mean value increases in Bortezomib group and remain unaltered in non-bortezomib group. But the differences were not statistically significant. Future perspective score was similar in both group at baseline and follow-up study. No significant improvement was observed in both groups.

Table V: Mean scores of the EORTC QLQ-C30 domains in non-bortezomib based chemotherapy (n=11)

EORTC QLQ-C30 scale	Mean	±SD	Mean Difference	OR*	95% CI Lower-upper	P-value
Function scale						
Baseline	35.0	±20.0				
One month	38.9	±20.7	3.9	0.49	0.27-1.25	0.666^{ns}
Three months	39.0	±22.7	4.0	0.41	0.05-1.42	0.999^{ns}
Symptom scales/ items						
Baseline	61.4	±14.3				
One month	47.5	±14.8	-13.9	0.02	0.01-0.90	0.056^{ns}
Three months	25.0	±17.4	-36.4	0.19	0.13-0.99	0.005^{s}
Global health status/QoL						
Baseline	76.1	±20.2				
One month	80.2	±11.7	4.1	1.24	0.38-2.35	0.288^{ns}
Three months	88.6	±10.7	12.5	1.35	0.29-3.00	0.032^{s}

Note: At one month, one patient dropout due to lost follow up and one patient dropout due to death.
At three-month, two patients dropout due to lost follow up and two patients dropout due to death.
s=significant, ns= not significant; P value reached from paired t-test
*OR and 95% CI was used linear regression

Table VI: Mean scores of the EORTC QLQ-MY20 domains in bortezomib based chemotherapy (n=24)

EORTC QLQ-MY20 scale	Mean	±SD	Mean Difference	OR*	95% CI Lower-upper	P-value
Disease symptom						
Baseline	50.8	±23.7				
One month	46.3	±22.4	-4.5	0.64	0.26-1.03	0.093ns
Three months	39.4	±20.2	-11.4	0.63	0.10-1.16	0.012s
Side effects of treatment						
Baseline	28.1	±11.3				
One month	28.3	±14.1	0.2	0.42	0.15-0.68	0.450ns
Three months	22.5	±15.6	-5.6	0.12	0.11-0.36	0.596ns
Body image						
Baseline	4.2	±8.3				
One month	61.9	±26.0	57.7	1.20	0.77-1.63	0.004s
Three months	89.5	±68.5	85.3	2.52	1.43-3.62	0.001s
Future perspective						
Baseline	43.0	±15.2				
One month	61.1	±19.6	18.1	0.48	0.15-1.40	0.001s
Three months	69.0	±17.3	26.0	0.20	0.01-1.59	0.001s

Note: At one month, two patients dropout due to lost follow up and one patient dropout due to death.

At three-month, two patients dropout due to lost follow up and three patients dropout due to death.

s=significant, ns= not significant; P value reached from paired t-test

*OR and 95% CI was used linear regression

Table VII: Mean scores of the EORTC QLQ-MY20 domains in non bortezomib based chemotherapy (n=11)

EORTC QLQ-MY20 scale	Mean	±SD	Mean Difference	OR*	95% CI Lower-upper	P-value
Disease symptom						
Baseline	53.5	±17.1				
One month	43.2	±22.7	-10.3	0.13	0.01-0.38	0.690ns
Three months	51.4	±20.0	-2.1	0.33	0.01-0.72	0.674ns
Side effects of treatment						
Baseline	23.9	±11.6				
One month	26.4	±9.9	2.5	0.65	0.11-1.20	0.062ns
Three months	30.8	±12.0	6.9	0.06	0.01-0.96	0.108ns
Body image						
Baseline	36.4	±7.6				
One month	42.9	±2.4	6.5	1.00	0.97-1.04	0.392ns
Three months	43.3	±3.3	6.9	0.97	0.95-0.99	0.154ns
Future perspective						
Baseline	37.1	±9.0				
One month	66.1	±11.5	29.0	0.77	0.75-1.91	0.008s
Three months	56.4	±21.1	19.3	0.24	0.02-0.54	0.130ns

Note: At one month, one patient dropout due to lost follow up and one patient dropout due to death.

At three-month, two patients dropout due to lost follow up and two patients dropout due to death.

s=significant, ns= not significant; P value reached from paired t-test

*OR and 95% CI was used linear regression

Table VIII: Comparison between EORTC QLQ-C30 domains in bortezomib and non bortezomib based chemotherapy (n=35)

EORTC QLQ-C30 scale	Bortezomib			Non bortezomib			Mean Difference	P-value
	n	Mean	±SD	n	Mean	±SD		
Function scale								
Baseline	24	34.6	±19.5	11	35.0	±20.0	-0.4	0.956[ns]
One month	21	46.6	±18.7	9	38.9	±20.7	7.7	0.325[ns]
Three months	19	57.9	±20.7	7	39.0	±22.7	18.9	0.055[ns]
Symptom scales/ items								
Baseline	24	68.7	±19.1	11	61.4	±14.3	7.3	0.268[ns]
One month	21	51.1	±26.5	9	47.5	±14.8	3.6	0.707[ns]
Three months	19	29.6	±19.8	7	25.0	±17.4	4.6	0.593[ns]
Global health status/QoL								
Baseline	24	70.2	±21.9	11	76.1	±20.2	-5.9	0.454[ns]
One month	21	70.7	±18.2	9	80.2	±11.7	-9.5	0.162[ns]
Three months	19	81.7	±14.1	7	88.6	±10.7	-6.9	0.253[ns]

Bortezomib group: At one month, two patients dropout due to lost follow up and one patient dropout due to death.
At three-month, two patients dropout due to lost follow up and three patients dropout due to death.
Non bortezomib group: At one month, one patient dropout due to lost follow up and one patient dropout due to death.
At three-month, two patients dropout due to lost follow up and two patients dropout due to death
ns= not significant; P value reached from unpaired t-test

Table IX: Comparison between EORTC QLQ-MY20 domains in bortezomib and non bortezomib based chemotherapy (n=35)

EORTC QLQ-MY20 scale	Bortezomib			Non bortezomib			Mean Difference	P-value
	n	Mean	±SD	n	Mean	±SD		
Disease symptom								
Baseline	24	50.8	±23.7	11	53.5	±17.1	-2.7	0.737[ns]
One month	21	46.3	±22.4	9	43.2	±22.7	3.1	0.732[ns]
Three months	19	39.4	±20.2	7	51.4	±20.0	-12	0.191[ns]
Side effects of treatment								
Baseline	24	28.1	±11.3	11	23.9	±11.6	4.2	0.319[ns]
One month	21	28.3	±14.1	9	26.4	±9.9	1.9	0.717[ns]
Three months	19	22.5	±15.6	7	30.8	±12.0	-8.3	0.216[ns]
Body image								
Baseline	24	4.2	±8.3	11	36.4	±7.6	-32.2	0.001[s]
One month	21	61.9	±26.0	9	42.9	±2.4	19	0.039[s]
Three months	19	89.5	±68.5	7	43.3	±3.3	46.2	0.091[ns]
Future perspective								
Baseline	24	43.0	±15.2	11	37.1	±9.0	5.9	0.243[ns]
One month	21	61.1	±19.6	9	66.1	±11.5	-5	0.483[ns]
Three months	19	69.0	±17.3	7	56.4	±21.1	12.6	0.133[ns]

Bortezomib group: At one month, two patients dropout due to lost follow up and one patient dropout due to death.
At three-month, two patients dropout due to lost follow up and three patients dropout due to death.
Non bortezomib group: At one month, one patient dropout due to lost follow up and one patient dropout due to death.
At three-month, two patients dropout due to lost follow up and two patients dropout due to death
s= significant, ns= not significant; P value reached from unpaired t-test

Table X: Distribution of the study patients by outcome (n=35)

Outcome	Number of patients	Percentage
Alive	26	74.3
Death	5	14.3
Lost follow up	4	11.4

Table XI: Comparison between outcome with bortezomib and non bortezomib based chemotherapy (n=9)

Outcome	Total N	Bortezomib		Non Bortezomib		P-value
		n	%	n	%	
Death	5	3	60.0	2	40.0	0.764^{ns}
Lost follow up	4	2	50.0	2	50.0	

ns= not significant; P value reached from chi square test.

Table X shows almost three fourth (74.3%) patients were alive, 5(14.3%) were death and 4(11.4%) were lost follow up.

Table XI shows total death was found in 5 patients, out of which 3(60.0%) in bortezomib group and 2(40.0%) in non-bortezomib group. Four patients were lost of follow up, among them 2 (50.0%) in bortezomib group and 2(50.0%) in non-bortezomib group. The difference was not statistically significant (p>0.05) between bortezomib and non-bortezomib chemotherapy.

DISCUSSION

In my study mean score of EORTC QLQ-C30 in baseline and follow up it was observed that at baseline there was high symptom scale and reduced functional scale. At one month (OR= 0.54; 95% CI 0.23 to 1.86%) and three month (OR= 0.15; 95% CI 0.01 to 1.63%) functional scale was significantly improved when compared with baseline. Mean changes of functional scale were found 9.5 at one month and 18.0 at three months. There was significant reduction of symptom scale at one and three months. Mean changes of symptoms scales/items were -16.4 and -28.3 at one and three months respectively. No significant improved of global health status/QoL was noticed at one month but at three months follow up it was improved significantly. Mean changes of global health status/QoL was 1.5 at one month and 11.4 at three months. Similarly, Proskorovsky et al.[10] (2014) showed their study the mean QLQ-C30 Global Health Status/QoL score was 60.1 ± 25.5 and the IQR was 41.7 to 83.3. The HRQoL scales identified in this analysis as significant predictors of utility values, such as Global Health Status/QoL, Physical Functioning, and Pain, are similar to HRQoL scales that have been pre-selected as clinically relevant in previous assessments (Dimopoulos et al. 2013).[11] Another study conducted by Khalafallah et al. (2011)[12], which showed physical (OR 6.78; 95% CI 2.81 to 16.4; P for trend T<0.001) and social functioning (OR 3.16; 95% CI 1.42 to 7.02; T=0.021 T2=0.009) were moderately improved in the follow-up period, as well as the patient's assessment of their global health status (OR 7.99; 95% CI 2.67 to 23.9; P for trend T<0.001) and quality of life (OR 7.06; 95% CI 2.74 to 18.2; P for trend T<0.001) and remained the same in the 3 monthly follow up. Sonneveld et al.[13] (2013) observed their study fifteen baseline HRQoL parameters were significant in predicting mortality during treatment when univariate logistic regression was used, but only the QLQ-C30 fatigue and physical sub scores were significant predictors of survival in a subsequent multivariate regression. QLQ-C30 revealed no significant median change (45 points MID) from baseline in 14 of 15 domains for patients completing questionnaires at baseline and 24 weeks. Alegre et al.[14] (2012) reported further HRQoL data from 63 patients enrolled in the Spanish cohort. At week 24, 42 patients were available for HRQoL assessment. In addition to the reported improvement in Future Perspective, a non-significant impairment in the Physical Functioning domain of the QLQ-C30 functional scores was also observed (<5 points MID).

In this present study mean scores of the EORTC QLQ-MY20 domains at baseline and follow up, it was observed at one month and three-month disease symptoms was improved but not statistically significant (p>0.05) when compared with baseline. Mean changes of disease symptom were -6.1 at one month and -9.2 at three months. Side effect of treatment scale was unaltered throughout the assessment period. Mean changes of side effects of treatment scale were 1.0 at one month and -2.2 at three months. Mean changes of body image were 42.8 at one month and 61.7 at three months. There was a steady increased in future perspective at one and three months. Mean changes of future perspective were -21.4 at one month and 24.4 at three months. Similarly, Proskorovsky et al.[10] (2014) found their study for the QLQ-MY20 instrument, Body Image scores were generally high (77.9 [IQR 66.7 to 100]), but Future Perspective scores appeared to be relatively more affected (59.9 [IQR 33.3 to 77.8]).

In my study comparison between EORTC QLQ-C30 domains in bortezomib and non-bortezomib based chemotherapy. Initial symptom burden was similar in both groups. Significant symptom relief was achieved in both group but the differences was not statistically significant. Significant differences of functional scale between groups was shown at three-month follow-up (P value 0.055). Global health status/QoL appeared to be unaltered at one month in both group but improved at three months. There was no statistically significant difference was observed in both arms. QLQ-C30 analysis found significantly better HRQoL in the bortezomib group vs dexamethasone, although a declining trend in mean GHS score was observed in both arms. The impact of bortezomib dose on HRQoL in a study by (Delforge et al. 2012)[15] showed patients receiving a lower dose intensity of bortezomib (<5.6 mg/m^2/cycle) for at least two cycles before achieving overall response or before their end-of-treatment visit generally reported

better HRQoL vs the higher dose intensity group. Leleu et al. (2017)[16] showed the results that HRQoL was not substantially impaired under continued treatment with either lenalidomide- or bortezomib-based regimens. Only a change indicating a worsening in the Diarrhoea domain from baseline to month 6 was observed in the lenalidomide cohort, and a change indicating a worsening in the Global health status/QoL domain was observed in the bortezomib cohort. At study completion (month 6), HRQoL reductions from baseline reaching MID were observed for 1 of the 22 domains in each cohort**.** For all other domains, changes over time did not reach the MID. A slight deterioration in HRQoL was consistently observed over time in both lenalidomide and bortezomib cohorts for all other domains, except Financial difficulties, Pain, Disease symptoms and Future perspective domains, where a slight improvement was observed. However, in the new era of novel agents for treatment of MM such as proteasome inhibitor; bortezomib and the immunomodulatory agents; thalidomide and lenalidomide, there is a significant improvement of quality of life in the management of older patients and/or those not eligible for transplantation [17] (Richardson et al. 2010). Leleu et al. (2017)[16] found their study for patients who discontinued the study prior to 6 months owing to disease progression or discontinuation of treatment, clinically meaningful declines in HRQoL exceeding the MID were observed in 8 of the 22 domains for the bortezomib cohort (Global health status/QoL, Role functioning, Social functioning, Fatigue, Dyspnoea, Diarrhoea, Motor scale and Sensory scale domains) and in 1 of the 22 domains in the lenalidomide cohort (Motor scale domain). The study focusses on RRMM; however, with the approval of lenalidomide in combination with dexamethasone in frontline MM in February 2015 by the European Medicines Agency (EMA), the question on bortezomib vs lenalidomide has also become relevant for newly diagnosed MM (NDMM) patients. Improvements in HRQoL were generally maintained for patients on continued treatment with lenalidomide –dexamethasone.

In this study comparison between EORTC QLQ-MY20 domains in bortezomib and non-bortezomib based chemotherapy. Disease symptom score gradually decreased in bortezomib arm and significant improvement was observed. In non-bortezomib arm though symptoms reduced initially at one month it was further increased at three months. No significant difference of side effect of treatment domain was observed in both group but increased score in non-bortezomib domain reflect increased side effect of treatment. Body image score was very low at baseline (mean 4.2±17.7) in bortezomib group and 36.4±17.7 in non-bortezomib group. Mean difference was significant. Gradually, mean value increases in Bortezomib group and remain unaltered in non-bortezomib group. But the differences were not statistically significant**.** A study conducted by Delforge et al.[18] (2015), which showed in the QLQ-MY20, lenalidomide and low-dose dexamethasone demonstrated a significantly greater reduction in the Disease Symptoms domain compared with melphalan, prednisone, thalidomide at Month 3**.** Continuous lenalidomide and low-dose dexamethasone delays disease progression *versus* melphalan, prednisone, thalidomide and has been associated with a clinically meaningful improvement in health-related quality-of-life. Statistically significant symptom relief, as measured by the QLQ-MY20 Disease Symptoms domain, was achieved in both arms. Both treatment arms showed statistically significant (P<0.05) reductions in pain (QLQMY20 Disease Symptoms domains) at all post-baseline assessments.

In this present study it was observed that almost three fourth (74.3%) patients were alive, 5(14.3%) were death and 4(11.4%) were lost follow up. Similarly, Khalafallah et al. (2011)[12] found their study alive patients was 16(88.9%) and deceased due to disease progression 2(11.1%). Another study done by Blimark et al. (2015)[19], which showed at one year of follow up, infection was the underlying cause in 22% of deaths in multiple myeloma patients.

LIMITATIONS

1. Small sample size was also a limitation of the present study. Therefore, in future further study may be undertaken with large sample size.
2. The sample was taken purposively, so there may be change of bias which can influence the result.

RECOMMENDATIONS

There are some recommendations for further study. Study period may be extended. Further multi-centered prospective analytical study with larger sample size is recommended.

ABBREVIATIONS

ASCT: Autologus Haemopoietic Stem Cell Transplantation; **BM:** Bone Marrow; **BMP:** Bortezomib, Melphalan, Prednisolone; **BSMMU:** Bangabandhu Sheikh Mujib Medical University; **ECOG:** European Cooperative Oncology Group; **EORTC QLQ:** European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire; **DMCH:** Dhaka Medical College Hospital; **FDA:** Food and Drug Administration; **HDT:** High-dose chemotherapy; **HRQoL:** Health Related Quality of Life; **Ig:** Immunoglobulin; **IMWG:** International Myeloma Working Group; **IPD:** In Patients Department; **IRB:** Institutional Review Board; **ISS:** International Staging System; **KRD:** Carfilzomib - Lenalidomide - Dexamethasone; **MM:** Multiple Myeloma; **MP:** Malphalan and Prednisolone; **MPT:** Melphalan, Prednisone and Prednisolone; **OB:** Osteoblast; **OC:** Osteoclast; **OPD:** Out Patients Department; **OS:** Overall Survival; **QoL:** Quality of Life; **SD:** Standard Deviation; **SPSS:** Statistical Package of Social Science; **VCD:** Bortezomib - Cyclophosphamide-Dexamethasone; **VRD:** Bortezomib – Lenalidomide - Dexamethasone; **VTD:** Bortezomib – Thalidomide - Dexamethasone; **WHO:** World Health Organization.

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