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Systematic Review

Acute non-alcoholic nutritional neuropathies in high-income countries – a systematic review

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ABSTRACT

INTRODUCTION. We determined the semiology, causes, risk factors and outcomes of patients with acute nutritional neuropathies requiring hospitalisation in high-income countries.

METHODS. We searched PubMed, Cochrane Library and Embase for non-alcoholic malnutrition neuropathy cases published since 1990.

RESULTS. Thirty-six studies were identified, including 83 patients (mean age 39.8 years; 70% women) with deficient levels of thiamine (54%), pyridoxine (16%), copper (11%) or folate (7%). Common clinical signs were lower extremity weakness (100%), hypesthesia (63%), hypo-/areflexia (54%) and cranial nerve deficits (27%). Thirty-two (39%) patients also had Wernicke's encephalopathy. The mean time from symptom onset to hospitalisation was 4.2 weeks (range: 1-12). Ten (12.1%) patients required intensive care. Risk factors were weight loss (60%), vomiting (51%) and diarrhoea (11%). Aetiologies included bariatric surgery (n = 60, 72%), psychiatric disorders (n = 15, 18%) and hyperemesis gravidarum (n = 4, 5%). Electrophysiology showed axonal polyneuropathy in 60 (72.3%) patients, typically with sensorimotor involvement (n = 42). Besides nutritional supplements, 19 (23%) patients also received IVIG, plasmapheresis or steroids. Forty-nine patients had a one-year follow-up, with a good outcome (modified Rankin Scale Score ≤ 2) in 25 (51%).

CONCLUSIONS. Nutritional neuropathies may mimic axonal Guillain-Barré syndrome. Early recognition is crucial to avoid lasting deficits and unnecessary therapy like IVIG or plasmapheresis.

Guillain-Barré syndrome (GBS) is the most common cause of acute polyradiculoneuropathy worldwide [1-3], but thorough differential diagnostic considerations are important to identify GBS mimics [4-6].

In low-income countries, acute nutritional neuropathies are an important differential diagnosis to GBS due to high rates of malnutrition caused by inadequate food intake, poor dietary diversity with starch-rich staples and low rates of food fortification. In high-income countries, nutritional neuropathies are not infrequent either and most often caused by vitamin B_{12} deficiency or thiamine deficiency due to chronic alcohol abuse. However, a wide range of lesser-known and underdiagnosed risk factors of malnutrition exist, e.g., gastric surgery, diuretics, excessive vomiting or diarrhoea, and poor dietary habits in people with psychiatric disorders [7-9]. The spectrum of nutritional neuropathies may be chronic, subacute (< 3 months) or acute (< 4 weeks). Their diagnosis requires a high index of clinical suspicion. For acute onset neuropathies, the primary differential diagnosis is GBS, whereas subacute or chronic cases should prompt consideration of chronic inflammatory demyelinating polyneuropathy, among others. As acute nutritional neuropathies cause significant morbidity and mortality, it is

essential to consider the implications of these GBS mimics also in high-income countries.

We reviewed the literature to investigate adult patients from high-income countries with acute non-alcoholic nutritional polyneuropathies requiring hospitalisation. These neuropathies may mimic GBS but have distinct profiles that are recognisable in the clinical setting.

Methods

Standard protocol approvals and registrations

We followed the Preferred Reporting Items for Systematic Reviewers and Meta-Analysis guidelines [10]. The protocol was preregistered with PROSPERO (CRD42021293301). Objectives were phrased using the PICO (Population, Intervention, Comparison, Outcomes) approach.

Primary objectives

In patients with nutritional neuropathies of (sub)acute onset (< 3 months) requiring hospitalisation in high-income countries (P), what are the frequency, semiology, causes, associated risk factors (I) and clinical outcomes (i.e., in terms of mortality and morbidity) (O), compared to more common acute neuropathies such as GBS (C)?

Secondary objectives

- What are the neurological signs and symptoms, and are there cases with simultaneous central nervous system involvement?

- What is the clinical course from admission to follow-up?

- What are the results from CSF, electrophysiology, neuroimaging and blood tests?

Search strategy, patients and target conditions

We searched PubMed, Cochrane Library, and Embase for non-alcoholic malnutrition neuropathy cases published since 1990. The search strategy combined acute neuropathies and malnutrition. We included hospitalised adults (age ≥ 18 years) diagnosed with (sub)acute (< 3 months) nutritional neuropathy unrelated to alcohol consumption or nitride oxide abuse, irrespective of comorbidities, concomitant therapies and previous history of neurological disease. The target conditions were nutritional neuropathy due to an isolated deficiency or a complex deficiency resulting from several concurrent metabolic disorders [11]. Details are available from the appendix.

Results

We identified 36 suitable studies with 151 patients; individual data were available for 83 patients (**Figure 1, Table 1**). Studies were case reports (n = 31, 86.1%) or case series reporting on single-subject data in retrospective chart reviews (n = 5, 13.8%). Included studies were published in the USA (11 studies), Italy (five studies), Taiwan (five studies), Japan (three studies), Saudi Arabia (three studies), France (two studies), Canada, Ireland, Israel, Kuwait, Singapore, Spain and the UK (one each). Tables S1 and S2 provide details.

FIGURE 1 PRISMA flow chart of the systematic review. Among 11,876 papers screened, 36 were included, comprising 83 patients with acute nutritional neuropathies. Neuropathies caused by alcohol and nitric oxide abuse were excluded.

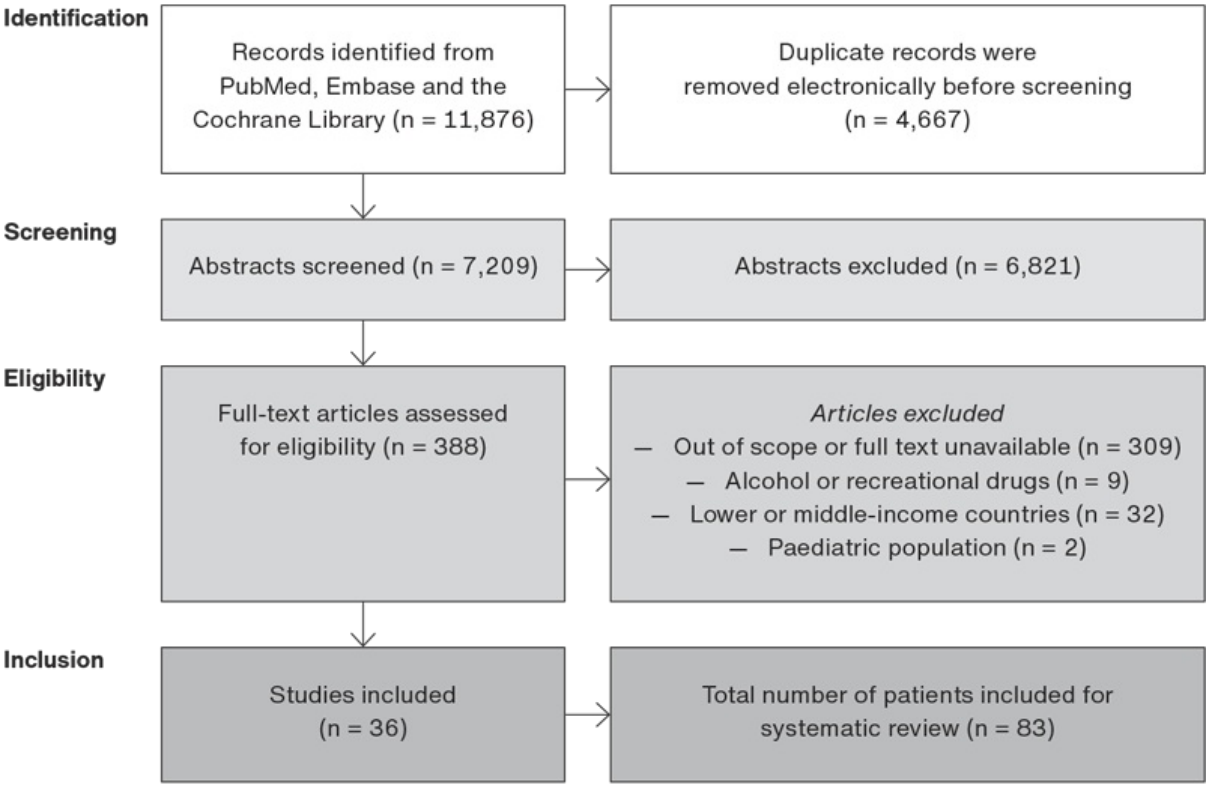


TABLE 1 Total and subdivided patient group characteristics: clinical course, symptomatology, laboratory findings, treatment and outcome.

	Total	Gastric surgery	Psychiatric disorder	Hyperemesis gravidarum	Malabsorption, other	p value
Demographics						
Patients, n (%)	83 (100)	60 (72.3)	15 (18.1)	4 (4.8)	4 (4.8)	
Age, mean (± SD), yrs	40.2 (± 16.7)	40.8 (± 16.2)	35.8 (± 17.8)	24 (± 5.0)	55 (± 14.6)	0.035
Females, n (%)	58 (69.8)	41 (66.7)	12 (80.0)	4 (100)	1 (25.0)	
Malignancy, n (%)	14 (16.9)	14 (23.3)	-	-	-	
Hypertension, n (%)	10 (12.1)	8 (13.3)	-	-	2 (50.0)	
Diabetes mellitus, n (%)	6 (7.2)	5 (8.3)	-	-	1 (25.0)	
Endocrinology, n (%)	4 (4.8)	2 (3.3)	1 (6.7)	-	1 (25.0)	
Nadir, mean (± SD), wks	4.2 (± 3.0)	3.8 (± 3.4)	6 (± 4.2)	4.8 (± 4.4)	3 (± 0.8)	0.281
Risk factors, prior, n (%)						
Weight loss	50 (60.2)	37 (61.7)	11 (73.3)	2 (50.0)	-	
Vomiting	43 (51.8)	33 (55.0)	7 (46.7)	3 (75.0)	-	
Diarrhoea	9 (10.8)	5 (8.3)	3 (20.0)	1 (25.0)	-	
Semiology						
Extremity weakness, n (%)	83 (100)	60 (100)	15 (100)	4 (100)	4 (100)	1.000
UE (MRC), median (range), score	4 (2-5)	4 (2-5)	3 (3-5)	4 (4-5)	3 (2-5)	0.166
LE (MRC), median (range), score	3 (0-5)	3 (0-5)	3 (1-4)	3 (3-4)	2 (2-3)	0.255
Paraesthesia, n (%)	52 (62.7)	42 (50.6)	6 (40.0)	1 (25.0)	1 (25.0)	0.028
Hypo- or areflexia, n (%)	45 (54.2)	29 (34.9)	7 (46.7)	4 (100)	4 (100)	
Wernicke's encephalopathy, n (%)	32 (38.6)	24 (40.0)	3 (20.0)	4 (100)	1 (25.0)	
CN deficits, n (%)	22 (26.5)	16 (19.3)	2 (13.3)	2 (50.0)	2 (50.0)	0.308
Autonomic symptoms, n (%)	12 (14.5)	10 (16.7)	-	-	2 (50.0)	
Organ complications, n (%)						
Cardiological	26 (31.3)	17 (28.3)	5 (33.3)	2 (50.0)	2 (50.0)	0.665
Respiratory	17 (19.3)	11 (18.3)	1 (6.7)	3 (75.0)	2 (50.0)	0.009
Nephrological	2 (3.6)	2 (33.3)	-	-	-	
Laboratory findings, n (%)						
MRI:						
Total MRI, cerebrum	25 (30.1)	16 (26.7)	3 (20.0)	4 (100)	2 (50.0)	
Wernicke's encephalopathy findings	16 (64.0)	10 (40.0)	2 (8.0)	3 (12.0)	1 (4.0)	0.034
Total MRI, spine	18 (21.7)	16 (26.7)	-	-	2 (50.0)	
Myelopathy findings	2 (11.1)	1 (5.6)	-	-	1 (5.6)	
Electrophysiology:						
Sensorimotor	60 (72.3)	49 (81.7)	6 (40.0)	2 (50.0)	3 (75.0)	0.006
Motor	7 (8.4)	3 (5.0)	1 (6.7)	2 (50.0)	1 (25.0)	0.010
Sensory	1 (1.2)	1 (1.7)	-	-	-	
Micronutrient deficiency:[a]						
Thiamin: vitamin B1	45 (91.8)	34 (69.4)	8 (16.3)	3 (6.1)	-	
Pyridoxine: vitamin B6	13 (61.9)	7 (33.3)	6 (28.6)	-	-	
Copper	10 (41.7)	7 (29.2)	2 (8.3)	-	1 (25.0)	
Folate: vitamin B9	6 (25.0)	4 (16.7)	1 (4.2)	-	1 (25.0)	
Cobalamin: vitamin B12	3 (5.6)	1 (1.9)	1 (1.9)	-	1 (25.0)	
Vitamin E	3 (16.7)	2 (11.1)	-	-	1 (5.6)	
Zink	1 (4.2)	1 (4.2)	-	-	-	
Treatment, n (%)						
Thiamin, parenteral	76 (91.6)	56 (93.3)	14 (93.3)	4 (100)	2 (50.0)	
Vitamin suppl.	31 (37.4)	25 (41.7)	3 (20.0)	-	3 (75.0)	
Copper infusion	7 (8.4)	6 (10.0)	-	-	1 (25.0)	
IVIG, PLEX, steroids	19 (22.9)	16 (26.7)	-	-	3 (75.0)	
Outcome						
ICU admission, n (%)	10 (12.1)	6 (10.0)	-	3 (75.0)	1 (25.0)	
Follow-up, n (%)	49 (59.0)	32 (38.6)	12 (14.5)	2 (50.0)	3 (3.6)	0.138
Follow-up time, mean (± SD), mos.	11.8 (± 17.9)	10.6 (± 15.9)	18.0 (± 24.8)	2.5 (± 0.7)	8.3 (± 5.8)	0.250
Monophasic, n (%)	77 (92.8)	55 (91.7)	14 (93.3)	4 (100)	2 (50.0)	
Multiphasic, n (%)	5 (6.0)	3 (5.0)	1 (6.7)	-	1 (25.0)	
mRS ≤ 2, n (%)	25 (51.0)	17 (28.3)	4 (26.7)	1 (25.0)	3 (75.0)	0.264
mRS ≥ 3, n (%)	24 (49.9)	14 (23.3)	8 (53.3)	1 (25.0)	1 (25.0)	0.150

CN = cranial nerve; ICU = intensive care unit; IVIG = intravenous immunoglobulins; LE = lower extremities; MRC = motor weakness as per the Medical Research Council Scale: 0-5; mRS = modified Rankin Scale; PLEX = plasma exchange; SD = standard deviation; UE = upper extremities.
a) Patients may have several micronutrient deficiencies simultaneously.

Patient population

Of 83 patients (Table 1), 58 (69.8%) were female and mean age was 40.2 years (median = 39, range: 14-72). Sixty patients (72.3%) had undergone recent gastric surgery for obesity (n = 46, 76.7%) or gastric malignancies (n = 14, 23.3%), 15 patients (18.1%) had psychiatric disorders, four patients (4.8%) were diagnosed with hyperemesis gravidarum and four patients (4.8%) had other gastrointestinal malabsorption conditions including gastritis, gastric phytobezoar and parenteral nutrition. Twenty-eight patients (33.7%) had comorbidities like hypertension (n = 10, 12.1%), diabetes mellitus (n = 6, 7.2%) and other endocrinological diseases (n = 3, 3.6%). All patients were admitted to hospital due to subacute (< 3 months) progression of lower extremity weakness, eventually leading

to a final diagnosis of nutritional neuropathy.

Patients were divided into sub-groups based on main associated malnutritional risk factor: gastric surgery, psychiatric disorder, hyperemesis gravidarum and other reasons for gastrointestinal malabsorption (Table S1). In all sub-groups, most were women. Women with hyperemesis gravidarum were younger (24 years, range: 18-29, p = 0.035) than the other sub-groups. Comorbidities were more frequent with older age and in patients with gastric surgery and other malabsorption conditions. All patients with gastric surgery were obese or had an underlying malignancy. Mean time from symptom onset to hospitalisation was 4.2 weeks (range: 0.5-12) but differed among subgroups, being shortest among patients with gastric surgery and patients with other malabsorption conditions. Symptom onset of five patients was not disclosed.

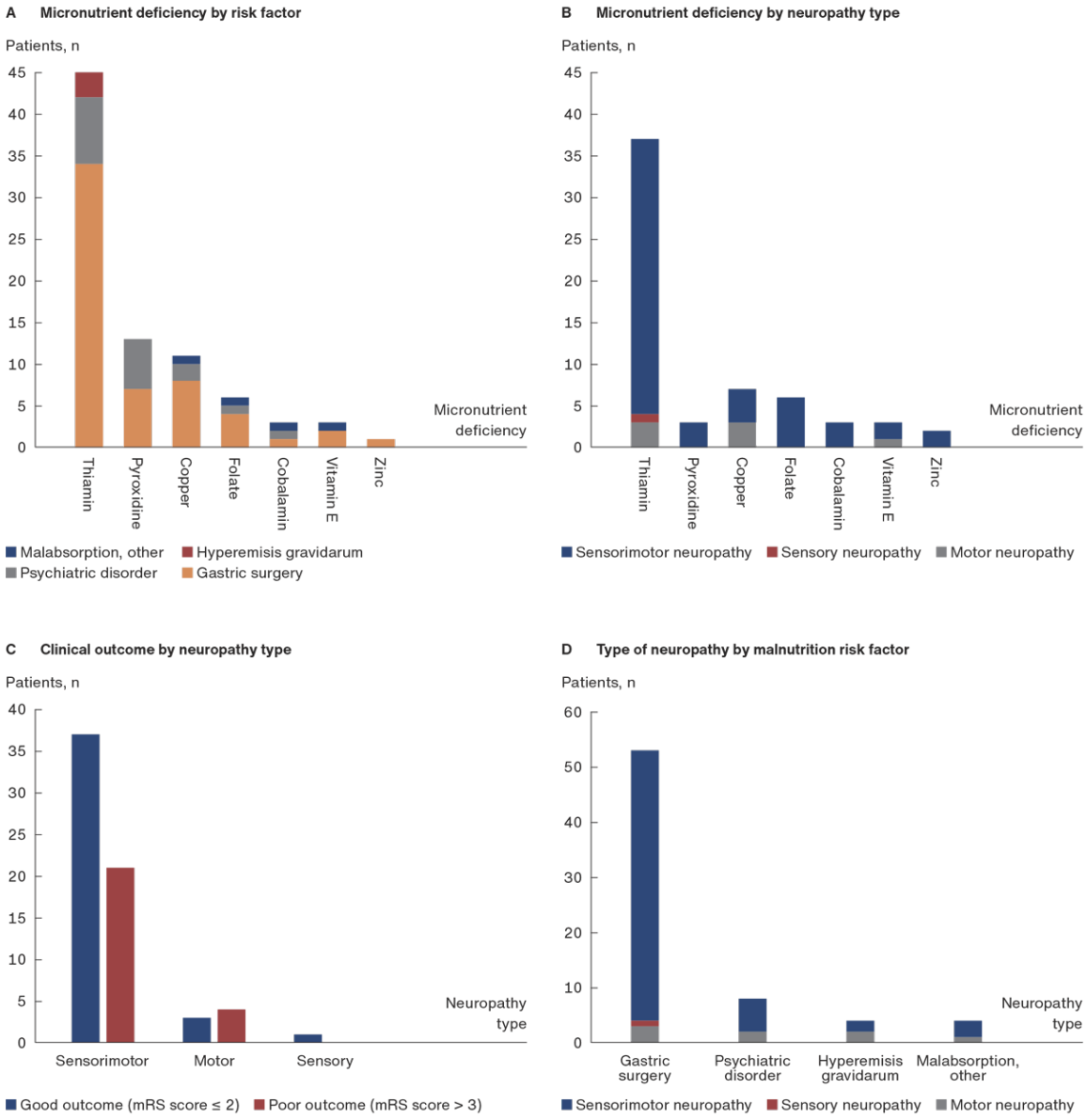
Clinical signs and symptoms

In descending order, patients presented with weakness of extremities (100%), sensory symptoms (62.7%), significant weight loss (60.2%), nausea and vomiting (51.8%), oculomotor symptoms (21.7%), respiratory symptoms including dyspnoea (19.3%), subject memory impairment and/or clinical signs of memory dysfunction (16.9%), autonomic symptoms including urinary incontinence and/or urinary retention (14.5%) and diarrhoea (10.8%). A total of 26 (31%) patients experienced some form of cardiac involvement; for example, chest pain or tachycardia. A total of 61 (81.9%) patients had documented neurologic examinations. Muscle strength according to the Medical Research Council scale was most decreased in lower distal extremities (median = 3, range: 0-5), most severely in patients with malabsorption conditions. Other neurological signs reported included paraesthesia (62.7%), hypo- or areflexia (54.2%), altered mental status (38.6%), Wernicke's encephalopathy (28.9%), cranial nerve deficits (26.5%), autonomic dysfunction (14.5%) and myelopathy (6%). Paraesthesia was associated with psychiatric origin (χ^2 test, n = 83; p = 0.028). Other organ complications (8.4%) included shock, coma, respiratory failure, heart failure due to cardiomegaly or pericarditis, which lead to intensive care unit admission in ten patients (12.1%). Respiratory complications were more frequent in patients with hyperemesis gravidarum (n = 83; p = 0.009).

Laboratory findings

Eighty-two (98.7%) patients were investigated for at least one micronutrient derangement in blood samples, but types and numbers of micronutrient markers varied, including different vitamins, minerals and/or trace elements. Micronutrient deficiency was documented in 61 (73.5%) patients, and evidence of above-range micronutrient levels was found in ten (12.1%) patients. A total of 53 patients had an isolated micronutrient deficiency. Thiamin was deficient in 45 (91%) of 49 patients in whom it was measured, pyroxidine in 13/21 patients (61.9%), copper in 10/24 patients (41.7%), folate in 6/24 patients (25.0%), vitamin E in 3/17 patients (17.6%), cobalamin in 3/57 patients (5.3%) and zinc in 1/24 patients (4.2%). Levels above the normal range were seen in cobalamin (8.4%), folate (2.4%) and copper (1.2%). Other associated laboratory abnormalities included hypoalbuminemia (31.3%), hypokalaemia (24.1%), elevated liver transaminases (9.6%) and increased mean corpuscular erythrocyte volume (4.9%), predominantly among patients with gastric surgery. Lumbar puncture with cerebrospinal fluid (CSF) analysis was performed in 52 patients (62.7%) and was normal in 48 patients; only four patients (4.8%) had elevated protein levels. Main malnutritional risk factors were not associated with a particular micronutrient deficiency (**Figure 2**).

FIGURE 2 Micronutrient deficiency types by risk factors (**A**) and type of neuropathy (**B**), as well as clinical outcomes by neuropathy type (**C**) and type of neuropathy by malnutrition risk factor (**D**). The y-axes in A-D show the number of patients. Sensorimotor neuropathy was associated with gastric surgery, and pure motor neuropathy with hyperemesis gravidarum. The only patient with a pure sensory neuropathy on nerve conduction studies had weakness due to a concomitant myelopathy.



mRS = modified Rankin Scale.

Table S3 in the appendix provides an overview of laboratory findings categorised by micronutrient deficiency. Nerve conduction studies (NCS) were performed in 81 (97.6%) patients and were abnormal in all. Sixty (72.3%) patients had decreased amplitudes on NCS indicative of axonal loss, of whom 42 (70.0%) patients had both motor and sensory nerve involvement, and three patients had pure motor nerve involvement (5.0%). Furthermore, eighteen (30.0%) patients showed signs of both axonal loss and demyelinating lesions with sensorimotor involvement. One (1.7%) patient presented with slow conduction velocity and prolonged F-wave, consistent with a demyelinating motor pattern. In two (3.3%) patients, pure motor involvement was reported without specifying the pathological patterns. Sensorimotor neuropathy was associated with gastric surgery (Fisher's exact test, n = 83; p = 0.01) and pure motor neuropathy with hyperemesis gravidarum (n = 83; p = 0.01). However, no

association between neuropathy type confirmed by NCS and micronutrient deficiency was observed (Figure 2).

Thirty-six (43.4%) patients were investigated with magnetic resonance imaging (MRI) of the brain. Twenty-five (30.1%) MRIs were performed, of which 16 (64.0%) showed hyperintense signal changes on T2- and fluid-attenuation inversion recovery (FLAIR)-sequences involving the thalamus and mammillary bodies, as well as third ventricle enlargement, indicative of Wernicke's encephalopathy, which was clinically diagnosed in 32 (38.6%) patients. MRI findings compatible with Wernicke's encephalopathy were more common in patients with hyperemesis gravidarum (n = 83; p = 0.03). Eighteen (21.7%) MRIs were performed of the spine, with positive findings in two patients (2.4%), suggesting myelopathy.

Treatment

First-line treatment for nutritional neuropathy is parenteral supplementation of deficient micronutrients (thiamin, copper, zinc, pyridoxine, folate, cobalamin), which was eventually initiated in all patients, including thiamin (n = 76, 91.6%), copper (n = 7, 8.4%) and unspecified vitamins (n = 31, 37.4%). However, GBS was initially suspected in 37 patients (44.5%), and 19 (22.9%) were treated accordingly with intravenous immunoglobulin (IVIG), plasmapheresis and/or steroids, often before initiating vitamin supplementation.

Outcomes

A total of 77 (92.7%) patients experienced a monophasic course of disease, and five (6.0%) patients had a polyphasic course. A good outcome (a modified Rankin Scale (mRS) score ≤ 2) was seen in 24 (49.9%) patients, including complete remission in three (6.1%). A poor outcome (an mRS score > 3) occurred in 25 (50.0%) patients. No deaths were registered. Forty per cent of men and 18.5% of women regained the ability to walk independently. Patients with good outcomes were younger (mean = 33.7 years, standard deviation: ± 13.8). Those with sensorimotor neuropathy had the best chance of a good outcome (63.8%), followed by those with pure motor neuropathies (57.1%) (Figure 2 C).

Discussion

Several key messages are available to clinicians from this review. First, acute nutritional neuropathies are not uncommon in high-income countries, and an increasing number of cases are being reported due to more prevalent risk factors like bariatric surgery, psychiatric disorders and other malabsorption disorders, as well as greater awareness. Second, nutritional neuropathies have varying clinical presentations, but most commonly present as progressive lower distal limb weakness with paraesthesia, occasionally including central nervous system signs (e.g., amnesia, ataxia and oculomotor symptoms) and systemic complications (e.g., respiratory symptoms and cardiac failure). Third, most common laboratory findings relate to thiamine deficiency and axonal sensorimotor polyneuropathy confirmed by blood tests and NCS, respectively. Still, there is no consistent correlation between the type of micronutrient deficiency and the type of neuropathy. Importantly, a third of patients has clinical and radiological findings consistent with Wernicke's encephalopathy. CSF analysis tends to be normal. Finally, almost every second patient has a poor outcome (mRS score ≥ 3) on follow-up despite vitamin supplementation. Predictors of good outcomes include young age, male sex and risk factors that are conveniently manageable or temporary, like gastrointestinal malabsorption and hyperemesis gravidarum, respectively. Restated, the prognosis is best among patients with actionable risk factors like hyperemesis gravidarum and malabsorption.

Even when neurophysiological findings are consistent with axonal GBS, interpretation should primarily be guided by the clinical context. Despite their heterogeneity, acute nutritional neuropathies in high-income countries are GBS mimics with a distinct clinical profile that should be recognised to prompt vitamin

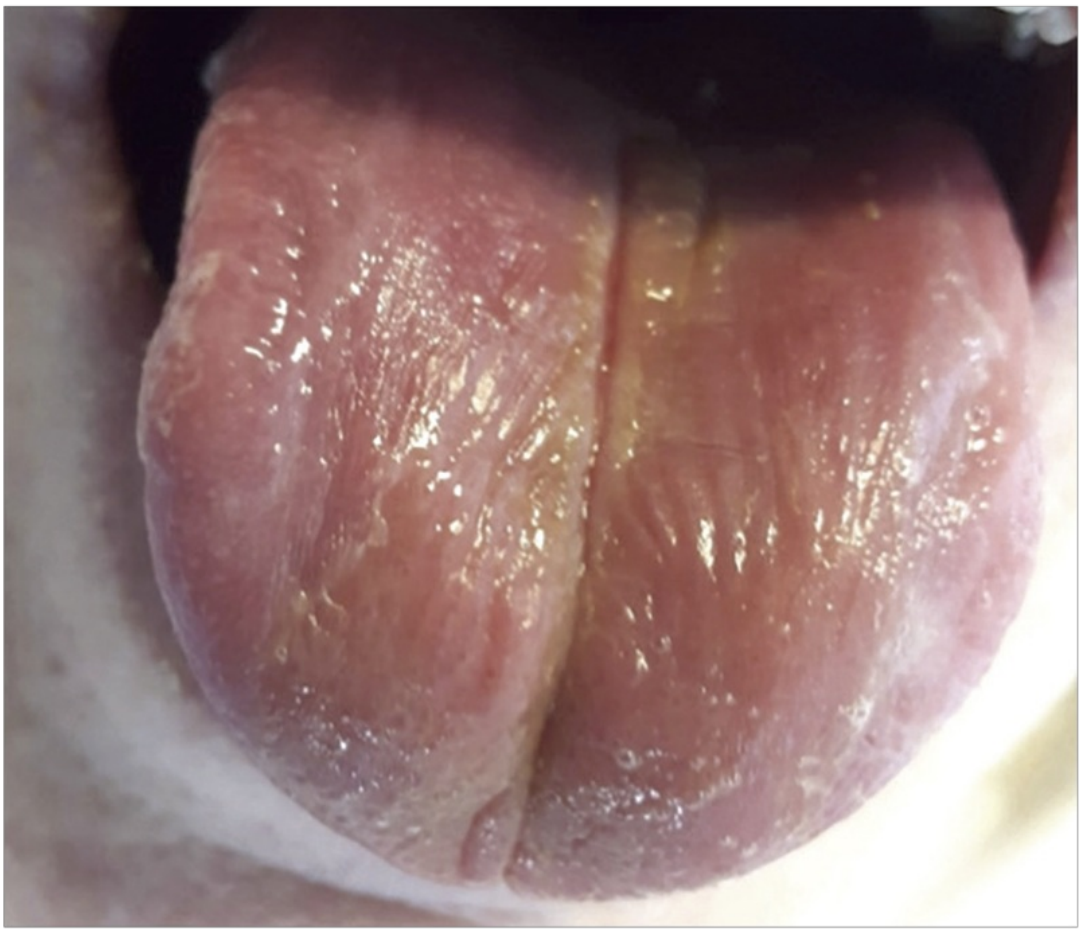
supplementation and avoid unnecessary treatments such as IVIG and plasmapheresis.

Epidemiology and semiology

The main risk factors for malnutrition were bariatric surgery and other malabsorption conditions, psychiatric disorders and hyperemesis gravidarum. Most of the studies (66.1%) were published within the preceding ten years, suggesting an increased awareness of this disorder, as well as an increased frequency of malnutritional risk factors in high-income countries [12]. A recent study confirmed the increase of non-alcohol-related thiamine deficiency in high-income countries [9]. In our study, most patients were women (70%). It is unclear whether women are more susceptible to malnutrition and develop symptoms of micronutrient deficiency more often or if nutritional neuropathy is underrecognised in men. However, some data indicate that micronutrient metabolism does indeed differ between men and women, with the latter being more prone to deficiencies [13]. By contrast, GBS is more prevalent in males than females (ratio 1.5:1), and the highest rates are observed in the youngest and oldest age groups [1]. Although precise data on the incidence and prevalence of nutritional neuropathies in high-income countries are lacking, the large number of case reports and case series suggests that these conditions are likely underdiagnosed.

The most common presentation of nutritional neuropathies was progressive weakness and sensory disturbances of the lower extremity and, with decreasing frequency, weight loss, vomiting, oculomotor symptoms, respiratory symptoms, memory impairment, autonomic symptoms and diarrhoea. Symptoms progressed over weeks, with an average of four weeks from onset to hospital admission. Around 10% of patients were admitted to the intensive care unit due to systemic complications like coma, hypotensive shock, respiratory failure and cardiac failure, including cardiomegaly and pericarditis. Clinical and electrophysiological presentations of acute nutritional neuropathy mimic those of axonal GBS variants like acute motor sensory axonal neuropathy (AMSAN) [14, 15]. However, the distinct clinical setting (i.e., a history of gastric surgery, psychiatric disease or hyperemesis gravidarum, suggesting the possibility of malnutrition), the lack of a preceding infectious illness and the somewhat more delayed onset over days to weeks rather than just a few days, all argue against AMSAN. It is important to realise that obesity (i.e., an excess of calories) does not exclude the possibility of deficient micronutrients. To secure the correct diagnosis, a thorough history and clinical examination are mandatory to identify malnutritional risk factors and physical stigmata, including systemic manifestations of anaemia and liver, kidney and skin involvement (**Figure 3**).

FIGURE 3 Atrophic glossitis associated with acute-onset nutritional neuropathy. Note the complete absence of filiform papillae on the dorsal surface of the tongue. Glossitis reflects deficiencies of micronutrients like riboflavin, niacin, pyridoxine, vitamin B12, folic acid, vitamin E, iron and zinc. Physical stigmata, like glossitis in a patient with sensorimotor polyneuropathy with axonal features on nerve conduction studies in the correct clinical setting (e.g., after gastric surgery or with chronic psychiatric disease), are suggestive of nutritional neuropathy.



Laboratory findings

Micronutrient status in blood was not measured or consistently reported, and when investigated, laboratory biomarkers varied in terms of type and number. We were unable to identify a single causative micronutrient deficiency; however, thiamine levels were most frequently measured and below the normal range in most patients at hospital admission. Thiamine was reported as the only micronutrient to be deficient in 30 patients, whereas 15 patients had decreased thiamine levels and other deficiencies like pyroxidine (vitamin B_6), copper, folate (vitamin B_9), cobalamin, (vitamin B_{12}), vitamin E and zinc. NCS most frequently showed axonal sensorimotor neuropathy. However, pure motor and sensory axonal neuropathy were also seen, and among

these types, demyelinating features were occasionally observed. Since AMSAN has similar electrophysiological characteristics and also typically normal CSF protein [16], NCS and lumbar puncture are not sufficient to establish a diagnosis; rather, results must be interpreted in the correct clinical context.

We found no association between specific micronutrient deficiencies and the type of neuropathy. However, some authors reported clinical characteristics of specific micronutrient deficiencies. Thus, thiamine and zinc deficiency were associated with axonal pure motor neuropathy or with sensory involvement, whereas pyroxidine, folate and vitamin E deficiencies were typically associated with a mild sensory neuropathy, copper deficiency with myelopathy, and cobalamin deficiency with a sensorimotor axonal with demyelinating features [17]. Others [18] found that patients with pure thiamine deficiency had a motor-predominant neuropathy. Another recent study [19] suggested that nerve fibre vulnerability to thiamine deficiency may be variable, selectively affecting motor or sensory fibre populations. On these grounds, it seems that it is not meaningful for clinicians to attempt to attribute certain types of micronutrients to specific electrophysiologic features.

Treatment and outcomes

All patients received relevant micronutrient supplementation; however, immunomodulatory therapies were also administered in 23% of patients, and in some cases, even before the initiation of vitamin supplementation. Overall, 59% of patients who were followed up after an average of four months had a favourable outcome (mRS score ≤ 2). Favourable outcome predictors were young age, male sex and malnutritional risk factors like malabsorption and hyperemesis gravidarum. The course was monophasic in most cases. Immunomodulatory therapies did not seem to be beneficial for either short- or long-term outcomes. Nutritional polyneuropathies are preventable when risk factors are recognised and managed properly. Still, one must keep in mind that patients with gastric surgery and eating disorders will need continuing supplementation to avoid relapses. Hence, the prognosis of acute nutritional neuropathy is not only dependent on prompt recognition and immediate supply of micronutrients but also requires continuous management of the underlying risk factors.

Limitations

We have probably underestimated the true frequency of clinical features of nutritional neuropathies, given the retrospective nature of this data analysis and the well-known limitations of systematic reviews, such as selection, reporting and publication biases. Furthermore, we were unable to quantify treatment effects and morbidity compared to GBS because data that directly compare these two disorders are unavailable. We focused on adults, and neuropathies in children may have different clinical presentations. Given that most data were from before the COVID-19 era, we may have missed potential modified phenotypes in nutritional neuropathies or GBS-mimickers in people with SARS-CoV2 infections [20]. Finally, nodopathies may be misdiagnosed as nutritional neuropathies [21], and there is an overlap between nutritional and toxic neuropathies, especially for manganese-related neuropathy [22].

Conclusions

Nutritional neuropathies occur in high-income countries worldwide. Recognition of these GBS mimics is important to promptly correct the underlying nutritional deficiency and avoid immunotherapies that are not indicated.

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KEY POINTS

- Acute non-alcoholic nutritional neuropathies are not uncommon in high-income countries and may mimic Guillain-Barré syndrome (GBS).
- Although heterogeneous, these GBS mimics have a distinct clinical profile that should be recognised to initiate immediate vitamin supplementation and avoid unnecessary treatments like intravenous immunoglobulin and plasmapheresis.
- One third of patients have clinical and radiological findings consistent with Wernicke's encephalopathy.
- Prognosis is best among patients with identifiable and treatable risk factors like hyperemesis gravidarum and malabsorption.

REFERENCES

1. Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. Neuroepidemiology. 2011;36(2):123-133. https://doi.org/10.1159/000324710
2. Shahrizaila N, Lehmann HC, Kuwabara S. Guillain-Barré syndrome. Lancet. 2021;397(10280):1214-1228. https://doi.org/10.1016/S0140-6736(21)00517-1
3. Papri N, Islam Z, Leonhard SE, et al. Guillain-Barré syndrome in low-income and middle-income countries: challenges and prospects. Nat Rev Neurol. 2021;17(5):285-296. https://doi.org/10.1038/s41582-021-00467-y
4. van Doorn PA, Van den Bergh PYK, Hadden RDM, et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of Guillain-Barré syndrome. Eur J Neurol. 2023;30(12):3646-3674. https://doi.org/10.1111/ene.16073
5. Yuki N, Kokubun N, Kuwabara S, et al. Guillain-Barré syndrome associated with normal or exaggerated tendon reflexes. J Neurol. 2012;259(6):1181-1190. https://doi.org/10.1007/s00415-011-6330-4
6. Fokke C, van den Berg B, Drenthen J, et al. Diagnosis of Guillain-Barré syndrome and validation of Brighton criteria. Brain. 2014;137(pt 1):33-43. https://doi.org/10.1093/brain/awt285
7. Fulgoni VL 3rd, Keast DR, Bailey RL, Dwyer J. Foods, fortificants, and supplements: where do Americans get their nutrients? J Nutr. 2011;141(10):1847-1854. https://doi.org/10.3945/jn.111.142257
8. Galvin R, Bråthen G, Ivashynka A, et al. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol. 2010;17(12):1408-1418. https://doi.org/10.1111/j.1468-1331.2010.03153.x
9. Gomes F, Bergeron G, Bourassa MW, Fischer PR. Thiamine deficiency unrelated to alcohol consumption in high-income countries: a literature review. Ann N Y Acad Sci. 2021;1498(1):46-56. https://doi.org/10.1111/nyas.14569
10. Schardt C, Adams MB, Owens T, et al. Utilization of the PICO framework to improve searching PubMed for clinical questions. BMC Med Inform Decis Mak. 2007;7:16. https://doi.org/10.1186/1472-6947-7-16
11. Lagueny A. Metabolic and nutritional neuropathies. Rev Prat. 2000;50(7):731-735
12. Buchwald H, Williams SE. Bariatric surgery worldwide 2003. Obes Surg. 2004;14(9):1157-1164. https://doi.org/10.1381/0960892042387057

13. Johnson PE, Milne DB, Lykken GI. Effects of age and sex on copper absorption, biological half-life, and status in humans. Am J Clin Nutr. 1992;56(5):917-925. https://doi.org/10.1093/ajcn/56.5.917
14. Feasby TE, Hahn AF, Brown WF, et al. Severe axonal degeneration in acute Guillain-Barré syndrome: evidence of two different mechanisms? J Neurol Sci. 1993;116(2):185-192. https://doi.org/10.1016/0022-510X(93)90324-R
15. Griffin JW, Li CY, Ho TW, et al. Pathology of the motor-sensory axonal Guillain-Barré syndrome. Ann Neurol. 1996;39(1):17-28. https://doi.org/10.1002/ana.410390105
16. Vargas-Cañas ES, Galnares-Olalde JA, León-Velasco F, et al. Prognostic implications of early albuminocytological dissociation in Guillain-Barré syndrome. Can J Neurol Sci. 2023;50(5):745-750. https://doi.org/10.1017/cjn.2022.288
17. Gwathmey KG, Grogan J. Nutritional neuropathies. Muscle Nerve. 2020;62(1):13-29. https://doi.org/10.1002/mus.26783
18. Koike H, Iijima M, Sugiura M, et al. Alcoholic neuropathy is clinicopathologically distinct from thiamine-deficiency neuropathy. Ann Neurol. 2003;54(1):19-29. https://doi.org/10.1002/ana.10550
19. Hamel JI, Logigian EL. Clinical spectrum and prognosis in patients with acute nutritional axonal neuropathy. Neurology. 2023;100(20):e2134-e2140. https://doi.org/10.1212/WNL.0000000000207215
20. Bocci T, Campiglio L, Priori A. Disorders of cranial and spinal nerves. In: Priori A, ed. Neurology of COVID-19. Milano University Press, 2021. https://doi.org/10.54103/milanoup.57.25
21. Gupta P, Mirman I, Shahar S, Dubey D. Growing spectrum of autoimmune nodopathies. Curr Neurol Neurosci Rep. 2023;23(5):201-212. https://doi.org/10.1007/s11910-023-01264-4
22. Peres TV, Schettinger MR, Chen P, et al. Manganese-induced neurotoxicity: a review of its behavioral consequences and neuroprotective strategies. BMC Pharmacol Toxicol. 2016;17(1):57. https://doi.org/10.1186/s40360-016-0099-0

