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To cite this article: Gamze Bozgeyik, Derya Ipekcioglu, Menekse Sila Yazar & Mehmet Cem Ilnem (2019) Behavioural and psychological symptoms of Alzheimer's disease associated with caregiver burden and depression, *Psychiatry and Clinical Psychopharmacology*, 29:4, 656-664, DOI: [10.1080/24750573.2018.1541646](https://doi.org/10.1080/24750573.2018.1541646)

To link to this article: <https://doi.org/10.1080/24750573.2018.1541646>



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Published online: 09 Nov 2018.



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Behavioural and psychological symptoms of Alzheimer's disease associated with caregiver burden and depression

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ABSTRACT

OBJECTIVE: The aim of the study was to investigate the relationship between behavioural and psychological symptoms of Alzheimer's disease with caregiver burden and depression.

METHODS: In this prospective and clinic-based study, 71 patients over 65 years of age diagnosed with Alzheimer's disease according to DSM IV diagnostic criteria who were admitted to Bakirkoy Prof. Dr. Mazhar Osman Research and Training Hospital for Psychiatry, Neurology and Neurosurgery between April 2014 and November 2014 and their 71 caregivers were included in the study. Information on patients and caregivers were assessed using the sociodemographic and clinical data form. The Standardized Mini Mental State Examination (SMMSE) and the Global Deterioration Scale (GDS) were used to determine disease severity and stage. The Neuropsychiatric Inventory (NPI) was used to assess the behavioural and psychological symptoms of the patients. Caregivers' burden and depression were assessed using the Zarit Caregiver Burden Scale (ZCBS) and the Hamilton Depression Rating Scale (HAM-D). SPSS 22.0 program was used for the statistical analysis of data.

RESULTS: The average age of the caregivers was 52, 81.7% (n: 58) were female and 53.5% (n: 38) were the patients' daughters. Caregiver burden was found to be mild in 50.7% (n: 36), moderate in 15.5% (n: 11) and heavy in 33.8% (n: 24) of caregivers. Depression was found to be mild in 19.7% (n: 14), moderate in 19.7% (n: 14) and severe in 4.2% (n: 3) of caregivers. The most common behavioural and psychological symptoms were; apathy (60.6%), delusions (57.7%), depression / dysphoria (56.3%), hallucinations (53.5%), irritability (47.9%), anxiety (32.4%), abnormal motor behaviour (29.6%), agitation / aggression (26.8%), eating-appetite changes (26.8%) and elation / euphoria (1.4%). Patient caregivers in the group with more behavioural and psychological symptoms had more caregiving burden and depression. Symptoms having a significant effect on caregiver burden were delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, apathy, disinhibition, irritability, abnormal motor behaviour. Behavioural and psychological symptoms that correlate with caregiver depression are agitation/aggression, anxiety, disinhibition, irritability. In the correlation analysis between NPI and ZCBS factor groups, only the factor 4 showing the economic burden did not show any significant correlation.

CONCLUSION: Results show that behavioural and psychological symptoms in Alzheimer's patients increase the caregiver burden and cause caregiver depression. Preventive measures to prevent the emergence of such symptoms and effective and rapid intervention are required. Further multi-center studies with a prospective design, involving different cultures, patients from a wider population, different care settings are required.

ARTICLE HISTORY

Received 12 May 2018
Accepted 24 October 2018



KEYWORDS

Alzheimer's disease;
behavioural and
psychological symptoms;
neuropsychiatric symptoms;
caregiver burden; caregiver
depression

Introduction

Alzheimer's Disease (AD) is the most common type of dementia, accounting for 50–70% of all dementia cases. This is a progressive and neurodegenerative disease of unknown etiology [1]. Alzheimer's patients are experiencing difficulties in communication, difficulty in orientation, and decreased the ability to reason because of cognitive decline. Behavioural problems and personality changes can also be seen in patients. The most commonly used terminology for these symptoms is “neuropsychiatric symptoms” or the “behavioural and psychological symptoms of dementia” (BPSD), as

defined by the International Association for Geriatric Psychiatry. Behavioural and psychological symptoms can be defined as non-cognitive symptoms and behaviours frequently seen in dementia patients. These heterogeneous symptoms can be divided into subgroups such as a set of mood disorders (depression, anxiety, apathy/indifference), a set of motor behaviour (walking back and forth, wandering and other unintended behaviour), and a set of inappropriate behaviours (agitation, disinhibition, euphoria). During the course of AD, neuropsychiatric symptoms are seen in at least two thirds of the patients [2–5].

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Different BPSDs can be more dominant in different phases of AD. Affective symptoms such as depression and anxiety are more common in the early stages of the disease. While the psychotic symptoms gain importance in the middle stage of the disease, disinhibition, wandering, repetitive behaviours and pronounced apathy are seen in the final stage. During the course of the disease, the course of the symptoms may also vary. In a study conducted by Devanand et al., It has been shown that affective symptoms show a rather fluctuating course during the months and years during the disease course, psychotic symptoms are seen relatively less frequently, and psychomotor agitation tends to increase as the disease progresses [6,7].

BPSD can lead to negative results for the caregiver. The caregiver is the person who supports the patient physically, emotionally, socially and economically. People who care for Alzheimer's patients are often the patients' spouse, children, and rarely friends, who do not get paid for care. This group accounts for about 85% of caregivers. Compared to those who do not care, caregivers have more physical and psychological symptoms, use more prescription medicines and need health care more. BPSD creates a burden on patient caregivers, leading to more stress and depression [8–12].

Caregiver burden; can be defined as a multidimensional response to physical, psychological, emotional, social, and economic stress factors associated with caregiver's care experience. Caregiver burden and depression can threaten caregivers family relationships, social relationships, physical health, can cause psychiatric morbidity in caregivers, and early institutionalization of patients. Shultz and Beach also reported that caregiver burden in primary caregivers is an independent risk factor associated with increased mortality rates [10,13–15].

Studies have reported that specific BPSD is more closely related to caregiver burden. Symptoms such as aggression, agitation, and night shift were closely associated with caregiver burden and depression [16,17]. Allegri et al. reported that hallucinations, abnormal motor behaviours, and abnormal night-time behaviours are more likely to be associated with caregiver burden while apathy and depression are more common, but not affecting the caregiving burden [18].

In our study, we have defined the demographics and clinical characteristics of Alzheimer's patients and their caregivers and aimed to investigate the relationship between BPSD in patients with caregiver burden and depression.

Methods

Patients and caregiver

In this prospective clinic-based study, 71 patients over 65 years of age diagnosed with Alzheimer's disease

according to DSM IV diagnostic criteria [19] who were admitted to Bakirkoy Prof. Dr. Mazhar Osman Research and Training Hospital for Psychiatry, Neurology and Neurosurgery between April 2014 and November 2014 and their 71 caregivers who were caring for them more than three days a week were included in the study. Exclusion criteria for the patients as follows; serious visual and/or hearing problems, mental retardation, alcohol and/or substance abuse, disorder related to general medical condition that may affect cognitive functions. Information of the patients and caregivers were assessed using the socio-demographic and clinical data form. Standardized Mini Mental Test (SMMT), Global Deterioration Scale (GDS) were applied to patients. The neuropsychiatric inventory (NPI) was filled with the patient's caregiver. Zarit Caregiver Scale (ZCBS) and Hamilton Depression Rating Scale (HAM-D) were applied to caregivers.

Participants were informed about the study before inclusion and the patient and/or guardian and caregivers who agreed to participate in the study signed the informed consent form. The study was approved by the local Ethics Committee of Bakirkoy Prof. Dr. Mazhar Osman Research and Training Hospital for Psychiatry, Neurology and Neurosurgery at 27.03.2014 with the protocol number of 21209 and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice.

Assessment and outcome measures

Sociodemographic and clinical data form (Prepared for patients)

It is a form prepared by the investigators who record patient characteristics such as age, gender, occupation, education level, marital status, income level and disease duration.

Standardized mini mental state examination (SMMSE)

The Standardized Mini Mental State Examination is a short, useful and standardized test that can be used to determine the cognitive level globally which was published by Folstein et al. [20]. It consists of eleven items collected under five main headings as management, recording memory, attention and calculation, recall, and language and is evaluated on a total score of 30. According to the test scores, the cognitive loss is considered as mild between 20–24 points, moderate between 10–19 points, and severe if less than 10 points. Validity and reliability study in Turkish was performed by Güngen et al. In the study of validity and reliability 23/24 threshold value of SMMSE was found to be highly sensitive and specific in the case of mild dementia in Turkish elderly [21].

Global Deterioration Scale (GDS)

It is developed by Reisberg et al. in order to assess the severity of the general deterioration in dementia. It consists of 7 stages. Stage 1 represents the normal cognitive state, while stage 7 represents the most advanced dementia [22].

Neuropsychiatric Inventory (NPI)

It was developed by Cummings et al. in 1994 [23] and a total of 12 behavioural areas (Delusions, Hallucinations, Agitation / Aggression, Depression / Dystrophy, Anxiety, Elation / Euphoria, Apathy / Indifference, Disinhibition, Irritability / Lability, Abnormal motor behaviour, Sleep / night behaviour, Appetite and eating changes) are questioned whether the related symptom is found. Otherwise the next area is questioned. If the patient's relative confirms the presence of the symptom, it is elaborated by more specific questions about that area. Subsequently, the numerical values given for the frequency of symptom ("1 rare", "4 very often-every day") and severity ("1 light", "3 heavy") are multiplied to obtain the score of that item. The maximum score can be 144. For each item, the distress that the symptom causes for the patient's relative is calculated separately on 5 points (0 no, 5 very heavy). Turkish adaptation and validity-reliability study was performed by Akça-Kalem et al. [24].

Sociodemographic and Clinical Data Form (Prepared for caregivers)

It is a form prepared by investigators including information such as age, gender, duration of education, marital status, occupation, level of income, social security, homeownership, closeness to patient and care experience.

Zarit Caregiver Burden Scale (ZCBS)

It is a Likert-type, self-assessment scale that was developed by Zarit et al. in 1980 [25] and consists of 19-items. The items of the Zarit Caregiver Burden Scale show 5 dimensions. These dimensions are grouped under 5 factors. Factor 1 includes item 2,3,10, 11, 12, 17 and 19 indicating psychological distress and disruption of private life, Factor 2 includes item 5,9,22 for irritability and restrictedness, Factor 3 includes item 6, 13, 18 for disruption of social relationships, factor 4 includes item 15, 20, 21 and 7 for economic burden and factors 5 includes item 8 and 14 for addiction. In our study, 22–46 points was considered mild, 47–55 points moderate, 56 points severe caregiver burden. Validity and reliability study in Turkish was performed by Ozlü et al. in 2009 [26].

Hamilton Depression Rating Scale (HAM-D)

It was developed by Hamilton in 1960 to measure the severity of depression [27]. It is composed of 17 items which question the symptoms of depression

experienced within the last week. In our study, 0–7 points was considered as no depression, 8–15 as mild depression, 16–28 as moderate depression and 29 and above as severe depression. Validity and reliability study in Turkish was conducted by Akdemir et al. in 1996 [28].

Statistical method

The SPSS for windows 22.0 statistical package program was used for statistical analysis. Mean, standard deviation, median lowest, highest values were used in the descriptive statistics of the data. The distribution of the variables was checked by the Kolmogorov Simirnov test. Mann–Whitney u test was used for the analysis of quantitative data. Chi-square test in the analysis of qualitative data, Fischer test in the absence of chi-square conditions. Spearman correlation analysis was used for correlation analysis.

Results

Sociodemographic and clinical characteristics of patients and caregivers

The average age of the patients was 79, 69% (n: 49) women, 60.6% (n: 43) housewives, average education level 3.1 (SD \pm 3.7) years. The average age of caregivers was 52, 81.7% (n: 58) women, the average duration of education was 8 years, 74.6% (n: 53) were married and 90.1% (n: 64) were unemployed. 53.5% (n: 38) of caregivers were the daughter of the patient, and 84.5% (n: 60) had no care experience. Caregiver burden was found to be mild in 50.7% (n: 36), moderate in 15.5% (n: 11) and heavy in 33.8% (n: 24) of caregivers. Depression was found to be mild in 19.7% (n: 14), moderate in 19.7% (n: 14) and severe in 4.2% (n: 3) of caregivers (Table 1).

Frequency of behavioural and psychological symptoms of the patients

When we look at the frequency of behavioural and psychological symptoms seen in patients; 60.6% (n:43) apathy, 57.7% (n: 41) delirium, 56.3% (n: 40) depression / dysphoria, 53.5% (n:31) anxiety, 35.2% (n: 25) disinhibition, 32.4% (n:23) sleep-night behaviour, 29.6% (n:21) abnormal motor behaviour, 26.8% (n:19) agitation / aggression, 26.8% (n: 19) eating-appetite changes and 1.4% (n: 1) elation / euphoria were observed (Table 2)

The effect of the behavioural and psychological symptoms of the patients on caregiver burden

When the effect of BPS on the caregiver burden is assessed; the level of distress caused by caregiver

Table 1. Sociodemographic and clinical characteristics of patients and caregivers.

| Patient Information | | Med (Min–Max) | Ave.±s.d. /n-% | |
|-------------------------------|------------------|---------------|----------------|-------|
| Age | | 79 65–91 | 78.4±5.8 | |
| Gender | Women | 49 | | 69.0% |
| | Men | 22 | | 31.0% |
| Occupation | Housewife | 43 | | 60.6% |
| | Retired | 28 | | 39.4% |
| Education duration (years) | | 0 0–15 | 3.1±3.7 | |
| Marital Status | Married | 31 | | 43.7% |
| | Single | 1 | | 1.4% |
| | Divorced | 6 | | 8.5% |
| | Deceased Partner | 33 | | 46.5% |
| Level of Income | <1000 TL | 48 | | 67.6% |
| | 1000–2000 TL | 23 | | 32.4% |
| Disease Duration (months) | | 48 12–168 | 54.8±29.0 | |
| Psychiatric disease history | None | 63 | | 88.7% |
| | Depression | 8 | | 11.3% |
| Mini Mental State Examination | Mild | 18 | | 25.4% |
| | Moderate | 31 | | 43.7% |
| | Severe | 22 | | 31.0% |
| Global Deterioration Scale | | 6 4–7 | 5.6±1.0 | |
| <i>Caregiver Information</i> | | | | |
| Age | | 52 27–79 | 52.9±11.5 | |
| Gender | Women | 58 | | 81.7% |
| | Men | 13 | | 18.3% |
| Education duration (years) | | 8 0–15 | 7.7±3.7 | |
| Marital Status | Married | 53 | | 74.6% |
| | Single | 11 | | 15.5% |
| | Divorced | 4 | | 5.6% |
| | Separated | 1 | | 1.4% |
| | Deceased Partner | 2 | | 2.8% |
| Occupation | Housewife | 42 | | 59.2% |
| | Employed | 7 | | 9.9% |
| | Retired | 22 | | 31.0% |
| Income | <1000 TL | 9 | | 12.7% |
| | 1000–2000 TL | 55 | | 77.5% |
| | 2000 TL < | 7 | | 9.9% |
| Social security | None | 3 | | 4.2% |
| | Yes | 68 | | 95.8% |
| House | Rented | 9 | | 12.7% |
| | Owner | 62 | | 87.3% |
| Kinship | Daughter | 38 | | 53.5% |
| | Partner | 14 | | 19.7% |
| | Son | 9 | | 12.7% |
| | Daughter-in-law | 8 | | 11.3% |
| | Other | 2 | | 2.8% |
| Care experience | None | 60 | | 84.5% |
| | Yes | 11 | | 15.5% |
| Care Support | None | 40 | | 56.3% |
| | Yes | 31 | | 43.7% |
| Home care fee | None | 57 | | 80.3% |
| | Yes | 14 | | 19.7% |
| Care Duration (month) | | 36 0–120 | 41.9±25.7 | |
| Social activity | None | 53 | | 74.6% |
| | Yes | 18 | | 25.4% |
| Physical activity | None | 53 | | 74.6% |
| | Yes | 18 | | 25.4% |
| Physical disease | None | 39 | | 54.9% |
| | I | 24 | | 33.8% |
| | II | 4 | | 5.6% |
| | III | 4 | | 5.6% |
| Psychiatric disease history | None | 59 | | 83.1% |
| | Depression | 11 | | 15.5% |
| | Anxiety | 1 | | 1.4% |
| Zarit Caregiver Burden | Mild | 36 | | 50.7% |
| | Moderate | 11 | | 15.5% |
| | Severe | 24 | | 33.8% |
| ZCBS I | | 15 7–35 | 16.6±7.3 | |
| ZCBS II | | 8 3–15 | 8.1±3.3 | |
| ZCBS III | | 5 3–15 | 6.1±3.1 | |
| ZCBS IV | | 11 3–20 | 10.6±4.1 | |
| ZCBS V | | 8 2–10 | 7.3±2.6 | |
| HAM-D | None | 40 | | 56.3% |
| | Mild | 14 | | 19.7% |
| | Moderate | 14 | | 19.7% |
| | Severe | 3 | | 4.2% |

Table 2. Frequency of behavioural and psychological symptoms of the patients.

| | n | % |
|---|----|-------|
| Neuropsychiatric Inventory (NPI) | | |
| Delirium | 41 | 57.7% |
| Hallucination | 38 | 53.5% |
| Agitation / Aggression | 19 | 26.8% |
| Depression / Dysphoria | 40 | 56.3% |
| Anxiety | 31 | 43.7% |
| Elation / Euphoria | 1 | 1.4% |
| Apathy | 43 | 60.6% |
| Disinhibition | 25 | 35.2% |
| Irritability | 34 | 47.9% |
| Abnormal Motor Behaviour | 21 | 29.6% |
| Sleep – Night Behaviour | 23 | 32.4% |
| Eating – Appetite | 19 | 26.8% |

burden and symptoms increased ($p = 0.000$) as the BPSD increased. BPS affecting caregivers with moderate to severe caregiver burden were delirium ($p = 0.031$), hallucination ($p = 0.023$), agitation / aggression ($p = 0.035$), depression / dysphoria ($p = 0.042$), anxiety ($p = 0.004$), apathy ($p = 0.011$), disinhibition ($p = 0.029$), irritability ($p = 0.017$) and abnormal motor behaviour ($p = 0.002$). These symptoms had statistically significant ($p < 0.05$) impact on caregivers with moderate and severe caregiver burden compared to those with mild caregiver burden (Table 3).

The effect of the behavioural and psychological symptoms on the level of caregiver depression

When the effect of BPS on caregiver depression is evaluated; caregiver depression increased as neuropsychiatric symptoms increased ($p = 0.000$). The symptoms of agitation/aggression ($p = 0.010$), anxiety ($p = 0.009$), disinhibition ($p = 0.011$) and irritability ($p = 0.001$) had a statistically significant impact on depressive caregivers ($p < 0.05$) compared to the group without depression (Table 4).

Correlation between behavioural and psychological symptoms, caregiver burden and caregiver depression

There was a significant positive correlation between delirium, hallucination, agitation/aggression, anxiety, apathy, disinhibition, irritability, abnormal motor behaviour and ZCBS I (mental tension and disruption of private life) ($p < 0.05$).

There was a significant positive correlation between delirium, hallucination, agitation/aggression, anxiety, disinhibition, irritability, abnormal motor behaviour and ZCBS II (irritability, restrictedness) ($p < 0.05$).

There was a significant positive correlation between delirium, hallucination, agitation/aggression, anxiety, apathy, disinhibition, irritability, abnormal motor behaviour, and ZCBS III (disruption in social relations) ($p < 0.05$).

There was a significant positive correlation between depression/dysphoria and ZCBS IV (economic burden) ($p < 0.05$).

There was a significant positive correlation between hallucination, apathy and eating/appetite and ZCBS V (addiction) ($p < 0.05$).

There was a significant positive correlation between agitation/aggression, depression/dysphoria, anxiety, apathy, disinhibition, irritability, abnormal motor behaviour and ZCBS total value ($p < 0.05$).

There was a significant positive correlation between agitation/aggression, depression/dysphoria, anxiety, apathy, disinhibition, irritability, abnormal motor behaviour and HAM-D ($p < 0.05$).

There was no significant correlation between Elation / Euphoria and sleep-night behaviour and ZCBS subscales, ZCBS total score and HAM-D ($p > 0.05$) (Table 5).

Correlation between neuropsychiatric symptoms total score and caregiver burden subgroups;

When we look at the correlation between BPS total value and caregiver burden subgroups; there was a significant positive correlation between ZCBS I (mental tension and disruption of private life) ($p = 0.000$), ZYBO II (nervousness, restrictedness) ($p = 0.000$), ZYBO III (disruption in social relations) ($p = 0.000$), ZYBO V (addiction) ($p = 0.001$) and BPS values. There was no significant correlation between neuropsychiatric symptoms total score and ZYBO IV (economic burden) ($p = 0.076$) (Table 6).

Discussion

In the systematic review study by Torti et al., the average age of caregivers for dementia patients was middle age and over [29]. The gender of the caregiver was female in the majority of the studies. In a multicentre study by Rinaldi et al. involving 419 dementia patients and their caregivers, 302 of the caregivers were female, 117 were male and their average age was 58.2. The majority of caregivers were children of patients, followed by their partners [30]. The caregiver profile in our study is in parallel with the literature in terms of age, sex, and degree of closeness with the patient.

The incidence of depression is high in patients with Alzheimer's disease. Caregivers have worried that their quality of life has deteriorated and show inadequate coping strategies. In many studies, clinical depression was detected in 10–83% of the caregivers screened for depression [10,14,31,32]. Dura et al. detected depression in 24% of patients with dementia [33]. In a study conducted by Mahoney et al., including 153 caregivers for Alzheimer's patients, depression was observed in 10.5% of caregivers [34]. In our study,

Table 3. The effect of the behavioural and psychological symptoms of the patients on caregiver burden.

| | ZCBS – Mild | | | ZCBS – Moderate – Severe | | | <i>p</i> |
|---|---------------|---------------|--------|--------------------------|---------------|---------|--------------|
| | Ave.±s.d./n-% | Med (Min–Max) | | Ave.±s.d./n-% | Med (Min–Max) | | |
| Neuropsychiatric Inventory (NPI) | | | | | | | |
| Total NPI Score | 22.0 ± 18.3 | 16 | 0 - 63 | 49.7 ± 30.8 | 54 | 0 - 105 | 0.000 |
| Delirium | 2.6 ± 3.8 | 1 | 0 - 12 | 5.4 ± 5.3 | 3 | 0 - 12 | 0.031 |
| Hallucination | 2.0 ± 3.8 | 0 | 0 - 12 | 3.8 ± 4.4 | 1 | 0 - 12 | 0.023 |
| Agitation / Aggression | 0.8 ± 2.0 | 0 | 0 - 9 | 2.7 ± 4.4 | 0 | 0 - 12 | 0.035 |
| Depression / Disphoria | 2.8 ± 4.0 | 0 | 0 - 12 | 5.2 ± 5.0 | 4 | 0 - 12 | 0.042 |
| Anxiety | 1.6 ± 3.1 | 0 | 0 - 12 | 4.9 ± 4.8 | 6 | 0 - 12 | 0.004 |
| Elation / Euphoria | 0.0 ± 0.0 | 0 | 0 - 0 | 0.1 ± 0.7 | 0 | 0 - 4 | 0.310 |
| Apathy | 4.6 ± 5.5 | 0 | 0 - 12 | 8.0 ± 4.9 | 12 | 0 - 12 | 0.011 |
| Disinhibition | 1.2 ± 3.1 | 0 | 0 - 12 | 3.6 ± 4.9 | 0 | 0 - 12 | 0.029 |
| Irritability | 1.8 ± 3.3 | 0 | 0 - 12 | 5.0 ± 5.2 | 4 | 0 - 12 | 0.017 |
| Abnormal Motor Behaviour | 0.8 ± 2.4 | 0 | 0 - 12 | 4.2 ± 5.5 | 0 | 0 - 12 | 0.002 |
| Sleep – Night Behaviour | 2.2 ± 3.8 | 0 | 0 - 12 | 3.4 ± 5.2 | 0 | 0 - 12 | 0.532 |
| Eating – Appetite | 2.0 ± 4.3 | 0 | 0 - 12 | 3.5 ± 5.3 | 0 | 0 - 12 | 0.160 |
| Caregiver Distress | 9.2 ± 7.5 | 9 | 0 - 26 | 21.2 ± 11.6 | 21 | 0 - 41 | 0.000 |

Note: Mann–Whitney U test.

43.7% of caregivers were found to have depression. Development of depression in the caregiver may be affected by different variables such as social, cultural, sociodemographic, and clinical characteristics. In different societies, we believe that different results can be detected due to the mentioned properties.

Different results have been obtained in different studies investigating the frequency of BPS seen in Alzheimer's patients. The most common symptoms resulting from the individual evaluation of BPS in patients with dementia are apathy, depression, irritability, agitation and anxiety while the least frequent are euphoria, hallucinations and disinhibition. Clinically the most significant symptoms are depression, apathy and anxiety. At least four neuropsychiatric symptoms occur in 50% of patients [35]. In a study by Bergh and Selbaek to determine the prevalence of neuropsychiatric symptoms, 19 trials were reviewed. Four of these studies involved patients from general population, ten from outpatient clinic and five from nursing houses and the most common neuropsychiatric manifestations regardless of the characteristics of the patients' habitat are apathy, irritability, agitation / aggression, depression and anxiety, while the least frequent neuropsychiatric symptoms are deliriums,

hallucinations, disinhibition, abnormal motor behaviour and euphoria [36]. In our study, apathy, irritability, depression, and anxiety were higher than in other studies. The least common neuropsychiatric symptom in our study is euphoria similar to other studies. Differences in the results may be due to differences in the characteristics of the sample group and the assessment tools.

In the study of Matsumoto et al. involving 67 dementia patients and their caregivers assessed by the NPI scale, to investigate the association of neuropsychiatric symptoms seen in patients with dementia in the community with the distress caused in caregiver showed higher levels of distress in caregivers of patients with more neuropsychiatric symptoms, similarly to our results [37]. In a study conducted by Huang et al. with 88 dementia patients and their caregivers, the NPI scale was used and it was found that high neuropsychiatric symptoms increased caregivers' burnout [38].

When the effects of each BPS on caregiver burden were examined, the results of our study revealed that delirium, hallucinations, agitation/aggression, depression/dysphoria, anxiety, apathy, disinhibition, irritability and abnormal motor behaviour were correlated with the caregiver burden level ($p < 0.05$). Most

Table 4. The effect of the behavioural and psychological symptoms on the level of caregiver depression.

| | HAM-D Depression-None | | | HAM-D Depression-Yes | | | <i>p</i> |
|---|-----------------------|---------------|--------|----------------------|---------------|---------|--------------|
| | Ave.±s.d./n-% | Med (Min–Max) | | Ave.±s.d./n-% | Med (Min–Max) | | |
| Neuropsychiatric Inventory (NPI) | | | | | | | |
| Total NPI Score | 25.1 ± 21.6 | 21 | 0 - 84 | 49.4 ± 31.1 | 54 | 1 - 105 | 0.001 |
| Delirium | 3.1 ± 4.2 | 2 | 0 - 12 | 5.1 ± 5.3 | 3 | 0 - 12 | 0.137 |
| Hallucination | 2.4 ± 3.8 | 1 | 0 - 12 | 3.6 ± 4.6 | 1 | 0 - 12 | 0.315 |
| Agitation / Aggression | 0.8 ± 2.3 | 0 | 0 - 9 | 2.9 ± 4.5 | 0 | 0 - 12 | 0.010 |
| Depression / Disphoria | 3.0 ± 4.1 | 1 | 0 - 12 | 5.3 ± 5.1 | 4 | 0 - 12 | 0.074 |
| Anxiety | 2.0 ± 3.5 | 0 | 0 - 12 | 4.9 ± 4.8 | 6 | 0 - 12 | 0.009 |
| Elation / Euphoria | 0.0 ± 0.0 | 0 | 0 - 0 | 0.1 ± 0.7 | 0 | 0 - 4 | 0.256 |
| Apathy | 5.2 ± 5.6 | 3 | 0 - 12 | 7.6 ± 5.1 | 9 | 0 - 12 | 0.075 |
| Disinhibition | 1.1 ± 2.9 | 0 | 0 - 12 | 4.1 ± 5.0 | 0 | 0 - 12 | 0.011 |
| Irritability | 1.6 ± 3.3 | 0 | 0 - 12 | 5.5 ± 5.2 | 4 | 0 - 12 | 0.001 |
| Abnormal Motor Behaviour | 1.6 ± 3.8 | 0 | 0 - 12 | 3.5 ± 5.2 | 0 | 0 - 12 | 0.105 |
| Sleep – Night Behaviour | 2.1 ± 3.8 | 0 | 0 - 12 | 3.6 ± 5.3 | 0 | 0 - 12 | 0.405 |
| Eating – Appetite | 2.3 ± 4.7 | 0 | 0 - 12 | 3.3 ± 5.1 | 0 | 0 - 12 | 0.389 |
| Distress caused by symptoms | 10.2 ± 8.6 | 11 | 0 - 34 | 21.5 ± 11.5 | 23 | 1 - 41 | 0.000 |

Note: Mann–Whitney U test.

Table 5. Correlation between behavioural and psychological symptoms, caregiver burden and caregiver depression.

| | | ZCBS I | ZCBS II | ZCBS III | ZCBS IV | ZCBS V | ZCBS Total | HAM-D |
|--------------------------|----------|--------------|--------------|--------------|--------------|--------------|--------------|--------------|
| Delirium | <i>r</i> | 0.302 | 0.271 | 0.274 | 0.112 | 0.153 | 0.214 | 0.214 |
| | <i>p</i> | 0.010 | 0.022 | 0.021 | 0.351 | 0.202 | 0.073 | 0.073 |
| Hallucination | <i>r</i> | 0.318 | 0.249 | 0.501 | −0.051 | 0.291 | 0.167 | 0.167 |
| | <i>p</i> | 0.007 | 0.036 | 0.000 | 0.675 | 0.014 | 0.164 | 0.164 |
| Agitation / Aggression | <i>r</i> | 0.357 | 0.356 | 0.277 | 0.146 | 0.128 | 0.383 | 0.383 |
| | <i>p</i> | 0.002 | 0.002 | 0.019 | 0.223 | 0.288 | 0.001 | 0.001 |
| Depression / Disphoria | <i>r</i> | 0.232 | 0.126 | 0.146 | 0.341 | 0.093 | 0.245 | 0.245 |
| | <i>p</i> | 0.051 | 0.295 | 0.225 | 0.004 | 0.439 | 0.040 | 0.040 |
| Anxiety | <i>r</i> | 0.305 | 0.421 | 0.308 | 0.201 | 0.213 | 0.349 | 0.349 |
| | <i>p</i> | 0.010 | 0.000 | 0.009 | 0.093 | 0.074 | 0.003 | 0.003 |
| Elation / Euphoria | <i>r</i> | 0.129 | 0.029 | 0.077 | 0.009 | 0.135 | 0.075 | 0.075 |
| | <i>p</i> | 0.285 | 0.808 | 0.524 | 0.942 | 0.261 | 0.536 | 0.536 |
| Apathy | <i>r</i> | 0.353 | 0.080 | 0.270 | 0.132 | 0.337 | 0.253 | 0.253 |
| | <i>p</i> | 0.003 | 0.508 | 0.023 | 0.271 | 0.004 | 0.033 | 0.033 |
| Disinhibition | <i>r</i> | 0.372 | 0.303 | 0.385 | 0.092 | 0.185 | 0.313 | 0.313 |
| | <i>p</i> | 0.001 | 0.010 | 0.001 | 0.445 | 0.122 | 0.008 | 0.008 |
| Irritability | <i>r</i> | 0.307 | 0.408 | 0.305 | 0.138 | 0.188 | 0.485 | 0.485 |
| | <i>p</i> | 0.009 | 0.000 | 0.010 | 0.251 | 0.116 | 0.000 | 0.000 |
| Abnormal Motor Behaviour | <i>r</i> | 0.327 | 0.402 | 0.412 | 0.005 | 0.136 | 0.248 | 0.248 |
| | <i>p</i> | 0.005 | 0.001 | 0.000 | 0.965 | 0.259 | 0.037 | 0.037 |
| Sleep – Night Behaviour | <i>r</i> | 0.211 | 0.190 | 0.205 | −0.047 | 0.098 | 0.158 | 0.158 |
| | <i>p</i> | 0.078 | 0.112 | 0.087 | 0.696 | 0.416 | 0.188 | 0.188 |
| Eating – Appetite | <i>r</i> | 0.208 | 0.150 | 0.110 | 0.190 | 0.300 | 0.105 | 0.105 |
| | <i>p</i> | 0.082 | 0.212 | 0.360 | 0.113 | 0.011 | 0.384 | 0.384 |

Note: Spearman correlation

correlated neuropsychiatric symptoms with caregiver burden were abnormal motor behaviour and anxiety ($p < 0.01$). Elation/euphoria, sleep-night behaviour, eating appetite changes did not affect the level of caregiver burden. In a study of 82 Alzheimer's patients and caregivers Allegri et al. compared each sub-factor of the NPI scale with the caregiver burden level and found that positive neuropsychiatric symptoms such as hallucinations, abnormal motor behaviours, and abnormal sleep-night behaviours correlated significantly with caregiver burden. In the same study, negative neuropsychiatric symptoms such as apathy and depression did not correlate with caregiving burden, while delirium, anxiety, disinhibition, agitation and eating-appetite changes correlated with caregiver burden at lower extent [18]. In our study, the relation of some neuropsychiatric symptoms with the caregiver burden varied with the results of Allegri et al. This was considered to be due to differences in the populations and assessment tools in the studies.

In our study, the evaluation of the relationship between BPS seen in patients and the caregiver depression showed more depression in the group of caregivers for patients with more neuropsychiatric symptoms. In a study by Mohamed et al. of 421 outpatients with Alzheimer's and their caregivers participating in the CATIE-AD study, a multicenter randomized double-blind placebo-controlled study, the severity of

neuropsychiatric symptoms seen in patients was significantly associated with caregiver depression [39]. In a study by Clyburn et al. involving 613 dementia patients and their caregivers living in community and nursing homes, behavioural and psychiatric problems seen in patients were closely related to the presence of depressive symptoms of caregivers [40]. In our study, consistent results were obtained with the results of similar studies in the literature.

In our study, the evaluation of ZCBS's 5 subscales in the group with more neuropsychiatric symptoms compared to that with less symptoms showed that individual scores of each factor were higher. Correlation analysis of NPI scores and ZCBS factor groups revealed that only factor 4 representing the economic burden did not show a significant correlation. Factor 4, which indicates the economic burden in the ZCBS, is not expected to correlate with neuropsychiatric symptoms because it is related to the economic burden on the caregiver of the patient.

Conclusion

If we summarize the results of our study;

- The average age of caregivers is 52.9 and 81.7% are women.
- Depression were mild in 19.7% of the caregivers, moderate in 19.7% and severe in 4.2%. The incidence is 43.7% in total.
- The most common BPS in patients are; apathy, delirium, depression/dysphoria, hallucinations, irritability, anxiety, disinhibition, sleep-night behaviour, abnormal motor behaviour, agitation/aggression, eating-appetite changes, elation/euphoria.

Table 6. Correlation between neuropsychiatric inventory total score and caregiver burden subgroups.

| | | ZCBS I | ZCBS II | ZCBS III | ZCBS IV | ZCBS V |
|----------------------------------|----------|--------------|--------------|--------------|---------|--------------|
| Neuropsychiatric Inventory (NPI) | <i>r</i> | 0.503 | 0.413 | 0.481 | 0.212 | 0.376 |
| | <i>p</i> | 0.000 | 0.000 | 0.000 | 0.076 | 0.001 |

Note: Spearman correlation.

- The NPI score of caregiver's distress is higher in the group with more BPS.
- Caregiver's burden and depression are higher in the group of patients with more BPS.
- Symptoms having a significant effect on caregiver burden were delusions, hallucinations, agitation/aggression, depression/dysphoria, anxiety, apathy, disinhibition, irritability, abnormal motor behaviour.
- Symptoms having a significant effect on caregiver's depression are agitation/aggression, anxiety, disinhibition, irritability.
- Agitation /aggression, anxiety, disinhibition, and irritability are common symptoms that affect caregiver's burden and depression.
- There was no significant correlation between Elation / Euphoria and sleep-night behaviour and ZCBS subscales, ZCBS total value and HAM-D.
- In the correlation analysis between NPI and ZCBS factor groups, only the factor 4 showing the economic burden did not show any significant correlation.

We tried to investigate the relationship between behavioural and psychological symptoms in Alzheimer patients and caregiver burden and depression. We discussed the results in light of the literature. While some of our findings were consistent with the results of the literature, some of them were different. We emphasized that the results can be affected by various factors such as social, cultural, sociodemographic and clinical characteristics, number and characteristics of the sample, study design, scales used.

Due to the increase in the geriatric population, the needs in this area are increasing day by day. The identification of behavioural and psychological symptoms that increase the burden of caregivers of Alzheimer's patients and affect the development of depression in caregivers will enable this process with great difficulties for both the patient and the caregiver to be carried out more healthily. The results indicate that BPS seen in AD increase the caregiver burden and cause caregiver depression. Preventive measures to prevent the emergence of such symptoms and effective and rapid intervention are required. For this reason, we believe that our study is meaningful despite the small number of populations. Further multi-center studies with a prospective design, involving different cultures, patients from a wider population, different care settings are required.

Acknowledgement

This study is performed for the dissertation of Spec. Dr. Gamze Bozgeyik and her thesis supervisor was Spec. Dr. Derya Ipekcioglu. Both authors have equal rights in the study.

Disclosure statement

No potential conflict of interest was reported by the authors.

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