Effect of Active versus Passive Humidification on Airway Complications and Clinical Outcomes in Trauma ICU Patients with Prolonged Mechanical Ventilation

Protocol of Thesis

Submitted for Partial Fulfillment of the Requirements of Doctorate Degree in Critical Care and Emergency Nursing

By

Mostafa Muhammad Ahmad Ali

Assistant lecturer of Critical Care and Emergency Nursing

Thesis Supervisors:

Prof. Dr. Mervat Anwar Abdel Aziz

Professor of Critical Care and Emergency Nursing

Prof. Dr. Mostafa Samy Abbas

Professor of Anesthesia, Intensive Care and Pain Management

Dr. Mona Abdel Elezim Ahmed

Assistant professor of Critical Care and Emergency Nursing

Faculty of Nursing
Assiut University

13/5/2026

Introduction:

Effective humidification of inspired gases is an essential component of invasive mechanical ventilation for making breathing easier, because artificial airways bypass the upper respiratory tract's natural mechanisms for warming and moistening inhaled air **(Lellouche, 2023 & Fiorentino et al., 2023).** Inadequate humidification results in dryness of the respiratory mucosa, impaired mucociliary clearance, increased secretion viscosity, and potential airway obstruction, which can contribute to ventilator-associated complications and impaired gas exchange **(Re et al., 2024).**

Two primary methods of humidification are used in clinical practice: active heated humidifiers (HHs), which add heat and moisture via an external water reservoir, and passive heat-and-moisture exchangers (HMEs), which recycle exhaled heat and moisture back to the airway **(Bernatzky et al., 2020 & Campodoni et al., 2023)**. International standards recommend that HMEs deliver at least 30 mg H_2O/L and HHs deliver 33–44 mg H_2O/L with gas temperature of 34–41°C and 100 % relative humidity at the circuit Y-piece to approximate physiologic conditions **(Fiorentino et al., 2023)**.

It's necessary to measure the temperature and humidity of delivered air for patients on invasive mechanical ventilation by thermo-hygrometry probe; to achieve the over mentioned criteria **(Bernatzky et al., 2020).** These devices have advantages and limitations; HHs attains a greater humidity and temperature, no contraindications, but has higher cost and risk of contamination due to possible condensation. In opposite, HMEs are simpler, disposable, portable, cost-effective and advantageous; those remove condensation, but associated with increased airway resistance, work of breathing and dead space, leading to decreases alveolar ventilation **(Yin et al., 2020).**

Systematic reviews and clinical guidelines have found no consistent overall superiority of one humidification method over the other for general ICU populations with regard to ventilator-associated pneumonia, duration of mechanical ventilation, or mortality, highlighting the need for context-specific evidence rather than broad comparisons **(Goodfellow et al., 2024)**. Trauma ICU patients frequently present unique challenges, including prolonged MV, impaired cough, and variable airway secretion characteristics influencing the effectiveness of humidification devices **(Yin et al., 2020)**.

For example, copious, thick, or bloody secretions can occlude HMEs, increasing airway resistance and the risk of tube obstruction, whereas active humidifiers may better maintain airway patency under these conditions. Additionally, prolonged MV may ennhance these differences, emphasizing the clinical relevance of device choice in this population **(Deokar et al., 2025)**. Despite these concerns, there is lack of high-quality, clinical trials directly comparing the effects of humidification methods on airway and clinical outcomes specifically in trauma ICU patients with prolonged MV **(Plotnikow et al., 2025)**.

Operational definitions:

Active humidifiers, also known as heated humidifiers, are devices that comprise of a plastic humidification chamber with a metallic base, containing sterile water, which is placed on top of an electric heater plate connected with inspiratory limb of the ventilator circuit, proximal to the ventilator **(Gaffney & Dalton, 2024)**.

Passive Humidifiers are disposable Heat and moisture exchanger (HME), some with a particle filters, also called artificial noses because they mimic the action of nasal cavity in gas humidification **(Gaffney & Dalton, 2024).**

Significance of the study:

Mechanical ventilation is required in up to 70% of ICU patients, making appropriate gas humidification essential for all invasively ventilated individuals via HH or HMEs. Numerous studies conducted in general ICU populations have consistently reported no significant differences between HH and HME regarding ventilator-associated pneumonia, duration of MV, or mortality **(Goodfellow et al., 2024);** these findings may not apply to trauma ICU patients requiring prolonged ventilation. Such patients often present with heavy airway secretions and increased risk of airway obstruction, which may influence the clinical effectiveness of humidification devices.

With approximately **90%** of **1,029** patients admitted to Trauma ICUs in Assiut University Hospital in **2025**, requiring prolonged invasive mechanical ventilation (MV), there is a critical need to compare the effect of active versus passive humidification on patients' outcomes. This study investigates the clinical differences between active and passive humidification regarding airway complications, VAP, temperature fluctuations, length of stay, and mortality **(Al Dorzi et al., 2022).**

Aim of the study:

1- To compare effect of active versus passive humidification on airway complications and clinical outcomes in trauma ICU patients with prolonged mechanical ventilation.

Research hypotheses:

To fulfill the study aim, the following research hypotheses are formulated for trauma ICU patients requiring prolonged invasive mechanical ventilation:

Alternative Hypothesis (H_1):

1- Patients with heat and moisture exchanger experience more viscous tracheobronchial secretions and a higher frequency of airway-obstruction events requiring tube change compared with those with heated humidifier.
2- Patients with heated humidifier have higher ventilator associated pneumonia than patients with heat and moisture exchanger.
3- Patients with heat and moisture exchanger demonstrate significant differences in arterial blood gases, hemodynamic status, and ventilator data compared with those with heated humidifier.
4- There are statistically significant differences in clinical outcomes (duration of mechanical ventilation, length of stay and ICU mortality) between patients with heat and moisture exchanger and those with heated humidifier.

Null hypothesis (H_0):

- There are no statistically significant differences between effects of heat and moisture exchanger and heated humidifier on outcomes of traumatized patients with prolonged invasive mechanical ventilation.

Patients and method:-

Research design:

It is a randomized controlled trial (RCT) comparing the effects of HH versus HME on trauma ICU patients requiring prolonged invasive MV **(Deokar et al., 2025).**

Setting:

This study will be conducted at Trauma ICUs of Assiut University Hospital, Egypt. Trauma ICU1 include 25 beds in five separated rooms , 11 head nurses, 59 nurses, 8 assistant nurses , nurse patient ratio 1:2, and trauma ICU2 composed of 20 beds in four separated rooms , 9 head nurses, 51 nurses, 7 assistant nurses , nurse patient ratio 1:2.

Sample size:

The sample size was calculated based on the primary outcome of the study, which is the incidence of airway obstruction, a binary clinical outcome. The calculation will be performed using G*Power software (version 3.1) for comparison between two independent proportions (HH vs. HME) **(Farahani & RoshanChesli, 2023)**. Accordingly, the initial required sample size will include 148 patients (74 patients per group).

To account for potential dropouts or attrition (~10%), the total sample size increased to 162 patients, with 81 patients in the HH group and 81 patients in the HME group.

Inclusion criteria:

1- Adult age 18–65 years.

2- Trauma ICU patients receiving invasive mechanical ventilation.

3- Anticipated to require prolonged mechanical ventilation, defined as ≥7 days of invasive ventilatory support **(Rubulotta et al., 2024)**.

Exclusion criteria:

1- Immunosuppression such as HIV, cancer or AIDS.

2- Blood leukocyte count <1,000 cells/mm3.

3- Withdrawal of life-sustaining treatment within 5 days.

4- Use of HME in conjunction with an HH.

5- Contraindications of HME including body temperature < 32°C, copious, thick, or bloody secretions, significant air leak (exhaled VT >70% of VT inspired) or broncopleural fistula **(Palanisamy et al., 2025)**.

Types of outcome measures

Primary endpoint is clinically significant **airway obstruction**, defined as an unexplained increase in airway resistance (>15 $cmH_2O/L/s$) and/or peak airway pressure (>35 cmH_2O or a sudden increase of 5–10 cmH_2O above the patient's baseline) is accompanied by evidence of secretion retention, thick secretions with increased suction burden, mucus plugging, partial or complete

tube occlusion, difficulty in suction catheter passage, or the need for airway intervention such as bronchoscopy or endotracheal tube/tracheostomy tube exchange **(Mattson et al., 2024)**.

Secondary outcomes

These are the main clinical outcomes that directly reflect the effect of humidification:

1. Airway and secretion-related outcomes

- Delivered gas conditions at Y-piece (temperature & absolute humidity).
- Tracheobronchial secretion characteristics
- Suctioning burden
- Frequency of endotracheal/tracheostomy tube exchange due to obstruction
- Artificial airway-related complications
- Grading of airway obstruction severity

2. Infectious outcomes

- Ventilator-associated pneumonia (VAP) diagnosed based on predefined clinical, radiological, and microbiological criteria, with the Clinical Pulmonary Infection Score (CPIS) used as a supportive tool.
- Ventilator-associated events (VAE: VAC, IVAC, PVAP)

3. Ventilation and respiratory outcomes

- Duration of mechanical ventilation
- Weaning and liberation outcomes
- Gas exchange and hemodynamic parameters
- Ventilatory efficiency indices
- Respiratory mechanics and oxygenation status

4. Patient-centered outcomes

- ICU length of stay
- ICU mortality

Exploratory outcomes

These are useful for additional interpretation, but they should not compete with the main clinical endpoints:

- Resource utilization
- Estimated cost analysis
- Comparative economic burden

Randomization and Allocation Concealment:

Patients will be randomly assigned in a 1:1 ratio to either the heated humidifier (HH) group or the heat-and-moisture exchanger (HME) group using block randomization with variable block sizes (4 and 6), generated using Microsoft Excel prior to patient enrollment. The randomization sequence will be prepared by an independent researcher not involved in patient recruitment or outcome assessment. Allocation concealment will be ensured using sequentially numbered, opaque, sealed envelopes (SNOSE), which will be opened only after patient enrollment.

Blinding and Bias Mitigation

While full double-blinding is not feasible due to the visible differences between the two humidification systems, scientific rigor will be implemented to ensure a 'PROBE' design (Prospective Randomized Open-label Blinded Endpoint). To minimize detection bias, an independent outcome assessor and a blinded statistician will remain unaware of group assignments until the final analysis is complete. Furthermore, objective clinical data (e.g., laboratory and imaging results) will be adjudicated by clinicians blinded to the intervention.

Handling Missing Data:

All data will be screened for completeness and consistency prior to analysis. Missing data will be managed according to the Intention-to-Treat (ITT) principle, ensuring all randomized patients are included in the final analysis. If the proportion of missing outcome data exceeds 5%, appropriate

imputation methods (e.g., multiple imputation or last observation carried forward) will be applied to maintain statistical power and minimize bias.

Data collection tools:

Four tools will be used to collect patient's data, as following:

Tool I: Trauma ICU patients' assessment profile:

This tool will be developed by the researcher based on national and international literatures review **(Cheng et al 2021, Naderi, 2022 & Hickey et al., 2024).** Composed of ten parts, as the following:

Part 1: Demographic and medical data:

This part will include patient's code, age, gender, educational level, marital status, residence place, employment and smoking. Also, this part will assess patient's diagnosis, present complaints, past medical history, surgical history, date of admission and date of discharge from intensive care unit (to calculate length of stay)**.**

Part 2: Trauma-related clinical data:

This part will assesses trauma characteristics including type of trauma (blunt or penetrating), mechanism of injury (road traffic accident, fall from height, assault, or burn injury), anatomical injury sites (head injury, chest trauma, abdominal trauma, spinal fractures, or multiple trauma), and the number of injured body regions. In addition, it evaluates severity of trauma by using injury severity score (ISS), revised trauma score (RTS), and glasgow coma scale (GCS).

Physiological status at admission will be assessed using shock index (heart rate/systolic blood pressure) as an indicator of hemodynamic instability. Associated injuries and complications will include hemorrhagic shock, traumatic brain injury, spinal injury, rib fractures or flail chest, and pneumothorax or hemothorax. Emergency interventions prior to ICU admission

will be recorded, including surgical procedures, chest tube insertion, emergency laparotomy, and orthopedic or external fixation procedures **(Mew et al., 2022).**

Part 3: APACHE (Acute Physiology and Chronic Health Evaluation) IV score:

This scale will be adopted from **(Zimmerman et al., 2006)**, validated and widely used **Gaikwad et al., (2026)** as a severity-of-illness scoring system to assess baseline patient condition and predict in-hospital mortality. It consists of the Acute Physiology Score (APS), age score, comorbidity score, and other admission-related variables. APS is derived from the worst physiological values recorded during the first 24 hours of ICU admission, including cardiovascular, respiratory, renal, gastrointestinal, hematologic, and neurologic parameters.

Part 4: Hemodynamic parameters assessment:

This part will include assessment of hemodynamic parameters such as vital signs (body temperature, heart rate, respiratory rate and blood pressure as systolic, diastolic and mean arterial pressure), oxygen saturation, central venous pressure (CVP), capillary refill time, lactate, urine output and body weight.

Part 5: Laboratory and radiological investigations assessment:

This part will compose of arterial blood gases parameters (PH, PaO2, PaCO2, HCO3 and BE), bacterial biomarkers (white blood cells, C-reactive protein, procalcitonin and sputum culture) and chest radiograph.

Part 6: Antibiotic Exposure Assessment:

This part will assess antibiotic exposure as a potential confounding factor affecting infectious and respiratory outcomes. Antibiotic administration will be recorded from the initiation of invasive MV until extubation or termination of ventilation. Data will include the type of antibiotic, spectrum (broad vs. narrow), timing of initiation, duration of therapy, and indication when available. Antibiotic exposure will be documented as a time-dependent variable to

account for its potential influence on ventilator-associated pneumonia, ventilator-associated events, and airway secretion characteristics.

Part 7: Sequential Organ Failure Assessment (SOFA) score:

The Sequential Organ Failure Assessment (SOFA) score will be will be adapted from **(Vincent et al., 1997)** and still used as an indicator of the severity of organ dysfunction **(Li et al., 2025)**. SOFA score will be assessed within the first 24 hours of ICU admission to establish baseline severity of illness and then recorded daily at a fixed time point throughout the period of mechanical ventilation to monitor changes in organ dysfunction over time.

Part 8: Chest Physiotherapy Exposure:

Chest physiotherapy will be recorded as a potential confounding factor influencing secretion clearance and airway patency. Data will include whether chest physiotherapy was applied (yes/no) and frequency of sessions per day, from the initiation of invasive MV until extubation or termination of ventilation. This information will be used to account for variability in airway clearance practices that may affect secretion burden, airway obstruction, and ventilator-associated outcomes.

Part 9: Sedation and analgesia assessment:

This part will assess the level of sedation and analgesia in mechanically ventilated trauma patients as a potential confounding factor affecting airway clearance, cough reflex, secretion burden, and ventilatory outcomes. Sedation level will be evaluated daily during the period of MV using the Richmond Agitation–Sedation Scale (RASS), recently used by **(Adams et al., 2026).** In addition, variability in sedation depth over time will be considered to reflect sedation stability during mechanical ventilation. The type of sedation will be categorized based on the primary sedative agent (propofol, benzodiazepine, mixed, or no sedation). Analgesic use, particularly opioid administration, will also be recorded.

Part 10: Fluid Balance Assessment

This part will evaluate fluid status as a potential confounding factor influencing lung mechanics, secretion characteristics, and gas exchange. Fluid balance will be assessed daily until extubation, including measurement of fluid intake and output, including all intravenous fluids, medications, nutrition, urine output, and other measurable losses.

Tool II: Humidification and Mechanical Ventilation Assessment:

This tool will be developed by researcher after reviewing related literature (**Hickey et al., 2024).** It will comprise of five parts:

Part 1: Humidification type and adequacy indicators:

This part includes the type of humidification used, either active or passive humidifier with assessment for presence of condensation and its amount daily. In addition, the adequacy of humidification will be assessed by measuring inspired gas humidity and temperature at the Y-piece using a hygrometer probe.

Part 2: Artificial airway interface and ventilator settings:

This part includes the type of artificial airway interface between the patient and the mechanical ventilator, either endotracheal tube or tracheostomy. Endotracheal tube cuff pressure will be monitored and maintained within recommended limits as a confounding factor influencing microaspiration and airway contamination.

It also includes ventilator mode, tidal volume, minute ventilation, flow, peak airway pressure (PIP), mean airway pressure (Pmean), plateau pressure (Pplat), positive end-expiratory pressure (PEEP), fraction of inspired oxygen (FiO_2), inspiratory time (Tinsp), and pressure support (Ps). These data will be extracted from the ventilator monitoring system.

Part 3: Respiratory Mechanics Parameters:

This part will assess ventilator-derived respiratory mechanics to evaluate lung function, airway resistance, and pulmonary compliance in mechanically

ventilated trauma patients. It will include driving pressure (ΔP = Pplat − PEEP), which reflects lung stress and strain during mechanical ventilation. Static compliance (Cstat = tidal volume / [Pplat − PEEP]) and dynamic compliance (Cdyn = tidal volume / [PIP − PEEP]) will be calculated to assess lung elasticity and changes in respiratory system mechanics over time.

Work of breathing (WOB= (Ppeak−PEEP)×Vt2) will be estimated using ventilator-derived parameters when available to reflect patient respiratory effort and ventilatory load. Airway resistance (Raw = [PIP − Pplat] / inspiratory flow) will also be measured as an indicator of airway narrowing and secretion-related obstruction. All pressures will be recorded in cmH_2O and flow in L/min.

<u>Part 4:</u> Ventilatory Efficiency Indices:

This part will evaluate ventilatory efficiency as a physiological domain reflecting gas exchange efficiency and ventilatory inefficiency. It will include physiologic dead space fraction (VD/VT) and ventilatory ratio (VR) as complementary indices. VD/VT will be calculated using the Enghoff modification of the Bohr equation: VD/VT = ($PaCO_2$ − $P\bar{E}CO_2$) / $PaCO_2$, where $PaCO_2$ is obtained from arterial blood gas analysis and mixed expired CO_2 ($P\bar{E}CO_2$) is measured using volumetric capnography.

Ventilatory ratio (VR) will be calculated using the standard equation (VR = (Minute ventilation × $PaCO_2$) / (Predicted minute ventilation × 37.5), where minute ventilation (VE) is expressed in L/min, $PaCO_2$ in mmHg, and predicted minute ventilation is calculated from predicted body weight to estimate global ventilatory inefficiency and gas exchange impairment.

<u>Part 5:</u> Oxygenation Status Assessment:

This part will assess oxygenation status as a clinical outcome reflecting pulmonary gas exchange efficiency in mechanically ventilated trauma patients. Oxygenation will be evaluated using the PaO_2/FiO_2 ratio as the primary indicator of oxygenation impairment. Lower values indicate worse oxygenation

and higher severity of respiratory dysfunction. PaO_2/FiO_2 ratio will be interpreted in relation to FiO_2 levels to minimize oxygen supplementation bias.

Measurements for all parameters included in this tool will be performed daily at the same time of day whenever feasible, during MV under stable conditions, defined as no ventilator setting changes for at least 30–60 minutes and hemodynamic stability, until extubation to ensure standardized and comparable repeated longitudinal measurements over time. Measurements will be deferred during airway suctioning, patient transport, or acute instability. All measurements will be performed by the investigator or trained ICU personnel to ensure consistency.

Tool III: Airway Complications Assessment:

This tool will be developed by the researcher after reviewing relevant literature **(Goodfellow et al., 2024; & Nejatian et al., 2025).** It is designed to evaluate airway complications during mechanical ventilation in trauma patients. It will comprise of three parts:

Part 1: Airway obstruction assessment:

Airway obstruction will be recorded as present (Yes) when an unexplained increase in airway resistance (>15 $cmH_2O/L/s$) and/or peak airway pressure (>35 cmH_2O or a sudden increase of 5–10 cmH_2O above the patient's baseline) is accompanied by evidence of secretion retention, thick secretions with increased suction burden, mucus plugging, partial or complete tube occlusion, difficulty in suction catheter passage, or the need for airway intervention such as bronchoscopy or endotracheal tube/tracheostomy tube exchange.

If none of these criteria are present, airway obstruction will be recorded as absent (No). In addition, the number of obstruction events per patient and the time to first obstruction will be documented as event-based secondary variables. Airway obstruction will be assessed continuously throughout the period of MV, with the exact date and time of each event recorded. **(Goodfellow et al., 2024).**

<u>Part 2:</u> Grading of Airway Obstruction Severity:

Airway obstruction severity will be classified as a study-defined exploratory severity classification based on a combined clinical and objective assessment. Mild obstruction will be defined by increased secretion burden requiring more frequent suctioning without significant ventilatory compromise. This may be accompanied by mild increases in PIP or airway resistance, while ventilation remains adequate.

Moderate obstruction will be defined by partial airway compromise associated with increased secretion burden, difficulty in secretion clearance, and/or a clinically significant rise in airway resistance or PIP requiring active intervention beyond routine suctioning, such as repeated suction attempts, or patient repositioning.

Severe obstruction will be defined by complete or near-complete airway compromise resulting in marked ventilatory deterioration, inability to pass a suction catheter, mucus plugging or tube occlusion, severe hypoxemia, or the need for bronchoscopy or endotracheal/tracheostomy tube exchange. This classification will be used as a study-defined exploratory measure to further characterize the clinical impact of humidification strategy on airway patency **(Goodfellow et al., 2024)**.

<u>Part 3:</u> Artificial Airway-Related Complications:

This part will document complications associated with artificial airways during MV, including complete tube obstruction, bronchoscopy requirement, endotracheal or tracheostomy tube exchange, accidental extubation, and clinically confirmed tube malposition requiring intervention.

Data recorded for each event will include occurrence (yes/no), frequency, date and time, and underlying cause when applicable. Continuous monitoring will be performed throughout MV, with daily review of patient records to ensure completeness and accuracy of event reporting. In addition, re-intubation

cause (e.g., airway obstruction, excessive secretion, or respiratory failure) will be identified, allowing integrated analysis of airway complications and clinical outcomes in relation to humidification (**Nejatian et al., 2025)**.

Tool IV: Clinical Outcomes Assessment:

This tool will be developed by researcher after reviewing related literature (**Al Dorzi et al., 2022, Jongh & Somhorst, 2025 & Rubulotta et al., 2024).** This tool includes assessment of secondary outcomes related to effects of active or passive humidifier during invasive mechanical ventilation on intensive care patients such as tracheobronchial secretion, VAP, duration of MV, weaning, ICU length of stay, mortality and cost. Composed of nine parts as following:

Part 1: Tracheobronchial secretion assessment:

This assessment will be done by using visual analog scale, which adopted from **(Gross &Park, 2012)**, and still used by **(Sorensen et al., 2024),** to rate viscosity of tracheal secretion (e.g., 0 = thin, 10 = extremely thick), divided into three types thin, moderate and thick. In addition assessment of suctioning burden (frequency/day), volume (mL/day) and color (Clear/White/Yellow/Green/Bloody).

Part 2: Ventilator-Associated Pneumonia (VAP) assessment:

VAP will be assessed as lower respiratory tract infection occurring after at least 48 hours of invasive mechanical ventilation. VAP diagnosis will be established based on a composite of clinical, radiological, and microbiological criteria. These include the presence of new or progressive pulmonary infiltrates on chest radiography, in addition to clinical evidence of infection such as fever, leukocytosis or leukopenia, and purulent tracheal secretions. Microbiological confirmation will be based on tracheal aspirate cultures when available. VAP will be recorded as a clinical event with documentation of its occurrence (yes/no) and the exact date of onset to allow time-to-event analysis when applicable **(Howroyd et al., 2024)**.

<u>Part 3:</u> Ventilator-Associated Events (VAE):

VAE will be assessed as objective indicators of respiratory deterioration during MV using standardized criteria established by the Centers for Disease Control and Prevention. VAE will be identified using a tiered algorithm comprising ventilator-associated condition (VAC), infection-related ventilator-associated complication (IVAC), and possible ventilator-associated pneumonia (PVAP) **(Centers for Disease Control and Prevention 2023).**

A VAC will be defined as a sustained deterioration in oxygenation following a period of stability or improvement of at least two consecutive days, evidenced by an increase in the daily minimum fraction of inspired oxygen (FiO_2) of ≥0.20 or an increase in positive end-expiratory pressure (PEEP) of ≥3 cmH_2O, persisting for at least two consecutive days. IVAC will be identified when VAC criteria are met in conjunction with clinical indicators of infection or inflammation, including abnormal body temperature or white blood cell count, and the initiation and continuation of a new antimicrobial agent for at least four days.

PVAP will be confirmed when IVAC criteria are fulfilled along with microbiological evidence suggestive of pulmonary infection, based on predefined CDC/NHSN laboratory and diagnostic criteria. VAE will be assessed daily based on ventilator parameters and clinical data. Each event will be assigned a date of onset, defined as the first day of sustained deterioration in oxygenation following a period of stability or improvement, in accordance with CDC/NHSN criteria.

<u>Part 4:</u> Clinical Pulmonary Infection Score (CPIS):

This score will be adopted from **(Pugin et al., 1991).** It is widely used as a supportive and secondary assessment tool to quantify the likelihood and severity of VAP; however, it is not recommended as a standalone diagnostic criterion.

Therefore, it should be used in conjunction with bacterial biomarkers and chest radiography for the diagnosis of VAP **(Miron et al., 2024).**

The score ranges from 0 to 12 points and evaluates six clinical, radiographic, and microbiological parameters: body temperature, white blood cell (WBC) count, tracheal secretions, oxygenation status (PaO_2/FiO_2 ratio), chest radiographic infiltrates, and tracheal aspirate culture results.

Each parameter is assigned a score from 0 to 2 based on the severity or presence of abnormal findings. A CPIS value >6 is generally considered suggestive of a higher probability of VAP.

Part 5: Duration of mechanical ventilation:

Duration of MV will be defined as a continuous variable representing the total number of days from initiation of invasive mechanical ventilation until successful extubation, ICU discharge, or death. **(Rubulotta et al., 2024).**

Part 6: Weaning and Liberation Outcomes:

Weaning outcome will be assessed as a final clinical endpoint reflecting the ability of patients to successfully discontinue MV. Weaning will be classified into successful or failed outcomes. Successful weaning is defined as sustained liberation from invasive MV without the need for re-intubation or ventilatory support within 48 hours following extubation. Failed weaning is defined as the need for re-intubation or resumption of MV within 48 hours due to respiratory failure or clinical deterioration.

In addition, time to first weaning attempt will be recorded as the number of days from initiation of invasive mechanical ventilation to the first documented spontaneous breathing trial or reduction in ventilatory support, according to ICU weaning protocols **(Jaber & De Jong, 2023)**.

Part 7: Length of stay (LOS):

It will be defined as the number of days from the date of admission to the date of discharge, transfer, or death. LOS divided into short (0 – 5 days), medium **(**6 – 10 days) and long (more than 10 days).

Part 8: Mortality outcome:

This part includes recording of death occurrence as a binary variable, where the patient died or survived**.**

Part 9: Resource Utilization and Estimated Cost Analysis:

This part will assess healthcare resource utilization associated with mechanical ventilation and humidification in trauma ICU patients using procedural indicators reflecting ICU resource consumption, including suctioning frequency and total episodes, bronchoscopy, airway-related tube exchange, reintubation, and duration of mechanical ventilation. ICU length of stay will also be recorded as a global measure of resource utilization.

For exploratory analysis, standardized unit costs will be applied to key consumables and airway-related interventions based on institutional averages and/or published estimates to derive a comparative economic burden between study groups. This analysis will provide a preliminary, non-formal estimation of relative resource costs without conducting a formal cost-effectiveness or cost-utility evaluation **(Karagiannidis et al., 2024)**.

Methods:

The study will be conducted throughout three main phases:

1- Preparatory phase
2- Implementation phase
3- Evaluation phase

1- Preparatory phase:

- Official approval to carry out this study will be obtained from the Dean of Faculty of Nursing - Assiut University, Director of Trauma Assiut University Hospital, responsible authorities in trauma ICUs after explaining

the aim and nature of the study to be able to conduct study and collect the necessary data for present study.

- The study tools will be developed after an extensive review of the relevant literature and will be evaluated for content validity by a panel of experts in critical care nursing and medicine to ensure clarity, relevance, and comprehensiveness of all items. Necessary modifications will be performed based on their feedback.
- The reliability of study tools will be checked by using correlation coefficient and it will be estimated by Alpha Cronbach's test for this study.
- A pilot study will be conducted on a sample representing 10% of the total study population to assess the feasibility, clarity, and applicability of the data collection tools.

Ethical considerations:

1- Research proposal will be approved from Ethical Committee at Faculty of Nursing, Assiut University prior the implementation of the present study.
2- There is no risk from study for participants during application of the research.
3- The study will follow common ethical principles in clinical research.
4- Informed consent will be taken from participants in present study.
5- Study participants have the right to refuse or to withdraw from the study without any justification at any time.
6- Confidentiality and anonymity will be assured.
7- Study participants privacy will be considered during collection of data.

Trial Registration and Reporting:

This study will be prospectively registered at ClinicalTrials.gov prior to patient enrollment. The trial registration number will be included in all future publications (Registration number: xxxxxxxxxx). Reporting of study methods and results will adhere to the CONSORT 2010 guidelines for randomized

controlled trials to ensure transparency, reproducibility, and standardized reporting of outcomes, participant flow, randomization, blinding, and data analysis.

2- Implementation phase:

- When the trauma ICU patients fulfilling the research criteria, the researcher started to collect data.
- The patients' permission for voluntary participation was obtained from patients after the process and purpose of the study are explained.
- Each patient receiving invasive MV with either an active humidifier or a heat-and-moisture exchanger will be followed prospectively from the time of ICU admission and/or initiation of mv until extubation, discharge, or death.
- At baseline, the researcher will collect socio-demographic and medical data, trauma related clinical data and calculate the APACHE IV score within the first 24 hours of ICU admission.
- Hemodynamic status, laboratory and radiological investigations, antibiotic exposure, SOFA score, chest physiotherapy exposure, sedation and analgesia assessment, and fluid balance will then be recorded daily throughout the period of mechanical ventilation.
- Humidification type, ventilator settings, artificial airway interface, respiratory mechanics, ventilatory efficiency indices, and oxygenation status will also be assessed daily at a fixed time whenever feasible under stable conditions, using the same standardized procedure to ensure consistency and minimize measurement variability.
- Airway complications will be monitored continuously throughout MV. Airway obstruction events, grading of obstruction severity, and artificial airway-related complications will be documented with the exact date and time of occurrence.

- In addition, tracheobronchial secretion characteristics, VAP, VAE, CPIS, weaning outcome, duration of MV, length of stay, mortality, and resource utilization indicators will be recorded according to the predefined study tools. Event-based outcomes will be updated continuously, whereas physiological and clinical variables will be collected daily until extubation or termination of ventilation.
- **Measurement procedure using a hygrometer probe:**

  Temperature and humidity were measured using a hygrometer probe. This device was calibrated according to the manufacturer's instructions before the start of the study. All measurements were taken at the Y-piece of the ventilator circuit **once daily at fixed time** by the researcher to ensure standardization of data collection and minimize inter-observer variability. The probe was disinfected using 70% alcohol before and after each patient to prevent cross-infection. All measurements were performed using the same device and following the same standardized procedure.
- Routinely changed the HMEs every 48- 96hrs or if excessive condensation and secretion present on it, or according manufacture recommendation.
- The active humidifier is set to deliver gas at a target temperature of 36°C at the Y-piece, ensuring 100% relative humidity to maintain optimal mucociliary function and prevent secretion inspissation.

3- Evaluation phase:

- The researcher evaluates the impacts of HHs or HMEs on mechanically ventilated trauma ICU patientspatients.

Statistical analysis:

Data collected throughout the study will be statistically analyzed using the Statistical Package for the Social Sciences (SPSS), version 27. Categorical variables (such as the incidence of airway obstruction events, ventilator-associated pneumonia, and mortality rates) will be expressed as frequencies and

percentages, and compared between the two independent study groups (Heated Humidifier group vs. Heat and Moisture Exchanger group) using the Chi-square test (or Fisher's exact test when appropriate).

Continuous variables (such as patient demographics, hemodynamic parameters, arterial blood gases, and duration of mechanical ventilation/ICU length of stay) will be tested for normality. Normally distributed continuous data will be presented as Mean ± Standard Deviation (SD) and compared using the independent Student's t-test, whereas non-normally distributed data will be expressed as Median and range and analyzed using the Mann-Whitney U test. A p-value of less than 0.05 (< 0.05) will be considered statistically significant for all statistical comparisons.

Results:

Results of present study will be tabulated, analysed by computer and using appropriate statistical tests.

Discussion:

In the light of scientifically & international references, discussion of the obtained results will be done based on the study results.

Conclusion:

Appropriate conclusion will be written based on the study results.

Recommendations:

Recommendations will be derived from the study results.

Summary:

Brief description for all the work done will be provided.

References:

Adams, A. M. N., Chamberlain, D., Brun Thorup, C., Maiden, M. J., Waite, C., Dafny, H. A., ... & Conroy, T. (2026). Patient agitation in the intensive care unit: a concept analysis. Journal of Advanced Nursing, 82(2), 1737-1749.

Al Dorzi, H. M., Ghanem, A. G., Hegazy, M. M., AlMatrood, A., Alchin, J., Mutairi, M., ... & Arabi, Y. M. (2022). Humidification during mechanical ventilation to prevent endotracheal tube occlusion in critically ill patients: A case control study. Annals of Thoracic Medicine, 17(1), 37-43.

Bernatzky, A., Galletti, M. F., Fuensalida, S. E., & Mariani, G. L. (2020). Heated humidifier versus heat-and-moisture exchanger during positive pressure ventilation with a T-piece resuscitator in rabbits. Respiratory Care, 65(9), 1295-1300.

Campodoni, E., Artusi, C., Vazquez Iglesias, B., Nicosia, A., Belosi, F., Vandini, A., ... & Sandri, M. (2023). Nature-Inspired Heat and Moisture Exchanger Filters Composed of Gelatin and Chitosan for the Design of Eco-Sustainable "Artificial Noses". ACS Applied Polymer Materials, 5(5), 3468-3479.

Centers for Disease Control and Prevention. (2023). Ventilator-associated event (VAE)-for use in adult locations only.

Cheng, P., Wu, H., Yang, J., Song, X., Xu, M., Li, B., ... & Zhou, X. (2021). Pneumonia scoring systems for severe COVID-19: which one is better. Virology Journal, 18(1), 33.

de Jongh, F., & Somhorst, P. (2025). Technical aspects of the ventilator. In ERS Practical Handbook of Invasive Mechanical Ventilation (pp. 252-261). European Respiratory Society.

Deokar, K., Plotnikow, G. A., Singhal, S., Mina, B., ElShazly, M., Wooldridge, M., ... & Esquinas, A. (2025). Humidification insights in

Mechanical ventilation and respiratory support. A narrative review. *Expert Review of Respiratory Medicine*, (just-accepted).

Farahani, H., & RoshanChesli, R. (2023). Calculation and justification of sample size in researches of psychological sciences: Application of G* Power software. Clinical Psychology and Personality, 20(2), 221-234.

Fiorentino, G., Lanza, M., Annunziata, A., & Esquinas, A. M. (2023). Humidification Tracheostomy: Physiology and Device. In Humidification in the Intensive Care Unit: The Essentials (pp. 159-170). Cham: Springer International Publishing.

Gaffney, S., & Dalton, A. (2024). Humidification devices. Anaesthesia & Intensive Care Medicine, 25(7), 465-468.

Gaikwad, A., Karnik, S., & Chaudhary, H. (2026). Evaluating Predisposition, Infection, Response, and Organ Dysfunction, Acute Physiology and Chronic Health Evaluation, and Sequential Organ Failure Assessment Scores for Mortality Prediction in Geriatric Sepsis: Toward Age-adapted Prognostic Models. Annals of African Medicine, 10-4103.

Goodfellow, L. T., Miller, A. G., Varekojis, S. M., LaVita, C. J., Glogowski, J. T., & Hess, D. R. (2024). AARC clinical practice guideline: patient-ventilator assessment. Respiratory Care, 69(8), 1042-1054.

Gross, J. L., & Park, G. R. (2012). Humidification of inspired gases during mechanical ventilation. Minerva Anestesiol, 78(4), 496-502.

Hickey, S., Sankari, A., & Giwa, A. (2024). Mechanical ventilation. StatPearls.

Howroyd, F., Chacko, C., MacDuff, A., Gautam, N., Pouchet, B., Tunnicliffe, B., ... & Veenith, T. (2024). Ventilator-associated pneumonia: pathobiological heterogeneity and diagnostic challenges. Nature communications, 15(1), 6447.

Intagliata, S., Rizzo, A., & Gossman, W. (2023). Physiology, lung dead space. In StatPearls [Internet]. StatPearls Publishing.

Jaber, S., & De Jong, A. (2023). Weaning from mechanical ventilation in intensive care units: a call for new international consensus guidelines. The Lancet Respiratory Medicine, 11(5), 398-400.

Karagiannidis, C., Krause, F., Bentlage, C., Wolff, J., Bein, T., Windisch, W., & Busse, R. (2024). In-hospital mortality, comorbidities, and costs of one million mechanically ventilated patients in Germany: a nationwide observational study before, during, and after the COVID-19 pandemic. The Lancet Regional Health–Europe, 42.

Lellouche, F. (2023). Humidification during invasive mechanical ventilation. In Humidification in the Intensive Care Unit: The Essentials (pp. 97-120). Cham: Springer International Publishing.

Li, D., Wei, Y., Zhang, C., Yang, Y., Wang, Z., Lu, Y., & Liu, L. (2025). Value of SOFA score, APACHE II score, and WBC count for mortality risk assessment in septic patients: A retrospective study. Medicine, 104(20), e42464.

Mattson, J. R., Gada, K. D., Jawa, R., Zhang, X., & Ahmad, S. (2024). Impact of humidification modality on incidence of endotracheal tube occlusion in COVID-19 patients. Journal of Intensive Care Medicine, 39(10), 965-973.

Mew, E. J., Koenen, K. C., & Lowe, S. R. (2022). Trauma as a public health issue: Epidemiology of trauma and trauma-related disorders. In Evidence based treatments for trauma-related psychological disorders: A practical guide for clinicians (pp. 13-40). Cham: Springer International Publishing.

Miron, M., Blaj, M., Ristescu, A. I., Iosep, G., Avădanei, A. N., Iosep, D. G., ... & Luca, M. C. (2024). Hospital-acquired pneumonia and ventilator-associated pneumonia: a literature review. Microorganisms, 12(1), 213.

Misganaw, A., & Ayenew, N. T. (2025). Intensive care unit nurses' knowledge and compliance with ventilator associated pneumonia bundle at a resource

limited setting in East Gojam and West Gojam Zones, Ethiopia. a cross-sectional study. International Journal of Surgery Open, 63(2), 94-100.

Naderi, N. (2022). Hemodynamic study. In Practical Cardiology (pp. 201-216). Elsevier.

Nejatian, A., Forsberg, I. M., Thorö, U., Sjöblom, A., & Kåhlin, J. (2025). Impact of Checklist Implementation on Endotracheal Intubation-Related Complications in Critically Ill Adults—A Retrospective Before and After Study. *Acta Anaesthesiologica Scandinavica*, *69*(7), e70103.

Palanisamy, S., Sreevilasan, S. K., Venkatesh, L., Jose, D., Gowtham, B. C., & Parameswaran, N. (2025). Effect of heat and moisture exchanger vs heated humidifier on ventilator-related adverse events in children: A pilot randomized controlled trial. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine, 29(9), 746.

Plotnikow, G. A., Moracci, R. S., Gutiérrez, F. J., Setten, M., & Mariani, J. (2025). Knowledge and Practice of Mechanical Ventilation Humidification Systems in Latin American ICUs. Respiratory Care, 70(11), 1387-1394.

Pugin, J., Auckenthaler, R., Mili, N., Janssens, J. P., Lew, D. P., & Suter, P. M. (1991). Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage fluid. American Journal of Respiratory and Critical Care Medicine, 143, 1121-1129.

Re, R., Lassola, S., De Rosa, S., & Bellani, G. (2024). Humidification during Invasive and non-invasive ventilation: a starting tool kit for correct setting. Medical Sciences, 12(2), 26.

Rokeman, N. R. M. (2024). Likert measurement scale in education and social sciences: explored and explained. EDUCATUM Journal of Social Sciences, 10(1), 77-88.

Rubulotta, F., Torra, L. B., Naidoo, K. D., Aboumarie, H. S., Mathivha, L. R., Asiri, A. Y., ... & Soussi, S. (2024). Mechanical ventilation, past, present, and future. Anesthesia & Analgesia, 138(2), 308-325.

Sorensen, E., Oleson, J., Kutlu, E., & McMurray, B. (2024). A Bayesian hierarchical model for the analysis of visual analogue scaling tasks. Statistical Methods in Medical Research, 33(6), 953-965.

Vincent, J. L. (1997). Organ dysfunction as an outcome measure: The SOFA Score. Sepsis, 1(1), 53-54.

Yin, X., Yang, L., Sun, H., Yun, Z., Wang, Y., & Ma, B. (2020). A comparative evaluation of three common airway humidification methods for patients with severe traumatic brain injury. Annals of Palliative Medicine, 9(6), 4137145-4134145.

Zeleke, S., & Kefale, D. (2021). Nurses' supplemental oxygen therapy knowledge and practice in Debre Tabor general hospital: a cross-sectional study. Open Access Emergency Medicine, 51-56.

Zimmerman, J. E., Kramer, A. A., McNair, D. S., & Malila, F. M. (2006). Acute Physiology and Chronic Health Evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. Critical care medicine, 34(5), 1297-1310.