International Journal of Scientific Reports
Saha V et al. Int J Sci Rep. 2022 Feb;8(2):43-52
http://www.sci-rep.com
pISSN 2454-2156 | eISSN 2454-2164

DOI: https://dx.doi.org/10.18203/issn.2454-2156.IntJSciRep20220102

Original Research Article

Quality of life in patients with multiple myeloma: early rehabilitation is need of the hour

Vasundhara Saha*, Hafis Rahman M. C.

Department of Physical Medicine and Rehabilitation, AIIMS, New Delhi, India

Received: 10 December 2021
Revised: 14 January 2022
Accepted: 15 January 2022

***Correspondence:**
Dr. Vasundhara Saha,
E-mail: drvasus199@gmail.com

ABSTRACT

Background: Multiple myeloma (MM) is a debilitating disease leading to reduced functioning. Evaluation of rehabilitative needs is necessary to provide rehabilitative care which may improve the functional status and quality of life (QOL) of such patients. We aimed to assess the rehabilitative needs, as well as levels of QOL in patients diagnosed with MM.

Methods: Ninety consecutive patients were included in this cross-sectional survey. All patients (new and relapsed), irrespective of disease status and duration from diagnosis, underwent baseline evaluation following which they completed a scale exploring their functional status by Barthel mobility index scoring and QOL with the European organization of research and training in cancer QOL questionnaire with its MM module. Mean score and frequency (%) were calculated. Comparison of scores between different categories was analyzed.

Results: Mean age was 57 years±10.1 (32 to 85 years). The QOL was low (39±18.2), with key areas of impairment being physical (100%), emotional (95.5%), role (91%), social (87.7%) and cognitive (68.8%) functioning. Low mean QOL score was found in all patients irrespective of treatment, clinical response and duration from diagnosis. There was improvement in quality-of-life score with treatment, though it did not cross the minimal important difference range.

Conclusions: There was significant reduction in quality-of-life score and functioning. This study emphasizes the need to assess rehabilitation needs among patients of MM to optimize the management.

Keywords: Assessment, Functioning, MM, QOL, Rehabilitation

INTRODUCTION

Multiple myeloma (MM), a B cell disorder of malignant plasma cells, is the second most common hematological malignancy with a higher incidence in North America and a lower incidence in Asia.[1-5] During the past 15 years, prognosis of MM has improved significantly, attributed to induction therapy using novel agents e.g. immunomodulators-(Thalidomide, Lenalidomide, Pomalidomide), proteasome inhibitors (e.g. Bortezomib, carfilzomib), high dose chemotherapy plus stem cell transplantation and maintenance therapy.[6-12] While there has been significant improvement in survival of these patients, many patients continue to have symptoms related to bone damage (pain, deformity, limited range of motion, upper and lower extremity dysfunction or persistent neurological deficits), therapy related side effects (fatigue, anorexia, constipation, dysphagia, neuropathy, gait disturbance, myopathy, osteoporosis etc.), sleep disturbance, anxiety, depression, along with co morbidities of old age. These factors prevent a return to a normal functioning, and better QOL.[13] A few studies have assessed the rehabilitative needs and effects of rehabilitation interventions in the improvement of patient's functional status and the QOL.[14-21] These studies have revealed that significant numbers of rehabilitative problems could be improved with rehabilitative care. Identification of these needs and timely referral to rehabilitation team is important for improvement in functional status and QOL of myeloma patients. To the best of the author's knowledge, no such previous study has been conducted in view of the Indian population.

The aim of this study was therefore to assess the functional well-being and needs with respect to activities of daily living (ADL) along with QOL in terms of physical, role, emotional, cognitive and social functioning; and evaluating the extent and severity of various symptoms in these patients.

METHODS

Study design and ethics

In this cross-sectional study, MM patients consecutively attending outpatients' myeloma clinic in the department of medical oncology at our institute during the period of November 2014 to January 2016 were recruited using simple random sampling. The study was approved by the institute ethics committee and informed written consent was obtained. Eligibility criteria included a diagnosis of MM based on standard evaluation (serum and/or urine electrophoresis, bone marrow examination and skeletal survey) and those willing to participate in the study. All patients, newly diagnosed (naïve and on 1st line treatment) and relapsed; irrespective of disease status and duration from diagnosis were included. Patients with cognitive deficits or communication defects, those with pre-existing (before being diagnosed with MM) disabling conditions and those not willing to take part in the study were excluded.

Data collection

Patients were explained about the disease and assessment procedure. Baseline evaluation included detailed history, physical examination and investigations. The data was split into three subsets. First, newly diagnosed patients (naïve and on 1st line treatment) and relapsed categories. Second, according to disease status; and third as per duration from diagnosis (<6 months, 6-12 months, 12-24 months and >24 months). The functional status and QOL was assessed using the Barthel index scoring and European organization of research and training in cancer QOL questionnaire (EORTC QLQ C-30) with the myeloma (MY20) module.

EORTC QLQ C30 includes 5 multi-item functional scales, that is physical, role, emotional, cognitive, social function and a global health related QOL (HRQOL) scale; with 3 multi-item symptom scales for fatigue, pain, nausea and vomiting; along with 6 single item symptom scales for dyspnea, insomnia, appetite loss, diarrhea, constipation and financial problems.[22,23] All scales and single item measures range in score from 0-100. Higher scores represent better functioning for 5 function scales and global QOL scale. For symptom scale, higher scores are suggestive of more symptoms. For scoring, raw score was calculated by estimating average score of the items followed by standardization of raw score using linear transformation so that scores range from 0-100. Cut off values were taken as mean score of the respective variables of the reference myeloma population.[24] For global QOL, it was taken as 55.

Barthel index is an effective tool for functional assessment. It is simple to administer, easy to interpret and has a widespread use in routine clinical practice. It assesses current level of activity for the following ten items: bowel & bladder function, bathing, grooming, feeding, transfers, mobility, climbing stairs and dressing.[25-27] The total possible score ranges from 0-100, with lower scores indicating increased disability. Cut off value for low and high score was taken as 60.[28]

Statistical analysis

Data was analyzed by Stata 14 and presented in mean (standard deviation/ median/ min and max) and frequency (%). Categorical variables were compared by Chi square test. Continuous variables following normal distribution were compared by one way ANOVA followed by post hoc comparison using Bon ferroni correction (2 groups). On other hand, continuous data not following normal distribution were compared by Kruskal Wallis test followed by multiple comparison using Dunn's test with Bonferroni correction. $P \leq 0.05$ was considered significant.

Minimal important difference (MID), for assessment of change in mean scores between groups was taken as a change of ≥5 points from the mean score for the EORTC QLQ C30 and ≥20 points for the Barthel mean score.[29,30]

RESULTS

Participants' demographic characteristics

A total of 90 patients were enrolled in the study. Mean age was 57 years±10.1 (range 32 to 85 years), 58% were less than 60 years of age and 71% were males. Most of the patients (92%) belonged to the middle socioeconomic status group. Modified Kuppuswamy scale was used to define socioeconomic status.[31] Baseline characteristics of the participants are presented in Table 1.

Clinical features

The most common symptom in all participants was fatigue (96%), followed by excessive worry in 94%, and being tense in 91% of patients. Backache and bone pains were present in 84% and 56% of patients respectively, whereas 84% reported pain increasing with activity, with significant pain in 48%. Insomnia in 75% while 58% reported being depressed. Limited leisure was reported by 86%. Weakness of limbs-14%; loss of bowel and bladder sensations and control-10%; and sensory loss in 8%.

Examination revealed tenderness of spine in 57%, with restricted range of motion in 24% and neuro deficit (including weakness of limbs, reduced sensations and neurogenic bowel and bladder) in 14% of patients. Kyphotic deformity of spine was present in 6%, with 10.0% of patients being non ambulatory and 31% being ambulatory under supervision. Mobility assistive devices in the form of cane, crutches, walker, wheelchair, spinal and lower limb orthosis were used by 41% of patients.

Reduced QOL and physical functioning was reported by 100% of patients, while 95.6% had reduced emotional functioning, 90% had reduced role functioning, 86.7% had reduced social functioning and 67.8% had reduced cognitive functioning.

The proportion of participants with various disease symptoms, reduced function and examination findings, in newly diagnosed (both naïve and on 1st line treatment) and relapsed categories are presented in Table 2.

EORTC QLQ C30 mean scores of groups in the "newly diagnosed and relapsed" category

The mean global QOL score for naïve patients, those on 1st line treatment, and relapsed patients was low (<55). Statistically significant mean difference was found between naïve and 1st line treatment groups for appetite loss (23.27; 95% CI: 6.48, 40.06); and between naïve and relapsed groups for appetite loss (21; 95% CI: 4.77, 37.22). The mean differences for the rest of the scores were not found to be statistically significant. The EORTC QLQ C30 mean scores for naïve, 1st line treatment and relapsed groups are presented in Table 3.

EORTC QLQ C30 mean scores of groups in "disease status" category

The mean Global QOL score for the complete response/near complete response (CR/nCR), partial response/ very good partial response (PR/VGPR), relapsed groups and patients whose disease status was not evaluated at the time of recruitment, was found to be low (<55). Statistically significant mean differences were found between unevaluated and CR/nCR groups for pain (17.54; 95% CI: 1.40, 33.68), appetite loss (23.68; 95% CI: 7.60, 39.76), and Global QOL (-15.31; 95% CI: -25.47, -5.15); between unevaluated and PR/VGPR groups for appetite loss (17.91; 95% CI: 2.76, 33.06), and Global QOL (-9.89; 95% CI: -19.74, -0.04); between CR/nCR and relapsed groups for pain (-24.29; 95% CI: -40.27, -8.31), insomnia (-21.35; 95% CI: -38.08, -4.62), and global QOL (17.02; 95% CI: 5.07, 28.96); between PR/VGPR and relapsed groups for insomnia (-17.64; 95% CI: 32.92, -2.36) and Global QOL (11.60; 95% CI: 0.07, 23.13). Mean differences for the rest of the scores were not found to be statistically significant. The EORTC QLQ C30 mean scores for the unevaluated, CR/nCR, PR/VGPR and relapsed groups are presented in Table 4.

EORTC QLQ C30 mean scores of groups in the "duration from diagnosis" category

The mean global QOL score for the groups with duration of diagnosis being <6 months, 6-12 months, 12-24 months and >24 months was found to be low (<55). Statistically significant mean difference was found between groups with duration from diagnosis of <6 months and 12-24 months for appetite loss (24.58; 95% CI: 5.63, 43.53). Mean difference for the rest of the scores were not found to be statistically significant. The EORTC QLQ C30 mean scores for all four groups are presented in Table 5.

Barthel mean score

The mean Barthel score for all the three categories was found to be high (>60). No statistically significant mean difference of the same was found between the groups. The Barthel mean score for all the three categories are presented in Table 3-4.

Table 1: Participant characteristics.

Characteristic	No. of patients (%)
Age (Years)	
40-49	27 (30)
50-59	25 (28)
60-69	29 (32)
70-79	9 (10)
ISS* stage	
I	23 (26)
II	17 (19)
III	46 (51)
Missing data	4 (4)
Type of myeloma	
IgG	69 (76)
IgA	18 (20)
Missing data	3 (3)
Renal failure† **(S. creatinine >2 mg%)**	31 (34)

Continued.

Characteristic	No. of patients (%)
Treatment received	81 (90)
Naive	11 (12.2)
On 1st line treatment	58 (64.4)
Salvage therapy (R)[‡]	21 (23.3)
Novel agents	75 (83.3)
Radiotherapy	9 (10)
ASCT[§]	11 (12.2)
Maintenance	33 (36.7)
Disease status	
CR[‖]/nCR[**]	19 (21.1)
PR[††]/VGPR[‡‡]	15 (16.6)
Relapsed	21 (23.3)
Not evaluated	35 (38.8)
DOD[§§]	
<6 months	49 (54.4)
6-12 months	15 (16.6)
12-24 months	8 (8.8)
>24 months	18 (20)

*: International staging system; †: Values at the time of assessment; ‡: Relapsed; §: Autologous stem cell transplantation; ‖: Complete response; **: near complete response; ††: partial response; ‡‡: very good partial response; §§: duration of diagnosis

Table 2: Proportions of participants with disease symptoms, reduced functioning and examination findings in newly diagnosed patients (naïve), newly diagnosed (on 1st line treatment) and those on salvage therapy (relapsed).

Variables	Naïve, (n=11) (%)	On 1st line treatment, (n=58) (%)	On salvage therapy, (n=21) (%)
Backache	8 (73)	49 (84)	19 (90)
Bone pain	6 (55)	30 (52)	15 (71)
Fatigue	10 (91)	56 (97)	21 (100)
Significant pain	6 (55)	27 (47)	11 (52)
Pain with activity	9 (82)	47 (81)	20 (95)
Inability for strenuous work	11 (100)	57 (98)	21 (100)
Inability for long walk	11 (100)	56 (97)	20 (95)
Dyspnea	3 (27)	18 (31)	7 (33)
Insomnia	9 (82)	41 (71)	18 (86)
Appetite loss	9 (82)	39 (67)	17 (81)
Constipation	6 (55)	34 (59)	14 (67)
Diarrhea	0 (0)	3 (5)	1 (5)
Memory loss	3 (27)	13 (22)	7 (33)
Tense	11 (100)	52 (90)	19 (90)
Worry	11 (100)	54 (93)	20 (95)
Depression	8 (73)	32 (55)	12 (57)
Hair loss	0 (0)	6 (10)	1 (5)
Dry mouth	5 (45)	29 (50)	10 (48)
Tingling	0 (0)	13 (22)	11 (52)
Heartburn	3 (27)	22 (38)	9 (43)
↓ADL[*]	7 (64)	46 (79)	18 (86)
↓QOL[†]	11 (100)	58 (100)	21 (100)
↓Physical function	11 (100)	58 (100)	21 (100)
↓Role function	11 (100)	52 (90)	19 (90)
↓Emotional function	11 (100)	55 (95)	20 (95)
↓Social function	9 (82)	49 (84)	21 (100)
↓Cognitive function	9 (82)	39 (67)	14 (67)
Limited leisure	10 (91)	48 (83)	19 (90)
Spine deformity	0 (0)	6 (10)	0 (0)
Spine tenderness	5 (45)	34 (59)	12 (57)
Neuro deficit	1 (9)	8 (14)	4 (19)

Continued.

Variables	Naïve, (n=11) (%)	On 1st line treatment, (n=58) (%)	On salvage therapy, (n=21) (%)
Vertebral collapse	5 (45)	44 (76)	18 (86)
Co morbidity	3 (27)	27 (47)	10 (48)
Psychiatric illness	0 (0)	1 (2)	1 (5)
Future perspectives	11 (100)	56 (97)	21 (100)

*: Activities of daily living; †: Quality of life

Table 3: Barthel and EORTC QLQ C30 mean scores of newly diagnosed (Naïve and on 1st line treatment) and Relapsed (on salvage therapy) groups with their comparison (ANOVA and Kruskal Wallis).

Variables	Naïve, mean ± SD (95% CI)	1st line treatment, mean ± SD (95% CI)	On salvage therapy, mean ± SD (95% CI)	$\chi^2/F_{2,87}$	P value
Barthel score	68±32 (46.6-89.7)	84±20 (78.7-89.1)	83±20 (74.0-92.1)	2.52*	0.08
EORTC function					
Physical function	43±28 (24.5-62.1)	50±24 (44.3-56.6)	48±20 (39.1-57.1)	0.78†	0.67
Role function	38±22 (22.6-52.6)	55±27 (47.4-61.7)	53±26 (41.2-64.4)	4.52†	0.10
Emotional function	55±23 (40.0-70.7)	62±19 (57.4-67.2)	58±21 (48.1-67.5)	0.80*	0.45
Social function	51±35 (27.5-74.9)	55±28 (47.6-62.5)	48±20 (39.1-56.9)	0.93†	0.62
Cognitive function	69±21 (55.3-83.4)	80±18 (75.7-85.1)	78±19 (69.4-87.0)	1.66*	0.19
Symptom					
Fatigue	61±25 (43.9-78.0)	55±18 (50.6-60.2)	57±18 (48.8-65.6)	0.41*	0.66
Nausea/ vomiting	27±28 (8.3-45.8)	11±21 (5.6-16.6)	11±19 (3.1-26.3)	4.43†	0.10
Pain	57±34 (34.6-79.7)	45±26 (37.7-51.6)	54±27 (42.3-66.4)	2.90†	0.23
Dyspnea	15±27 (-3.1-33.1)	13±21 (6.9-18.1)	17±27 (5.1-29.5)	0.26†	0.87
Insomnia	45±27 (27.1-62.9)	30±24 (23.8-36.5)	42±26 (30.1-54.3)	5.91†	0.06
Appetite loss	54±27 (36.1-71.9)	31±25 (24.1-37.4)	33±18 (24.7-41.2)	8.32†	0.01‡
Constipation	27±29 (7.6-46.3)	27±26 (20.3-34.2)	28±24 (17.3-39.2)	0.06†	0.96
Diarrhea	3±10 (-3.6-9.6)	3±13 (-0.5-6.2)	2±7 (-1.7-4.8)	0.27†	0.87
Financial difficulty	24±37 (-0.5-48.7)	26±32 (17.7-34.6)	22±26 (10.1-33.9)	0.20†	0.9
Global QOL§	30±17 (18.9-41.1)	42±18 (37.5-46.8)	36±18 (27.9-44.3)	4.70†	0.09

*: *F*-statistic value; †: χ^2 value (df: 2), ‡: statistically significant (p≤0.05), §: Quality of Life

Table IV: Barthel and EORTC QLQ C30 mean scores of unevaluated, CR/nCR, PR/VGPR and relapsed groups with their comparison (ANOVA and Kruskal Wallis).

Variables	Not evaluated, mean ± SD (95% CI)	CR/nCR, mean ± SD (95% CI)	PR/VGPR, mean ± SD (95% CI)	Relapsed, mean ± SD (95% CI)	$\chi^2/F_{3,86}$	P value
Barthel score	80±24 (71.5-88.2)	87±18 (77.3-92.1)	86±17 (76.4-94.9)	79±23 (68.8-88.7)	0.71*	0.54
EORTC function						
Physical	48±25 (39.8-56.8)	55±23 (43.3-67.5)	53±19 (42.3-63.9)	43±23 (33.8-53.2)	3.08†	0.37
Role	49±26 (40.1-58.3)	64±26 (50.2-78.4)	53±23 (40.4-65.6)	48±28 (35.7-59.6)	4.85†	0.18
Emotional	63±20 (56.1-69.6)	64±21 (53.5-75.6)	58±16 (49.4-67.4)	55±21 (46.6-64.3)	0.96*	0.41
Social	53±28 (43.2-62.8)	62±31 (45.8-78.6)	57±27 (42.3-72.5)	44±22 (34.9-53.2)	4.57†	0.20
Cognitive	77±20 (70.0-83.7)	79±19 (68.7-88.9)	84±15 (75.8-92.4)	77±19 (69.5-85.5)	0.56*	0.64
Symptom						
Fatigue	59±22 (52.1-66.9)	53±17 (43.7-61.7)	52±17 (42.7-62.1)	57±17 (49.9-64.9)	0.74†	0.53
N/V§	19±28 (9.9-28.9)	8±15 (0.4-16.1)	9±15 (0.4-17.1)	10±18 (2.6-17.9)	2.67†	0.44
Pain	50±29 (40.7-60.4)	33±21 (21.9-44.1)	46±27 (3.1-61.5)	57±26 (46.1-68.5)	7.33†	0.05‡
Dyspnea	16±27 (6.8-25.4)	12±16 (3.6-21.2)	9±15 (0.43-17.2)	15±26 (4.3-25.9)	0.43†	0.93
Insomnia	38±25 (28.9-46.5)	23±26 (8.7-36.7)	26±18 (16.2-36.6)	44±25 (33.4-54.7)	8.81†	0.03‡
Appetite loss	44±26 (35.2-53.4)	20±27 (6.5-34.8)	26±18 (16.2-36.6)	33±19 (24.8-41.2)	12.12†	0.007‡
Constipation	25±29 (15.5-35.4)	29±27 (14.7-43.1)	24±19 (13.4-35.1)	32±25 (21.2-42.1)	1.24†	0.74
Diarrhea	5±16 (-0.9-10.3)	0 (0)	2±8 (-2.5-6.9)	1±7 (-1.5-4.2)	1.70†	0.63
Financial prob	30±36 (17.8-42.7)	16±24 (3.7-29.3)	24±32 (6.6-41.9)	23±27 (12.1-34.6)	1.35†	0.71
Global QOL‖	35±16 (29.8-40.9)	51±18 (41.3-60.1)	45±15 (37.1-53.4)	34±19 (25.8-41.6)	11.57†	0.009*

*: F-statistic value; †: χ^2 value (df: 3), ‡: statistically significant (p≤0.05), §: Nausea/Vomiting; ‖: Quality of life.

Table 5: Barthel and EORTC QLQ C30 mean scores of groups with participants diagnosed <6 months, 6-12 months, 12-24 months and >24 months with their comparison (ANOVA and Kruskal Wallis).

Variables	<6 months, mean ± SD (95% CI)	6-12 months, mean ± SD (95% CI)	12-24 months, mean ± SD (95% CI)	>24 months, mean ± SD (95% CI)	$\chi^2/F_{3,86}$	P value
Barthel score	82±23 (74.9-88.5)	79±20 (68.1-89.9)	76±28 (52.9-99.6)	87±16 (78.8-95.1)	0.57[*]	0.63
EORTC function						
Physical	49±24 (42.6-56.7)	47±22 (35.2-60.0)	36±23 (16.8-55.8)	54±19 (44.8-63.7)	3.08[†]	0.37
Role	50±27 (42.-58.2)	54±27 (39.2-69.2)	43±28 (20.2-66.8)	59±24 (46.8-71.0)	2.12[†]	0.54
Emotional	61±20 (55.6-67.1)	61±20 (52.4-72.9)	52±11 (42.5-61.0)	61±22 (49.9-71.9)	0.56[*]	0.64
Social	53±29 (44.9-61.9)	57±29 (41.2-73.8)	39±23 (19.7-58.8)	54±20 (44.1-64.4)	2.30[†]	0.51
Cognitive	78±20 (72.2-83.7)	82±16 (72.9-90.9)	72±20 (55.9-89.1)	80±16 (71.9-88.5)	0.50[*]	0.68
Symptom						
Fatigue	57±21 (51.4-63.5)	56±13 (48.6-63.8)	61±21 (43.9-78.7)	52±16 (44.0-60.5)	0.49[*]	0.68
N/V[‡]	17±25 (10.0-24.4)	7±14 (0.1-15.3)	0 (0)	13±20 (2.8-22.8)	5.52[†]	0.13
Pain	49±29 (40.5-57.3)	44±21 (32.7-55.3)	53±30 (28.2-79.5)	48±28 (34.7-62.9)	0.53[†]	0.91
Dyspnea	13±23 (6.8-20.2)	13±21 (1.6-24.8)	12±24 (-8.2-32.9)	16±26 (3.6-29.4)	0.23[†]	0.97
Insomnia	36±25 (28.5-42.9)	26±22 (14.0-38.8)	37±21 (19.4-54.8)	38±30 (23.3-53.8)	2.04[†]	0.56
Appetite loss	41±25 (33.7-48.5)	26±22 (14.0-38.8)	16±17 (1.8-31.3)	29±22 (18.2-40.4)	10.03[†]	0.01[§]
Constipation	27±28 (18.8-35.1)	26±25 (12.2-40.6)	37±21 (19.4-54.8)	25±21 (15.1-36.3)	1.45[†]	0.69
Diarrhea	3±14 (-0.6-7.4)	2±8 (-2.5-6.9)	4±11 (-5.6-13.9)	0 (0)	1.78[†]	0.61
Financial difficulty	26±35 (16.3-36.5)	22±27 (7.1-36.9)	41±23 (21.7-60.8)	16±23 (4.9-28.1)	4.52[†]	0.21
Global QOL[‖]	38±16 (33.5-42.7)	44±23 (31.2-56.9)	35±19 (19.5-51.0)	40±18 (31.2-49.4)	1.30[†]	0.72

*: *F*-statistic value; †: χ^2 value (df: 3), ‡: Nausea/ vomiting; ‖: Quality of life, §: statistically significant ($p \le 0.05$).

DISCUSSION

In this study, most of the participants (>50%) were found to have low QOL with reduced functioning in all aspects. This was irrespective of the disease and treatment status or duration from diagnosis.

Only a few studies have assessed the health related QOL with the use of novel agents and chemotherapy in patients with MM.[29] In these studies, QOL has been identified as a primary outcome apart from response and survival in such patients. Various scales for assessment like EORTC QLQ C30 (most common) with MY20, Functional assessment of cancer therapy, etc., have been used. Studies have compared QOL at before initiation of treatment, and thereafter assessed at specified intervals, during the induction phase, at end of induction and maintenance phases.

The results of previous studies have reflected an improvement in HRQOL with treatment, with the MID or clinical meaningful response being achieved during induction phase; with the peak reaching at the end of induction phase. Thereafter scores being maintained below the peak throughout the maintenance phase. The MID for HRQOL score was taken as a change of 6-17 points or ≥5 points of mean score.[29] The values for MID were obtained from the standard error of measurement. The MY20 module, which depicts the disease symptoms, side effects of treatment, future perspectives and body image, has depicted increased scores for side effects of treatment in various studies. But the increased scores for adverse effects had no impact over improvement in HRQOL score with treatment in such patients.[29] A few studies have also shown to have improved QOL score in patients who received inpatient rehabilitation.[32] Thus we require assessing further, if rehabilitation could be started at an earlier stage, so as to improve the QOL and functioning. For this, we required to understand the key deficit areas as per the QOL and function for all patients, new and relapsed both, and those with any clinical response.

The functioning and QOL scores in the present study were assessed as per the treatment status, clinical response, and duration from being diagnosed with MM. Though the study population did not represent the whole, but only a part of the Indian population, the scores helped in identifying the key features related to reduced QOL and functioning in this subset, for which rehabilitation plan can be assessed and established further.

The median age of patients in this study was about a decade earlier as compared to those reported from North America and Western Europe.[4] Younger median age in our population reflects the younger population being diagnosed with MM. The prevalence of disease symptoms and reduced functioning were found comparable for naïve, those on 1st line treatment and patients who were on salvage therapy for relapse, with no statistically significant difference between the groups. Significantly higher proportion of patients in each group reported backache, bone pain, fatigue, appetite loss, constipation, insomnia, depression, and reduction in role, emotional, social and cognitive functioning along with ADL. All the patients in each group reported having reduced physical functioning and QOL. Hair loss was higher in those on 1st line treatment, whereas paresthesia was present in half of the patients on salvage therapy for relapse. All these findings reflect the higher prevalence of morbidity in all patients irrespective of treatment or disease status.

The MID with improved score was found in patients on 1st line treatment for physical, role, cognitive and emotional function, fatigue, nausea and vomiting, pain, insomnia, appetite loss and global QOL, in comparison to naïve patients; and for pain, insomnia, social function and global QOL in comparison to relapsed patients. Overall, global QOL and pain scores were found to be improved in patients who were on 1st line treatment. Though the difference between scores were found to be in the range of 5-20, which was not higher than the MID. These findings reflect some improvement in symptoms and functioning with the initiation of treatment (majorly being on novel agents and chemotherapy). But the improvement could not reach to a significant high level. Though, statistically significant difference between the group means could be found only for the scores for appetite loss, which could be due to less number of patients in the cohort.

With respect to clinical response, relapsed patients were found to have low mean scores for global QOL and physical, role and social function, with high scores for pain, insomnia and appetite loss, as compared to patients with CR/nCR and PR/VGPR. Emotional function score in patients with a relapse was low in comparison to CR/nCR, whereas cognitive functioning was low in comparison to PR/VGPR. Patients in CR/nCR had improved scores for role, emotional and social function, pain and global QOL in comparison to those with PR/VGPR. Thus, patients in the relapsed status had lower function, more symptoms and low QOL as compared to CR/nCR and PR/VGPR status. Overall QOL was better in the CR/nCR. This reflects improvement in QOL with the treatment. These findings were in the relation to the MID.

Patients with duration of diagnosis between 12-24 months had lower physical, role, social and emotional functioning as compared to those diagnosed less than 12 months, and more than 24 months. The global QOL was low as compared to patients diagnosed between 6-12 months. Patients diagnosed less than 6 months had higher mean score for nausea and vomiting, and appetite loss. The findings indicate improvement in functioning during induction, with reduction in QOL post the induction phase or during maintenance phase. It reflects improvement following initiation of treatment. These findings of change in scores with respect to MID was not comparable to statistically significant mean difference between the groups, found only for appetite loss, which could be explained owing to low sample size.

There was no change with respect to MID found for Barthel scores in any of the categories above. Barthel scale used in this study is an ordinal scale of functional measure, with respect to motor function inclusive of personal care. As it is an ordinal scale, so any change of score at different points may not mean the same.[27] Numerically equal gains may have different meaning based on baseline clinical status.[33] The steps on Barthel scale are large, so any small change may not be considered. It also has a ceiling effect, which makes people score higher and still be dependent in daily activities.[27] Our study has reflected the same, wherein participants having scored higher in Barthel mobility assessment, but still being low in functioning, as reflected in the EORTC scores.

Table 6: EORTC QLQ C30 mean scores of the whole MM cohort in the present study and the rest of the world.

Subscales (EORTC)	Mean score present study	UK myeloma[20]	Reference myeloma[24]	Reference all cancer patients[24]
Global QOL	39	60.0	55.7	61.3
Physical function	48.7	62.7	67.7	76.7
Role function	52.1	55.0	60.1	70.5
Social function	53.0	60.0	63.2	75
Emotional function	60.0	73.3	71.3	71.4
Cognitive function	79.1	73.3	78.1	82.6
Fatigue	56.1	44.4	48.7	34.6
Pain	49.4	38.3	47.1	27.0
Insomnia	34.8	36.7	28.9	28.9
Appetite loss	33.7	20.0	23.2	21.1
Constipation	26.4	20.0	23.2	21.1
Financial difficulty	25.7	23.3	16.1	16.3
Dyspnea	13.5	30.0	26.0	21.0
Nausea/vomiting	12.8	10.0	10.5	9.1
Diarrhea	2.5	11.7	9.6	9.0

Thus, lower functioning in all aspects with lower QOL was found to be there in all patients, but severely in newly diagnosed patients not receiving any treatment, those with a relapsed status and those evaluated between 12-24 months of diagnosis (after the end of induction phase). Though treatment had shown improvement in the mean scores of functioning and QOL, but the improvement or change of scores was found to be within the MID of scores. So, a higher significant gain was not found. Similar results have been found in other studies, suggesting improvement in QOL with treatment, but the maximum improvement being in the moderate range. Compared to earlier studies or reference patients,[24] patients in present study had lower physical, role and social functioning along with a lower global QOL score. There was a higher incidence of fatigue, insomnia, appetite loss and financial difficulty as shown above in the Table 6.

Most patients in this study reported having anxiety and depression. Depression scoring used in the QOL scale has only been identified with patients' self-reported depressed mood, rather than a standard criteria or scale which requires to be fulfilled to diagnose a patient with depression. This limitation in our study probably labeled more number of patients to be depressed. However, this aspect is frequently ignored. Majorly, patients were worried for the future and the status of having a malignancy, which may decline the emotional state. So, patients may require appropriate psychological counseling, medications and appropriate referral. However, these findings are similar to those found in other studies.[18-20,34-36] The requirement of mobility assistive device and other aids for activities of daily living has also to be ascertained pertaining to the high number of patients with vertebral collapse and tenderness of spine (>50%).

Future research may be needed to assess if rehabilitation interventions can further improve QOL and functioning in such patients, and when should they be initiated during the course of management. An individualized assessment for new, relapsed and patients with any clinical response will help in devising their rehabilitation plan for a higher improvement in QOL.

There were some limitations in the study. First, comparison of results of present study with other population groups may not be appropriate, as it depends on the demographic profile, assessment technique and stage of the disease.[20,24] Moreover, the QOL also depends on timing of assessment (during, pre and post treatment), family support and financial status etc. Second, comparison may also require a higher sample size. Third, reduced emotional functioning may affect other functioning and symptoms like perception of pain, insomnia, fatigue etc. and their interrelationship was not studied. Further, the effect of co morbidity on scores was not found.

CONCLUSION

Present study confirms low level of QOL and functioning with respect to ADL and physical, role, emotional, social and cognitive function in majority of patients. Treatment alone with novel agents and chemotherapy may result in an inadequate improvement in QOL and functioning. This affects the overall clinical enhancement which could have been improvised with inclusion of rehabilitative services. Thus, early identification and evaluation of details of deficit in functioning can lead to focused interventions, with subsequent formulation of rehabilitation plan in respective area of deficit. This study helps to understand the importance of a well targeted rehabilitation, the incorporation of which may improve the overall functioning of patients suffering from a debilitating disease, helping to provide them with a level QOL.

ACKNOWLEDGEMENTS

Author would like to thanks to who were participated in the study and helped to facilitate the research process.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Kyle RA, Rajkumar SV. Multiple Myeloma. Blood. 2008;111:2962-72.
2. Comert M, Guines AE, Satin F, Saydem G. Quality of life and supportive care in Multiple Myeloma. Turk J haematol. 2013;30(3):234-46.
3. Kumar L, Verma R, Radhakrishnan VR. Recent advances in management of multiple myeloma. Natl Med J India. 2010;23:210-8.
4. Rebecca S, Kimberley M, Ahmedin J. Cancer statistics, 2017. CA Cancer J Clin. 2017;67:7-30.
5. Charles A, Lloyd E. Blood Disorders. In: Stephen J, Maxine A, Michael W, (ed). Current Medical Diagnosis and Treatment. 56th ed. San Francisco (CA): McGraw-Hill; 2015:499-545.
6. Palumbo A, Rajkumar SV, San Miguel JF, Larocca A, Niesvizky R, Morgan G et al. International Myeloma Working Group consensus statement for the management, treatment, and supportive care of patients with myeloma not eligible for standard autologous stem-cell transplantation. J Clin Oncol. 2014;32(6):587-600.
7. Bergsagel PL, Mateos MV, Gutierrez NC, Rajkumar SV, San Miguel JF. Improving overall survival and overcoming adverse prognosis in the treatment of cytogenetically high-risk multiple myeloma. Blood. 2013;121(6):884-92.
8. Castelli R, Gualtierotti R, Orofino N, Losurdo A, Gandolfi S, Cugno M. Current and Emerging Treatment Options for Patients with Relapsed

Myeloma. Clin Med Insights Oncol. 2013;7:209-19.

9. Ocio EM, Richardson PG, Rajkumar SV. New drugs and novel mechanisms of action in multiple myeloma in 2013: a report from the International Myeloma Working Group (IMWG). Leukemia. 2014;28(3):525-42.
10. Kouroukis CT, Baldassarre FG, Haynes AE, Imrie K, Reece DE, Cheung MC. Bortezomib in multiple myeloma: a practice guideline. Clin Oncol (R Coll Radiol). 2014;26(2):110-19.
11. Scott LJ. Pomalidomide: a review of its use in patients with recurrent multiple myeloma. Drugs. 2014;74(5):549-62.
12. Fratino L, Rupolo M, Mazzuccato M, Berretta M, Lleshi A, Tirelli U et al. Autologus stem cell transplatation as a care option in elderly patients. Anticancer Agents Med Chem. 2013;13(9):1419-29.
13. Who.int. Geneva (CH): WHO. Rehabilitation. Available at: http://www.who.int/topics/rehabilitation/en/. Accessed on 18 Oct 2021.
14. Galvao DA, Newton RU. Review of exercise intervention studies in cancer. J Clin Oncol. 2005;23:900-909.
15. Mikkelsen TH, Sondergaard J, Jensen AB, Olesen F. Cancer rehabilitation: psychosocial rehabilitation needs after discharge from hospital. Scand J Prim Care. 2008;26(4):216-21.
16. Groeneveldt L, Mein G, Garrod R, Jewell AP, Van Soeren K, Stephens R et al. A mixed exercise training programme is feasible and safe and may improve quality of life and muscle strength in multiple myeloma survivors. BMC Cancer. 2013;13:31.
17. Holm LV, Hansen DG, Johansen C, Vedsted P, Larsen PV, Kragstrup J et al. Participation in cancer rehabilitation and unmet needs: a population-based cohort study. Support Care Cancer. 2012;20(11):2913-24.
18. Johnsen AT, Tholstrup D, Petersen MA, Pedersen L, Groenvold M. Health related quality of life in a nationally representative sample of hematological patients. Eur J Haematol. 2009;83(2):139-48.
19. Movsas SB, Chang VT, Tunkel RS, Shah VV, Ryan LS, Millis SR. Rehabilitation needs of an inpatient medical oncology unit. Arch Phys Med Rehabil. 2003;84(11):1642-6.
20. Molassiotis A, Wilson B, Blair S, Howe T, Cavet J. Unmet supportive care needs, psychological well-being and quality of life in patients living with multiple myeloma and their partners. Psychooncology. 2011;20(1):88-97.
21. Slovacek L, Slovackova B, Pavlik V, Hrstka Z, Maingova Z, Jebavy L et al. Health-related quality of life in multiple myeloma survivors treated with high dose chemotherapy followed by autologous peripheral blood progenitor cell transplantation: a retrospective analysis. Neoplasma. 2008;55(4):350-55.
22. Fayers P, Aaronson NK, Bjordal K, Groenvold M, Crran D, Bottomley A et al. The EORTC QLQ-C30 Scoring Manual. Brussels: European Organization for Research and Treatment of Cancer. 2001. Available at: https://www.eortc.be/qol/files/SCManualQLQ-C30.pdf. Accessed on 18 Oct 2021.
23. Cocks K, Cohen D, Wisloff F, Sezer O, Lee S, Hippe G et al. An international field study of the reliability and validity of a diseases specific questionnaire module (the QLQ-MY20) in assessing the quality of life of patients with multiple myeloma. Eur J Cancer. 2007;43:1670-8.
24. Scott NW, Fayers PM, Aoronson NK, Bottomley A, Graeff A, Groenvold et al. EORTC QLQ-C30 Reference Values. Brussels: 2008. Available at: https://www.eortc.org/app/uploads/sites/2/2018/02/reference_values_manual2008.pdf. Accessed on 18 Oct 2021.
25. Mahoney F, Barthel DW. Functional evaluation: The Barthel Index. Md State Med J. 1965;14:56-61.
26. Stroke center.org. Dallas (TX): The Internet Stroke Center. Available at: www.strokecenter.org/professionals/stroke-diagnosis/stroke-assessment-scales/barthel/. Accessed on 19 Oct 2021.
27. Young J. Rehabilitation: General principles. In: Fillit HM, Rockwood K, Woodhouse K, (ed). Brocklehurst's Textbook of Geriatric medicine and Gerontology. 7th ed. Philadelphia (PA): Elsevier. 2010:1-21.
28. Lewis C, Shaw K. The (Original) Barthel Index of ADLs. Physical therapy Rehab Med. 2006;17(21):8.
29. Sonneveld P, Verelst SG, Lewis P, Grey-Schopfer V, Hutchings A, Nixon V et al. Review of health-related quality of life data in multiple myeloma patients treated with novel agents. Leukemia. 2013;27:1959-69.
30. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. Int Disabil Stud. 1988;10(2):61-3.
31. Bairwa M, Rajput M, Sachdeva S. Modified Kuppuswamy's Socioeconomic Scale: Social researcher should include updated income criteria, 2012. Indian J Community Med. 2013;38(3):185-6.
32. Gan JH, Cim CYL, Santorelli LA. The effectiveness of exercise programmes in patients with multiple myeloma: A literature review. Critical Reviews in Oncology/Hematology. 2016;98:275-89.
33. Stucki G, Daltry L, Katz JN, Johannesson M, Liang MH. Interpretation of change scores in ordinal clinical scales and health status measures: the whole may not equal the sum of parts. J Clin Epidemiol. 1996;49(7):711-7.
34. Parker PA, Baile WF, De Moor C, Cohen L. Psychosocial and demographic predictors of quality of life in a large sample of cancer patients. Psychooncology. 2003;12:183-93.
35. Kim YM, Kim DY. Cancer Rehabilitation: Experience, Symptoms, and Needs. J Korean Med Sci 2011;26(5):619-24.

36. Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. Cancer. 2008;112(11):2577-92.

Cite this article as: Saha V, Rahman HMC. Quality of life in patients with multiple myeloma: early rehabilitation is need of the hour. Int J Sci Rep 2022;8(2):43-52.