DEPRESSION AND ITS ASSOCIATED FACTORS IN THE CAREGIVERS OF HOSPITALIZED PATIENTS WITH CANCER

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Abstract – Objective: Cancer diagnosis can confront the patients' first care and support source, their family and caregivers, with a serious crisis, likewise, they may show depressive symptoms. Paying attention to such an issue is of special importance in promoting the patients' health. Therefore, this study was conducted to determine the extent of depression and related factors in hospitalized cancer patients' caregivers.

Materials and Methods: In the present descriptive-analytical study, 152 caregivers of hospitalized patients with cancer in Imam Khomeini hospital in Sari (Mazandaran, Iran) were selected using available sampling in 2018. The data gathering instruments included demographic and medical information questionnaire of both the caregivers and patients, and 21-item Beck depression inventory. The data were analyzed using SPSS 16 along with the descriptive statistics and inferential statistical tests such as Chi-square and Pearson correlation coefficients.

Results: According to the results, the mean depression of caregivers was 13.97±10.19, suggesting the minimum level of depressive symptoms. Nevertheless, 25.6% had moderate to severe depression. Variables such as care hour, marital status, place of residence, depression history, incidence of depression over the past six months, financial status, and the relation between the patient and caregivers had a significant relationship with depression (p<0.05). There was no significant relationship between caregivers' depression and caregivers' age, patient's age, caregivers' gender, as well as duration of disease diagnosis (p>0.05).

Conclusions: Considering the supportive role of caregivers and their impact in promoting the patients' health, it is recommended that training programs and classes be developed to reduce depression, as well as the possibility of periodic screening of companions in hospitals and, if necessary, referral to a psychiatrist in severe cases should be provided.

KEYWORDS: Cancer, Depression, Family, Caregivers

Cancer is one of the most important health-related issues worldwide[1,2]. Despite the significant advances in medical sciences, cancer is still one of the most important diseases of the current century, it is the second leading cause of death worldwide. Generally, about one of every six deaths is caused by cancer[2,3]. In Iran, according to the cancer statistical center report, around 51000 new cases of cancer are identified annually[4]. Unfortunately, the diagnosis of cancer has unpleasant consequences that affect not only the patient, but also their families, so that the diagnosis of cancer in any member of the family is accompanied by a serious and severe crisis for other members[5-7]. In many cases, the family members of the patients, in addition to the psychological trauma resulting from the possible death of

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their beloved ones, face the other new and anxious-prone experiences associated with the patients' treatment. These include constant presence in the hospital, taking care of the patients at home, observation of their suffering and pain, fatigue caused by disrupting the order of life or accepting new responsibilities that may, at least initially, be beyond their control[8-10]. Psychological stresses are also one of the most common consequences following cancer diagnosis in patients with cancer and their families[11-13]. Anxiety and depression have the highest incidence rate, with the prevalence of anxiety and depression reported in most studies from one-third to almost one-second[9,14,15]. Researchers in Iceland found that 41% of family members of patients with cancer who had been hospitalized for at least three days experienced definite or possible symptoms of depression[16]. The results of another study indicated that 36.4% of mothers and 25% of fathers experienced severe depression, and 18.2% of mothers and 4.5% of fathers of children with cancer undergoing treatment had moderate symptoms of depression[17]. Mild-to-moderate depression symptoms were observed in 60% of caregivers in another study[18]. In this regard, since development of depression in patients with cancer and their caregivers can impair their personal and social responsibilities as well as physical health, and eventually, their quality of life[19-21], and can cause increased vulnerability of individuals in applying coping strategies and controlling stress as well as available social support[15,22], thus it seems that studies about the depression assessment in the caregivers of patients with cancer and its associated factors are required for planning and increasing support of the caregivers in order to promote the patients' and their caregivers' quality of life. A review of the available databases also showed that most studies in this field have been conducted in other countries with different psychological, social and cultural contexts, which may be different depending on the culture and conditions of each society which needs to be checked. Also, in most of the studies conducted in this field, only the spouses or caregivers of cancer patients were examined. Therefore, according to the above-mentioned cases, the present study was designed to determine the extent of depression and related factors in the caregivers of cancer patients hospitalized in the hospital to be a guide for planning to maintain and improve the caregivers' health.

MATERIALS AND METHOD

The present research is a descriptive analytical study performed in Imam Khomeini hospital, Sari (Mazandaran, Iran) in 2018. This study was a census type in which 152 caregivers of hospitalized patients with cancer in Imam Khomeini hospital of Sari were chosen through available sampling method (in all of the wards where patients with cancer were hospitalized including oncology, gastroenterology, internal medicine, etc.). Entry criteria included adult caregivers of hospitalized patients with a definitive diagnosis of cancer who were at least 18 years old, with the least literacy ability, and willingness to participate in the study. After obtaining permission from the Ethics Committee and relevant authorities, the researcher referred to the hospital for conducting the sampling. Describing the goals and methods of the study, she identified the qualified caregivers, received written informed willingness from these caregivers and assured them about the confidentiality of their information.

The data gathering instruments included: 1) demographic and medical questionnaire (information on age, gender, occupational status, marital status, education level; and the caregivers' information included: age, gender, education level, marital status, religion, place of residence, occupational status, financial adequacy, the relation between caregivers and patient, the number of hours for direct daily care of the patient, previous depression history, incidence of crisis including death of spouse or other family members, divorce, serious disease and other disasters over the past six months) and, 2) Beck depression inventory (BDI-II).

The BDI-II consists of 21 items, based on the principal symptoms of depression and their severity, some degrees are created for every item scored between 0-3. This questionnaire included 21 items about depression each of which had four options with a score between 0-3. In every item, 0 indicated the absence of the symptom, while 3 indicated the maximum severity. The overall scores less than 14 suggested minimum symptoms, 14-19 mild depression, 20-28 moderate depression, and 29-63 severe depression[23]. In a study on the elderly South Koreans, Cronbach's Alpha coefficient was calculated to be 0.88[21]. This questionnaire was translated into Persian and its validity and reliability were investigated. When examining the validity and reliability of the Beck Depression Inventory in the Iranian population, Cronbach's alpha was calculated to be 0.93[20]. The data were analyzed by SPSS 16 (SPSS Inc., Chicago, IL, USA) along with descriptive statistic tests including mean, frequency, percentage, and median, also considering the inferential statistics such as Chi-square and Pearson correlation coefficient.

RESULTS

The average age of the caregivers was 40.42±12.90 and their age range was 18-81 years. The patients' average was 59.11±15.10 and their age range was 15-

TABLE 1. The demographic and medical characteristics of the patients' caregivers.

Variable	Number (Percent), N (%)
Gender	
Male	57 (37.5)
Female	95 (62.5)
Level of education	
Under Diploma	55 (36.2)
Diploma	45 (29.6)
Associate degree	14 (9.2)
Bachelor	31 (20.4)
Master's degree	5 (3.3)
PhD and above	2 (1.3)
Marital status	
Single	27 (17.6)
Married	122 (80.4)
Divorced	3 (2)
Religion	
Shia	150 (98.7)
Sunni	2 (1.3)
Place of residence	
City	88 (57.99)
Village	64 (42.1)
Occupational status	
Employee	23 (15.1)
Freelancer	32.2 (49)
Unemployed	80 (52.6)
Financial adequacy	
Poor	30 (19.7)
Average	95 (62.5)
Good	24 (15.8)
Very good	3 (2)
Relation to the patient	
First-degree1	108 (71.1)
Second-degree 2	44 (28.9)
History of depression	
With a history of depression	22 (14.5)
No history of depression	130 (85.5)
Experience of crisis over the last six months	
Yes	58 (38.2)
No	94 (61.8)

Note: 1. First-degree relatives including parents, children, spouse; 2- second-degree relatives including brothers and sisters, the children of brothers and sisters.

TABLE 2. Demographic and medical characteristics of patients.

Variable	Number (Percent), N (%)
Gender	
Male	62 (40.8)
Female	90 (59.2)
Marital status	
Single	3 (2)
Married	140 (92)
Divorced	4 (6)
Deceased spouse	2 (3)
Occupational status	
Employee	8 (5.3)
Freelancer	49 (32.2)
Unemployed	91 (59.9)
Retired	4 (2.6)
Education level	
Sub-diploma	116 (76.3)
diploma	23 (15.1)
Associate degree	6 (3.9)
BS/BA	5 (3.3)
MA/MS	2 (1.3)
History of underlying disease	
Yes	86 (56.6)
No	66 (43.4)
Treatments received	
Pharmacological	60 (39.5)
Surgery	29 (19.1)
Radiotherapy	3 (2)
Combined	60 (39.4)

(r=-0.4, p=0.6). No significant difference existed between the patient's age and caregiver's depression (p=0.96, r=0.004). However, there was a significant relationship between care hour and caregivers' depression level (p=0.001, r=0.33). On the other hand, no significant difference existed between duration of disease diagnosis and the caregivers' depression level (p=0.07, r=0.14). No significant difference was found between the caregivers' depression level and their gender (p=0.57, X2=1.98). Regarding the variable of religion, only two cases were Sunni while 150 were Shi'a. Thus, they could not be compared with each other. No significant difference existed between the kind of cancer disease and caregiver's depression level (p=0.12, r=0.13). There was no significant difference between anticancer treatment and caregiver's depression (p=0.30, r=0.05).

Based on Fisher's test, there was a significant relationship between marital status and the caregivers' depression level (p=0.001). Specifically, the maximum level of depression was related to married individuals. Based on Fisher's test, a significant relationship was observed between the place of residence and the caregivers' depression (p=0.003), with the maximum frequency of severe depression relating to the villagers. Using Fisher's test, the hi-
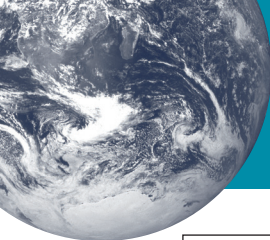
95 years. The average care- hour was 13.09±9.28 and its range was 1-24 hours. The average duration of disease diagnosis was 66.59±26.02 months ranging from 1 to 408 months. Other details of demographic and medical information of the caregivers and patients are provided in Tables 1 and 2.

The depression level was 0-52 with the average of 13.97±10.19, suggesting the minimum level of depressive symptoms. Other details regarding the individual's depression level are shown in Figure 1.

Pearson correlation coefficient showed no significant relationship between the age of the patients' caregivers and their level of depression

Fig. 1. Caregivers' depression of patients with cancer.

story of previous depression had a significant relationship with the caregivers' depression level of patients with cancer ($p<0.001$). Based on Fisher's test, crisis over the past six months had a significant relationship with the caregivers' depression level ($p=0.004$). According to Fisher's test, there was a significant relationship between caregivers' financial status and their depression ($p<0.001$), with the maximum frequency of depression being associated with average income adequacy. Finally, Fisher's test indicated that there was a significant relationship between caregivers' depression and their relation to the patient ($p=0.03$).

DISCUSSION

The present study was performed to determine the depression and its associated factors among the caregivers of hospitalized patients with cancer. Accordingly, the results of the present study indicated that most participants had minimum depressive symptoms. Unlike the present research findings, the findings obtained by Friðriksdóttir et al[25] suggested that most caregivers were asymptomatic. One of the possible reasons for this difference can be the different instruments used for measuring depression. In the study by Friðriksdóttir et al[25], the hospital anxiety and depression scale (HADS) had been used, while here, the Beck depression inventory (BDI) was used. Further, the present research was conducted in Iran, while the mentioned study had been performed in Iceland. The results obtained by Li et al[26] also showed that most caregivers had mild depression; the results in that study were not in line with the present study results. This can be due to the occupational status of participants in these studies. In this study, most patients' caregivers had no occupation, while in the study by Li et al[26] most of them were employed. Another reason can be the financial status of caregivers; in the present study, most had average financial adequacy, while in the

study by Li et al[26], most of the caregivers had been tolerating a heavy financial burden for treating the patients' cancer. This can cause differences in the results of the mentioned study and our results. Besides, a research reported that depression is more frequent at lower economic levels[27].

Another result of the present study was a significant relationship between marital status and the caregivers' depression level, which was in line with the study by Cho et al[28]. Also, in the research by Han et al[29], the caregivers' depression level was significantly correlated with marital status. However, unlike the present study, the depression level was greater among singles than married individuals in the study by Han et al[29]. As a justification, since the mentioned study and the present one were performed in two different countries (Korea and Iran) with different cultures, thus, the differences in the quantity and quality of emotional relations as well as the supports received from spouses have caused differences in the depression level among singles and married individuals. On the other hand, unlike the present research, in the study by Rhee et al[30], no significant relationship was found between caregivers' marital status and their depression level. Also, in the study by Karabekiroğlu et al[31], no significant difference existed between caregivers' marital status and depression level. One possible reason for the such differences between other studies and our results can be the different place and time of research. Indeed, different place and time of conducting research can affect the personal and social characteristics as well as vulnerability of individuals towards depression. The study by Karabekiroğlu et al (31) was conducted on the caregivers of patients with stage 4 cancer in 2015. Also, the study by Rhee et al (2007) was performed in Korea in 2008, while the present research was performed in Iran in 2018.

Another result of the present study was the relationship between financial status of the family and the caregivers' depression level. Congruent with the present study, Cho et al[28] found a signi-

ficant relationship between financial status of the family and fathers' depression and despair level. Indeed, there was a significant difference between depression scores of high, middle, and low income-fathers. Also, in the study by Omranifard et al[32], a relationship was found between the patients' financial dependence and caregivers' depression of. Another study concluded that lower income is associated with more depression (33), which is in line with the results of the present study.

Another notable result here was a significant relationship between the caregivers' depression and their relation to the patient. First-degree relatives would suffer more depression than second-degree relatives. In line with the present study, in the research by Otani et al[19], a significant relationship was observed between the caregivers' depression level and the caregiver-patient relation (more depression in spouses). Also, Shine et al[33] had reported a significant relationship between caregivers' depression and the caregiver-patient relationship. Unlike the results of the present study, another research found no significant relationship between caregivers' depression and their relation to the patient[32]. One of the reasons for this difference can be the different patients' diseases. In the present study, the patients had cancer, while in the mentioned study, the patients had been suffering from dementia. Justifying the discrepancies between these two studies, it can be stated that since patients' relatives with cancer find themselves in a very critical and difficult situation in the course of hospitalization and receiving different treatments, and for some reasons such as lack of inadequate awareness about the course of disease and its prognosis as well as long-term presence in hospital; they may tend to develop crisis and experience psychological disorders more than the relatives of patients with dementia. It also seems that since those with dementia are increasingly dependent on others to perform their routine daily activities because of their impaired cognitive functioning and behavior, and their complex needs and management can involve both the relatives and other acquaintances in a wider scale, accordingly, the diversity and the degree of care may cause the patient- caregiver relationship not to be significantly related to caregivers' depression. Indeed, possibly not only the relatives but also other acquaintances may also equally suffer from psychological problems such as depression[34,35].

CONCLUSIONS

Considering the caregivers' supportive role, depression in the caregivers, and their impact on promoting the patients' health, it is suggested that educational classes and training programs be developed for reducing depression. It also seems necessary to perform periodic screening and examination on caregivers' psychological health in hospitals, so that the severe cases of depression would be referred to psychiatrists. Since the maximum frequency of severe depression was related to villagers, it is suggested that provision of psychological and psychiatric services be increased in villages.

CONFLICT OF INTERESTS:
The authors declare that they have no conflict of interest.

REFERENCES

1. Angtuaco EJ, Fassas AB, Walker R, Sethi R, Barlogie B. Multiple myeloma: clinical review and diagnostic imaging. Radiology 2004; 231: 11-23.
2. Prasad S, Pandey MK, Yadav VR, Aggarwal BB. Gambogic acid inhibits STAT3 phosphorylation through activation of protein tyrosine phosphatase SHP-1: potential role in proliferation and apoptosis. Cancer Prev Res (Phila) 2011; 4: 1084-1094.
3. Stearn W. Vinca L. In Flora of Turkey and the East Aegean Islands, PH, D., Ed. Edinburgh University Press: Edinburgh, 1978; 6: pp. 161-163.
4. Stearn WT. Synopsis of the genus Vinca including its taxonomic and nomenclatural history. In The Vinca alkaloids botany, chemistry, pharmacology, Taylor, W. Farnsworth, N., Eds. 1973; pp. 19-94.
5. Güner A. Türkiye bitkileri listesi (damarlı bitkiler). ANG Vakfı 2012.
6. Koyuncu M. A new species of Vinca (Apocynaceae) from eastern Anatolia, Turkey. Turk J Bot 2012; 36: 247-251.
7. Koyuncu M, Ekşi G, Özkan AMG. Vinca ispartensis (Apocynaceae), a new species from Turkey. Ann Bot Fenn 2015; 52: 340-344.
8. Evans WC. Trease and Evans Pharmacognosy E-Book. Elsevier Health Sciences 2009.
9. Şimşek-Sezer EN, Uysal T. Anti-proliferative and Apoptotic Effects of Vincristine and Vinblastine on Multiple Myeloma. Fresenius Envir Bull 2019; 28: 4001-4006.
10. Şimşek-Sezer EN, Uysal T. Volatile and Phenolic Compositions of the Leaves of Two Vinca L. Species from Turkey. Cupmap 2018; 1: 51-58.
11. Rzeski W, Stepulak A, Szymański M, Sifringer M, Kaczor J, Wejksza K, Zdzisińska B, Kandefer-Szerszeń M. Betulinic acid decreases expression of bcl-2 and cyclin D1, inhibits proliferation, migration and induces apoptosis in cancer cells. Naunyn Schmiedebergs Arch Pharmacol 2006; 374: 11-20.
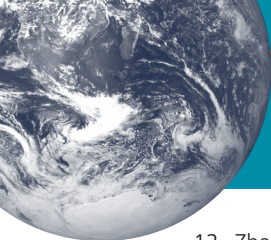
12. Zhao M, Ma J, Zhu HY, Zhang XH, Du ZY, Xu YJ, Yu XD. Apigenin inhibits proliferation and induces apoptosis in human multiple myeloma cells through targeting the trinity of CK2, Cdc37 and Hsp90. Mol Cancer 2011; 10: 104.

13. Yang LJ, Chen Y, He J, Yi S, Wen L, Zhao S, Cui GH. Effects of gambogic acid on the activation of caspase-3 and downregulation of SIRT1 in RPMI-8226 multiple myeloma cells via the accumulation of ROS. Oncol Lett 2012; 3: 1159-1165.

14. Li W, Wang Y, Song Y, Xu L, Zhao J, Fang B. A preliminary study of the effect of curcumin on the expression of p53 protein in a human multiple myeloma cell line. Oncol Lett 2015; 9: 1719-1724.

15. Canturk Z, Dikmen M, Artagan O, Ozarda MG, Ozturk N. Cytotoxic Effects of Resveratrol, Rutin and Rosmarinic Acid on ARH-77 Human (Multiple Myeloma) Cell Line. Nat Prod Commun 2016; 11 : 1441-1444.

16. Tibullo D, Caporarello N, Giallongo C, Anfuso CD, Genovese C, Arlotta C, Puglisi F, Parrinello, NL, Bramanti V, Romano A, Lupo G, Toscano V, Avola R, Brundo MV, Di Raimondo F, Raccuia SA. Antiproliferative and Antiangiogenic Effects of Punica granatum Juice (PGJ) in Multiple Myeloma (MM). Nutrients 2016; 8: 611.

17. Kiraz Y, Neergheen-Bhujun VS, Rummun N, Baran Y. Apoptotic effects of non-edible parts of Punica granatum on human multiple myeloma cells. Tumour Biol 2016; 37: 1803-1815.

18. Koru Ö, Avcu F, Tanyüksel M, Ural AU, Araz RE, Şener K. Cytotoxic effects of caffeic acid phenethyl ester (CAPE) on the human multiple myeloma cell line. Turk J Med Sci 2009; 39: 863-870.

19. Han Y, Zhang S, Wu J, Yu K, Zhang Y, Yin L, Bi L. Matrine induces apoptosis of human multiple myeloma cells via activation of the mitochondrial pathway. Leuk Lymphoma 2010; 51: 1337-1346.

20. Neergheen VS, Bahorun T, Taylor EW, Jen LS. Aruoma OI, Targeting specific cell signaling transduction pathways by dietary and medicinal phytochemicals in cancer chemoprevention. Toxicology 2010; 278: 229-241.

21. Shahneh FZ, Baradaran B, Orangi M, Zamani F. In vitro cytotoxic activity of four plants used in Persian traditional medicine. Adv Pharm Bull 2013; 3: 453.

22. Cory S, Adams JM. The Bcl2 family: regulators of the cellular life-or-death switch. Nat Rev Cancer 2002; 2: 647-656.

23. Derenne S, Monia B, Dean NM, Taylor JK, Rapp MJ, Harousseau JL, Bataille R, Amiot M. Antisense strategy shows that Mcl-1 rather than Bcl-2 or Bcl-xL is an essential survival protein of human myeloma cells. Blood 2002; 100: 194-199.

24. Zhang B, Gojo I, Fenton RG. Myeloid cell factor-1 is a critical survival factor for multiple myeloma. Blood 2002; 99: 1885-1893.

25. Song G, Mao Y, Cai Q, Yao L, Ouyang G, Bao S. Curcumin induces human HT-29 colon adenocarcinoma cell apoptosis by activating p53 and regulating apoptosis-related protein expression. Braz J Med Biol Res 2005; 38: 1791-1798.

26. Salakou S, Tsamandas A, Bonikos D, Papapetropoulos T, Dougenis D. The potential role of bcl-2, bax, and Ki67 expression in thymus of patients with myasthenia gravis, and their correlation with clinicopathologic parameters. Eur J Cardiothorac Surg 2001; 2: 712-721.

27. Degterev A, Boyce M, Yuan J. A decade of caspases. Oncogene 2003; 22 : 8543-67.

28. Li F, Rajendran P, Sethi G. Thymoquinone inhibits proliferation, induces apoptosis and chemosensitizes human multiple myeloma cells through suppression of signal transducer and activator of transcription 3 activation pathway. Br J Pharmacol 2010; 161: 541-554.

29. Zhao M, Ma J, Zhu HY, Zhang XH, Du ZY, Xu YJ, Yu XD. Apigenin inhibits proliferation and induces apoptosis in human multiple myeloma cells through targeting the trinity of CK2, Cdc37 and Hsp90. Mol Cancer 2011; 10: 104.

30. Kannaiyan R, Hay HS, Rajendran P, Li F, Shanmugam MK, Vali S, Abbasi T, Kapoor S, Sharma A, Kumar AP. Celastrol inhibits proliferation and induces chemosensitization through down-regulation of NFκB and STAT3 regulated gene products in multiple myeloma cells. Br J Pharmacol 2011; 164: 1506-1521.

31. Kudo C, Yamakoshi H, Sato A, Ohori H, Ishioka C, Iwabuchi Y, Shibata H. Novel curcumin analogs, GO-Y030 and GO-Y078, are multi-targeted agents with enhanced abilities for multiple myeloma. Anticancer Res 2011; 31: 3719-3726.