# INTRODUCTION

Critical illness is characterized by disruptions in homeostasis that result in single- or multiple-organ injury and reversible or irreversible organ dysfunction. To a large extent, the duration of exposure to injurious stimuli/conditions determines the reversibility or irreversibility of organ dysfunction in critical illness. Therefore, it is highly important that organ system dysfunction in critically ill patients is recognized as early as possible and appropriate therapeutic interventions are applied to improve outcomes in these patients ***(Anderson et al., 2008).***

Traditionally, recognition of organ dysfunction in patients has relied on its clinical signs and symptoms (eg, oliguria and/or elevated creatinine levels for the kidney). Historically, recognition of circulatory failure and the likelihood of tissue hypoperfusion relied on the presence of persistent or refractory (to fluid resuscitation) hypotension. This approach is complicated by a relative lack of sensitivity of clinical signs and symptoms to predict the presence or absence of organ injury or tissue hypoperfusion. In addition, some clinical examination techniques lack standardization, for example, the assessment of capillary refill time as an index of peripheral hypoperfusion **(Anderson et al., 2008).**

The incidence of elderly patients being admitted to intensive care units (ICUs) has increased globally **(Marik, 2006).**

Serum lactate is one of the most widely used biomarkers for sepsis. Lactate levels rise early in the disease course and, hence, can be used as an early marker for organ failure and detection of occult shock before any detectable changes occur in the patient's vital signs **(Jansen et al., 2008).**

Crucial to implementing the guidelines of resuscitation and the severe sepsis bundles is the utilization of lactate as an indicator of global organ hypoperfusion and shock, while the aetiology of lactate elevations in severe sepsis is debatable, it is well accepted as a resuscitation endpoint, an indicator of severity, and a predictor of short-term and long-term mortality **(Okorie and Dellinger., 2011)**. Additionally, persistent elevation of lactate has been shown to be associated with poor outcome, such that a decrease in lactate (or lactate clearance) during resuscitation is an independent predictor for improved mortality **(Arnold et al., 2009).**

The predictive value of a single elevated blood lactate on mortality is demonstrated in a number of studies in patients admitted to ICU. Admission lactate >2 mEq/l was a significant independent predictor of mortality in adult patients admitted to

ICU in a large retrospective study by Khosravani et al., 2009, they found that Odds Ratio (OR) for mortality increased from 1.94 to 10.89 dependent on the level of hyperlactatemia **(Khosravani et al., 2009).**

# AIM OF THE WORK

The aim of our study is to determine the relation between serum lactate level and outcome in critically ill elderly patients.

# ELDERLY IN ICU

With increased frequency, the consumers of critical care services are older adults. More than one-half (55.8%) of all intensive care unit (ICU) days are incurred by patients over the age of sixty-five. This number is expected to increase to unprecedented levels over the years as the population ages **(Angus et al., 2000).**

While older adults are an extremely heterogeneous group, they do share some age-related characteristics and are susceptible to a variety of geriatric syndromes and diseases that may influence both their ICU utilization rates and outcomes. Americans over the age of sixty-five are living longer; are more racially and ethnically diverse; frequently suffer from chronic conditions such as hypertension, heart disease, diabetes and cancer; and over one-quarter report difficulty performing one or more activities of daily living (ADL) **(Administration on Aging, 2005).**

They are also more likely to be diagnosed as having two of the most common and costly ICU diagnoses, acute respiratory failure and sepsis. Reports of the incidence of these conditions increase exponentially with age **(Martin et al., 2006).**

Ideally, the goals of providing medical care to the critically ill older adult include restoring physiologic stability, preventing complications, maintaining comfort and safety, and preserving or preventing decline in pre illness functional ability and quality of life (QOL).

## Risk Factors for poor outcome:

There is evidence, however, suggesting many critically-ill older adults are at risk for poor outcomes. A critical review of the literature found that once hospitalized for a life-threatening illness, older adults suffer from high ICU, hospital and long-term crude mortality rates and are at risk for deterioration in functional ability and post-discharge institutional care **(Williams et al, 2008).**

Older age is also one of the factors that may lead to physician bias in refusing ICU admission**(Mick and Ackerman, 2004)**, the decision to withhold mechanical ventilation, surgery, or dialysis, a provision of lower intensity of care **(Thompson et al., 2008)**

Despite these findings, most critically-ill older adults demonstrate resiliency, report being satisfied with their QOL post discharge and, if needed, would reaccept ICU care and mechanical ventilation **(Guentner et al., 2006)**. Although research identifying specific factors responsible for undesirable

outcomes is conflicting, it has become increasingly clear that chronologic age alone is not an acceptable predictor of poor outcomes after critical illness **(Marik, 2006)**. In other words, older patients demonstrate considerable variability in outcomes following an ICU stay.

There are many factors, supported by research, that influence an older adult's ability to survive a catastrophic illness. These factors include severity of illness, nature and extent of co-morbidities, diagnosis, reason for/duration of mechanical ventilation, impaired level of consciousness, complications, length of ICU/hospital stay, preadmission nursing home residence, pulmonary artery catheterization, pre-hospitalization functional ability, gender and ethnicity **(Soares et al., 2006).**

## Preadmission Risk Factors for Critical Care:

Older adults who experience an illness or accident that brings them to an ICU can have a number of preexisting conditions or may be relatively healthy. In addition to the acute event that precedes the person's admission, it is essential to recognize the complex interaction of physiological, cognitive, psychological, developmental and social influences that are a part of every older adult's life. Within a critical care context, some of these factors can increase the risk of poor outcomes for the older adult with a complex illness. Therefore, the completion

of a comprehensive assessment of a critically ill older adult's preadmission health status and functional ability helps to identify risk factors for cascade iatrogenesis, the development of life-threatening conditions and frequently encountered geriatric syndromes. The cascade of interactions between the effects of usual aging and the older adults' critical care stay can compound their efforts to recover from critical illness and lead to additional post-hospitalization disability, particularly for those older adults who enter into a critical illness with some functional impairment **(Creditor, 1993).**

## Pre-existing Cognitive Impairment:

There are many anatomic and physiologic changes that occur in the aged central nervous system. It is important the critical care nurse recognize that these age-related neurological changes are not necessarily synonymous with cognitive impairment **(Urden et al., 2005)**.

The presumption that outcomes from critical care are less favorable in patients with dementia, is not supported in the literature, and should not solely drive treatment decisions in the ICU **(Pisani et al., 2005).**

Knowledge of preexisting cognitive impairment can also further aid Practitioners in making anesthetic and analgesic

choices, considering one-to-one care options, weaning from mechanical ventilation and helping in the discharge planning process. It is, therefore, vitally important that the nurse assess for the presence of prior cognitive impairment and acknowledge its potential influence on critically ill older adults' outcomes and risks for adverse events.

Relatives or other caregivers should be asked for baseline information about memory, executive function and overall functional ability in daily living prior to critical care admission, finally, doctor should obtain a list of all prescription and non-prescription medications taken prior to hospitalization and review it for potential withdrawal syndromes **(Broyles et al., 2008).**

## Developmental and Psychosocial Factors:

According to the Administration on Aging (2005), 55 percent of older non institutionalized persons in United States reported living with a spouse, while 31 percent lived alone. While many older adults have adult children or other relatives who care for them, it is important to note that many of these elders are also caregivers themselves—caring for their aging spouses, relatives, grandchildren, and friends **(Administration on Aging, 2005)**.

Living alone or having few significant others nearby is likely to increase an older, critically ill adult's risk for additional issues related to their overall assessment and management.

The lack of presence of family or a significant other threatens the nurse's ability to obtain accurate data about the person, which is often needed urgently to make important management decisions. Flexible, longer, and more open visitation in ICUs has become accepted practice in the ICU and is particularly important in the care of older critically ill patients **(Henneman and Cardin, 2002).**

Family members are, therefore, often a crucial source for obtaining important preadmission information such as past medical and surgical history, drug and alcohol use, nutritional status, sensory impairments, home environment and medication use **(Broyles et al., 2008).**

The spouse or significant other of a critically ill older adult is also often the person responsible for communicating with the healthcare team what the patient wants in terms of aggressiveness and goals of care, quality of life values, Do Not Resuscitate (DNR) status and advanced directives. Consequently, when a spouse or significant other is absent from the bedside and additional information sources are unavailable,

additional risks to the overall plan of care can ensue from inadequate communication.

## Functional Ability:

Although the majority of older adults report having at least one chronic condition and many report having multiple conditions, they remain relatively independent **(Administration on Aging, 2005).**

Disability data from 2000 person in United States shows that only 10 percent of persons sixty five and older reported a disability that restricted their ability to dress, bathe or get around inside their home, while 29 percent reported a disability restricting a physical activity, such as ambulating **(Waldrop and Stern, 2003).**

The importance of evaluating preadmission functional status cannot be over emphasized; some studies have shown functional status to be a major determinant in the recovery of critically older adults **(Mick and Ackerman, 2004).**

# SERUM LACTATE

## Lactate production, metabolism, and excretion:

Glycolysis is the first step in the metabolism of glucose and its end product is pyruvate. Once formed, pyruvate can follow several metabolic pathways. It can cross the mitochondrial membranes into the tricarboxylic acid pathway and produce energy (38 molecules of ATP) **(Handy, 2006).**

It can be converted into lactate by the action of the enzyme lactate dehydrogenase. It can be used as a substrate in gluconeogenesis for the production of glucose, or it can undergo transamination to alanine. The conversion of pyruvate to lactate is reserved primarily for excess pyruvate levels. Conversion of pyruvate to lactate is favored during hypoxic tissue conditions and several other clinically relevant conditions **(Handy, 2006).**

Hypoxia blocks mitochondrial oxidative phosphorylation, thereby inhibiting ATP synthesis and reoxidation of NADH. This leads to a decrease in the ATP/ADP ratio and an increase in the NADH/NAD ratio. A decrease in the ATP/ADP ratio induces both an accumulation of pyruvate, which cannot be utilised by way of phosphofructokinase stimulation and a decrease in pyruvate utilisation by inhibiting pyruvate

carboxylase, which converts pyruvate into oxaloacetate**(Levy, 2006)**. Consequently, the increase in lactate production in an anaerobic setting is the result of an accumulation of pyruvate, which is converted into lactate stemming from alterations in the redox potential; this results in an increase in the lactate/pyruvate ratio**(Levy, 2006)**.

Classic teaching suggests that increased production of lactate results in acidosis, known widely as lactic acidosis**(Vernon and LeTourneau., 2010)**. Close examination of glycolysis reveals that complete metabolism of glucose to lactate results in no net release of protons and, thus, does not contribute to acidosis. In fact, during the production of lactate from pyruvate, protons are consumed and acidosis is inhibited. Furthermore, lactate oxidation and lactate consumption via gluconeogenesis consume hydrogen ions and are alkalinising processes. This implies that 'lactic acidosis, is a condition that does not exist**(Robergs et al., 2004).**

The serum arterial lactate concentration reflects the balance between net lactate production and net lactate consumption and clearance. This concentration is generally less than 2 mmol/L, The daily production of lactate is about 1400 mmol, and although all tissues can produce lactate, physiologic lactate production is primarily from skeletal muscle (25%), skin (25%), brain (20%), intestine (10%), and red blood cells (20%),

in pathologic conditions, significant lactate production occurs in other organs **(Levy,2006).**

In the critically ill, lactate is produced in tissues outside the "usual lactate producers," including the lungs, white blood cells, and splanchnic organs. Physiologic lactate production by the lungs is negligible leading to an arteriovenous difference in lactate levels close to zero across the lungs under physiologic conditions **(Harris et al., 1963)**.

In critically ill patients, Weil and colleagues observed that venous blood samples from a pulmonary artery catheter yielded lactate concentrations equivalent to those in arterial blood **(Weil et al., 1987).**

This finding has been replicated in subsequent works in patients with severe sepsis and acute lung injury/acute respiratory distress syndrome, as well as in patients without significant hypoxemia **(De Backer et al., 1997).**

Similarly, lactate is released in supraphysiologic amounts from the sites of infection and inflammation and is thought to be related to the augmented glycolysis in the recruited and activated leukocytes at the sites of infection. White blood cells have a limited capacity for aerobic (mitochondrial) ATP generation, when activated; these cells rely primarily on augmented anaerobic glycolysis to meet energy requirements, which leads

to the production of large amounts of lactate unrelated to oxygen deprivation. In experimental models, following exposure to endotoxin, significant increases were noted in blood lactate levels and were thought to be a result of augmented leukocyte lactate production **(Haji-Michael et al., 1999).**

Lactate is metabolized primarily in the liver (60%), kidneys (30%), and heart (10%). In the liver, the periportal hepatocytes directly use lactate to produce glycogen and glucose via the Cori cycle. In patients with chronic liver disease, lactate clearance may be diminished and this can lead to its elevated blood levels **(Mizock, 2001).**

Levraut and colleagues challenged hemodynamically stable septic patients with an external lactate load and found that in patients with normal lactate clearance, normal lactate levels were noted. However, mildly elevated levels (2–4 mEq/L) were observed in patients with reduced lactate clearance **(Levraut et al., 1998).**

The renal cortex is very sensitive to reduction in renal blood flow, and renal lactate clearance can be impaired in critically ill patients with compromised renal blood flow, leading to elevated lactate levels. Lactate can be excreted by the kidney if the renal threshold is exceeded (approximately 5–6 mmol/L).