

## **Post-Intensive Care Syndrome: A Comprehensive Review**

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### **Abstract**

**Background:** Post-Intensive Care Syndrome (PICS) is a recognized condition encompassing physical, cognitive, and psychological impairments experienced by ICU survivors. **Objectives:** The objective of this review article is to provide a comprehensive overview of PICS, including its definition, prevalence among ICU survivors, and its impact on patients' quality of life. The review aims to highlight the growing recognition of PICS as a distinct syndrome and emphasize the importance of addressing its long-term consequences. Additionally, the review aims to discuss strategies for prevention and management of PICS, such as early mobility programs, rehabilitation interventions, psychological support, and follow-up care. It also explores the role of interdisciplinary collaboration in optimizing patient outcomes. **Conclusions:** PICS has a profound impact on the long-term outcomes and quality of life of ICU survivors. The prevalence of PICS highlights its significance as a healthcare issue, necessitating comprehensive care strategies. Early recognition, comprehensive care, and interdisciplinary collaboration are essential in preventing and managing PICS. By addressing the physical, cognitive, and psychological aspects of PICS, healthcare professionals can improve patient outcomes and enhance the overall well-being of ICU survivors.

**Keywords:** PICS, Perioperative Care, Clinical Manifestations, Assessment, Monitoring, Prevention, Management.

### **1. Introduction**

Post-Intensive Care Syndrome (PICS) is a cluster of physical, cognitive, and psychosocial deficits that may emerge when a patient is released from an intensive care unit (ICU). PICS may impact people across several medical disciplines, but its significance in the setting of anesthesiology is especially noteworthy. Patients undergoing anaesthesia and intensive care are exposed to many variables that increase their risk of acquiring PICS [1].

Patients often face lengthy immobility, mechanical breathing, exposure to sedatives and analgesics, and systemic inflammation during anaesthesia. In conjunction with the underlying severe disease, these variables may lead to muscular weakness, deconditioning, and weariness. In addition, anaesthesia and surgery may cause a systemic inflammatory response, which can result in organ malfunction and possible long-term problems [2].

PICS is increasingly recognized as a distinct syndrome due to the growing awareness of its prevalence and the unique set of challenges it presents. While the exact prevalence rates vary depending on factors such as the specific ICU population and the duration of follow-up, studies consistently indicate that a significant proportion of ICU survivors experience some form of PICS.

Physical impairments are a common manifestation of PICS. Extended periods of immobility, muscle wasting, and prolonged

mechanical ventilation during the ICU stay can result in muscle weakness, deconditioning, and physical deconditioning. These physical impairments can persist long after the patient's discharge from the ICU and can significantly impact their ability to perform daily activities, leading to functional disability and reduced quality of life.

Cognitive impairments are another important aspect of PICS. Many ICU survivors report difficulties with memory, attention, concentration, and executive function. These cognitive impairments can be a result of various factors, including delirium, sedative medications, hypoxia, and underlying medical conditions. They can significantly affect the individual's ability to return to work, engage in social activities, and function independently.

Psychological impairments are prevalent among PICS patients as well. ICU stays can be traumatic experiences, characterized by high levels of stress, anxiety, and fear. The prevalence of anxiety, depression, post-traumatic stress disorder (PTSD), and sleep disturbances is higher in ICU survivors compared to the general population. These psychological challenges can further exacerbate the physical and cognitive impairments experienced by PICS patients and can have a profound impact on their overall well-being and quality of life.

The recognition and understanding of PICS have led to increased efforts in improving the long-term outcomes of ICU survivors. Healthcare providers and researchers are

focusing on prevention strategies and interventions aimed at mitigating the impact of PICS. Early mobility programs, rehabilitation interventions, and interdisciplinary care have shown promise in addressing the physical, cognitive, and psychological aspects of PICS and promoting recovery.

## 2. Prevalence and Risk Factors

The prevalence of PICS varies according to the examined population, the degree of disease, and the length of follow-up. However, 50-70 percent of ICU survivors may suffer some type of PICS, according to estimates [3].

Several risk factors that lead to the development of PICS have been identified. These risk factors may be classified as patient-related, intensive care unit-related, and treatment-related. Understanding these risk variables is critical for early detection, prevention, and individualised therapies [4].

### ➤ Patient-related factors:

#### 1. Age

Age is connected with a greater likelihood of acquiring PICS. Often, the diminished physiological reserve of elderly people might result in a more severe and protracted disease [5].

#### 2. Pre-existing comorbidities

Patients with preexisting illnesses such as cardiovascular disease, chronic lung disease, or compromised renal function are particularly prone to PICS. These comorbidities may interact with the severe disease and impede healing over the long run [6].

#### 3. Severity of illness

Significant risk factors for PICS include the severity of the first illness necessitating ICU admission, as determined by scoring systems such as Acute Physiology and Chronic Health Evaluation (APACHE) and Sequential Organ Failure Assessment (SOFA). Higher rates of complications and organ dysfunction are connected with more severe diseases, increasing the probability of developing PICS [7].

#### 4. Pre-existing cognitive impairment

PICS patients with preexisting cognitive impairments, such as dementia or cognitive decline, are more likely to have cognitive dysfunction [8].

### ➤ ICU-related factors:

#### 1. Duration of ICU stay

A lengthy ICU stay is a major risk factor for PICS. The longer a critical illness lasts, the higher the chance of physical, cognitive, and psychological deficits [9].

#### 2. Mechanical ventilation

Patients who need extended mechanical breathing are at a greater risk of developing

PICS. Mechanical ventilation may cause diaphragmatic dysfunction and muscular weakness, which contribute to long-term physical disabilities [10].

#### 3. Sedation and delirium

Inadequately managed sedation and bouts of delirium during ICU stay are related to an increased prevalence of PICS, specifically cognitive deficits [11].

### ➤ Treatment-related factors:

#### 1. Invasive procedures

The invasiveness of ICU operations, including as intrusive catheterizations, surgical interventions, and extracorporeal support, might lead to the onset of PICS [12].

#### 2. Sepsis

Intensive care unit (ICU) patients who acquire sepsis have an increased chance of acquiring PICS. Sepsis induces a systemic inflammatory response that may have long-lasting repercussions on a number of organ systems [13].

#### 3. Administration of sedatives and analgesics

Sedatives and analgesics, especially benzodiazepines and opioids, have been linked to cognitive and psychological deficits in PICS. The excessive or extended use of these drugs should be closely monitored [14].

### 3. Clinical Manifestations:

Patients with Post-Intensive Care Syndrome (PICS) may suffer from a broad spectrum of physical, cognitive, and psychosocial problems. These manifestations may have a substantial effect on their overall health and enjoyment of life. It is essential to detect and treat these deficiencies in order to give proper care and support to PICS patients [15].

### ➤ Physical impairments:

**Muscle weakness:** Muscle weakness, which may impact both the respiratory and peripheral muscles, is one of the defining physical symptoms of PICS. Patients may have trouble with everyday tasks, limited mobility, and a diminished general functional ability [16].

**Fatigue:** PICS Even after moderate physical exercise, patients typically experience lingering weariness. Fatigue may inhibit their capacity to participate in everyday activities and reduce their quality of life [17].

**Pain:** Numerous PICS survivors suffer from ongoing discomfort, which may be caused by the underlying severe disease, invasive operations, or protracted immobility. This discomfort might restrict movement and perpetuate a cycle of physical deconditioning [18].

### ➤ Cognitive impairments:

**Memory deficits:** PICS may lead to memory problems, especially in terms of short-term

memory and the capacity to remember recent events or information. Patients may have difficulty recalling recent events or discussions, which might impair their everyday functioning [19].

**Attention and concentration difficulties:** PICS is characterised by difficulties with sustained focus, split attention, and multitasking. Patients may have difficulty focusing on activities or following complicated directions [20].

**Executive dysfunction:** PICS may affect executive functions including problem-solving, decision-making, planning, and organisation. Patients may struggle with activities requiring superior cognitive skills [21].

➤ **Psychological impairments:**

**Anxiety:** Anxiety issues are widespread among PICS patients. They may feel excessive anxiety, agitation, and a sense of impending doom, which may have a substantial impact on their daily functioning and well-being [22].

**Depression:** PICS Depression is more likely to emerge in cancer survivors. Symptoms may include chronic depression, lack of interest or pleasure in activities, changes in eating or sleep habits, and feelings of worthlessness or despair [23].

**Post-traumatic stress disorder (PTSD):** Intensive care unit (ICU) stays may be distressing for many patients, and PICS can be accompanied with PTSD symptoms. In PICS patients with PTSD, flashbacks, nightmares, hypervigilance, and avoidance of reminders of the ICU stay are typical [24].

**6. Critical Care Management:**

The handling of critically sick patients in the intensive care unit (ICU) may have a substantial effect on the development of Post-Intensive Care Syndrome (PICS). Several areas of critical care treatment, including as sedation procedures, ventilator control tactics, and the use of neuromuscular blockade, have been studied for their potential influence on PICS results [3].

In order to maximise patient comfort, facilitate mechanical breathing, and reduce possible deleterious effects on cognitive function, proper sedation management in the ICU is necessary. Targeted sedation methods, such as the use of sedation scales (such as the Richmond Agitation-Alertness Scale), try to create a balance between sedative depth and patient wakefulness. By avoiding heavy sedation and conducting regular sedation breaks and spontaneous breathing trials, the length of mechanical ventilation and risk of PICS-related problems may be decreased [25].

Mechanical ventilation is a frequent intervention in the ICU, but improper

management may lead to lung damage and the development of PICS. It has been shown that lung-protective ventilation methods, such as low tidal volumes, restricted plateau pressures, and positive end-expiratory pressure (PEEP), minimise the risk of ventilator-induced lung damage. These measures attempt to reduce the production of pro-inflammatory mediators, avoid atelectrauma, and reduce the likelihood of future lung dysfunction and PICS [3].

Neuromuscular blocking in the ICU is a contentious and difficult subject. In spite of the fact that neuromuscular blockade may assist mechanical breathing and increase patient-ventilator synchronisation, it bears the potential for adverse effects. Long-term or severe neuromuscular blockade has been linked to muscle weakening and atrophy, which may lead to physical deficits and a protracted recovery in PICS. Therefore, careful planning and monitoring of neuromuscular blockade usage, with a focus on reducing its duration and dose, are essential [25].

Early mobility and rehabilitation in the ICU have attracted considerable interest because to their ability to prevent the onset of PICS. It is possible to avoid muscular deconditioning, weakness, and functional deterioration by encouraging and supporting early out-of-bed movements, such as sitting, standing, and walking. Early mobility programmes have shown positive outcomes in terms of enhancing physical function, decreasing the length of mechanical ventilation, and maybe lowering the incidence and severity of PICS [3].

In critically sick patients, delirium is prevalent and is related with an increased risk of cognitive impairment and PICS. Implementing techniques to avoid and treat delirium, such as the use of established delirium assessment instruments (e.g., the Confusion Assessment Method for the Intensive Care Unit) and the management of sleep-wake cycles, may help reduce the effect of delirium on long-term cognitive results [25].

**7. Assessment and Monitoring:**

Identification and monitoring of Post-Intensive Care Syndrome (PICS) symptoms in patients are critical for prompt intervention and therapy. Assessing and monitoring patients throughout the perioperative and critical care phases may aid in identifying possible risk factors, tracking the development of PICS-related deficits, and determining the most effective therapies. Several evaluation instruments and monitoring methods may assist in this procedure [26].

Regular physical examinations are essential for recognising PICS-related physical limitations.

These evaluations may involve testing for muscular strength, range of motion, functional ability, and respiratory health. The Medical Research Council (MRC) Scale for muscular strength and the Six-Minute Walk Test may give objective assessments and help monitor improvements over time [27].

Cognitive abnormalities are prevalent in PICS, and frequent cognitive examinations may help identify them. Standardized instruments such as the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Confusion Assessment Method for the ICU (CAM-ICU) may be used to evaluate cognitive function and diagnose delirium. Serial evaluations may be used to monitor changes and direct treatments [26].

Psychological health is an essential component of PICS. Screening instruments such as the Hospital Anxiety and Sadness Scale (HADS) and the Impact of Event Scale (IES) may assist in identifying anxiety, depression, and post-traumatic stress disorder symptoms (PTSD). Regular evaluation of psychological symptoms may lead appropriate therapies, such as psychotherapy, medication, and referral to mental health experts, as necessary [26].

Evaluating the quality of life of PICS-affected individuals gives vital information into the syndrome's effect on their everyday functioning and well-being. The Short Form Health Survey (SF-36) and the EuroQol-5D (EQ-5D) questionnaire may be used to evaluate many dimensions of quality of life, such as physical, mental, and social components [28].

The objective of functional evaluation is the patient's capacity to execute activities of daily living (ADLs) and instrumental activities of daily living (IADLs) (IADLs). The Barthel Index and the Lawton Instrumental Activities of Daily Living Scale (IADL) may give a standardised evaluation of functional capability and aid in identifying limits or impairments that may need focused treatments [26].

Various monitoring approaches may help in the early diagnosis of issues associated to PICS and guide their treatment. In a critical care situation, this may include continuous monitoring of vital signs, oxygenation, and ventilator settings. In addition, monitoring techniques like as pulse oximetry, cardiac telemetry, and end-tidal carbon dioxide monitoring may offer crucial real-time data on the patient's physiological state [29].

#### **4. Long-term outcomes:**

Long-term outcomes of Post-Intensive Care Syndrome (PICS) have significant implications for both patients and healthcare systems. The consequences of PICS extend beyond the

initial ICU stay and can persist for months or even years, impacting various aspects of individuals' lives.

One key long-term outcome of PICS is increased healthcare utilization. ICU survivors with PICS often require ongoing medical care and frequent visits to healthcare providers. The physical, cognitive, and psychological impairments associated with PICS can lead to complications, recurrent hospital admissions, and the need for specialized healthcare services. This increased healthcare utilization places a substantial burden on the healthcare system, both in terms of financial costs and resource allocation.

Functional disability is another significant long-term consequence of PICS. The physical impairments resulting from ICU stay, such as muscle weakness and deconditioning, can lead to limitations in activities of daily living, reduced mobility, and functional dependency. These limitations can persist even after discharge from the ICU, impairing patients' ability to return to work, engage in social activities, and maintain independence. Functional disability not only affects the quality of life of PICS patients but also poses challenges for their caregivers and the overall support system.

Reduced quality of life is a common outcome of PICS. The physical, cognitive, and psychological impairments experienced by ICU survivors can have a profound impact on their overall well-being and day-to-day functioning. PICS patients may struggle with decreased physical endurance, persistent cognitive difficulties, anxiety, depression, sleep disturbances, and post-traumatic stress symptoms. These factors can lead to a diminished sense of well-being, social isolation, and a lower overall quality of life.

The implications of these long-term outcomes extend beyond the individual patients and affect the healthcare system as a whole. The increased healthcare utilization associated with PICS puts additional strain on already burdened healthcare resources. It necessitates the provision of specialized care, rehabilitation services, and ongoing support to address the complex needs of PICS patients. Healthcare systems need to allocate resources effectively and develop integrated care models that consider the long-term consequences of ICU stays.

Addressing the long-term outcomes of PICS is essential for improving patient outcomes and optimizing healthcare resource utilization. Early identification, comprehensive follow-up care, and targeted interventions can play a crucial role in mitigating the long-term

consequences of PICS. Multidisciplinary approaches involving healthcare professionals from various specialties, including critical care, rehabilitation, mental health, and primary care, are necessary to provide holistic care and support to PICS patients.

#### **5. Prevention and management:**

Prevention and management strategies are crucial in addressing Post-Intensive Care Syndrome (PICS) and optimizing patient outcomes. Various approaches can be employed to mitigate the risk of developing PICS and effectively manage its physical, cognitive, and psychological impairments.

One important strategy for preventing and managing PICS is the implementation of early mobility programs. Encouraging early mobilization and physical activity during the ICU stay can help mitigate muscle weakness, deconditioning, and physical impairments. Early mobilization protocols involving physical therapy, occupational therapy, and dedicated rehabilitation teams have shown promising results in improving patients' functional outcomes and reducing the incidence of PICS.

Rehabilitation interventions play a significant role in the management of PICS. Comprehensive rehabilitation programs tailored to the specific needs of ICU survivors can address physical impairments and facilitate functional recovery. These programs may include exercises, strength training, gait training, and pulmonary rehabilitation to improve muscle strength, endurance, and respiratory function. Involving a multidisciplinary team of physiotherapists, occupational therapists, and respiratory therapists is essential for providing comprehensive rehabilitation care.

Psychological support is another crucial aspect of preventing and managing PICS. Providing psychological interventions, such as cognitive-behavioral therapy, counseling, and trauma-focused therapies, can help address anxiety, depression, PTSD, and other psychological symptoms experienced by ICU survivors. Incorporating mental health professionals into the care team can support patients in processing their ICU experiences, managing emotional distress, and promoting psychological well-being.

Follow-up care plays a vital role in the long-term management of PICS. Establishing structured post-ICU clinics or follow-up programs can facilitate ongoing monitoring, assessment, and intervention for PICS patients. These programs allow healthcare professionals to track patients' progress, identify emerging issues, and provide targeted interventions.

Regular follow-up visits also provide an opportunity to address ongoing physical, cognitive, and psychological impairments, optimize medication management, and ensure appropriate referrals to specialized services.

Interdisciplinary collaboration is essential for optimizing patient outcomes in the prevention and management of PICS. Involving a diverse team of healthcare professionals, including intensivists, physiotherapists, occupational therapists, psychologists, social workers, and primary care providers, promotes a comprehensive and holistic approach to care. Collaborative decision-making, care coordination, and shared knowledge across disciplines are essential for delivering patient-centered care and addressing the multidimensional aspects of PICS.

#### **6. Future Directions and Research:**

Future directions in the field of Post-Intensive Care Syndrome (PICS) encompass ongoing research efforts and emerging interventions that aim to improve our understanding and management of this complex syndrome. By exploring these directions, we can identify potential areas of improvement in clinical practice and highlight opportunities for future studies.

Ongoing research efforts are focused on deepening our understanding of PICS and its underlying mechanisms. These efforts involve investigating the biological, psychological, and social factors that contribute to the development and persistence of PICS. By unraveling the complex interactions between these factors, researchers strive to identify potential biomarkers, risk factors, and predictive models for PICS. This ongoing research holds the potential to improve early identification, prevention, and targeted interventions for ICU survivors at risk of developing PICS.

Emerging interventions are being explored to address the multifaceted nature of PICS. These interventions include innovative approaches in physical rehabilitation, cognitive training, and psychological support. For example, novel rehabilitation techniques such as virtual reality-based exercises and task-specific training are being investigated to enhance functional recovery and mitigate physical impairments. Cognitive interventions, such as computer-based training programs and cognitive rehabilitation strategies, aim to improve cognitive function and reduce the cognitive deficits associated with PICS. Additionally, interventions that integrate psychological therapies, peer support groups, and resilience-building programs show promise in addressing the psychological

impact of PICS and promoting emotional well-being in ICU survivors.

## 7. Conclusions

In conclusion, Post-Intensive Care Syndrome (PICS) is a recognized and complex syndrome that significantly impacts the quality of life of ICU survivors. The long-term consequences of PICS, including increased healthcare utilization, functional disability, and reduced quality of life, have substantial implications for both patients and healthcare systems. Strategies such as early mobility programs, rehabilitation interventions, psychological support, and follow-up care play a crucial role in preventing and managing PICS. Interdisciplinary collaboration is essential for optimizing patient outcomes. Further research and emerging interventions offer opportunities for improving clinical practice and enhancing the understanding and management of PICS, ultimately leading to better long-term outcomes for ICU survivors.

## References

- [1] C.S. Vrettou, V. Mantziou, A.G. Vassiliou, S.E. Orfanos, A. Kotanidou, I. Dimopoulou. Post-intensive care syndrome in survivors from critical illness including COVID-19 patients: A narrative review. *Life*;12:107. 2022
- [2] G. Voiriot, M. Oualha, A. Pierre, C. Salmon-Gandonnière, A. Gaudet, Y. Jouan, et al. Chronic critical illness and post-intensive care syndrome: from pathophysiology to clinical challenges. *Ann Intensive Care*;12:58. 2022
- [3] S. Inoue, J. Hatakeyama, Y. Kondo, T. Hifumi, H. Sakuramoto, T. Kawasaki, et al. Post-intensive care syndrome: its pathophysiology, prevention, and future directions. *Acute medicine & surgery*;6:233-46. 2019
- [4] M. Lee, J. Kang, Y.J. Jeong. Risk factors for post-intensive care syndrome: A systematic review and meta-analysis. *Aust Crit Care*;33:287-94. 2020
- [5] M.H. Ahmad, S.P. Teo. Post-intensive Care Syndrome. *Ann Geriatr Med Res*;25:72-8. 2021
- [6] B. Bigdelou, M.R. Sepand, S. Najafikhoshnoo, J.A.T. Negrete, M. Sharaf, J.Q. Ho, et al. COVID-19 and Preexisting Comorbidities: Risks, Synergies, and Clinical Outcomes. *Front Immunol*;13:890517. 2022
- [7] M.M. El-Kholy, S.H. Sadek, R.M. El-Morshedy, A.S. Ali. Severity scoring systems and different biochemical markers as predictors of mortality in the respiratory ICU. *The Egyptian Journal of Chest Diseases and Tuberculosis*;71:179-86. 2022
- [8] G. Livingston, J. Huntley, A. Sommerlad, D. Ames, C. Ballard, S. Banerjee, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet*;396:413-46. 2020
- [9] A.F. Rousseau, H.C. Prescott, S.J. Brett, B. Weiss, E. Azoulay, J. Creteur, et al. Long-term outcomes after critical illness: recent insights. *Crit Care*;25:108. 2021
- [10] H.Y. Huang, C.Y. Huang, L.F. Li. Prolonged Mechanical Ventilation: Outcomes and Management. *J Clin Med*;11. 2022
- [11] M.F. Mart, S. Williams Roberson, B. Salas, P.P. Pandharipande, E.W. Ely. Prevention and Management of Delirium in the Intensive Care Unit. *Semin Respir Crit Care Med*;42:112-26. 2021
- [12] S. Rajsic, R. Breitkopf, M. Bachler, B. Treml. Diagnostic Modalities in Critical Care: Point-of-Care Approach. *Diagnostics (Basel)*;11. 2021
- [13] J.C. Mira, L.F. Gentile, B.J. Mathias, P.A. Efron, S.C. Brakenridge, A.M. Mohr, et al. Sepsis Pathophysiology, Chronic Critical Illness, and Persistent Inflammation-Immunosuppression and Catabolism Syndrome. *Crit Care Med*;45:253-62. 2017
- [14] A.N. Edinoff, C.A. Nix, J. Hollier, C.E. Sagrera, B.M. Delacroix, T. Abubakar, et al. Benzodiazepines: Uses, Dangers, and Clinical Considerations. *Neurol Int*;13:594-607. 2021
- [15] C. Yuan, F. Timmins, D.R. Thompson. Post-intensive care syndrome: A concept analysis. *Int J Nurs Stud*;114:103814. 2021
- [16] A. Jaitovich, E. Barreiro. Skeletal Muscle Dysfunction in Chronic Obstructive Pulmonary Disease. What We Know and Can Do for Our Patients. *Am J Respir Crit Care Med*;198:175-86. 2018
- [17] S.T. Thomas, A. Sav, R. Thomas, M. Cardona, Z. Michaleff, T.T. Titus, et al. Patient and physician perspectives

- on treatment burden in end-stage kidney disease: a nominal group technique study. *BMJ Open*;12:e064447. 2022
- [18] G.K. Alaparthi, A. Gatty, S.R. Samuel, S.K. Amaravadi. Effectiveness, Safety, and Barriers to Early Mobilization in the Intensive Care Unit. *Crit Care Res Pract*;2020:7840743. 2020
- [19] M. Cascella, Y. Al Khalili. Short Term Memory Impairment.[Updated 2021 Jul 21]. *StatPearls* [Internet] Treasure Island (FL): StatPearls Publishing. 2022
- [20] G. Contemori, M.S. Saccani, M. Bonato. Multitasking Effects on Perception and Memory in Older Adults. *Vision (Basel)*;6. 2022
- [21] P. Cristancho, L. Kamel, M. Araque, J. Berger, D.M. Blumberger, J.P. Miller, et al. iTBS to relieve depression and executive dysfunction in older adults: an open label study. *The American Journal of Geriatric Psychiatry*;28:1195-9. 2020
- [22] M. Ayalew, B. Deribe, B. Duko, D. Geleta, N. Bogale, L. Gemechu, et al. Prevalence of depression and anxiety symptoms and their determinant factors among patients with cancer in southern Ethiopia: a cross-sectional study. *BMJ Open*;12:e051317. 2022
- [23] C. Kraus, B. Kadriu, R. Lanzenberger, C.A. Zarate Jr, S. Kasper. Prognosis and improved outcomes in major depression: a review. *Translational psychiatry*;9:127. 2019
- [24] O.J. Bienvenu, T.A. Gerstenblith. Posttraumatic Stress Disorder Phenomena After Critical Illness. *Crit Care Clin*;33:649-58. 2017
- [25] M.D. Hashem, A.M. Parker, D.M. Needham. Early Mobilization and Rehabilitation of Patients Who Are Critically Ill. *Chest*;150:722-31. 2016
- [26] S. Smith, O. Rahman. Post intensive care syndrome. 2020
- [27] Z. Turan, M. Topaloglu, O. Ozyemisci Taskiran. Medical Research Council-sumscore: a tool for evaluating muscle weakness in patients with post-intensive care syndrome. *Crit Care*;24:562. 2020
- [28] O. Alzahrani, J.P. Fletcher, K. Hitos. Quality of life and mental health measurements among patients with type 2 diabetes mellitus: a systematic review. *Health Qual Life Outcomes*;21:27. 2023
- [29] S. Ayad, A.K. Khanna, S.U. Iqbal, N. Singla. Characterisation and monitoring of postoperative respiratory depression: current approaches and future considerations. *British journal of anaesthesia*;123:378-91. 2019