PROFILE OF POLYURIA IN PICU WITH SPECIFIC REFERENCE TO CENTRAL DIABETES INSIPIDUS AND CEREBRAL SALT WASTING SYNDROME

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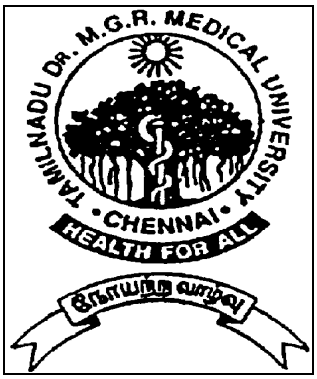

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CERTIFICATE

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INTRODUCTION

Polyuria a commonly encountered problem in paediatric intensive care unit (PICU) is defined as urine output more than 4 ml/kg/hr lasting for atleast 24hrs.[1,2]

Causes of polyuria in critically ill children include [1,2]

1. Diabetic ketoacidosis
2. Renal tubular acidosis
3. Chronic renal failure with concentration defects
4. Osmotic diuresis(mannitol,urea,sorbitol)
5. Central diabetes insipidus (CDI)
6. Nephrogenic diabetes insipidus
7. Cerebral salt wasting syndrome (CSWS
8. Non oliguric ARF
9. Stress hyperglycemia
10. Hyperaldostrenosim
11. Systemic or metabolic disease (eg,hypercalcemic or hypokalemic nephropathy, sickle cell disease).

Among these causes, diabetic ketoacidosis, renal tubular acidosis and chronic

renal failure with concentration defects are the common causes of polyuria in intensive care unit. They usually will present with polyuria and associated complications. Other than these, there are diseases which deserves special attention in PICU like central diabetes insipidus (CDI), nephrogenic diabetes insipidus, cerebral salt wasting syndrome (CSWS), non oliguric ARF, stress hyperglycemia and hyperaldostrenosim which are not uncommon in PICU.

DIABETES INSIPIDUS

Central diabetes insipidus (DI) is characterized by decreased secretion of arginine vasopressin (AVP or ADH), that results in polyuria and polydipsia by diminishing the patient's ability to concentrate urine. Diminished or absent ADH can be a result of a defect in one or more sites involving the hypothalamic osmoreceptors, supraoptic or paraventricular nuclei, or the supraopticohypophyseal tract [3,4,5.]

Nephrogenic DI is characterized by a decrease in the ability to concentrate urine due to a resistance to ADH action in the kidney. Nephrogenic DI can be observed in chronic renal insufficiency, hypercalcemia, hypokalemia, and tubulointerstitial disease [5.]

Pathophysiology

ADH is the primary determinant of free water excretion in the body. Its main target is the kidney, where it acts by altering the water permeability of the cortical and medullary collecting tubules. Water is reabsorbed by osmotic equilibration with the hypertonic interstitium and returned to the systemic circulation. The actions of ADH are mediated through at least 2 receptors—V1 mediates vasoconstriction, enhancement of

corticotrophin release, and renal prostaglandin synthesis; V2 mediates the antidiuretic response [3,4].

DI is uncommon, with a prevalence of 1 case per 25,000 population.

No significant sex difference exists in central or nephrogenic DI[6].

CLINICAL FEATURES

The most common form of DI is that which follows trauma or surgery to the region of the pituitary and hypothalamus. It may exhibit 1 of 3 patterns—transient, permanent, or triphasic. The triphasic pattern is observed more often clinically [5].

First, a polyuric phase occurs and lasts 4-5 days. Inhibition of ADH causes the polyuric phase. An immediate increase in urine volume and a concomitant fall in urine osmolality occur.

Second, an antidiuretic phase of 5-6 days occurs, which results from release of stored hormone. The urine osmolality rises.

The third phase can be permanent DI, when stores of ADH are exhausted and the cells that produce more ADH are absent or unable to produce.

Polyuria, polydipsia, and nocturia (from 3-18 liters) are the predominant symptoms [5].

In infants, crying, irritability, growth retardation, hyperthermia, and weight loss may be the most apparent signs.

In children, enuresis, anorexia, linear growth defects, and fatigability typically predominate.Patients with a nontraumatic onset typically have a much more insidious course.

Signs of dehydration and an enlarged bladder may be present; otherwise, no specific signs of DI exist.

Causes [5,7]

Recent literature indicates 30% of cases to be idiopathic, 25% related to malignant or benign tumors of the brain or pituitary, 16% secondary to head trauma, and 20% following cranial surgery.

- Idiopathic DI is associated with destruction of cells in the hypothalamus, often as part of an autoimmune process.

- DI after neurosurgery or trauma varies with the extent of damage. Approximately 10-20% of patients will experience DI following transsphenoidal removal of an adenoma. This percentage increases to 60-80% with large tumors. Not all cases of DI are permanent. The common causes of postoperative polyuria are excretion of excess fluid given during surgery and an osmotic diuresis as a result of treatment for cerebral edema.

- Primary intracranial tumors causing DI include craniopharyngioma, or pineal tumors. Appearance of other hypothalamic manifestations may be delayed for as long as 10 years. Thus, periodic follow-up of patients diagnosed with

idiopathic DI is necessary to detect slowly growing intracranial lesions.

- Other causes include cancer (eg, lung cancer, lymphoma, leukemia), hypoxic encephalopathy, infiltrative disorders (histiocytosis X, sarcoidosis), anorexia nervosa, and vascular lesions such as arteriovenous malformations or aneurysms.

Lab Studies

The diagnosis of diabetes insipidus (DI) often is made clinically, while the laboratory tests provide confirmation. Perform testing with the patient maximally dehydrated as tolerated, ie, at a time when ADH release would be highest and urine would be most concentrated. Ruling out secondary causes, such as diabetes mellitus, also is important.

The clinician should measure serum electrolytes and glucose, urine specific gravity, urinary sodium, simultaneous serum and urine osmolality, and ADH levels. A urine specific gravity of 1.010 or less and a urine osmolality less than 200 mOsm/l is the hallmark of DI. Random plasma osmolality generally is greater than 285 mOsm/l [5,6].

The water deprivation test (ie, Miller-Moses test), a semiquantitative test to ensure adequate dehydration and maximal stimulation of ADH for diagnosis, is performed in ambiguous clinical circumstances [7,8].

1. The water deprivation test is the simplest and most reliable method for diagnosing CDI but should be performed only while the patient is under constant

supervision. Serious dehydration may result. The test is started in the morning by weighing the patient, obtaining venous blood to determine electrolyte concentrations and osmolality, and measuring urinary osmolality. Voided urine is collected hourly, and its specific gravity or preferably, osmolality is measured.

Dehydration is continued until orthostatic hypotension , postural tachycardia appear and $\geq$ 5% of the initial body weight has been lost. Serum electrolytes and osmolality are again determined and vasopressin should be given.

A normal response produces maximum urine osmolality after dehydration (often > 1.020 sp gr or 700 mOsm/L), exceeding the plasma osmolality; osmolality does not increase more than an additional 5% after injection of vasopressin .

Patients with CDI are generally unable to concentrate urine to greater than the plasma osmolality but are able to increase their urine osmolality by > 50% after vasopressin.

Patients with partial CDI are often able to concentrate urine to above the plasma osmolality but show a rise in urine osmolality of > 9% after vasopressin administration. Response to AVP is not informative in this case. Further testing must be done to distinguish partial central vs. partial nephrogenic DI.

Patients with NDI are unable to concentrate urine to greater than the plasma osmolality and show no additional response to vasopressin

2. Concurrent measurements of plasma AVP (measured before and during a

fluid deprivation test) should be plotted against Posm, and Uosm. In partial central DI, AVP levels will be low for the concurrent level of Posm, while in partial nephrogenic DI, AVP levels are elevated (more reliable in general than low-normal values). For this method to be accurate, one must achieve Posm of 295 mOsm/l during water deprivation; if not, infuse 3% saline (at 0.1 mL/kg/min)[7,8.]

3. Therapeutic trial of desmopressin (10-20 µg intranasally bid). In central DI, this will abolish polyuria and in nephrogenic DI, it will have no effect [7,8.]

All these tests can be performed easily in stable patients. But in critically ill children, doing water deprivation test is very much crucial. The concept of water deprivation test is to induce atleast 3% dehydration, to rise the serum osmolality. For the rise in serum osmolality, pituitary should secrete ADH to concentrate urine for the maintenance of osmotic equilibrium. In most of the critically ill patients with polyuria, there will be more than 5% dehydration at the time of suspicion of diagnosis unlike stable patients. In stable patients, there will be an increase in thirst following rise in serum osmololity. So that they will present with normal hydration. Before making diagnosis and doing investigations, atleast 3% dehydration is essential in these patients.

So in critically ill patients water deprivation test is not essential. In general, if the serum osmolality is more than 295 meq/l, there is no need of water deprivation test.[2]

TREATMENT [9,10]

Medical Care.

- Replace losses with IV fluid according to the patient's urinary sodium level.

Avoid hyperglycemia, volume overload, and a correction of hypernatremia that is too rapid. Desmopressin is the drug of choice. Generally, it can be administered 2-3 times per day. Frequent electrolyte monitoring is recommended [9,10.]

- Pharmaceutical therapy for DI includes subcutaneous, nasal, and oral preparations of vasopressin analogues, as well as chlorpropamide, carbamazepine, clofibrate, thiazides, and indomethacin (limited efficacy).

Surgical Care [9,10]

Postoperatively, administer the usual dose of desmopressin to patients with DI and administer (hypotonic) IV fluids to match urine output.

After pituitary surgery, administer parenteral desmopressin every 12-24 hours, along with adequate fluid to match losses. Follow the specific gravity of the urine and administer the next dose of desmopressin when the specific gravity has fallen to less than 1.008-1.005 with an increase in urine output. When the patient can tolerate oral intake, thirst can become an adequate guide.

CEREBRAL SALT WASTING SYNDROME [11,12]

Cerebral salt-wasting syndrome (CSWS) is defined by the development of excessive natriuresis and subsequent hyponatremic dehydration in patients with intracranial disease. Differentiation of this disorder from the syndrome of inappropriate secretion of antidiuretic hormone (SIADH), another common cause of hyponatremia in this setting, is critical to initiate appropriate therapy .[11,13]

Pathophysiology

The exact mechanism of underlying renal salt wasting in this syndrome remains unclear. One hypothesis is that involves release of natriuretic factors, possibly including brain natriuretic peptide, C-type natriuretic peptide or an oubainlike peptide, by the injured brain .[12]

Exact data regarding the incidence of this disorder is not available. Approximately 60% of children with brain injuries or tumors develop hyponatremia during their hospital course. Some experts suggest that CSWS is responsible for hyponatremia at least as often as SIADH, particularly in neurosurgical patients. [12]

Mortality/Morbidity

CSWS usually appears in the first week after brain injury and spontaneously resolves in 2-4 weeks. Death and complication rates for this syndrome are not available. Failure to distinguish CSWS from SIADH as the cause of hyponatremia will lead to improper therapy (ie, fluid restriction), thereby exacerbating intravascular volume depletion and potentially jeopardizing cerebral perfusion. [12]

Age

CSWS can occur at any age. Published reports include patients aged 6 months to 65 years.[12]

Clinical features [11,12]

Symptoms include lethargy, agitation, headache, altered consciousness, seizures, and coma. Severity of symptoms typically reflects the magnitude and rapidity of the

decrease in serum sodium concentration.

Physical signs include those associated with severe hyponatremia or intravascular volume depletion. Hyponatremia can manifest as acute central nervous system (CNS) dysfunction such as altered mental status, seizures, and coma.

Causes

CSWS occurs in the setting of acute CNS disease. Conditions include the following.[11,12,14]

- Head injury
- Brain tumor
- Intracranial surgery
- Stroke
- Intracerebral hemorrhage
- Tuberculous meningitis
- Craniosynostosis repair

Lab Studies [11,12]

- Patients with untreated CSWS are often hyponatremic, with elevated urine osmolality and low serum osmolality. Serum uric acid concentrations are often low in SIADH but can be normal in CSWS.

- Urine sodium concentrations are typically elevated in both SIADH and CSWS (>40 mEq/L). However, urinary sodium excretion (urine sodium concentration [mEq/L] X urine volume [L/24 h]) is substantially higher than sodium intake in

CSWS but generally equals sodium intake in SIADH. Therefore, net sodium balance (intake minus output) is negative in CSWS.[11,12,13]

- Fractional excretion of uric acid (FEUA) is defined as the percentage of urate filtered by glomeruli that is excreted in urine. It is calculated by dividing the product of (urinary uric acid [mg/mL] X serum creatinine [mg/mL]) by the product of (serum uric acid [mg/mL] X urine creatinine [mg/mL]) and multiplying the result by 100%.Normal values are less than 10%. Patients with either CSWS or SIADH have elevated FEUA. However, after correction of hyponatremia, FEUA normalizes in SIADH but remains elevated in CSWS.[11,12]

Medical Care [12,15]

- Evaluation and treatment typically occurs in the inpatient setting because most patients are seriously ill with acute CNS disease.
- Management centers on correction of intravascular volume depletion and hyponatremia as well as replacement of ongoing urinary sodium loss with intravenous isotonic or hypertonic saline solutions.
- Once the patient is stabilized, enteral salt supplementation can be considered.
- Some clinicians have reported a favorable response to mineralocorticoid therapy in CSWS which acts on fluid and electrolyte balance. It enhances sodium reabsorption in the kidney by direct action on renal tubule cell, resulting in expansion of extracellular fluid volume. It increase renal excretion of potassium and hydrogen ion.

Prognosis [11,12]

CSWS usually develops in the first week following a brain insult. Its duration is usually brief (spontaneously resolves in 2-4 weeks), although it can last for several months.

NON OLIGURIC RENAL FAILURE

Nonoliguric acute renal failure is being recognized more commonly as a frequent initial observation for azotemia. Use of automated biochemical monitoring, aminoglycoside antibiotic utilization, and administration of potent diuretics and mannitol in settings of oliguria all contribute to its increased incidence.[16,17]

- There appears to be less morbidity and mortality in patients with nonoliguric acute renal failure, and diagnostic urinary indices suggest less of an insult to renal function. Aim is to compare nonoliguric acute renal failure with the oliguric form because there are important differences to be recognized by the clinician.

Pathophysiology

The driving force for glomerular filtration is the pressure gradient from the glomerulus to the Bowman space. Glomerular pressure is primarily dependent on renal blood flow (RBF) and is controlled by combined resistances of renal afferent and efferent arterioles. Regardless of the cause of ARF, reductions in RBF represent a common pathologic pathway for decreasing GFR.[18]

Recovery from ARF is first dependent upon restoration of RBF. Early RBF normalization predicts better prognosis for recovery of renal function. In prerenal

failure, restoration of circulating blood volume is usually sufficient. Rapid relief of urinary obstruction in postrenal failure results in a prompt decrease of vasoconstriction. With intrinsic renal failure, removal of tubular toxins and initiation of therapy for glomerular diseases decreases renal afferent vasoconstriction.[18]

Mortality rates are generally lower for nonoliguric ARF (>400 mL/day) than for oliguric (<400 mL/day) ARF, reflecting the fact that nonoliguric ARF is usually caused by drug-induced nephrotoxicity and interstitial nephritis, which have few other systemic complications.

Intrinsic renal failure [19,20]

Causes are [19,20]

1. ATN, ischemia, toxins (eg, aminoglycosides, radiocontrast, heme pigments, cisplatin, myeloma light chains, ethylene glycol)
2. Interstitial diseases - Acute interstitial nephritis, drug reactions, autoimmune diseases (eg, systemic lupus erythematosus [SLE]), infiltrative disease (sarcoidosis, lymphoma), infectious agents (Legionnaire disease, hantavirus)
3. Acute glomerulonephritis
4. Sepsis and septic shock.[17,21,22,23]

Out of these septic shock needs special mention. Serious bacterial infections at any body site, with or without bacteremia, usually are associated with important changes in the function of every organ system in the body. These changes are mediated mostly by elements of the host immune system against infection. Shock is deemed present when

volume replacement fails to increase blood pressure to acceptable levels and associated clinical evidence indicates inadequate perfusion of major organ systems, with progressive failure of organ system functions.[24,25]

Multiple organ dysfunction syndrome (MODS): This is the presence of altered organ function in a patient who is acutely ill and in whom homeostasis cannot be maintained without intervention.

The evidence that sepsis results from an exaggerated systemic inflammatory response induced by infecting organisms is compelling; inflammatory mediators are the key players in the pathogenesis.[22,24,25]

The gram-positive and gram-negative bacteria induce a variety of proinflammatory mediators, including cytokines. Such cytokines play a pivotal role in initiating sepsis and shock. The bacterial cell wall components are known to release the cytokines; these include lipopolysaccharide (gram-negative bacteria), peptidoglycan (gram-positive and gram-negative bacteria), and lipoteichoic acid (gram-positive bacteria).

The predominant hemodynamic feature of septic shock is arterial vasodilation. Diminished peripheral arterial vascular tone may result in dependency of blood pressure on cardiac output, causing vasodilation to result in hypotension and shock if insufficiently compensated by a rise in cardiac output. Early in septic shock, the rise in cardiac output often is limited by hypovolemia and a fall in preload because of low cardiac filling pressures. When intravascular volume is augmented, the cardiac output

usually is elevated (the hyperdynamic phase of sepsis and shock). Even though the cardiac output is elevated, the performance of the heart, reflected by stroke work as calculated from stroke volume and blood pressure, usually is depressed. Factors responsible for myocardial depression of sepsis are myocardial depressant substances, coronary blood flow abnormalities, pulmonary hypertension, various cytokines, nitric oxide, and beta-receptor down-regulation.[22,23,26]

Renal dysfunction [21,22,23,24,25,26]

Sepsis often is accompanied by acute renal failure caused by acute tubular necrosis. The mechanism is by systemic hypotension, direct renal vasoconstriction, release of cytokines (eg, TNF), and activations of neutrophils by endotoxins and other peptides, which contribute to renal injury.

Inappropriate polyuria leading to hypovolemia and hypotension occurs frequently in patients with severe sepsis. Its etiology was studied in three patients with polyuria and systolic hypotension.

Glomerular filtration rate and renal blood flow were measured by the standard renal clearance techniques. Renal blood flow distribution to the outer cortex, inner cortex-outer medulla and the inner medulla were measured by radioactive xenon. The glomerular filtration rate, renal blood flow and renal blood flow distribution were normal.

Polyuria does not result from a maldistribution of renal blood flow. Antidiuretic hormone did not alter the polyuric syndrome. These data suggest that sepsis produces a

blockade at either the distal tubule or the collecting duct, thereby preventing salt and water conservation. This blockade may be due to either a toxin or a toxic metabolic breakdown product of sepsis.

Emergency Care

Treatment of ARF ideally should begin before the diagnosis of ARF is firmly established. A high index of suspicion often is necessary to diagnose early ARF. Significant decrease in GFR frequently occur before indirect measures of GFR reveal a problem. ARF should be included in differential diagnosis of all critically ill patients.[27,28]

- Fluid management [27]
    - Fluid management in patients with ARF is challenging
    - Hypovolemia potentiates and exacerbates all forms of ARF.
    - Reversal of hypovolemia by rapid fluid infusion often is sufficient to treat many forms of ARF. However, rapid fluid infusion can result in life-threatening fluid overload in patients with ARF.
    - Accurate determination of a patient's volume status is essential and may require invasive hemodynamic monitoring if physical examination and laboratory results do not lead to a definite conclusion.
    - Urinary obstruction often is an easily reversible cause of ARF.
    - Placement of a urinary catheter early in the workup of a patient with ARF not only allows diagnosis and treatment of urethral and bladder outlet urinary obstruction, but also allows for accurate measurement of urine output.

STRESS HYPERGLYCEMIA [29,30]

Hyperglycemia is frequent during critical illness and is perceived by the clinician as part of the systemic metabolic response to stress.

Today, it is well known that any type of acute illness or injury results in insulin resistance, glucose intolerance, and hyperglycemia, a constellation termed "diabetes of injury". Illness or trauma increases hepatic glucose production with ongoing gluconeogenesis despite hyperglycemia and abundantly released insulin. Hepatic insulin resistance is further characterized by elevated circulating levels of IGF–binding protein–1 (IGFBP-1). Also, in skeletal muscle and heart, insulin-stimulated glucose uptake is impaired. Glucose uptake in critically ill patients, however, is increased but takes place mainly in the tissues that are not dependent on insulin for glucose uptake, such as, the nervous system and the blood cells. The most severe cases of stress-induced hyperglycemia and highest levels of circulating IGFBP-1 are observed in patients with the highest risk of death. Orchestrated "counterregulatory" hormonal responses, cytokine release, and signals from the nervous system, all affecting glucose metabolic pathways, bring about the diabetes of injury. The hormones involved include catecholamines, cortisol, glucagon, and growth hormone (GH). Proinflammatory cytokines affect glucose homeostasis indirectly, by stimulating counterregulatory hormone secretion, and directly, by altering insulin receptor signaling .

Furthermore, both endogenous and exogenous catecholamines promptly inhibit insulin secretion from ß cells, and catecholamines as well as angiotensin II exert anti-insulin effects.

Contemporary medical practice states that hyperglycemia under these conditions should be treated with insulin only if blood glucose levels are > 200 mg/dl. A recent trial showed that intensive insulin treatment of critically ill patients in the intensive care unit with the goal of maintaining blood glucose levels between 80 and 110 mg/dl significantly reduced morbidity and mortality without significant risk of hypoglycemia.[29,30]

These benefits of insulin treatment are not yet well understood, but some pathophysiological evidence suggests that hyperglycemia perpetuates the systemic proinflammatory response, and insulin –a natural endogenous hormone that has a major role in the intermediary metabolism– participates actively in the systemic anti-inflammatory response. As a result of these findings, we recommend that hyperglycemia during critical illness should be treated with insulin in order to achieve blood glucose levels in a normal range, regardless of whether or not these patients have diabetes mellitus.[29,30]

HYPERALDOSTERONISM[31,32,33,34,35,36,37]

Aldosterone is a steroid hormone produced exclusively in the zona glomerulosa of the adrenal cortex. It is the major circulating mineralocorticoid in humans. The principal regulators of its synthesis and secretion are the renin-angiotensin system and potassium ion concentration.

The principal site of action of aldosterone is the distal nephron, although several other sites of aldosterone-sensitive sodium regulation exist, including the sweat glands

and GI tract. Hyperaldosteronism is characterized by excessive secretion of aldosterone causing increase in sodium reabsorption and loss of potassium and hydrogen ions. It may be either primary (autonomous) or secondary.

Primary aldosteronism or primary hyperaldosteronism refers to a renin-independent increase in the secretion of aldosterone. Approximately 99% of cases of primary aldosteronism are due to either an aldosterone-producing adenoma ([APA] approximately 40% of cases) or idiopathic hyperaldosteronism ([IHA] approximately 60% of cases, almost all of which are bilateral). Primary hyperaldosteronism is principally a disease of adulthood.[31,32,33]

Inherited forms of primary hyperaldosteronism account for only 1% of cases of primary aldosteronism but are more likely to occur during childhood years. These include familial hyperaldosteronism types I,II.[33]

Secondary hyperaldosteronism, represents a diverse group of disorders characterized by physiologic activation of the renin-angiotensin-aldosterone (R-A-A) axis as a homeostatic mechanism designed to maintain serum electrolyte concentrations or fluid volume. In the presence of normal renal function, it may lead to hypokalemia. Secondary hyperaldosteronism can be divided into 2 categories depending on whether associated hypertension exists. The former category includes renovascular hypertension, which results from renal ischemia and hypoperfusion leading to activation of the R-A-A axis. The common causes of renal artery stenosis in children are fibromuscular hyperplasia and neurofibromatosis. Hypokalemia may occur in up to 20% of patients.[35]

Secondary hyperaldosteronism in the absence of hypertension occurs as a result of homeostatic attempts to maintain sodium or circulatory volume or to reduce potassium such as in diarrhea, excessive sweating, low cardiac output states and hypoalbuminemia due to liver or renal disease or nephrotic syndrome.[35]

Clinical features

Primary hyperaldosteronism may be asymptomatic, particularly in its early stages. When present, symptoms are related to hypertension (if severe), hypokalemia or both.[31,32,36]

The spectrum of hypertension-related symptoms are, headache, facial flushing and if severe, weakness, visual impairment, impaired consciousness and seizures (hypertensive encephalopathy).

Hypokalemia can be precipitated by non–potassium-sparing diuretics or sodium loading. Symptoms of hypokalemia include constipation, polyuria and polydipsia (because of impaired renal concentrating ability), weakness. If low enough, paralysis and disturbances of cardiac rhythm can occur.

If secondary hyperaldosteronism is suspected as the cause of hypertension, history should include questions about flushing, diaphoresis, anxiety attacks and headaches (pheochromocytoma) and about hematuria and abdominal fullness (Wilms or other renal tumor) in addition to the above symptoms.[35,36]

For patients in whom secondary hyperaldosteronism is suggested, questions

should be specifically directed at potential causes (eg, the presence and duration of edema the child's exercise tolerance).[35,36]

Information should be sought about a family history of essential hypertension and familial syndromes that include the following:

Neurofibromatosis (associated with renal artery stenosis and pheochromocytoma), multiple endocrine neoplasia (MEN) type 2, von hippel-lindau syndrome

Hypermineralocorticoidism should be considered in any patient with associated hypokalemia, although it should not be excluded in its absence.

Patients with significant hypertension should have their blood pressure repeated several times, preferably with an automated device after a supine rest.

Causes:

The following is a list of conditions causing hyperaldosteronism and conditions that mimic hyperaldosteronism:

Primary hyperaldosteronism [31,32,33]

- APA (Aldosterone-producing adenoma) - High aldosterone, low Plasma renin activity (PRA).
- IHA (Idiopathic hyperaldosteronism). Responds to posture
- Primary adrenal hyperplasia - Responds to posture
- GRA (Glucocorticoid remediable hyperaldosteronism) Sustained suppression

of aldosterone (<4 ng/dL) with dexamethasone.

- FH-II - Familial (probably autosomal dominant)

Secondary hyperaldosteronism [35]

- Edema disorders (eg, cardiac failure, nephrotic syndrome) - High aldosterone, nonsuppressed plasma renin activity (>2 ng/mL)
- Renovascular hypertension
- Renin-producing tumors

Lab Studies [37]

The evaluation of a patient in whom hyperaldosteronism is suggested has several distinct stages. The finding of hypertension, hypokalemia or both most commonly precipitates the decision to screen. The presence of these 2 features together has a 50% predictive value.

The first step entails confirmation that hyperaldosteronism is present and if it is not present, exclusion of other conditions that produce a similar picture.

The next step involves differentiating primary from secondary causes of hyperaldosteronism.

Medical Care [31,31,35]

Surgical excision of the affected adrenal gland is recommended for all patients with proven APA. Ensuring good control of blood pressure and replenishment of potassium levels preoperatively is important.

Medical care for IHA is as follows: Although bilateral adrenalectomy corrects hypokalemia in patients with IHA, it has not been shown to be effective at controlling blood pressure..

Control of hypokalemia and hypertension in IHA can be achieved with sodium restriction (to <2 g/d) and spironolactone or amiloride, but additional antihypertensives are often needed to achieve good control

Glucocorticoid-remediable hyperaldosteronism

- In adult patients with GRA, control of hypertension can be achieved by treatment with physiologic doses of dexamethasone. However, in children, avoiding dexamethasone is best because of its adverse effects on growth and bone density. Hydrocortisone is a better choice because of its short half-life (typical dose is 10-12 mg/m^2), but it is not as efficient at reducing mineralocorticoid levels as dexamethasone.

1. Segura matute S, Balaguer Gargallo *et al* did the study to determine the incidence and characteristics of fluid and electrolyte disorders in the immediate postoperative period after surgery for CNS tumors in children treated in their hospital [38]They retrospectively analyzed clinical and laboratory data in all infants and children who underwent surgery for CNS tumors in their hospital from January 1998 to June 2005 and who met the laboratory criteria for diabetes insipidus, SWS or SIADH.

RESULTS

Twenty-three electrolyte disorders were identified in 149 surgical patients (an incidence of 15.4%).. The most frequent electrolyte disturbance was diabetes insipidus (65.2% of all electrolyte disorders. The second most frequent electrolyte disturbance was SWS (26.1%).

2. Wong MF *et al* aimed to determine the incidence, profile and outcome of patients admitted to an 18-bedded neurosurgical intensive care unit who developed DI.[39] The overall incidence was 3.7% (29/792 admissions). Overall mortality was 72.4%. There were no deaths in the patients who underwent excision of tumours.

3. According to Michael coperman MD *et al* study, there is no sex predilection in central diabetes insipidus.[6]

4. Garcia Garcia et al did the study on central diabetes insipidus. The aim of this study was to document the etiology of central diabetes insipidus (CDI) in children under fourteen years of age: A descriptive-retrospective study using the

records of 33 children diagnosed to have CDI between January 1988 and December 1997 was performed.[40,41,42,43,44]

RESULTS: Brain death produced CDI in seventeen patients, intracranial tumors in five (after excision of the tumor) and other causes in seven. No etiology was detected in four.

5. The etiology of diabetes insipidus (DI) was determined in 73 children evaluated from 1962 through 1983 by Greger NG, Kirkland RT *et al.*Intracranial tumors produced DI in 34 children, but 27 of these 34 children developed DI only after excision of the tumor. Diabetes insipidus occurred in ten children with intracranial birth defects, eight with severe central nervous system infections, and six with histiocytosis. Six had other causes. No etiology was detected in nine.[5,7,45]

6. Jaruratanasirikul S et al, retrospectively reviewed the records of children with central DI identified at Songklanagarind Hospital from 1985 to 2000. Of the total 29 patients identified, 16 patients were males and 13 were females. All patients received computed tomography or magnetic resonance imaging of the brain to differentiate the etiologies of central DI.[5,7,46]

The etiologies of central DI were intracranial tumors in 7 patients (24.1%), histiocytosis in 3 patients (10.3%), septooptic dysplasia in 1 patient (3.5%), empty-sella syndrome in 1 patient (3.5%), pituitary abscess in 1 patient (3.5%), and idiopathic in 16 patients (55.1%)

7. Maghnie M, Cosi G *et al*, studied all 79 patients with central diabetes insipidus who were seen at four pediatric endocrinology units between 1970 and 1996. There were 37 male and 42 female patients whose median age at diagnosis was 7.0 years (range, 0.1 to 24.8). All patients underwent magnetic resonance imaging (MRI) and periodic studies of anterior pituitary function .[5,7,47]

RESULTS:

The causes of the central diabetes insipidus were Langerhans-cell histiocytosis in 12 patients, an intracranial tumor in 18 patients, a skull fracture in 2 patients, and autoimmune polyendocrinopathy in 1 patient; 5 patients had familial disease. The cause was considered to be idiopathic in 41 patients (52 percent).

8. Amar Agha, Evan Thornton *et al* aimed to evaluate the prevalence of posterior pituitary dysfunction in a large cohort of survivors of TBI(Traumatic brain injury).[5,7,48] One hundred two consecutive patients (85 males) who suffered severe or moderate TBI were evaluated for diabetes insipidus (DI) at a median of 17 months (range 6–36 months) after the event, using the 8-h water deprivation test (WDT). Their results were compared against normative data obtained from 27 matched, healthy controls. Patients' medical records were retrospectively reviewed for the presence of abnormalities of salt and water balance in the immediate post-TBI period.

Twenty-two patients (21.6%) developed DI in the immediate post-TBI period (acute DI group), Patients in the acute and permanent DI groups were more likely to have more severe TBI, compared with the rest of the cohort ($P < 0.05$). In the immediate post-TBI period, 13 patients (12.9%) had syndrome of inappropriate secretion of

antidiuretic hormone, which persisted in one patient, and one other patient developed cerebral salt wasting.

Permanent DI was present in 6.9% of patients who survived severe or moderate TBI, which is higher than traditionally thought. Identification of patients with partial posttraumatic DI is important because appropriate treatment may reduce morbidity and optimize the potential for recovery. [5,7,48]

9. Gu F,Jin Z *et al,* studied clinical data of 408 cases with CDI treated in Peking Union Medical College Hospital between 1956 and 2000, including 113 cases caused by tumors in sella region, were analyzed retrospectively. Follow-up for three months to 16 years was made to 35 cases of CDI without etiological diagnosis during the first visit.[5,7,49]

10. Kabakus N Yilmaz B *et al* reported transient DI as a complication of Escherichia coli (E.coli) meningitis due to ventriculoperitoneal shunt in an 18-month-old boy is presented. [50]

11. Lee YJ, Huang FY,Shen FY *et al* studied diabetes insipidus in hypoxic encephalopathy babies.Hypoxic encephalopathy is rarely mentioned as a cause of neurogenic diabetes insipidus (DI) in children.They reported six cases of DI which occurred after severe hypoxic/ischaemic brain damage and include a review of the literature on 28 paediatric cases of neurogenic DI due solely to severe hypoxia/ischaemia. Airway obstruction, haemorrhagic shock and sudden infant death syndrome are the three major causes of hypoxia/ischaemia, Nineteen cases (82.6%)

developed DI within 6 days after the hypoxic/ischaemic insult. Only two neonates survived with developmental delay. The remaining 26 cases died.[51,52,53]

12. Arisaka O, Arisaka M *et al* described two children who after cardiopulmonary arrest developed hypernatremia at the terminal stage. Urinary antidiuretic hormone concentration was very low, indicating central diabetes insipidus. These cases illustrate the necessity of alertness to the development of central diabetes insipidus in patients with severe hypoxic brain damage.[51,52,54]

13. According to Hojo M,Kumo T *et al* study, Central diabetes insipidus: an ominous sign in severe hypoxic encephalopathy.[51,52,55]

14. Adunsky A, Yaretsky A *et al* reported a 13-year-old girl was admitted with meningeal signs. A lumbar puncture was followed shortly by cardiorespiratory arrest. In spite of intensive resuscitation she remained comatose and had severe polyuria diagnosed as diabetes insipidus.[51,52,56]

15. Outwater KM,Rockoff MA *et al* studied,diabetes insipidus (DI) developed in 14 of 16 children who satisfied criteria for brain death.

The occurrence of DI after an hypoxic/ischemic insult may represent midbrain death and seems to be a clinically useful sign in the diagnosis of brain death in children. In two patients, DI resolved spontaneously.[40,41,42,43,44,51,52,57]

16. Fisser DH,Jimenez JF *et al* studied, central diabetes insipidus (DI) in patients suffering from overwhelming CNS injuries leading to brain death. The purpose

of this study was to describe the clinical presentation of DI in children with brain death. The medical records of 34 patients with a diagnosis of brain death were reviewed. Diuresis was present in 76% of patients; however, DI was present only in 38% of patients.[40,41,42,43,44,58]

They concluded that DI is present in many, but not all, patients who experience brain death and therefore, cannot be relied on solely as a marker of brain death.

17. Jayakumar Indira, Ranjit S, Balasubramaniam S *et al* did the study in intensive care unit. The objective of the study was to determine the etiology, evaluate treatment modalites and assess the outcome in children with an underlying acute neurologic disease who were hyponatremic. All these children were admitted to the Intensive Care Unit (ICU).

Out of 1371 Pediatric Intensive Care Unit (PICU) admissions over a 30-month period, 385 (28%) had primary CNS disorders and of these, 58 were hyponatremic. The causes were SIADH in 19 (33%), hyponatremic dehydration in 16 (28%), drug-induced hyponatremia in 13 (22%) and CSW in 10 (17%) patients. The overall incidence of salt wasting syndrome is 0.7%. About 10 of the 58 hyponatremic patients expired. All deaths were due to the severity of the underlying neurological condition .[11,12,13,14,15,59]

18. Bussmann C, Bast T, Rating D *et al* conducted a retrospective analysis of electrolyte disturbances in 195 children with various acute CNS diseases. In 20 children (10.3%) hyponatraemia with plasma sodium below 130 mmol/l was identified. On the basis of clinical and laboratory data 7 of these 20 children were diagnosed as SIADH,

and the other 9 children, as CSW. Our data suggest that hyponatraemia attributable to CSW is at least as frequent in children as SIADH. The incidence of saltwasting among cases with electrolyte imbalance is 4.6%.[11,12,13,14,15,60]

19. James Springate *et al* study on the salt wasting syndrome, showed no sex predilection.[12]

20. Jimenez R, Casado-Flores J *et al* have done a study to describe the causes, clinical pattern and treatment of cerebral salt wasting syndrome in children with acute central nervous system injury. This retrospective study focused on patients<15 years old diagnosed with cerebral salt wasting syndrome, over a period of 7 years, in the pediatric intensive care unit of a tertiary care hospital.[12,14]

Fourteen patients were identified with cerebral salt wasting syndrome, 12 after a neurosurgical procedure (8 brain tumor, 4 hydrocephalus) and 2 after severe brain trauma. In 11 patients the cerebral salt wasting syndrome was diagnosed during the first 48 hours of admission.

In conclusion, cerebral salt wasting syndrome can complicate the postoperative course of children with brain injury; it is frequently present after surgery for brain tumors and hydrocephalus and in patients with severe head trauma.[12,14]

21. John W., Christopher W *et al* reported, Cerebral Salt Wasting Syndrome following Brain Injury in Three Pediatric Patients.[61]

22. Askar Akram, Tarif Nauman *et al,* reported a case of CSW in a patient with head trauma without evidence of cerebrovascular injury or brain edema. They have diagnosed on the basis of high fractional excretion of urinary sodium and uric acid along with extremely low serum uric acid.[62]

23. Lee SJ *et al*, made a diagnosis of CSW syndrome in two craniosynostosis children manifesting postoperative hyponatremia and supplied them an appropriate amount of water and sodium via intravenous route. The hyponatremia or natricuresis of the children improved .[63]

24. Berger TM *et al*, reported a 3-yr-old boy with a cerebral infarct secondary to traumatic carotid artery dissection who developed hyponatremia associated with weight loss and excessive renal sodium excretion on the sixth day after hospitalization. [64]

25. Namba T, Harada T *et al* reported a case of Cerebral salt wasting syndrome in a patient with viral meningoencephalitis.[65]

26. Huang SM *et al*, described a 3-year-old boy with tuberculous meningitis complicated by hydrocephalus and CSWS and emphasize the different clinical presentation and management of patients with CSWS. [66]

27. Dass R, Nagaraj R *et al*, reported a12-year-old boy with tuberculous meningitis and hydrocephalous, after undergoing revision of ventriculo-peritoneal shunt had persistent impairment of sensorium and episodes of hyponatremia (serum sodium 104 to 125 mmol/l), accompanied by polyuria, signs of poor peripheral perfusion

hypotension and low CVP and high urinary sodium excretion (114-60 mmol/l).A diagnosis of cerebral salt wasting syndrome (CSWS) was made.[67]

28. Craig G.N. Campbell *et al* studied the, Medical and Cognitive Outcome in Children with Traumatic Brain Injury. This study describes a population of Canadian children who suffered moderate or severe traumatic brain injury. Initial GCS was the best predictor of mortality and cognitive outcome.[68,69,70]

29. Barsic E, Marton *et al*, in this prospective study the Glasgow Coma Scale (GCS) score was evaluated in 107 critically ill infectious disease (ID) patients admitted to the Intensive Care Unit (ICU) during a 1-year period. Univariate logistic regression analysis confirmed a significant relationship between the first ICU day GCS score and the subsequent ICU mortality in the group of patients with CNS infections (r=0.3152, p=0.0015) but not in the group with infections not affecting the CNS.[68,69,71]

30. P.C. Nayana Prabha, P. Nalini, V *et al* done a study to know the role of glasgow coma scale in non traumatic coma. They concluded that ocular, motor response scores and brainstem reflexes are more predictive of the short-term outcome than the total GCS score. A score incorporating ocular response, motor response and brain stem reflexes should be evaluated to assess the outcome in nontraumatic coma in the pediatric population.[68,69,72]

31. Springer Berlin and Heidelberg *et al*, studied the severity of illness, particularly the presence of shock or coma, in meningitis was significantly associated with poor outcome in PICU. All admissions with a diagnosis of meningitis between

1995 and 2000 in the Pediatric Intensive Care Unit Evaluations (PICUEs) database.[73,74,75]

32. Peter Lindvall, Clas Ahlm *et al* have reported findings concerning continuous intracranial pressure (ICP) and cerebral perfusion pressure (CPP) measurements and mortality in patients with severe bacterial meningitis treated on the basis of an ICP targeted approach.[76,77]

Eighteen patients with severe bacterial meningitis were admitted for neurointensive care at Umeå University Hospital (Umeå, Sweden). In 15 patients, ICP was measured continuously through an ICP measuring device. During care, all patients but one developed intracranial hypertension with an ICP of 15 mm Hg (14 [93%] of 15 patients). Ten (67%) of 15 patients survived and were discharged and 5 patients (33%) died.

Mean ICP was significantly higher and CPP was markedly decreased in nonsurvivors compared with survivors. Among the survivors, ICP was gradually reduced.[76,77]

33. Singh D, Chopra A *et al* done a prospective study to determine the frequency, etiology, type and outcome of shock in hospitalized children in the age group of 1 month to 15 years.

Compensated stage was common in hypovolemic shock (88.9%) whereas majority of patients with septic shock (73.5%) presented in decompensated stage. Diagnosis and management of shock in compensated stage carried better prognosis than in uncompensated shock irrespective of the age of the patient.[73,74,78]

34. Post hoc analysis of the Leuven *et al* revealed a linear correlation between the degree of hyperglycemia and the risk of death, which persisted after correction for insulin dose and severity of illness scores.

Patients in the conventional insulin treatment group who showed only moderate hyperglycemia (110–150 mg/dl or 6.1–8.3 mmol/l) had a lower risk of death than those with frank hyperglycemia (150–200 mg/dl or >8.3 mmol/l) but a higher risk of death than those who were intensively treated with insulin to restore blood glucose levels to below 110 mg/dl (6.1 mmol/l)

Similarly, for the prevention of morbidity effects such as acute renal failure, bacteremia, and anemia, it appeared crucial to reduce blood glucose to below 110 mg/dl. The risk of developing critical illness polyneuropathy in particular correlated linearly with blood glucose levels.

Multivariate logistic regression analysis confirmed the independent role of blood glucose control in achieving most of the clinical benefits of intensive insulin therapy and underlined the importance of lowering the blood glucose level to strict normoglycemia.[30]

35. Srinivasan V, Spinella PC, Drott HR *et al* study its clear that, patients with higher peak blood glucose levels, higher % of PICU days with hyperglycemia, and median blood glucose levels > 150 for the first 48 hours had a higher risk of mortality. Also, there was an 8.3% mortality rate among patients with a 24 hour blood glucose < 100 while the mortality rate rose to 28.5% in those with a 24 hour blood glucose > 180.

In multivariate analysis, the authors found four significant variables that were

independently predictive of mortality: 24-hr PRISM score, use of epinephrine, peak blood glucose and duration of hyperglycemia. When adjusted for age, severity of illness and use of epinephrine, two variables remained independently associated with mortality in this population: peak blood glucose and duration of hyperglycemia.[30]

STUDY JUSTIFICATION

Polyuria is a significant co morbid condition in critically ill children which has to be recognized with reference to its etiology, as management is specific. In a critical care unit CDI and CSWS has to be differentiated since onset of CDI predicts a poor prognosis whereas CSWS is a self limiting and a treatable condition which is often overlooked.[11,12,13,14]

Central diabetes insipidus (DI) occurs in patients suffering from overwhelming CNS injuries leading to brain death. Although hypoxic/ischemic encephalopathy is very rarely associated with central diabetes insipidus, this is very common in intensive care set up. Generally it is an ominous sign of severe brain damage.[3,4,5,7,51,52,53,54,55,56]

Hyponatremia is a common electrolyte disturbance following intracranial disorders. Hyponatraemia in patients with acute central nervous system disease can be caused by two different mechanisms: (1) retention of free water, i.e. the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and (2) excessive sodium excretion, i.e., the cerebral salt wasting syndrome (CSWS). Although the concept of CSWS is well known in adult medicine, it is still not established in child neurology.

Especially two syndromes leading to hyponatremia in intracranial disorders need to be distinguished, as they resemble each other in many, but not all ways. These are the syndrome of inappropriate ADH secretion (SIADH) and the cerebral salt wasting syndrome (CSWS). The syndrome of inappropriate ADH secretion is characterized by water retention, caused by inappropriate release of ADH, leading to dilutional hyponatremia. The cerebral salt wasting syndrome on the other hand, represents primary

natriuresis, leading to hypovolemia and sodium deficit. SIADH should be treated by fluid restriction, whereas the treatment of CSWS consists of sodium and water administration.[11,12,13,14,59,60,61]

So these diseases have to be addressed appropriately in intensive care unit.

AIM OF THE STUDY

1. To study the incidence,etiology and outcome of polyuria in critically ill children.

2. To study the incidence,etiology and outcome of central diabetes insipidus (CDI) and cerebral salt wasting syndrome (CSSW) in critically ill children

3. To study the risk factors determining the outcome of polyuria.

SUBJECTS AND METHODS

Study design : Descriptive study

Study place : PICU, ICH&HC

Study period : October 2006 TO September 2007

Inclusion criteria : All cases admitted in PICU in the above mentioned period

EXCLUSION CRITERIA

Diabetic ketoacidosis(DKA),renal tubular acidosis(RTA),chronic renal failure(CRF) with concentration defect and structural abnormalities of kidney are excluded

MANEUVRE

All children developing polyuria in PICU were subjected to a detailed case history followed by meticulous clinical examination.

Depending upon the clinical presentation, necessary investigations were done like complete blood count, smear study, blood sugar, urea creatinine, electrolytes, calcium, arterial blood gas analysis,liver function tests, blood culture, urine for specific gravity, sugar, ketones, albumin,chest x ray , ultrasound abdomen and KUB.

After excluding DKA, RTA, CRF with concentration defects and structural abnormalities of kidney, the remaining cases were registered and followed up in PICU.

Further specific investigations like, serum osmolality,uric acid,urine specific gravity and osmolality, urine sodium were done simultaneously .

Depending upon the results further diagnosis was made.

Hypernatremia(S.Na >145Meq/L), urine specific gravity of 1.010 or less, a urine osmolality less than 300 mOsm/L and serum osmolality of more than 300 mosm/L are the hallmark of diabetes insipidus. After diagnosing diabetes insipidus, nasal desmopressin (10-20microgram) was given to differentiate CDI from NDI.[3,4,5,7,8,9,10.]

Repeat urine osmolality was done after 12 hrs of nasal desmopressin. Diagnosis of CDI was made with the evidence of increasing urine osmolality of more than 50% from the previous value .

Dignosis of cerebral salt wasting syndrome was made by the following criteria.[12,15]

Serum sodium : <135Meq/L.

Serum osmolality : less than 285 Meq/L

Urine osmolality : more than s.osmolality

Urine sodium : > 40Meq/L(often >150meq/L)

Urine sodium concentrations are typically elevated in both SIADH and CSWS (>40 mEq/L). However, urinary sodium excretion (urine sodium concentration [mEq/L] X urine volume [L/24 h]) is substantially higher than sodium intake in CSWS but generally equals sodium intake in SIADH. Therefore, net sodium balance (intake minus output) is negative in CSWS.[12]

Diagnosis of stress hyperglycemia was made by hyperglycemia glycosuria and elevated serum and urine osmolality. Before making diagnosis, the other causes of hyperglycemia and elevated serum and urine osmolality was excluded.[29,30]

Diagnosis of tubular dysfunction in septic shock was made by elevated renal parameters, polyuria, lower serum osmolality and urine specific gravity along with normal serum osmolality.[16,17]

STATISTICAL ANALYSIS

Meticulous data entry was made. All these parameters are formulated into tables and percentages. Statistical significance was arrived using Fischer exact test and Chi square test separetly. P value less than 0.05 was considered for statistical significance. Finally univariate analysis was done.

RESULTS

1. INCIDENCE OF POLYURIA

Total number of PICU admissions during study period = 947

Total number of polyuria cases included in study = 26

Incidence of polyuria = 26 (2.7%) ; 95% C.I. = (1.8 , 4.0)

2. ETIOLOGY OF POLYURIA

Diagnosis	n	%
Central diabetes insipidus	17	65.4
Cerebral salt wasting syndrome	7	26.9
Non-oliguric acute renal failure	1	3.8
Stress hyperglycemia	1	3.8

Out of 26 cases of polyuria, majority of cases were contributed by central diabetes insipidus (65.4%), followed by cerebral salt wasting syndrome (26.9%), non oliguric acute renal failure and polyuria induced by stress hyperglycemia contributed one case(3.8%) each.

3. INCIDENCE

Central diabetes insipidus = 17/947=1.79%

Cerebral salt wasting syndrome = 7/947 =0.7%

4. OUTCOME OF POLYURIA

Diagnosis	Improved		Death		p-value
	n	%	n	%	
Central diabetes insipidus	-	-	17	100.0	0.005
Cerebral salt wasting syndrome	3	42.9	4	57.1	
Non oliguric acute renal failure	1	100.0	-	-	
Stress hyperglycemia	-	-	1	100.0	

In this study , we studied about 26 cases. Out of 26 cases, 22 cases died and only 4 cases improved. Of the 26 cases of polyuria , 17 cases were diagnosed to have central diabetes insipidus. All those cases with central diabetes insipidus died (100% mortality). 7 cases were diagnosed to have cerebral salt wasting syndrome. Out of these 7 cases, 3 cases improved and remaining 4 cases died showing 57% mortality.

Death	n	%
Death within 48 hours	20	76.9
Death 3 to 5 days	1	3.8
Death after 5 days	1	3.8
Improved	4	15.4

Out of 22 death cases, 20 cases died within 48 hrs of onset of polyuria.

5. PRIMARY ETIOLOGY

Central diabetes insipidus

S.NO	DISEASE	N	%
1.	Tuberculous meningitis	5	29.4%
2.	Meningoencephalitis	3	17.6%
3.	Acute CNS infection	3	17.6%
4.	Intra cranial bleed	3	17.6%
5.	Acute demyelinating disorder	1	5.8%
6.	Brain tumour	1	5.8%
7.	Congenital hydrocephalus	1	5.8%
8.	Idiopathic central diabetes insipidus	1	5.8%

The primary etiology of central diabetes insipidus was mainly contributed by CNS infections. Tuberculous meningitis leads the list followed by meningoencephalitis.Diagnosis of acute CNS infection was mainly made by clinical criteria, because in these cases neuro imaging and CSF analysis were not done due to poor general condition. One child was already a known case of idiopathic CDI.

Cerebral salt wasting syndrome

S.NO	DISEASE	N	%
1.	HSV Encephalitis	2	28.5%
2.	Toxic Encephalopathy	1	14.2%
3.	Meningoencephalitis	1	14.2%
4.	Acute CNS infection	1	14.2%
5.	Tuberculous meningitis	1	14.2%
6.	Seizure disorder	1	14.2%

6. SEX RATIO

S.NO	DISEASE	BOY	GIRL
1.	Central diabetes insipidus	6 (35.2%)	11 (64.8%)
2.	Cerebral salt wasting syndromee	4 (57.1%)	3 (42.9%)

There is a male predominance in cerebral salt wasting syndrome and female predominance in central diabetes insipidus in our study

7. FACTORS DETERMINING OUTCOME

SYMPTOMS

Symptoms	Improved		Death		p-value
	n	%	n	%	
Fever					
Yes	1	5.6	17	94.4	0.07
No	3	37.5	5	62.5	
Seizure					
Yes	4	25.0	12	75.0	0.14
No	0	-	10	100.0	
Posturing					
Yes	2	11.1	16	88.9	0.56
No	4	25.0	6	75.0	
Altered level of consciousness					
Yes	4	15.4	22	84.6	-
No	-	-	-	-	

Out of 22 cases who died, 17 cases (77%)presented with fever, 12 cases presented with seizures and 16 cases with posturing.

Out of the 4 cases who improved, all the 4 presented with seizures, 2cases with posturing and one with fever.

All 26 cases had altered level of consciousness at the time of PICU admission.

GLASGOW COMA SCALE

Glasgow coma scale	Improved		Death		p-value
	n	%	n	%	
At the time of PICU admission					
3	1	9.1	10	90.9	
4 – 8	-	-	10	100.0	0.007
>8	3	60.0	2	40.0	
During polyuria					
3	-	-	18	100.0	
4 – 8	3	42.9	4	57.1	0.002
>8	1	100.0	-	-	
24 hrs after the correction of polyuria					
3	-	-	21	100.0	
4 – 8	1	50.0	1	50.0	0.00
>8	3	100.0	-	-	

Glasgow coma scale was compared at the time of admission, at the time of polyuria and 24 hours after the correction of polyuria

In these 22 death cases, 20 cases had GCS less than 8 at the of admission itself. Out of 22 cases, 18 cases had GCS 3 at the time polyuria and 21 cases had GCS 3 at 24 hours after the correction of polyuria. All the cases died.

SHOCK

Shock	Improved		Death		p-value
	n	%	n	%	
At the time of PICU admission					
Decompensated	-	-	-	-	1.00

Compensated	2	13.3	13	86.7	
No	2	18.2	9	81.8	
During polyuria					
Decompensated	-	-	9	100.0	0.008
Compensated	1	8.3	11	91.7	
No	3	60.0	2	40.0	
24 hrs after the correction of polyuria					
Decompensated	-	-	11	100.0	0.02
Compensated	1	11.1	8	88.9	
No	3	50.0	3	50.0	

Of the 22 cases which died, 13 cases had compensated shock at the time of admission itself. Proportion of cases with decompensated shock increased during hospital stay. 11 cases developed decompensated shock after admission and all of them died.

INOTROPIC SUPPORT

Inotropic support	Improved		Death		p-value
	n	%	n	%	
At the time of PICU admission					
Adrenaline	1	50.0	1	50.0	0.29
Dopamine or dobutamine	1	7.7	12	92.3	
No	2	18.2	9	81.8	
During polyuria					
Adrenaline	-	-	8	100.0	0.02
Dopamine or dobutamine	1	8.3	11	91.7	
No	3	50.0	3	50.0	
24 hrs after the correction of polyuria					
Adrenaline	-	-	9	100.0	
Dopamine or dobutamine	1	9.1	10	90.9	
No	3	50.0	3	50.0	0.02

Only one of survived cases required adrenaline infusion at the time of admission, because of post cardiac arrest state and subsequently improved. Those cases required

adrenaline infusion(10 cases) at the time of polyuria, had 100% mortality. These are statistically significant.

SIGNS

Signs	Improved		Death		p-value
	n	%	n	%	
Signs of raised intracranial tension					
Yes	1	4.5	21	95.5	0.006
No	3	75.0	1	25.0	
Required mechanical ventilation					-
Yes	4	15.4	22	84.6	
No	-	-	-	-	

Out of the 26 cases, 22 had signs of raised intracranial pressure and 21 died. All these are statistically significant.

Interestingly all 26 cases of polyuria required mechanical ventilation.

BLOOD SUGAR

Blood sugar	Improved		Death		p-value
	n	%	n	%	
At the time of PICU admission					
More than 200 mg/dl	1	100.0	-	-	0.05
More than 126 mg/dl	-	-	3	100.0	
Normal range	3	13.6	19	86.4	
During polyuria					
More than 200 mg/dl	-	-	6	100.0	0.06
More than 126 mg/dl	3	42.9	4	57.1	
Normal range	1	7.7	12	92.3	
24 hrs after the correction of polyuria					0.53

More than 200 mg/dl	-	-	5	100.0	
More than 126 mg/dl	1	25.0	3	75.0	
Normal range	3	17.6	14	82.4	

URINE SUGAR

Urine sugar	Improved		Death		p-value
	n	%	n	%	
Urine sugar at the time of PICU admission					
Glycosuria	1	100.0	-	-	0.15
Normal	3	12.0	22	88.0	
Urine sugar during polyuria					
Glycosuria	1	20.0	4	80.0	1.00
Normal	3	14.3	18	85.7	
Urine sugar at 24 after the end of polyuria					
Glycosuria	-	-	4	100.0	1.00
Normal	4	18.2	18	81.8	

Out of 26 cases, 3 cases had hyperglycemia at the time of admission and 10 cases had at the time of polyuria. Out of 10 hyperglycemic cases, 9 cases died. Out of these 10 cases, 6 had hyperglycemia of more than 200mg/dl. These cases had 100% mortality.

Out of 6 cases with hyperglycemia of more than 200mg/dl. Only 4 cases showed glycosuria.

SERUM SODIUM

Serum sodium	Improved		Death		p-value
	n	%	n	%	
At the time of PICU admission					
More than 145meq/l	-	-	3	100.0	0.71
Less than 135meq/l	1	14.3	6	85.7	
Normal range	3	18.8	13	81.3	
During polyuria					
More than 145meq/l	1	5.6	17	94.4	0.06
Less than 135meq/l	3	42.9	4	57.1	
Normal range	-	-	1	100.0	
24 hrs after the correction of polyuria					0.61
More than 145meq/l	1	9.1	10	90.9	

Less than 135meq/l	-	-	-	-	
Normal range	3	20.0	12	80.0	

Depending upon the etiology and physiological status, serum sodium level showed abnormalities. But none of them was statistically significant.

Out of 26 cases, 18 cases showed hypernatremia during polyuria. 17 cases died because of underlying etiology .i.e. central diabetes insipidus. Among 26 polyuria cases, 7 cases had hyponatremia during polyuria. Though hyponatremia was corrected in all the cases, only 3 cases improved and remaining 4 cases died due to underlying etiology.

SERUM POTASSIUM LEVEL

Serum potassium	**Improved**		**Death**		**p-value**
	n	**%**	**n**	**%**	
At the time of PICU admission					
Less than 2.5 meq/l	-	-	1	100.0	0.91
2.5 to 3.5 meq/l	1	16.7	5	83.3	
Normal range	3	15.8	16	84.2	
During polyuria					
Less than 2.5 meq/l	1	14.3	6	85.7	0.19
2.5 to 3.5 meq/l	-	-	9	100.0	
Normal range	3	30.0	7	70.0	

In the total 26 cases studied, 17 cases were found to have hypokalemia. In these 17 cases, 7 had severe hypokalemia.

Urine specific gravity showed exact correlation with urine osmolality. Out of 26 cases of polyuria, 18 cases showed low specific gravity at the time of polyuria. Of the 18 cases, 17 cases were diagnosed to have central diabetes insipidus and remaining one was

diagnosed to have non oliguric renal failure.

8 cases showed high specific gravity at the time of polyuria. Of which 7 cases diagnosed to have cerebral salt wasting syndrome and remaining one was found to have stress hyperglycemia.

URINE SPECIFIC GRAVITY

Urine specific gravity	Improved		Death		p-value
	n	%	n	%	
At the time of PICU admission					
Less than 1.010	-	-	2	100.0	1.00
More than 1.025	-	-	-	-	
Normal range	4	16.7	20	83.3	
During polyuria					
Less than 1.010	1	5.5	17	94.4	0.29
More than 1.025	3	37.5	5	62.5	
Normal range	-	-	-	-	

P0LYURIA

Polyuria	Improved		Death		p-value
	n	%	n	%	
Duration					
More than 3 days	-	-	6	100.0	0.04
1 to 3 days	3	15.8	16	84.2	
12 to 24 hrs	1	100.0	-	-	
Quantity					
More than 10 ml/kg/hr	2	22.2	7	77.8	0.59
Less than 10 ml/kg/hr	2	11.8	15	88.2	

In 22 cases of polyuria, 6 cases showed polyuria of more than 3 days duration. All those cases died.

UNIVARIATE LOGISTIC REGRESSION

RISKFACTORS FOR DEATH AMONG IN CHILDREN WITH POLYURIA IN PICU

	OR	CI	P
GCS at the time of PICU admission			
<=8	30.0	2.0 , 441.8	0.01
>8	1.0	Reference	
Shock during polyuria			
Yes	30.0	2.0 , 441.8	0.01
No	1.0	Reference	
Shock at 24 hrs after the correction of polyuria			
Yes	19.0	1.5 , 248.2	0.03
No	1.0	Reference	
Requires inotropic support during polyuria			
Inotropes	19.0	1.5 , 248.2	0.03
No inotropes	1.0	Reference	
Requires inotropic support at 24 hrs after the correction of polyuria			
Inotropes	19.0	1.5 , 248.2	0.03
No inotropes	1.0	Reference	
Signs of raised intracranial tension			
Yes	63.0	3.1 , 1296.5	0.007
No	1.0	Reference	

Factors associated with poor outcome are GCS<8 at the of admission (O.R 30), shock during polyuria(OR 30), shock at 24hrs after the correction of polyuria(OR 19), requirement of inotropic support during polyuria (OR 19), at 24 hrs after the correction of polyuria (OR19) and signs of increased intra cranial pressure(OR 63).

DISCUSSION

Polyuria is a common condition in paediatric intensive care unit.

Common causes in critically ill children include [1,2]

Diabetic ketoacidosis

Renal tubular acidosis

Chronic renal failure with concentration defects

Osmotic diuresis(mannitol,urea,sorbitol

After excluding all the common causes of polyuria in our study, remaining diseases are,

1.Central diabetes insipidus

2.Cerebral salt wasting syndrome

3. Non oliguric renal failure

4. Stress hyperglycemia

5. Hyperaldosteronism

Out of these 5 diseases, central diabetes insipidus, and Cerebral salt wasting

syndrome are the leading causes of polyuria in paediatric intensive care unit.

Incidence of polyuria in our study is 2.7%. There is no similar study to compare the incidence of polyuria in intensive care unit. Most of the studies concentrated around the diabetes insipidus.

In our study, central diabetes insipidus tops the list (65.4%), closely followed by cerebral salt wasting syndrome(26.9%).Non oliguric acute renal failure and stress hyperglycemia contributed 3.8% each.

According to Segura matute S,Balaguer Gargallo *et al* study, the most frequent electrolyte disturbance was diabetes insipidus (65.2% of all electrolyte disorders. The second most frequent electrolyte disturbance was SWS (26.1%). Only two patients developed SIADH.[38]

In both our study and study of these authors, central diabetes insipidus is the common disease followed by Cerebral salt wasting syndrome.

Central diabetes insipidus

The overall incidence of central diabetes insipidus in our study is 1.79%. We had 17 cases of central diabetes insipidus, out of 947 admissions during study period.

Wong MF, Chin NM *et al*, did a similar study in neurosurgical intensive care unit. The overall incidence was 3.7% (29/792 admissions).[39]

The incidence in our study is less than wong MF et all study. The reason may be,

we studied the disease in genereal ICU unlike their study .

In our study, there is a female predominance CDI. But as such there is no predilection in sex in other study. According to Michael coperman MD *et al* study, there is no sex predilection.[6]. The difference may be due to smaller sample size in our study.

The primary etiology of central diabetes insipidus in our study being,

Tubercular meningitis	29.4%
Meningoencephalitis	17.8%
Intracranial bleed	17.8%.

Garcia Garcia et al have done a similar study. He concluded that the most frequent etiology of CDI in children was brain death (51%).[40,41,42,43,43]

The etiology of diabetes insipidus (DI) was determined in 73 children evaluated from 1962 through 1983 by Greger NG, Kirkland RT *et al.*Diabetes insipidus occurred in 34 children with intracranial tumors, ten children with intracranial birth defects, eight with severe central nervous system infections, and six with histiocytosis. Six had other causes. No etiology was detected in nine.[5,7,45]

Jaruratanasirikul S et al, retrospectively reviewed the records of children with central DI identified at Songklanagarind Hospital from 1985 to 2000. He concluded that the common etiologies of central DI are intracranial tumor and idiopathic,[5,7,46]

Maghnie M, Cosi G *et al*, studied all 79 patients with central diabetes insipidus who were seen at four pediatric endocrinology units between 1970 and 1996. The causes of the central diabetes insipidus were Langerhans-cell histiocytosis in 12 patients, an intracranial tumor in 18 patients, a skull fracture in 2 patients, and autoimmune polyendocrinopathy in 1 patient; 5 patients had familial disease. The cause was considered to be idiopathic in 41 patients (52 percent). [5,7,47]

All these 4 studies were retrospective studies. They studied the etiology of the disease over the years and except the study by Garcia et al, all studies were done in stable patients. From all these studies, we know that most common cause is idiopathic, followed by tumors. The only comparable study to our study is Garcia et al study, which was done in PICU. They found that the most common cause was brain death without considering about the primary diagnosis.

In our study also, most of the cases had GCS <8, absent brainstem reflexes, decompensated shock and required adrenaline infusion. More than that all our 17 cases of CDI have died. So it is clear that both Garcia et al study and our study are almost similar.

In our study, 17 cases were diagnosed to have central diabetes insipidus. These cases had 100% mortality.

According to Wong MF *et al* study, Overall mortality was 72.4%. There were no deaths in the patients who underwent excision of tumours. Careful diagnosis and management of DI after hypothalamo-neurohypophyseal surgery did not result in any

permanent neurological sequelae.[39]

Amar Agha, Evan Thornton *et al* **,** aimed to evaluate the prevalence of posterior pituitary dysfunction in a large cohort of survivors of traumatic brain injury(TBI). They concluded that identification of patients with partial posttraumatic DI is important because appropriate treatment may reduce morbidity and optimize the potential for recovery.[5,7,48]

Kabakus N Yilmaz B *et al* reported transient DI as a complication of Escherichia coli (E. coli) meningitis due to ventriculoperitoneal shunt.[50]

Lee YJ, Huang FY,Shen FY *et al* studied diabetes insipidus in hypoxic encephalopathy babies. They reported six cases of DI which occurred after severe hypoxic/ischaemic brain damage .[51,52,53]

Arisaka O, Arisaka M *et al* described two children who after cardiopulmonary arrest developed hypernatremia at the terminal stage. Urinary antidiuretic hormone concentration was very low, indicating central diabetes insipidus.[51,52,54]

According to Hojo M,Kumo T et all study, Central diabetes insipidus: an ominous sign in severe hypoxic encephalopathy.[51,52,55]

According to Garcia Garcia et al ,study the most frequent etiology of CDI in children was brain death (51%) in PICU .[40]

In Adunsky A, Yaretsky A *et al* study,he concluded that the differential diagnosis of dehydration and polyuria in patients after cardiorespiratory arrest and resuscitation

should include hypothalamic injury causing diabetes insipidus.[51,52,56]

By comparing our study with all these 7 studies,it is clear that prognosis of central diabetes insipidus depends upon the primary etiology. Those cases of idiopathic CDI, secondary to brain tumors and intracranial surgery have a good prognosis provided it is suspected, diagnosed and treated appropriately. But those cases developed secondary to cardiac arrest, decompensated shock and episodes of airway obstruction will have a grave prognosis. In our study, we had 17 cases, all these cases had any two of above risk factors.

Of these 17 cases of CDI, 14 cases had GCS 3 at the time of diagnosis. More than 90% died within 48 hours of diagnosis. Those cases with GCS 3, had non reactive pupils, absent dolls eye movement and absent gag reflexes. This is to say that 14 out of 17 cases had clinical signs of brain death.

By observing all these findings, in a background of CNS etiology and hypoxic episodes as described earlier, can we say the occurrence of CDI as a clinical marker of brain death?

This is very controversial. Supporting studies are there on either side.

According to Outwater KM,Rockoff MA *et al* study, the occurrence of DI after an hypoxic/ischemic insult may represent midbrain death and seems to be a clinically useful sign in diagnosing brain death in children.[40,41,42,43,43,51,52,57]

But Fisser DH, Jimenez JF *et al*, concluded that DI is present in many, but not all, patients who experience brain death and therefore, cannot be relied on solely as a marker of brain death. So this aspect needs further studies.[40,41,42,43,44,58]

CEREBRAL SALT WASTING SYNDROME

We had 7 cases of cerebral salt wasting syndrome out of 947 admissions during the study period. The overall incidence of cerebral salt wasting syndrome in our study is 0.73%

Jayakumar Indira, Ranjit S, Balasubramaniam S et al have done a similar study. The overall incidence of salt wasting syndrome is 0.7%.[11,12,13,14,15,59]

Bussmann C, Bast T, Rating D et al conducted a retrospective analysis of electrolyte disturbances in 195 children with various acute CNS diseases. On the basis of clinical and laboratory data 7 of these 20 children were diagnosed as having SIADH, and the other 9 children, as having CSW. Their data suggest that hyponatraemia attributable to CSW is atleast as frequent in children as SIADH. The incidence of saltwasting among the cases with electrolyte disturbances is 4.6%.[11,12,13,14,15,60]

By comparing with Jayakumar et al study, the incidence of salt wasting is almost similar. Both the studies were done in PICU admitting all the cases. Bussman et all study was done in only those childrens with electrolyte disturbances. So as expected, incidence was high in second study.

In our study, there is a male predominance. In the study by James Springate *et al,* there was no sex predilection.[12]

In general, cerebral salt wasting syndrome, will have a primary CNS pathlogy. It can be due to tumors,infections.hemorrhage and congenital anomalies. In our study, we

had 7 cases of CSSW out of 26 cases.

In these, infections lead the list.

HSV Encephalitis	28.5%
Tuberculous meningitis	14.2%
Toxic Encephalopathy	14.2%
Meningoencephalitis	14.2%
Acute CNS infection	14.2%
Seizure disorder	14.2%

As a whole, salt wasting syndrome is not a well recognised disease. The association between hyponatremia and intracranial pathology has been well described. When accompanied by natriuresis, hyponatremia has most commonly been attributed to inappropriate secretion of antidiuretic hormone. However, there is growing evidence to suggest that many of these patients may actually have cerebrally mediated salt losses, a disorder referred to as the cerebral salt wasting syndrome (CSWS). While this syndrome has been reasonably well described in adults, data regarding CSWS in pediatric-aged patients remains sparse.

Jimenez R, Casado-Flores J *et al* have done a study, to describe the causes, clinical pattern, and treatment of cerebral salt wasting syndrome in children with acute central nervous system injury. In conclusion, cerebral salt wasting syndrome can complicate the postoperative course of children with brain injury.[11,12] John W.,

Christopher W *et al* reported, Cerebral Salt Wasting Syndrome following Brain Injury in 3 Pediatric Patients. [61]

Askar Akram, Tarif Nauman *et al*, reported a case of CSW in a patient with head trauma without evidence of cerebrovascular injury or brain edema.[62]

Lee SJ *et al,* made a diagnosis of CSW syndrome in two craniosynostosis children manifesting postoperative hyponatremia.[63] Berger TM *et al*, reported, a 3-yr-old boy with a cerebral infarct secondary to traumatic carotid artery dissection who developed hyponatremia [64]. Namba T, Harada T *et al* reported a case of Cerebral salt wasting syndrome in a patient with viral meningoencephalitis.[65] Huang SM *et al*, described a CSWS in a 3-year-old boy with tuberculous meningitis complicated by hydrocephalus. [66.]Dass R, Nagaraj R *et al*, reported a 12-year-old boy with tuberculous meningitis and hydrocephalus, after undergoing revision of ventriculo-peritoneal shunt.[67]

By comparing with all these studies, we know that cerebral salt wasting is also having a definite CNS pathology.

In our study, we had 7 cases of salt wasting syndrome. Out of these 4 cases died contributing to 57% mortality. But in general CSWS usually appears in the first week after brain injury and spontaneously resolves in 2-4 weeks. The mortality in salt wasting syndrome depends on primary disease, associated risk factors like decompensated shock, raised ICP and failure to recognise it as a separate entity from SIADH.

Failure to distinguish CSWS from SIADH as the cause of hyponatremia will lead to improper therapy (ie, fluid restriction), thereby exacerbating intravascular volume

depletion and potentially jeopardizing cerebral perfusion.

In our study, we had 4 deaths out of 7. All these 4 cases had GCS<8, decompensated shock and raised ICP signs. All these factors are well emphasized in Jayakumar *et al* study.

FACTORS DETERMINING OUTCOME OF POLYURIA

Out of so many factors observed during the study, the following factors are statstically significant.

1. Low Glasgow coma scale along with absent brainstem reflexes
2. Signs of raised intra cranial pressure
3. Presence of circulatory shock during PICU stay
4. Requiring inotropic support during polyuria
5. Hyperglycemia >200mg/dl during PICU stay

In our study 22 cases died out of 26 cases, having 84% mortality.

In all these 22 death cases, 20 cases had GCS less than 8 at the of admission itself. Out of 22 cases, 18 cases had GCS 3 at the time polyuria. All the cases died. At the same time ,those cases having GCS 3 ,had non reactive pupils,absent dolls eye movements and absent gag reflexes.

According to Craig G.N. Campbell *et al* and Barsic E, Marton *et al*,initial GCS was the best predictor of mortality.[68,69,70,71]

P.C. Nayana Prabha, P. Nalini, V *et al* done a study to know the role of glasgow coma scale in non traumatic coma. They concluded that ocular, motor response scores and brainstem reflexes are more predictive of the short-term outcome than the total GCS score. [68,69,72.]

Springer Berlin and Heidelberg *et al*, concluded that the severity of illness, particularly the presence of shock or coma, in meningitis was significantly associated with outcome in PICU.[73,74,75]

In our study, 21 out of 22 death cases had signs of raised intracranial pressure.

Peter Lindvall, Clas Ahlm *et al* have, reported findings concerning continuous intracranial pressure (ICP) and cerebral perfusion pressure (CPP) measurements and mortality in patients with severe bacterial meningitis treated on the basis of an ICP targeted approach.[76,77]

In our study, those cases presented with decompensated shock any time during hospital stay and those cases required adrenaline infusion at the time of polyuria, had 100% mortality.

Singh D, Chopra A *et al* concluded that diagnosis and management of shock in compensated stage carried better prognosis than in uncompensated shock irrespective of the age of the patient.[73,74,78]

Out of 26 cases,10 cases had hyperglycemia at the time of polyuria. Out of 10 hyperglcemic cases, 9 cases died. Out of these 10 cases ,6 had hyperglycemia of more than 200mg/dl. These cases had 100% mortality.

A post hoc analysis of the Leuven study revealed a linear correlation between the

degree of hyperglycemia and the risk of death, which persisted after correction for insulin dose and severity of illness scores.[30]

From the Srinivasan V, Spinella PC, Drott HR *et al* study its clear that patients with higher peak blood glucose levels, higher number of PICU days with hyperglycemia, and median blood glucose levels > 150 mg/dl for the first 48 hours had a higher risk of mortality. In multivariate analysis, the authors found four significant variables that were independently predictive of mortality: 24-hr PRISM score, use of epinephrine, peak blood glucose, and duration of hyperglycemia.[30]

By comparing with all these 7 studies, low Glasgow coma scale along with absent brainstem reflexes, signs of raised intra cranial pressure, presence of circulatory shock during PICU stay, requiring ionotropic support during polyuria, hyperglycemia during PICU stay have much significance in determining outcome in PICU patients with polyuria.

SUMMARY

1. Polyuria is not an uncommon entity in paediatric intensive care unit with an incidence of 2.7%.

2. In our study, central diabetes insipidus (65.4%) is the common cause of polyuria.[38]

3. Any pathology that involves central nervous system can cause central diabetes insipidus and cerebral salt wasting syndrome.[3,4,5,7],[11,12,13,14,15]

4. The outcome of central diabetes insipidus depends upon its etiology.Those diseases that develop secondary to hypoxic events like decompensated shock, airway obstruction, cardiac arrest and raised intra cranial pressure, will have grave prognosis. In our study all 17 cases died (100% mortality).[3,4,5,7,51,52,53,54,55,56]

5. Development of central diabetes insipidus, is an ominous sign indicating hypoxic encephalopathy.[3,4,5,7,51,52,53,54,55,56]

6. Cerebral salt wasting syndrome is being recognized in PICU only in recent times.[12,14]

7. Hyponatremia in CNS disorders is not always due to SIADH. This can be also due to salt wasting syndrome. This is has to be addressed because, both the entities need entirely different management.[11,12,13,14,15,59,60,61]

8. Stress hyperglycemia is a common entity in PICU.But stress hyperglycemia

causing polyuria is very rare.[29,30]

9. Septic shock patients also can develop polyuria because of associated toxin mediated tubular dysfunction.[16,17,18,21]

10. Low Glasgow coma scale along with absent brainstem reflexes, signs of raised intra cranial pressure, presence of circulatory shock during PICU stay, requirement of inotropic support during polyuria and hyperglycemia are statistically significant factors for determining outcome of polyuria.[68,69,70,71,72,73,74,75,76,77,78]

CONCLUSION

1. Polyuria is not uncommon in paediatric intensive care unit.[1,2,3,5,7,9,11,12,14]

2. Development of central diabetes insipidus, is an ominous sign of hypoxic encephalopathy. [3,4,5,7,51,52,53,55,56]

3. Cerebral salt wasting syndrome is a emerging cause of polyuria in critically ill children.[11,12,14]

4. Hyponatremia in CNS disorders is not always due to syndrome of inappropriate secretion of antidiuretic hormone and cerebral salt wasting syndrome should be considered for optimal management.[11,12,13,14,15,59,60,61]

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ANNEXURE

PROFORMA

Name

Age

M/F

Weight

I.P No

PICU No

SYMPTOMS:

Fever

Altered level of consciousness

seizures

Posturing

Weakness

Breathlessness

Headache

Vomiting

Bleeding tendencies

Loose stools

Edema

FTT

Abd.pain

Trauma

CLINICAL FEATURES:

Glasgow coma scale

Respiratory distress

Resp.failure

Shock

Blood pressure

Dehydration

Tone

Power

Deep tendon reflex

Plantar reflex

Pupils

Dolls eye movement

Gag reflex

Fundus

Signs of ICP

Bleeding manifestations

Other systems

Episodes of pneumothorax

Cardiac arrest

Urine output

INVESTIGATIONS

Complete blood count

Smear study

Blood sugar

Urea

Creatinine,

Electrolytes,

Calcium,

Liver function tests

Arterial blood gas analysis,

Blood culture

Urine culture,

HIV

Viral studies

CSF analysis

Urine for specific gravity, sugar, ketones, albumin,

Chest x ray ,

Ultrasound abdomen and KUB.

Computed tomography

MRI brain

SERUM SODIUM		**IN**	
SERUM OSMOLALITY		**TER**	
SERUM URICACID		**VEN**	
URINE SODIUM		**TI**	
URINE OSMOLALITY		**ON**	

OUTCOME