Fear of Recurrence and Somatic Symptom Severity in Multiple Myeloma Patients: An Institution-Based Cross-Sectional Study

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Abstract

Introduction Psychosocial concerns especially fear of cancer recurrence (FCR) is less commonly addressed among patients with multiple myeloma in India. Myeloma being incurable, an understanding of this problem is essential for adequately addressing them.

Objectives To study the prevalence of FCR among patients with multiple myeloma and determine the prevalence of somatic symptoms among patients with multiple myeloma.

Materials and Methods A cross-sectional study was performed at our institution among patients with multiple myeloma who had been on treatment for 1 year or more. The study was conducted between July 01 and July 31, 2015. At least 49 patients were required to be recruited into this study to meet its first objective. Patients were administered fear of cancer recurrence inventory (FCRI) questionnaire and Physical Health Questionnaire-15 (PHQ-15) questionnaire.

Results Sixty-four patients participated in the study. The median age was 60 years (34–80 years) and majority were females ($N = 38$, 60%). ISS staging information was available in 53 (83%) patients. Of 53, 24 (45%) were ISS stage 3, 12 (23%) were ISS stage 2 and remaining stage 1. The mean total FCRI score in the study population was 27.95 (SD: 24.5). Moderate to high levels of FCR were seen in 40% ($N = 26$). Using PHQ-15, 54 (84%) patients had mild or lesser somatic symptom burden. Disease status of patients at the time of this study had a significant statistical association with PHQ-15 scores (mean score in partial response (PR) or more group 6.02 versus 8.00 in less than PR group, $p = 0.02$).

Conclusions Overall, FCR scores and somatic symptom severity were low among our patients with multiple myeloma. However, a significant proportion had moderate to high levels of FCR. Further studies involving larger numbers in a prospective manner required to confirm our findings of fear of cancer recurrence among patients with multiple myeloma.

Keywords
- fear of recurrence
- multiple myeloma
- PHQ-15
- FCRI

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Introduction

Fear of cancer recurrence/relapse (FCR) is one of the most distressing problems among cancer survivors.[1] FCR is defined as the fear or worry that the cancer will return or progress in the same organ or in another part of the body.[2,3] Higher FCR is associated with many problems such as higher physical symptom burden, higher emotional distress, and certain maladaptive behaviors such as alcohol use and lower physical activity.[4] Cancer patients with high FCR have higher unmet supportive care needs and in fact FCR has been one of the most important concerns among cancer patients and survivors.[5,6] FCR has been well studied among cancer survivors who had solid tumors and certain hematological cancers.[7–11]

Multiple myeloma survival has improved over time due to advances in diagnosis, risk stratification, and treatment.[12] However, myeloma is still incurable with patients experiencing multiple relapses and eventually becoming treatment refractory.[13] Myeloma is associated with significant symptom burden due to the nature of the illness and prolonged treatment required.[14] The presence of physical symptoms may be considered as disease not getting controlled or as a sign of reappearance of disease.[15]

There are limited studies exploring the fear of recurrence/relapse among myeloma patients.[13,16,17] With improvement in survival of myeloma, patients are in a state of persistent confrontation with likelihood of progression. In the studies by Hulin et al and Kelly et al, the issue of FCR was studied in a qualitative manner.[13,16] In the study by Xiaochun et al, it was observed that 56.4% of patients with myeloma had a high level of FCR using the Fear of Progression Questionnaire short form.[17] Persistent and high FCR are debilitating. Early recognition of FCR is essential as psychological interventions have shown to alleviate FCR-related symptoms.[18] Studies focusing on FCR in myeloma are lacking from India and hence we decided to undertake this study to assess the baseline prevalence of FCR among patients with multiple myeloma on treatment for 1 year or more and the prevalence of somatic symptoms among them. It is important to have a baseline assessment of the degree of FCR and somatic symptom burdens in our population. This will help us guide our intervention in the future to improve the patient well-being.

Materials and Methods

This cross-sectional study was conducted at the hematology outpatient department (OPD) at our center. All patients with multiple myeloma fulfilling the inclusion criteria mentioned below were recruited in to this study. The study was conducted between July 01 and July 31, 2015. Approval was obtained from the Institutional Review Board (IRB) before the start of the study. A single interviewer who was a qualified psychiatrist administered the fear of cancer recurrence inventory (FCRI) questionnaire and Patient Health Questionnaire-15 (PHQ-15) to all patients who satisfied inclusion criteria and came to OPD during the study period. The interview was conducted in the regional language, i.e., Malayalam. All patients were aware of the diagnosis. Patients were told about the prognosis by the treating doctor if they explicitly asked for such information. Responsible caregivers of patients were appraised about the prognosis. Socioeconomic status assessment was done using modified Kuppuswamy's scale.[19]

Inclusion Criteria

1. Patients with multiple myeloma on treatment for 1 year or more from the date of their diagnosis.
2. Patients who give informed consent to participate in the study.
3. Age 18 years and above.

Exclusion Criteria

1. Patients who were not willing to participate in the study or unwilling to provide informed consent.
2. Patients who were diagnosed with and on treatment for any psychiatric illness.

Fear of Cancer Recurrence Inventory

FCRI is a multidimensional questionnaire. Seven components of fear of cancer recurrence (FCR) along a continuum of severity are evaluated using this questionnaire. There are 42 items and key domains evaluated include triggers, severity, psychological distress, functioning impairments, insight, reassurance, and coping strategies. Each item is rated on a Likert scale ranging from 0 to 4. Score is obtained for each subscale and for the total scale by summing the items. A higher score indicates higher levels of FCR. Score ranges from 0 to 168.[2,6] If FCR mean scores are below the mid-points of these scales, it indicates low-to-moderate levels of FCR.[6] For the purpose of this study, patients were classified as having low FCR if they had FCR scores below the mean score, moderate if observed scores were between mean and 84 (midpoint of the total FCR score), and high if they had observed scores above 84.

PHQ-15

PHQ-15 is a somatic symptom subscale that was derived from the full patient health questionnaire (PHQ). It deals with the assessment of severity of 15 somatic symptoms commonly reported in outpatient settings. PHQ-15 score is a continuous measure. However, using cut offs of 5, 10, and 15, the PHQ-15 score can be demarcated into four classes. These are minimal, mild, moderate, and high. Scoring is done by asking patients how often they are bothered due to each symptom in the past 7 days. If a patient is not at all bothered due to the symptoms, it will be scored as "0," 1 if bothered a little; and 2 if bothered a lot. Range of PHQ-15 score is 0 to 30.[20]

Sample Size Calculation

Sample size was calculated using the formula of $4pq/d^2$ where p is the expected prevalence, q is 100-p, and d is the precision level. The prevalence of FCR was expected to be 67.[10] Assuming 20% as relative precision, sample size = 4

$\times 67 \times (100–67)/13.4 \times 13.4 = 49$. Thus, at least 49 patients were required for this study.

Statistical Analysis

The data were tabulated electronically in Microsoft Excel and analyzed using the software IBM SPSS 20.0 version (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp). The demographic details of the participants are expressed in frequency and percentage. The associations between scores of FCR, PHQ, and other continuous demographic variables were examined by Pearson's correlation analysis if they were normally distributed, or Spearman's correlation if they were not. Independent samples *t*-test was used for comparison of means of FCR and PHQ with gender and response to treatment. For analysis in this study, response to treatment was divided into two groups, i.e., patients who had partial response or more and patients who had less than partial response (PR or more vs. less than PR). The response defined as one documented just before recruitment into this study. One-way analyses of variance (ANOVAs) were conducted to compare FCR and PHQ scores with socioeconomic class.

Results

A total of 64 patients participated in this study. The median age was 60 years (range: 34–80 years). More than half of patients were females ($N = 38$, 60%). The majority of participating patients were married ($N = 53$, 82%). Most of the study participants ($N = 57$, 89%) had education of primary school level or more. A significant number of participants were either unemployed (22, 34%) or were unskilled laborers (18, 28%). Forty-seven (73%) patients were from upper lower socioeconomic status. Other demographic details are mentioned in ►**Table 1**. Complete ISS staging information was available in 53 (83%). Of these 53 cases, 24 (45%) were ISS stage 3, 12 (23%) were ISS stage 2, and remaining stage 1. First-line treatment received by these patients is listed in ►**Table 1**. The majority received melphalan prednisolone thalidomide (MPT) (25, 39%) followed by lenalidomide dexamethasone (20, 31%). Three (5%) patients had undergone autologous stem cell transplant. After first-line treatment, responses observed were very good partial response (VGPR) in 44 (69%) patients, 16 (25%) had partial response (PR), and 4 (6%) had stable disease. At the time of this study, 15 (23%) had complete remission, 25 (39%) had VGPR, 11 (17%) had PR, 2 (3%) had stable disease, and 7 (11%) had progressive disease. Data were missing in 4 (6%). The mean duration from diagnosis to enrolment into this study was 28 months.

Table 1 Patient Characteristics

Parameter		*N* (%)
Median age (in years)		60 (range 34–80)
Gender	Male	26 (40)
	Female	38 (60)
Marital status	Married	53 (80)
	Single	11 (20)
Educational status	Illiterate	7 (11)
	Primary school	17 (27)
	Middle school	26 (41)
	High school	11 (17)
	Intermediate/ diploma	2 (3)
	Graduate	1 (1)
	Professional degree	0 (0)
Occupational status	Unemployed	22 (34)
	Unskilled	18 (28)
	Semiskilled	8 (12)
	Skilled	12 (19)
	Clerical/shop/farm	1 (2)
	Semi-profession	2 (3)
	Professional	1 (2)
Socioeconomic class	Lower	4 (6)
	Upper lower	47 (73)
	Lower middle	12 (19)
	Upper middle	0 (0)
	Upper class	1 (2)
ISS stage*	Stage 1	17 (32)
	Stage 2	12 (23)
	Stage 3	24 (45)
First-line treatment	MPT	25 (39)
	Lenalidomide-dexamethasone	20 (31)
	CyBorD	10 (16)
	Thalidomide dexamethasone	9 (14)
Treatment response to first line	VGPR or better	44 (69)
	Partial response	16 (25)
	Stable disease	4 (6)

Abbreviations: CyBorD, cyclophosphamide bortezomib dexamethasone; MPT, melphalan prednisolone thalidomide; VGPR, very good partial response.
*International Staging system (ISS) details were available only in 53 patients.

Fear of Cancer Recurrence

The mean total FCRI score in the study population was 27.95 (SD: 24.5). The mean score was numerically higher in females compared with males (29.42 vs. 25.81, $p = 0.56$). Moderate to high levels of FCR were seen in 40% ($N = 26$). One patient (2%) had FCR score more than the mid-point of this scale, indicating high levels of FCR. There was no correlation between total FCRI scores and age ($r = -0.192$, $p = 0.130$) or with duration of disease ($r = -0.072$, $p = 0.57$). There was no significant difference in the mean total FCRI score between patients who had partial response or more compared with those who had less than partial response at the time of this study (mean

Table 2 PHQ-15 Somatic Symptom Severity Scale

Levels of somatic symptom severity	Number (%)
Minimal (0–4)	25 (39)
Low (5–9)	29 (45)
Moderate (10–14)	10 (16)
High (15–30)	0 (0)

Abbreviation: PHQ-15, Patient Health Questionnaire-15.

score in PR or more group 29.37 vs. 22.67 in less than PR group, $p = 0.47$) or among socioeconomic groups ($p = 0.289$).

PHQ-15

Somatic symptom severity assessed by PHQ-15 revealed that the majority (84%, $N = 54$) had mild or lower somatic symptom burden. Frequency of patients in each class based on somatic symptom severity scale is listed in ►**Table 2**. There was a significant difference in mean PHQ-15 scores between patients who had partial response or more compared with those who had less than partial response at the time of this study (mean score in PR or more group 6.02 vs. 8.00 in less than PR group $p = 0.02$). There was no significant statistical difference in means of PHQ-15 between either gender ($p = 0.56$) or different socioeconomic groups ($p = 0.39$). There was no significant correlation of total PHQ-15 score with the duration of disease ($r = 0.05$, $p = 0.65$) or with FCRI total scores ($r = 0.140$, $p = 0.27$). Symptoms reported by patients to cause a little or a lot of bother in more than half of study subjects were feeling tired, nausea or indigestion, and pain in arms, legs, or joints.

Discussion

We studied FCR among myeloma patients on treatment for a year or more utilizing FCRI, which is a multidimensional tool with 42 items. We observed a mean FCRI score of 27.95 among our study participants. There are no studies assessing FCR among Indian patients with multiple myeloma using the FCRI tool. In our study, the mean total FCRI score observed was lower compared with other solid tumors in which the fear of recurrence has been studied using this tool.[2] The mean FCRI score has been reported as 39 among prostate cancer patients, 60 among breast cancer survivors, and 58 among colorectal cancer survivors and lung cancer survivors respectively.[2] Low FCRI scores may have been due to multiple factors. One reason could be that the majority of subjects in our study had disease under control and had lower symptom burden. Lower symptom burden and the thought that disease is under control would have led to lower FCR scores.[4,15] In India, patients may be aware of the diagnosis of cancer. However, they may not be fully aware of their prognosis.[21] In our society, a responsible family member, mostly a male is the decision maker on cancer management. Patients are kept in the dark especially about their prognosis. This is because relatives fear that a complete information regarding cancer to the patient may negatively impact a patient's physical and mental health.[21] Hence, the responsible caregiver comes to an understanding with treating oncologists and chooses in majority to conceal a lot of information regarding the patient's cancer.[21] Patient's lack of knowledge about prognosis of disease may be another reason for lower mean FCRI scores. A thorough knowledge can induce FCR.[22] However, we have not specifically looked into what extent patients themselves were aware of their disease prognosis. Across different cancer sites and with different assessment strategies, on an average, 49% of cancer survivors reported to have moderate to high levels of FCR.[6] In our study, we observed that 40% of patients had moderate to high levels of FCR and this is similar to what has been observed in lymphoma survivors.[9] However, tools used to assess FCR differ. It has been seen in some studies that patients are less apprehensive about recurrence or disease progression when they undergo frequent checkups including blood tests or when they are on some form of treatment.[23] Myeloma patients are continually on one or other forms of treatment and they undergo periodic blood testing as well. It is notable that the mean duration from diagnosis to enrollment into this study was around 28 months. Thus, patients would have developed a sense of understanding about the chronicity of their disease. This may also have contributed in some to the development of a sense of coherence and possibly altering their perception about the disease.[11,24] The majority of patients at the time of this study had disease in remission and this could be the reason for lower symptom burden. Most of the study subjects reported feeling tiredness, nausea, or indigestion and pain in arms, legs, or joints. These are common symptoms reported by myeloma patients on treatment.[14,25] These might be due to disease or due to drugs such as steroids used to treat these patients. Pain is one of the main somatic symptoms a myeloma patient would complain of because of involvement of the skeletal system by the disease process. There was a significant difference in the mean PHQ-15 scores between patients who had partial response or more compared with those who had less than partial response at the time of this study. Patients with progressive or non-responding disease have higher symptom burden.[26] A large majority of patients (84%) had mild or lower somatic symptom burden. This means that 16% had moderate-to-high symptom burden. This is lower than that reported in a population based data among transplant ineligible patients.[27] In this study from Canada, symptom burden was assessed among patients with myeloma within an year of their diagnosis. In our study, patients enrolled had been diagnosed with multiple myeloma for a year or more. The lower symptom burden seen in our study was possibly due to greater proportion of patients with partial response or better. In the study by Mian et al, the symptom burden was observed to steadily decrease over time.[27] Their study did not capture symptom burden in specific lines of treatment and other myeloma-related variables such as stage and response. Also, this study used a different tool—Edmonton symptom assessment scale (ESAS) to measure symptom burden among myeloma patients. ESAS is a validated tool for general cancer symptoms.[27] Females had a higher symptom burden in their study.[27] However, we

did not observe any difference in symptom burden based on gender.

There are a few strengths to our study. This is one of the few studies looking into fear of cancer recurrence among myeloma patients. In the study from the Chinese group, FCR was assessed among myeloma patients using the Fear of Progression Questionnaire short form which contains 12 items.[17] We have used the FCRI tool which contains 42 items. Longer multidimensional scales such as FCRI may be more useful where FCR is the primary outcome of interest.[28] Studies focusing on FCR in myeloma are lacking from India and this study provides initial reports regarding FCR among myeloma patients. There are no studies from India looking into symptom burden among myeloma patients on treatment. We provide here initial reports of symptom burden among myeloma patients who are on treatment for a year or more. However, this study is not without limitations. The FCRI tool has 42 items and is extensive. Hence, a shorter tool is recommended for administration on a day today basis in the outpatient department. The PHQ-15 tool has not been validated for use in cancers. Also, PHQ-15 tool does not capture all symptoms specifically related to multiple myeloma. It is important to have a baseline assessment of FCR among patients with myeloma. This will help us to guide psychosocial interventions to improve patient well-being.

Conclusions

This study has shown that patients with multiple myeloma have overall lower fear of cancer recurrence compared with solid tumors. One possible explanation for this may be related to our cultural practice of non-disclosure of prognosis to the patients. In our study, patients had lower physical symptom burden especially in patients who had partial response or better at the time of this study. However, a significant proportion had moderate to high levels of fear of cancer recurrence. Further studies involving larger numbers in a prospective manner are required to confirm our findings about fear of cancer recurrence among patients with multiple myeloma.

Ethics Approval and Consent to Participate

Approval was obtained from the Institutional Review Board before the start of the study.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Ethics

The procedures followed were in accordance with the ethical standards of the IEC and with the Helsinki Declaration of 1964, as revised in 2013. An approval was obtained from the Institutional Review Board (IRB) at Malabar Cancer Center, Thalassery before the start of the study. IRB number – 1616/IRB-SRC/13/MCC/04–07–15/4. Informed consent was obtained from all the patients prior to the study.

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None.

Conflict of Interest

None declared.

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