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Health-related quality of life in multiple myeloma in Kurdistan Iraq

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Abstract:

BACKGROUND: Health-related quality of life (HRQoL) in multiple myeloma (MM) gained increasing importance to ensure that the improved survival is associated with improved life quality.

OBJECTIVES: The aim of this study was to assess the HRQoL in a cohort of myeloma patients from Kurdistan region in Iraq.

MATERIALS AND METHODS: This observational, cross-sectional, multi-center study enrolled 138 patients with symptomatic MM patients. The patients' records were retrieved and they were also clinically assessed and appropriately investigated at the time of enrolment. HRQoL was assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Multiple Myeloma module (EROTC QLQ-MY20.

RESULTS: The 138 patients included had a mean age of 60.4 years and included 83 males and 55 females. Significant predictors of worse HRQoL disease symptoms and side effects of treatment domains included increasing age, female sex, and increase number of treatment courses. Other predictors associated with worse disease symptom domain include presence of bone lesions and nonsecretory myeloma versus light chain myeloma. Basic parameters including the concentration of monoclonal band, hemoglobin, serum creatinine, calcium, and albumin were not significant associated with scores in any of the domain while serum LDH was associated with worse side effects of treatment scores. Furthermore, it was noted that patients who had underwent autologous stem cell transplants had better HRQoL in all domains compared to other modalities of therapy, though this did not reach significance.

CONCLUSIONS: HRQoL in MM treated in Iraqi Kurdistan is not much different from their Western counterparts and several predictors of worse QoL were identified in this cohort of patients.

Keywords:

Health-related quality of life, multiple myeloma, quality of life questionnaire-multiple myeloma module

Introduction

Health-related quality of life (HRQoL) have recently gained widespread attention in the assessment of patients' perspective toward their management and treatment options in a multitude of hematological disorders.[1] They are also gained importance in the process of new drugs approvals in these disorders.[2] Multiple myeloma (MM) is a bone marrow-based multifocal plasma cell neoplasm, usually associated with an M-protein in serum and/or urine.[3] It is essentially an incurable malignancy, though its prognosis has improved markedly over the past 20 years as new treatment options continue to be introduced.[4]

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The current therapy protocols of newly diagnosed plasma cell myeloma involves induction treatment with repeated cycles of two or more drug combinations followed in legible patients by autologous stem cell transplant.[5,6] However, eventually, the disease will progress or relapse, and initiation of a rescue treatment will be necessary.[7] Different therapeutic modalities cause a multitude of adverse effects which may have an impact on the patients' quality of life.[4,8-10] Treatment in MM is complex and involves several factors such as disease stage, prognostic risk stratification, and severity of myeloma symptoms and complications.[7,11-13]

MM is a frequently encountered hematological malignancy in Iraq with a multitude of the management options available. No study has addressed the HRQoL in this disease in our region. Thus, the current study had been initiated to tackle such paucity.

Subjects and Methods

A total of 138 patients diagnosed with MM and visiting the three main hematology/oncology centers in Iraqi Kurdistan (Hiwa Hospital-Sulemiani, Azadi hospital-Duhok and Nana Kelly Hospital in Erbil) were available for inclusion in this cross-sectional study. The patients records were retrieved and their clinical, radiological, and laboratory data at diagnosis were recorded. The patients were assessed clinically, and various laboratory investigations were performed at the time of enrollment. Furthermore, the treatment protocols were reviewed in detail in each, and the current therapy was recorded. The original diagnosis of Myeloma was based on the WHO criteria which is basically marrow plasma cells in excess of 10% with evidence of organ damage (hypercalcemia, increased creatinine, bone lesions, and anemia).[3]

Myeloma-specific HRQoL instrument namely the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Multiple Myeloma module (EORTC QLQ-MY20) was used in all patients. This questionnaire has been validated, and is recommended as a MM disease specific instrument.[14] The module consists of 20 questions that cover four myeloma-specific HRQoL domains: Disease Symptoms, Side Effects of Treatment, Future Perspective, and Body Image. Three of these domains are multi-item scales: disease symptoms (includes bone aches or pain, back pain, hip pain, arm or shoulder pain, chest pain, and pain increasing with activity); side effects of treatment (includes drowsiness, thirst, feeling ill, dry mouth, hair loss, upset by hair loss, tingling hands or feet, restlessness/agitation, acid indigestion/heartburn, and burning or sore eyes); and future perspective (includes worry about death and health in the future, and thinking about illness). The body image scale, on the other hand, is a single-item scale that tackles physical attractiveness. Average of each of EROTC QLQ-MY20 domain scores is calculated, and transformed linearly to a score ranging from 0 to 100. A high score for Disease Symptoms and Side Effects of Treatment represents a high level of symptomatology or problems, whereas a high score for future perspective and body image represents better outcomes.

Informed consent was obtained from all recruited patients, and the study was approved by the ethical committee at the Kurdistan board of medical Specialties in Erbil, Iraq.

Statistical analysis utilized the Statistical Package for the Social Sciences (SPSS) (SPSS, Illinois, USA). Means (standard deviations) or range and medians were used as appropriate. Pearson correlations were used evaluate correlation between continuous variables, while Mann–Whitney U test and Kruskal Wallis test were used as non-parametric tests to determine associations, as appropriate. A $P < 0.05$ was considered statistically significant.

Results

The age of the enrolled patients ranged from 35 to 89 years (mean 60.4 ± 11.5 years), and included 83 males and 55 females. Table 1 shows the main characteristics of the enrollees at diagnosis.

The HRQoL was evaluated in all 138 enrolled patients using EROTC QLQ-MY20 myeloma-specific instrument. The evaluation was done at a median of 24 months from diagnosis (range 1–106 months), and the numbers of therapy courses and current treatment received at the time of enrolment is presented in Table 2. The mean and standard deviation of each of the four domains of EROTC QLQ-MY20 instrument namely: disease symptoms, side effects of treatment, body image, and future perspectives are shown in Table 3.

Correlation between EROTC QLQ-MY20 domain scores and various continuous variables using Pearson correlation revealed that disease symptoms and side effects of treatment scores increased with increasing age and with number of treatment courses received, and these correlations were significant [Table 4]. Other significant correlations include a positive correlation between time since diagnosis and future perspective as well as LDH with side effects of treatment. Otherwise, none of the basic continuous parameters outlined in Table 4 is correlated to any of the four domains of EROTC QLQ-MY20 instrument. Furthermore, it was found that

Table 1: The main features of the 138 enrolled patients at diagnosis

Parameter	Mean (SD)
Age, mean±SD	60.4±11.5
Sex (male:female)	1.5:1
Hb (g/dl), mean±SD	10.2±2.1
WBC (×10^9/L), mean±SD	7.6±4.5
Platelets (×10^9/L), mean±SD	217±90
ESR (mm/h), mean±SD	90.3±40.5
M-band Serum detected* (%)	117 (84.8)
M-band concentration (g/dL) (%)	3.02 (2.23)
Bence-Jones Protein in Urine (of 127 tested)* (%)	75 (59.05)
Nonsecretory myeloma*(%)	8 (5.8)
Light chain myeloma*(%)	13 (9.4)
Serum immunoglobulin (IF) (of 93 tested)*	
IgG*, mean±SD	67±72.0
IgA*, mean±SD	24±25.8
IgM*, mean±SD	1±1.1
Biclonal (IgG/A)*, mean±SD	1±1.1
Serum creatinine (mg/dl), mean±SD	1.7±2.9
Bone lesions* (%)	109 (78.99)
Calcium (mg/dl), mean±SD	9.4±1.5

*n (%). SD=Standard deviation, Hb=Hemoglobin, ESR=Erythrocyte sedimentation rate, EBC=White blood cell, Ig=Immunoglobulin

Table 2: The time since diagnosis, courses received and current therapy at the time of enrolment in 138 patients with myeloma

Parameter	Range (median)
Time since diagnosis (months)	1-106 (24)
Number of courses received	1-12 (4)
Therapy at time of enrollment	
Proteasome inhibitors±chemotherapy	36
Immunomodulatory agents (IMiDs) maintenance	58
IMiDs + chemotherapy	7
ASCT followed by IMiDs + Chemotherapy	11
Autologous stem cell transplant, currently off therapy	7
Off therapy	19

IMiDs=Immunomodulatory drugs, ASCT=Autologous stem cell transplant

Table 3: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Multiple Myeloma module scores at the time of enrolment of 138 patients with Myeloma

Domain	Mean±SD
Disease symptoms	28.41±21.40
Side effects of treatment	25.12±17.13
Future perspective	66.83±28.98
Body image	66.43±33.09

SD=Standard deviation

females have higher disease symptoms scores compared to males, finding which was significant ($P = 0.001$), while there were no significant correlations with other domain scores. The presence of bone lesions was also associated with higher disease symptom scores ($P = 0.009$), but not with other domain scores. When the type of monoclonal immunoglobulin was assessed (IgG versus IgA), it was found that disease symptoms scores were higher in those with IgA, though it just failed to reach significance ($P = 0.056$). Moreover, a comparison between nonsecretory myeloma, light chain myeloma, and myelomas with serum monoclonal bands revealed that the highest disease symptom scores were in those with non-secretory myeloma and the least were in light chain myeloma, a finding which was significant ($P = 0.045$), while other domain scores were not significantly different. As shown in Table 5, the mean ranks of the four domain scores relevant to modality of therapy at the time of enrollment, it is clear that the least disease symptoms and side effect scores were encountered in those who have underwent autologous stem cell therapy and are off therapy, while the highest ones are in those on IMiDs. Moreover, the highest scores for body image and future perspective were in those who had ASCT and are on no medication now. Overall, however, none of the variations was significant

Discussion

MM remains and despite the introduction of novel agents and a multitude of drug combinations an incurable disease. The main aim in the management is to prolong survival, delay progression, and deal with various complications by providing rather continuous therapy. This leads to an increasing role of health-related quality of life tools and scrutiny of their methodological aspects to ensure not only prolonged survival, but also a better quality of life and suitability of novel agents or drug combinations in management.[15]

The mean scores obtained for the disease symptoms domain of 28.4% in the current study were comparable to reports from some European countries of 23%–36.6%. The same could be also said of side effects of therapy domain score, where scores of 25.1% was observed, compared to 16.8%–30% in European countries. On the other hand, our rates for future perspectives of 66.8% are also similar to those in Western counterparts at 59.9%–73.3%. Body image scores were lower than some European reports of 77.9%–82.3%, but nearer to others of 63.3%.[16-19] The overall similarities in the HRQoL results between our study and those of developed countries may be related to similarities in the clinical characteristics and treatment modalities used in Europe and our country.

The current study documented that disease symptoms and side effects of the treatment domains of HRQoL were correlated with age and that females fared worse than males. These finding has also been documented by previous studies including studies from various European countries, where symptoms tend to be more severe in older patients and in females as opposed to males.[16,20-22]

Table 4: Pearson correlation Coefficients and Nonparametric *P* values of some of the major variables and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Multiple Myeloma module domain scores (significant *P* values are bold)

Domain	Pearson correlation coefficient (*P*)									Nonparametric *P*			
	Age	Time since Dx	Number of courses	M-band	Hb	Creat	Cal	Alb	LDH	Sex	IgG versus IgA	NSM versus LCM	Bone lesions
Disease symptoms	0.281 (**0.001**)	−0.055 (0.521)	0.291 (**0.001**)	−0.094 (0.276)	−0.110 (0.198)	−0.003 (0.970)	−0.049 (0.564)	0.123 (0.150)	0.081 (0.343)	**0.001**	0.056	**0.045**	**0.009**
Side effects of treatment	0.190 (**0.026**)	0.125 (0.145)	0.181 (**0.034**)	−0.039 (0.652)	−0.156 (0.067)	−0.033 (0.704)	−0.100 (0.242)	0.176 (0.059)	0.201 (**0.018**)	**0.038**	0.172	0.238	0.791
Body image	−0.002 (0.978)	−0.012 (0.888)	−0.15 (0.078)	0.140 (0.103)	0.083 (0.335)	0.163 (0.056)	0.002 (0.983)	−0.03 (0.723)	−0.224 (0.008)	0.133	0.467	0.697	0.136
Future perspective	0.091 (0.288)	0.185 (**0.03**)	−0.138 (0.107)	0.045 (0.601)	0.091 (0.288)	0.032 (0.711)	0.003 (0.975)	0.034 (0.695)	−0.119 (0.165)	0.130	0.938	0.336	0.089

Dx=Diagnosis, Hb=Hemoglobin, Creat=Creatinine, Cal=Serum Calcium, Alb=Albumin, NSM=Non-Secretory Myeloma, LCM=Light chain Myeloma, Ig=Immunoglobulin

The increase of disease symptoms and side effects of therapy scores with number of therapy of courses is expected, and has also been documented by previous studies including that of Despiegel *et al*., which demonstrated such an increase in disease symptoms and side effects of therapy in their study on cohort of routine clinical practice of French myeloma patients.[19]

Immunoglobulin A (IgA) myeloma is well known to be worse prognostically from IgG myeloma and is associated with worse cytogenetic categories[23] and it appears to be associated with worse quality of life in the current study, though it did not reach significance.

Myeloma bone disease is one of the most important complications of MM and is due to bone destruction and lack of bone formation mediated by several complex pathways, and it is a main cause of morbidity and disability in this disease.[24] Thus, the observation of significant association with worse quality of life as manifested by increased symptom disease domain scores is quite expected.

The observation that disease symptoms scores were significantly higher in NSM compared to secretory myelomas is likely to be related to the higher frequencies of renal insufficiency, bone lesions, and number of treatment courses received in the former patients. Studies on NSM are really scarce due to rarity of this entity, with contradictory observations regarding biological behavior and prognosis, and in the absence of monoclonal protein difficulties in monitoring as opposed to secretory myeloma.[25]

The observation that patients who were autologous stem cell transplant and are currently off therapy having a rather better quality of life than those receiving other forms of therapy, has been observed by earlier studies from Croatia and the Netherlands.[16,26]

The limitations of the current study include it being a cross-sectional and not a longitudinal study. The latter type of study by following patients up and determining their quality of life through various period in their illness and various forms of therapy maybe more informative. Furthermore, the addition of EORTC QLQ C30 cancer HRQoL assessment to the specific Myeloma EORTC QLQ MY20 would have made the assessment more comprehensive.[19,17]

Conclusions

It appears that HRQoL in Myeloma patients treated by the three major Hematology/Oncology centers in Iraqi Kurdistan is not much different from their Western counterparts and that age, sex, number of treatment

Table 5: Mean Ranks of the four European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Multiple Myeloma module domains in each treatment Category at the time of the interview

Treatment category at the time of interview	Mean ranks of HRQoL EROTC QLQ-MY20 domains			
	Disease symptoms	Side effects of treatment	Body image	Future perspective
Proteasome inhibitors±chemotherapy	69.65	55.54	74.76	64.14
Immunomodulatory agents (IMiDs)	77.63	80.72	64.12	74.02
IMiDs+chemotherapy	67.29	55.36	74.0	59.36
Autologous stem cell transplant followed by IMID + chemotherapy	66.05	74.14	63.91	63.59
Autologous stem cell transplant, currently off therapy	33.64	57.93	97.57	82.07
Off therapy	60.4	68.5	67.18	68.39
P Kruskal-Wallis test	0.102	0.06	0.297	0.72

IMiDs=Immunomodulatory drugs, HRQoL=Health-related quality of life, EROTC QLQ-MY20=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Multiple Myeloma module

courses, bone disease, and the subtype of the Monoclonal band or its absence are predictors of this quality of Life. Future studies should be longitudinal and include more comprehensive HRQoL testing should be encouraged.

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Conflicts of interest
There are no conflicts of interest.

References

1. Basch E, Rogak LJ, Dueck AC. Methods for implementing and reporting patient-reported outcome (PRO) measures of symptomatic adverse events in cancer clinical trials. Clin Therapeutics 2016;38:821-30.
2. European Medicine Agency. Appendix 2 to the Guideline on the Evaluation of Anticancer Medicinal Products in Man. The Use of Patient-Reported Outcome (PRO) Measures in Oncology Studies. EMA/CHMP/292464/2014. London: European Medicine Agency; 2016. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/04/WC500205159.pdf. [Last accessed on 2016 Apr 01].
3. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, *et al*. WHO Classification of Tumors of Haemopietic and Lymphoid tissue. Revised 4th ed.: International Agency for Research on Cancer (IARC) Lyon; 2017.
4. Delforge M, Ludwig H. How I manage the toxicities of myeloma drugs. Blood 2017;129:2359-67.
5. Lenhoff S, Hjorth M, Holmberg E, Turesson I, Westin J, Nielsen JL, *et al*. Impact on survival of high-dose therapy with autologous stem cell support in patients younger than 60 years with newly diagnosed multiple myeloma: A population-based study. Nordic Myeloma Study Group. Blood 2000;95:7-11.
6. Mateos MV, Leleu X, Palumbo A, San Miguel JF. Initial treatment of transplant-ineligible patients in multiple myeloma. Expert Rev Hematol 2014;7:67-77.
7. Laubach J, Garderet L, Mahindra A, Gahrton G, Caers J, Sezer O, *et al*. Management of relapsed multiple myeloma: Recommendations of the International Myeloma Working Group. Leukemia 2016;30:1005-17.
8. Mateos MV. Management of treatment-related adverse events in patients with multiple myeloma. Cancer Treatment Rev 2010;36:S24-32.
9. 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. Psycho Oncol 2011;20:88-97.
10. Boland E, Eiser C, Ezaydi Y, Greenfield DM, Ahmedzai SH, Snowden JA. Living with advanced but stable multiple myeloma: A study of the symptom burden and cumulative effects of disease and intensive (hematopoietic stem cell transplant-based) treatment on health-related quality of life. J Pain Symptom Manag 2013;46:671-80.
11. Mikhael JR, Dingli D, Roy V, Reeder CB, Buadi FK, Hayman SR, *et al*. Management of newly diagnosed symptomatic multiple myeloma: Updated mayo stratification of myeloma and risk-adapted therapy (mSMART) consensus guidelines. Mayo Clin Proceed 2013;88:360-76.
12. Tariman JD, Doorenbos A, Schepp KG, Becker PS, Berry DL. Patient, physician and contextual factors are influential in the treatment decision making of older adults newly diagnosed with symptomatic myeloma. Cancer Treat Commun 2014;2:34-47.
13. Leleu X, Mateos M, Delforge M, Lewis P, Schindler T, Bibson C, *et al*. Assessment of multiple myeloma patient preferences on treatment choices: An international discrete choice study. Blood 2015;126:2086.
14. Cocks K, Cohen D, Wisløff F, Sezer O, Lee S, Hippe E, *et al*. EORTC Quality of Life Group. An international field study of the reliability and validity of a disease-specific questionnaire module (the QLQ-MY20) in assessing the quality of life of patients with multiple myeloma. Europ J Cancer 2007;43:1670-8.
15. Nielsen LK, Abildgaard N, Jarden M, Klausen TW. Methodological aspects of health-related quality of life measurement and analysis in patients with multiple myeloma. Br J Haematol 2019;185:11-24.
16. Ficko SL, Pejsa V, Zadnik V. Health-related quality of life in Croatian general population and multiple myeloma patients assessed by the EORTC QLQ-C30 and EORTC QLQ-MY20 questionnaires. Radiol Oncol 2019;53:337-47.
17. Proskorovsky I, Lewis P, Williams CD, Jordan K, Kyriakou C, Ishak J, *et al*. Mapping EORTC QLQ-C30 and QLQ-MY20 to EQ-5D in patients with multiple myeloma. Health Qual Life Outcomes 2014;12:35.
18. Ludwig H, Moreau P, Dimopoulos MA, Mateos MV, Kaiser M, Hajek R, *et al*. Health-related quality of life in the ENDEAVOR study: Carfilzomib-dexamethasone vs bortezomib-dexamethasone in relapsed/refractory multiple myeloma. Blood Cancer J 2019;9:23.
19. Despiégel N, Touboul C, Flinois A, Saba G, Suzan F, Gonzalez-McQuire S, *et al*. Health-related quality of life in patients with multiple myeloma treatment in routine clinical practice in France. Clin Lymphoma Leukemia 2019;19:e13-38.
20. Schwarz R, Hinz A. Reference Dana for the quality of life questionnaire EORTC QLQ-C30 in the general German population. Europ J Cancer 2001;37:1345-51.

21. Hjermstad MJ, Fayers PM, Bjordal K, Kaasa S. Health related quality of life in the general Norwegian population assessed by the European organization for research and treatment of cancer core quality of-life questionnaire: The QLQ=C30 (+3). J Clin Oncol 1998;16:1188-96.
22. Velenik V, Secerov-Ermenc A, But-Hadzic J, Zadnik V. Health-related quality of life assessed by the EORTC QLQ-C30 questionnaire in the general Slovenian population. Radiol Oncol 2017;51:342-50.
23. Wang L, Jin FY, Li Y, Sun JN, Zhang JJ, Tang R, *et al*. IgA type multiple myeloma, clinical features, and prognosis. Chin Med J (Engl) 2018;131:1249-50.
24. Hameed A, Brady JJ, Dowling P, Clynes M, O'Gorman P. Bone disease in multiple myeloma: Pathophysiology and management. Cancer Growth Metastasis 2014;7:33-42.
25. Dupuis MM, Tuchman SA. Non-secretory multiple myeloma: From biology to clinical management. Onco Targets Ther 2016;9:7583-90.
26. Uyl-de Groot CA, Buijt I, Gloudemans IJ, Ossenkoppele GJ, Berg HP, Huijgens PC. Health related quality of life in patients with multiple myeloma undergoing a double transplantation. Eur J Haematol 2005;74:136-43.