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Acquired muscle weakness among Critical Ill Patients: Leading Agents and Prevention

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Abstract: Background: ICU-AW is considered one of the most important complications occurs in the ICU. Critical care nurses (CCNs) have an important role in the prevention of ICU-AW through applying early mobilization and applying of range of motion exercises. **Purpose:** The purpose of the study is to examine the leading agents and preventive measures for acquired muscle weakness among Critical Ill Patients. **Design:** A descriptive exploratory design was utilized to achieve purpose of this study. Setting: the study was carried out in intensive care units **Sample:** A Purposive sample of seventy-five patients admitted in the previous mentioned setting. **Instruments:** Patient assessment tool, muscle strength scale and indicators to incidence of ICU-AW and agents affecting to ICU-AW assessment tool. **Results:** revealed that, more than half of studied patients had ICU-AW, most studied patients who had muscle weakness were old patients. Administration of corticosteroid and malnutrition was higher in the ICU-AW patients than the Non-ICU-AW patients. There was no statistically significant relation between incidence of ICU-AW and gender, insulin therapy and application of positioning, walking exercises. **Conclusion:** More than half of studied patients developed ICU-AW. The contributing agents of ICU-AW are patient age, malnutrition, no applying range of motion and chair sitting exercise to ICU patients, administration of corticosteroid. Mobilization as rang of motion exercise and well nutrition is a preventive measures. **Recommendations:** Further research is recommended to study extensively the effect of nutritional status on incidence of ICU-AW.

Key words: - *Acquired Muscle Weakness, Critical Ill Patients, Leading Agents& Prevention.*

Introduction

Patients with critical illnesses are at risk of developing long-term conditions that may include neuromuscular impairment, cognitive impairment, and mental health disorders. These conditions, known as Post-Intensive Care Syndrome (PICS). One of the most studied aspects of

post-intensive care syndrome is ICU-acquired muscle weakness (ICUAW). This complication is characterized by atrophy and/or loss of muscle mass in critically ill patients, caused by myopathy, polyneuropathy, or both, in the absence of other plausible etiology (Fan et al., 2020).

ICU-acquired muscle weakness is frequently found in critically ill patients, and is characterized by a generalized, symmetric weakness, affecting limb (proximal more than distal) and respiratory muscles. Facial and ocular muscles are most often not affected. No demyelination is seen, as is the case in Guillain–Barré syndrome. The condition was first acknowledged in the 1980's and has through the years had a large variety of names, for example: Polyneuropathy in critically ill patients, acute necrotizing myopathy of intensive care, Critical illness myopathy and/or neuropathy or Critical illness neuromuscular syndrome. (Hermans et al., 2019).

The exposure to leading agents, patient population under study, assessment scheduling, diagnostic approaches, and inconsistent accounting for patients' pre-hospital muscular function or general functional condition all have a significant impact on the prevalence of ICU-acquired weakness. ICU-AW is prevalent and ranges from 26–65% for patients intubated for a period of 5-7 days to up to 67% for patients intubated for extended durations of time (>10 days). An estimated 25% of the ICU patients experienced ICU-AW for at least another 7 days after being extubated. ICU-AW is thought to develop in 60% of individuals with acute respiratory distress syndrome (ARDS). Sepsis patients have a much greater incidence of ICU-AW, with estimates ranging from 50% to 100%. (Nakamura & Yonclas, 2019).

The development of ICU-AW is correlated to two major agents (not modifiable leading agent and modifiable agenrts), not modifiable leading agents include a higher illness severity score, patients with systemic inflammation or sepsis and patients with multiorgan failure seem to be of particular risk, especially with neurological failure. Also, high lactate and both prolonged mechanical ventilation and prolonged critical illness has been linked with a higher risk of ICUAW. Female sex and older age indicate a higher risk. (Kress & Hall, 2019).

Some leading agents are modifiable; these include hyperglycemia, both caused by the stress of critical illness and by parenteral nutrition, Several drugs such as vasoactive drugs (beta-agonists in particular), some antibiotics, sedatives, corticosteroids, and neuromuscular blocking agents. Sedatives, and deep sedation in particular, is associated with increased risk, Immobilization is recognized as a very important leading agent for ICUAW Several studies have shown that mobilization in the ICU is feasible and safe, even when initiated at an early stage, where the patients might require for example mechanical ventilation, vasopressor infusions or renal replacement. (Latronic et al., 2020).

The mainstay of ICU-AW prevention is through the minimization of the leading agents. Current strategies to limit ICU-AW and optimize recovery from critical illness are focused around minimizing sedation and targeting early mobilization of patients, even while they are still undergoing mechanical ventilation. Passive exercise for patients who are immobile may help hasten recovery. Limiting patient exposure to corticosteroids and neuromuscular blocking agents, good glycemic control and adequate nutritional intake are helping in the

prevention of this syndrome (Latronic et al., 2020).

Significance of the study

Intensive care unit-acquired weakness (ICU-AW) is a common neuromuscular complication associated with cases in the ICU, It is a type of skeletal muscle dysfunction that commonly occurs following sepsis, mobility restriction, hyperglycemia, and the use of neuromuscular blocking agents or glucocorticoids. ICU-AW can lead to delayed weaning of mechanical ventilation and extended hospitalization (Vanhorebeek et al., 2020), identifying leading agents and prevention for acquired muscle weakness among critical ill patients could provide the basis for more research into ICUAW, its possible treatment.

Purpose

To examine leading agents and prevention for acquired muscle weakness among critical ill patients.

Research Questions

1. What are the leading agents for acquired muscle weakness among critical ill patients?
2. What are the preventive measures for acquired muscle weakness among critical ill patients?

Methods

Research design

A descriptive design was utilized in this study.

Research setting

The study was carried out in three intensive care units (ICUs) of Cairo University Hospital (chest, general and internal medicine ICU).

Sampling

A purposive sample of 75 patients admitted to the previously mentioned setting.
The sample was selected based on statistical power analysis test (the confidence level of 90% and margin of error of 5%).

Inclusion Criteria:

- Patients above 18 years in the ICU.
- Patients should be fully conscious and able to follow simple commands.

Exclusion Criteria:

- Patient with systemic vascular disorders such as lupus erythematous and with neuromuscular blocking agents and preexisting neuromuscular disease (myasthenia gravis, Guillain-Barre syndrome, spinal cord injury and stroke) were excluded from study.

Instruments

In order to achieve the aim of the study the following tools were being used:

<u>Instrument One</u>:- Patients assessment tool:

It was developed by investigators based on scientific review of literature which consist of one part:

- Patient Demographic data which includes age, gender, level of education, occupation and residence.

<u>Instrument two</u>: - Muscle Strength Scale/Medical Research Council (MRC) and Indicators to incidence of ICU-AW:

This instrument was adopted from Hrmans et al., (2012). It was used to monitor critically ill patients' indicators of ICU-AW and to assess

limb movement manually. This scale was used to assess muscle strength of upper limb (right and left hand) and lower limb (right and left leg).

The diagnosis of ICU-AW is made through grading muscle strength in the upper and lower extremities. The assessment of muscle strength include; wrist extension, elbow flexion, and bilateral shoulder abduction, for the upper limbs. Hip flexion, knee extension and foot dorsiflexion for the lower limps.

Scoring; muscle strength in each group was scored according to the six-point MRC system. Zero was given for no visible contraction, one degree for visible contraction without movements of the limbs, two degrees for movements of the limbs but not against the gravity, three degrees for movement against gravity over (almost) the full range, four degrees for active movement against gravity and resistance and five was scored for presence of normal muscle power.

Scoring system:

- If muscle strength score was < 48, this indicates that the patient had ICU- AW.
- If muscle strength score ranged from 48 to 60, this indicated the absence of ICU- AW.

<u>Instrument three:</u> - Agents affecting Intensive Care Unit Acquired Muscle Weakness (ICU-AW).

This instrument was developed by the researcher after reviewing the related literatures (Goldman & Andrew, 2015) to assess contributing agents for the occurrence of acquired muscle weakness in intensive care units. It consisted of three parts:

- **Part one: preventive measures observational checklist:-**

It was used to assess application of ICU-AW preventive measures and contains four main items as follows: Positioning and repositioning, Range of motion exercises, walking exercises and Chair sitting exercises.

Scoring system

- Each procedure done to the patient was given one degree.
- Each procedure not done to the patient was given zero.

- **Part Two: Drug related agents:**

It includes prescribed medications during the ICU stay such as glucocorticoid therapy and insulin therapy. The response format is measured using scale of yes (present), no (not present).

Scoring system

- Patient who took corticosteroid therapy or insulin therapy, Yes = 1 degree.
- Patient who didn't take corticosteroid therapy or insulin therapy, No = zero.

- **Part Three: Nutritional related agents:**

- The actual nutritional intake was compared versus the ideal nutritional requirements needed for each patient to know if the patient had enough or not enough nutrition.
- The ideal nutritional intake for each patient was calculated using the following equations: (Harris & Benedict, 1919) equations to calculate the ideal nutritional intake.

Basal Energy Expenditure (BEE) equal

For men, B.E.E. = 66.5 + (13.75 x Weight (kg) + (5.003 x height (cm) - (6.775 x age (year).

For women, B.E.E. = 655.1 + (9.563 x weight (kg) + (1.850 x height (cm) - (4.676 x age (year).

Total Caloric Requirements= B.E.E. x the sum of the stress and activity factors.

Stress plus activity factors range from 1.2 to over 2.

- Then the researcher calculated the actual nutritional intake for each patient, through measuring the food and fluids the patient took during the day and calculated how many calories the food and fluids the patient took during the day.
- If the patient was well nourished, the actual nutritional intake was equal to the ideal nutritional requirements.
- If the patient was malnourished, then the actual nutritional intake was less than the ideal nutritional requirements.

Scoring system

- One degree was provided for well nourished patients, Zero was provided for malnourished

Content validity of the tools

The instruments were reviewed for appropriateness of items by a jury of 7 experts, one of them was a professor and three assistant professors of critical care Nursing Department at Faculty of Nursing, Cairo University and two were lecturers of ICU medicine at Faculty of Medicine in Cairo University and one assistant professor at Faculty of Physiotherapy in Cairo University. The expertise tools clarity, relevance, they reviewed the tools for clarity on relevance, comprehensiveness, simplicity and applicability, minor modification was done.

Reliability

Reliability of intensive care unit acquired muscle weakness (ICU-AW) assessment instrument tool was done by Alpha Cronbach testa= 0.95

Ethical considerations

The research approval was obtained from the Ethical and |Research committee in faculty of nursing Cairo University.

Approaches to ensure the ethical issues were considered in the study regarding confidentiality and informed consent. Confidentiality was achieved by the use of locked sheets without names of the participants and were replaced by numbers. All participants were informed that the information they provided during the study would be kept confidential and used only for statistical purpose. Each parent was informed that participation in the study was voluntary, and had the right to withdraw from the study at any time.

Pilot study

A pilot study was conducted to test the feasibility and applicability of the study instruments used in this study. It was carried out on 10% of patients (8 patients) with critical illness in the previous mentioned setting. No modifications were done.

Procedure:

Data were collected in 7 months, from beginning of August 2021 to the end of February 2022. Filling out the data collection instrument took about 75 to 95 minutes as follows:

- Assessment of patient demographic data, and medications (Patient file) took about 15 minutes.
- Assessment of muscle strength for each patient took about 30 minutes for each study patient.
- Assessment of nutritional status for each studied patient took about 20-30 minutes to calculate the ideal and actual nutritional intake.
- Each patient was observed in the morning and afternoon shifts by the researcher during the actual performance of preventive measures (positioning, range of motion, chair sitting and walking) and it took about 15-20 minutes to see if preventive measures were done or not.

Statistical analysis

All Data were collected, tabulated and subjected to statistical analysis, which is performed by SPSS in general (version 22). While Microsoft office Excel is used for data handling and graphical presentation. Data were presented in tables and graphs. The statistical analysis included: number (No.), percentage (%), the arithmetic mean ($\bar{X}$), chi-square ($\chi 2$) and Z-Test.

The observed differences and associations were considered as follows:

-P.> 0.05 no statistical significant difference (No difference) P. ≤ 0.05 statistical significant difference. A highly statistical significant was considered if P.≤ 0.001

Standard Deviation (SD) and arithmetic mean ($\bar{X}$) were used for quantitative data e.g. age and muscle strength score. Frequency (number and percentage) were used for qualitative categorical variables.Meanwhile,

chi-square and Z-test were used to test the association between incidence of ICU-AW and some study variables .

Results

Table 1: indicates the frequency distribution of studied patients according to their characteristics. Nearly one half (49.3) of studied patients have 50 years or more, with Mean ± SD equals 48.29 ± 16.22. More than half (52.0%) of studied patients were males. Less than half (42.7%) of them were illiterates. In relation to occupation of studied patients, one third (33.3%) were housewives and more than three quarter (76.0%) were from rural area. According to their admission medical diagnosis, the results revealed that less than half (46.7%) of studied patients had respiratory disorder. Meanwhile,(1.3%) of studied patients had cancer, infectious and endocrine disorders.

Figure 1: reveals that more than half (53.3%) of studied patients had intensive care unit acquired muscle weakness. While less than half (46.7%) of studied patients did not have intensive care unit acquired muscle weakness.

Table 2: shows frequency distribution of Preventive Measures application contributing to intensive care unit acquired muscle weakness among studied patients. For the Non ICU-AW patients, the application of Preventive Measures was majority (80.0%) for walking exercise, more than half (51.4%) for chair sitting, less than half (45.7%) for range of motion, and minority (2.9%) for positioning. While for the ICU-AW patients, the application of Preventive measures was more than three fifth (62.5%) for walking exercise, less than fifth (15.0%) for chair sitting exercise and none of them (0.0%) for positioning and range of motion.

Table 3: illustrate the frequency distribution of drug and nutritional related agents that contributing to intensive care unit acquired muscle weakness among studied patients. In the Non ICU-AW patients, less than fifth (17.1%) received corticosteroid, more than quarter (28.6 %) received insulin therapy and one quarter (25.7%) were malnourished, While in the ICU-AW patients, three fifths (60.0%) received corticosteroid, less than half (45%) received insulin therapy and less than three quarters (72.5%) were malnourished.

Table 4: reveals that there was a highly statistically significant relation between incidence of intensive care unit acquired muscle weakness and application of preventive measures as range of motion and chair sitting at P .00002 and .00988 respectively.

While, there was no statistical significant relation between the incidence of intensive care unit acquired muscle weakness and application of other preventive measures as positioning and walking exercise.

Table 5: reveals that there was a highly statistical significant relation between incidence of intensive care unit acquired muscle weakness and both usage corticosteroid and nutritional related agents, While, there was no statistical significant relation between the incidence of intensive care unit acquired muscle weakness and administration of insulin therapy.

Table (1) Frequency distribution of studied patients according to their characteristics (n = 75).

Patient's characteristics	No	%
Age:		
18 - < 30 years	9	12.0%
30 - < 40 years	18	24.0%
40 - < 50 years	11	14.7%
≥ 50years	37	49.3%
Mean ± SD	**48.29±16.22**	
Gender:		
Male	39	52.0%
Female	36	48.0%
Level of education		
Illiterate	32	42.7%
Read/Write	15	20.0%
Secondary education	13	17.3%
Higher education	15	20.0%
Occupation		
Student	4	5.3%
Worker	17	22.7%
Employee	14	18.7%
Retired	15	20.0%
House wife	25	33.3%
Residence		
Rural	57	76.0%
Urban	18	24.0%
Admission medical diagnosis		
Cardiovascular disorders	11	14.7%
Respiratory disorders	35	46.7%
Infectious disorders	1	1.3%
Gastrointestinal disorders	5	6.7%
Endocrine/metabolic disorders	1	1.3%
Renal disorders	9	12.0%
Cancer	1	1.3%
Poisoning	3	4.0%
Falling from height	3	4.0%
Postoperative care	6	8.0%

Figure (1): Incidence of Intensive Care Unit Acquired Muscle Weakness among the studied sample (n=75).

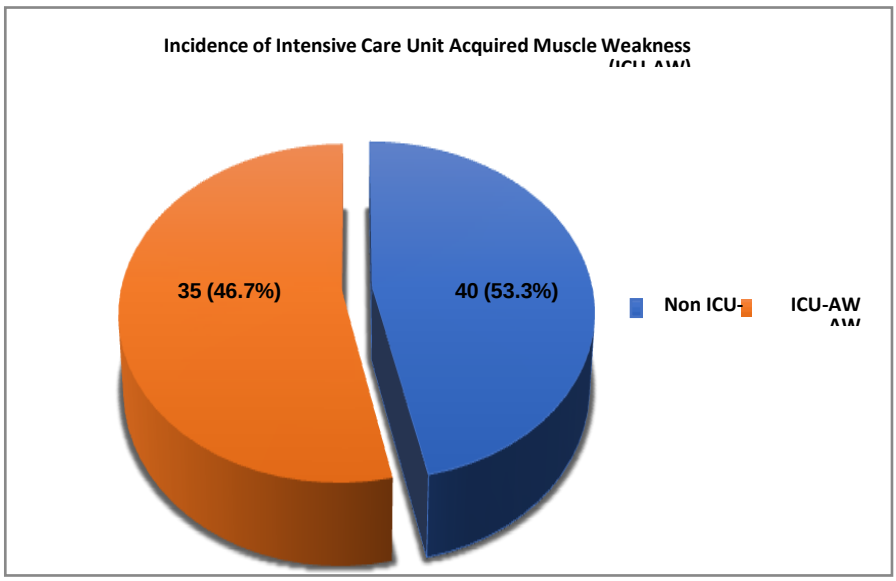

Table (2): Distribution of Critically Ill Patients according to their Practising of Preventive Measures for Acquired Muscle Weakness

Preventive Measures	Non ICU-AW (n=35)				ICU-AW (N=40)			
	Done		Not Done		Done		Not Done	
	NO.	%	NO.	%	NO.	%	NO.	%
Positioning	1	2.9%	34	97.1%	0	0.0%	40	100%
Range of motion exercises	16	45.7%	19	54.3%	0	0.0%	40	100%
Walking exercises	28	80.0%	7	20.0%	25	62.5%	15	37.5%
Chair sitting exercises	18	51.4%	17	48.6%	6	15.0%	34	85.0%

Table (3): Distribution of Critically Ill Patients according to Their Administration of Corticosteroids, Insulin Therapy and Level of Nutrition

Leading agents	Non ICU-AW (n = 35)		ICU-AW (n = 40)	
	No.	%	No.	%
Corticosteroid				
-No	29	82.9%	16	40.0%
-Yes	6	17.1%	24	60.0%
Insulin Therapy				
-No	25	71.4%	22	55.0%
-Yes	10	28.6 %	18	45.0%
Level of Nutrition				
-Well Nourished	26	74.3%	11	27.5%
-Malnourished	9	25.7%	29	72.5%

Table (4): Distribution of Critically Ill Patients (ICU-AW and non ICU_AW) according to Their Positioning, Performing Range of Motion Exercises

Preventive Measures	Non ICU-AW (n=40) Done		ICU-AW (n=40) Done		Test (Z)	P Value
	No.	%	No.	%		
Positioning	1	2.9%	0	0.0%	.94	.34634
Range of Motion Exercises	16	45.7%	0	0.0%	4.22	.00002*
Walking Exercises	28	80.0%	25	62.5%	.14	.89217
Chair Sitting Exercises	18	51.4%	6	15.0%	2.58	.00988*

HS (Highly Significant) *P value < 0.01 NS (No Significance) P value > 0.05

Table (5) Distribution of Critically Ill Patients (ICU-AW and non ICU_AW) according to Their Administration of Corticosteroids, Insulin and Level of Nutrition

Leading agent	Non ICU-AW (n=35) %	ICU-AW (n=40) %	Test x2	P Value
Drug related agent (corticosteroid)				
-NO	82.9%	40.0%	14.29	.00016*
-Yes	17.1%	60.0%		
Drug related agent (insulin therapy)				
-NO	71.4%	55.0%	3.31	.19062
-Yes	28.6 %	45.0%		
Nutritional related agent				
-Well Nourished	74.3%	27.5%	16.35	.00005*
-Malnourished	25.7%	72.5%		

HS (Highly Significant)*P value < 0.01 NS (No Significance) P value > 0.05

Discussion

Intensive care unit (ICU)-acquired weakness (ICUAW), is observed in many survivors of critical illness following various critical diseases. Clinical consequences of muscular weakness include, for example, impaired mobilization, prolonged bed rest, and extended ICU and/or hospital length of stay. This may induce a secondary complication and necessitates repeated and/or intensified medical therapy, which may again result in increased morbidity and mortality Kramer, (2019) So, the current study aimed to examine leading agents and prevention for acquired muscle weakness among critical ill patients.

Concerning the incidence of ICU- AW, the current study indicated that more than half of studied patients developed ICU-AW. From the researcher point of view, this result was due to the largest sector of the studied patient were old age, receiving corticosteroids and malnourished All these factors decrease protein synthesis in the muscle leading to decrease muscle strength and tone.

This findingas in the same line with Appleton et al., (2019) who showed that more than half of studied patients developed Intensive Care Unit Acquired weakness (ICUAW) in a study titled " The incidence of intensive care unit acquired weakness syndromes " However, this finding was

inconsistent with Yu et al., (2018) who found that only one quarter of studied patients had ICU-AW in their study entitled "Analysis of high risk factors of intensive care unit-acquired weakness in patients with sepsis ".

Regarding the application of preventive measures contributing to intensive care unit acquired weakness, the current study stated that the majority of Non ICU-AW patients were walking exercise, more than half were sitting on chair and less than half were performing range of motion exercises. No one in the ICU-AW patients had done positioning and range of motion exercises. From the researcher point of view, the application of preventive measures were inadequate in the ICU-AW patients because some patients were immobilized due to their medical condition and some procedures not applied to them e.g. walking and chair sitting exercise.

These findings were in agreement with Asfour, (2016) who found that no one in the ICU-AW cases had done range of motion and in the Non ICU-AW cases nearly half of patients had done range of motion exercise. Also Mohamed et al., (2019) indicated that the majority of patients in the Non ICU-AW cases had done walking exercise and No one in the ICU-AW cases had done positioning and range of motion exercises in their study entitled "Factors Contributing to Acquire Muscle Weakness among Critical Ill Patients".

Concerning to distribution of drug and nutritional related agents contributing to intensive care unit acquired muscle weakness, The current study found that two third of patients in the ICU-AW received corticosteroid, more than quarter received insulin therapy and one quarter of them were malnourished,. While less than one fifth in the Non ICU-AW patients were received corticosteroid, less than half received insulin therapy and less than three quarter were malnourished. From the researcher point of view, this finding may be due to high incidence of respiratory disorders in ICU-AW cases; so they were in need for systemic or inhaled corticosteroid to treat airway obstruction and inflammation.

This finding was similar to Michael et al., (2020), who found less than three quarters of patients with ICU-AW were malnourishe. in a study entitled "Muscle weakness and nutrition therapy in ICU ". Also, this finding consistent with Li et al., (2020) who stated that two thirds in the ICU-AW received cortisone. While, less than one fifth in the Non ICU-AW patients was received the drug.

Concerning the relation between application of preventive measures contributing to muscle weakness and the incidence of intensive care unit acquired muscle weakness among studied patients; the current study revealed that there was a was a negative relation between the incidence of ICU-AW and application of preventive measures as range of motion exercise and chair sitting exercise. While, there was no statistically significant relation between incidence of ICU-AW and application of other preventive measures as positioning and walking exercise.

From the researcher point of view, this result may be due to mobilization could increase muscle excitability, improve muscle strength and prevent incidence of disuse muscle atrophy. So, not applying these measures to ICU cases increase incidence of muscle weakness.

These findings agreed with Zhang et al., (2019) who conducted a study "Early mobilization of critically ill patients in the intensive care unit" and

found that not applying preventive measures e.g chair sitting, walking and range of motion exercise

Regarding the relation between drug, nutritional related agents and incidence of intensive care unit acquired muscle weakness among studied patients: The finding of the current study revealed that there was highly statistically significant relation between incidence of ICU-AW and both usage of corticosteroid and nutritional related agent, While, there was no statistical significant relation between incidence of intensive care unit acquired muscle weakness and admiration of insulin therapy. In the researcher point of view, corticosteroid had dangerous side effect on muscle mass and its strength. Also, well nutrition is essential for function of skeletal muscular system.

This finding agreed with Hermans et al., (2019) who conducted a study about " Impact of intensive insulin therapy on neuromuscular complications and ventilator dependency in the medical intensive care unit " and found that no significant relation between insulin therapy and incidence of ICU-AW. Also, Vanhorebeek et al., (2020) supported this result in a study entitled "ICU-acquired weakness" and reported that there was highly significant relation between incidence of ICU-AW and using of corticosteroid in ICU. Additionally, Michael et al., (2020), agreed that there was significant relationship between incidence of ICU-AW and nutritional status of critically ill patients. On the other hand; this finding contradicted with Yang et al., (2021), who found no significant effect of corticosteroids on the incidence of ICU-AW among ICU patients on their a study on "Hyperlactacidemia as a risk factor for intensive care unit-acquired weakness in critically ill adult patients".

Conclusion

From the result of the present study, one can conclude that:

The study concluded that further than half of studied cases developed intensive care unit acquired muscle weakness (ICU-AW). Operation of positioning and range of motion exercises were not done in the ICUAW patients. As well, less than half of ICU-AW patients received insulin therapy, half corticosteroid drug and less than three quarters were malnourished.

Recommendations

- Critical care nurses should be provided with knowledge about exercises that should be performed by critically ill patients to avoid muscle weakness
- Application of mobility protocol in ICU and engagement of patients in achievement of safety mobilization protocol.
- Collaboration of occupational team consists of (intensives, nutritionist, physical therapist, and CCNs) to provide a preventive program to decrease incidence of ICU-A.
- Critically ill patients should perform range of motion exercises for all joints, perform adduction and abduction three times /daily
- Further studies by using larger probability sample for generalization of the results.
- Further studies are needed to examine the incidence of ICU-AW in unconscious and sedated patients.
- Further studies are needed to assess the effectiveness of other types of exercises on muscle weakness.

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