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Medicine

"Study of Clinical Profile, Pathophysiological Process and Outcome in Patients Having Hyponatremia in Tertiary Care Hospital"

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Abstract **Original Research Article**

This study is aimed to study the cases of hyponatremia with regard to pathophysiology, clinical picture and outcome of treatment. In this study patients of hyponatremia admitted in ward [1, 14] and ICU of tertiary care hospital of Ahmedabad were taken. It is an observational and prospective study. Patients were more than 18 years of age various tests were performed on this patients e.g. C.B.C., ESR , ECG, chest x-ray, urine urea, urine sodium, urine glucose, blood sugar, urea, Serum creatinine. In selected cases thyroid function, cortisol level, USG abdomen, city scan were done depending on clinical suspicion. In this study 100 patients were selected from patients having serum sodium less than 130 mEq /L .in this study majority of patients were more than 45 years (78%). Irrespective of gender [6-8]. In this study severe hyponatremia (S. Na+ < 110 mEq/L) was seen in 24%. Commonest gastrointestinal symtems was vomiting, nurological symptoms were irritability, drowsiness, fatigue and coma. State of hydration showed 72% euvolemia 14% hypoeuvolemia and 14% had hypereuvolemia. In this study clinical examination showed that 42% were conscious, 30 % drowsy, 24% unconscious and 4% were restless. In patient with euvolemich hyponatremia S I A D H was commonest (58.3%) they had underline nurological or respiratory problems. In this study mortality was 16 %. Mortality was higher in euvolemic and hypervolemichyponatremia[16,17]. Two patients had hypothyroidism and two patients had hypoadrenalisum. Among patients with hypervolemic hyponatremia 3 had C.C.F [18, 19], two had CRF and 1 had cor-p and 1 had cirrhosis [20]. This study concluded that hyponatremia is common in elderly age group 72% had euvolemic hyponatremia. S I A D H was commonest cause of hyponatremia. It also concluded that rapid fall of sodium creates severe symptoms. Nausea, Vomiting, irritability and seizer were common symptoms.

Keywords: Hyponatremia, SIADH, Drowsy, Hypovolemic, CSW.

INTRODUCTION

Hyponatremiais the most common electrolyte disorder among hospitalizeed patients and has been associated with increased mortality hyponatremia is defined as serum concentration ([Na+]) less than 135 mEq/L. Hyponatremia is common In non-critical and neurocritical care patients admitted in ICU and ward[1-3]. It has significant morbidity and mortality [4]. Common pathology resulting in hyponatremia in neuro intensive care includes acute brain injury (ABI) subarachnoid haemorrhage (SAH) and traumatic brain injury. Despite plenty of research in syndrome of inappropriate antidiuretic hormone (SIADH and cerebral Salt wasting (CSW), there underline pathophysiological mechanisms are not still well understood. In this paper we will review the understanding of pathophysiology of hyponatremia in neurological and non-neurological patients. We will also review current and future challenges to diagnose and manage hyponatremia. Such challenges include distinguishing, CSW, SIADH, Hypovolemic, Hypervolemic and euvolemich hyponatremia. Greater understanding of pathophysiological of hyponatremia in critical and non-critical care patients remain our biggest challenge. The clinical manifestations of hyponatremia are produced by brain swelling and are primarily a function of the rate of fall of serum sodium concentration and not the absolute level. Symptoms occurring early in hyponatremia is usually anorexia, nausea, vomiting. Some patients may have headache and irritability. As serum sodium levels falls further patients develop neuropsychiatry symptoms. These symptoms range from restlessness, altered consciousness, lethargy, seizures to coma. In this paper

we tried to understand pathophysiology, clinical presentation and outcome of hyponatremia.

MATERIALS AND METHODS

The present study was conducted in patients admitted in the medical wards of a tertiary care hospital in western part of India over a period of two years.

SELECTION CRITERIA

Inclusion criteria

- Patients admitted to the hospital in medical wards with serum sodium levels less than or equal to 130 mEq/L are selected for the study.
- Age of the patients greater than 18years.

Exclusion criteria

- Age of the patients less than 18years.
- Patients admitted to the hospital in medical wards with serum sodium levels greater than 130mEq/L.
- Post-operative patients.
- Patients who had sodium correction already elsewhere.

STUDY PROTOCOL

Over a period of two years data on patients admitted to tertiary care hospital in the medical wards with hyponatremia were collected. Patients admitted to hospital suspected to have metabolic derangement were evaluated for biochemical abnormalities. The blood samples of these patients were sent for analysis within twenty minutes from the collection of samples. 100 patients with serum sodium level less than or equal to 130 mEq/L were randomly selected for the study. A detailed history was delineated with special thrust to the events occurred prior to admission and the symptomatology whatsoever these patients manifested at the time of admission were recorded. These patients were then evaluated clinically to access their fluid status. Based on this they were further divided as hypovolumic, euvolumic or hypervolumic patients.

The routine investigations done in these patients were the hemoglobin, total count, differentiacount, erythrocyte sedimentation rate, electrocardiogram, chest x-ray, 24 hours urine sample for urine sodium, urine urea and urine glucose, blood sugar, urea and creatinine. Patients suspected with other causes were investigated accordingly. Other investigations like thyroid function, cortisol levels, abdominal sonography, and computer tomographic scans were performed on some patients depending on the clinical suspicion.

Based on serum sodium level, these patients were divided into mild hyponatremia with serum sodium 121-130 mEq/L, moderate hyponatremia with serum sodium 111-120 mEq/L and severe hyponatremia with serum sodium less than or equal to 110 mEq/L. Based on the hydration of these cases they were further divided into hypovolumic, euvolumic and hypervolumic hyponatremia. Based on symptoms these patients were divided into symptomatic and asymptomatic patients. Symptomatic patients were further divided into mild, moderate and severe. Nausea, vomiting and headache were considered as mild symptoms, fatigue, irritability and cramps as moderate symptoms and seizures, unconsciousness as severe symptoms.

STATISTICAL METHODS

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Analysis of variance (ANOVA) has been used to find the significance of age between four groups of patients. 2x3 Fisher Exact test has been used to find the significance of study parameters on categorical scale between two groups.

1. Significant figures
+Suggestive significance (P value: $0.05<P<0.10$)
* Moderately significant (P value: $0.01<P \leq 0.05$)
**Strongly significant (P value: $P \leq 0.01$)

METHODS OF COLLECTION OF DATA

Blood samples for serum sodium, blood urea and random blood sugar. 24 hrs urine sample for urine sodium, urine urea and urine glucose

Calculation of serum and urine osmolality

$$\text{Mosm/kg} = 1.86\,(Na^{+}\ \text{m mol/L}) + \text{glucose (mg/dl)}/18 + \text{urea N (mg/dl)}/2.8+9$$

RESULTS

For this study, 100 patients were selected at random from the patients with serum sodium less than 130 mEq/L.

Among the 100 subjects studied 58 (58%) were males and 42 (42%) were females (Table-4 and Figure-5). The male to female ratio was 1.38:1

Table-1: Gender distribution

Gender	Number	%
Males	58	58
Female	42	42.0
Total	100	100.00

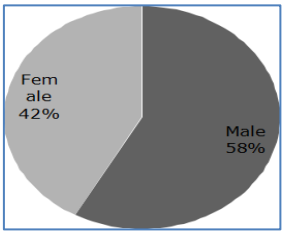

Fig-1

As reflected in total number of patients, majority were males in most of the age groups except 71-80 years, where both genders were equal. Age group of more than 80 comprised of only females.

Table-2: Age and gender distribution

Age in Years	Male		Female		Total	
	No.	%	No.	%	No.	%
20-30	4	6.9	2	4.8	6	6.0
31-40	6	10.3	2	4.8	8	8.0
41-50	12	20.7	6	14.3	18	18.0
51-60	12	20.7	10	23.8	22	22.0
61-70	14	24.1	6	14.3	20	20.0
71-80	10	17.2	10	23.8	20	20.0
>80	0	0.0	6	14.3	6	6.0
Total	58	100.00	42	100.0	100	100.0
Mean + SD	56.24 + 15.64		61.90 + 17.14		58.62 + 16.3	

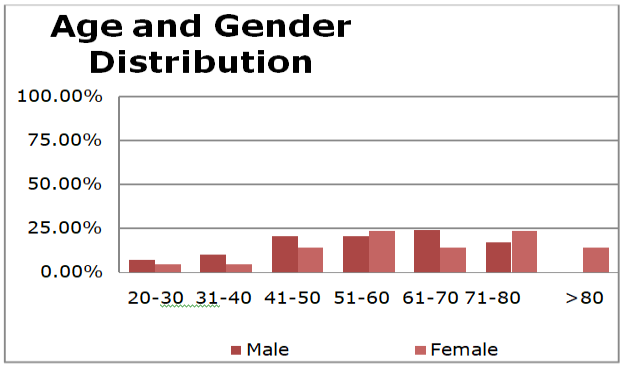

Fig-2: Graph of page 6

Patients with mild hyponatremia with serum sodium 121-130 mEq/L were 36, 40 patients had moderate hyponatremia with serum sodium between 111-120 mEq/L and 24 patients had severe hyponatremia with serum sodium less than or equal to 110 mEq/L. (Table-3 and Figure-3).

Table-3: Severity of hyponatremia

Severity of Hyponatremia	Number	%
Mild hyponatremia	36	36.0
Moderate hyponatremia	40	40.0
Severe hyponatremia	24	24.0
Total	**100**	**100.0**

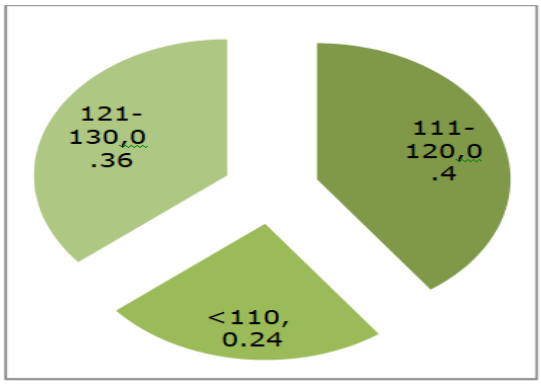

Fig-3

Based on severity of hyponatremia and age distribution (Table-4 and Figure-4) patients above the age of 45 years were found to be more in mild and moderate hyponatremia. In severe hyponatremia there were equal categories of both the age groups. Of 36 patients with mild hyponatremia, 10 patients were less than 45 years and 26 patients were more than 4 years. All 40 patients with moderatehyponatremiawereabove45years.Inseverehypo natremia, among 24patients, 12patients were above 45years and12patients were below 45 years. All the values were statistically significant.

Table-4: Age group v/s severity of hyponatremia

Age in Years	Hyponatremia			Total (n=100)
	Mild (n=36)	oderate (n=40)	Severe (n=24)	
< 45 Years	10 (27.7%)	0 (0.0%)	12(50.0%)	**22 (22.0%)**
> 45 Years	26 (72.2%)	40 (100%)	12(50.0%)	**78 (78.0%)**

(P-value=0.00001)

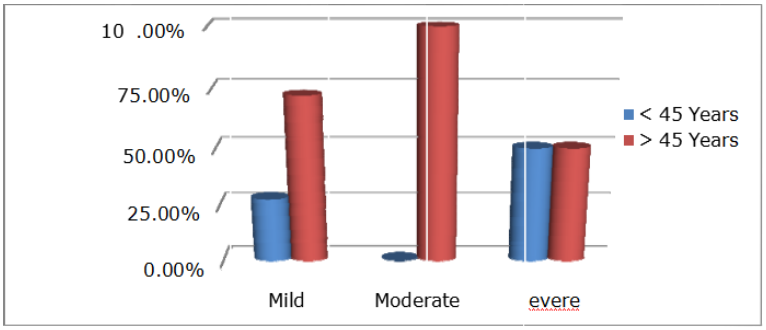

Fig-4

The symptoms of these patients varied from gastrointestinal to neurological symptoms. The gastrointestinal symptoms were predominantly nausea and vomiting and the neurological symptoms were fatigue, cramps, irritability, seizures, drowsiness and unconsciousness.

In the present study the commonest gastrointestinal symptom was vomiting and neurological symptoms were fatigue, irritability and drowsiness. The symptoms observed are represented in Table-5.

Table-5: Association of symptoms with severity of hyponatremia

Symptoms	Hyponatremia			Total (n=100)	P value
	Mild (n=36)	oderate (n=40)	Severe (n=24)		
Nausea	4 (11.1%)	16(40.0%)	14(58.3%)	34(34.0%)	0.0004
Vomiting	6(16.7%)	24(60.0%)	20(83.3%)	50(50.0%)	<0.001
Headache	2(5.6%)	6(15.0%)	8(33.3%)	16(16.0%)	0.015
Fatigue	26(72.2%)	18(45.0%)	20(83.3%)	64(64.0%)	0.036
Irritable	6(16.7%)	28(70.0%)	24(100.0%)	58(58.0%)	<0.001
Seizures	0	0	22(91.7%)	22(22.0%)	<0.001
Cramps	0	0	2(8.3%)	4(4.0%)	<0.001
Drowsiness	4(11.1%)	20(50.0%)	6(25.0%)	30(30.0%)	0.0009

Patients (72%) had euvolumia, 14 patients (14%) had hypovolumia and 14 patients (14%) had hypervolumia.

Table-6: Hydration and levels of hypnatremia

Hydration	Hyponatremia			Total (n=100)
	Mild (n=36)	oderate (n=40)	Severe (n=24)	
Euvolumia	22(61.1%)	30(75.0%)	20(83.3%)	**72(72.0%)**
Hypovolumia	4(11.1%)	6(15.0%)	4(16.7%)	**14(14.0%)**
Hypervolumia	10(27.8%)	4(10.0%)	0	**14(14.0%)**

(P-value= 0.038)

In this study, comparison was made with the severity of hyponatremia and the state of hydration of these patients (Table-6 and Figure-5). Among the 72 patients with euvolumic hyponatremia, 22 had mild hyponatremia, 30 had moderate hyponatremia and 20 had severe hyponatremia. In the 14 patients with hypovolumichyponatremia, 4had mild hyponatremia, 6 had, oderate hyponatremia and 4 had severe hyponatremia. In the 14 patients with hypervolemichyponatremia, 10 had mild hyponatremia and 4 had moderate hyponatremia.

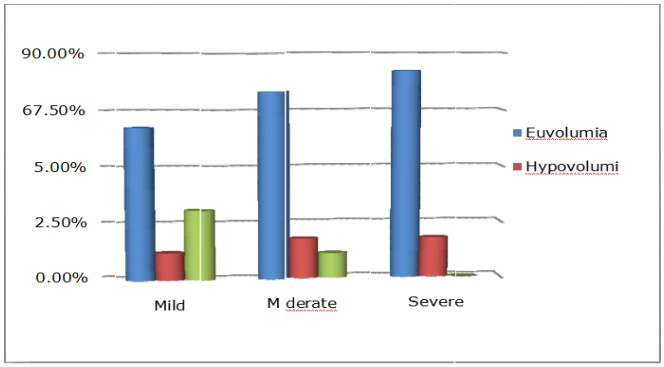

Fig-5

Table -7: Association of sensorium with severity of hyponatremia

Sensorium	Hyponatremia			Total (n=100)
	Mild (n=36)	Moderate (n=40)	Severe (n=24)	
Conscious	32(88.9%)	10(25.0%)	0	**42(42.0%)**
Restless	0	0	4(16.7%)	**4(4.0%)**
Drowsiness	4(11.1%)	20(50.0%)	6(25.0%)	**30(30.0%)**
Unconscious	0	10(25.0%)	14(58.3%)	**24(24.0%)**

(P-value = <0.001)

In patients with euvolemich Hyponatremia, syndrome of inappropriate anti diuretic hormone (SIADH) was the commonest. There were 42 (58.3%) patients with SIADH in the present study (Table-9). Most of these patients had evidence of underlying neurological (28) andrespiratory (14) causes. Among neurological causes, cerebrovascular accident and in respiratory causes, infections like bacterial pneumonia were the commonest.

Table-8: Syndrome of inappropriate anti diuretic hormone (siadh) in different levels of euvolumic hyponatremia

SIADH	Euvolumic Hyponatremia			Total (n=72)
	Mild (n=22)	oderate (n=30)	Severe (n=20)	
Present	10 (45.5%)	18(60.0%)	14(70.0%)	42(58.3%)
Absent	12(54.5%)	12(40.0%)	6(30.0%)	30(41.7%)

(P-value = 0.265)

The mortality was 16% in this study. Among these, 8 patients belonged to the mild hyponatremia group, 4 patients to the moderate hyponatremia group and 4 patients to the severe hyponatremia group (Table-9). 1 patient in the severe hyponatremia group was HIV positive.

Table-9: Outcome in different levels of hyponatremia

Hyponatremia	Number of Patients (n=100)	Outcome	
		Death (n=16)	scharge (n=84)
Mild	36 (36.0%)	8(22.2%)	28(77.8%)
Moderate	40(40.0%)	4(10%)	36(90%)
Severe	24(24.0%)	4(12.5%)	20(87.5%)

(P-value = 0.34)

The outcomes of the patients were related with the different levels of hydration. Mortality was found to be higher in euvolemic and hypervolemich Hyponatremia (Table-10).

Table-10: Outcome in different levels of hydration

Hydration	Number of Patients (n=50)	Outcome	
		Death (n=16)	Present (n=84)
Euvolumia	72 (72.0%)	8(50.0%)	64(76.2%)
Hypovolumia	14(14.0%)	0	14(16.7%)
Hypervolumia	14(14.0%)	8(50.0%)	6(7.1%)

(P-value=0.002)

DISCUSSION

The present study included patients with serum sodium less than 130 mEq/L. There were 58 males and 42 females with ratio of 1.38:1, which was comparable to the study of Baji PP[12], Borkar SS where male: female ratio is 1.17:1. In general, in our hospital population, there were more males than females. This ratio was more or less constant in all age groups[6]. But in the age group above 70 years both genders were equal and in the age group of above

80 years comprised of only females. In study by Hochman *et al*. [9] there were 39 % patients with mild hyponatremia and rest 61% had moderate to severe hyponatremia. The presence or absence of symptoms and severity was more related to rapidity of fall of serum sodium rather than the amount of fall.

In the study done by Hochman[9], there were 43.4% patients who were asymptomatic, 39.9% who had mild symptoms and 16.7% patients has severe neurological symptoms with stupor and coma.In the study of Dr Mahavir Agrawal[13] and Dr Aparna Agrawal at el,confusion was seen in 30 per cent of the patients and altered sensorium in 17.1 percent.In the study of Nandini Chatterjee, Nilanjan Sengupta,1 Chanchal Das,

Atanu Roy Chowdhuri, Ashis Kumar Basu and Salil Kumar Pal at el- 11.94% patients were unconscious at admission, 31.8% patients were disoriented while 4.47% patients had seizures. The largest percentage of patients (48.21%) was asymptomatic.

Table-11

Symptoms	Hochman[9]		Present Study	
	% Patients	Mean serum	% Patients	Mean Serum Na
Asymptomatic	43.4	123	4	125
Mild-Moderate	39.1	121	64	117.2
Severe	17.5	120	32	102.3

The hydration status of the patients was diagnosed on the basis of clinical examination and was divided into euvolumic, hypovolumic and hypervolumic states. In the present study, 72 patients were euvolumic, 14 patients were hypovolumic and 14 patients were hypervolumic representing 72%, 14% and 14% of the patients respectively. Even 50.4% patients were present in study done by Nandini Chatterjee, Nilanjan Sengupta, 1Chanchal Das, Atanu Roy Chowdhuri, Ashis Kumar BasuandSalil Kumar Pal *et al*. Like our study Bennani et al andDr Rajesh padhi at el in a study on hyponatremia found that euvolumich Hyponatremia was the most common (50.6%) type of hyponatremia.

Table-12

Hyponatremia	Hochman [9] (%)	Anderson (%)	Present study (%)
Euvolumia	50	34	72
Hypovolumia	30.5	35	14
Hypervolumia	19.5	31	14

This correlated with other studies where euvolumich Hyponatremia was the commonest. Further SIADH was the most common diagnosis among this group of patients as also was seen study of Bennani *et al*. andDr Rajesh padhi at el. In study by Anderson 9, 34% had euvolumia, 35% had hypovolumia and 31% had hypervolumia. In study by Hochman [9] 50% patients had euvolumia, 30.5% had hypovolumia and 19.5% had hypervolumia.

In the study done by Vurgese[11] the incidence of hyponatremia was 3.6%., with the definition of hyponatremia as serum sodium levels ≤ 130 m mol/L. The study population consisted of 66 patients with 56% males and 44% females. The mean age was 57.05 ± 2SD. The commonest agegroup affected was 45 to 64 years (72. 8%) and the least affected group was 12 to 25 years. The common cause for hyponatremia was SIADH and pneumonia was the commonest cause of SIADH leading to hyponatremia. One of the causes of SIADH was due to HIV infection. Renal failure and congestive cardiac failure was the next frequent causes of hyponatremia. A majority of the patients (82%) showed mild to moderate hyponatremia (120-130 m mol/L). Seasonal variation was noted in the study with 59.1% patients presenting in the summer months. The comparison of the present study with the study done by Vurgese[11] is given in Table-13.

Table - 13

	Vurgese[11]	Present Study
Study Population		
Male	56%	58%
Female	44%	42%
Mean Age	57.95± 2SD	58.62 ±16.36
> 45 years with Hyponatremia	72.8%	78%
Common Causes	SIADH	SIADH
Other Causes	Renal Failure, CCF	CCF, Renal Failure
Grade of Hyponatremia	Mild to Moderate	Mild to Moderate

On the whole, SIADH was the most common cause of hyponatremia in the present study representing 58.3% of cases. In other studies by Hochman [9], SIADH represented 28.3% of cases, 34% in the study by Anderson9 and 34.8% in the study byVurgese[11].

2 patients had hypothyroidism and 2 had hypoadrenalism. Patient with hypothyroidism and hypoadrenalism had presentation similar to SIADH. However, other features associated with these condition help to differentiate them from SIADH. Before the

diagnosis of SIADH, the above diseases should be excluded by appropriate investigations.

Patients with hypovolumic hyponatremia also had predominant moderate hyponatremia. Among 14 patients with hypovolemic hyponatremia. 6 patients had acute gastroenteritis,2hadentericfever,2hadhypothyroidism, and 2 had diabetic ketoacidosis and pneumonia and 2 had metabolic encephalopathy.Majority of patients with hypervolumic hyponatremia had mild hyponatremiaand severe hyponatremia was not seen. Among 7 patients with hypervolumic hyponatremia, 3 had congestive cardiac failure, 2 had chronic renal failure, 1 had corpulmonale, and 1 had cirrhosis. 2 patients had hypothyroidism and 2 had hypoadrenalism. Patient with hypothyroidism and hypoadrenalism had presentation similar to SIADH. However, other features associated with these condition help to differentiate them from SIADH. Before the diagnosis of SIADH, the above diseases should be excluded by appropriate investigations.

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CONCLUSION

Hyponatremia is more common in the elderly age group. The symptoms of Hyponatremia increased with severity of Hyponatremia. Most patients in this study were euvolemic. SIADH was the commonest cause of Hyponatremia; most patients with SIADH had evidence of neurological and respiratory cause. More severe The Hyponatremia and rapid the fall of sodium is more severe the symptoms are.

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ADH : Antidiuretichormone
AIDS : Acquired immunodeficiencysyndrome
ANOVA: Analysis ofvariance
ARC : Aids-relatedcomplex
ATPase: Adenosinetriphosphatase
AVP : Argininevasopressin
C: Centigrade
cAMP: Cyclic adenosinemonophosphate
CHF: Congestive cardiacfailure
Cl- : Chloride
COPD: Chronic obstructive pulmonarydisease
CO3- : Carbonate
dl: Deciliter
FE : Fractionalexcretion
G: Gram
GFR : Glomerular filtrationrate
H+ : Hydrogenion
H202 : Hydrogenperoxide
H2O : Water
HCo3-: Bicarbonate
HIV: Human immunodeficiencyvirus
hrs : Hours
IHD: Ischemic heartdisease
ISE : Ion selectiveelectrodes
K+ : Potassium
Kg : Kilogram
L : Litre
MDMA: 3,4methylenedioxymethamphetamine
mEq : Milliequivalents
mg : Milligram
Mmol: Millimoles
mOsm: Milliosmoles
N2 : Nitrogen
Na+: Sodium
NAD+: Nucleotide adeninedinucleotide
NAD(P): Nucleotide adenine dinucleotidephosphate
NADH: Nucleotide adenine dinucleotidehydrogenase
ng : Nanogram
NH4+: Ammonium
NSAID's: Non-steroidal anti-inflammatorydrugs
O2 : Oxygen
Pg : Picogram
PTB: Pulmonarytuberculosis
SIADH: Syndrome of inappropriate antidiuretic hormone secretion.
SD : Standarddeviation
% : Percentage