Effect of Multimodal Integrative Interventions on Pain-Related Outcomes among Critically Ill Patients

Amal S. Taha[1], Safaa H. Mohamed[2], Doaa M. Mahmoud[3]

[1]Medical-Surgical Nursing, Faculty of Nursing, Benha University, Benha, Egypt.
e-mail:Amal.said22@yahoo.com
[2]Medical-Surgical Nursing, Faculty of Nursing, Zagazig University, Zagazig, Egypt.
e-mail:drsafaa488@gmail.com
[3]Medical-Surgical Nursing, Faculty of Nursing, Benha University, Benha, Egypt.
e-mail:drdoaamohamed1710@gmail.com

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ABSTRACT

Context: Pain, a persistent problem in critically ill patients, adversely affects outcomes. Despite recommendations, no evidence-based non-pharmacological approaches for pain treatment in critically ill patients have been found.

Aim: To evaluate the effect of multimodal integrative interventions on pain-related outcomes among critically ill patients.

Methods: A quasi-experimental design (pre / post-test) was utilized to fulfill the aim of this study. A convenience sample of sixty adult critically ill patients was recruited from the intensive care unit at Benha University Hospital affiliated to Benha University at Qualyubia Governorate, Egypt. Three tools were used to conduct this study as follows: Critically ill patients' assessment record; The Critical-Care Pain Observation Tool (CCPOT); The Groningen Sleep Quality Scale.

Results: The results show decreased frequency of pain occurrence in the post intervention periods (75%) immediately post to 50% after 48 hours of intervention compared with pre-intervention (100%). The results show a highly statistically significant differences at $p \leq 0.001$ between pre and post of intervention periods regarding the intensity of the pain mean score among studied patients. It also shows statistically significant differences with p-value ≤ 0.05 regarding all items of sleep quality immediately after and after 48 hours of intervention compared to pre-intervention, except related to having a deep sleep last night, and feel like a slept poorly last night with a p-value ≥ 0.05. There was a highly positive statistically significant correlation at p-value ≤ 0.001 between pain intensity and other secondary outcomes, including quality of sleep, blood pressure, heart rate and respiratory rate.

***Conclusion*:** Multimodal integrative interventions effectively decrease pain and improve pain-related outcomes among critically ill patients. Appropriate pain assessment must be partnered with an adequate, multimodal, evidence-based management strategy that incorporates both pharmacologic and non-pharmacologic modalities of pain control.

Keywords: Critically ill patients, multimodal integrative interventions, outcomes, pain

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1. Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage and is the third most common healthcare problem. Inadequate pain relief can result in short and long-term physical and psychological conditions such as hemodynamic dysfunction, hyperglycemia, infection, delirium, and anxiety *(Kia, et al., 2021; Devlin, et al., 2018; Papathanassoglou & Park, 2016).*

Critical illness, regardless of etiology, is a painful condition. Studies have noted that at least half of all critically ill patients have moderate to severe pain at rest. More than 5 million patients are admitted to ICUs in the United States annually, with an average length of stay of 3-8 days. Unfortunately, over half of these patients experience moderate to severe pain at rest associated with their admission and 80% have pain during procedures *(Carrillo, et al., 2018).*

Traditionally, pain management tended to emphasize pharmacological agents. However, intensive use of analgesics has negative implications as it can greatly affect some physiological functions, with side effects, drug dependency and increasing health care costs. It puts a burden on the country's economy. Inadequately managed pain negatively affects patient's quality of life, leading to more frequent outpatient visits, higher readmission rates, causing longer stays in the hospital and increased stress and anxiety levels for the patient and families *(Carrillo, et al., 2018).*

Pain can fluctuate over time, present at rest, and escalate during procedures or movement. Moreover, anxiety, fear and negative expectations are common in critically ill patients and may contribute to a heightened perception of pain. Thus, the multifactorial nature of ICU pain calls for approaches that address physiological and psychosocial responses to pain *(Damico, et al., 2020).*

The Society of Critical Care Medicine (SCCM) ICU Liberation Bundle recommends four primary non-pharmacologic methods for pain relief: Massage therapy, cold therapy, music and sound and relaxation therapy to address both physical and sensory pain pathways (massage therapy, cold therapy) as well as the emotional, affective, and cognitive

[1]*Correspondence author: Amal Said Taha*

elements of pain perception (music and sounds, relaxation therapy) *(Richard, et al., 2019).*

Pain perception entails a complex interaction among sensory, affective, and social components. Relaxation, guided imagery and music therapy are mind-body interventions, whereas touch and massage are body-based practices. Massage therapy for ICU patients typically involves massage on the back, feet and hands. Depending on the patient's clinical status, 20 minutes of light pressure massage at least twice in 24 hours. Hands-only massage is also acceptable. Massage therapy, when done consistently, has been shown to reduce visual numeric pain scores by up to two points *(Jagan, et al, 2019).*

Music or sound therapy has been associated with moderate decreases in pain scores in ICU patients. It is another area that needs the patient's family involvement, as the family will likely know what music the patient would best enjoy. Relaxation therapy includes techniques such as guided imagery, breathing exercises, biofeedback and self-hypnosis, with guided imagery, which typically involves having the patients imagine a calm and relaxing location of their choice to take them psychologically out of the current painful environment and breathing exercises being the most frequently used in critically ill patients. Relaxation promotes a sense of calmness often associated with parasympathetic activation. These therapies have shown a 2.6-point reduction in visual scale pain scores *(Aktas & Karabulut, 2019).*

2. Significance of the study

Globally, it has been estimated that 1 in 5 adults suffers from pain and another 1 in 10 adults is diagnosed with chronic pain each year *(Lui, et al., 2021; Critical Care Statistics, 2021).* Despite advances in pain management, critically ill patients continue to have unacceptably high rates of uncontrolled pain *(Ayasrah, 2016).* More than 50% of critically ill patients experience pain during their stay in ICU, even during rest. Patients in ICU experience pain due to multiple causes such as their underlying health condition, catheters or tubes inserted into them and because they are immobile. They also experienced pain because of the care-related procedures performed on them *(Al-Sutari, et al., 2014).*

In recent years, various studies have examined pharmacological pain management methods, but only a few have focused on using non-pharmacological pain management methods in ICUs. Therefore, this study evaluated the effect of multimodal integrative interventions on pain-related outcomes among critically ill patients.

3. Aim of the study

This study aimed to evaluate the effect of multimodal integrative interventions on pain-related outcomes among critically ill patients.

3.1. Operational Definitions

Multimodal Integrative Interventions in this study included multiple therapeutic modalities such as massage therapy and relaxation therapy (music, guided imagery).

Pain-related outcomes in this study include the primary and secondary outcomes. The primary outcome was the frequency of pain. The secondary outcomes included pain intensity, hemodynamic measurements (blood pressure, respiratory and pulse rate) and sleep quality.

3.1. Research Hypotheses

The following research hypotheses have been developed to achieve the aim of the study:

H1: Critically ill patients exposed to multimodal integrative interventions will exhibit less frequent pain episodes than before implementation.

H2: Critically ill patients exposed to multimodal integrative interventions will exhibit less pain intensity than before implementation.

H3: Critically ill patients exposed to multimodal integrative interventions will exhibit better sleep quality than before implementation.

H4: Critically ill patients exposed to multimodal integrative interventions will exhibit more stable physiological responses than before implementation.

4. Subject & Methods

4.1. Research Design

A quasi-experimental research design (pre/ post-test) was utilized to fulfill the aim of this study. A quasi-experimental design aims to establish a relationship between an independent and dependent variable. Contrary to an actual experiment, a quasi-experiment does not rely on randomization; instead, the classification of individuals is based on non-random criteria. A quasi-experimental design is beneficial when real trials cannot be used for ethical or practical considerations *(Reichardt, 2019).* The independent variables in this study were the multimodal integrative interventions, while the dependent variables were pain-related outcomes.

4.2. Study setting

The current study was conducted in the intensive care unit at Benha University Hospital, affiliated to Benha University at Qualyubia Governorate, Egypt. Intensive care unit locates on the second floor of the medical building; it contains three rooms with six beds and four counters, each counter contains four beds.

4.3. Subjects

The target population of this study consisted of a convenience sample of sixty adult critically ill patients admitted to the setting mentioned above; the subjects were recruited according to the following inclusion and exclusion criteria:

Inclusion criteria

Patients were eligible for the study if they were more than 18 years old and had a score greater than nine on the Glasgow Coma Scale (GCS) at the time of inclusion.

Exclusion criteria

Patients were excluded if they had an expected ICU length of stay of fewer than 48 hours, had a current history of severe mental health problems or dementia, suffered from blindness, deafness, hearing impairment or conditions that

did not permit the use of headphones and patients who had seizures or brain stem death or receiving neuromuscular blockers.

They were assessed on admission (pre-intervention), immediately after (post-intervention) and two days after the intervention based on recommendations of a study done by *Papathanassoglou et al. (2018)* to avoid post-intervention attrition.

4.4. Tools of data collection

Three tools were used to conduct this study as follow:

4.4.1. Critically Ill Patients' Assessment Record

It was developed by the researchers after reviewing related literature *Damico et al. (2020); Younis and Ahmed (2015)* to assess critically ill patients' clinical condition. It was divided into three parts:

Part 1: Patients' demographic and baseline data, including age, gender, marital status, residence, occupation, and level of education. Medical and surgical history including associated comorbidities, previous surgeries, medication history and family history of chronic diseases.

Part 2: A physiological parameter record. It aimed to record physiological parameters including, pulse rate, respiration rate, systolic and diastolic blood pressure of the studied patients based on *Papathanassoglou et al. (2018).* The researchers manually measured the pulse and respiration rates in beats per minute and breaths per minute, respectively. The same sphygmomanometer measured systolic and diastolic blood pressure throughout the study in millimeters of mercury (mmHg). Normal reference values of all the selected physiological parameters given inbox.

Table (1): Reference values for normal and abnormal physiological parameters.

Physiological parameters	Normal range	Abnormal range
Pulse rate (PR) (Beats per minute)	**60–90**	<60 bradycardia or >90 tachycardia
Respiration rate (RR) (Cycle per minute)	16–24	<16 bradypnea or >24 tachypnea
Blood Pressure Systolic / Diastolic Blood pressure (in mmHg)	*120/80±20/15*	>140/95 hypertension <100/65 hypotension

Part 3: Chronic Pain Assessment Questionnaire: A self-administered questionnaire assesses the two parts of chronic pain that often change over time; persistent baseline and breakthrough pain. It was adapted from *Nordness et al. (2021)* and modified by the researchers; it included seven questions as follows; frequency of pain occurrence, duration of pain (last most of the day), rate of baseline pain, site of pain, description of pain, time of feeling worst pain and if the pain awakes the patient from sleep.

Scoring system

Regarding questions concerning frequency, duration of pain and if pain awakens the patient from sleep, the answer for each question included two options: yes, which scored one grade, or no, which scored a zero. The total score for each question was calculated and converted into percent.

A Numeric Pain Rating Scale Assessment (NPRSA) was used for rating baseline pain. The scale is displayed as a line numbered from zero to ten degrees. The 11-point numeric scale ranges from '0' representing one pain extreme (e.g., "no pain"), to '10' representing the other pain extreme (e.g., worst pain imaginable). The values on the pain scale correspond to the pain levels as follows; higher scores indicate greater pain level:

- No pain scores 0.
- Mild pain scores 1-3.
- Moderate pain scores 4-6.
- Severe pain scores 7-10.

Regarding the question concerning the site of pain; a body map was used to identify the location of pain either on the neck, shoulder, lower back or leg and a closed-ended question was asked to describe the character of pain, whether aching, burning, cramping or stabbing and time of feeling worst pain whether on the morning, afternoon or at night.

4.4.2. The Critical-Care Pain Observation Tool

It was adopted from *Gelinas et al. (2006); Devlin et al. (2018); Hylén et al. (2016); Chen et al. (2016); Modanloo, et al. (2019)* to assess pain intensity as the secondary outcome. The Critical Care Pain Observation Tool (CCPOT) included four sections with different behavioral categories; facial expression, body movements, compliance with the ventilator or vocalization for extubated patients and muscle tension.

Scoring system

Each item of CCPOT scored from (0-2) with a total score of 8. It was divided as follows:

- No pain (0 degree).
- Mild pain (1-3 degrees).
- Moderate pain (4-6 degrees).
- Severe pain (above 6 degrees).

4.4.3. The Groningen Sleep Quality Scale

This scale was adopted from **Chaiard, et al., (2019)** to assess the quality of sleep as a secondary outcome of pain. It consists of 15 questions that examine a person's sleeping habits, such as feeling tired after waking up this morning, waking up several times last night and feeling rested after waking up this morning.

Scoring system

The first question does not count toward the total score. One point if answer is "no" for questions 2, 3, 4, 5, 6, 7, 9, 11, 13, 14, 15. One point if the answer is "yes" for questions 8, 10 and 12. The measure ranges from 0 to 14, with a higher score indicating a lower subjective sleep quality. Normal refreshing sleep is represented by a total score of (0-2). The range of (3-9) was deemed slightly disturbed sleep in this study, whereas the range of (10-14) was considered poor sleep quality.

4.5. Procedures

Validity and reliability of the study tools: Tools of data collection were reviewed for their content validity by five experts (four professors of Medical-Surgical Nursing and one professor of critical care medicine), Benha University who were selected to revise the data collection instruments for thoroughness, applicability, and legibility to ascertain the content and face validity.

Reliability: The internal consistency of the Critical Care Pain Observational Tool (CCPOT) was 0.880, which indicated that the tool was reliable. The correlation coefficient (α) was 0.88 for the Groningen sleep quality scale.

Pilot Study: A pilot study was conducted after the development of the tools and before starting the actual data collection to test the clarity, applicability of the study tools and the time needed to fill in the tool and to assess the feasibility of the research process. The pilot study was done on ten percent of the sample (n=6) who were included in the main study sample because they did not add any modifications to the study tools.

The Scientific Research and Ethics Committee of the Faculty of Nursing at Benha University approved the current study. Further, permission to conduct the current study was taken from the hospital authorities after an explanation of the aim of the study. The study was conducted with careful attention to the ethical standards of research and the rights of the participants to accept or refuse to contribute to this study. Their information was treated with confidentiality and for research. The respondents' anonymity was maintained as they were not required to mention their names. Patients' relatives were also assured that the quality of care provided would not be affected if they did not wish to participate in the study.

Fieldwork: Data were collected in 6 months from the beginning of January 2022 to the end of June 2022. The multimodal integrative interventions are applied through the following phases:

The preparatory phase included reviewing the available literature and studies related to the research problem and theoretical knowledge using textbooks, evidence-based articles, internet periodicals and journals.

The assessment phase:

- The researchers approached the responsible nursing supervisors of determined areas daily to identify the number of newly admitted patients to the intensive care unit and within inclusion criteria.
- The researchers explained the aim and nature of the study to all patients who were included in the study after taking their verbal approval of participation.
- The researchers interviewed the studied patients (pre-multimodal integrative interventions) to complete the socio-demographic and baseline data, assess chronic pain as a primary outcome. The researcher assessed the secondary outcomes of pain intensity and sleep quality. The researchers recorded baseline physiological parameters such as pulse rate, respiratory rate and blood pressure. The interview lasted between 25 to 35 minutes.

Planning Phase **(**Multimodal Integrative Interventions' Development): Objectives were designed based on predetermined patients' needs, relevant recent literature and validated by nursing experts. These were revised and modified based on the experts' comments to be implemented using various methods, including a booklet containing major headlines of the multimodal integrative interventions for critically ill patients, which were designed by researchers and written in very simple Arabic language supplemented by photos.

Implementation phase: The implementation of multimodal integrative interventions was carried out by the researchers. The intervention was delivered daily (between 9:30 am and 11:30 am). The multimodal integrative interventions with approximately 55 minutes were based on a literature review; by *Posa, et al. (2020).* Interventions included relaxation and guided imagery (15 minutes) and moderate-pressure massage (40 minutes).

Relaxation therapy includes techniques such as guided-imagery therapy, which typically involves having the patients imagine a calm and relaxing location of their choice to take them psychologically out of the current painful environment and listen to music through headphones for 15 minutes. The selection of music from Mozart's piano sonata KV 283 was based on previous evidence of its physiological effects on critically ill patients *(Richard, et al., 2019).*

Massage therapy for ICU patients typically involves massage on the back, feet and hands depending on the patient's clinical status. Massage is typically paired with decreasing sensory stimuli such as dimming lights and either muting alarms or decreasing the volume and providing earplugs or an eye mask to the patient *(Jagan, et al., 2019; Boitor, et al., 2018).*

Swedish massage included stroking, effleurage, vibrations, or kneading. Areas with inflammation, petechiae, ecchymosis, subcutaneous hemorrhage or wounds were not messaged. Baby oil was used to make the area slippery and easy to massage (about 1-2 cc per foot) and it had no other therapeutic value. A napkin used to remove the residual oil from the patient's body. The massage was performed when the workload of the intensive care unit was low. Pain and its related outcomes were reexamined immediately and two days after the intervention. Each message session was carried out as follows:

- *Back message technique* (approximately 10 minutes): The researchers messaged the middle of the patient's back in a circular motion. The areas over the right and left shoulder blades were stroked upward and messaged again using circular motion. The same areas were stroked downward and ended by messaging the iliac crests in the femur. These processes were repeated three times.
- *Feet and legs message technique* (approximately 10 minutes): The patient was placed in a supine position with a pillow under the feet so that the feet were bent slightly, and the head of the bed was at an angle of 30–45 degrees. The massage area was uncovered from ten cm above the patient's knee. The researchers began to massage after examining the feet for the presence of the massage barriers. The researchers performed five light strokes on top of the patient's foot and

then spread the metatarsals using thumb glides. After that, the sole of the foot was petrissaged and the plantar fascia was stripped three times. The researchers used both hands to effleurage up the lower leg and petrissage the medial aspect of the lower leg, then performed a figure of eight around the knee using both hands and a loose fist on the quadriceps. These processes were repeated three times.

- *Abdominal massage technique* (approximately 4 minutes): The researchers massaged the abdomen in the direction of peristalsis or a clockwise direction. Then slid the hands with gentle, even pressure up the middle of the patient's abdomen until the patient's ribs were felt. The researcher put both hands on the lower right side of the abdomen and then moved her palms up to the top of the navel until they reached the patient's ribs. The researchers swept their hands across the abdomen just below the ribs and down to the lower side of the patient's abdomen. The navel-circling message was repeated three times.
- *Hands and arm massage technique* (approximately 10 minutes): The researchers gently rubbed over the metacarpals in a circular motion and then gentle stretches were performed to open the patient's hand. The researchers stretched out the patient's fingers, performed circular rubbing and then stroked along the bones of the patient's palm. Both sides of the forearm were gently stroked back toward the heart using a thumb glide. Then, shoulder stretch and traction were performed.
- *Chest message technique* (approximately 5 minutes): The researcher slid a flat hand firmly but gently up to the middle of the patient's chest. Before the researcher's hand reached the collarbones, she fanned hands out toward the patient's shoulders and applied gently. However, firm pressure on the muscles in the upper chest, once the researcher's hand reached the patient's shoulders, pushed them over under the shoulder area, then back up over the upper arm, the researcher's hands moved into the ribcage area, started at the armpits, researcher's hands were slid down the length of the ribcage. After that researcher's hands were pulled back up into the chest area where the researcher began, and the message was repeated three times.
- *Gum message technique* (approximately 1 minute): The researcher placed the thumb on the outer gum line and the index finger on the inner gum line, directly behind the thumb. Then patient's gum was gently massaged in a circular motion.

After completing the intervention, the patients rested for about 15 minutes without physical activities such as suctioning, positioning and hygiene measures until the researchers obtained the last reading of physiological responses and pain levels based on recommendation of a study done by *Younis and Ahmed (2015).*

Evaluation phase aimed to reassess critically ill patients after the intervention phase to identify differences in their level of response from baseline. The evaluation made immediately after and 48 hours post multimodal integrative interventions. The researchers measured physiological responses, CCPOT scores and sleep quality three times (pre, immediately post and 48 hours post multimodal integrative interventions). The researchers compared them to explore any significant changes in the findings using the same tools.

4.6. Limitations of the Study

The study findings could not be generalized because of the following reasons:

- The study was confined to a specific geographical area that limits any larger generalization.
- The massage therapy was carried out in one session due to the critical condition of ICU patients.
- The sample size was relatively small, thus restricting the statistical inferences of results.

4.7. Data analysis

Data were analyzed using the statistical package for social science (SPSS), version 25. Numerical data were expressed as mean, standard deviation (SD) and range. Qualitative data were expressed as frequency and percentage. The Chi-square test was used to examine the difference between qualitative variables and the paired t-tests for comparing the mean scores between two periods within the same group. Correlation between different numerical variables was tested using Pearson product-moment correlation coefficient and spearman correlation for categorical variables. A p-value ≤ 0.05 was considered significant and ≤ 0.001 was considered highly significant.

5. Results

Table 2 shows demographic characteristics of critically ill patients. The table shows that 41.7% of studied patients aged from 40-<50 years old with a mean of 49.00±0.92. 60% of the studied patients were males; 55% were widowed. Regarding residence, 58.3% were from urban areas. It was also noticed that 68.3% of studied patients were employed and 51.7% had secondary education.

Table 3 reveals the distribution of studied patients according to their medical data. The table shows that the present history of associated comorbidities included diabetes mellitus and liver diseases represented 33.3% of the studied patients. The past history revealed that 83.3% of the studied patients had no previous surgeries. Regarding medication history, all studied patients took medications, as 53.3% on anti-inflammatory medication. Also, 75% of the studied patients had a family history of chronic disease such as diabetes mellitus, which represented 46.7% of them.

Table 4 shows the persistent baseline and breakthrough pain as a primary outcome among studied patients. The table shows decreased frequency of pain occurrence in the post intervention periods (75% immediately post to 50 % after 48 hours of intervention) compared with pre-intervention (100%). Regarding the length of pain stay, all studied patients had pain most of the day pre-intervention compared with 66.7% immediately post-intervention and 58.3% after 48 hours of intervention.

Concerning pain rate, it was found that pain severity had significantly decreased in the post intervention periods (25% immediately post to 16.7% after 48 hours of intervention) compared with pre-intervention (33.3%). There were highly statistically significant differences between pre- and post-

periods of intervention regarding description of pain, the timing of feeling pain, and awakening of sleep due to pain at p ≤0.001.

Table 5 shows the comparison of pain intensity among the studied patients pre and post intervention. The table shows a highly statistically significant difference at p ≤0.001 between pre and post of intervention periods regarding the intensity of the pain mean score (as a secondary outcome) among studied patients.

Regarding facial expression, there was marked relaxation of tense facial expressions from 41.7% pre and immediate post to 33.3% post-48 hours of intervention. Regarding body movement, it was noticed that agitation had decreased from 41.7% pre-intervention to 31.7% immediate post and 25% after 48 hours of intervention. Regarding vocalization, there was a marked improvement in talking in a normal tone from 20% pre to 31.7% immediate post to 35% after 48 hours of intervention. The muscle tension revealed a marked increase in relaxation of muscle rigidity from 21.7% pre to 26.7% immediate post to 35% after 48 hours of intervention with a statistically significant difference among the three study phases.

Table 6 shows statistically significant differences with p-value ≤0.05 regarding all items of sleep quality immediately after and after 48 hours of intervention compared to pre-intervention, except related to having a deep sleep last night and feel like a slept poorly last night with a p-value ≥0.05.

Figure 1 shows a percentage distribution of sleep quality level pre, immediately post and after 48 hours of intervention. There was marked improvement in the studied patients' total quality of sleep from 55% had poor sleep pre-intervention decreased to 48.3% immediately post-intervention and only 36.7% after 48 hours of intervention.

Table 7 shows highly statistically significant differences at p ≤0.001 between pre and post intervention-periods of hemodynamic measurements (as secondary outcomes) among studied patients. Regarding blood pressure, 50% of the studied patients had hypertension pre-intervention decreased to 41.7% immediately post-intervention and 33.3% after 48 hours of intervention. Regarding heart rate, 41.7% of the studied patients had tachycardia pre-intervention decreased to 36.7% immediately after post-intervention and 21.7% after 48 hours of intervention. Regarding the respiratory rate, 56.7% of the studied patients had tachypnea pre-intervention compared with 53.3% immediately post-intervention and this decreased to 45.0% after 48 hours of intervention.

Table 8 reveals a highly statistically significant positive correlation at p-value ≤ 0.001 between behavioral domains of pain intensity and other secondary outcomes, including quality of sleep, blood pressure, heart rate and respiratory rate.

Table (2): Frequency and percentage distribution of critically ill patients' demographic characteristics (n= 60).

Demographic characteristics	(No.)	%
Age		
20-<30	5	8.3
30-< 40	10	16.7
40-<50	25	41.7
50-60	20	33.3
Mean±SD	49.00±0.92	
Gender		
Male	36	60.0
Female	24	40.0
Marital status		
Single	0	0.0
Married	22	36.7
Divorced	5	8.3
Widowed	33	55.0
Residence		
Rural	25	41.7
Urban	35	58.3
Occupation		
Employed	41	68.3
Unemployed	19	31.7
Level of education		
Cannot read and write	0	0.0
Basic education	14	23.3
Secondary education	31	51.7
High level of education	15	25.0

Table (3): Frequency and percentage distribution of critically ill patient's medical and surgical history (n=60).

Medical and surgical history	No.	%
Comorbidities		
Diabetes mellitus	20	33.3
Liver diseases	20	33.3
Renal diseases	10	16.7
Cardiovascular diseases	10	16.7
Previous surgery		
Yes	10	16.7
No	50	83.3
Medication history		
Yes	60	100.0
No	0	0.0
If yes, type of medication (n=60)		
Ant inflammatory	32	53.3
Antibiotics	14	23.3
Analgesics	8	13.3
Diuretics	6	10.0
Family history of chronic diseases		
Yes	45	75.0
No	15	25.0
If yes, what is the disease (n=45)		
Diabetes Mellitus	21	46.7
Liver diseases	3	6.7
Renal diseases	14	31.0
Cardiovascular diseases	7	15.6

Table (4): Comparison of the persistent baseline and breakthrough pain among critically ill patients during pre and post intervention periods (n=60).

Incidence of Persistent Baseline pain (primary outcome)	Pre-intervention		Immediately post intervention		Post 48 hours of intervention		X^2 (1)	p-value (1)*	X^2 (2)	p-value (2)**
	No.	%	No.	%	No.	%				
Frequency of pain occurrence										
Frequent	60	100.0	45	75.0	30	50.0	N.A#	N.A	N.A	N.A
Not frequent	0	0.0	15	25.0	30	50.0				
Duration of pain (pain lasted most of the day)										
Yes	60	100.0	40	66.7	35	58.3	N.A	N.A	N.A	N.A
No	0	0.0	20	33.3	25	41.7				
On average, rate baseline pain										
Mild	15	25.0	15	25.0	30	50.0	29.55	<0.001	17.37	0.002
Moderate	25	41.7	30	50.0	20	33.3				
Severe	20	33.3	15	25.0	10	16.7				
Site of pain										
Neck	5	8.3	5	8.3	6	10.0	47.84	<0.001	47.11	<0.001
Shoulder	10	16.7	16	26.7	17	28.3				
Lower back	24	40.0	20	33.3	18	30.0				
Leg	21	35.0	19	31.7	19	31.7				
Description of pain										
Aching	17	28.3	16	26.7	20	33.3	81.69	<0.001	57.69	<0.001
Burning	15	25.0	20	33.3	19	31.7				
Cramping	23	38.3	18	30.0	17	28.3				
Stabbing	5	8.3	6	10.0	4	6.7				
Time of feeling the worst pain										
Morning	15	25.0	13	21.7	12	20.0	16.29	0.003	13.62	0.009
After noon	20	33.3	20	33.3	18	30.0				
Night	25	41.7	27	45.0	30	50.0				
Awake from sleep										
Yes	45	75.0	40	66.7	30	50.0	10.000	0.002	20.00	<0.001
No	15	25.0	20	33.3	30	50.0				

**Difference between pre and immediate post-periods of intervention, **Difference between pre and post 48 hours periods of intervention, #Not applicable*

Table (5): Comparison of pain intensity among critically ill patients during pre and post intervention periods (n=60).

Critical-Care Pain Observation Tool (CPOT)	Pre-intervention		Immediately post intervention		Post 48 hours of intervention		X^2 (1)	p-value (1)	X^2 (2)	P-value (2)
	No.	%	No.	%	No.	%				
Facial expression										
Relaxed, neutral	15	25.0	15	25.0	30	50.0				
Tense	25	41.7	25	41.7	20	33.3	62.94	<0.001	45.00	<0.001
Grimacing	20	33.3	20	33.3	10	16.7				
Mean±SD	1.08±0.76		1.00±0.71		0.67±0.75		*t=1.21	0.028	t=4.21	<0.001
Body movements										
Absence of movements or normal position	15	25.0	16	26.6	20	33.3				
Protection	20	33.3	25	41.7	25	41.7	60.27	<0.001	62.21	<0.001
Restlessness/Agitation	25	41.7	19	31.7	15	25.0				
Mean±SD	1.17±0.81		1.05±0.77		0.92±0.77		t=1.72	0.050	t=3.22	0.002
Vocalization (extubated patients)										
Talking in a normal tone or no sound	12	20.0	19	31.7	21	35.0				
Sighing, moaning	28	46.7	24	40.0	25	41.7	34.33	<0.001	35.93	<0.001
Crying out, sobbing	20	33.3	17	28.3	14	23.3				
Mean±SD	1.13±0.72		0.97±0.78		0.88±0.76		t=1.80	0.050	t=2.66	0.010
Muscle tension										
Relaxed	13	21.7	16	26.7	21	35.0				
Tense, rigid	27	45.0	26	43.3	24	40.0	46.69	<0.001	37.70	<0.001
Very tense or rigid	20	33.3	18	30.0	15	25.0				
Mean±SD	1.12±0.74		1.03±0.76		0.90±0.77		t=1.04	0.030	t=2.27	0.027
Total score	4.50±2.95		4.05±2.95		3.37±2.95		t=1.57	0.021	t=3.31	0.002

**(t) Paired T-test, (1) Difference between pre and immediate post-periods of intervention, (2) Difference between pre and post 48 hours periods of intervention*

Table (6): Comparison of sleep quality among studied patients pre and post-periods of intervention (n=60).

The Groningen Sleep Quality Scale	Pre-intervention				Immediately post intervention				Post 48 hours of intervention				X^2 (1)	(p-value) (1)*	X^2 (2)	(p-value) (2)**
	No		Yes		No		Yes		No		Yes					
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%				
Had a deep sleep last night	0	0.0	60	100.0	0	0.0	60	100.0	30	50.0	30	50.0	N.A	N.A	N.A	N.A
Feel like slept poorly last night	0	0.0	60	100.0	0	0.0	60	100.0	30	50.0	30	50.0	N.A	N.A	N.A	N.A
Took more than half an hour to fall asleep last night	30	50.0	30	50.0	28	46.7	32	53.3	29	48.3	31	51.7	52.50	<0.001	56.12	<0.001
Felt tired after waking up this morning	35	58.3	25	41.7	16	26.7	44	73.3	19	31.7	41	68.3	3.89	0.048	4.86	0.027
Woke up several times last night	25	41.7	35	58.3	15	25.0	45	75.0	18	30.0	42	70.0	5.14	0.023	6.61	0.010
Feel like did not get enough sleep last night	25	41.7	35	58.3	13	21.7	47	78.3	15	25.0	45	75.0	8.48	0.004	14.28	<0.001
Got up in the middle of the night	30	50.0	30	50.0	33	55.0	27	45.0	26	43.3	34	56.7	49.09	<0.001	45.88	<0.001
Felt rested after waking up this morning	15	25.0	45	75.0	27	45.0	33	55.0	30	50.0	30	50.0	16.36	<0.001	20.00	<0.001
Feel like only had a couple of hours of sleep last night	25	41.7	35	58.3	16	26.7	44	73.3	15	25.0	45	75.0	3.89	0.048	10.08	0.001
Feel slept well last night	35	58.3	25	41.7	42	70.0	18	30.0	49	81.7	11	18.3	6.61	0.010	13.43	<0.001
Did not sleep a wink last night	25	41.7	35	588.3	16	26.7	44	73.3	17	28.3	43	71.7	3.89	0.048	8.72	0.003
Did not have any trouble falling asleep last night	35	58.3	25	41.7	46	76.7	14	23.3	43	71.7	17	28.3	6.65	0.010	8.72	0.003
After woke up last night, had trouble falling asleep again	25	41.7	35	58.3	30	50.0	30	50.0	15	25.0	45	75.0	1.71	0.190	5.14	0.023
Tossed and turned all night last night	30	50.0	30	50.0	26	43.3	34	56.7	17	28.3	43	71.7	45.88	<0.001	23.72	<0.001
Did not get more than 5 hours of sleep last night	24	40.0	36	60.0	34	56.7	26	43.3	21	35.0	39	65.0	30.58	<0.001	21.53	<0.001
Total	9.20 ± 5.13				7.63 ± 4.29				6.28 ± 4.71				t=2.03	0.046	t=2.621	0.011

**(1) Difference between pre and immediate post-periods of intervention, ** (2) Difference between pre and post 48 hours periods.*

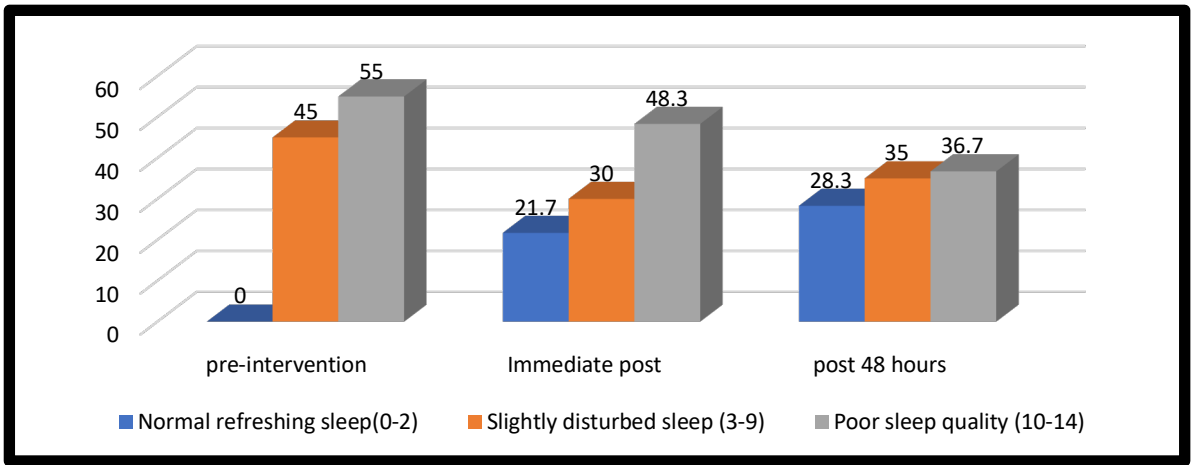

Fig (2): Percentage distribution of critically ill patients according to their total level of quality of sleep (n = 60).

Table (7): Comparison of hemodynamic measurements among critically ill patients during pre and post-periods of intervention (n=60).

Hemodynamic measurements	Pre-intervention		Immediately post intervention		Post 48 hours of intervention		X^2 (1)	(p-value) (1)*	X^2 (2)	(p-value) (2)**
	No.	(%)	No.	(%)	No.	%				
Blood pressure										
Normal	10	16.7	12	20.0	22	36.7				
Hypotension	20	33.3	23	38.3	18	30.0	48.913	<0.001	42.27	<0.001
Hypertension	30	50.0	25	41.7	20	33.3				
Heart rate										
Normal	15	25.0	20	33.3	27	45.0				
Tachycardia	25	41.7	22	36.7	13	21.7	42.545	<0.001	29.05	<0.001
Bradycardia	20	33.3	18	30.0	20	33.3				
Respiratory rate										
Normal	15	25.0	16	26.7	22	36.7				
Tachypnea	34	56.7	32	53.3	27	45.0	37.346	<0.001	36.09	<0.001
Bradypnea	11	18.3	12	20.0	11	18.3				

**(1) Difference between pre and immediate post-periods of intervention, ** (2) Difference between pre and post 48 hours periods*

Table (8): Correlation coefficient between patients' pain intensity and pain-related outcomes (n=60).

Other Secondary outcomes	Patients' pain intensity	
	r	P value
Quality of sleep	0.875	<0.001
Blood pressure	0.938	<0.001
Heart rate	0.921	<0.001
Respiratory rate	0.945	<0.001

6. Discussion

Despite several decades of research, pain is still a significant problem for critically ill patients throughout their stay in the intensive care unit (ICU). Inaccurate pain assessment and the resulting inadequate treatment of pain in critically ill adults can have significant physiological and psychological consequences. So, the current study was conducted with the aim to evaluate the effect of multimodal integrative interventions on pain-related outcomes among critically ill patients.

The results of the current study show the demographic characteristics of critically ill patients; it was found that, less than half of studied patients aged from forty to less than fifty years old with a mean age of 49.00±0.92. This age is the average age for ICU patients, as the people getting older, they are expected to suffer chronic disease, this findings are revealed in this study as two third of the studied patients had either diabetes mellitus or liver disease.

In the same line, *Hill et al., (2016)* in their study entitled "Long-term outcomes and Healthcare utilization following Critical Illness – a population-based study" and reported that most study subjects were above the age of forty. Similarly, *Jaskirat et al. (2021)* examined the effect of music therapy on ICU-induced anxiety and physiological parameters among ICU patients and stated that less than half of the studied patients were forty-four to fifty years old.

Concerning gender, the current study reveals that two-thirds of the studied patients were males. This finding may be due to the rapid lifestyle and lack of safety precautions among young adult males. Supporting this finding, *Othman et al., (2020)* in their study entitled "Effect of integrative

nursing practices on cognitive recovery among severe traumatic brain injury patients." And indicated that most of the studied patients were males and middle-aged. This finding is also supported by the results of a recent controlled trial conducted by *Rezaeikia (2020)* to investigate the effect of passive movements of the lower extremity on hemodynamic parameters of patients under a ventilator and found that nearly two-thirds of the study group subjects were males.

Regarding marital status, more than half of the studied patients were widowed, residents in urban areas. These findings referred to the location of the study setting as it serves wide geographical urban areas. These results disagree with the results of a study done by *Mahadeo and Shabana (2014),* who showed that nearly half of the patients were married, two-thirds of them were females, and more than half were from rural areas.

Regarding medical data, the current study demonstrates that less than half of the patients had diabetes mellitus and liver diseases. More than half of them had taken medications such as anti-inflammatories. Also, three-quarters of the studied patients had a family history of chronic diseases such as diabetes mellitus. This might be because diabetes mellitus is a common diagnosis in patients requiring critical care. Although diabetes is sometimes the reason for admission to intensive care units, it is a more commonly comorbid condition that complicates patient management and may increase the severity of primary illness.

This finding agrees with *Silva-Perez, (2017)* in a study entitled "Management of Critically Ill Patients with Diabetes" and reported that the main cause for intensive care admission is diabetes mellitus. This result disagrees with *Fahmy et al., (2021)*, who conducted a study entitled "The effect of passive range of motion exercises on hemodynamic parameters of mechanically ventilated patients," which revealed that less than half of the studied patients were suffering from neurosurgical disorders without a history of diabetes.

Regarding the primary outcome of the persistent baseline and breakthrough pain of the studied patients, it was observed that the frequency of recurrence of persistent baseline pain among studied patients had decreased post intervention periods compared with pre-intervention. These findings are referred to the effect of massage therapy in the multimodal integrative intervention and support the first research hypothesis.

These results agree with the results of a study done by *Ghodela, et al. (2019)* in a study entitled "Effectiveness of progressive muscle relaxation therapy on anxiety and depression: A pre-experimental study on elderly people of old age homes." and showed a marked significant decrease in the incidence of pain post-intervention. Also, *Leutualy, et al. (2022)* in their study entitled "non-pharmacology interventions on pain in critically ill patients" and indicated that pain problems in critically ill patients decreased by multimodal integrative interventions than pharmacological interventions.

Regarding the intensity of the pain (as a secondary outcome) among studied patients, the results of the current study indicated highly statistically significant differences at $p \leq 0.001$ between pre and post-periods of intervention regarding the total mean score of pain intensity. These findings are referred to the effect of massage therapy and relaxation therapy (music, guided imagery) in the multimodal integrative intervention and support the second research hypothesis.

The reported decreasing in pain intensity is in line with *Kukimoto et al. (2017),* who conducted a recent meta-analysis showing decreased postoperative pain with massage interventions. These results also agree with the results of a study by *Mahadeo and Shabana, (2014),* who showed that self-reported pain indicated that on the first day after the intervention, mean CPOT scores indicated a significant decrease in pain in the intervention group.

Regarding the studied patients' total level of quality of sleep (as a secondary outcome), the results of the current study indicated a statistically significant improvement in the studied patients' total sleep quality, as more than half of studied patients had poor sleep pre-intervention decreased to more than one-third after 48 hours of intervention. This finding supports the third research hypothesis and may be because the physical effects of therapeutic massage include the release of muscle tension, increased blood circulation, and initiation of the relaxation response. The release of muscle tension resulting in more restful sleep and lessening the need for pain medication and narcotics. Similarly, *Golino et al. (2019)* in a study about "Impact of an active music therapy intervention on intensive care patients" and stated that after the intervention, outcomes differed between the two intervention groups. Patients receiving the relaxation intervention often fell asleep.

Regarding hemodynamic measurements as secondary outcomes of pain among the studied patients, the results of the current study indicates highly statistically significant differences at $p \leq 0.001$ between pre and post-intervention periods of all hemodynamic measurements. These findings are referred to the effect of massage therapy and relaxation therapy (music, guided imagery) in the multimodal integrative intervention and support the fourth research hypothesis.

Regarding blood pressure, half of the studied patients had hypertension pre-intervention decreased to one-third post-48 hours of intervention. *Ciftci and Otzunc, (2015)* supported these findings on their experimental study entitled "The effect of Music Therapy on Comfort, Anxiety, and Pain in the Intensive Care Unit" and concluded that music has beneficial outcomes on physiological parameters as the mean score of systolic blood pressure was 142 mm/Hg at the beginning of the study and reduced to 138 mm/Hg after they received music.

Similarly, in a Cochrane review, *Bradt et al. (2016)* found that music had a moderate pain-reducing effect and led to a small reduction in heart rate, respiratory rate and blood pressure in cancer patients. *Johnson et al. (2018); Khan et al. (2020)* stated that within the ICU setting, music is cited to reduce delirium and decrease vital signs.

On the other hand, the results of the current study disagree with the results of a study conducted by *Boitor, et al. (2018)* stated non-significant differences between groups in terms of blood pressure or heart and respiratory rates at

any time point across the two data collection sets. However, heart and respiratory rates decreased by two beats/breaths per minute with the administration of hand massage and hand holding.

Regarding heart rate, nearly half of the studied patients had tachycardia pre-intervention decreased to more than one-third immediately post-intervention and one-fifth post 48 hours of intervention. This might be because the association between pain and heart rate tends to vary considerably across critically ill patients. Those patients have complex conditions and comorbidities that may confound the classically established relationship between increased heart rate and acute pain severity.

This finding disagrees with *Dayoub and Jena, (2015)* in their study entitled "Does pain lead to tachycardia" and found no association between heart rate and self–reported pain among patients and concluded that heart rate and pain might be not strongly related in the real-world clinical settings.

Regarding the respiratory rate, more than half of the studied patients had tachypnea pre-intervention compared to less than half post-48 hours of intervention. These results agree with the results of a study by *Golino et al., (2019).* They stated that after the intervention, significant decreases were found in respiratory, heart and self-reported pain. The findings are supported by *Jaskirat et al. (2021),* who reported that music therapy was highly effective in reducing anxiety and stabilizing physiological parameters among experimental group subjects during post-test as compared to the conventional care group where no intervention was given except routine care. Similarly, *Golino et al. (2019)* demonstrated that after the music intervention, significant changes were found in respiratory rate, heart rate and anxiety levels at ($p < 0.001$).

The current study' results reveal a highly positive statistically significant correlation between pain intensity and other secondary outcomes, including sleep quality, blood pressure, heart rate and respiratory rate. These findings emphasized the concept of association between pain intensity, physiological parameters and sleep quality, just the pain intensity controlled, the physiological parameters and sleep quality could be improved

This finding is supported by *Mandel et al. (2019); Millett and Gooding (2017),* who stated that the field of music therapy is an evidence-based health profession built on a strong foundation of research. Specifically, within medical settings. Music therapy has been found to significantly reduce stress, anxiety, pain, provide procedural support and improve the overall quality of life and patient satisfaction.

7. Conclusion

According to the results of this study, study hypotheses are approved as it can be concluded that multimodal integrative interventions delivered including multiple therapeutic modalities such as massage therapy and relaxation therapy (music, guided imagery) are effective in decreasing persistent baseline and breakthrough pain and improving pain-related outcomes (intensity of pain, sleep quality and hemodynamic parameters of blood pressure, heart rate and respiratory rate in critically ill patients.

8. Recommendations

Based on the results of the current study, the following recommendations can be suggested:

- The approach to the assessment and treatment of pain in the ICU should be well-protocolized and multimodal, focusing on adequate and frequent assessment of pain at rest and during procedures.
- Appropriate pain assessment must be partnered with an adequate, multimodal and evidence-based management strategy that incorporates pharmacologic and non-pharmacologic pain control modalities.
- Further research is needed to identify modifiable risk factors or interventions that can reduce the development of chronic pain syndromes in ICU survivors.
- The link between systematic pain assessment in critical care and patient satisfaction needs to be explored.
- The use of massage therapy, relaxation techniques and music therapy are recommended in clinical practice as a routine method.

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