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Metabolic Encephalopathy in Elderly with a Special Focus on Thyroid Function and Hashimotos Encephalopathy

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ABSTRACT

Objective: *Metabolic encephalopathy is a common cause for morbidity and mortality in elderly. Metabolic disturbances are frequent causes of impaired consciousness and their presence must always be considered when there are no focal signs of cerebral disease. An underdiagnosed but potentially treatable cause of metabolic encephalopathy in elderly is Hashimoto's encephalopathy (HE). It has huge clinical relevance since it is not uncommon and shows very good response to immunosuppressive treatment. The aim of the study was to analyse the various causes of metabolic encephalopathy in elderly patients. Various presenting features of encephalopathy particularly involuntary movements have also been studied. Cases of Hashimoto's encephalopathy have been specifically sought for and looked into to characterise the specific clinical manifestations that can point towards its diagnosis.*

Materials and Methods: *Our study was a hospital based descriptive study conducted in elderly patients above the age of 60 years admitted with altered sensorium. Patients with documented sepsis, hepatic failure ,renal failure, cerebrovascular accident, CNS infection and head injury were excluded from the study. A thorough clinical examination including detailed neurological examination was done. Blood was sent for investigations including serum electrolytes, hepatic, renal and throid function tests. Those patients who did not had any obvious cause for encephalopathy and not responding to treatment were further evaluated with anti TPO antibodies in CSF.*

Results: *Of the 132 patients enrolled in the study there were 55males (41.7%) and 77 females (58.3%). Seizures was seen in 15.9% and myoclonus in 3.8% patients. Study showed that 92.4% of patients had hyponatremia and 7.6% had normonatremia. The patients having blood glucose values above 500 mg% and below 50 mg% were 4.5%, and 7.6%. Thus our study showed 7.6% of patients had hypoglycaemic encephalopathy Thyroid status of the patients showed that clinical hypothyroidism was seen in 3.8% and subclinical hypothyroidism in 15.4%. Majority of the patients were euthyroid(80.8%).The CSF examination showed 14 patients (10.6%) positive for anti TPO antibodies and were diagnosed to have hashimotos encephalopathy.Among the patients with hashimotos encephalopathy 71.4% were females , 57.2 % patients had abnormal movements at presentation , 64.3 % patients had hyponatremia and 78.5 % had a euthyroid status.*

Conclusion: *Hyponatremia and altered blood glucose levels were the major causes leading to metabolic encephalopathy in elderly patients. About 10.6% of the elderly patients presented with hashimotos encephalopathy. Abnormal movements were an important presenting feature of hashimotos encephalopathy. A Significant proportion of patients with hashimotos encephalopathy had euthroid status. A high level of clinical suspicion is needed for the diagnosis, as it is a treatable condition.*

Keywords: *Hasimotos encephalopathy, seizures, anti TPO antibodies, hyponatremia, euthyroid.*

Introduction

Metabolic encephalopathy is a common cause for morbidity and mortality in elderly. Metabolic disturbances are frequent causes of impaired consciousness and their presence must always be considered when there are no focal signs of cerebral disease. They usually occur in the setting of an underlying systemic disease and these encephalopathies are often reversible if the systemic disease is brought under control. The common causes of metabolic encephalopathy in elderly are hyponatremia, hypoglycemia, hyperglycemia, hepatic or renal failure, hypoxia, hypercapnoea and endocrine disturbances. Hyponatremia is the most commonly encountered electrolyte disturbances occurring in approximately one of every three hospitalized patients.(1)

An underdiagnosed but potentially treatable cause of metabolic encephalopathy in elderly is Hashimoto's encephalopathy (HE). It has huge clinical relevance since it is not uncommon and shows very good response to immunosuppressive treatment. This has led to the renaming of Hashimoto encephalopathy as "steroid- responsive encephalopathy associated with autoimmune thyroiditis" (SREAT) or "nonvasculitic autoimmune meningoencephalitis" (NAIM).(2) The clinical, laboratory, and radiologic findings in patients HE have to be characterised to potentially improve recognition of this treatable entity. Several studies conducted in this field shows that all patients were assigned an alternative misdiagnosis at presentation, most commonly viral encephalitis, Creutzfeldt-Jacob disease or a degenerative dementia. Clinical manifestations of HE may include encephalopathic features such as seizures, behavioral and psychiatric manifestations, movement disorders, and coma. Although it has been linked to cases of hashimoto's thyroiditis or thyroid dysfunction, the most common immunological feature of HE is the presence of high titers of antithyroglobulin or anti-TPO (antimicrosomal) antibodies.(3)

Seizures including status epilepticus may also occur in patients with hashimotos encephalopathy .Seizures appear to be extremely common in HE and deserves consideration in the differential diagnosis of adult onset recurrent epileptic seizures. An excessive, central release of TRH was held responsible for the epileptic seizures.(4) HE patients with seizures were unresponsive to anticonvulsant medication, but showed rapid neurological improvement following steroid treatment. Thus HE must be considered in all cases of investigation negative encephalopathies and unexplained recurrent seizures.

Acute and/or severe electrolyte imbalances frequently cause seizures, and these seizures may be the sole presenting symptom. Seizures are especially common in patients with sodium disorders. Seizures generally occur if the plasma sodium concentration rapidly decreases to <115 mEq/L; they represent an ominous sign and also a medical emergency, as they are associated with high mortality.(5). Hyponatraemic encephalopathy can be difficult to recognize, as the most frequent symptoms are nonspecific and can easily be incorrectly attributed to other causes.(6) An important treatable cause of euvolemic hyponatremia include endocrine disorders like hypothyroidism and adrenal insufficiency. Hyponatremia has been reported in upto 10% of hypothyroid patients.(7) When hyponatremia is the result of hypothyroidism it can be treated with thyroid hormone substitution.(8)

The aim of the study was a sincere attempt to analyse the various causes of metabolic encephalopathy in elderly patients. Various presenting features of encephalopathy particularly involuntary movements have also been studied. Focus was also given on the thyroid function of patients with encephalopathy. Cases of Hashimoto's encephalopathy have been specifically sought for and looked into to characterize the specific clinical manifestations that can point towards its diagnosis.

Material and Methods

Our study was a hospital based descriptive study conducted in elderly patients above the age of 60

years admitted with altered sensorium. The study was conducted in medical wards and Intensive care unit under Department of Medicine, in a tertiary care hospital in South Kerala over a period of six months. Our exclusion criteria were (1) Patients with documented sepsis, hepatic and renal failure.(2) Patients with cerebrovascular accident, CNS infection and head injury.

A thorough clinical examination of all the patients were done focussing on their hydration status, vital signs, level of consciousness. The characteristics of the encephalopathy and associated symptoms including memory loss, incordination, weakness, sleep disturbances and abnormal movements were studied. A detailed neurological examination was also done. Special emphasis was given on abnormal movements particularly seizures and myoclonus. Past history of thyroid illness was sought.

Patients were evaluated with routine haemogram, serum electrolytes, blood glucose, liver function tests,renal function and throid function tests. Those patients who did not had any obvious cause for encephalopathy and not responding to treatment were further evaluated with anti TPO antibodies in CSF. Anti TPO antibody positive were considered to have hashimotos encephalo-pathy.

Data was collected and analysed using statistical tools. Mean,median, percentage sampling were used for quantitative analysis and statistics package for social sciences, SPSS (VERSION 11)) was used for qualitative analysis to derive the values of probability(p value). Chi square test was used appropriately for analysis of variables.

Results

Of the 132 patients enrolled in the study there were 55males (41.7%) and 77 females (58.3). The age group of the patients varied from 60 years to 90 years. The number of patients were more in the age groups between 70 and 79years.There was 62 patients(62%) in age groups 60 to 69 years and 64patients (48.5%) in the age group between 70 to 79 years.(Table 1)

The presence of abnormal movements were studied. Seizures was seen in 21patients (15.9) and myoclonus in five patients (3.8%).(Table 2).The Serum Sodium levels of all the patients were evaluated. About 74 patients (56.1%) had serum sodium levels between 100 to 119 meq/L. (Table 3).Study showed that 122 patients (92.4%) had hyponatremia and 10 patients (7.6%) had normonatremia.(Figure 1).

The blood sugar status of the patients were studied. The number of patients having blood sugar values above 500 mg%, 100 to 500 mg%, 50 to 100 mg%, less than 50 mg% were six patients (4.5%), 102(77.3%),14(10.6%), 10(7.6%) respectively. So our study showed 7.6% of patients had hypoglycaemic encephalopathy. (Figure 2)

The serum TSH values were studied.Serum TSH value above 5 mIU/L was seen in 25 patients (18.9%) (Table 4).Thyroid status of the patients were evaluated and showed that clinical hypothyroidism was seen in five patients (3.8%) and subclinical hypothyroidism in 20 patients (15.4%).Majority of the patients were euthyroid (80.8%) (Table 5).

The CSF examination showed 14 patients (10.6%) positive for anti TPO antibodies. These patients were diagnosed as hashimotos encephalopathy. (Figure 3). A Clinical spectrum of patients with HE was studied. HE was comparatively more common in 60 to 69 year group,10 patients (71.4%) were females,57.2 % patients had abnormal movements at presentation,64.3 % patients had hyponatremia Abnormal movements including seizures and myoclonus was seen in 57.2 % of patients. Around 11 patients (78.5 %) were having a euthyroid status. (Table 6). Abnormal movements occurred only in 15.2% in non hashimotos group as against 57.2% in hashimotos group. This was statistically signicant (Table 7).

Table 1 Distribution according to age

Age	Count	Percent
60 – 69	62	47.0
70 – 79	64	48.5
≥ 80	6	4.5
Mean ± SD	70.3 ± 5.9	
Median	70	

Table 2 Distribution according to abnormal movements

Abnormal movements	Count	Percent
None	106	80.3
Seizure	21	15.9
Myoclonus	5	3.8

Table 3: Distribution of the sample according to Serum Sodium

S. Na	Count	Percent
> 145	2	1.5
135 – 145	8	6.1
120 – 134	46	34.8
100 – 119	74	56.1
< 100	2	1.5
Mean ± SD	117.7 ± 9.9	
Median	116	

Table 4 Distribution according to serum TSH levels

S. TSH	Count	Percent
0.3 – 5.0	107	81.1
> 5.0	25	18.9
Mean ± SD	3.9±1.6	
Median	3.95	

Table 5 Distribution according to thyroid status

Thyroid	Count	Percent
Clinical Hypothyroidism	5	3.8
Euthyroid	105	80.8
Subclinical Hypothyroidism	20	15.4

Table 6: Clinical spectrum of patients with Hashimoto's Encephalopathy

14 patients		Hashimotos Encephalopathy	
		Count	Percent
Age	60 – 69	8	57.1
	70 – 79	6	42.9
	≥ 80	0	0.0
Gender	Male	4	28.6
	Female	10	71.4
Abnormal movements	None	6	42.9
	Seizure	6	42.9
	Myoclonus	2	14.3
Serum sodium	Hyponatremia	9	64.3
	Normonatremia	5	35.7
Thyroid status	Clinical Hypothyroidism	1	7.14
	Euthyroid	11	78.5
	Subclinical Hypothyroidism	2	14.3

Table 7: Comparison of Hashimotos vs Non hashimoto's Encephalopathy

		TPO				χ^2	P
		Non hashimotos Enceph		Hashimotos Enceph			
		Count	Percent	Count	Percent		
Age	60-69	54	45.8	8	57.1	1.16	0.560
	70-79	58	49.2	6	42.9		
	>=80	6	5.1	0	0.0		
Gender	Male	51	43.2	4	28.6	1.1	0.293
	Female	67	56.8	10	71.4		
Abnormal Movements	None	100	84.7	6	42.9	14.44**	0.001
	Seizure	15	12.7	6	42.9		
	Myoclonus	3	2.5	2	14.3		
Serum sodium	Hyponatremia	113	95.8	9	64.3	17.71**	0.000
	Normonatremia	5	4.2	5	35.7		
Thyroid	Clinical Hypothyroidism	4	3.3	1	7.14	4.63	0.099
	Euthyroid	94	79.6	11	78.5		
	Subclinical Hypothyroidism	18	15.5	2	14.3		

Fig. 1: Percentage distribution of the sample according to Serum sodium

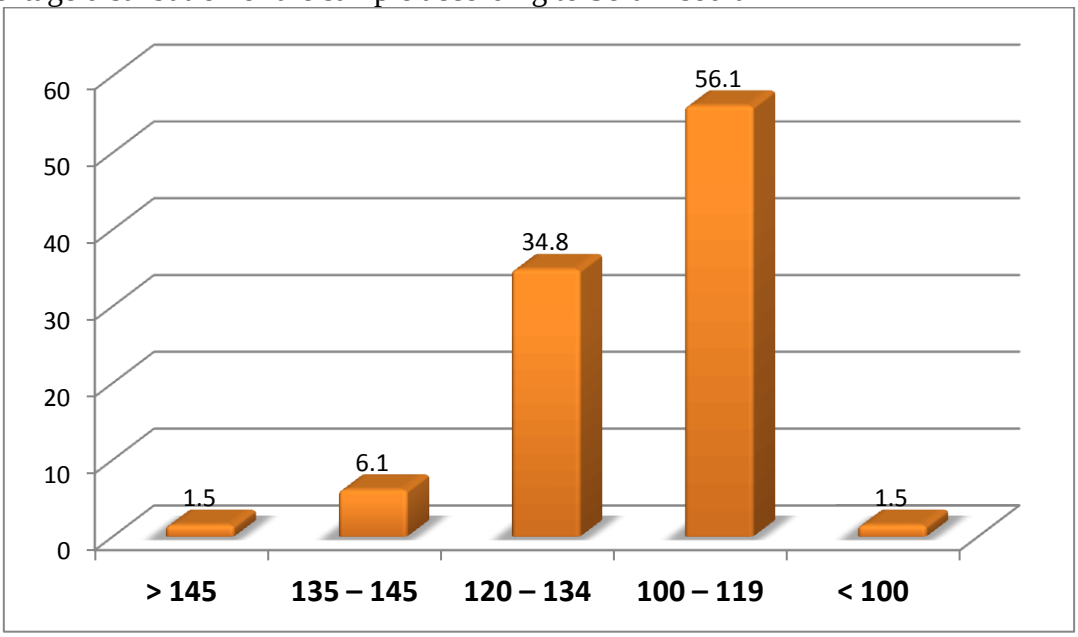


Fig 2: Percentage distribution of the sample according to RBS

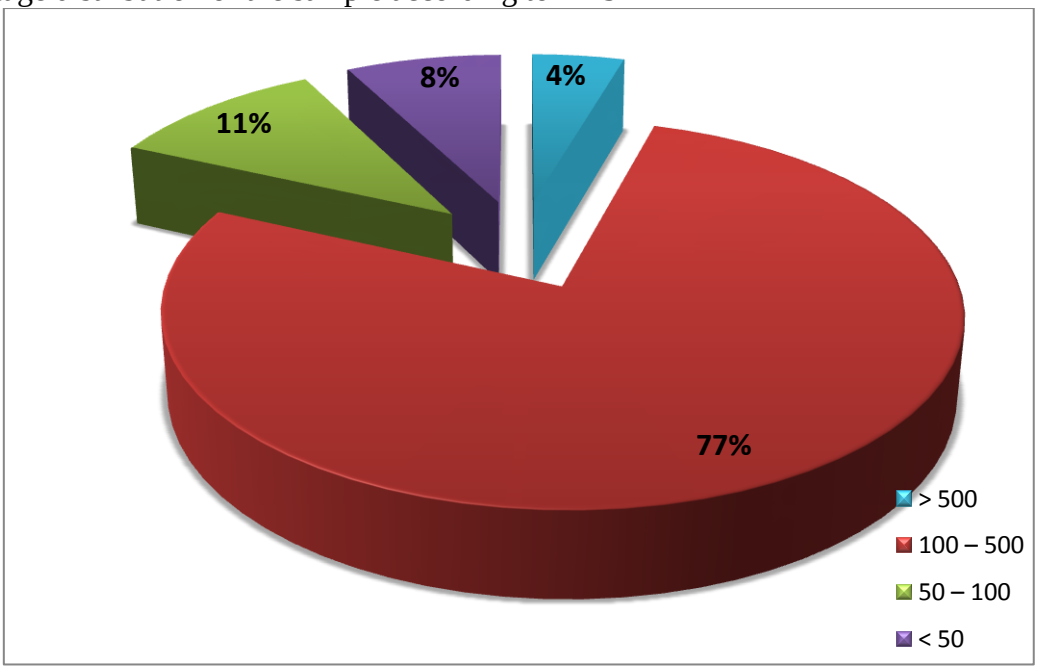
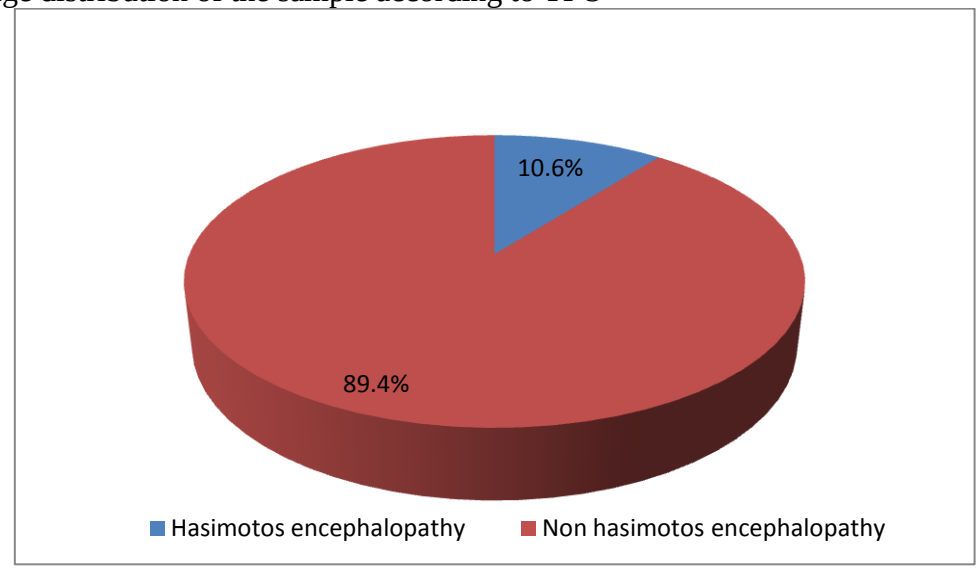


Fig. 3: Percentage distribution of the sample according to TPO



Discussion

Although hyponatremia was the major cause for metabolic encephalopathy in elderly in our study it also showed that 10.6% of the total 132 patients had Hashimoto's encephalopathy. A major proportion of 57.1% were in 60- 69yr age group.; 42.9% were in 70- 79yr age group. None of the patients were older than 80 years. In a study by Chong et al[9] the mean age at onset was 44 years the range being 9-78 years; Matsunaga et al[10] identified two age peaks 20-30 yrs and 50-70yrs. Chaudhuri et al[11] observed that the age range of patients was 21-65 years.

In the study 71.4% of the total 14 patients with HE were females and 28.6% were males. This female preponderance was similar to those of previous studies. Chong et al observed that 62% patients were females, study by Chaudhuri et al had 72% and Matsunaga et al found that 69% of the patients with Hashimoto's Encephalopathy were females.

The present study showed that abnormal movements occur only in 15.2% in non Hashimoto's group as against 57.2% in Hashimoto's group. 42.9% of patients with Hashimoto's Encephalopathy had seizures and

14.3% had myoclonus. Seizures appear to be extremely common in Hashimoto's encephalopathy and deserve consideration in the differential diagnosis of adult onset recurrent epileptic seizures. In the meta analysis by Chong et al 66% of the patients with HE had seizures . In the study by Chaudhuri et al 67% of Hashimoto's Encephalopathy patients had seizures, with recurrent seizures in 6% of patients.. Gayatri et al[12] observed that 87% of children with Hashimoto's encephalopathy had seizures at the time of presentation.

In the present study it was observed that the prevalence of normonatremia was high (35.7%) in the Hashimoto's group compared with the non Hashimoto's group(4.2%). Mention has not been made in the previous studies regarding the Sodium levels at which Hashimoto's Encephalopathy occurs.

In the present study, 78.5% among the total 14 patients with HE were clinically and biochemically euthyroid. 7.14% had clinical hypothyroidism and 14.3% had subclinical hypothyroidism. Matsunaga et al observed that most patients with Hashimoto's Encephalopathy were in euthyroid state. In the meta analysis by Chong et al 35% patients had subclinical hypothyroidism. In the Mayo Clinic series by Sawka et al[13] among the nine patients, three were clinically hypothyroid, four were subclinically hypothyroid, and two were euthyroid. . The study by Chaudhuri et al had not evaluated patients in terms of their thyroid function. Inspite of all these studies literature states that though Hashimoto's encephalopathy may be associated with hypothyroidism, thyroid function is usually clinically and biochemically normal.[14][15] Neurologic symptoms and signs are similar in patients irrespective of their thyroid status.[9]

All previous studies had in common TPO positivity in almost all patients with Hashimoto's encephalopathy. However, anti TPO antibodies have also been found in rheumatoid arthritis, insulin-dependent diabetes mellitus, and a low percentage of euthyroid subjects (14.4% in men and 25.8% in women). Matsunaga et al stressed the importance of a novel test- Anti-alpha-enolase antibodies in the serum of patients with Hashimoto's Encephalopathy which is specific more for Hashimoto's Encephalopathy than for Hashimoto's Thyroiditis. They concluded that patients with anti NAE antibodies tended to exhibit acute encephalopathy and that anti-NAE autoantibodies were positive in 44% of patients with HE.[I0]

Majority of the patients(92.4%) in the present study had hyponatremia. They were further evaluated with thyroid function tests to see if there was any association between hypothyroidism and hyponatremia. Literature gives strong correlation between hypothyroidism and hyponatremia. Hyponatremia is reported in up to 10% of hypothyroid patients, although it is usually mild and rarely causes symptoms.[16] The relationship between hypothyroidism and hyponatremia, although described earlier, was recently questioned by Warner et al. [17] Although they showed a statistical association between hyponatremia and hypothyroidism (for every 10 mU/1 rise in thyroid-stimulating hormone, serum sodium decreased 0.14 mmol/1), the clinical relevance of this association seems minute. If the relationship does exist, a low cardiac output and/or a low glomerular filtration rate could explain its pathophysiology. Georgios et al , University of Vienna had investigated kidney function changes in thyroidectomised patients and found that none had hyponatremia.[18] In the present study too there was no significant association between hypothyroidism and hyponatremia as 92.4% of euthyroid individuals and 95% of hypothyroid individuals had hyponatremia.

Another finding in this study was the occurrence of seizures in hyponatremia. The mean Sodium values at which seizures occurred was 112 meq/1 and thus seizures could be considered as an indicator of severity of hyponatremia. A study by Riggs et al showed that complications of severe and rapidly evolving hyponatremia include

seizures, usually-generalized tonic clonic. Seizures generally occur if the plasma sodium concentration rapidly decreases to <115 mEq/L; they represent an ominous sign and also a medical emergency, as they are associated with high mortality.[19]

This study was conducted in a small population in a tertiary care centre and may not reflect the clear picture in the community. Further studies may be carried out in larger population to characterise the clinical and laboratory features of hashimotos encephalopathy in a better way to improve recognition of this treatable entity.

Conclusions

Hyponatremia and altered blood glucose levels were major causes leading to metabolic encephalopathy in elderly patients. About 10.6% of the elderely patients presented with hashimotos encephalopathy. Abnormal movements were an important presenting feature of hashimotos encephalopathy. A Significant proportion of patients with hashimotos encephalopathy were in euthroid status. A high level of clinical suspicion is needed for the diagnosis, as it is a treatable condition.

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