NARRATIVE REVIEW

Antecedent infections, recent developments and future directions in Guillain-Barré syndrome

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Abstract

The Guillain-Barré syndrome is an autoimmune polyradiculoneuropathy causing symmetrical weakness of limbs. After poliomyelitis, it is the second most common cause of paralysis, with an annual incidence of 0.84-1.91 per 100,000 individuals. The syndrome affects both men and women, showing a male preponderance. Campylobacter jejuni, epstein-barr virus, cytomegalovirus, mycoplasma pneumoniae and haemophilus influenzae are amongst the most common causative agents of Guillain-Barré syndrome. Several immunological and genetic factors have been recognised as the risk factors. Human leukocyte antigen, cluster of differentiation 1, and tumour necrosis factor-alpha alleles are among the frequently investigated loci in Guillain-Barré syndrome. Genome-wide association studies have found no significant association of Guillain-Barré syndrome with common variants. Many vaccines against Campylobacter jejuni infection have been proposed, but there are concerns about the efficacy and safety of these vaccines. So far, there is no approved vaccine against Campylobacter jejuni.

Keywords: Guillain-Barré syndrome, Variants, Preceding infections, Genetic factors, Vaccine.

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Introduction

The Guillain-Barre syndrome (GBS), which was initially diagnosed in 1916, is characterised by albuminocytologic dissociation (increased protein values with normal white blood cells or leucopenia) in cerebrospinal fluid (CSF) and acute flaccid paralysis (AFP). At present, the most frequent cause of flaccid paralysis globally is GBS, because poliomyelitis has almost been eradicated.[1] The morbidity rate of GBS is about 20% while the mortality rate is estimated to be about 5%, and most of the patients die from cardiac rhythm disturbances.[2]

The GBS begins with subtle paraesthesia in the fingertips and toes, after that lower extremity weakness starts that can progress over hours and days to include the cranial nerves, limbs, and in extreme cases respiratory muscles. The presence of respiratory muscle dysfunction is a not-so-good prognostic indicator. The GBS is a rare peripheral nervous system (PNS) disorder and has been reported all over the world. Both sensory and motor nerves are damaged by this disorder. The annual frequency of GBS is 0.84-1.91 per 100,000 individuals, and studies have reported that the occurrence increases with age, and men are more susceptible than women.[3]

There are four main subclasses of GBS based on axonal degeneration and myelin sheath damage. Variants based on axonal degeneration are acute motor axonal neuropathy (AMAN) causing damage to motor nerves, and acute motor-sensory axonal neuropathy (AMSAN) causing damage to both motor and sensory nerves. Acute inflammatory demyelinating polyneuropathy (AIDP) is based on myelin sheath and Schwann cell damage. Miller-Fisher Syndrome (MFS) is an infrequent illness caused by ocular nerve damage of the nodal regions. The epitopes of the causative agent have structural resemblance with lipopolysaccharides of human gangliosides and, hence, the immune system attacks the nerves, causing degeneration of axons.[4]

Almost 60-80% of GBS patients develop the syndrome following several infections of the gastrointestinal and respiratory tracts. Several pathogens trigger GBS, and both viral and bacterial factors are implicated in this disorder. Campylobacter (C.) jejuni is the foremost origin of GBS, followed by cytomegalovirus (CMV) and Epstein-Barr virus (EBV). C. jejuni could be recovered from stool culture of GBS patients for a median of 16 days after diarrhoea occurrence. Generally, almost two weeks after the infection, paralysis begins to set in and reaches its

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peak in a month. Antecedent infections of GBS could be fever, cough, flu and abdominal disturbances.[5]

The GBS patients are diagnosed through nerve conduction study (NCS), electromyography (EMG), and CSF analysis. Axonal and demyelination both can be appreciated on NCS. CSF analysis is performed to differentiate between GBS and poliomyelitis by studying albuminocytologic dissociation (ACD). GBS treatment is subdivided into rehabilitation and management therapy. Plasma exchange, or plasmapheresis, is performed to remove autoantibodies from the blood, followed by intravenous immunoglobulin (IVIG) therapy. The IVIG is the addition of healthy antibodies to the patient's blood.[6]

GBS Epidemiology

The GBS is reported from across the world. All age groups and both genders are affected by it. The epidemiological characteristics of the GBS have been reported from England, North America, Iceland and Norway before 1979. The population frequency of GBS in Italy, the United States, Canada, Sweden and Spain ranged from 0.62-2.66 patients per 100,000 people per year. The GBS occurrence rises by 20% for each 10-year increase in age. The relative ratio of the incidence of Fisher syndrome among GBS patients in Japan was higher than in other Asian countries.[7]

GBS Variants

Acute inflammatory demyelinating polyneuropathy (AIDP)

Taheraghdam et al. reported that the AIDP is more frequently linked with CMV and EBV. CMV infection in the past has been linked to cranial nerve dysfunction and extreme sensory deficits in young females. Plasma antibodies contrary to ganglioside monosialic 2 (GM2) were found in some CMV-related GBS patients, but their specificity and significance in the development of GBS are unknown. Degeneration of Schwann cells and myelin results in demyelination which is a salient feature of AIDP.[8]

Acute motor axonal neuropathy (AMAN)

Axonal degeneration has been divided into two subgroups of GBS involving axonal motor nerve degeneration and axonal motor and sensory nerve degeneration. The leading cause of AMAN and AMSAN is C. jejuni, which causes gastroenteritis worldwide. Patients who have previously been infected with C. jejuni frequently experience serious involvement of cranial nerve and pure-motor neuropathy with unusual pathology. AMAN in childhood during the summer is more common in Asia than in the US, Europe and other regions, and is highly prevalent in China.[5]

Acute motor sensory axonal neuropathy (AMSAN)

AMSAN is comparable to AMAN, except that it has sensory involvement. It varies from AMAN in the later age of onset, nerve conduction involvement of sensory fibres, a greater geographical distribution, a longer duration, and slower and partial improvement. Acute and extensive axonal sensory and motor neuropathy without demyelinating characteristics is revealed by nerve conduction studies. The sensory nerve involvement that distinguishes AMSAN from AMAN is present in AMAN patients sub-clinically, too.[9]

Miller-Fischer syndrome (MFS)

The MFS is a rare subgroup of GBS and is found only in 5% of GBS cases. Eye muscle involvement is reported in this disorder which comprises ophthalmoplegia, ataxia and areflexia. Ataxia is mainly noted through gait, with a smaller contribution of the limbs. The MFS is associated with facial nerves and lower cranial nerves.[10]

Antecedent infections of GBS

GBS patients have a history of infection about 3-4 weeks before the onset of the disease. Preceding infections could be viral or bacterial. the main viral factors include CMV and EBV, while bacterial factors are C. jejuni and Mycoplasma (M.) pneumoniae. Signs and symptoms of GBS include cough, fever, flu, nasal discharge, diarrhoea, ascending weakness, areflexia, numbness, and tingling

Table-1: Clinical features of the two major subtypes of Guillain-Barré Syndrome (GBS).

Feature	Acute inflammatory demyelinating polyneuropathy	Acute motor axonal neuropathy
Preceding infection	Cytomegalovirus Epstein-Barr virus Mycoplasma peneumoniae mostly respiratory infection	Campylobacter jejuni, Haemophilus influenzae mostly Gastrointestinal infection
Trigger factors	Monoclonal antibodies Vaccination	Monoclonal antibodies Vaccination
Epidemics	None	Children
Clinical features	Cranial nerve palsies, Sensory deficits	Rarely involve cranial nerves without sensory loss Motor deficits
Involved nerves	Autonomic, cranial and sensorimotor nerves	Motor nerves

sensation. The GBS patients' serological data of preceding event of 16 pathogens was matched to that of gender- and age-matched controls by Jacobs et al. who discovered that 4 pathogens were linked with the emergence of GBS; CMV, C. jejuni, M. pneumoniae, and EBV. The most prevalent antecedent pathogen in GBS was C. jejuni (Table-1). The presence of an antecedent pathogen may be a key factor in distinguishing GBS patients into clinical subtypes.[11]

The role of C. jejuni in GBS

C. jejuni is the principal microbial source of diarrhoeal infection occurring before the onset of GBS and is reported in 30-40% of GBS cases. C. jejuni is a food-borne bacterium, inhabits the chicken gut, and is widely distributed in poultry and poultry products. Nonetheless, other animals like pigs, pet animals, sheep, and cattle may also serve as a source of C. jejuni which is a microaerophilic, gram-negative bacterium requiring a small amount of carbon dioxide (CO2), and grows best at 37- 42°C. The pathogen is most likely transmitted by faeces-infested meat surfaces. Untreated milk, water and waste pollution are some of the other causes of campylobacteriosis.[4]

The involvement of CMV in GBS

The CMV was found to be the most commonly diagnosed viral source of GBS, with prevalence ranging from 10% to 22%. The CMV, unlike C. jejuni-associated axonal GBS, develops AIDP, showing electrophysiological signs of demyelination. The cranial and sensory nerves are often involved in CMV-associated GBS. CMV infection in the past has been linked with extreme sensory deficits in young females.[12]

Haemophilus influenzae involvement in GBS

Haemophilus (H.) influenzae is a usual element of the flora of 80% of humans, occurring in the upper respiratory tract, and isolation might happen in combination with other infectious agents of the GBS. There are six serotypes of capsular strains of H. influenzae (a-f), while type b is found in severe chest infections and seems to be linked with GBS. H. influenzae b is the most important cause of fatal infections.[13] A few type b strains were found to bear lipooligosaccharide (LOS) structures, like human gangliosides. Many children were found to develop GBS after H. influenzae type b conjugate vaccination.[14]

Serological proof of H. influenzae infection was reported in 6(13%) of 41 consecutive GBS patients in a Japanese study. Electro diagnosis and antiganglioside antibodies of AMAN were discovered in some GBS patients with H. influenzae infection, which were similar to those found in GBS patients having C. jejuni infection. The occurrence of monosialotetrahexosylganglioside-1 (GM1) molecules on the surface of H. influenzae pathogens extracted from GBS patients was verified by cytochemical staining with cholera toxin. Axonal GBS may be caused by a GM1-like structure in a specific strain of H. influenzae.[13]

M. pneumoniae's involvement in GBS

M. pneumoniae is a frequent source of lower and upper respiratory tract infections (RTIs) in humans, as well as GBS, and has been linked with the development of many neurological complications, such as cerebellar ataxia, transverse myelitis, and encephalitis. M. pneumoniae exposures are uncommon, and microbial cultures are often negative, finding it challenging to examine the unexplained relationship between antecedent infection and immunological or clinical features. A case-control study published recently reported antecedent M. pneumoniae infection in 3% adult GBS and 21% paediatric GBS cases.[13]

EBV involvement in GBS

EBV can cause complications and diseases other than infectious mononucleosis. Consistent with the increased plasma concentrations of molecules linked with T-cell migration and activation, EBV-related GBS may have a mechanism analogous to CMV-linked GBS. Infections with EBV were found more frequently in mildly affected patients.[15]

Hepatitis E virus involvement in GBS

Hepatitis E virus (HEV) infection has recently been linked with a variety of systemic problems. According to a retrospective cohort report, 7.5% cases of HEV infection had neurological symptoms, including vestibular neuritis, brachial neuritis, and GBS. GBS after HEV infection has been confirmed to have a wide range of clinical manifestations. HEV genome sequences have been discovered in the blood of GBS patients with anti-HEV immublobulin M (IgM) antibodies, suggesting that antiviral drugs can be effective therapies for treating GBS development if the ongoing HEV infection is still impacting the immune reaction at the time of neurological progression.[16]

Zika-virus involvement in GBS

The Zika virus (ZIKV) is a flaviviridae virus that is spread by mosquito bites, sexual contact, and blood transfusions. ZIKV infection may lead to a variety of complications, but only two of them are thought to be autoimmune-related: GBS and idiopathic thrombocytopenic purpura. ZIKV has widely spread in the US following two major outbreaks in 2007 on the Micronesian island of Yaq and in French

Polynesia from October 2013 to April 2014.[17]

Association of GBS with gender

Being male is a risk factor for the onset of GBS, which involves the presence of at least one Y chromosome. Male predominance is an uncommon trait of autoimmune disorders, which are generally more common in women. At least 27 proteins are encoded by the Y chromosome, and a few of them are restricted to the testes. The hereditary risk of developing GBS by being a man might be because of the effects of male hormones produced by gonads.[18]

Association of GBS with age

People of all ages are thought to be affected by GBS. Several epidemiological types of research indicate a small upsurge in late adolescence and early adulthood, possibly because of an elevated risk of C. jejuni infections, and CMVs. This may be due to more vulnerability to autoimmune diseases and compromised immune suppressor mechanisms in old age.[19]

Seasonal trends of GBS

Although most studies did not show seasonal patterns, a few exhibited seasonal clustering in the fall and winter. Yakoob et al. reported spring (March-May), fall (September-November) and winter (December-February) seasonal clustering. Only three patients in that study presented in the summer (June-August).[20]

Role of anti-ganglioside antibodies

Antiganglioside antibodies are found in the blood of patients suffering from autoimmune neuropathies and these antibodies react with self-gangliosides. The underlying mechanism for antibody-mediated neuropathy includes modulation of ion channel function at the nodes of Ranvier, complement-dependent cytotoxicity at the nodes, motor nerve terminals, and interference with nerve regeneration. These antibodies were developed against tetrasialylated lactosylceramide-3 (GQ3), disialoganglioside-3 (GD3), glycosyltransferase-1 (GT1), and GM1 displaying a well-determined association with subgroups of GBS. AMAN often has IgG against GM1, disialoganglioside-1a (GD1a), and N-acetylgalactosaminyl disialoganglioside-1a (GalNAc-GD1a) (Table-2). Patients with Miller Fisher syndrome have reactivity against tetrasialylated lactosylceramide-1b (GQ1b), which is expressed at the para-nodal regions of extraocular motor nerves.[21]

Table-2: Classification of typical antiganglioside antibodies found in Guillain-Barre´ Syndrome (GBS).

Variant	Antibody
Acute inflammatory demyelinating polyneuropathy (ADIP)	No specific antibody
Acute motor axonal neuropathy (AMAN)	GD1a, GalNac-GD1a, GM1a, GM1b
Acute motor sensory axonal neuropathy (AMSAN)	GD1a and GM1
Miller-Fischer syndrome (MFS)	GT1a and GQ1b
Acute motor conduction block neuropathy	GD1a and GM1
Pharyngeal-cervical brachial variant	GD1a, GQ1b, GT1a
Acute ataxic neuropathy (without ophthalmoplegia)	GT1a and GQ1b
Bickerstaff encephalitis	GT1a, GQ1b
Pure sensory ataxic variant	GT1a, GQ1b, GD1b

Molecular mimicry and cross-reactivity

GBS is caused by autoimmunity, where the immune system attacks the axons and myelin sheath of neurons by mistake, and signals in and out of the brain travel through the nerves. This "mistaken immune attack" may ascend due to the C. jejuni surface which contains polysaccharides resembling glycoconjugates of the human ganglions. This similarity was named "molecular mimicry," which is described as the recognition by a receptor of T or B-cell of a structural molecule of a microbe and host antigen. It is the process through which infections induce reactive antibodies or T cells that may progress to autoimmune diseases.[22]

Doorn et al. reported that there exists molecular mimicry amongst lipopolysaccharides of C. jejuni and human gangliosides. When C. jejuni attacks the human body, macrophages attack the pathogen, phagocytose and digestion occurs in the proteasome. There may be a cross-presentation of major histocompatibility complex-I (MHC-I) and MHC-II. Antigenic peptides of C. jejuni are displayed to T-cells by their binding to antigen-presenting cells. T-cells, in turn, activate B-cells which produce antibodies. These antibodies are usually cross-reactive and attack gangliosides, causing demyelination and axonal degeneration.[23]

GBS pathogenesis

The GBS is a post-infectious disorder triggered by an immune reaction to an infectious pathogen. The GBS has been known as a heterogeneous syndrome whose intensity was correlated with the degree of axonal and demyelination-related injury. However, several phenotypes, including AIDP (in which myelin sheath and associated Schwann cells are damaged by immune-related injury) and AMAN (in which axons are affected by immune-related injury) are now well-understood. It is a rare disorder that is mainly humoral regulated instead of mediated by T cells, causing inflammation. The AMAN is an antibody-linked molecular mimicry-driven attack between microbial and axolemmal surface molecules.[24]

Immunological responses in GBS

T-lymphocytes take part in cell-mediated immunity. T-helper 17 (Th17) cells are a subclass of T-cells implicated in cell-mediated immunity and inflammatory responses. These cells synthesise several signalling molecules (interleukins [IL]), such as IL-17A, IL-22, IL-17F and IL-21. IL-17 is implicated in neutrophil aggregation and has a central role in immune-mediated and autoimmune responses. The Th17 cells defend the host against many extracellular fungal and bacterial infections on the mucosal surfaces of the skin, gut and lungs. Endothelial cells, fibroblasts, epithelial cells, macrophages and keratinocytes amongst other cell types have IL-17A and IL-17F receptors.[25]

Genetic basis to GBS susceptibility

Being a hereditary disorder, GBS has been reported in many families. The MFS, the important variant of GBS, which occurs concurrently has also been reported in two siblings.[26] Twelve families with GBS were found in the largest study from the Netherlands.[26] Geleijns et al. revealed that the observed incidence among siblings of GBS subjects was 2.6 times higher than the predicted occurrence. The likely role of hereditary factors in GBS is reinforced by these studies (Table-3).[26]

Table-3: Preceding events of Guillain-Barre´ Syndrome (GBS).

Events	Factors
Th 17 and IL-17	Immunological responses
CD1 gene	Genetic predisposition
TNF α gene	Genetic predisposition
TLR2 gene	Genetic predisposition
Vaccine	Swine flu & Rabies
Bacterial infections	Campylobacter jejuni, Mycoplasma pneumoniae, Haemophilus influenzae
Viral infections	Epstein barr virus, Cytomegalovirus, Zika virus, Hepatitis E virus
Gastrointestinal infection	Bacterial infection
Respiratory infection	Viral infection

Th 17: T Helper 17, IL-17: Interleukin-17, CD1L Cluster of differentiation 1, TNF: Tumour necrosis factor, TLR2; Toll like receptor 2.

Involvement of CD1 syste

Lipid antigens are displayed to T-cells by cluster of differentiation 1 (CD1) macromolecules. As the myelin sheath of gangliosides consists of glycolipids and these lipid antigens are presented to T lymphocytes by CD1 molecules, therefore polymorphism of CD1 genes may have a crucial role in GBS pathogenesis. There exist five CD1 genes on human chromosome 1; CD1At to CD1-E. The CD1 gene polymorphisms can influence GBS susceptibility. A research looked into CD1 gene polymorphisms in GBS cases from a population of Chinese Han. In 126 cases and 138 healthy controls, exon 2 of the CD1E and CD1A genes were genotyped. CD1A gene polymorphisms were found to be related to GBS. Moreover, subjects with CD1A*01/02 had a 2.9-fold lower risk of developing GBS than the controls, and those with CD1A*02/02 had a 2.5-fold higher risk, whereas CD1E gene polymorphisms had no connection with GBS susceptibilities.[27]

Genetic contribution of Tumour necrosis factor alpha (TNF-α) gene

Tumour necrosis factor alpha (TNF-α) is a cytokine synthesised by various cells and may play a significant role in the aetiology of immune-related diseases, especially those with an inflammatory and autoimmune component. Utilising polymorphisms, numerous studies have proposed relations amongst TNF region and autoimmune ailments, like insulin-dependent diabetes, systemic lupus erythematosus (SLE), and multiple sclerosis. Earlier research has shown that serum TNF-α values are higher in patients with GBS, showing that serum levels correlate with the seriousness of the disease. The TNF polymorphisms, nevertheless, have not been explored in GBS to date.[28]

Association of Toll-like receptor 2 (TLR-2) polymorphism with GBS

Toll-like receptors (TLRs) are involved in several autoimmune diseases, including GBS, and play a significant role in host defenses. Polymorphism in the genes encoding TLRs may result in reduced or overexpression of TLR proteins. Genetics, demographics and environmental factors influence the magnitude of the connection between polymorphisms and autoimmune disease. TLR-2 polymorphisms were linked to an increased risk of autoimmune disease in several studies. However, certain TLR-2 polymorphisms may not be linked to rheumatoid arthritis (RA) as an autoimmune illness. Kharwar et al. conducted a study in India to see if there was a connection between TLR-2 and IL-8 expression and gene polymorphism in GBS patients. TLR-2 polymorphisms were found to have a vital link with GBS, and elevated expressions and higher levels of IL-8 can play a vital role in GBS progression. Also, polymorphisms in TLR-2 could be used as a genetic marker for GBS susceptibility.[29]

Genome-wide association study (GWAS) of GBS

Until now, there is only one genome-wide association study (GWAS) of GBS in which Blum et al. found no significant association of imputed human leukocyte antigen (HLA) alleles and individual single nucleotide polymorphisms (SNPs) with GBS. They reported that common SNPs contribute up to 25% susceptibility of GBS.[30]

Vaccination: A possible cause of GBS

Epidemiological research has shown that GBS may develop after vaccination against a variety of pathogens. Polio (oral vaccine), influenza, rabies, measles/mumps/rubella, measles, hepatitis B, tetanus toxoid, and further vaccinations are examples of certain vaccines. GBS symptoms can appear anywhere from a day to some weeks after vaccination, peaking around two weeks. GBS induced by vaccination was first observed in 1976-77, within 6-8 weeks of obtaining the swine flu vaccine during an influenza vaccination campaign.[31]

A study found that monovalent inactivated influenza A (H1N1) vaccines were linked with a slight increase in GBS risk. This meant that for every 100,000 vaccinated applicants, there were around 1.6 extra cases of GBS though there are contradictory accounts. However, trials of influenza vaccine used for the subsequent years have found a little to no rise in the risk of GBS.[32]

GBS diagnosis

Although there are clinical diagnostic criteria for GBS, no neurophysiological classification criterion has been established. Electrodiagnostic research aid in the diagnosis, classification and prognosis of patients. In electrodiagnostic studies performed within 10 days of GBS onset, abnormal late responses are the utmost common finding with partially blocked motor conduction, distal temporal dispersion (TD), the presence of several A-waves, as well as an irregular blink reflex (BR).[33]

The GBS includes ancillary testing, such as CSF and serum analysis. CSF protein levels increase in more than three-quarters of patients with a regular or irregular mononuclear cell count. During the first week of infection, CSF proteins may be normal. But after 2-3 weeks, there is an upsurge in the albumin level, most probably due to demyelination of myelin sheath and axonal degeneration. Extractable nuclear antibodies, antinuclear antibodies, anti-neutrophil cytoplasmic antibodies, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), electrolyte, creatinine, urea, serum delta-aminolevulinic acid levels, and blood sugar levels are all measured for porphyria, but the findings are non-specific. Porphobilinogen is occasionally detected in urine.[34]

GBS treatment

IVIG is just as effective as plasma exchange for treating GBS. The American Academy of Neurology (AAN) practice parameters on GBS immunotherapy reached this conclusion in 2003, which has been subsequently confirmed by several studies, including a 2006 meta-analysis of five trials involving mainly adult non-ambulatory patients, contrasting IVIG with plasmapheresis for the treatment of GBS patients, and a systematic study of GBS immunotherapy published in 2007.[35]

GBS vaccines

In recent years, knowledge of bioinformatics has made it much easier to obtain information about genomics, proteomics and new bacteria vaccines. Predicting the production of recombinant vaccines has benefits over other approaches in terms of vaccine development. In silico vaccines can be thought of as quick and easy way to detect antigens and allergens while also reducing laboratory errors. They are less expensive than other conventional methods, but epitope region anticipation is not always 100% accurate, and the results of multiple servers are unlikely to be identical.[36]

Earlier researches have indicated that an effective C. jejuni vaccine may be produced. Some scientists, for example, have employed whole-cell vaccines against C. jejuni, which have succeeded in animal models, but have failed in human trials and the results have not been approved in terms of human safety thus far. Moreover, various studies have suggested that bacteria's polysaccharide capsule (cps) may be used to treat campylobacteriosis, but this method has only been tested in phase 1 clinical trials, Besides, there are concerns about the mimicry amongst human gangliosides and bacterial polysaccharides. Other antigens, such as ATP-binding cassette (ABC) transporter periplasmic binding protein-1 (PEB1), which is an immunogenical and defensive protein, may be used in C. jejuni vaccination development. It is possible that the immune system's inverse PEB1 protein response, which is formed by lymphocytes, will prevent the disease from progressing. This vaccine, on the other hand, is only in pre-clinical testing. Further pathogenic proteins of C. jejuni have also been studied. Despite multiple attempts to create a vaccine, no C. jejuni vaccine has yet been approved for human use.[37]

There is a need to understand more about the aetiology of GBS. Immunological factors that trigger GBS may be explored through large sample sizes. There appear to be

genes that make subjects susceptible to the development of the disease. There would be a benefit in repeating GBS studies by studying the genes that predispose to the disease. Such genes are a promising candidate for further studies. Further, GWAS should be repeated in a larger cohort to look for more common SNPs associated with GBS. There is a dire need to develop an effective vaccine for GBS.

Conclusions

About two-thirds of GBS patients develop the syndrome following an antecedent infection. Both viral and bacterial factors are implicated in this disorder. GBS has been reported all over the world. All age groups and both genders are affected by this syndrome. GBS, being a hereditary disorder, has shown genetic predisposition. T-lymphocytes take part in cell-mediated immunity and IL-17 levels trigger autoimmunity. GBS may rarely develop after vaccination. Despite multiple attempts to create a vaccine, no vaccine has yet been approved for human use against pathogens implicated in GBS.

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