Evaluation of Hypernatremia as a Predictor of Multiple Organ Dysfunctions Compared to Clinical Scores in Medical Critically Ill Patients

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Abstract: Hypernatremia is common in intensive care units. It has detrimental effects on various physiologic functions and was shown to be an independent risk factor for increased mortality in critically ill patients. Mechanisms of hypernatremia include sodium gain and/or loss of free water and can be discriminated by clinical assessment and urine electrolyte analysis. Because many critically ill patients have impaired levels of consciousness, their water balance can no longer be regulated by thirst and water uptake but is managed by the physician. Therefore, the intensivists should be very careful to provide the adequate sodium and water balance for them. Hypernatremia is treated by the administration of free water and/or diuretics, which promote renal excretion of sodium. The rate of correction is critical and must be adjusted to the rapidity of the development of hypernatremia. **Aim of the Work**: To evaluate the acquired hypernatremia as a predictor of multiple organ dysfunction in sever critical illness and to assess the prognostic value of acquired hypernatremia in medical critically ill patients. **Methods:** This study include 300 critically ill patients admitted to critical care department in the Alexandria Main University Hospital, and the Intensive Care Unit in Alexandria Armed Force Hospital due to medical cause and exclude all patients with hypernatremia on admission, Patients received hyperosmotic agents like (sodium bicarbonate - mannitol), chronic kidney disease patients,Patients on renal replacement therapy and regular hemodylasis, Sequential Organ Failure Assessment score(SOFA) score on admission and daily, APACHE II score on admission and NA level on admission and daily done for all patients. **Monitoring of outcome:** Development of multiple organ systemic failure, Development of septic shock, ICU length of stay, Duration of mechanical ventilation in mechanically ventilated patients. **Results:** There was positive significant correlation between the mean SOFA and the mean serum sodium level in the MOD and NOMD patients (p=0.003,p=o.ooo) respectively. As regard to patients outcome in the MOD group 18(16.4%) out of the patients had increase duration of mechanical ventilation, 27(24.5%) out of the patients had increase duration of stay in ICU, 35(31.8%) out of the patients had increase mortality through As regard to patients outcome in the NMOD group 26(26.7%) out of the patients had increase duration of mechanical ventilation, 26(26.7%) out of the patients had increase duration of stay in ICU, 15(16.7%) out of the patients had increase mortality through 28 day and 27(30%) out of the patients had developing of septic shock.28 day and 30(27.3%) out of the patients had developing of septic shock. **Conclusion:** Hypernatremia can affect the morbidity and mortality markedly among ICU patients this is proved from our study as the level of Hypernatremia was high the SOFA score also was increased indicating multiple organ failure., Hypernatremia is a common finding upon ICU patients. Hypernatremia is caused by both a positive solute balance due to intake of sodium rich infusion therapy and loss of free water. We should daily measure the sodium levels for all ICU admitted patients to give the chance for very early discovered of any Hypernatremia. Rapid correction of any Hypernatremia should be adopted to prevent its hazardous side effects.

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Keyword: Hypernatremia, multiple organ failure (MOF), non multiple organ failure (NMOF), mortality, length of stay in ICU, duration of mechanical ventilation, developing of septic shock

Introduction

Definition of critical illness:

Critical illness is any disease process which causes physiological instability leading to disability or death within minutes or hours

There are many reasons for this including a lack of a systematic approach to these patients **(Cullinane et al, 2005)[(1)]:**

Initial approach to a potentially critically ill ward patient:

Clinical observations commonly associated with critical illness include hypotension, tachycardia, tachypnoea, a reduced level of urine output and altered consciousness.

The sensitivity and specificity of these findings for critical illness are greatly improved if they are considered all together.

The presence of two or more of these signs strongly suggests that the patient is critically ill and at risk of death. Indeed inpatient mortality can be defined by the number of physiological abnormalities, being 0.7% with none, 4.4% with one, 9.2% with two, and 21.3% with three or more time, based on appearance and simple clinical observations, it should be possible to triage the patient into one of three possible categories: critically ill, potentially critically ill and not critically ill.

Management of the critically ill patient:

Resuscitation is the first priority and the simplest elements of this are unaltered by the underlying disease. Providing a safe airway, administering an appropriate concentration of oxygen and establishing venous access is never wrong and may be life saving in the short term. However, the longer-term outcome depends on the diagnosis and it is fundamentally important to establish this. It may be difficult or even impossible to take a history directly from the patient. If communication is possible then a balance has to be struck between eliciting key information and needlessly exhausting the patient with less relevant questions. The patient best describes important symptoms such as pain but other elements of the history should be obtained from relatives, nurses or the medical notes.

Physical examination has to be conducted in such a way that minimizes any physical effort by the patient. Prolonged, irrelevant examination, particularly if associated with patient exertion and inappropriate positioning, can easily precipitate cardiac arrest. The emphasis should be on eliciting clinical signs, such as those associated with meningitis or peritonitis, that will influence further management and cannot be reliably obtained should the patient require general anaesthesia.

A blood gas is useful to measure adequacy of ventilation ($PaCO_2$), oxygenation (PaO_2, A-a gradient) and circulation (pH and lactate) and can guide response to treatment or alert to further deterioration.

Careful consideration has to be given before requesting investigations, particularly if these involve moving the patient, as this can be extremely hazardous. If the investigation is for diagnostic refinement but will not affect immediate management, then it is best deferred. Where possible diagnostic imaging such as ultrasonography should be done at the patient's bedside. Transfer may be required for other imaging modalities, such as computed tomography.

In the early stages of this diagnostic process, advice should be sought from a senior clinician. This is particularly important if there is uncertainty about the appropriateness of resuscitation **(General Medical Council, 2002)[8].** At this stage a decision will be taken as to whether the patient should remain on the ward or be transferred. Once a definitive plan is made it should be carefully communicated to staff, the patient and the patient's family.

Management of the potentially critically ill patient:

This category of patient is quite difficult to deal with, as there is uncertainty about the clinical course that the patient will take.

Although these patients have adverse clinical observations, not all develop critical illness and it is difficult to prospectively identify those that will.

The first step should be a thorough reappraisal of the admission diagnosis and treatment. Occasionally misdiagnosis can lead to inappropriate treatment or prescribed therapy may not have been given.

Alternatively the patient may have developed a complication of the presenting disease or even a new illness. It is useful to seek a senior clinical opinion in these cases.

Regardless of the cause, adverse trends in clinical observations should be interpreted as evidence for deteriorating physiology and measures should be taken to ameliorate this. The patient may require additional intravenous fluid or an increase in supplemental oxygen. More frequent clinical observations by the bedside nurse are often required as is enhanced monitoring, for example by the use of a pulse oximeter or the passage of a urinary catheter to measure urine output. Medical and nursing staff must remain vigilant and frequent review to assess progress is mandatory.

Sometimes because of staff constraints all of this may not be possible on a general ward and these patients may need transfer to a high dependency unit. Finally, as with a critically ill patient, it is imperative that the definitive management plan is carefully communicated to staff, the patient and the patient's family.

Multiple Organ Dysfunction Syndrome (MODS):

Definition:

Dysfunction or failure of multiple organ or system happened simultaneously or sequentially due to various etiological factors.

Etiology:

- Infection: Gram positive/negative bacteria, fungal, Virus.
- Shock, hemorrhage, etc.
- Allergy.
- Burns.
- Trauma.
- Severe acute pancreatitis.

Classification of MODS:

- Immediate Type (Primary): Dysfunction is happened simultaneously in two or more organs due to primary disease.
- Delayed type (Secondary): Dysfunction happened in a organ, other organs sequentially

happened dysfunction or failure.

- Accumulation type: Dysfunction leaded by chronic disease.

Treatments of MODS:

- Combined therapy:
- Correction of ischemia: fluid resuscitation, mechanical ventilation
- Prevention of infection：drainage, antibiotics
- Interruption of pathological reaction: hemofiltration
- Stabilization of internal environment: water, electrolyte,
- acid-base imbalance
- Regulation of immunity: cellular and humor
- Support of organ function:
- Ventilator
- Artificial kidney
- Artificial liver
- Protection of enteral mucosa
- Drugs of protection of heart

Pathogenesis and management of multiple organ dysfunction:

Important in initial resuscitation efforts coupled with advancements in technological support and knowledge of disease process have improved the survival of critically ill patients and resulted in a relatively new disorder, multiple organ dysfunction.[2,3,4] These advances in supportive care coupled with longer survival time allow the critically ill patient to develop later stages of their illness and become susceptible to the common complications of critical illness.[5] In prior years, patients would have died much earlier in their disease course, long before they would develop the evidence of organ dysfunction that we now refer to as multiple organ dysfunction syndrome (MODS) or multiple organ failure (MOF). The initial reports of MOF were in 1969.[6] It was evident that survival was dependent on factor other than the initial disease process for which the patient was admitted. Multiple organ dysfunction/failure is now regarded as the most common cause of death among patients in the non coronary critical care unit and also is a frequent cause of morbidity, prolonged hospitalization, and increased cost of care.[2]

Systemic inflammatory response syndrome (SIRS)

The systemic inflammatory response to a wide variety of severe clinical insults, manifested by two or more of the following conditions:

1. Temperature > 38C or < 36C.
2. Heart rate > 90 beats/min.
3. Respiratory rate > 20 breaths/min or Pa CO_2 < mm Hg.
4. WBC count > 12,000/mm3, < 4000/mm3, or > 10% immature (band) forms.

Sepsis:

The systemic inflammatory response to infection. In association with infection, manifestations of sepsis are the same as those previously defined for SIRS. It should be determined whether they are a direct systemic response to the presence of an infectious process and represent an acute alteration from baseline in the absence of other known causes for such abnormalities.

- Severe Sepsis/SIRS. (SIRS) associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status.
- Sepsis (SIRS) Induced Hypotension. A systolic blood pressure < 90 mm Hg or a reduction of 40 mm Hg from baseline in the absence of other causes for hypotension.
- Septic Shock/SIRS Shock. A subset of severe sepsis (SIRS) and defined as sepsis (SIRS) induced hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but limited to, lactic acidosis, oliguria, or an acute alternation in mental status. Patients receiving inotropic or vasopressor agents may no longer be hypotensive by the time they manifest hypoperfuction abnormalities or organ dysfunction, yet they would still be considered to have septic (SIRS) shock.

It also was recognized that the initial injury may produce direct organ system injury or be accompanied by hemodynamic alterations, such as hypotension and/or decreased cardiac output, which could result in organ dysfunction/failure.[7] This condition has been termed primary MODS. Secondary MODS is the term used to describe the ones or organ dysfunction/failure that develops later in the course of illness and is frequ Potential Mediators Involved in the Pathogensis of MODS/MOF.

Potential humoral mediators:

- Complement.
- Products of Arachidonic Acid **Metabolism**.
- Lipoxygenease products.
- Cyclooxgenase products.
- Tumor Necrosis Factors.
- Interleukins (1-13).
- Growth Factors.
- Adhesion Molecules.
- Platelet Activating Factor.
- Procoagulants.
- Fibronectin and Opsonins.
- Toxic Oxygen Free Fadicals.
- Endogenous Opioids-Endrophins.
- Vasocative Polypeptides and Amines.
- Bradykinin and Other Kinins.
- Neutoendocrine Factors.
- Myocardial Depressant Factor.

- Coagulation Factors and Their Degradation Products.

Cellular inflammatory mediators:

- Polymorpho nuclear Leukocytes.
- Monocytes/Macrophages.
- Platelets.
- Endothelial Cells.

Exogenous mediators:

- Endotoxin.
- Exotoxin and Other Toxins.
- ently related to shock and sepsis.[7]
- Pathophysiologic Mechanism(s) Involved in the Production of MODS/MOF.
- Primary cellular injury.
- Inadequate tissue/organ perfusion.

- Hypoperfusion.
- Ischemia/Reperfusion.
- Microaggregation and/or disseminated intravascular coagulation.

- Diffuse endothelial cell injury
- Circulating humoral factors (i.e., myocardial depressant substance).
- Circulating immune/inflammatory mediators.
- Protein calorie malnutrition.
- Bacterial-toxin translocation.
- Defective red blood cells.
- Adverse effect of directed treatment or medication.

Hypernatremia:

Definition:

- Hypernatremia is a disorder of water metabolism and is usually defined as a plasma sodium concentration above 145 mEq/L. Hypernatremia generally results from a net loss of body water relative to sodium and can occur with or without a loss or even in body sodium content [8].
- Hypernatremia can be classified into borderline (145 < Na ≤ 150 mmol/l), mild (150 < Na ≤ 155mmol/l) and severe hypernatremia (Na > 155 mmol/l) [9].
- **Epidemiology of hypernatremia:**
- Hypernatremia is particularly common in critically ill patients, but there are no prospective data available on the prevalence of hypernatremia in intensive care unit (ICU). The reported prevalence of hypernatremia in ICU patients varies in different retrospective studies due to the difference in sodium level used to define hypernatremia (> 145 mEq/L or > 150 mEq/L), type of critical care population studied (medical, surgical, or neurosurgical), and the time of occurrence of hypernatremia (prior to ICU admission or ICU acquired) [10].
- Hypernatremia (≥ 150 mEq/L) has been reported in 7% to 16% of patients admitted to medical ICU and nearly 8% of neurosurgical ICU (Funk et al., 2010). Another retrospective study reported ICU-acquried hypernatremia (≥ 145 mEq/L) in almost 25% of combined medical, surgical, and neurosurgical ICU patients with a dose response relationship and increased risk of hospital mortality [11].

Causes of hypernatremia:

- The origin of hypernatremia requies several factors to develop in ICU patients such as: the administration of hypertonic sodium bicarbonate solutions; renal water loss through a concentrating defect from renal disease or the use of diuretics or solute dieresis from glucose or urea in patients on high protein feeds or in a hypercatabolic state; gastroin testinal fluid losses through nasogastric suction and lactulose administration, and water losses through fever, drainages, and open wounds. Thus, most etiologies of hypernatremia involve states of impaired water access in conjunction with excessive free water losses [12].
- The causes of hypernatremia in critically ill ICU patients are numerous and can be subdivided based on the type of underlying fluid loss (pure water or hypotonic fluids) as well as changes in body salt content (normal, decreased, or increased

Symptoms:

Primarily neurological and reflected changes in brain volume (shrinkage). They range in severity and include:

- Headache.
- Confusion
- Nausea and vomiting
- Lethargy
- Irritability
- Seizures
- Nystagmus
- Myoclonic jerks.
- Loss of consciousness.
- Coma.

There is no specific concentration at which they may occur and hypernatraemia developing over days to weeks may be relatively asymptomatic, even with Na > 160 mmol/ L. there may be additional symptoms which reflect the underlying cause.

Even mild hypernatraemia is an extremely potent stimulus of thirst, although this diminishes over time. Therefore it usually only develops if there is restricted access to fluids or an inability to express thirst.

Orthostatic hypotension and other signs of hypovolaemia may also be present, although are late signs, due to the fact that free water losses are primarily from the intracellular fluid space. The intravascular fluid volume is relatively protected until Na reaches around 170 mmol/L.

Risk Factors for Hypernatraemia:

- Ag > 65
- Dementia, other mental or physical disability.
- Residential care settings.

What are the main causes of hypernatraemia?

Hypernatraemia is almost always due to excess water loss or inability to replace normal insensible loss by drinking.

Excessive intake of sodium is an uncommon cause, but may be suggested by a non elevated urea, and could raise the possibility of deliberate self harm or abuse. This is difficult to diagnose, but if suspected it is useful to check serial weights and paired blood and random urine samples.

There are three common causes for hypernatraemia:

Low fluid intake

Anything which impairs thirst, swallowing or access to water. Fluid losses will be exacerbated by fever, high ambient temperature or thyrotoxicosis.

Diabetes Insipidus (DI)

This may be central (pituitary), due to lack of ADH secretion, or nephrogenic, due to renal resistance to ADH. Polyuria and polydipsia are the main symptoms. The commonest cause is treatment with lithium which causes nephrogenic DI. Any history of current of previous lithium use is relevant: even if levels have always been within the therapeutic range. Central DI may result from head injury or pituitary disease.

Hyperosmolar hyperglycaemic state (HHS), previously called Hyperosmolar non ketotic state ("HONK").

This is a decompensated from of type 2 diabetes. Severe, prolonged hyperglycaemia causes osmotic dieresis with a net loss of free water. Plasma sodium tends to be diluted by the osmotic pull of water from the intracellular to the extracellular space, thus the "ture" sodium is higher still.

Subjects All critically ill patients admitted to Alexandria Main University Hospital Critical Care Department and the Intensive Care Unit in Alexandria Armed Force Hospital due to medical cause will included till reach the number of 300 patients.

Inclusion patients:

All critically ill patients admitted to critical care department due to medical cause.

Exclusion patients

1. Hypernatremia on admission.
2. Patient received hyperosmotic agents like (sodium bicarbonate - mannitol).
3. Chronic kidney disease.
4. Patient on renal replacement therapy and regular hemodylasis.

Methods

All patients included in the study will be subjected to the following:

1- History Taking:

- Personal data: age, gender and cause of admission.
- Past history: of chronic diseases; chronic kidney disease, diabetes milletus, hypertension, cardiao-pulmonary, neurological, and hepatic disease.
- Drug history: including corticosteroids, mannitol, bicarbonate

2- Clinical examination:

- Vital signs (blood pressure (mmHg), heart rate (beat/ min), temperature (degree°), respiratory rate (cycle/ minute).
- Comprehensive physical examination.

3- Recording of the following scores:

The following clinical scores will be recorded on admission and daily for one week or till the development of multiple organ dysfunction (MOD).

a- Acute Physiology and Chronic Health Evaluation II score (APACHE II score) (Appendix 1)[13] on admission.

b- Glasgow Coma Scale (GCS) (Appendix 2)[14] on admission and daily.

c- Sequential Organ Failure Assessment score (SOFA) (Appendix 3)[15] on admission and daily.

4- Laboratory evaluation:

- Serum sodium level (m Eq/ L) (on admission and daily)

Will be measured on admission and daily during patient stay in critical unit.

Serum sodium level will be measured by taken blood sample using Machine (easylyte). Easylyte is an automated microprocessor controlled analyzer for measurement of sodium in serum and plasma, whole blood and urine to optain accurte results. The easylyte must be operated with medical's speacially packaged calibrant and bovine-Based control materials. The analyzer takes 55-60 seconds and requires only 100 ul of serum plasma or whole blood or 400 ul of diluted urine. The analyzer for the measurement of capillary blood sample with volume as low as 60 ul, the analyzer measure sodium in biological fluid using Ion selective electrode technology:

- Complete blood count (CBC).
- Serum albumin (mg/dl).
- Coagulation profile (prothrombin time – partial thromplastin time – international normalization ratio) (PT – PTT – INR).
- Blood urea (mg/dl) – blood urea nitrogen (mg/ dl).
- Creatinine (mg/ dl) – alanine transferase ALT (u/L) – asptate transaminaze AST (mg/dl).
- Potassium (mEq/L) – magnesium (mg/dl) – serum.
- Bicarbonate (mEq/L) – Bilrubin (mg/dl).

5- Arterial Blood gasses:

(ABG) to record (PH – PAO_2 – HCO_3- FIO_2) on admission and when needed.

6- Chest X ray (CXR):

On admission and when needed.

All included patients will be monitored during their ICU stay by the continous monitoring of:

- Arteril oxygen saturation by (pulse oximetry).
- Continous ECG monitoring.
- Daily fluid balance and urine output will be recorded for each patient.

- All patients involved in the study will be managed with the same protocol for:

1- Fluid management.

2- Mechanical ventilator management.

Monitoring of outcome:

1- Development of multiple organ systemic failure.

2- Development of septic shock.

3- ICU length of stay.

4- Duration of mechanical ventilation in mechanically ventilated patients.

Results

As regard to patients age, 74(24.7%) out of the patients was ≤50 years, 69(23%) out of the patients their ages ranged between 51-60 years, 74(24.7%) out of the patients their ages ranged between 61-70 years and 83(27.7%) out of the patients was over 70 years; in general, patients age ranged between 40-80 years with mean±S.D. 61.09 ± 11.99 years and the median value was 62 years. (Table (IV), Figure (1))

As regard to patients sex, 159(53%) out patients was male and 141(47%) out of the patients was female. (Table (IV), Figure (2))

As regard to patients past history, 20(6.7%) out of the patients didn't had past history while 280(93.3%) out of the patients had past history, 135(48.2%) out of this patients had DM history, 124(44.3%) out of the patients had HTN history and 21(7.5%) out of the patients had cardiac history.(Table (IV), Figure (3))

Table (I): Distribution of studied sample according to demographic data (n=300).

	No.	%
Age		
≤50	74	24.7
51 – 60	69	23
61 – 70	74	24.7
>70	83	27.7
Min. – Max.	40 – 80	
Mean ± SD.	61.09 ± 11.99	
Median	62	
Sex		
Male	159	53
Female	141	47
Past History		
No	20	6.7
Yes	280	93.3
DM	135	48.2
HTN	124	44.3
Cardiac	21	7.5
Drug History		
No	234	78
Manitol	15	5
Corticosteroid	15	5
Bicarbonate	36	12

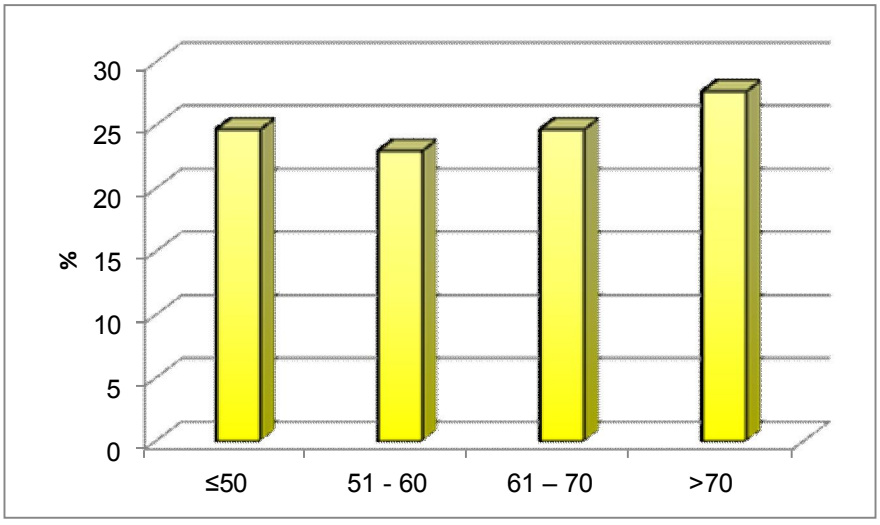

Figure (1): Distribution of studied sample according to patients age (n=300).

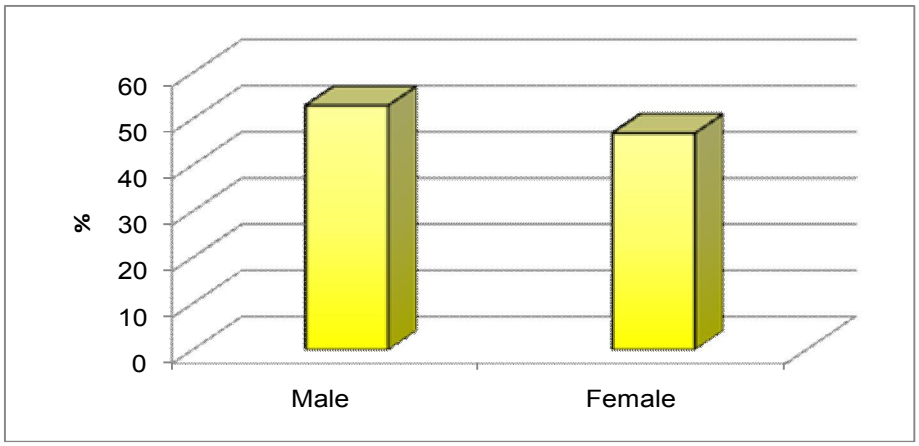

Figure (2): Distribution of studied sample according to patients sex (n=300).

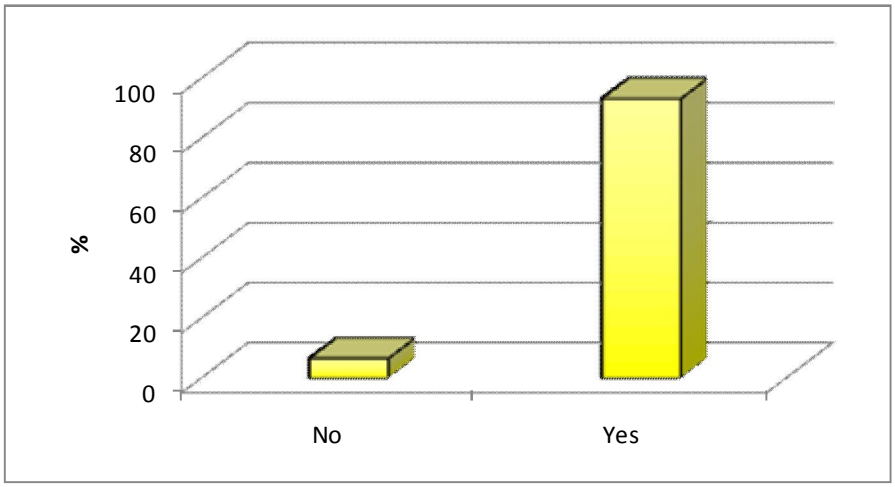

Figure (3): Distribution of studied sample according to patients past history (n=300).

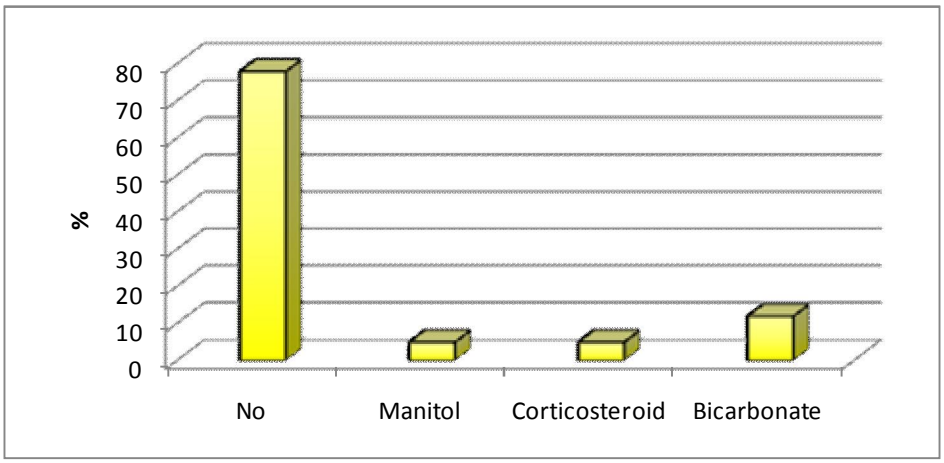

Figure (4): Distribution of studied sample according to patients Drug History (n=300).

As regard to patients Drug history, 234(78%) out patients had no drug history, 30(10%) out patients had Manitol and 36(12%) out of the patients had Bicarbonate. (Table (IV), Figure (4))

As regard to patients examination, 60(20%) out of the patients was normal, 40(13.3%) out of the patients was hyponatrmia while 200(66.7%) out of the patients was hyper (110(55%) of the hypernatrmia patients was

multiple organ dysfunction (MOD) and 90(45%) of the hyper patients was non multiple organ dysfunction (NMOD)).(Table (V) Figure (5)).

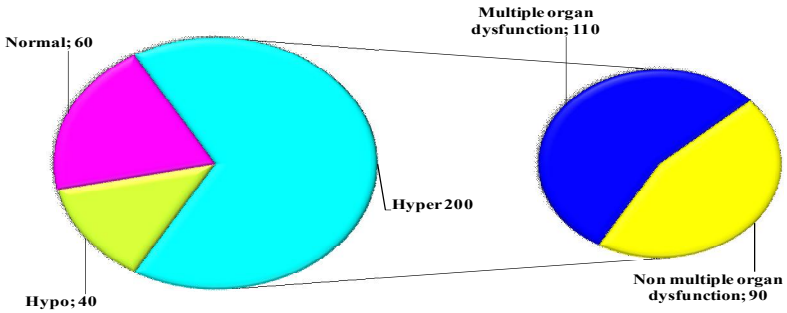

Figure (5): Distribution of the studied cases according to Patients examination.

Table (II): Distribution of the studied cases according to Patients examination.

	No.	%
Examination		
Normal	60	20
Hyponatrmia	40	13.3
Hypernatrmia	200	66.7
Multiple Organ Dysfunction (MOD)	110	55
Non Multiple Organ Dysfunction (NMOD)	90	45

As regard to patients outcome, in the MOD group 41(37.3%) out of the patients was died and 69(62.7%) out of the patients was survived while in the in the NMOD group 14(15.6%) out of the patients was died and 76(84.4%) out of the patients was survived. There was no statistically significant differences between the two groups while P=0.114 (P significant leval at P less than 0.05). (table (VI), figure (6))

Table (III): Comparison between the studied groups according to outcome.

	MOD (n=110)		NMOD (n=90)		Total			p
	No.	%	No.	%	No.	%		
Outcome								
Died	41	37.3	14	15.6	55	27.5	0.135	0.114
Survived	69	62.7	76	84.4	145	72.5		

χ^2: Chi square test

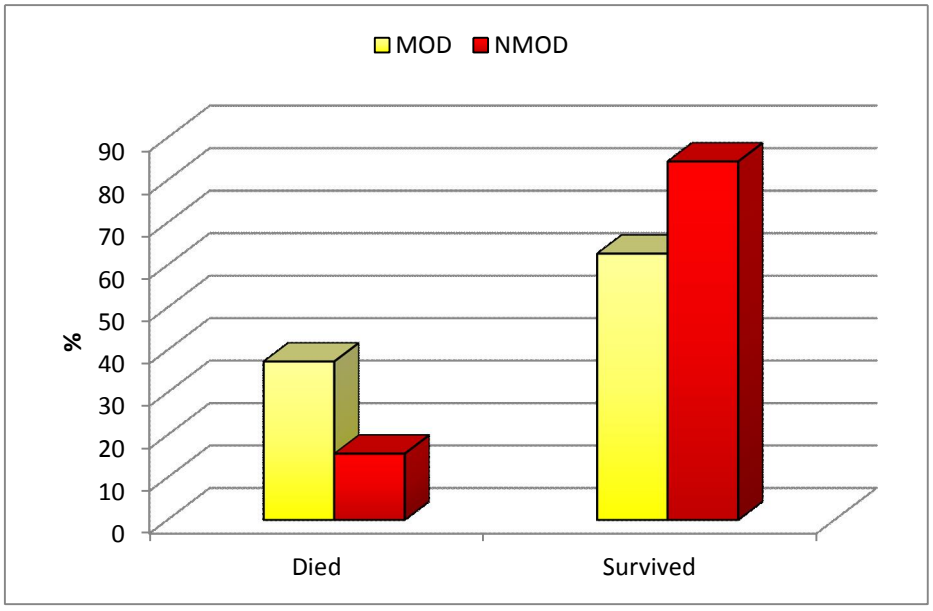

Figure (6): Comparison between the studied groups according to outcome.

As regard to patients APACHE II score, in the normal group it ranged between 5-20 with mean±S.D. 13.15±4.498 and the median value was 13.5, in the hyponatrmia group it ranged between 5-20 with mean±S.D. 12.15±4.406 and the median value was 11 while in the hypernatrmia group the MOD patients it ranged between 24-35 with mean±S.D. 27.81±2.621 and the median value was 28 and in the NMOD patients it ranged between 19-30 with mean±S.D. 24.12±3.381 and the median value was 23.5. There was statistically significant differences between groups while P=0.000 (P significant leval at P less than 0.05).(table (VII), figure (7)).

Table (IV): Comparison between the studied groups according to APACHE II.

	Normal (n=60)	Hyponatrmia (n=40)	Hypernatrmia		p
			MOD (n=110)	NMOD (n=90)	
APACHE II					
Min.	5	5	24	19	
Max.	20	20	35	30	
Mean	13.15	12.15	27.81	24.12	0.000*
SD.	4.498	4.406	2.621	3.381	
Median	13.50	11.00	28.00	23.50	

*: Statistically significant at $p \leq 0.05$

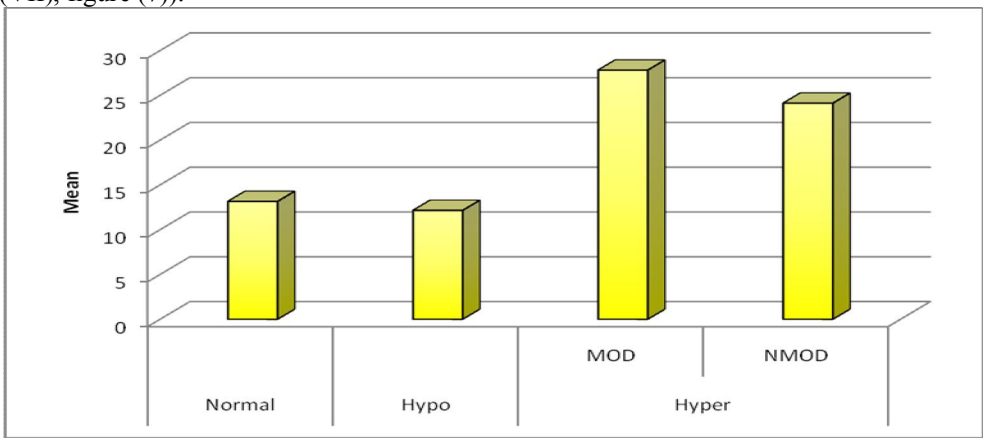

Figure (7): Comparison between the studied groups according to APACHE II.

Table (V): Comparison between different stages of SOFA in the hyper cases group (n=200).

	SOFA							Mean SOFA
	1	2	3	4	5	6	7	
Min.	7.00	8.00	9.00	10.00	11.00	11.00	11.00	9.57
Max.	12.00	13.00	14.00	15.00	15.00	15.00	15.00	13.71
Mean	9.36	10.47	11.37	12.23	12.86	13.09	13.24	11.80
SD.	1.88	1.84	1.83	1.79	1.42	1.56	1.66	1.60
Median	10.00	11.00	12.00	12.00	13.00	14.00	14.00	13.00
p		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	

As regard to SOFA, in the 1st stage ranged between 7-12 with mean±S.D. 9.36±1.88 and the median value was 10 it found that SOFA increase significantly in the 2nd, 3rd, 4th, 5th,6th and 7th stage (10.47,11.37,12.23,12.86,13.09 and 13.24 respectively) while the mean SOFA ranged between 9.57-13.71 with mean±S.D. 111.8±1.6 and median value 13. (table (VIII), figure (8)).

As regard to Serum Sodium, in the 1st stage Serum Sodium ranged between 144-150 with mean±S.D. 146.72±1.87 and the median value was 146 it found that Serum Sodium increase significantly in the 2nd, 3rd, 4th, 5th,6th and 7th stage (150.11, 155.35, 160, 162.01, 164.99 and 166.72 respectively) while the mean Serum Sodium ranged between 154.29-161.57 with mean±S.D. 157.98±2.64 and median value 159.57. (table (IX), figure (9)).

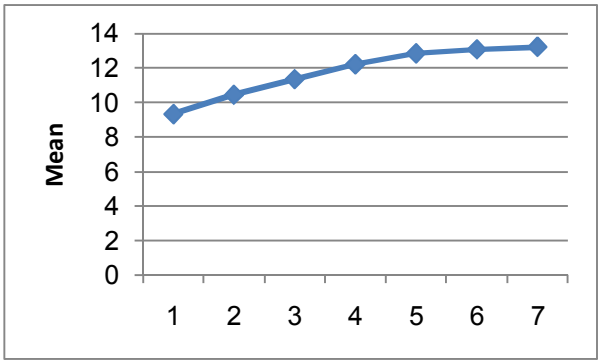

Figure (8): Comparison between different stages of SOFA in the hyper cases group (n=200).

Table (VI): Comparison between different stages of Serum Sodium in the hyper cases group (n = 200).

	Serum Sodium							Mean Serum Sodium
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	
Min.	144.00	147.00	149.00	155.00	158.00	161.00	163.00	154.29
Max.	150.00	155.00	160.00	165.00	168.00	169.00	170.00	161.57
Mean	146.72	150.11	155.35	160.00	162.01	164.99	166.72	157.98
SD.	1.87	2.80	3.46	3.70	3.22	2.84	2.58	2.64
Median	146.00	150.00	156.00	161.00	161.00	166.00	168.00	159.57
p		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	

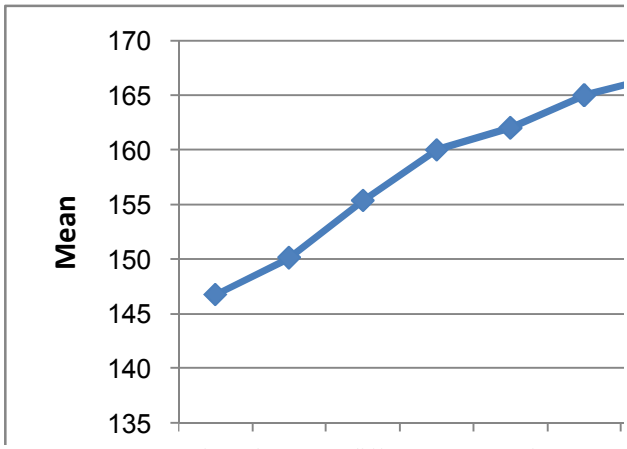

Figure (9): Comparison between different stages of Serum Sodium in the hyper cases group (n = 200).

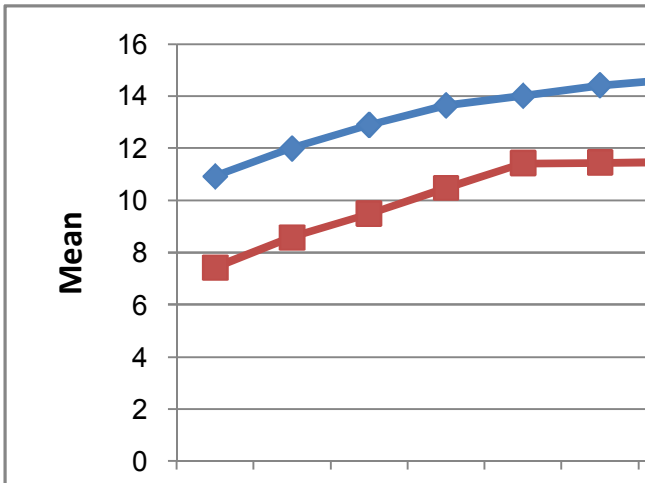

Figure (10): Comparison between different stages of SOFA.

As regard to SOFA, in the MOD patients the 1st stage ranged between 10-12 with mean±S.D. 10.93±0.82 and the median value was 11 it found that SOFA increase significantly in the 2nd, 3rd, 4th, 5th,6th and 7th stage (12,12.90,13.65,14.01,14.42 and 14.66 respectively) while the mean SOFA ranged between 12.57-13.71 with mean±S.D. 13.22±0.23 and median value 13.21 while in the NMOD patients the 1st stage ranged between 7-8 with mean±S.D. 7.43±0.5 and the median value was 7 it found that SOFA increase significantly in the 2nd, 3rd, 4th, 5th, 6th and 7th stage (7.43, 8.59, 9.49, 10.48, 11.44, 11.46 and 11.49 respectively) while the mean SOFA ranged between 9.57-10.57 with mean±S.D. 10.05±0.19 and median value 10. There was statistically significant differences between the two groups as regard to the SOFA stages 1,2,3,4,7 and the mean of SOFA. (table (X), figure (10)).

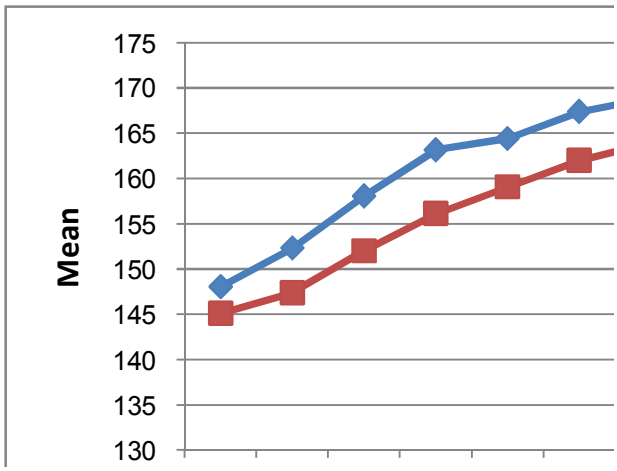

Figure (11): Comparison between different stages of SOFA.

As regard to Serum Sodium, in the MOD patients the 1st stage Serum Sodium ranged between 146-150 with mean±S.D. 148.04±1.4 and the median value was 148 it found that Serum Sodium increase significantly in the 2nd, 3rd, 4th, 5th,6th and 7th stage (152.31, 158.07, 163.16, 164.42, 167.4 and 168.93 respectively) while the mean Serum Sodium ranged between 159.14-161.57 with mean±S.D. 160.33±0.53 and median value 160.29 while in the NMOD patients the 1st stage Serum Sodium ranged between 144-146 with mean±S.D. 145.11±0.80 and the median value was 145 it found that Serum Sodium increase significantly in the 2nd, 3rd, 4th, 5th, 6th an 7th stages (147.42, 152.01, 156.12, 159.07, 162.04 and 164.01 respectively) while the mean Serum Sodium ranged between 154.29-155.86 with mean±S.D. 155.11±0.36 and median value 155.14. There was statistically significant differences between the two groups as regard to the serum sodium day and the mean of serum sodium day where P=0.000 in all (P significant leval at P less than 0.05). (table (XI), figure (11)).

Table (VII): Comparison between different stages of SOFA.

	SOFA							Mean SOFA
	1	2	3	4	5	6	7	
MOD (n=110)								
Min.	10.00	11.00	12.00	12.00	13.00	14.00	14.00	12.57
Max.	12.00	13.00	14.00	15.00	15.00	15.00	15.00	13.71
Mean	10.93	12.00	12.90	13.65	14.01	14.42	14.66	13.22
SD.	0.82	0.84	0.80	1.02	0.71	0.50	0.47	0.23
Median	11.00	12.00	13.00	14.00	14.00	14.00	15.00	13.21
p		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	
NMOD (n=90)								
Min.	7.00	8.00	9.00	10.00	11.00	11.00	11.00	9.57
Max.	8.00	9.00	10.00	11.00	12.00	12.00	12.00	10.57
Mean	7.43	8.59	9.49	10.48	11.44	11.46	11.49	10.05
SD.	0.50	0.49	0.50	0.50	0.50	0.50	0.50	0.19
Median	7.00	9.00	9.00	10.00	11.00	11.00	11.00	10.00
p		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	
F	18.471	17.32	14.076	59.280	0.041	0.978	10.545	5.783
P	0.000*	0.000*	0.000*	0.000*	0.840	0.324	0.001*	0.017*

Table (VIII): Comparison between different days of Serum Sodium.

	Serum Sodium							Mean Serum Sodium
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	
MOD (n=110)								
Min.	146.00	150.00	156.00	161.00	161.00	166.00	168.00	159.14
Max.	150.00	155.00	160.00	165.00	168.00	169.00	170.00	161.57
Mean	148.04	152.31	158.07	163.16	164.42	167.40	168.93	160.33
SD.	1.40	1.81	1.49	1.42	2.30	1.12	0.75	0.53
Median	148.00	152.00	158.00	163.00	165.00	167.00	169.00	160.29
p		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	
NMOD (n=90)								
Min.	144.00	147.00	149.00	155.00	158.00	161.00	163.00	154.29
Max.	146.00	148.00	155.00	157.00	160.00	163.00	165.00	155.86
Mean	145.11	147.42	152.01	156.12	159.07	162.04	164.01	155.11
SD.	0.80	0.50	1.89	0.76	0.83	0.76	0.85	0.36
Median	145.00	147.00	152.00	156.00	159.00	162.00	164.00	155.14
p		0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	
F	24.057	189.856	5.836	44.492	123.568	30.202	4.387	15.667
p_1	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*

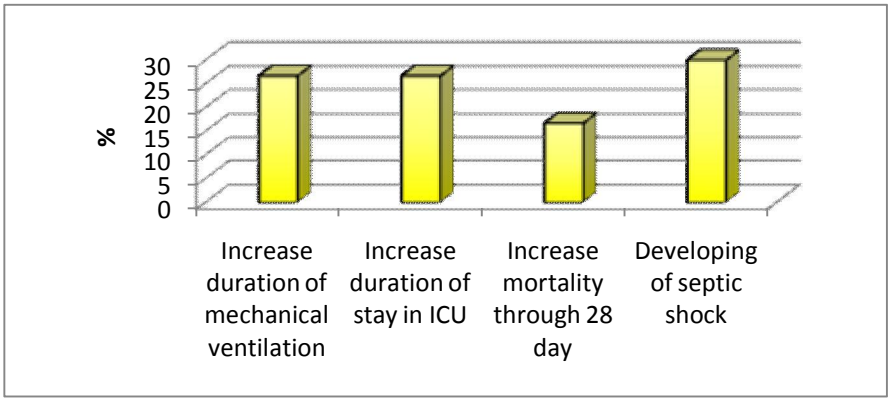

Figure (12): Distribution of the studied cases according to NMOD Patients outcome.

As regard to patients outcome in the MOD group 18(16.4%) out of the patients had increase duration of mechanical ventilation, 27(24.5%) out of the patients had increase duration of stay in ICU, 35(31.8%) out of the patients had increase mortality through 28 day and 30(27.3%) out of the patients had developing of septic shock.(table (XIV), figure (13)).

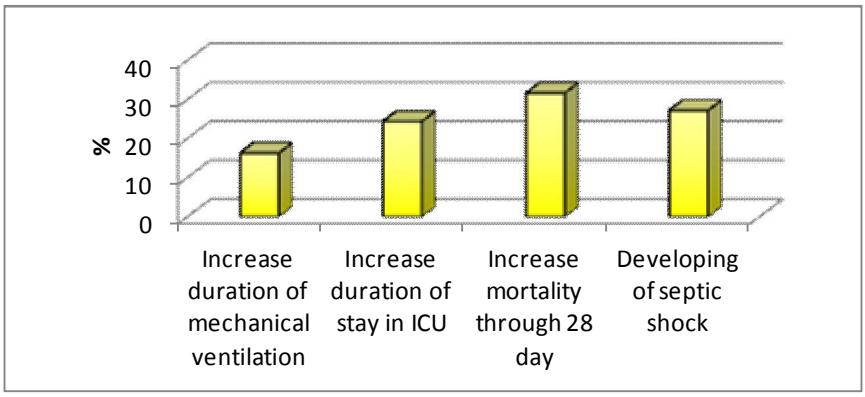

Figure (13): Distribution of the studied cases according to MOD Patients outcome.

There was positive significant correlation between the mean SOFA and the mean serum sodium day in the MOD and NOMD patients. (Table (XII)).

Table (IX): Correlation between mean SOFA and Mean Serum Sodium Day.

Mean Serum Sodium Day	Mean SOFA	
	r	p
MOD	**0.283**	**0.003***
Survived	0.247	0.039*
Died	0.331	0.037*
NMOD	**0.855**	**0.000***
Survived	0.831	0.000*
Died	0.875	0.000
Total (n=200)	0.981	0.000*

r: Pearson coefficient

As regard to patients outcome in the NMOD group 26(26.7%) out of the patients had increase duration of mechanical ventilation, 26(26.7%) out of the patients had increase duration of stay in ICU, 15(16.7%) out of the patients had increase mortality through 28 day and 27(30%) out of the patients had developing of septic shock.(table (XIII), figure (12)).

Table (X): Distribution of the studied cases according to NMOD Patients outcome.

	NMOD (n=90)	
	No.	%
Outcome		
Increase duration of mechanical ventilation	24	26.7
Increase duration of stay in ICU	24	26.7
Increase mortality through 28 day	15	16.7
Developing of septic shock	27	30

Table (XI): Distribution of the studied cases according to MOD Patients outcome.

	MOD (n=110)	
	No.	%
Outcome		
Increase duration of mechanical ventilation	18	16.4
Increase duration of stay in ICU	27	24.5
Increase mortality through 28 day	35	31.8
Developing of septic shock	30	27.3

Discussion

Hypernatremia is a frequent and potentially life-threatening electrolyte disturbance in hospitalised patients. About 7–9% of critically ill patients in the ICU develop hypernatremia, and this kind of serum sodium disturbance condition were termed ICU acquired hypernatremia[1-3]. Hypernatremia is usually caused by progressive loss of water from the kidney or gastrointestinal tract and insensible perspiration, which is sometimes accompanied by insufficient fluid intake or inappropriate treatment with electrolyte solution. Patients with TBI (traumatic brain injury) have disordered consciousness, loss of sensation of thirst and concomitant fever, and are usually treated with diuretics to control intracranial pressure which results in loss of body fluid. In contrast to community-acquired hypernatremia, in the ICU, there are fewer cases of hypovolemic and more cases of euvolemic or hypervolemic hypernatremia.

Predicting prognosis in MOF is of paramount importance. Clinical assesmements and the usual biological surrogates for organ dysfunction are still widely used and help us to provide care for critically ill patients in everyday practice[4]. The main objective in this setting is clearly to intervene early and in an appropriate manner,especially regarding to fluid management[5].

The aim is to predict organ failure before it become obvious by which time it is very often too late this makes sense if intervention likely to prevent end organ dysfunction and improved survival[6].The challenge is therefore to find biomarkers that give the physician accurate information regarding the risk of apoor outecome within the stay in intensive care unite. These reasons have led to the search for biomarker or lab investigation for effectively identifying the prognosis of the disease rapid, simple, cost effective and reliably guiding the management.

We conducted a observational study on 200 patient of 300 patients 66.5% developed acquired hypernatremia after admission to the ICU which is

large percentage conicoides other study with agreement observation of mortality occurance from acquired hypernatremia in ICU reported by Hadjizacharaia et al this study conducted on 267 patients.

In present study, the mean age was (41.97± 10.49) the highest patient age as a risk factor was between (31-40) years 86 patient (28.7%) which is contraducting findings with study reported by O Donoghue et al which reported the highest patient age as risk factor was >61 y.

As regard reporting serum sodium level for all patient we found 100 patient either they NA level stay normal during they stay in ICU 20% (60) patients or became hyponatremic 13.3%(40) patients whose we did not reported their outcome in our study because they did not developed hypernatrmia, and they consider the smallest groub in our study.

As the incidence of development acquired hrpernatremia among ICU patients due to loss of thirst effect or receiving osmotic dieresis and not treated by hypertonic saline so we had 66.7% (200) patients suffering from hypernatremia, 55%of these 66.7% developed MOF (110) patients, and 45%(90) patients not developed MOF and still their laboratory investigations showing hypernatremia. As regard to Sunder varun et al reported in critical care department Sri Ramarchandra India medical college the sudy reported on 670 patients 64 developed HAH 21 patients out of them developed MOF and 43 not developed MOF, reset of the total patients 381 became normal NA level and 225 developed hyponatremia.

Measuring of NA level in our study on admission and daily the maximum NA level was 170 mg/l.The average duration of hypernatremia was (7-10) days in agreement with AmJ et al reported by national kidney foundation shows the maximum reported NA level (160-170)mg/l and its average duration (6-11)days.

The factors contributing hypernatremia was fever found in 45% of patients, 18% due to dialysis,38% due to polyurea and 35% had volume overload as most patients administred sodium chloride solution.

For predicting mortality among our patients APACHE II scored for all groubs the mean score among normal NA groub was 13.5 while in hyponatremic groub was 12.5 but the hyernatemic patient who developed MOF was scored 27.81 on admission and among the patients with preserved organ functions their score was 24.21 so hypernatremia affect the patient health (p 0.000). Zhongguo wei et al reported in emergency department of China capital university hospital shows increase the incidence of mortality in relation to APACHE II scoring on admission of patient developed hypernatremia during hospital admission and ICU stay as result mean score for patient developed hypernatremia (28.16)and (16) for nonhypernatremic patient that show high significant relation for developing MOF (0.001).

For the assessment of developing of MOF, SOFA scoring done on admission and daily with close observation of the relation between increase NA level above normal range and daily SOFA for 7 days during stay in ICU as the mean duration of hypernatremic level in patient serum (7-10) days.

The mean SOFA for 200 patients developed hypernatremia at the first day of increasing NA level above the normal range was 9.36 and on day 2 was 10.47 and on day 3 was 11.37and on day 4 was 12.23 and on day 5 was 12.86 and day 6 was13.09 and on day 7 was 13.24, the subgroub of patients developed MOF 37.3%(41) patients not survived and 15.6% (14) patient whose not developed MOF also not survived (P0.000).Another method for estimation of MOF reported by varun s. et al in relation to hypernatremic effect using the median SOFA score for the patients every day that range (2-24) for hypernatremic patient and (1-16) for non-hypernatremic patients that shows difference in result with our study but not show close obervation during hypernatremic state or the state of outcome for those patients and cannot determine the cutpoint Of NA level for occurance of MOF to some extend Darmon et al shows observation between also mean SOFA score and serum sodium level but the study done through 13 days and the mean SOFA for hypernatremic patient was 12 and 10 for non-hypernatremic patient which and was nearly equal in observational result with our study (P<0.0001).

As observation for NA level in our patients,mean NA level in first day of hypernatremia 146.72 and on day 2 was 150.11and on day 3 was 155.35 and on day 4 was 160 and on day 5 was 162.01 and on day 6 was 164.99 and on day 7 was 166.72 so in realtion with SOFA score in the same days we can observe the mean SOFA score increases with increase hypernatremic state of the patients that correlate with the damage effect during increase hypernatremic state (P0.000), that result highly agreement with Darmon et al observation for a prognostic value of dysnatremia in medical ICU patients which shows the harmfull effect of increase NA level on patient health but this study aim to show not only hypernatremic effect but also hyponatremic effect on patient health and subdivided hypernatrmia to mild, moderate, sever and don't show the cutpoint of NA level which MOF occure in contrary with our study which aim to show only hypernatremic effect and determine cutpoint of occurance of MOF but with agreement of the same mortality precentage between the two studies 66%.

For observation of MOF occurance in our studied groubs SOFA score calculated which shows the mean ranges (12-12.9) in relation to serum NA level observed in the same days ranges (152.31-158.07)

which was between day 2 and 3 at which when referral to SOFA score guideline [8] we conclude that NA level shows the massive harmfull effect on different organs and ocurrance of MOD.

In this study observation of outcome regarde the mortality and morbitidy in the groub which developed MOD 37.3% (41) patients out of 110 patients was nonsurvived (P0.037), 62.7% (69) patients survived (P0.039), while 90 patients with preserved organ functions 15.6% (14) patients not survived (P0.000), while 84.4% (76) patients survived (P0.000), in relation to studied reported by Aiyagari et al and Hadjizacharia et al showed patients developed HAH were so critical on admission as regard high APACHE II score and low GCS and have five fold higher mortality rate in contrary to the type of patients studied which selected from neurological ICU as regard sever TBI patients, 21.8% mortality for observed patients by Aiyagari et al and 22%whose studed by Hadjizacharia et al contrary to our study on medical ICU patients mortality ranges 32%-66% with agreement to similar study Mandal et al 180 out of 267 patients developed hypernatremia, mortality for patients developed NA level >150mmol/l was 67.4%.

As regard for control groubs observed by Mandal et al mortality rate was 2% lower than reported by O Donoghue et al 7.7%,the NA level in the last studies for nonsurvived patients was 164 mmol/l ($p<0.001$), in contrary to our study did not include control groub due to randomized selection of patients. Mandal etal subdivided observed hypernatremia to mild, moderate amd sever in contrary to our study no subgroubs of hypernatremia included.

As regard to our aim to evaluate the prognosis of hypernatremia in critically ill patients, we observed 200 patient who developed hypernatremia,90 patients out of them not developed MOF result in 24 patients increased duration of mechanical ventilation, other 24 patients showed increase duration in ICU stay,15 patients increase risk for mortality through 28 days, 27 patients developed septic shock while 110 patients who developed MOF result in 35 patients increase risk of mortality through 28 days,30 patients developed septic shock, 18 patients increasing duration of mechanical ventilation and 27 patients increasing duration of stay in ICU, as an observational point of view reported by Darmon et al which evaluate the prognostic outcome for dysnatremic patient to some extend toward hyernatremic observed patients result in 100 patient out of 750 developed MOF, 200 patients increase length of stay in ICU, 250 patients showed sepsis,100 patients result to increase duration of mechanical ventilation,100 patients increase possibility for readmission to ICU, 200 patients increase possibility to increase mortality through 30 days.

As we reported in our study the major risk factors for HAH age >60 years, AKI on admission, mechanical ventilation, worsening of SOFA score,need for inotropes,enteral feeding, negative fluid balance which additionaly identidied hypokalemia, hypercalcemia, hypoalbuminemia, sodium bicarbonate administration, hyperglycemia and gastrointestinal losses as other risk factor for HAH[6-9], in an attempt to explain pathophysiology of HAH renal concentrating defect was postulated and it was attributed to disease associated with central diabetes insipidus, drugs causing nephrogenic diabetes insipidus, hypokalemia, hypercalcemia, loop diuretic and renal dysfunction [6-7]. In our study we were not able to establish a direct cause relationship effect between hypernatremia and renal concentrating defect as the study was best supporting that case discussion.

As the physiological principles that explain ocurrance of hypernatremia due lack of access to water in contrary to these principles observed that decreased free water administration may not be a major risk factor for HAH for the majority of patients, but at the sametime free water administration <100 ml/day was associated with HAH among patients on mechanical ventilation and those enteral feeds, this observation raises the possibility of renal concentrating defects in patients who develop HAH.

Individually with lack of access to water need not necessary if kidneys retain water appropriate often called appropriate renal response during hypernatremia.

Such response could be expected to prevent hypernatremia in cohort study of patients who received inadequet volumes of electrolyte free water.

In fact 60 of 64 patients developed HAH points to renal concentrating defect as a major mechanism of the abnormality.

As the incidence of ocurrance of hypernatrmia was as high as 51.55% in a cohort study of patient in ICU when compared with patients treated in internal medicine department and surgery department the incidence of hypernatremia is higher in patients treated in the neurological ICU

Donoghue et al found that the incidence of acquired hypernatremia was 7.7%in the general ICU in a 5 year study in which patients having burn and neurosurgical diagnoses and those receiving treatment with hypertonicsaline solution were excluded.

Aiyagari et al found that the incidence of hypernatremia was 24.3% in patient receiving mannitol for treatment for dehydration in the neurological ICU [9]

By reporting of all refrences of different studies of which is consistent with earlier reports of hypernatremic effect, HAH IS associated with high inhospital mortality ranging from 30-50% [6,2,7,8,26,28]

Mortality among patients who developed HAH was higher (34.3%) compared with those did not (19.4%).

Hypernatraemia was an independent predictor for mortality. In the patients who died, hypernatraemia was both more acute and more severe, while no association was found between mortality and the generally modest cor As regard to our study the median APACHE II was 28 to MOD patients and 23.5 to NMOD patients (P0.000) but the mean age was (41.97± 10.49), GCS recorded for all patient but we conider it's a part of SOFA scoring and APACHE`II scoring, so our study was nearly agreement in result with the other studies.

Rection rates of hypernatraemia.

In conclusion, ICU-acquired hypernatremia is caused by both a positive solute balance because of inadequate sodium-rich infusion therapy and the loss of free (renal and extrarenal) water. This is induced mainly by osmotic dieresis, diuretic use, and renal dysfunction. Daily assessment of water balance in the intensive care setting is mandatory. This allows for the early identification of mechanisms that will lead to changes in serum sodium levels and the avoidance of hypernatremia, which presents an independent risk factor for poor prognosis this was clearly seen in our results as the level of sodium increases the SOFA score increases indicating the harmful effects of hypernatremia on various body organs which needs a rapid diagnosis and an urgent interference to decrease the incidences of different morbidities and occurrence of different organ complications and decrease the time of mechanical ventilation and ICU stay and also help to decrease the incidence of mortalities.

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