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An Unusual Case of Transient Cortisol Deficiency and Profound Hyponatremia in a Pregnant Female with Pre-Eclampsia

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***Abstract*— Pre-eclampsia is a multisystem disorder that complicates 3-8% of pregnancies and accounting 18% of maternal deaths. Pre-eclampsia is defined as hypertension and proteinuria with associated signs and symptoms such as pedal edema, headache, visual disturbances, and epigastric pain which starts at the onset of 20 weeks of pregnant state. Usually in pre-eclampsia we found no electrolyte disturbances except lower levels of magnesium in most of the cases. Pre-eclampsia with profound hyponatremia is one of the rare complications encountered during pregnancy and as per the literature we found only 14-16 cases have been reported. In such situation patient may predispose to convulsions, maternal mortality and fetal damage.**

Normally pregnancy is a state of hypercortisolemia (glucocorticoid excess) particularly in the latter stages and testing of HPA axis (hypothalamic-pituitary-adrenal axis) using validated stimulation or confirmation test during pregnancy are lacking. Adrenal insufficiency in pregnancy is relatively rare with reported incidence of 1:3,000 births and it is associated with significant maternal and fetal morbidity if untreated during gestation or in the puerperium. Pregnancy induced metabolic and endocrine changes with related symptoms is difficult to recognize, and a challenge to confirm the diagnosis of cortisol deficiency. Clinical features such as excessive dizziness, syncope, nausea, protracted vomiting, weight loss, profound hyponatremia, hypoglycemia and salt craving should raise the suspicion of Adrenal insufficiency.

We report a rare case admitted with history of dizziness, headache and abdominal pain found to have profound hyponatremia in 3rd trimester of pregnancy with pre-eclampsia and transient cortisol deficiency.

***Index Terms*— pre-eclampsia, cortisol, adrenal insufficiency, pregnancy.**

I. Introduction

A 32 week pregnant lady, with pre-eclampsia was admitted with history of abdominal pain and headache. She was referred to the physician by the obstetrician, for low sodium levels. History revealed that the patient she had headache previous night which she attributes to disturbed sleep.

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Patient had mild nausea without any episodes of vomiting. She denied any history of fever, cough, chest pain, palpitations or loss of consciousness. Patient complained of increased lower limb swelling which was noticed during 2nd trimester of her pregnancy. However she had have normal blood pressure readings in the antenatal clinics, till she was admitted to the hospital. On admission to the hospital she was found to have high blood pressure readings along withproteinuria and increasing lower limb edema. She was then started on oral anti-hypertensive medications for a diagnosis of pre-eclampsia. Her routine metabolic panel revealed her sodium levels to be 125 mmol/l which further dropped to 115 mmol/L in next 12 hours. On physical examination, she was conscious, comfortable and oriented. She respondedwell to all verbal commands. Her vitals were within normal limits , with a pulse rate of 80 bpm and blood pressure of 130/80mmhg. Her systemic examination was normal, except for bilateral diffuse pedal edema.

II. Discussion

Pre-eclampsia is a multi-system disorder that complicates 3-8% pregnancies and accounting 18% maternal deaths. It is characterized by hypertension and proteinuria with associated pedal edema, headache, visual disturbances and epigastric pain which usually starts at the onset of 20th week of pregnancy. Pre-eclampsia associated hyponatremia is a quite rare and life threatening condition which carries high maternal and fetal mortality and morbidity. (1,2)

In pregnancy , plasma osmolality falls to a new set point of about 270 mosmol/kg along with fall in the serum sodium concentration of about 5meq/l. The release of human chorionic gonadotropin during pregnancy may be responsible for mild hyponatremia (3), additionally within the brain oxytocin is proposed to suppress salt appetite and a peptide hormone relaxin also increases fluid intake and vasopressin secretion in pregnancy and leads to hyponatremic hypervolemia of pregnancy.(4,5)

Hyponatremia is defined as serum sodium below 135 meq/L, mild when it is 130-135 meq/L and severe when the serum sodium level falls below 120 meq/l. Severe hyponatremia can cause coma , seizures and even death if not treated (6) .Hyponatremia is broadly classified in three different types depending upon volume status as shown in the figure1 down.(7)

Table 1. Patient labs:

Lab Values	Pregnancy	Post partum	6 weeks after pregnancy
Sodium	125-121-118-115 mosmol/l	122-128-137 mosmol/l	140 mosml/l
Urine osmolality	667 mosml/kg		
Plasma osmolality	270 mosm/kg		
Urine Protien	256 mg/mmol		
Urine Sodium	16 mmol/l		
Cortisol AM	27 nmol/l (135-580)	172 nmol/l	
Synacten test: AM Cortisol 30 min Cortisol 60 min	 24 23		 272 330
ACTH a.m	6 pg/ml (5-60)		24
TSH	1.09 (0.27 – 4.20)		
Ft4	12.8		
Aldosterone	84 pmol/l (48 – 644)		

Hyponatremia in presence of edema indicates increased total body sodium and water. Increase in total body water is greater than the total body sodium levels resulting in edema. Resultant hypervolemic hyponatremia are found in heart failure, nephrotic syndrome, liver cirrhosis and inappropriate administration of IV fluids (8).

SIADH in the setting of preeclampsia can be explained by, preeclampsia causing decrease in effective circulating volume, non-osmotic release of ADH. A defective placenta in patient with preeclampsia does not produce sufficient vasopressinase an enzyme that rapidly inactivates ADH.(9)

Pregnancy is usually a state of hypercortisolemia (glucocorticoid excess) particularly in the latter stages and testing of HPA axis (hypothalamic-pituitary-adrenal axis) using validated stimulation or confirmation test during pregnancy are lacking (10). Adrenal insufficiency in pregnancy is relatively rare with reported incidence of 1:3,000 births. It is associated with significant maternal and fetal morbidity if left untreated during gestation or in the puerperium.(11)Pregnancy induced metabolic and endocrine changes with related symptoms creates difficulty in recognition and poses a great challenge to confirm the diagnosis of cortisol deficiency. Clinical features such as excessive dizziness, syncope, nausea, protracted vomiting, weight loss, profound hyponatremia, hypoglycemia and salt craving should raise the suspicion of Adrenal insufficiency.

In our patient renal and non-renal causes were excluded , and she neither had a past medical history of cardiac, thyroid, liver disorders, however she had new onset proteinuria from 32 week of pregnancy with hypertension. There was no evidence of diarrhea, vomiting nor administration of any drugs that could have caused hyponatremia. In our case we found, the patient having profound hyponatremia along with preeclampsia, whose workup of hyponatremia revealed her to have cortisol deficiency which is suspected to be a confounding factor for her profound hyponatremia.

Review of literature, mentions 15 cases of preeclampsia-induced hyponatremia caused by various mechanisms including nephrotic syndrome, SIADH and inappropriate administration of IV fluids. However inthe described case, we discovered severe cortisol deficiency along with preeclampsia, leading to severe hyponatremia. Till date there has been no similar reported case , with cortisol deficiency and preeclampsia.

Our patient's sodium levels dropped steeply from 122, 120, 118, 115mosmol/l during the initial 24 hours of patient's admission in the hospital. Despite fluid restriction the patient's sodium levels did not improve and the decision of immediate cesarean section was taken. On her first postpartum day, severe cortisol deficiency was confirmed by short synacten (cosyntropin) test, which was suggestive of cortisol deficiency. The patient was followed up closely for next 3 days and her sodium levels reached near normal levels. Since the patient was hemodynamically stable with sodium levels reaching near normal levels, she was not initiated on corticosteroid therapy and was discharged with a close follow-up and frequent Blood pressure monitoring . After 6 weeks of postpartum, she was called in for reevaluating cortisol deficiency and surprisingly was found to have normal cortisol levels.

We therefore report this case of life threatening hyponatremia with preeclampsia along with associated transient cortisol deficiency in which the single mechanism could not be explained, which is multifactorial and could be a confounding factors in her profound hyponatremia.

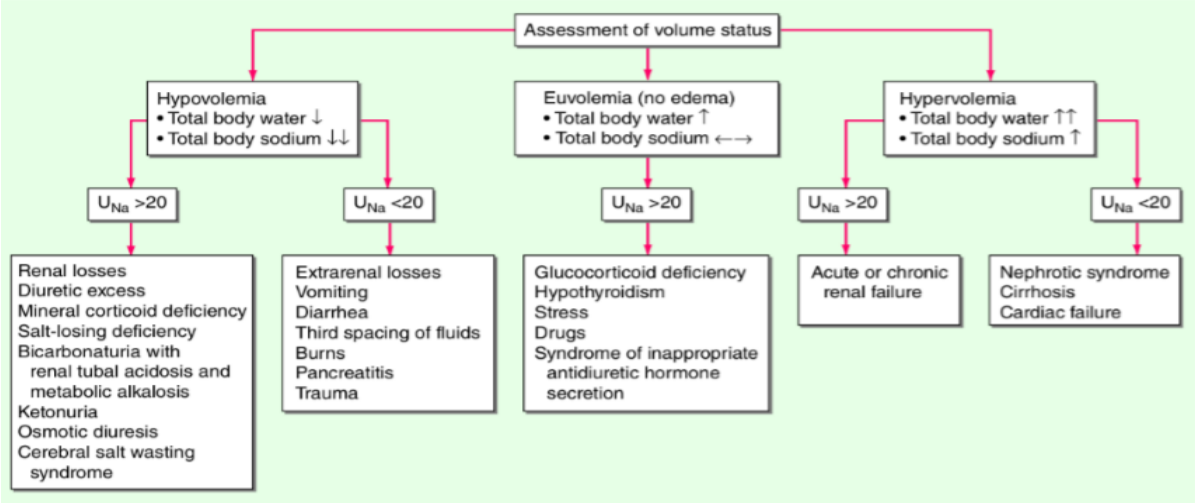

Table 2:

Few Case Reports of Hyponaremia in Pre eclampsia										
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Maternal Age	31	35	41	35	30	30	33	41	30	26
Gestational Age	32	33	37	33	33	32	38	38	32	32
Parity	1	1	1	1	4	1	1	3	1	1
Nephrotic proteinuria	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
Initial Serum Sodium meq/l	128	121	117	129	126	120	122	120	123	125
Urine Osmalality mosm/kg	348	628	372	675	630	311	270	537	325	667
Plasma Osmolality mosm/kg	256	258	236	264	263	261	257	249	266	270
Urine sodium meq/l	20	10	16	1	Not Reported	Not Reported	31	Not Reported	77	20
Postulated Mechanism	Hyervoluemic Hyponatremia	Hypervolemic Hyponatremia	SIADH	Hypervolemic Hyponatremia	Hypervolemic Hyponatremia	Hypervolemic Hyponatremia	SIADH	SIADH	SIADH	**SIADH/Cortisol Deficiency**
Treatment Strategy	Fluid Restriction	Fluid Restriction	Fluid Restriction	Fluid Restriction	Fluid Restriction	Labor Induction	Labor Induction	Labor Induction	Fluid Restriction	Fluid Restriction Induction of labor
Indication of Labor induction	Hyponatremia Hypotension	Fetal Distress	Fetal Distress	High BP	Hyponatremia	Pre term labor Hyponatremia	High BP Hyponatremia	Hyponatremia	High BP Hyponatremia	Acute Drop in Sodium levels
Time to sodium Normalization	8 hours	48	72	Not Reported	72	48	48	48	48	72
Cortisl Levels nmol/l	//	//	//	//	//	//	//	//	//	27
Time to resolve proteinuria	NA	1 week	1 week	4 weeks	Not Reported	Not Reported	Not Reported	NA	48	2 weeks

Case 10 – our case at Al Khor Hospital; Case 1 – Bruell and de et al; Case 2,3,4 – Hayalett et al;Case 5,6 – Magriples et al;Case 7 – Ravid et al;Case 8 – stutton et al;Case 9 – Kaharmngul et al

// - not available ; NA- not applicable

III. TAKE HOME POINTS

1.Hyponatremia in pregnancy can be serious life threatening condition if not addressed aggressively

2.Complete evaluation of hyponatremia should be done specially when dealing with special cases like pregnancy.

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