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A STUDY ON ACUTE HYPERDYPSIA AS AN EARLY PREDICTOR OF SHOCK IN PATIENTS WITH ACUTE FEBRILEILLNESS

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ABSTRACT

Background: Thirst is an underreported and under evaluated symptom in clinical practice. Like pain, it is often a neglected symptom which the clinician should properly enquire in history taking. The reason for undertaking this study is to throw light on the prevalence of sudden unquenchable thirst in patients admitted with acute febrile illness. Surprisingly no similar study was done in fever patients. The aims and objectives of the study are to study the prevalence of clinical symptoms in acute febrile illness, to study the prevalence of thirst in patients with normal blood pressure and in shock, to study the prevalence of hyperdipsia in dengue patients, to correlate the onset of hyperdipsia with prolongation of capillary refill time and increase in hematocrit. **Materials and methods:** 200 patients admitted in the fever unit of Tirunelveli medical college during the epidemic from august 2017 to January 2018 were studied. This study is a prospective observational study. **Results:** Hyperdipsia was present in 64% of fever cases. 42.18% of hyperdipsia patients were in shock. Excess thirst was prevalent even in patients with normal blood pressure ($p<0.001$), which suggests that onset of thirst preceded development of shock. 85.4%of dengue patients had hyperdipsia ($p<0.001$).The correlation of thirst with prolonged capillary refill time and increased hematocrit we're also statistically significant. **Conclusion:** Hyperdipsia is a valuable symptom as its onset precedes Hemodynamic and hematologic abnormalities in fever patients and guides the clinician in appropriate management.

KEYWORDS: Hyperdipsia, shock, haematocrit.

BACKGROUND

Thirst is an important symptom in the setting of illness. This is the first study on the prevalence of hyperdipsia in patients admitted with acute febrile illness. It is a prospective observational study conducted on 200 patients admitted with acute febrile illness. Hyperdipsia was the commonest symptom(64%). Hyperdipsia was prevalent even in patients with normal blood pressure, which suggested that it is an early predictor of shock ($P<0.001$). 29 out of 62 dengue patients had hyperdipsia, and all the dengue patients in shock were hyperdipsic($P<0.001$).

The association of hyperdipsia with prolonged capillary refill time and significant rise in hematocrit were also significant. As the duration of thirst increases, there is more tendency to the development of shock ($P<0.001$).

Thirst is an under evaluated and understudied symptom in clinical evaluation. Though it is a subjective symptom, the intensity and pervasiveness of thirst imply that this sensation needs to be further studied.Intense thirst or hyperdipsia can be an early warning signal of osmotic or fluid imbalance.Thirst, the desire for water is due to a complex system of neuro humoral signalling that regulated the body's water and sodium balance. Many critically ill patients due to poor communication cannot self report to the treating physicians. It could be a vital symptom that predicts the development of shock especially in fever cases. Hence, thirst must be enquired before it can be treated. Though there are various studies on thirst prevalence in ICU patients[1], chronically ill patients[2], cancer patients[3] and haemodialysis patients[4], no studies were done on the prevalence of thirst in fever patients.

This is the first study to analyse the prevalence of hyperdipsia or intense thirst with specific emphasis on the acuteness of onset of thirst in patients admitted with acute febrile illness.

MATERIALS AND METHODS

This is an observational study which was conducted in Intensive Medical Care Unit of Tirunelveli Medical

College and Hospital form August 2017 to January 2018.Totally 200 patients admitted with acute febrile illness were studied. Detailed history regarding quality of fever, duration history of thirst with specific emphasis on the sudden onset of hyperdipsia.

Clinical examination, complete blood count, renal, liver function tests were done. Only those patients with normal sodium level, calcium and glucose level and plasma osmolality were included in this study.
Serum osmolality was calculated using the formula

$$2(Na^+ + K^+) + \frac{BUN}{2.8} + \frac{glucose}{18}$$

Exclusion criteria were systemic illnesses like renal failure, heart diseases,liver failure, rheumatologic illness, hematologic malignancies, fluid loss from other causes like acute diarrhoeal disease, acute gastroenteritis, patients on dipsogenic drugs, anticholinergics, diuretics, opioids, tricyclic antidepressants, nonsteroidal anti-inflammatory drugs, steroids, proton pump inhibitors, antihypertensives.

Correlation between duration of hyperdipsia and the development of shock in patients with acute febrile illness, correlation between hyperdipsia and increased Capillary refill time and increase in haematocrit were studied.

All the patients were conscious and oriented to time, place, person. Patients who were able to self-report sudden unquenchable thirst were enrolled. All the patients with hyperdipsia were given fluids according to dengue guidelines irrespective of BP. For clinically stable and no change or minimal change in haematocrit, intravenous fluid at the rate of 2-3 ml/Kg/hr for 2-4 hrs was given. For worsening vital signs and rapidly increasing haematocrit crystalloid 5-10 ml/kg/hr for 1-2 hrs was given which was tapered on improvement to 3-5 ml/kg/hr for 2-4 hrs & 2-3 ml/kg/hr for 2-4 hrs. Management was according to CDC guidelines [Centres for disease control and prevention].

Thirst was assessed by numeric rating score from 1-10.Scores 1-5 were considered increasing degrees of thirst, 6, 7 – severe thirst, 8 – 10 extreme thirst to thirst distress. Shock is the clinical syndrome that results from inadequate tissueperfusion. Clinical shock included patients with a) Mean arterial pressure <60mmHg, b) Hypotension – Systolic BP < 90mmHg or c) Narrow pulse pressure <30mmHg. Capillary refill time was defined as ≤ 2 sec.

Shock is the clinical syndrome that results from inadequate tissue perfusion. Clinicalshock is usually accompanied by hypotension(i.e a mean arterial pressure (MAP<60 mmHg).The most common form of shock is hypovolemic shock, which results from the loss of blood and plasma or plasma alone due to extravascular fluid sequestration.

Mild hypovolemia (<20% of blood volume) generates mild tachycardia. Withmoderate hypovolemia (20-40% of blood volume), patient develops anxiety, tachycardia, normal blood pressure while supine and postural hypotension. In severe hypovolemia (40% loss of blood volume), the classic signs of shock appear; the BP falls, patient develops anxiety, tachycardia, oliguria and confusion[5]. Mental obtundation is an ominous sign.

RESULTS

Prevalence of clinical symptoms in acute febrile illness.

TABLE:1 Analysing the clinical profile of patients.

S.NO	SYMPTOMS	NUMBER	PERCENTAGE
1	Fever	200	100%
2	Petechial Rash	10	6%
3	Hyperdipsia	128	64%
4	Arthralgia	72	36%
5	Retroorbital pain	48	24%
6	Headache	84	42%
7	Facial puffiness	50	25%
8	Bleeding	27	13.5%
9	Jaundice	8	4%

Table: 2 Prevalence of normal BP, narrow pulse pressure and low systolic BP in relation to hyperdipsia.

S.no.	Quality of Thirst	No of patients with normal bp	No of patients with narrow pulse pressure	No of patients with systolic bp < 90mmhg	Total
1	Hyperdipsia	74(57.8%)	25(19.5%)	29(22.7%)	128
2	Normodipsia	59(81.9%)	5(6.9%)	8(11.2%)	72
	Total	133(66.5%)	30(15%)	37(18.5%)	200

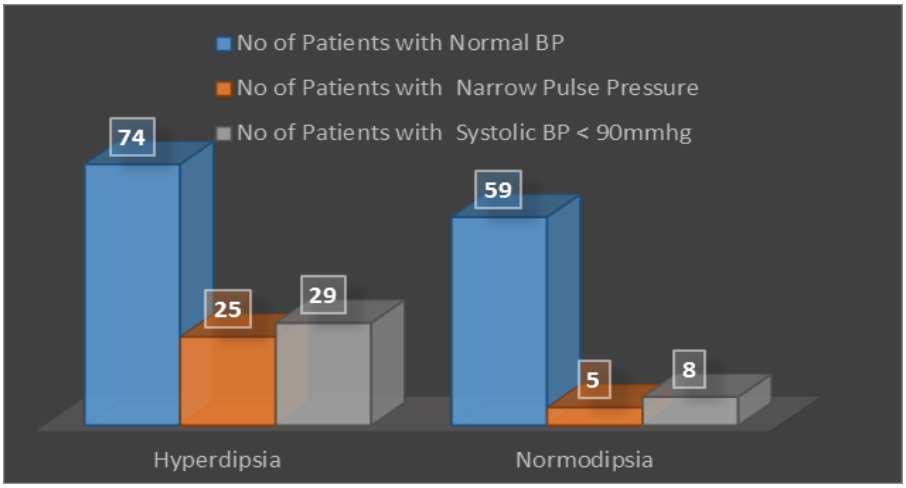

Figure:1 Distribution of febrile patients with normal and hyperdipsia in comparison with blood pressure.

TABLE 3: Prevalence of normal and hyperdipsia in relation to shock.

S.no.	Quality of Thirst	No of patients with normal bp	No of patients with shock	P value
1	Hyperdipsia	74 (55.6%)	54 (80.6%)	P< 0.001 (Chi square 12.0, df=1)
2	Normodipsia	59 (44.4%)	13 (19.4%)	
3	Total	133	67	

Table:4 Prevalence of shock in relation to the dengue serology positivity.

S.NO	Quality of Thirst	Normal BP		Narrow PP		SBP <90		Total
		D+ve	D-ve	D+ve	D-ve	D+ve	D-ve	
1	Hyperdipsia	26	48	16	9	11	18	128
2	Normodipsia	9	50	0	5	0	8	72
3	Total	35	98	16	14	11	26	200
4		133	30		37			
5	P value	0.0097(Chi square= 6.69)	0.014(Fisher exact)		0.076(Fisher exact)			

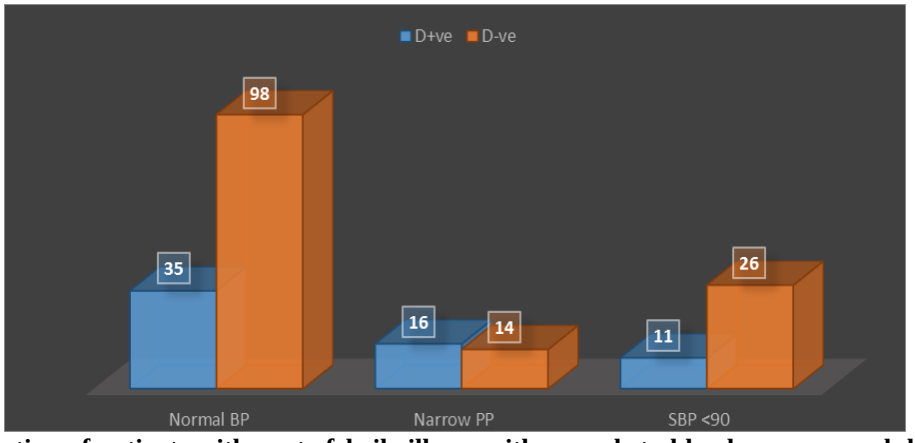

Figure:2 Distribution of patients with acute febrile illness with regards to blood pressure and dengue positivity (PP=pulse pressure, SBP= systolic blood pressure).

Table: 5 Prevalence of hyperdipsia in dengue patients.

S.no.	Quality of thirst	No of Patients with Normal BP n=133	No of Patients with Shock n=67		Total
		D+ve	D-ve	D+ve	D-ve	
1	Hyperdipsia	26	48	27	27	128
2	Normodipsia	9	50	0	13	72
3	TOTAL	35	98	27	40	200
	P value	0.0097 (Chi square)		0.0009 (Fisher exact)		

Table: 6 Correlation of hyperdipsia with increase in PCV.

S.no	Quality of Thirst	20% increase in pcv (no of patients)	No significant rise (no of patients)	Total	P value
1	Hyperdipsia	14 (10.9%)	114 (89%)	128	<0.001
2	Normodipsia	0 (0%)	72 (100%)	72	
3	Total	14 (7%)	186 (93%)	200	

Table:7 Comparison of capillary refill time in patients with normal BP and in shock

Capillary refill time	No of Patients with Normal BP (n=133)	No of Patients with Shock (n=67)	P VALUE
Increase in CRT>2 sec	0	12	<0.001
Normal CRT≤2sec	133	55	

Table: 8 Distribution of hyperdipsic patients with normal BP and shock with regards to duration of hyperdipsia.

S.NO.	Duration of Thirst	No. of hyperdipsic Patients with Normal BP (n=74)	No. of hyperdipsic Patients with Shock (n=54)	p value
1	< 6 hrs	50 (67.6%)	19 (35.2%)	<0.001
2	6-12 hrs	20 (27%)	19 (35.2%)	
3	> 12 hrs	4 (5.4%)	29 (53.7%)	

Table: 9 Comparison of onset of hyperdipsia and onset of shock in relation to day of fever.

S.NO	Onset of hyperdipsia on fever day	No of Patients with hyperdipsia and Shock (n=54)
1	1-2 days	6 (11.1%)
2	3-5 days	39 (72.2%)
3	> 5 days	9 (16.7%)

Hyperdipsia was the commonest symptom (64%) followed by headache (42%) and arthralgia (36%) (Table 1).

133 patients had normal BP and 67 patients developed shock including 30 patients with narrow pulse pressure and 37 with systolic BP<90 mmHg. In our study out of the200 patients admitted with acute febrile illness, hyperdipsia was noted is 128(64%) patients; out of the 128 patients 54 patients were in shock (42.18%) (Table 2, Figure: 1).

Out of the 133 patients with normal BP, 74 had complained of hyperdipsia(55.63%) which suggest that even with normal BP, patients can perceive thirst, or even develop unquenchable thirst and this was found to be statistically significant (P<0.001). Whereas only 13(19.4%) patients in the normal thirst group of 72 patients developed shock. (p value= <0.001). The result shows that patients who had complained of hyperdipsia had more chance of developing shock. (Table 3)

Out of 200 patients, 62 were positive for dengue IgM antibody.

The prevalence of hyperdipsia in patients with normal BP and narrow pulse pressure was statistically significant, but thirst was not significantly correlating when patients developed shock (P=0.076). Probably, the patients who developed shock instantaneously were not able to complain of thirst (table:4).

Out of 62 denguepatients, 53 (85.4%) patients had intense unquenchable thirst.27out of 53hyperdipsic dengue patients presented with shock (50.94%). All the 9 dengue patients with normal thirst did not develop shock. These findings were found to be statistically significant (P <0.001)This is an important observation that the symptom of acute onset hyperdipsia predicts hemodynamic compromise especially in dengue. (Table 4, Table 5, Figure:2)

Out of 200 patients, only 14 (7%) patients had significant rise in PCV. All the 14 had complained of hyperdipsia which implies that hyperdipsia arises hours before the hematological abnormalities (P value<0.001) (Table 6)

12 out of 200 patients had prolonged capillary refill time. All the 12 patient were in shock on admission. Out of them 10 patients had history of hyperdipsia and all the 10 patients had intense thirst for >12 hours'duration. This finding implies that hyperdipsia predicts development of shock even >12 hours earlier, the association of prolonged capillary refill time with shock was statistically significant (p<0.001) (Table 7).

In our study, out of 67 patients with in shock, 19 patients had thirst duration of less than 6 hours and another 19 patients had 6-12 hours duration of thirst and remaining 29 patients had more than 12 hours duration of thirst. The finding suggests that patients with hyperdipsia for more than 12 hrs, are more likely to develop shock which indirectly suggests that if appropriate fluid bolus was

given on the development of hyperdipsia, impending shockcould be prevented. (Table 8).

Out of 54 acute febrile illness patients with shock and unquenchable thirst, 39 patients had developed thirst on 3rd to 5th day of fever, 6 patients developed thirst on day of fever 1-2, 9 patients developed thirst on day of fever more than 5 days.72.2% of patients complained of onset of hyperdipsia between3rd to 5th day of fever.(Table 9).

DISCUSSION

This is the first study on the prevalence of hyperdipsia in patients with acute febrile illness. The age of the patients was not related to presence of thirst, though there are studies which demonstrated decreasing thirst in elderly. Probably thirst response differs in patients with acute febrile illness.[1]

The mean age of the patients with hyperdipsia was 42+11.2 years and those with normodipsia 41.2 + 11 years. The male and female distribution was not statistically significant. Male to female ratio is 1:0.87

Myalgia, arthralgia and headache were the common symptoms in our study and was comparable to other studies.[6,7]

The most commonsymptom among patients with acute febrile illness is thirst and about 64% patients had complained about acute onset of intense thirst. Though thirst prevalence was studied in cancer(70.%) and critically ill patients (70%) and patients on hemodialysis (86%), no studies are available on fever patients.[8,9]

Upto 7 patients(57.8%) who complained of intense thirst still had normal BP, which could imply that they were treated with fluid bolus at the right time to prevent the development of shock. The prevalence of shock in our study is 33.5% (n=67).

Out of 133 patients with normal BP 55.6% (n=74) had hyperdipsia and 80.6% of patients in shock(n=54) had hyperdipsia which is highly significant (P<0.001).31% of cases (n=62) were dengue positive. Of which 43.5% cases developed shock. All the normodipsic dengue patients (n=9) did not develop shock. 114 out of 186 (61.3%) patients with hematocrit rise, still had hyperdipsia and all were effectively treated and developed no further shock.

Only 12 out of 67(61.3%) patients with shock had prolonged capillary refill time, which implies hyperdipsia sets in hours before these clinical signs.

53(85.4%) hyperdipsic patients who presented with shock had the intense unquenchable thirst for more than 6 hours.

Most patients (67.6%) with normal BP presented to hospital with hyperdipsia or complained of intense thirst of duration less than 12 hours during hospital stay.

The anterior cingulate cortex and insula are activated in thirsty human beings as shows by functional brain imaging techniques. Osmoreceptors within the organum vasculosum of the lamina terminalis and subfornical organ detect systemic hypertonicity. The subfornical organ mediates the dipsogenic actions of circulating angiotensin II and relaxin. Major integrative sites are the nucleus tractus solitarius, the lateral para brachial nucleus, the midbrain raphe nuclei, the median preoptic nucleus and the septum.[10]

The immediate response to hypovolemiais activation of sympathetic nervous system, which increases the vascular tone, venous return, heart rate and contractility and renal and water reabsorption. Increased plasma vasopressin, renin-angiotensin, aldosterone, epinephrine / norepinephrine, ACTH and glucocorticoides act to retain sodium and water or to redistribute blood and interstitial fluids in an attempt to maintain blood flow to vital organs. The dipsogenic action of angiotensin requires sensing by structure of the lamina terminalis. Inhibition and facilitation of thirst is also mediated by cardiopulmonary and arterial baroreceptors from where afferent input is carried by the IX and X cranial nerves terminating in the nucleus tractussolitarius.[11] Angiotensin II is considered as the endogenous antagonist of atrial natriuretic peptide.[12] It causes sodium and water retention to restore plasma volume.[13]

In our study the patients who werehyperdipsic were able to pinpoint the sudden onset of thirst sensation and intensity. This could be explained by the threshold stimulus point and activation of dynamic core of neuronal groups.

Microcirculatory shock itself leads to progressive shock and enters a vicious cycle of cardiovascular deterioration. The threshold stimulus point for vasopressin release varies widely in individuals and it sets lower than the threshold associated with activation of the thirst sensation.[14,15] According to crick “at any moment, some active neural processescorrelatewith consciousness while others do not". Edelman and Tononi postulate that there is a cluster of “dynamic core" neuronal groups and integrated parts. From neuroimaging studies, the dynamic core common to primary emotions including thirst are anterior and posterior cingulate gyri, insula, parahippocampus orbitofrontal gyri and thalamus16, 17. The urge to drink water is driven by the central regulation of extracellular tonicity, termed osmotic thirst and by the need to replace fluid deficits, termed hypovolemic thirst.[5,18]

A decrease in 10% of plasma volume is required to initiate hypovolumic thirst, whereas 1% to 2% increase in plasma osmolality can stimulate thirst and

drinking.[19,20] This suggest the hypovolemic thirst mechanisms associated with changes in intravascular volume are less sensitive than those associated with osmotic changes.[21]

In our study we analysed the fever patients who had normal serum osmolality. More detailed study on hypo and hyperosmolar states with fever would throw more light on hyperdipsia. Though studies have not shown any correlation of thirst with same osmolality.[22,23,24]

CONCLUSION

Thirst was the commonest symptom in patients with acute febrile illness. Acute onset hyperdipsia was also more prevalent in patients who present with or subsequently developed shock. Emergence of hyperdipsia precedes changes in hematocrit or prolonged capillary refill time. Hyperdipsia follows soon after defervescencei.e in the third to fifth days of fever onset. Hence, hyperdipsia could be an early predictor of development of shock in patients with acute febrile illness and prompt treatment with intravenous fluid bolus appropriately prevents morbidity and mortality.

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