RESEARCH PAPER

EFFECT OF MIRTAZAPINE ON DEPRESSION IN ELDERLY CANCER PATIENTS UNDERGOING PALLIATIVE CARE

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ABSTRACT

Depression affects 2-3 times more cancer patients than the general population, significantly impacting quality of life, treatment compliance, and survival outcomes. In elderly cancer patients receiving palliative care, depression management remains challenging due to complex comorbidities and polypharmacy concerns. Mirtazapine, a noradrenergic and specific serotonergic antidepressant (NaSSA), offers potential advantages in this population through its rapid onset of action and beneficial side effects including appetite stimulation and sedation. **This study aims to** evaluate the effectiveness of mirtazapine in managing depression among elderly cancer patients in a geriatric palliative care unit at Ain Shams University Hospitals. The current prospective cohort study enrolled 60 elderly cancer patients (≥60 years) with DSM-5 diagnosed depression receiving palliative care over a two-month period. Fifty-six patients (93.3%) completed follow-up assessments. Patients with cognitive impairment, delirium, or terminal cancer (survival <6 weeks) were excluded. Participants received mirtazapine starting at 15mg daily, with dose escalation to 30mg based on clinical response. Comprehensive assessments were conducted at baseline, one month, and two months using validated instruments including HADS, Hamilton Depression Rating Scale (HAMD), PHQ-9, Mini Nutritional Assessment (MNA), and quality of life measures. The mean age of patients was 73.03±8.32 years, with 55% male participants. Significant improvements were observed in depression scores: HADS-D cases decreased from 86.7% to 5.4% ($p<0.001$), and HAMD scores improved from 18.28±3.06 to 11.45±2.5 ($p<0.001$). Anxiety symptoms also improved significantly, with HADS-A cases declining from 71.7% to 1.8% ($p<0.001$). Additional benefits included improved nutritional status (malnourished patients decreased from 41.7% to 8.9%), enhanced appetite (normal appetite increased from 16.7% to 83.9%), better sleep satisfaction (35% to 89.3%), and improved quality of life scores (median 2 to 4, $p<0.001$). Pain reduction was more significant in patients receiving concurrent opioid therapy. The most common side effect was sedation (15.5% at one month, 10.7% at two months), with no serious adverse events reported.

In conclusion mmirtazapine demonstrated significant effectiveness in managing depression and anxiety in elderly cancer patients receiving palliative care, with additional benefits for appetite, sleep, nutritional status, and quality of life. The medication was well-tolerated with manageable side effects. These findings support mirtazapine as a valuable therapeutic option for depression management in this vulnerable population, though individualized dosing and careful monitoring are essential. Further randomized controlled trials are needed to establish optimal dosing strategies and long-term outcomes.

Keywords: Mirtazapine, Depression, Elderly, Cancer, Palliative Care, Geriatric Oncology, Antidepressant

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INTRODUCTION

Depression represents one of the most prevalent and debilitating psychiatric conditions affecting cancer patients, with studies consistently demonstrating prevalence rates two to three times higher than those observed in the general population **(Gharib et al., 2026).** The psychological burden of cancer diagnosis and treatment creates a complex interplay of factors that significantly increase vulnerability to mood disorders, particularly among elderly patients who face additional age-related challenges and comorbidities **(Gharib et al., 2026).**

The clinical significance of depression in oncology settings extends far beyond psychological distress, as it profoundly impacts multiple dimensions of patient care and outcomes**.** Depression in cancer patients has been associated with reduced treatment compliance, prolonged hospital stays, decreased quality of life, and increased healthcare utilization, creating substantial challenges for both patients and healthcare systems **(Perusinghe et al., 2021).**

Among elderly cancer patients, the management of depression becomes particularly complex due to age-related physiological changes, increased comorbidity burden, and heightened sensitivity to medication side effects**.** The intersection of aging, cancer, and depression creates a vulnerable population that requires specialized therapeutic approaches, with careful consideration of drug interactions, polypharmacy concerns, and altered pharmacokinetics (**Mohamed et al., 2024).**

Palliative care settings present unique challenges for depression management, as patients often experience concurrent physical symptoms, existential distress, and anticipatory grief while facing life-limiting illness **(Economos et al., 2022).** Traditional antidepressant therapies may be less suitable in this context due to delayed onset of action, problematic side effect profiles, or contraindications related to cancer treatments and comorbid conditions **(Arrieta et al., 2024).**

Mirtazapine, a noradrenergic and specific serotonergic antidepressant (NaSSA), has emerged as a promising therapeutic option for depression management in cancer patients due to its unique

pharmacological profile and beneficial ancillary effects **(Hughes et al., 2025).** Unlike selective serotonin reuptake inhibitors, mirtazapine offers additional advantages including appetite stimulation, sedation, and antiemetic properties, which may address multiple symptoms commonly experienced by cancer patients (**Crampton & Weisse, 2023).** The rapid onset of antidepressant action associated with mirtazapine, with clinical improvements reported within 1-2 weeks of initiation, makes it particularly valuable in palliative care settings where time-sensitive symptom relief is crucial**.** This faster therapeutic response, combined with its favorable side effect profile for cancer patients, positions mirtazapine as an attractive option for managing depression in elderly oncology populations **(Crampton & Weisse, 2023).**

Although, expert consensus and clinical guidelines have increasingly recognized mirtazapine as one of the preferred antidepressants for palliative care settings, based on its multisymptomatic benefits and suitability for patients with complex medical conditions (Davis, 2024), yet comprehensive studies specifically evaluating its effectiveness in elderly cancer patients receiving palliative care are limited. Therefore, this study aimed to evaluate Effect of Mirtazapine in the management of depression in elderly patients with cancer in geriatric palliative care unit in Ain Shams University Hospitals.

PATIENTS AND METHODS

Study Design and Setting

Study Design: A prospective cohort study was conducted over a two-month period to evaluate the effects of mirtazapine on depression in elderly cancer patients receiving palliative care.

Study Setting: The study was carried out in the geriatric inpatient palliative care unit at Ain Shams University Hospitals, Cairo, Egypt.

Participants: A total of 60 elderly inpatients, aged 60 years or older, were enrolled in the study. All participants had confirmed diagnoses of both cancer and depression according to established clinical criteria. Patients were consecutively recruited from the inpatient geriatric palliative care unit.

Sample Size Calculation: Based on previous research by Stacey **DaCosta Byfield et al. (2021**), who reported 48% proportion of depression/anxiety in elderly cancer patients, sample size calculations were performed. A minimum sample of 51 participants was determined to achieve 80% statistical power for detecting clinically meaningful differences between pre- and post-treatment measurements, with an expected improvement rate of at least 75% using McNemar's test for paired proportions at a significance level of 0.05.

Inclusion Criteria

Participants were eligible if they were aged 60 years or older with confirmed cancer diagnoses requiring palliative care and DSM-5 diagnosed depression (five or more symptoms within two weeks). Additional requirements included adequate cognitive function (MMSE score ≥24) and predicted survival exceeding six weeks (PPI score <4).

Exclusion Criteria

Patients were excluded for unwillingness to participate, severe sensory impairments interfering with assessments, cognitive impairment (MMSE <24), terminal status with survival <6 weeks (PPI ≥4), active delirium (positive CAM), or contraindications to mirtazapine therapy.

Treatment Protocol

Mirtazapine Administration

All participants received mirtazapine following a standardized dosing protocol, with an initial dose of 15 mg administered at bedtime consistent with established guidelines for elderly patients **(U.S. Food and Drug Administration, 2020).** Dose adjustments were made based on clinical response and tolerability assessments at one-month follow-up visit. Dosing decisions followed established clinical guidelines: starting dose of 15 mg once daily at bedtime, with dose escalation to 30 mg if insufficient improvement occurred after one month and the medication was well-tolerated. The 15 mg dose was maintained if adequate improvement was observed or limited tolerance noted, with all dosing decisions individualized based on clinical response and tolerability.

Follow-up Schedule

Comprehensive assessments were conducted at three time points: baseline assessment prior to mirtazapine initiation, then one-month follow-up assessment, and two-month follow-up assessment. Follow-up visits were conducted in person at the outpatient clinic, with medication adherence monitored through weekly telephone contacts or face-to-face encounters to ensure treatment compliance and safety monitoring.

Baseline Assessments

Comprehensive Geriatric Assessment (CGA)

All participants underwent comprehensive geriatric assessment at baseline, encompassing demographic and clinical evaluation including detailed demographic information, medical history and comorbidity assessment using the Charlson Comorbidity Index, medication reconciliation with documentation of polypharmacy, and cancer-specific information including type, stage, metastatic status, and treatment modalities. Depression diagnosis and severity assessment included DSM-5 criteria for Major Depressive Disorder diagnosis and Patient Health Questionnaire-9 for depression severity quantification with scores interpreted as minimal (0-4), mild (5-9), moderate (10-14), moderately severe (15-19), or severe (20-27). Cognitive assessment utilized the Mini-Mental State Examination using validated Arabic version (**Kabalan et al., 2025)** and Confusion Assessment Method to exclude delirium (**Zhou et al., 2024).** Functional and frailty assessment incorporated the Palliative Performance Index for survival prediction **(Blanes-Selva et al., 2022),** Timed Up and Go Test for mobility and fall risk assessment, and Clinical Frailty Scale for frailty categorization (**Strini et al., 2021).**

Serial Assessment Measures

The following validated instruments were administered at baseline, one month, and two months. Mood assessment included the Hospital Anxiety and Depression Scale, a 14-item scale with separate anxiety

and depression subscales scored 0-21 for each domain (**Palmer, 2020),** and the Hamilton Depression Rating Scale, a 17-item clinician-administered scale for objective depression severity rating **(Byrne et al., 2024).** Functional assessment encompassed Activities of Daily Living for basic self-care activities assessment **(Pashmdarfard & Azad, 2020)** and Instrumental Activities of Daily Living for complex daily functioning evaluation (**Pashmdarfard & Azad, 2020).** Nutritional assessment utilized the Mini Nutritional Assessment for comprehensive nutritional status evaluation using validated Arabic version (**Shamlan et al., 2024**) and self-rated appetite assessment as normal or decreased. Symptom assessment included the Numerical Pain Rating Scale using a 0-10 pain intensity scale (**Wikström et al., 2024),** structured interview assessment of sleep quality and daytime napping, and self-rated quality of life using a 0-7 scale for overall health and well-being satisfaction. Safety monitoring involved systematic evaluation of common mirtazapine-related adverse effects including sedation, fatigue, dry mouth, dizziness, and constipation, along with medication adherence assessment through patient/caregiver interviews using non-judgmental questioning techniques **(Necyk et al., 2026).**

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics Version 27.0 (IBM Corp., Armonk, NY). Quantitative data were presented as means with standard deviations for parametric distributions and medians with interquartile ranges for non-parametric data. Qualitative variables were expressed as frequencies and percentages. Receiver operating characteristic (ROC) curve analysis was utilized to determine optimal cut-off points for depression screening instruments, with calculation of sensitivity, specificity, positive and negative predictive values, and area under the curve (AUC). Statistical significance was set at 95% confidence interval with 5% margin of error:

P-value > 0.05: Non-significant (NS), P-value < 0.05: Significant (S), P-value < 0.01: Highly significant (HS)

Ethical Considerations

The study was conducted following approval from the Research Ethics Committee at Ain Shams University Hospitals. Written informed consent was obtained from all participants or their legal guardians prior to enrollment.

RESULTS

Depression and anxiety of patients at start :

The dataset in Table (1) evaluates baseline depression and anxiety levels in 60 patients using four standard clinical screening tools. The Patient Health Questionnaire-9 (PHQ-9) indicates that 10% of patients with severe clinically significant depression (PHQ-9> 19), while 45% scored in the Moderately Severe range (15–19).

The Hospital Anxiety and Depression Scale for Anxiety (HADS-A) demonstrates that severe anxiety is nearly universal in this cohort, i.e. 71.7% (n = 43) met the strict diagnostic criteria for a definitive "case" of clinical anxiety (11–21). The depression subscale of the same instrument (HADS-D) mirrors the PHQ-9 findings but suggests even higher definitive clinical case rates, 86.7% (n = 52) met the threshold for a definitive clinical case of depression. The Hamilton Rating Scale for Depression (HAM-D) provides an external clinical evaluation of the sample. 33.3% (n = 20) were rated with Mild depression (13–25), 66.7% (n = 40) were rated with Moderate depression, while 86.7% (n = 52) met the threshold for a definitive clinical case of depression.

The baseline psychological assessments of the investigated 60 patients reveal high rates of significant morbidity, with 100% of participants scoring in the clinically significant range for depression (PHQ-9) and anxiety (HADS). The data indicates universal distress across all measures, characterized by a high burden of comorbid anxiety (71.7% clinical) and depression (86.7% clinical) with no patients falling into the normal range (Table 1). The strong agreement between the self-reported measures (PHQ-9, HADS) and the clinician-rated scale (HAM-D) confirms that psychological distress is severe, pervasive, and heavily comorbid with anxiety.

Table (1): Depression and anxiety at start among the studied patients.

		At start
		No. = 60
PHQ 9	Mild Moderate 10-14 Moderately Severe 15-19 Severe above 19	0 (0%) 27 (45.0%) 27 (45.0%) 6 (10.0%)
HADS-A	Normal (0-7) Borderline cases (8-10) A case (11-21)	0 (0%) 17 (28.3%) 43 (71.7%)
HADS-A	Mean ± SD Range	14.18 ± 3.41 8 – 20
HADS-D	Normal (0-7) Borderline cases (8-10) A case (11-21)	0 (0%) 8 (13.3%) 52 (86.7%)
HADS-D	Mean ± SD Range	15.08 ± 3.02 10 – 21
HAMD-D	Normal Mild (10-13) Moderate (14-17) Severe (more than 17)	0 (0%) 20 (33.3%) 40 (66.7%) 0 (0%)
HAMD-D	Mean ± SD Range	18.28 ± 3.06 13 – 25

PHQ-9: Patient Health Questionnaire-9, HADS-D: Hospital Anxiety and Depression Scale for depression, HADS-A: Hospital Anxiety and Depression Scale for anxiety, HAM-D: Hamilton Rating Scale for Depression.

Effect of mirtazapine on Depression and anxiety

Data in Table (2) revealed a rapid, highly significant reduction in both anxiety and depression symptoms following the initiation of mirtazapine therapy over the 2-month study period. For anxiety, self-reported HADS-A scores demonstrated substantial improvement. The proportion of patients meeting the criteria for a definitive clinical case plummeted from 71.7% at baseline to 13.8% at one month, and nearly resolved entirely to 1.8% by month two. Concurrently,

the percentage of patients achieving a normal anxiety score rose from 0% to 41.1% at the final endpoint. The mean HADS-A score decreased significantly from 14.18 ± 3.41 at baseline to 9.22 ± 1.75 at one month, reaching a low of 7.29 ± 1.85 at two months .

Parallel improvements were observed in self-reported depressive symptoms via the HADS-D scale. Definitive clinical cases of depression dropped from 86.7% at baseline to 25.9% at one month, and down to 5.4% by month two. By the study's conclusion, 35.7% of patients had achieved total symptom remission, placing them within the normal range ($0–7$). The mean HADS-D score reflected a highly significant, steady decline from 15.08 ± 3.02 at the start to 9.43 ± 1.94 at month one, and 8.36 ± 1.68 at month two.

Clinician-rated depression via the HAM-D mirrored these self-reported trends, verifying robust clinical remission. At baseline, 66.7% of patients presented with moderate depression, whereas by month two, 64.3% had downgraded to mild symptoms, and 19.6% achieved clinical remission (0% at baseline vs. 19.6% at 2 months). Mean HAM-D scores continuously and significantly decreased across the timeline, falling from 18.28 ± 3.06 at baseline to 14.22 ± 2.82 at one month, and 11.45 ± 2.50 at two months. The total sample attrition remained low, with only 4 patients lost to follow-up over the course of the study (N = 60 at baseline; N = 56 at 2 months).

Table (2): Effect of mirtazapine on Depression and anxiety at start, after 1 month and 2 months among the studied patients.

		At start	After 1 month	After 2 months	Test value	P-value	Sig.
		No. = 60	No. = 58	No. = 56			
HADS-A	Normal(0-7)	0 (0%)	9 (15.5%)	23 (41.1%)	92.526*	0.007	HS
	Borderline cases (8-10)	17 (28.3%)	41 (70.7%)	32 (57.1%)			
	A case (11-21)	43 (71.7%)	8 (13.8%)	1 (1.8%)			
HADS-A	Mean ± SD	14.18 ± 3.41	9.22 ± 1.75	7.29 ± 1.85	162.754•	0.007	HS
	Range	8 – 20	5 – 15	4 – 11			
HADS- D	Normal (0-7)	0 (0%)	3 (5.2%)	20 (35.7%)	106.601*	<0.001	HS
	Borderline cases (8-10)	8 (13.3%)	40 (69%)	33 (58.9%)			
	A case (11-21)	52 (86.7%)	15 (25.9%)	3 (5.4%)			
HADS- D	Mean ± SD	15.08 ± 3.02	9.43 ± 1.94	8.36 ± 1.68	207.878•	<0.001	HS
	Range	10 – 21	4 – 17	5 – 14			
HAM D-D	Normal	0 (0%)	0 (0%)	11 (19.6%)	53.488*	0.000	HS
	Mild (10-13)	20 (33.3%)	24 (41.4%)	36 (64.3%)			
	Moderate (14-17)	40 (66.7%)	30 (51.7%)	8 (14.3%)			
	Severe (more than 17)	0 (0%)	4 (6.9%)	1 (1.8%)			
HAM D-D	Mean ± SD	18.28 ± 3.06	14.22 ± 2.82	11.45 ± 2.5	110.586•	0.000	HS
	Range	13 – 25	10 – 24	5 – 18			

HADS-D: Hospital Anxiety and Depression Scale for depression, HADS-A: Hospital Anxiety and Depression Scale for anxiety, HAM-D: Hamilton Rating Scale for Depression

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

*: Chi-square test; •: Repeated Measures ANOVA test

Comparison of different doses of Mirtazapine regarding Depression and anxiety

The total sample size evaluated in this baseline (Table 3) is 56 patients and this matches our final month 2 follow-up count, indicating that this specific analysis focused only on the patients who completed the entire trial duration. It was obvious from analysis of data that there was no statistically significant difference (p > 0.05) in levels of baseline Depression Severity (PHQ-9) or Baseline Anxiety (HADS-A) for patients who treated with a lower dose (15 mg) (n=21) versus a higher dose (30 mg) (n=35) of mirtazapine. Assessment of baseline depression via the PHQ-9 demonstrated a highly comparable distribution of symptom severity between the 15 mg and 30 mg cohorts, respectively, including moderate (42.9% text vs. 48.6%), moderately severe (47.6% vs. 42.9%), and severe symptoms (9.5% vs. 8.6%; Chi-square test, p = 0.917). Similarly, self-reported anxiety scores on the HADS-A subscale showed no significant differences in clinical case distribution, with definitive anxiety cases ("A case") identifying in 71.4% of the 15 mg group and 68.6% of the 30 mg group (Chi-square test, p = 0.822). The mean HADS-A scores were likewise statistically equivalent between the 15 mg (14.76pm 3.67) and 30 mg (13.57 pm 3.27) cohorts (Independent t-test, p = 0.214).

Finally, the HADS-D subscale yielded an identical clinical case rate of 85.7% for both the 15 mg and 30 mg patient groups (Chi-square test, p = 1.000). Mean baseline HADS-D scores mirrored this uniform distribution, tracking at 15.57\pm 3.08 in the 15 mg group compared to 14.69pm 3.03 in the 30 mg group (Independent t-test, p = 0.297). Taken together, these data confirm that baseline psychological distress was uniform across groups and did not bias subsequent dosage allocation.

Table (3): Comparison of different doses of Mirtazapine regarding Depression and anxiety at start.

		Mirtazapine dose		Test value	P-value	Sig.
		15	30			
		No. = 21	No. = 35			
PHQ 9	Moderate 10-14	9 (42.9%)	17 (48.6%)	0.172*	0.917	NS
	Moderately Severe 15-19	10 (47.6%)	15 (42.9%)			
	Severe above 19	2 (9.5%)	3 (8.6%)			
HADS-A at start	Normal (0-7)	0 (0.0%)	0 (0.0%)	0.051*	0.822	NS
	Borderline cases (8-10)	6 (28.6%)	11 (31.4%)			
	A case (11-21)	15 (71.4%)	24 (68.6%)			
HADS-A at start	Mean ± SD	14.76 ± 3.67	13.57 ± 3.27	1.258•	0.214	NS
	Range	9 – 20	8 – 20			
HADS-D at start	Normal (0-7)	0 (0.0%)	0 (0.0%)	0.000*	1.000	NS
	Borderline cases (8-10)	3 (14.3%)	5 (14.3%)			
	A case (11-21)	18 (85.7%)	30 (85.7%)			
HADS-D at start	Mean ± SD	15.57 ± 3.08	14.69 ± 3.03	1.054•	0.297	NS
	Range	10 – 20	10 – 21			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

*: Chi-square test; •: Independent t-test

HADS-D: Hospital Anxiety and Depression Scale for depression, HADS-A: Hospital Anxiety and Depression Scale for anxiety, HAM-D: Hamilton Rating Scale for Depression; PHQ-9: Patient Health Questionnaire-9

Comparison of different doses of Mirtazapine with different geriatric domains

Baseline evaluation of geriatric domains across the two dosing cohorts revealed statistical homogeneity across most functional parameters, with the notable exception of nutritional status (Table 4). The Mini Nutritional Assessment (MNA) at baseline demonstrated a significant discrepancy between groups (Chi-square test, p = 0.045), wherein patients subsequently assigned to the 30 mg mirtazapine cohort exhibited a substantially higher burden of nutritional vulnerability, with 54.3% categorized as "at risk" and 42.9% classified as "malnourished," compared to 47.6% and 28.6% in the 15 mg cohort, respectively. Conversely, no significant differences were observed regarding self-rated decreased appetite (76.2% in the 15 mg group vs. 88.6% in the 30 mg group; p = 0.222) or severity of baseline pain on the Numerical Pain Scale (p = 0.805). Similarly, baseline functional dependencies measured via Activities of Daily Living (ADL; p = 0.930) and Instrumental Activities of Daily Living (IADL; p = 0.81) were equivalent between groups. Baseline sleep parameters, including unsatisfactory night sleep satisfaction (61.9% vs. 65.7%; p = 0.773) and unsatisfactory day naps (61.9% vs. 60.0%; p = 0.888), also demonstrated no statistical variance between the 15 mg and 30 mg cohorts.

To evaluate the diagnostic capacity of the HADS-D and HAM-D scales in identifying cases of moderately severe to severe depression (defined by the PHQ-9), a Receiver Operating Characteristics (ROC) curve analysis was performed (Fig. 1). The HADS-D, utilizing a clinical cutoff point of >12, demonstrated an Area Under the Curve (AUC) of 0.715, paired with a high sensitivity of 93.94% and a lower specificity of 40.74% (Positive Predictive Value [+PV] = 66.0%, Negative Predictive Value [-PV] = 84.6%). The clinician-rated HAM-D scale exhibited superior overall diagnostic accuracy at a cutoff point of >17, yielding an AUC of 0.778, a sensitivity of 87.88%, and a markedly improved specificity of 61.54% (+PV = 74.4%, -PV = 80.0%). These findings indicate that while both instruments are highly sensitive, the HAM-D provides superior diagnostic power for identifying severe depression within this geriatric oncology cohort.

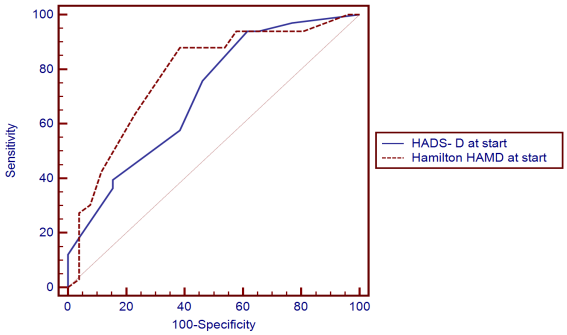
Table (4): Comparison of different doses of Mirtazapine with different geriatric domains at start.

		Mirtazapine dose		Test value	P-value	Sig.
		15	30			
		No. = 21	No. = 35			
Mininutritional assessment at start	Not at risk	5 (23.8%)	1 (2.9%)	6.205*	0.045	S
	At risk	10 (47.6%)	19 (54.3%)			
	Malnourished	6 (28.6%)	15 (42.9%)			
Self-rating appetite	Decreased	16 (76.2%)	31 (88.6%)	1.492*	0.222	NS
	Normal	5 (23.8%)	4 (11.4%)			
Numerical pain scale at Start	No pain	4 (19.0%)	5 (14.3%)	0.984*	0.805	NS
	1-3 mild	9 (42.9%)	12 (34.3%)			
	4-6 moderate	5 (23.8%)	12 (34.3%)			
	7-9 severe	3 (14.3%)	6 (17.1%)			
ADL at start	Independent	2 (9.5%)	6(17.1%)	0.144	0.930	NS

	Assisted	10(47.6%)	23(64.8%)			
	Dependent	9 (42.9%)	6(17.1%)			
IADL at start	Independent	1(4.8%)	6(17.1%)	0.413	0.81	NS
	Assisted	11(52.4%)	23(64.8%)			
	Dependent	9(42.9%)	6(17.1%)			
Sleep satisfaction at start	Satisfactory	8 (38.1%)	12 (34.3%)	0.083*	0.773	NS
	Not satisfactory	13 (61.9%)	23 (65.7%)			
Day naps at start	Satisfactory	8 (38.1%)	14 (40.0%)	0.020*	0.888	NS
	Not satisfactory	13 (61.9%)	21 (60.0%)			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
*: Chi-square test
ADL: Activities of daily living, IADL: Instrumental activities of daily living

Receiver operating characteristics curve to assess area under the curve (AUC), sensitivity and specificity HADS-D and Hamilton HAMD at start to detect cases with PHQ-9.



Variable	Cut off point	AUC	Sensitivity	Specificity	+PV	-PV
HADS- D at start	>12	0.715	93.94	40.74	66.0	84.6
Hamilton HAMD at start	>17	0.778	87.88	61.54	74.4	80.0

Fig. (1): Receiver operating characteristics curve to assess area under the curve (AUC), sensitivity, specificity, positive predictive value (+PV) and negative predictive (-PV) value of HADS-D and Hamilton HAMD at start to detect cases with moderately severe and severe PHQ-9.

DISCUSSION

This prospective cohort study aimed to assess the effects of mirtazapine on depression, anxiety, and related factors among elderly cancer patients experiencing depression in the geriatric palliative care unit at Ain Shams University over a duration of 2-month treatment period. Diagnosis of depression made by the DSM-5 and which is the gold standard for diagnosis of depression; PHQ-9 was used for assessment of the severity of depression, and also using different depression assessment tools, including the Hospital Anxiety and Depression Scale (HADS) that is used widely to screen and diagnose hospital anxiety and depression (**Palmer, 2020)** and the Hamilton Depression Rating Scale (HAMD) that is one of the most widely used scales to objectively rate depression severity worldwide (**Byrne et al., 2024**). The study enrolled 60 cancer patients admitted from the geriatric palliative care unit in Ain Shams University Hospitals. Following the exclusion of those with cognitive impairment, terminal cancer, or delirium. The participants were treated with mirtazapine for two months, and 56 patients (93.3%) completed the follow-up assessments, allowing for a comprehensive evaluation of the medication's impact.

In 66.7% of participants experienced moderate depressive symptoms by HAMD, and 86.7% met the criteria for cases By HADS-D which is consistent with **Kaphle et al. (2024),** who reported that over 50% of cancer patients had mild depression, and nearly one-third had moderate symptoms. Also, **Naser et al. (2021**) showed that the prevalence of depression among the studied patients was 23.4%; they used HADS and PHQ-9.

Also, depressive symptoms were more prevalent in the inpatient setting (37.1%) compared to patients in the outpatient setting (14.5%) ($p < 0.001$).

The present study assessed anxiety levels using the Hospital Anxiety and Depression Scale-Anxiety subscale (HADS-A). The results showed that 52.0% of patients exhibited clinically significant anxiety, as indicated by the HADS-A (with a score of 8 or higher), **Eriksen et al. (2023**) reported similar results where HADS-A-defined anxiety in 44% of elderly radiotherapy patients. Similarly, Kirkhus et al. (2020) reported clinically relevant anxiety in approximately 50% of older adults with cancer using HADS-A. Studies using Hamilton anxiety test, such as by **Li et al. (2021),** found a 46–55% prevalence of moderate anxiety in comparable geriatric oncology settings. Also, **Kaphle et al. (2024)** found anxiety in more than 60% of patients, supporting the high rates seen in the present cohort. Similarly, **Naser et al. (2021)** identified depression in 23.4% and anxiety in approximately 19% of patients, though their lower rates may reflect differences in patient age, setting, or cancer stage. In contrast to the current findings Weiss Wiesel et al. (2015) observed that anxiety tends to decline with age, possibly due to better emotional regulation in older adults.

Mirtazapine treatment in this study was associated with a significant reduction in depressive and anxiety symptoms among cancer patients over two months. Anxiety improved as HADS-A dropped from

71.7% to 1.8% ($p < 0.001$). Regarding depression, HADS-D dropped from 86.7% to 5.4%, and HAMD-D scores also improved, with moderate cases decreasing from 66.7% to 14.3% and mean scores from 18.3 to 11.5 ($p < 0.001$). **Andrade (2024**) found no significant difference between mirtazapine and placebo for depressive symptoms in cancer patients.

The present findings indicated that mirtazapine, even when used alone, provides multidimensional symptom relief in oncology settings. This was in agreement with **Ali et al. (2024)** who showed that combining mirtazapine with psychotherapy in Egyptian breast cancer patients led to more significant improvements in depression, anxiety, and quality of life compared to psychotherapy alone.

When comparing patients receiving 30 mg versus 15 mg of mirtazapine, baseline depression and anxiety scores (measured by HADS-A, HADS-D, and HAM-D) showed no statistically significant differences between patients receiving 15 mg versus 30 mg of mirtazapine, indicating comparable psychiatric symptom burden prior to treatment.

The Hamilton HAMD and HADS-D tests demonstrated decent diagnostic performance in this study. However, the Hamilton HAMD test showed superior AUC, sensitivity, specificity, and predictive values compared to the HADS-D. This indicated that HADS-D still holds clinical value, mainly because of its high sensitivity, making it effective at identifying individuals with the condition.

The present study indicated that Hamilton Depression Rating Scale (HAMD) has superior diagnostic performance compared to HADS-D, which aligns with the long-term follow-up results. HAMD also showed predictive associations across multiple follow-up points.This in alignment with **Hung et al. (2022) who performed** long-term study on Major Depressive Disorder (MDD) and found that HAMD has strong predictive power and correlated significantly with future depressive symptoms.

Conclusion

This study demonstrates that psychological distress—characterized by highly severe, comorbid depression and anxiety—is universally pervasive among elderly cancer patients at the initiation of oncological care. The evaluation of screening methodologies indicates that while self-reported measures like the HADS-D provide exceptional diagnostic sensitivity, clinician-rated instruments like the Hamilton Rating Scale for Depression (HAM-D >17) offer superior diagnostic accuracy and specificity for identifying advanced depression in geriatric oncology populations.

The clinical findings establish mirtazapine as an exceptionally effective, rapid-acting, and well-tolerated supportive pharmacotherapy for this vulnerable cohort. Treatment initiated significant and sustained reductions in both depression and anxiety symptoms within the first month of therapy, leading to robust clinical remission by month two. Furthermore, the targeted clinical utilization of the higher 30 mg dose for patients exhibiting poorer baseline nutritional status and active malnutrition underlines mirtazapine's dual utility.

This study demonstrated that mirtazapine could be a valuable tool in palliative care, particularly for enhancing emotional well-being. However, its use should be individualized and carefully monitored, especially in elderly patients with multiple comorbidities. Further research is needed to investigate the long-term effects and optimal dosing of mirtazapine in this patient population to fully determine its role in palliative care.

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تأثير ميرتازابين على الاكتئاب لدى مرضى السرطان المسنين الخاضعين للرعاية التلطيفية

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المستخلص يُصيب الاكتئاب مرضى السرطان بمعدل يتراوح بين ضعفين إلى ثلاثة أضعاف مقارنةً بعامة السكان، مما يؤثر بشكل كبير على جودة الحياة، والالتزام بالعلاج، وفرص البقاء على قيد الحياة. ولا تزال إدارة الاكتئاب لدى مرضى السرطان المسنين الذين يتلقون الرعاية التلطيفية تمثل تحديًا نظرًا لتعدد الأمراض المصاحبة ومشاكل تناول الأدوية المتعددة. ويُقدم ميرتازابين، وهو مضاد اكتئاب نورأدرينالي وسيروتونيني نوعي، مزايا محتملة لهذه الفئة من المرضى بفضل سرعة بدء مفعوله وآثاره الجانبية المفيدة، بما في ذلك تحفيز الشهية والتهدئة. تهدف هذه الدراسة إلى تقييم فعالية ميرتازابين في إدارة الاكتئاب لدى مرضى السرطان المسنين في وحدة الرعاية التلطيفية لكبار السن في مستشفيات جامعة عين شمس. شملت هذه الدراسة المستقبلية الحالية 60 مريضًا مسنًا مصابًا بالسرطان (≤ 60 عامًا) تم تشخيص إصابتهم بالاكتئاب وفقًا لمعايير الدليل التشخيصي والإحصائي للاضطرابات النفسية، الإصدار الخامس (DSM-5)، والذين تلقوا رعاية تلطيفية على مدار شهرين. أكمل 56 مريضًا (93.3%) تقييمات المتابعة. تم استبعاد المرضى الذين يعانون من ضعف إدراكي، أو هذيان، أو سرطان في مراحله النهائية (معدل البقاء على قيد الحياة أقل من 6 أسابيع). تلقى المشاركون دواء ميرتازابين بجرعة ابتدائية قدرها 15 ملغ يوميًا، مع زيادة الجرعة تدريجيًا إلى 30 ملغ بناءً على الاستجابة السريرية. أُجريت تقييمات شاملة عند خط الأساس، وبعد شهر، وبعد شهرين باستخدام أدوات معتمدة، بما في ذلك مقياس هاملتون لتقييم الاكتئاب (HADS)، ومقياس هاملتون لتقييم الاكتئاب (HAMD)، ومقياس صحة المريض (PHQ-9)، والتقييم الغذائي المصغر (MNA)، ومقاييس جودة الحياة. بلغ متوسط عمر المرضى 73.03 ± 8.32 عامًا، وكان 55% منهم من الذكور. لوحظ تحسن ملحوظ في درجات الاكتئاب: انخفضت حالات الاكتئاب وفقًا لمقياس هاملتون للقلق والاكتئاب (HADS-D) من 86.7% إلى 5.4% ($p<0.001$)، وتحسنت درجات مقياس هاملتون للاكتئاب (HAMD) من 18.28±3.06 إلى 11.45±2.5 ($p<0.001$). كما تحسنت أعراض القلق بشكل ملحوظ، حيث انخفضت حالات القلق وفقًا لمقياس هاملتون للقلق والاكتئاب (HADS-A) من 71.7% إلى 1.8% ($p<0.001$). وشملت الفوائد الإضافية تحسن الحالة التغذوية (انخفضت نسبة المرضى الذين يعانون من سوء التغذية من 41.7% إلى 8.9%)، وتحسن الشهية (ارتفعت نسبة الشهية الطبيعية من 16.7% إلى 83.9%)، وتحسن جودة النوم (من 35% إلى 89.3%)، وتحسن درجات جودة الحياة (من الوسيط 2 إلى 4، $p<0.001$). وكان انخفاض الألم أكثر وضوحًا لدى المرضى الذين يتلقون علاجًا متزامنًا بالأفيونيات. كان التخدير أكثر الآثار الجانبية شيوعًا (15.5% بعد شهر، و10.7% بعد شهرين)، ولم تُسجّل أي آثار جانبية خطيرة. خلصت الدراسة إلى أن الميرتازابين أظهر فعالية ملحوظة في علاج الاكتئاب والقلق لدى مرضى السرطان المسنين الذين يتلقون الرعاية التلطيفية، مع فوائد إضافية تتعلق بالشهية والنوم والحالة التغذوية ونوعية الحياة. وقد تحمّل المرضى الدواء جيدًا مع آثار جانبية يمكن السيطرة عليها. تدعم هذه النتائج اعتبار الميرتازابين خيارًا علاجيًا قيّمًا لعلاج الاكتئاب لدى هذه الفئة من المرضى، مع التأكيد على أهمية تحديد الجرعة المناسبة لكل مريض والمتابعة الدقيقة. ولا تزال هناك حاجة إلى مزيد من التجارب السريرية العشوائية المضبوطة لتحديد استراتيجيات الجرعات المثلى والنتائج طويلة الأمد.

الكلمات المفتاحية: ميرتازابين، اكتئاب، مسنون، سرطان، رعاية تلطيفية، طب أورام المسنين، مضادات الاكتئاب