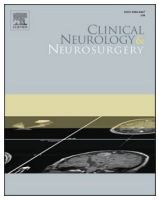
Clinical Neurology and Neurosurgery 249 (2025) 108719

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro



The overlap of diabetic and inflammatory neuropathies: Epidemiology, possible mechanisms, and treatment implications

Yusuf A. Rajabally [a,b,*], Young Gi Min [c]

[a] Inflammatory Neuropathy Clinic, Department of Neurology, University Hospitals Birmingham, UK
[b] Aston Medical School, Aston University, Birmingham, UK
[c] Department of Translational Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea

ARTICLE INFO

Keywords:
Diabetes
Chronic inflammatory demyelinating polyneuropathy
Guillain-Barré syndrome
Nodo-paranodopathy
Radiculoplexus neuropathy
Vasculitis

ABSTRACT

Diabetic polyneuropathy is the common neuropathy of diabetes. However, several inflammatory neuropathies may occur during diabetes. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) represents the most treatable example. There has been uncertainty about a higher risk of CIDP in subjects with diabetes. Contradicting earlier reports, subsequent epidemiological studies failed to confirm an association. However, more recent studies from different populations have shown a two-fold relative risk of concurrent diabetes with CIDP. Recognition of CIDP is important in diabetes as treatment response rates have been reported as comparable with or without diabetes. However, with diabetes, the clinical presentation of CIDP and the resulting disability may be more severe due to additional axonal loss from pre-existing diabetic polyneuropathy and delayed diagnosis. An association of nodo-paranodopathy has similarly been described with a three-fold relative risk of concurrent diabetes in seropositive subjects, particularly those harbouring anti-contactin 1 antibodies. Although rare, recognition of nodo-paranodopathy, with characteristic clinical features, in the context of diabetes is likewise important in view of treatment implications. Other inflammatory neuropathies in diabetes are the painful or painless, cervical, or lumbar, radiculoplexus neuropathies. These need distinguishing from variant, multifocal forms of CIDP, as are not treatable, although remit spontaneously over months or years. There are reports of possible association of Guillain-Barré syndrome (GBS), and particularly of greater GBS severity, with diabetes. Finally, vasculitic neuropathy may also occur in diabetes and requires early suspicion, urgent investigations and immunosuppressant treatment. As the worldwide prevalence of diabetes rises, prompt recognition of its concurrent inflammatory neuropathies, is essential.

1. Introduction

Diabetic polyneuropathy is the most common complication of diabetes. Diabetic polyneuropathy is a slowly progressive distal, symmetric, predominantly sensory neuropathy, which is present in one in six newly diagnosed patients with type 2 diabetes and occurs in about 40 % of subjects with over 10 years of diabetes [1,2]. The diagnosis of diabetic polyneuropathy is, above all, clinical. Conventional nerve conduction studies studying integrity of large fibres through motor and sensory amplitudes and conduction velocities in distal nerve segments [3], despite their documented limitations [4], skin biopsy assessing the intraepidermal fibre density [5], and confocal corneal microscopy evaluating corneal fibres [6], can be of help in confirming the clinical impression. Small fibre modalities are first involved, with pain, dysesthesiae, paraesthesiae and allodynia. Subsequent involvement of large fibres may result in vibratory and proprioceptive loss. However, challenging this concept, concurrent and parallel small and large fibre involvement from onset has also been postulated in diabetic polyneuropathy, both reversible with intervention [7,8]. Besides diabetic polyneuropathy, autonomic neuropathies are common and may produce multiple manifestations including cardiac, gastro-intestinal and uro-gentital [9].

Inflammatory neuropathies occur in a clinical pattern different to that of diabetic polyneuropathy. Although diabetic polyneuropathy has been reported as producing disability [10], the amplitude of functional impairment is characteristically greater, and usually reported as an

* Correspondence to: Inflammatory Neuropathy Clinic, Department of Neurology, Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham, Birmingham B15 2TH, UK.
E-mail address: y.rajabally@aston.ac.uk (Y.A. Rajabally).

https://doi.org/10.1016/j.clineuro.2025.108719
Received 28 November 2024; Received in revised form 2 January 2025; Accepted 3 January 2025
Available online 6 January 2025

unexpected feature of recent occurrence, in inflammatory neuropathies. Chronic inflammatory demyelinating polyneuropathy (CIDP) presents in its typical form, with proximal and distal weakness of the four limbs with large fibre-predominant sensory loss [11,12]. The commonest variant form of CIDP produces multifocal motor and sensory deficits. CIDP evolves over more than 2 months and is treatable by immunomodulatory agents. This distinguishes it from the diabetic lumbosacral or cervical radiculoplexus neuropathies, which have an acute course, with frequent but not constant, severe accompanying pain in the affected limb [13,14]. Radiculoplexus neuropathies may involve other limbs, making the distinction with CIDP more difficult in some cases. Importantly, radiculoplexus neuropathies are self-limiting although can have a protracted course over many months and may require aggressive pain management in the early stages as well as physical therapy. There is no evidence for immunomodulatory therapy in radiculoplexus neuropathies. Separate from the CIDP entity, nodo-paranodopathies occur with a characteristic clinical phenotype of often acute-onset, severe, ataxic and tremulous neuropathy, in presence of autoantibodies against cell adhesion molecules such as contactin-1, contactin-1 associated protein (Caspr-1) and neurofascin. Nodo-paranodopathies may, similarly to CIDP, be more frequent in diabetes. In addition, Guillain-Barré syndrome (GBS), an acute, frequently post-infectious, polyradiculoneuropathy [15,16], may occur in subjects with diabetes, possibly more frequently than in subjects without diabetes, as may vasculitic neuropathies, presenting with mononeuritis multiplex.

2. Potential mechanism of diabetes in inflammatory neuropathies

Pathological studies in patients with diabetic polyneuropathy have shown demyelination and axonal degeneration with loss of myelinated fibers [17]. Unmyelinated fibre pathology is characterized by a reduction in axon density and diameter [17]. Endoneurial microangiopathy occurs in subjects with pre-diabetes and worsens with diabetic polyneuropathy [18,19]. Although sural nerve biopsy studies in patients with CIDP can show similar pathological features to diabetic polyneuropathy, demyelination and remyelination, with onion bulb formation, is a characteristic feature [20]. Macrophage-induced demyelination is pathognomonic although rarely observed [20]. Endoneurial oedema may be another feature, particularly in acute-onset cases [21]. In a study of sural nerve biopsies, epineurial perivascular T-cell infiltrates and immunoreactivity for matrix metalloproteinase-9, was found in diabetic patients with CIDP, but was absent in patients with diabetic polyneuropathy, suggesting it could represent a biomarker for CIDP [22]. Several studies have demonstrated the microvasculitic nature of the radiculoplexus neuropathies, which appears pathologically similar with or without diabetes [23]. In presentations with mononeuritis multiplex pattern, on the other hand, necrotizing vasculitis of perineurial and endoneurial blood vessels, perineurial monocyte infiltrates and endoneurial haemorrhage, have been described [24]. Although there is specific limited evidence for diabetes as a risk factor for various types of inflammatory neuropathy, associations are well-documented for the radiculoplexus neuropathies, and, from recent studies, also for CIDP. Various biological backgrounds, detailed below, suggest that diabetes could either trigger the onset of inflammatory neuropathies or accelerate nerve damage caused by such conditions.

The potential mechanisms of inflammatory neuropathies in the context of diabetes are summarized in Fig. 1.

2.1. *Metabolic pathways*

Chronic hyperglycaemia induces oxidative stress, mitochondrial damage, apoptosis, and cellular apoptosis in neurons and Schwann cells [25,26]. These deleterious effects originate from the dysregulation of critical metabolic pathways, including the glycolytic pathway, polyol pathway, hexosamine pathway, and the formation of advanced glycation end products (AGEs) [27]. For instance, activated glycolysis in Schwann cells leads to an accumulation of lactate and pyruvate, inducing oxidative stress and mitochondrial damage. The polyol pathway heightens intracellular osmotic stress through sorbitol accumulation while depleting NADPH, which may further induce oxidative stress and inflammation. The proliferation of AGEs in diabetes alters protein structures and functions, promoting inflammation and oxidative stress in neurons and Schwann cells via the receptor for AGE (RAGE) [28].

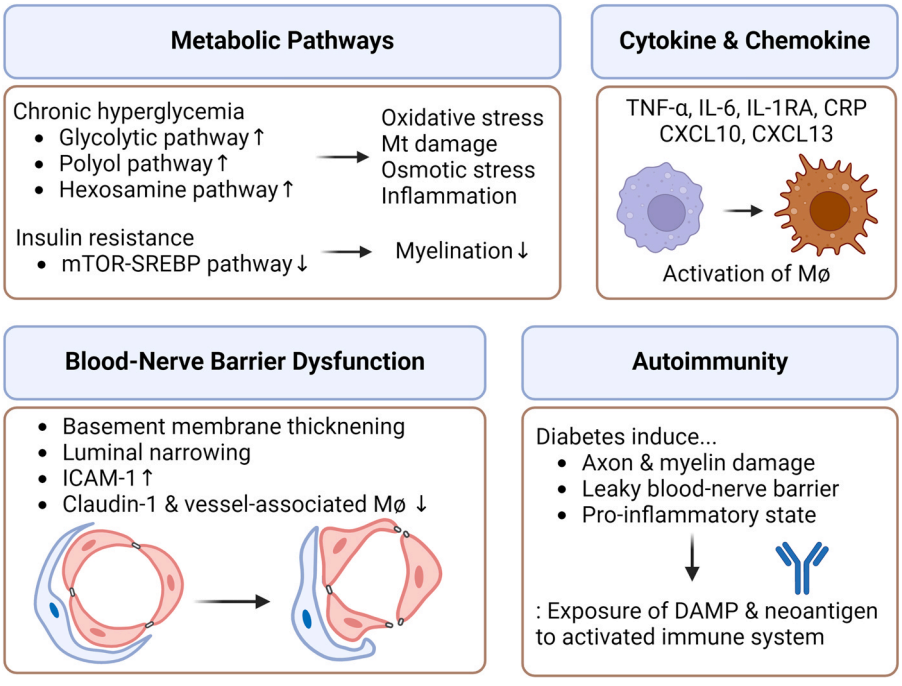


Fig. 1. Potential mechanisms of inflammatory neuropathies in the context of diabetes.

2.2. Cytokines and chemokines

Diabetes is associated with a systemic increase in various cytokines and chemokines, Tumor Necrosis Factor-alpha (TNF-alpha), Interleukin-6 (IL-6), Interleukin-1 Receptor Antagonist (IL-1RA), and C-Reactive Protein (CRP), which can shift the balance of macrophages towards a proinflammatory state. Such macrophages are pivotal cells that directly mediate demyelination in conditions like CIDP. In diabetic conditions, there is a surge of levels of chemokines like CXCL10 and CXCL13, which may be significantly implicated in autoimmune demyelinating neuropathies [29,30]. In spontaneous autoimmune neuropathy models, unlike in physically injured nerves, an increase in CXCL10, CCL5, and CXCL13 is observed, with the latest being highly expressed in macrophages that mediate demyelination in CIDP nerves [31]. Insulin resistance, another significant mechanism in diabetes, disrupts mTOR-SREBP (mammalian target of rapamycin-Sterol Regulatory Element-Binding Protein) signaling, hindering fatty acid and cholesterol synthesis [32], and may consequently also impact adversely on myelination.

2.3. Development of autoimmunity

Metabolic and inflammatory changes induced by diabetes can interact with the adaptive immune system, potentially contributing to the formation of autoimmunity. Diabetic patients, even those without neuropathic symptoms, exhibit higher serum levels of neurofilament light chain [33], indicating that nerves exposed to prolonged hyperglycemia may release internal substances into the extracellular fluid. Proteins that compose axons and myelin can meet with antigen-presenting cells, acting as neoantigens and potentially triggering autoimmunity. Moreover, the release of damage-associated molecular patterns (DAMPs) due to nerve damage can have pro-inflammatory effects [34], activate the immune system through pattern recognition receptors (PRRs) on immune cells [35].

2.4. Blood-nerve barrier dysfunction

Diabetes has been linked to microangiopathy with several possible mechanisms. In patients with diabetes, capillaries exhibit structural changes such as thickening of basement membrane and luminal narrowing [36]. There is a systemic increase in adhesion molecules, including intracellular adhesion molecule-1 (ICAM-1), which closely relates to electrophysiological functions. The blood-nerve barrier (BNB), which restricts the influx of substances from the blood to protect the nerves, consists of the tight junctions formed between endoneurial cells and pericytes of the perineurium. Diabetic nerves display BNB dysfunction, with increased permeability, inflammation, hypoxia, and damage to barrier cells being implicated as plausible mechanisms [37]. Recent studies on streptozotocin-induced experimental diabetes rats have found a reduction in pericyte expression of claudin-1 and diminishes vessel-associated macrophages, particularly increasing leakiness to small molecules [38]. This may allow leukocytes to infiltrate the PNS, exacerbating inflammation and nerve damage.

3. Epidemiology of inflammatory neuropathies in diabetes

The frequency of CIDP in diabetic patients has been uncertain. The current worldwide prevalence of all forms of CIDP is of around 3 per 100,000 [39], although with significant variations which may partly relate to diagnostic criteria used [40]. Although the association has been described for the past several decades [41], there have been successive contradictory reports on a link between the two disorders. A US non-population-based study described an 11-fold increased risk of CIDP in patients with diabetes compared to those without diabetes [42]. However, a large epidemiological study from Italy of over 4 million people reported a diabetes prevalence of just 9 % in 155 patients with CIDP giving a standardized morbidity ratio of only 1.07 (95 % C.I: 0.58–1.80) for diabetes in CIDP [43]. It is possible that methods used in this study to diagnose diabetes were suboptimal, relying on fasting glucose levels and documented use of antidiabetics. Using more rigorous diagnostic methods, a small U.S. epidemiological study of only a quarter of a million subjects, also contradicted the link between CIDP and diabetes, reporting a CIDP prevalence of 8.9/100,000 with only 1/23 patients (4.3 %) having concurrent diabetes, in contrast to 14 of 115 age and sex-matched controls [44]. A U.K. epidemiological study showed, on the other hand, results favouring an association, with about 15 % of patients with CIDP diagnosed as per the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) criteria, having concurrent diabetes [40]. The prevalence of diabetes in CIDP was subsequently investigated in an analysis published in 2016, from a health insurance claims database of over 100 million patients across the U.S [45]. Despite absence of defined diagnostic criteria, the prevalence of CIDP was found to be of 6 per 100,000 in patients without diabetes, consistent with other reports from other countries, but no less than 9-fold higher, of 54 per 100,000 in those with diabetes. This unexpectedly high figure however raised the issue of CIDP misdiagnosis in the U.S., for clinical and electrophysiological reasons [46,47], both more likely in subjects with diabetes.

More recently in 2020, the association was further evaluated in 2 European studies, including a total of 650 subjects with CIDP, from the U.K., Serbia, and Italy [48,49]. Both studies found a 2-fold increased risk of diabetes with CIDP, consistent in the 3 countries, considering local diabetes national prevalence figures. The U.K.-Serbian study showed that subjects affected by both disorders were more likely to present later in life, present with the typical form of CIDP, and had similar pre-treatment disability levels, as well as similar rates and amplitudes of improvement with therapy, compared to subjects without diabetes. Disability levels were greater and response to treatment were, on the other hand, found to be worse with concurrent diabetes in the Italian cohort. Subsequent reports in other countries have since supported these findings [39,50].

In summary, the prevalence of co-existing CIDP and diabetes may show variability attributable to difficulties in accurate case ascertainment, partly as a result of using different diagnostic criteria, as well as the populations studied. The extensiveness with which electrophysiological studies are undertaken may also lead to both over and under-recognition of CIDP, as may, in the first place, the rigor with which clinical evaluation is performed. Accumulation of recent reports from different cohorts makes it highly probable that CIDP is more common in subjects with diabetes, and heightened awareness and attention is required not to dismiss clinical changes, that may suggest the diagnosis in subjects with diabetes.

There are limited data regarding the incidence of lumbosacral or cervical radiculoplexus neuropathies in subjects with diabetes. Previous studies have suggested that the life-long incidence is about 1 % in type 2 diabetes [51]. More recently, the incidence of lumbosacral radiculoplexus neuropathy, including subjects without and with diabetes has been reported as high as 4 per 100,000 per year, i.e. significantly higher than that of CIDP, or Guillain-Barré syndrome (GBS) [52]. The incidence specifically in subjects with diabetes was of 2.79/100,000 per year. This study was on a relatively small population of less than 200,000 inhabitants in Olmsted County, U.S.A., and further confirmatory studies for other geographical regions and populations, are required. The same study found a 7.91 relative risk in subjects with diabetes and pre-diabetes.

The worldwide incidence of GBS is of 1–2/1000,000 per year [53]. Few studies have considered diabetes as a risk factor for GBS. In a recent Danish nationwide population-wide study, diabetes was found amongst the commonest co-morbidities diagnosed within the previous 5 months prior to GBS (O.R. 1.5, after adjustment for infection and surgery), with surgery, leukaemia and lymphoma [54]. Several other studies have otherwise found diabetes as a risk factor of severe prognosis in GBS [55-57]. This may relate to previous axonal damage from diabetic

polyneuropathy, although concurrent pro-inflammatory as well as ischaemic pathophysiological mechanisms, cannot be excluded.

Relatively recently identified nodo-paranodopathies are very rare [58], probably representing less than 2 % of CIDP cohorts [59]. A recent study has suggested a higher risk of these antibody-mediated neuropathies with diabetes [60], interestingly with no suggestion of implication of the autoantibodies in causing diabetes. Of note, other studies had previously also found higher than expected diabetes rates in cohorts of subjects harbouring anti-CNTN1 (contactin-1) antibodies [61], and Caspr1/CNTN1 antibodies [62], and these findings are supported by a recent systematic review on the subject [63], which suggests the association with diabetes mainly relates to subjects with antibody positivity to paranodal antigens.

How frequently vasculitic mononeuritis multiplex may occur in diabetes is unknown, as there have been no epidemiological studies performed. Literature descriptions [64] and clinical experience indicate it is encountered, although much less commonly than CIDP or lumbosacral radiculoplexus neuropathies.

4. Diagnosing inflammatory neuropathy in subjects with diabetes

CIDP is usually progressive, with increasing deficits over weeks to months, with, its typical form, symmetric proximal and distal muscle weakness of all 4 limbs, sensory loss to large fibre modalities and reduced or absent reflexes [11]. In contrast, in diabetic polyneuropathy, small fibre involvement predominates, motor impairment occurs late and remains distal, and the disease progresses slowly over years.

The diagnosis of CIDP is clinical but also relies upon detection of demyelinating features on electrophysiology. Several electrodiagnostic criteria for CIDP have been proposed in the last few decades [65]. Newly updated European Academy of Neurology/Peripheral Nerve Society (EAN/PNS) criteria have been shown to be of good sensitivity and specificity [66,67], comparable to those of previous versions [68,69]. As such, these criteria are reliable to separate the minimal degree of slowing that may be observed in diabetic polyneuropathy to that expected in CIDP, and, in our experience, combination of rigorous clinical evaluation and adequately exhaustive electrophysiology [70], suffices in most cases to reach the correct diagnosis. There are patients with diabetic polyneuropathy who may meet demyelinating CIDP criteria [71, 72], although these patients do not meet the essential clinical criteria for CIDP and should therefore not be considered as having the diagnosis. Although cerebrospinal fluid (CSF) protein levels are increased in most patients with CIDP, the value of a spinal tap is limited in presence of a clinical picture of CIDP and with compatible electrophysiology [11]. Furthermore, diabetes often causes increased CSF protein levels as well, limiting the value of CSF study [73]. Neuroimaging is today commonly used in the diagnostic evaluation of CIDP and associated disorders. However, its value is limited in the setting of concurrent diabetes, particularly as studies having demonstrated the presence of proximal lesions on MRI, like those with CIDP in patients with diabetes but without clinical evidence of CIDP [74,75]. Similarly, ultrasonography has been reported as showing nerve enlargement in both diabetic polyneuropathy and CIDP [76,77]. As regards neuropathology, its value in CIDP is today very limited because of poor sensitivity of characteristic findings, compounded by high reliance on the expertise of the set up offering the service. However, on occasion, nerve biopsy may prove helpful in unusual cases, to exclude potential differential diagnoses and in situations of failure of response to immunomodulatory therapy [78].

Diabetic lumbosacral radiculoplexus neuropathy, also known as diabetic amyotrophy, predominantly occurs in middle-aged or elderly males [79]. Diabetic lumbosacral radiculoplexus neuropathy presents with severe early pain and sensory symptoms with subsequent weakness and wasting, starting proximally, and then frequently extending distally. Contralateral involvement, as well as that of the upper limbs may occur, increasing diagnostic difficulty with CIDP. Weight loss is very commonly associated, and is frequently severe, leading to suspicion of a neoplastic disorder, which needs to be adequately excluded. The course is monophasic with slow improvement, albeit often partial, without treatment, however frequently prolonged for up to 3 years. Diabetic cervical radiculoplexus neuropathy has similar characteristics to those of diabetic lumbosacral radiculoplexus neuropathy [14]. Onset is acute in most, pain is a presenting feature in $>$ 60 % of cases, with weakness almost constant, sensory symptoms being frequent and weight loss also common. Pan-plexopathic involvement is frequent as is contralateral spreading, again on occasion resulting in diagnostic uncertainty, and difficulties separating with variant, upper limb predominant CIDP or Lewis-Sumner syndrome [80]. In addition, associated lumbosacral involvement may occur in a proportion of cases. Of note, in both cases, pain may be absent, contributing to the diagnostic difficulty with CIDP. CSF protein is often mildly elevated in both lumbosacral and cervical forms, and electrophysiology shows axonal involvement typically not meeting requirements for demyelination as observed in CIDP. Abnormal MRI findings may be frequent, with increased T2 signal, nerve hypertrophy and rarely contrast enhancement, which is therefore unhelpful in the differential diagnosis with CIDP, where similar findings may be expected. The disease course is monophasic, like that of its lumbosacral counterpart.

GBS is an acute, frequently post-infectious polyradiculoneuropathy, causing ascending weakness in four limbs, in its classical presentation [15]. Respiratory muscle weakness and cranial nerve involvement, as well as autonomic disturbances may occur during the disease course. GBS is a clinical diagnosis, with electrophysiology being of limited value as is the characteristic albumino-cytological dissociation on cerebrospinal fluid analysis, The clinical manifestations are of an acute nature and rapidly progressive and, as a result, easy to distinguish to those of diabetic polyneuropathy, or of other inflammatory neuropathies.

Nodo-paranodopathies are frequently misdiagnosed for CIDP, but have characteristic clinical features, which include distal predominance, ataxia and tremor [81]. It is important that such features, unexpected in diabetic polyneuropathy, are promptly recognised.

Vasculitic mononeuritis multiplex may also occur in diabetes and is also characteristically different from the length-dependent neuropathy of diabetes, and of other inflammatory neuropathies discussed above. Painful mononeuropathies appear in succession over days to weeks. An extensive work-up for vasculitis is mandatory, and nerve biopsy is also indicated for pathological diagnostic certainty, preferably targeting a clinically-affected sensory nerve [82].

5. Management of inflammatory neuropathies in subjects with diabetes

Identification of a neuropathic presentation, incompatible with diabetic polyneuropathy, and suggestive of an inflammatory aetiology, is essential in subjects with diabetes. On the clinical diagnosis depends decisions for further management. In the case of a clinical picture consistent with CIDP, particularly with proximal weakness and proprioceptive involvement [83], causing disability, it is noteworthy that, irrespective of investigation findings, in particular electrophysiology, it is frequently important to consider a therapeutic trial of immunomodulatory therapy, in view of the potential benefit on function and risk of irreversible decline, without treatment. This has to be counter-balanced by the essential use of outcome measures to determine initial disability level, as well as to ascertain changes with treatment in an as objective way as possible. Several disability measures are used for this purpose [84-86], complemented by strength scores including manual Medical Research Council (MRC) muscle testing and grip strength [87,88].

CIDP is treated by one of 3 first-line therapies, including intravenous immunoglobulins, corticosteroids, or plasma exchanges [11]. The evidence base is well-established [89], although treatment modalities vary, including for immunoglobulins which are extensively used in higher-income countries [90,91]. Therapeutic decisions are in practice

frequently conditioned by cost, availability and individual patient characteristics and circumstances [92]. In subjects with diabetes, corticosteroids, often preferred in pulse oral or intravenous form instead of daily oral therapy [93], are, as far as possible, avoided in view of their adverse effect on glycaemic control. Immunoglobulins are also however at greater risk of thromboembolic complications in presence of vascular risk factors, and hence have to be used with caution in subjects with diabetes, particularly in presence of other such risk factors [94,95]. Response rates in subjects with diabetes have been reported as equivalent as in those without diabetes [49], although presence of severe axonal loss pre-treatment, as may occur with pre-existing diabetic polyneuropathy, is a likely poor prognostic indicator [96,97]. In absence of response, switching to an alternative first-line agent, combination therapy and escalation to immunosuppressant therapy (mainly rituximab and cyclophosphamide [98]), all require consideration based on the level of functional impairment, in subjects with diabetes and similar to what is offered in absence of diabetes [99]. The importance of rigorously and systematically using adequate available outcome measures to objectively assess treatment response, is essential [98].

With regards to diabetic lumbosacral and cervical radiculoplexus neuropathies, there is currently no evidence for use of immunomodulatory therapy. Corticosteroids may be helpful for subjects affected by severe pain, refractory to basic analgesia [100]. In cases with clinical uncertainty about CIDP instead of microvasculitic radiculoplexus neuropathy, when electrophysiological criteria for demyelination are not met, treatment for CIDP is, in our opinion, frequently justified, as histopathological diagnostic confirmation may not be possible. Caution is however required to avoid unnecessary treatment in circumstances of a monophasic disease course [101].

Treatment of GBS presentations in subjects with diabetes is usually straightforward as similar to that of any patient, considering primarily the level of disability, and using either immunoglobulins or plasma exchanges [102]. Again, consideration of the thromboembolic risk with immunoglobulins is important.

Nodo-paranodopathies have poor immunoglobulin response [103]. Steroids may be helpful but need to be administered with caution in diabetics. Rituximab is the agent of choice [58,103].

Mononeuritis multiplex presentations suggestive of vasculitic neuropathy are managed in presence of diabetes similarly to all patients, with corticosteroids preferably pulse intravenous treatment, with careful glycaemic monitoring, with immunosuppressants (cyclophosphamide, azathioprine, methotrexate) considered in case of progression [82].

6. Conclusions

It is essential to accurately identify the inflammatory neuropathies that may occur at any time during the course of diabetes. Regular clinical evaluation allows identifying changes incompatible with the expected features and progression of diabetic polyneuropathy, and a high index of suspicion is desirable, to avoid dismissing patient-reported alterations in functional ability. CIDP is the main treatable diagnosis to consider and appears more common in the setting of diabetes but is often missed or diagnosed with delay, with in some cases, irreversible disability. Electrophysiology is useful to confirm the clinical impression of CIDP in suspected cases, but the clinical evaluation should take priority for therapeutic decisions, including in the differential with less treatable forms of inflammatory neuropathy. Further research is required to determine the potential underlying mechanisms of increased propensity for inflammatory neuropathy in subjects with diabetes, understand how and why presentations may vary, and may shed light on possible targeted treatment avenues, in future.

Disclosures

No relevant disclosures in relation to this work.

CRediT authorship contribution statement

Yusuf A. Rajabally: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Conceptualization. **Young Gi Min:** Writing – review & editing, Writing – original draft, Visualization, Validation.

References

[1] M.J. Young, A.J. Boulton, A.F. MacLeod, D.R. Williams, P.H. Sonksen, A multicentre study of the prevalence of diabetic peripheral neuropathy in the United Kingdom hospital clinic population, Diabetologia 36 (2) (1993) 150–154.
[2] UKPDS, Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33), UK Prospect. Diabetes Study (UKPDS) Group. Lancet 352 (9131) (1998) 837–853.
[3] I.W. Husstedt, S. Evers, K.H. Grotemeyer, Reproducibility of different nerve conduction velocity measurements in healthy test subjects and patients suffering from diabetic polyneuropathy, Electro Clin. Neurophysiol. 37 (6) (1997) 359–363.
[4] P.J. Dyck, C.J. Overland, P.A. Low, W.J. Litchy, J.L. Davies, P.J. Dyck, et al., Signs and symptoms versus nerve conduction studies to diagnose diabetic sensorimotor polyneuropathy: Cl vs. NPhys trial, Muscle nerve 42 (2) (2010) 157–164.
[5] D.N. Herrmann, J.W. Griffin, P. Hauer, D.R. Cornblath, J.C. McArthur, Epidermal nerve fiber density and sural nerve morphometry in peripheral neuropathies, Neurology 53 (8) (1999) 1634–1640.
[6] A. Kalteniece, M. Ferdousi, S. Azmi, S.U. Khan, A. Worthington, A. Marshall, et al., Corneal nerve loss is related to the severity of painful diabetic neuropathy, Eur. J. Neurol. 29 (1) (2022) 286–294.
[7] D. Ziegler, G.J. Bönhof, A. Strom, K. Straßburger, Y. Karusheva, J. Szendroedi, et al., Progression and regression of nerve fibre pathology and dysfunction early in diabetes over 5 years, Brain: a J. Neurol. 144 (10) (2021) 3251–3263.
[8] T.S. Jensen, N.B. Finnerup, Distal symmetric polyneuropathy in diabetes: a progressive disorder? Brain: a J. Neurol. 144 (10) (2021) 2912–2914.
[9] C.H. Gibbons, P. Schmidt, I. Biaggioni, C. Frazier-Mills, R. Freeman, S. Isaacson, et al., The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension, J. Neurol. (2017).
[10] S. Fatma, M.M. Noohu, Classification of functionality of people with diabetic peripheral neuropathy based on international classification of functioning, disability and health Core set (ICF-CS) of diabetes mellitus, J. Diabetes Metab. Disord. 19 (1) (2020) 213–221.
[11] P.Y.K. Van den Bergh, P.A. van Doorn, R.D.M. Hadden, B. Avau, P. Vankrunkelsven, J.A. Allen, et al., European academy of neurology/peripheral nerve society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force-second revision, Eur. J. Neurol. 28 (11) (2021) 3556–3583.
[12] P.Y. Van den Bergh, Y.A. Rajabally, Chronic inflammatory demyelinating polyradiculoneuropathy, Presse Med. (Paris, Fr.: 1983) 42 (6 Pt 2) (2013) e203–e215.
[13] P.J. Dyck, Norell JE. Non-diabetic lumbosacral radiculoplexus neuropathy: natural history, outcome and comparison with the diabetic variety, Brain: a J. Neurol. 124 (Pt 6) (2001) 1197–1207.
[14] R. Massie, M.L. Mauermann, N.P. Staff, K.K. Amrami, J.N. Mandrekar, P.J. Dyck, et al., Diabetic cervical radiculoplexus neuropathy: a distinct syndrome expanding the spectrum of diabetic radiculoplexus neuropathies, Brain: a J. Neurol. 135 (Pt 10) (2012) 3074–3088.
[15] P.A. van Doorn, P.Y.K. Van den Bergh, R.D.M. Hadden, B. Avau, P. Vankrunkelsven, S. Attarian, et al., European Academy of Neurology/Peripheral Nerve Society Guideline on diagnosis and treatment of Guillain-Barré syndrome, Eur. J. Neurol. 30 (12) (2023) 3646–3674.
[16] H.J. Willison, B.C. Jacobs, P.A. van Doorn, Guillain-Barré syndrome, Lancet 388 (10045) (2016) 717–727.
[17] R.A. Malik, S. Tesfaye, P.G. Newrick, D. Walker, S.M. Rajbhandari, I. Siddique, et al., Sural nerve pathology in diabetic patients with minimal but progressive neuropathy, Diabetologia 48 (3) (2005) 578–585.
[18] S. Thrainsdottir, R.A. Malik, L.B. Dahlin, P. Wiksell, K.F. Eriksson, I. Rosen, et al., Endoneurial capillary abnormalities presage deterioration of glucose tolerance and accompany peripheral neuropathy in man, Diabetes 52 (10) (2003) 2615–2622.
[19] H. Yasuda, P.J. Dyck, Abnormalities of endoneurial microvessels and sural nerve pathology in diabetic neuropathy, Neurology 37 (1) (1987) 20–28.
[20] W.M. Bosboom, L.H. van den Berg, H. Franssen, P.C. Giesbergen, H.Z. Flach, A. M. van Putten, et al., Diagnostic value of sural nerve demyelination in chronic inflammatory demyelinating polyneuropathy, Brain: a J. Neurol. 124 (Pt 12) (2001) 2427–2438.
[21] N. Uceyler, G. Necula, E. Wagemann, K.V. Toyka, C. Sommer, Endoneurial edema in sural nerve may indicate recent onset inflammatory neuropathy, Muscle Nerve 53 (5) (2016) 705–710.
[22] S. Jann, M.A. Bramerio, S. Beretta, S. Koch, C.A. Defanti, K.V. Toyka, et al., Diagnostic value of sural nerve matrix metalloproteinase-9 in diabetic patients with CIDP, Neurology 61 (11) (2003) 1607–1610.

[23] P.J. Dyck, J. Engelstad, J. Norell, P.J. Dyck, Microvasculitis in non-diabetic lumbosacral radiculoplexus neuropathy (LSRPN): similarity to the diabetic variety (DLSRPN), J. Neuropathol. Exp. Neurol. 59 (6) (2000) 525–538.
[24] G. Said, C. Lacroix, P. Lozeron, A. Ropert, V. Plante, D. Adams, Inflammatory vasculopathy in multifocal diabetic neuropathy, Brain: A J. Neurol. 126 (Pt 2) (2003) 376–385.
[25] A.R. Hackett, A. Strickland, J. Milbrandt, Disrupting insulin signaling in Schwann cells impairs myelination and induces a sensory neuropathy, Glia 68 (5) (2020) 963–978.
[26] G. Sloan, D. Selvarajah, S. Tesfaye, Pathogenesis, diagnosis and clinical management of diabetic sensorimotor peripheral neuropathy, Nat. Rev. Endocrinol. 17 (7) (2021) 400–420.
[27] Y. Cheng, Y. Chen, K. Li, S. Liu, C. Pang, L. Gao, et al., How inflammation dictates diabetic peripheral neuropathy: An enlightening review, CNS Neurosci. Ther. 30 (4) (2024) e14477.
[28] S.Y. Park, Y.A. Kim, Y.H. Hong, M.K. Moon, B.K. Koo, T.W. Kim, Up-regulation of the receptor for advanced glycation end products in the skin biopsy specimens of patients with severe diabetic neuropathy, J. Clin. Neurol. 10 (4) (2014) 334–341.
[29] Y.H. Kim, S.Y. Jang, Y.K. Shin, Y.R. Jo, B.A. Yoon, S.H. Nam, et al., Serum CXCL13 reflects local B-cell mediated inflammatory demyelinating peripheral neuropathy, Sci. Rep. 9 (1) (2019) 16535.
[30] H.J. Kim, C.G. Jung, M.A. Jensen, D. Dukala, B. Soliven, Targeting of myelin protein zero in a spontaneous autoimmune polyneuropathy, J. Immunol. 181 (12) (2008) 8753–8760.
[31] C. Cutellè, A. De Lorenzo, P.E. Doneddu, M.F. Creta, C. Selmi, G. Liberatore, et al., Cytokines and chemokines in patients with chronic inflammatory demyelinating polyradiculoneuropathy and multifocal motor neuropathy: A systematic review, J. Peripher. Nerv. Syst.: JPNS (2024).
[32] X. Dong, Y. Zhu, S. Wang, Y. Luo, S. Lu, F. Nan, et al., Bavachinin inhibits cholesterol synthesis enzyme FDFT1 expression via AKT/mTOR/SREBP-2 pathway, Int. Immunopharmacol. 88 (2020) 106865.
[33] L.L. Määttä, S.T. Andersen, T. Parkner, C.V.B. Hviid, L. Bjerg, M.A. Kural, et al., Longitudinal change in serum neurofilament light chain in type 2 diabetes and early diabetic polyneuropathy: ADDITION-Denmark, Diabetes care (2024).
[34] M. Ma, W. Jiang, R. Zhou, DAMPs and DAMP-sensing receptors in inflammation and diseases, Immunity 57 (4) (2024) 752–771.
[35] H. Block, J. Rossaint, A. Zarbock, The fatal circle of NETs and NET-associated DAMPs contributing to organ dysfunction, Cells 11 (12) (2022).
[36] H.W. Kan, J.H. Hsieh, H.F. Chien, Y.H. Lin, T.Y. Yeh, C.C. Chao, et al., CD40-mediated HIF-1alpha expression underlying microangiopathy in diabetic nerve pathology, Dis. Model Mech. 11 (4) (2018).
[37] Y. Takeshita, R. Sato, T. Kanda, Blood-nerve barrier (BNB) pathology in diabetic peripheral neuropathy and in vitro human BNB model, Int J. Mol. Sci. 22 (1) (2020).
[38] A. Ben-Kraiem, R.S. Sauer, C. Norwig, M. Popp, A.L. Bettenhausen, M.S. Atalla, et al., Selective blood-nerve barrier leakiness with claudin-1 and vessel-associated macrophage loss in diabetic polyneuropathy, J. Mol. Med (Berl.) 99 (9) (2021) 1237–1250.
[39] M.C. Broers, M. de Wilde, H.F. Lingsma, J. van der Lei, K.M.C. Verhamme, B. C. Jacobs, Epidemiology of chronic inflammatory demyelinating polyradiculoneuropathy in the Netherlands, J. Peripher. Nerv. Syst.: JPNS 27 (3) (2022) 182–188.
[40] Y.A. Rajabally, B.S. Simpson, S. Beri, J. Bankart, J.A. Gosalakkal, Epidemiologic variability of chronic inflammatory demyelinating polyneuropathy with different diagnostic criteria: study of a UK population, Muscle nerve 39 (4) (2009) 432–438.
[41] C. Vital, P. Dumas, D. Latinville, M. Dib, A. Vital, C. Brechenmacher, Relapsing inflammatory demyelinating polyneuropathy in a diabetic patient, Acta Neuropathol. 71 (1-2) (1986) 94–99.
[42] K.R. Sharma, J. Cross, D.R. Ayyar, A. Martinez-Arizala, W.G. Bradley, Diabetic demyelinating polyneuropathy responsive to intravenous immunoglobulin therapy, Arch. Neurol. 59 (5) (2002) 751–757.
[43] A. Chio, F. Plano, A. Calvo, M. Leone, R. Mutani, Cocito D. Comorbidity between CIDP and diabetes mellitus: only a matter of chance? Eur. J. Neurol. 16 (6) (2009) 752–754.
[44] R.S. Laughlin, P.J. Dyck, L.J. Melton, 3rd, C. Leibson, J. Ransom, P.J. Dyck, Incidence and prevalence of CIDP and the association of diabetes mellitus, Neurology 73 (1) (2009) 39–45.
[45] V. Bril, C.M. Blanchette, J.M. Noone, M.C. Runken, D. Gelinas, J.W. Russell, The dilemma of diabetes in chronic inflammatory demyelinating polyneuropathy, J. Diabetes Complicat. 30 (7) (2016) 1401–1407.
[46] J.A. Allen, R.A. Lewis, CIDP diagnostic pitfalls and perception of treatment benefit, Neurology 85 (6) (2015) 498–504.
[47] J.A. Allen, J. Ney, R.A. Lewis, Electrodiagnostic errors contribute to chronic inflammatory demyelinating polyneuropathy misdiagnosis, Muscle Nerve 57 (4) (2018) 542–549.
[48] P.E. Doneddu, D. Cocito, F. Manganelli, R. Fazio, C. Briani, M. Filosto, et al., Frequency of diabetes and other comorbidities in chronic inflammatory demyelinating polyradiculoneuropathy and their impact on clinical presentation and response to therapy, J. Neurol. Neurosurg. Psychiatry 91 (10) (2020) 1092–1099.
[49] Y.A. Rajabally, S. Peric, M. Cobeljic, S. Afzal, I. Bozovic, A. Palibrk, et al., Chronic inflammatory demyelinating polyneuropathy associated with diabetes: a European multicentre comparative reappraisal, J. Neurol. Neurosurg. Psychiatry 91 (10) (2020) 1100–1104.
[50] S. Kuwabara, A. Tsuneyama, S. Misawa, Chronic inflammatory demyelinating polyneuropathy and diabetes, J. Neurol. Neurosurg. Psychiatry 91 (10) (2020) 1035–1036.
[51] P.J. Dyck, K.M. Kratz, J.L. Karnes, W.J. Litchy, R. Klein, J.M. Pach, et al., The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the rochester diabetic neuropathy study, Neurology 43 (4) (1993) 817–824.
[52] P.S. Ng, P.J. Dyck, R.S. Laughlin, P. Thapa, M.V. Pinto, P.J.B. Dyck, Lumbosacral radiculoplexus neuropathy: Incidence and the association with diabetes mellitus, Neurology 92 (11) (2019) e1188–e1194.
[53] J.J. Sejvar, A.L. Baughman, M. Wise, O.W. Morgan, Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis, Neuroepidemiology 36 (2) (2011) 123–133.
[54] L.S. Levison, R.W. Thomsen, H. Andersen, Hospital-diagnosed morbidities and recent surgery as risk factors for developing Guillain-Barré syndrome, Eur. J. Neurol. 30 (10) (2023) 3277–3285.
[55] I. Štětkářová, E. Ehler, M. Židó, D. Lauer, J. Polák, J. Keller, et al., Influence of hyperglycaemia and CRP on the need for mechanical ventilation in guillain-barré syndrome, Front Neurol. 13 (2022) 875714.
[56] S. Peric, I. Bozovic, B. Bjelica, I. Berisavac, O. Stojiljkovic, I. Basta, et al., Diabetes mellitus may affect short-term outcome of Guillain-Barré syndrome, J. Peripher. Nerv. Syst.: JPNS 22 (2) (2017) 127–130.
[57] J.S. Bae, Y.J. Kim, J.K. Kim, Diabetes mellitus exacerbates the clinical and electrophysiological features of Guillain-Barré syndrome, Eur. J. Neurol. 23 (3) (2016) 439–446.
[58] L. Querol, J. Devaux, R. Rojas-Garcia, I. Illa, Autoantibodies in chronic inflammatory neuropathies: diagnostic and therapeutic implications, Nat. Rev. Neurol. 13 (9) (2017) 533–547.
[59] E. Delmont, A. Brodovitch, L. Kouton, T. Allou, S. Beltran, M. Brisset, et al., Antibodies against the node of Ranvier: a real-life evaluation of incidence, clinical features and response to treatment based on a prospective analysis of 1500 sera, J. Neurol. 267 (12) (2020) 3664–3672.
[60] L. Appeltshauser, J. Messinger, K. Starz, D. Heinrich, A.M. Brunder, H. Stengel, et al., Diabetes mellitus is a possible risk factor for nodo-paranodopathy with antiparanodal autoantibodies, Neurol. (R.) Neuroimmunol. Neuroinflamm. 9 (3) (2022).
[61] J. Fehmi, A.J. Davies, M. Antonelou, S. Keddie, S. Pikkupeura, L. Querol, et al., Contactin-1 links autoimmune neuropathy and membranous glomerulonephritis, PloS One 18 (3) (2023) e0281156.
[62] L. Appeltshauser, A.M. Brunder, A. Heinius, P. Körtvélyessy, K.P. Wandinger, R. Junker, et al., Antiparanodal antibodies and IgG subclasses in acute autoimmune neuropathy, Neurol. (R.) Neuroimmunol. Neuroinflamm. 7 (5) (2020).
[63] A. Tentolouris, M.I. Stefanou, A.V. Vrettou, L. Palaiodimou, C. Moschovos, M. Papadopoulou, et al., Prevalence and clinical implications of diabetes mellitus in autoimmune nodopathies: a systematic review, J. Diabetes Complicat. 38 (12) (2024) 108883.
[64] A.F. Vrancken, G. Said, Vasculitic neuropathy, Handb. Clin. Neurol. 115 (2013) 463–483.
[65] A. Breiner, T.H. Brannagan, 3rd, Comparison of sensitivity and specificity among 15 criteria for chronic inflammatory demyelinating polyneuropathy, Muscle Nerve 50 (1) (2014) 40–46.
[66] Y.A. Rajabally, S. Afzal, L.K. Loo, H.S. Goedee, Application of the 2021 EAN/PNS criteria for chronic inflammatory demyelinating polyneuropathy, J. Neurol., Neurosurg., Psychiatry (2022).
[67] P.E. Doneddu, A. De Lorenzo, F. Manganelli, D. Cocito, R. Fazio, C. Briani, et al., Comparison of the diagnostic accuracy of the 2021 EAN/PNS and 2010 EFNS/PNS diagnostic criteria for chronic inflammatory demyelinating polyradiculoneuropathy, J. Neurol. Neurosurg. Psychiatry (2022).
[68] P.Y. Van den Bergh, R.D. Hadden, P. Bouche, D.R. Cornblath, A. Hahn, I. Illa, et al., European federation of neurological societies/peripheral nerve society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the european federation of neurological societies and the peripheral nerve society - first revision, Eur. J. Neurol. 17 (3) (2010) 356–363.
[69] Y.A. Rajabally, G. Nicolas, F. Pieret, P. Bouche, P.Y. Van den Bergh, Validity of diagnostic criteria for chronic inflammatory demyelinating polyneuropathy: a multicentre European study, J. Neurol., Neurosurg., Psychiatry 80 (12) (2009) 1364–1368.
[70] Y.A. Rajabally, M. Narasimhan, Distribution, clinical correlates and significance of axonal loss and demyelination in chronic inflammatory demyelinating polyneuropathy, Eur. J. Neurol. 18 (2) (2011) 293–299.
[71] S.K. Dunnigan, H. Ebadi, A. Breiner, H.D. Katzberg, L.E. Lovblom, B.A. Perkins, et al., Comparison of diabetes patients with "demyelinating" diabetic sensorimotor polyneuropathy to those diagnosed with CIDP, Brain Behav. 3 (6) (2013) 656–663.
[72] S.K. Dunnigan, H. Ebadi, A. Breiner, H.D. Katzberg, L.E. Lovblom, B.A. Perkins, et al., Conduction slowing in diabetic sensorimotor polyneuropathy, Diabetes Care 36 (11) (2013) 3684–3690.
[73] H. Kobessho, K. Oishi, H. Hamaguchi, F. Kanda, Elevation of cerebrospinal fluid protein in patients with diabetes mellitus is associated with duration of diabetes, Eur. Neurol. 60 (3) (2008) 132–136.
[74] M. Pham, D. Oikonomou, B. Hornung, M. Weiler, S. Heiland, P. Baumer, et al., Magnetic resonance neurography detects diabetic neuropathy early and with proximal predominance, Ann. Neurol. 78 (6) (2015) 939–948.

[75] M. Vaeggemose, S. Ringgaard, N. Ejskjaer, H. Andersen, Magnetic resonance imaging may be used for early evaluation of diabetic peripheral polyneuropathy, J. Diabetes Sci. Technol. 9 (1) (2015) 162–163.
[76] S. Kang, S.H. Kim, S.N. Yang, J.S. Yoon, Sonographic features of peripheral nerves at multiple sites in patients with diabetic polyneuropathy, J. Diabetes Complicat. 30 (3) (2016) 518–523.
[77] A. Di Pasquale, S. Morino, S. Loreti, E. Bucci, N. Vanacore, G. Antonini, Peripheral nerve ultrasound changes in CIDP and correlations with nerve conduction velocity, Neurology 84 (8) (2015) 803–809.
[78] J.M. Vallat, F. Tabaraud, L. Magy, F. Torny, P. Bernet-Bernady, F. Macian, et al., Diagnostic value of nerve biopsy for atypical chronic inflammatory demyelinating polyneuropathy: evaluation of eight cases, Muscle Nerve 27 (4) (2003) 478–485.
[79] P.J. Dyck, A.J. Windebank, Diabetic and nondiabetic lumbosacral radiculoplexus neuropathies: new insights into pathophysiology and treatment, Muscle Nerve 25 (4) (2002) 477–491.
[80] Y.A. Rajabally, G. Chavada, Lewis-sumner syndrome of pure upper-limb onset: diagnostic, prognostic, and therapeutic features, Muscle Nerve 39 (2) (2009) 206–220.
[81] A. Uncini, Autoimmune nodo-paranodopathies 10years later: clinical features, pathophysiology and treatment, J. Peripher. Nerv. Syst.: JPNS 28 (2023). Suppl 3: S23-s35.
[82] K.G. Gwathmey, T.M. Burns, M.P. Collins, P.J. Dyck, Vasculitic neuropathies, Lancet Neurol. 13 (1) (2014) 67–82.
[83] U.J. Chaudhary, Y.A. Rajabally, Underdiagnosis and diagnostic delay in chronic inflammatory demyelinating polyneuropathy, J. Neurol. 268 (4) (2021) 1366–1373.
[84] R. Hughes, S. Bensa, H. Willison, P. Van den Bergh, G. Comi, I. Illa, et al., Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy, Ann. Neurol. 50 (2) (2001) 195–201.
[85] R.C. Graham, R.A. Hughes, A modified peripheral neuropathy scale: the overall neuropathy limitations scale, J. Neurol., Neurosurg. Psychiatry 77 (8) (2006) 973–976.
[86] S.I. van Nes, E.K. Vanhoutte, P.A. van Doorn, M. Hermans, M. Bakkers, K. Kuitwaard, et al., Rasch-built overall disability scale (R-ODS) for immune-mediated peripheral neuropathies, Neurology 76 (4) (2011) 337–345.
[87] E.K. Vanhoutte, N. Latov, C. Deng, K. Hanna, R.A. Hughes, V. Bril, et al., Vigorimeter grip strength in CIDP: a responsive tool that rapidly measures the effect of IVIG–the ICE study, Eur. J. Neurol. 20 (5) (2013) 748–755.
[88] Y.A. Rajabally, M. Narasimhan, Jamar hand-held grip dynamometry in chronic inflammatory demyelinating polyneuropathy, J. Neurol. Sci. 325 (1-2) (2013) 36–38.
[89] A.L. Oaklander, M.P. Lunn, R.A. Hughes, I.N. van Schaik, C. Frost, C.H. Chalk, Treatments for chronic inflammatory demyelinating polyradiculoneuropathy (CIDP): an overview of systematic reviews, Cochrane Database Syst. Rev. (1) (2017) CD010369.
[90] Y.A. Rajabally, S. Afzal, Clinical and economic comparison of an individualised immunoglobulin protocol vs. standard dosing for chronic inflammatory demyelinating polyneuropathy, J. Neurol. 266 (2) (2019) 461–467.
[91] A.M. Stino, E. Naddaf, P.J. Dyck, P.J.B. Dyck, Chronic inflammatory demyelinating polyradiculoneuropathy-Diagnostic pitfalls and treatment approach, Muscle Nerve 63 (2) (2021) 157–169.
[92] S. Mehreen, S. Iftikhar, A. Muhammad, R. Aatif Siddique, S. Shahid, Efficacy of azathioprine and methotrexate in patients with chronic inflammatory demyelinating polyneuropathy (CIDP), Pak. J. Pharm. Sci. 36 (4(Special) (2023) 1361–1365.
[93] R. Press, F.L. Hiew, Y.A. Rajabally, Steroids for chronic inflammatory demyelinating polyradiculoneuropathy: evidence base and clinical practice, Acta Neurol. Scand. 133 (4) (2016) 228–238.
[94] Y.A. Rajabally, D.A. Kearney, Thromboembolic complications of intravenous immunoglobulin therapy in patients with neuropathy: a two-year study, J. Neurol. Sci. 308 (1-2) (2011) 124–127.
[95] M. Kapoor, J. Spillane, C. Englezou, S. Sarri-Gonzalez, R. Bell, A. Rossor, et al., Thromboembolic risk with IVIg: Incidence and risk factors in patients with inflammatory neuropathy, Neurology 94 (6) (2020) e635–e638.
[96] M. Iijima, M. Yamamoto, M. Hirayama, F. Tanaka, M. Katsuno, K. Mori, et al., Clinical and electrophysiologic correlates of IVIg responsiveness in CIDP, Neurology 64 (8) (2005) 1471–1475.
[97] A. Al-Zuhairy, J. Jakobsen, Outcome in chronic inflammatory demyelinating polyneuropathy: a systematic review and meta-analysis, Muscle Nerve 68 (4) (2023) 388–396.
[98] Y.A. Rajabally, Contemporary challenges in the diagnosis and management of chronic inflammatory demyelinating polyneuropathy, Expert Rev. Neurother. 22 (2) (2022) 89–99.
[99] Y.A. Rajabally, Unconventional treatments for chronic inflammatory demyelinating polyneuropathy, Neurodegener. Dis. Manag. 7 (5) (2017) 331–342.
[100] Y.C. Chan, Y.L. Lo, E.S. Chan, Immunotherapy for diabetic amyotrophy, Cochrane Database Syst. Rev. (6) (2012) CD006521.
[101] Y.A. Rajabally, Long-term immunoglobulin therapy for chronic inflammatory demyelinating polyradiculoneuropathy, Muscle Nerve 51 (5) (2015) 657–661.
[102] P.A. van Doorn, P.Y.K. Van den Bergh, R.D.M. Hadden, B. Avau, P. Vankrunkelsven, S. Attarian, et al., European academy of neurology/peripheral nerve society guideline on diagnosis and treatment of guillain-barré syndrome, Eur. J. Neurol. (2023).
[103] M.C. Dalakas, IgG4-mediated neurologic autoimmunities: understanding the pathogenicity of IgG4, ineffectiveness of IVIg, and long-lasting benefits of anti-B cell therapies, Neurol. (R.) Neuroimmunol. Neuroinflamm. 9 (1) (2022).