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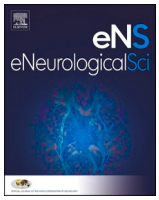

Review article

Is there a link between Hepatitis A virus and Guillain-Barré syndrome? A systematic review of case reports

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ABSTRACT

Introduction: Guillain-Barré syndrome (GBS) is an inflammatory disorder of the peripheral nervous system, causing acute flaccid paralysis. There have been occasional reports linking Hepatitis A virus (HAV) to GBS. Here we aimed to evaluate the current literature on the association between GBS and HAV, exploring potential mechanisms and clinical implications.

Methods: We conducted a systematic search using PRISMA guidelines in PubMed, Web of Science, Embase, and Scopus. Only published case reports or conference abstracts presenting cases of confirmed HAV infection and GBS were included. Data extraction was performed independently by two reviewers, and quality assessment was conducted using the Joanna Briggs Institute critical appraisal tool.

Results: Out of 581 studies identified, 46 studies encompassing 47 cases met the inclusion criteria. The mean age of patients was 29.47 years, with a male predominance (70.2 %). Geographically, most cases were reported in Asia (74.5 %). Clinical manifestations of HAV included fever, malaise, and jaundice, while GBS presented with muscle weakness and areflexia. Laboratory findings showed albuminocytological dissociation in 76.2 % of cases. Nerve conduction studies predominantly indicated AIDP subtype (32/46, 69.6 %). Treatment involved IVIG, plasmapheresis, and supportive care, with recovery times ranging from one week to 18 months. One fatality was reported.

Conclusions: This review suggests a potential link between HAV infection and GBS, proposing a mechanism: molecular mimicry. It emphasizes the need for increased awareness and preventive measures, especially in areas with lower health standards. However, further research is needed to clarify the possible mechanisms and deepen our understanding.

1. Introduction

Guillain-Barré syndrome (GBS) is a rare inflammatory disorder affecting the peripheral nervous system (PNS) and is the leading cause of acute flaccid paralysis globally. The estimated prevalence of GBS is approximately 1–2 cases per 100,000 individuals [1]. GBS encompasses several primary subtypes, including Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), and Acute Motor and Sensory Axonal Neuropathy (AMSAN). AIDP, characterized by demyelination affecting both motor and sensory nerves, often manifests with muscle weakness, paralysis, and autonomic dysfunction in severe cases [2,3]. AMAN, prevalent in Asia and Latin America, primarily affects motor nerves, leading to rapid-onset motor weakness, particularly in the lower limbs [4,5]. AMSAN affects both motor and sensory fibers, resulting in severe muscle weakness and sensory loss [6].

GBS exhibits a male predominance and its incidence increases with advancing age, although it can affect individuals across all age groups [1]. Notably, preceding symptoms indicative of respiratory or gastrointestinal tract infections occur in two-thirds of adult patients within a four-week timeframe preceding the onset of weakness [7]. Common pathogens associated with GBS include *Campylobacter jejuni*, *Mycoplasma pneumoniae*, *Haemophilus influenzae*, Cytomegalovirus (CMV), Epstein-Barr virus (EBV), Influenza A virus, and Zika virus [8].

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The hepatitis A virus (HAV), a positive-sense RNA virus, is predominantly spread through the fecal-oral route. It commonly results in self-limited infectious hepatitis. However, it can also lead to widespread epidemics through person-to-person transmission [9]. Rare instances of extrahepatic manifestations of HAV have been documented, including hemolytic anemia, pleural or pericardial effusion, acute reactive arthritis, and neurological complications such as GBS [10]. Recent studies have indicated a potential association between GBS and recent HAV infection, with approximately 5 % of GBS patients exhibiting positive serology for HAV [11]. While the exact mechanism remains unclear, it is hypothesized that an immune-mediated response, possibly involving molecular mimicry, triggers an autoimmune attack on peripheral nerves [12]. Given this gap in the current literature, this review aims to critically evaluate and synthesize the current literature on the association between Guillain-Barré syndrome and HAV, elucidating potential mechanisms and clinical implications.

2. Materials and methods

2.1. Search strategy and screening

To conduct this review, we adhered to the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [13]. We performed a systematic literature search across four major databases: PubMed, Web of Science, Embase, and Scopus, from the inception until May 2024. Customized search strategies incorporating the primary keywords “Guillain-Barre Syndrome” and “hepatitis A” were applied to each database (detailed in Supplement 1). To ensure the comprehensive collection of all relevant articles, an extensive search was conducted using Google Scholar, and the reference lists of all included studies were meticulously examined. Our review focused on cases involving both HAV and GBS.

2.2. Eligibility criteria

To ensure a homogeneous selection of studies, we included only published case reports or conference abstracts that presented cases meeting the following criteria. Each case must have satisfied both of the following conditions: (1) Hepatitis A infection confirmed through a combination of physical examination, clinical manifestations, and serum and cerebrospinal fluid (CSF) antibody tests; (2) Various subtypes of GBS confirmed via clinical presentation and diagnostic tests, including EMG-NCV and CSF studies. No age restrictions were applied to the presented cases, and studies in languages other than English were included in our review.

Studies were excluded if they met any of the following conditions: (1) Presence of other types of hepatitis infection; (2) Neurological involvement not confirmed as GBS, such as chronic inflammatory demyelinating polyneuropathy (CIDP), myasthenia gravis, acute flaccid myelitis (AFM), botulism, and critical illness polyneuropathy (CIP), or insufficient data to confirm the diagnosis; (3) Use of other study designs, including reviews, editorials, letters, commentaries, cross-sectional studies, cohort studies, case-control studies, and clinical trials.

2.3. Data extraction

Two independent reviewers (A.G. and N.B.L.) conducted the data extraction process autonomously. In instances of disagreement, a third author (A.S.) intervened to resolve discrepancies. The selected studies provided data on various variables, including study authorship, publication date, country of case origin, demographic details such as age and gender, clinical manifestations of GBS and its variants, presence of HAV IgM antibodies in serum and CSF, Guillain-Barre syndrome disability scores (GBSDS) computed from clinical data reported in the studies, results from hepatobiliary serological tests, CSF laboratory tests, EMG-NCV findings, treatments administered, and outcomes alongside patient follow-up status. The GBSDS is a standardized tool used to assess the functional impairment of patients with GBS [14]. It ranges from 0 to 6, with higher scores indicating greater disability. The score includes: 0 (healthy), 1 (minor symptoms, able to run), 2 (able to walk 10 m without assistance but unable to run), 3 (able to walk 10 m with assistance), 4 (bedridden or chairbound), 5 (requiring assisted ventilation), and 6 (death). This scale is essential in clinical practice to evaluate the severity and progression of GBS.

2.4. Quality assessment

We employed the Joanna Briggs Institute Critical Appraisal tools (JBI) tailored for case-report studies to evaluate the quality of included studies [15]. Two independent authors (A.G. and N.B.L.) conducted the assessment by answering 8 specific questions aiming at different aspects of the studies to gauge potential bias. Each question offered four response options (yes, no, unclear, not applicable). Discrepancies between reviewers were resolved through consensus discussion. Individual study bias was categorized based on thresholds: low risk ($\geq$70 % yes responses), moderate risk (50–69 % yes responses), and high risk ($<$49 % yes responses).

2.5. Data synthesis and analysis

Descriptive statistics were employed to summarize data, with means and standard deviations for continuous variables and frequencies and percentages for categorical variables. Statistical Package for the Social Sciences (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) was used for the analysis.

3. Results

3.1. Study selection

A comprehensive search was conducted across PubMed, Embase, Scopus, and Web of Science, yielding a total of 581 studies. Following the removal of duplicates and initial eligibility screening, 56 studies remained. However, full-text access was unavailable for five studies, and eight studies were excluded during full-text screening due to not meeting the eligibility criteria. An additional three eligible studies were identified through a meticulous manual search in Google Scholar and by examining the citations of included studies. Consequently, a total of 46 studies, encompassing 47 cases, were included in this review. Flow diagram of study selection process is shown in Fig. 1.

3.2. Study characteristics

The age of the reported patients ranged from 3 to 65, with a mean of 29.47 $\pm$ 16.95. Children (n = 8) [16–23] and adolescents (n = 5) [24–28] accounted for 28 % of the cases, while there was only one elderly individual (65 years). Male cases occurred 2.36 times more frequently than female cases (70.2 % vs. 29.8 %). Geographical distribution of cases indicated that 74.5 % of the cases were located in Asia [16–20,22–26,28–51], 14.9 % in Europe [27,52–57], 8.5 % in North America [58–61], and 2.1 % in Africa [21] (Fig. 2). Characteristics of the included studies are represented in Table 1.

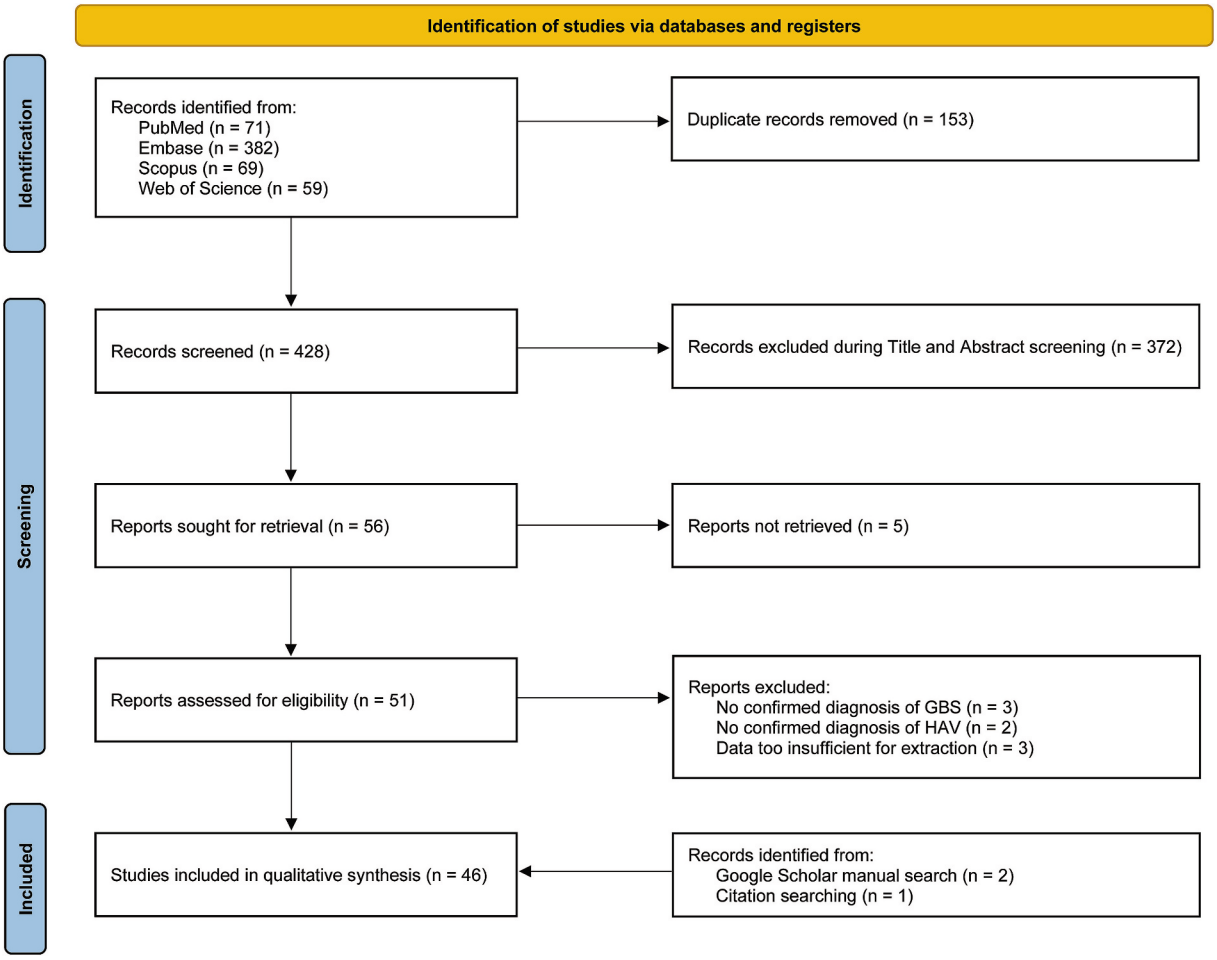

Fig. 1. PRISMA flow diagram of database searching and study selection.

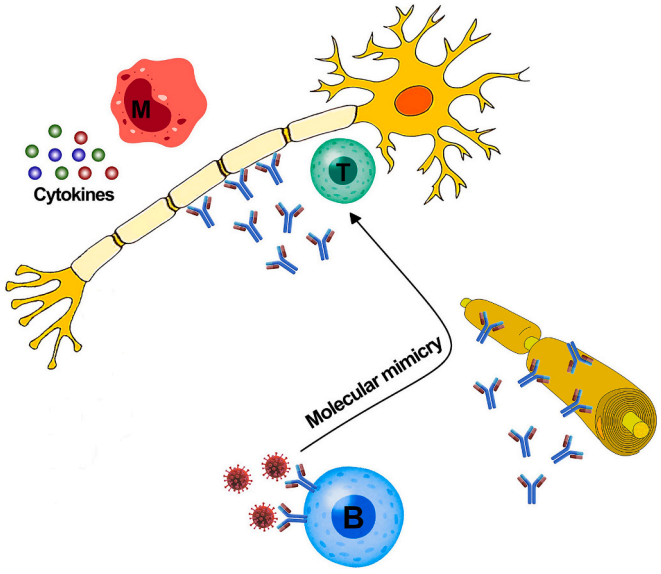

Fig. 2. Geographic distribution of the study cases categorized by continent and countries.

3.3. Quality assessment

Five studies exhibited a moderate risk of bias, while three studies demonstrated a high risk of bias, with 39 studies indicating a low risk of bias. Among studies categorized as high risk, a frequent deficiency was the inadequate detailing of clinical conditions and diagnostic methodologies employed for cases. Details of critical appraisal of included studies using JBI tool is shown in Table 2.

3.4. Clinical manifestations

Most common manifestations of HAV infection were prodromal symptoms, including fever, malaise, nausea, vomiting, and anorexia, followed by hepatomegaly and jaundice. The time interval between the first presentations of HAV and GBS ranged from 2 to 45 days, with a mean of 10.64 ± 7.84 days. In one case, HAV infection showed no signs and symptoms [16]. Forty-five cases had muscle weakness (41/45 both, 3/45 lower only, 1/45 upper only) with MRC grades ranging from 0 to 4. One case exhibited normal muscle strength in all four limbs [52], while another case did not provide any information regarding muscle strength [23]. Areflexia and hyporeflexia were present in 84.1 % and 11.4 % of the cases, respectively. Additionally, one case had normal deep tendon reflexes [48], and another had brisk DTRs [40]. Furthermore, cranial

Table 1
Characteristics of the included studies.

Author (Year-Country)	Age (Sex)	HAV IgM Ab		Interval (days)	clinical manifestations						Serum	CSF	GBSDS at nadir	Electrophysiology (Diagnosis)	Treatment	Outcome & Follow-Up
					Motor				Sensory	Reflex						
		Serum	CSF		Cranial Nerve Palsy	Limb										
						Upper		Lower								
						P	D	P	D							
Johnston et al. [52] (1981-England)	37 (M)	+	NR	14	NR	→	→	→	→	Numbness/ Paresthesia/ Absent vibration sense/ Impaired proprioception, light touch and pin-prick	Absent	ALT = 617 ALP = 198 ↑ T.Bil	Pr = 29 Glu = NL WBC < 3	3	No SNAP in right sural and right median nerves (Pure sensory AIDP)	Supportive	Six-month follow-up: Areflexia and mild sensory ataxia followed by general improvement.
Dunk et al. [53] (1982-England)	48 (M)	+	NR	3	VII, Dysarthria	↓↓	↓	↓↓	↓	Paresthesia/ Diminished joint-position sense and vibration sense	Absent	AST = 237 ALP = 458 ↑ T.Bil	Pr = 30 Glu = 63 No cells	4	Reduced motor conduction and increased terminal latency observed in the right median nerve (Sensory predominant AIDP)	Supportive	After five months, consistent facial paralysis persisted despite normal limb strength, showing overall improvement.
Igarashi et al. [29] (1983-Japan)	49 (M)	+	+	7	VII, Dysarthria	↓	↓	↓	↓	Paresthesia/ Decreased pin-prick, temperature and light touch sense/ Moderately decreased vibration and position sense	Absent	ALT = 412 AST = 105 T.Bil = 4.3	Pr = 165 Glu = 95 WBC = 8	3	Decreased motor conduction in right median, right peroneal and right posterior tibial nerves (AIDP)	Supportive	By the 70th day, limb power was nearly restored to normal, yet a mild facial nerve weakness persisted, indicating overall improvement.
Grover et al. [58] (1986-USA)	31 (M)	+	NR	7	VII	↓	↓	↓	↓	Ascending bilateral total extremity sensory loss	Absent	ALT = 8760 AST = 11,700 ALP = 130 T.Bil = 85	NR	4	F wave dispersion pattern (AIDP)	Supportive	Liver function tests and general health status within 30 days were found to be normal.
Marés-Segura et al. [54] (1986-Spain)	34 (F)	+	NR	7	VII	↓	↓	↓	↓	Paresthesia/ Impaired proprioception	Absent	ALT = 550 AST = 301	Pr = 156 Glu = 61 RBC = 5	3	Generalized alteration in nerve conduction velocity and an increased F-response conduction time (AIDP)	Supportive	After three months, the patient showed no symptoms except for persistent bilateral facial weakness.
Ono et al. [30] (1994-Japan)	62 (M)	+	NR	11	VII	↓	↓	↓↓	↓↓	Numbness/ Reduced pin-prick sensation/ Impaired vibratory and joint position sense	↓↓	ALT = 5062 T.Bil = 16.2	Pr = 181 Glu = 57 Cells = 1	4	Median and tibial sensory velocities within normal range, but decreased tibial and undetectable sural sensory velocities. Absence of F wave response in median and tibial nerves (AMSAN)	CS	Two months later, observed slight extremity weakness and a mild decline in proprioception.
Brunschwig et al. [55] (1995-France)	32 (F)	+	NR	10	NR	↓	↓	↓	↓	NR	Absent	ALT = 221 AST = 111	Pr = 36 No cells	4	Decrease in motor conduction velocities and increase in distal latencies (AIDP)	PP	One year later, there remains a minor motor

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Table 1 (*continued*)

Author (Year-Country)	Age (Sex)	HAV IgM Ab		Interval (days)	clinical manifestations					Sensory	Reflex	Serum	CSF	GBSDS at nadir	Electrophysiology (Diagnosis)	Treatment	Outcome & Follow-Up
		Serum	CSF		Motor												
					Cranial Nerve Palsy	Limb											
						Upper		Lower									
						P	D	P	D								
												T.Bil = NL					impairment in the lower extremities.
Lee et al. [31] (1997-Korea)	43 (F)	+	+	5	NR	→	→	3/5	3/5	Normal	Absent	ALT = 1748 AST = 1500 T.Bil = 2.7	NL	3	Bilateral absence of median F-wave, normal tibial F-wave latencies, motor, and sensory nerve conduction (AIDP)	PP and Platelet pheresis	Absent reflexes in all limbs but normal H-reflex and F-wave observed on day 70, indicating general enhancement.
Mihori et al. [32] (1998-Japan)	46 (M)	+	NR	2	NR	↓	↓	↓	↓	Dysesthesia/ Reduced pin-prick and soft-touch sensation/ Marked disturbance of vibratory and position sense	Absent	ALT = 399	Pr = 760 Cells = 3	4	Reduced ulnar and left sural sensory velocities observed, along with delayed motor conduction in lower limbs (MFS)	PP	Deep sensory disruption persisted for 18 months following the initial onset.
Azuri et al. [16] (1999-Israel)	3.5 (M)	+	NR	NR	NR	↓	↓	↓↓	↓↓	Normal	Absent	ALT = NL AST = NL T.Bil = NL	↑ Pr No cells	4	Nerve conduction velocity was prolonged with no F waves, consistent with acute demyelinating polyneuropathy (AIDP)	IVIG	After a month, regained muscle strength, but persistent areflexia in lower limbs remained.
Breuer et al. [33] (2001-Israel)	28 (F)	+	+	4	VII, Bulbar palsy	4/5	4/5	4/5	4/5	NR	Absent	ALT = 1586 AST = 868 ALP = 481 T.Bil = 7.3	Pr = 300 Cells = 4	5	AIDP	IVIG	General enhancement observed, discharged on the 21st day without signs of disease, delivered a healthy baby at term.
Ratnasari et al. [24] (2002-Indonesia)	19 (M)	+	NR	16	Normal	4/5	4/5	4/5	4/5	Paresthesia	↓	ALT = 197 AST = 140 T.Bil = 2.10	Pr = 53 Glu = 62 No cells	4	Prolonged distal motor latency and nerve conduction velocity of the right and left tibial nerves. Positive M and H waves. no reflexes (AIDP)	Supportive Antibiotics	NA
	43 (M)	+	NR	7	Normal	4/5	4/5	0	0	Hypoesthesia	↓	ALT = 342 AST = 163 T.Bil = 0.4	Pr = 19 Glu = 70 No cells	4	Prolonged distal motor latency and nerve conduction velocity of the right and left tibial nerves. Positive M and H waves. no reflexes (AIDP)	Supportive	NA
Özışık et al. [34] (2002-Turkey)	20 (M)	+	NR	7	VII, dysphagia	3/5	3/5	3/5	3/5	Lower & upper extremities sensory loss	Absent	ALT = 1792 AST = 521 ALP =	Pr = 161 No cells	5	Prolonged distal latencies in median, ulnar, peroneal and posterior tibial motor nerves. Normal motor nerve conduction velocities. No	IVIG	Normal liver function tests and overall improvement after three weeks.

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Table 1 (*continued*)

Author (Year-Country)	Age (Sex)	HAV IgM Ab		Interval (days)	clinical manifestations						Serum	CSF	GBSDS at nadir	Electrophysiology (Diagnosis)	Treatment	Outcome & Follow-Up
		Serum	CSF		Motor				Sensory	Reflex						
					Cranial Nerve Palsy	Limb										
						Upper		Lower								
						P	D	P	D							
											373 T.Bil = 10			sensory nerve responses in median and ulnar (AMSAN)		
Kocabas & Yildizdas [17] (2004-Turkey)	6 (M)	+	+	14	NR	2/5	2/5	2/5	2/5	NR	Absent	ALT = 900 AST = 1000 T.Bil = 12	Pr = 82 Glu = 41 No cells	3	Severe motor polyneuropathy associated with axonal damage in muscles and nerves in all extremities (AMAN)	IVIG	Restored muscular strength, normalized liver function tests, and achieved normal DTR within the initial month.
Gerenli et al. [18] (2004-Turkey)	4.5 (M)	+	NR	10	VII, Bulbar palsy	3/5	3/5	3/5	3/5	Severe reduction in vibratory and position senses, heat and touch sensations in all four limbs	↓	ALT = 276 AST = 836 T.Bil = 0.24	Pr = 14 Glu = 52 No cells	4	Myopathy with mixed peripheral neuropathy in both upper and lower extremities. Sensory and motor nerve conduction velocities were normal (AIDP + Myopathy)	CS	Full remission observed at 18-month follow-up
Çomoglu et al. [35] (2006-Turkey)	22 (M)	+	NR	10	NR	↓	↓	↓	↓	Paresthesia/ Hypoesthesia	Absent	ALT = 181 AST = 116 T.Bil = 1.6	Pr = 66 No cells	3	Nerve conduction velocities in peripheral nerves were prolonged with slightly decreased axonal amplitudes in electroneuromyography (AIDP)	CS	Complete recovery of motor weakness and partial improvement in paresthesia occurred within one month.
Chitambar et al. [25] (2006-India)	17 (M)	+	+	14	Normal	3/5	3/5	1/5	3/5	Tingling	Absent	ALT = 95 ALP = 148 T.Bil = 2	Pr = 100 Glu = 40 No cells	5	Severe motor neuropathy of axonal degeneration type (AMAN)	Supportive Antibiotics Physiotherapy	Three months later, the patient regained full power in both upper and lower limbs, proximally and distally, becoming asymptomatic and fully mobile.
Kadanali et al. [19] (2006-Turkey)	4 (M)	+	NR	14	VII	→	→	↓↓	↓↓	Normal	Absent	ALT = NL AST = NL T.Bil = NL	↑ Pr No cells	5	Prolonged distal latency, slowing of conduction velocity, conduction block, absent F responses (AIDP)	IVIG, Chest tube	Neurological improvements in muscle tone and strength were noted three weeks after admission.
Bae et al. [36] (2007-Korea)	32 (M)	+	NR	9	VII, Bulbar palsy	→	→	↓↓	↓↓	NR	Absent	ALT = 981 AST = 247 ALP = 270 T.Bil = 10.7	Pr = 115 Glu = 58 WBC = 1	5	Reduced nerve conduction velocity, prolonged distal latency, and F-wave absence. Bilateral median and ulnar nerves showed abnormal muscle action potentials of low amplitude (AIDP+ Secondary axonal)	IVIG	Day 90 of hospital stay showed normal LFT and general health improvement.

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Table 1 (*continued*)

Author (Year-Country)	Age (Sex)	HAV IgM Ab		Interval (days)	clinical manifestations						Serum	CSF	GBSDS at nadir	Electrophysiology (Diagnosis)	Treatment	Outcome & Follow-Up
		Serum	CSF		Motor				Sensory	Reflex						
					Cranial Nerve Palsy	Limb										
						Upper		Lower								
						P	D	P	D							
Kang et al. [37] (2007-Korea)	32 (M)	+	NR	4	VII	↓	↓	↓	↓	NR	Absent	ALT = 981 AST = 247 ALP = 400 T.Bil = 10.7	Pr = 115 Glu = 58 WBC = 1	5	Severe demyelinating sensorimotor polyneuropathy (AIDP)	IVIG CS	Fully recovered after three months.
Park et al. [38] (2008-Korea)	36 (M)	+	NR	7	Normal	3/5	3/5	2/5	2/5	Reduced pain, temperature, vibration, and proprioception in both upper limbs	Absent	ALT = 487 AST = 139 ALP = 283 T.Bil = 3.6	Pr = 112 Glu = 70 WBC = 1	4	Abnormalities in F-waves, prolonged distal latency, and reduced CMAP in the median, ulnar, and peroneal nerves. One week later: Asymmetrical, multifocal, demyelinating motor neuropathy (AIDP)	IVIG	Complete recovery, with residual mild muscle weakness (grade 4+) observed in bilateral lower limbs one-month post-admission.
Thapa et al. [20] (2009-India)	7 (M)	+	+	10	Bulbar palsy	2/5	1/5	5/5	5/5	Normal	Absent	ALT = 84 AST = 56 T.Bil = 3.2	Pr = 232 Cells = 8	NR	Acute motor axonal injury of the arms with sensory sparing (PCB)	IVIG	Improved muscle strength in arms and neck and overall recovery after three weeks.
Khan & Badshah [26] (2012-Pakistan)	17 (M)	+	NR	7	weak cough reflex	4/5	4/5	3/5	3/5	Normal	Absent	ALT = 111 ALP = 198 T.Bil = 4.4	Pr = 86 Glu = 67 Cell = 3	NR	Acute denervation in the upper and lower extremity muscles. Normal sensory responses. Reduction in amplitude of motor responses in legs (AMAN)	PP CS	NA
Jo et al. [39] (2013-Korea)	21 (M)	+	+	7	NR	4/5	2/5	4/5	2/5	Reduced pin-prick, vibratory, and joint position sensation	Absent	ALT = 376 AST = 385	Pr = 156 Glu = 61 No cells	5	Reduced CMAP and SNAP amplitudes in specific nerves with preserved velocities and latencies. Absent F-wave response in right median and both peroneal nerves (AMSAN)	IVIG	Gradual recovery observed. After four months, significant muscle atrophy and weakness persisted in the distal upper and lower limbs.
Sharma et al. [40] (2013-India)	25 (M)	+	NR	45	Normal	4/5	4/5	4/5	4/5	Normal	↑	↑ ALT ↑ AST ↑ ALP ↑ T.Bil	↑ Pr Glu = NL Cells = NL	3	Pure motor demyelinating affection of both upper and lower limbs (left>right) with increased distal latencies and increased F wave latencies (AIDP)	Supportive Physiotherapy	Fully recovered in two weeks.
Menon et al. [41] (2014-India)	28 (M)	+	NR	14	VII, neck muscle weakness	2/5	2/5	2/5	2/5	NR	Absent	ALT = 3058 AST = 1877 T.Bil = 5.6	Pr = 90 Cells = NL	5	Marked decrease in CMAP from bilateral tibial and peroneal nerves, with slightly longer latencies and conduction velocities. Absent SNAP amplitudes, except in	IVIG	He improved slowly and was asymptomatic at 12 months follow-up.

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Table 1 (*continued*)

Author (Year-Country)	Age (Sex)	HAV IgM Ab		Interval (days)	clinical manifestations						Serum	CSF	GBSDS at nadir	Electrophysiology (Diagnosis)	Treatment	Outcome & Follow-Up
					Motor				Sensory	Reflex						
		Serum	CSF		Cranial Nerve Palsy	Limb										
						Upper		Lower								
						P	D	P	D							
														bilateral median nerves (AMSAN)		
Nomani et al. [42] (2015-Pakistan)	24 (F)	+	NR	20	VII, Bulbar palsy	$\frac{3}{5}$	$\frac{3}{5}$	0	0	NR	Absent	ALT = 717 ALP = 178 T.Bil = 8.1	Pr = 25 Glu = NL Cells = 13	4	Extended distal latencies, decreased conduction velocities, dispersion, and reduced amplitudes (AIDP)	PP	Complete remission within 6 months without any sequela.
Patel et al. [43] (2015-India)	25 (F)	+	NR	7	VII, Bulbar palsy	$\frac{2}{5}$	$\frac{2}{5}$	$\frac{1}{5}$	$\frac{1}{5}$	Paresthesia	Absent	ALT = 1206 AST = 1070 T.Bil = 6.06	NR	4	CMAP reduced notably in several nerves, with lowered conduction velocities and prolonged distal latencies. F-responses were delayed or absent in certain nerves, and H-reflex was absent bilaterally. SNAP was also missing in specific nerves (AMSAN)	IVIG	Muscle strength regained, showing overall improvement by week 3.
Roşculeț et al. [57] (2016-Romania)	42 (M)	+	NR	11	VII	↓↓	↓↓	↓↓	↓↓	NR	Absent	NR	ACD	5	Markedly reduced amplitudes of CMAP (AIDP)	PP	Respiratory and motor improvement after 8 days.
Baltadzhiev et al. [27] (2018-Bulgaria)	12 (M)	+	NR	3	VII	↓	↓	↓	↓	Paresthesia	Absent	ALT = 2440 AST = 1816 ↑ T.Bil	Pr = 152 Glu = 61 Cells = NL	4	Low amplitude of CMAP, prolonged distal motor latency, temporal dispersion and reduced nerve conduction velocity in bilateral peroneal and facial nerves. Normal sensory nerve conduction velocities and SNAP (AIDP).	IVIG	At 4-month follow-up, normal CMAP, DTR, and motor function were observed.
Modi et al. [51] (2018-India)	20 (M)	+	NR	10	VII, Bulbar palsy	↓	↓	↓	↓	NR	Absent	↑ ALT ↑ AST ↑ T.Bil	ACD	4	Reduced nerve conduction velocity, prolonged distal latency, and nonrecordable F-wave (AIDP)	IVIG	Normal LFT and overall improvement after 3 weeks.
Saito et al. [44] (2018-Japan)	44 (F)	+	NR	12	VII, Bulbar palsy	$\frac{2}{5}$	$\frac{4}{5}$	$\frac{2}{5}$	$\frac{3}{5}$	Normal	Absent	ALT = 2946 AST = 1456 ALP = 819 ↑ T.Bil	Pr = 117 Cells = 13	5	Amplitude reduction and prolonged distal latency in median, ulnar, peroneal, and tibial nerves. Absent F-waves (AIDP)	IVIG CS	Positive treatment response observed, with enhanced muscle strength in all extremities and complete remission by day 47.
Chua et al. [50] (2018-Philippines)	58 (M)	+	NR	10	Bulbar palsy	$\frac{2}{5}$	$\frac{4}{5}$	$\frac{2}{5}$	$\frac{4}{5}$	Paresthesia	Absent	ALT = 1646 AST = 332 T.Bil = 6.22	Pr = 40.6 Glu = 66 WBC = 0	5	Prolonged distal latencies, reduced CMAP and SNAP amplitudes, absent sensory responses, and mixed axonal-demyelinating polyneuropathy with active	IVIG Tracheostomy Gastrostomy	After two months, the patient had mild right-hand weakness and minimal numbness. He had improved reflexes and muscle

(*continued on next page*)

Table 1 (*continued*)

Author (Year-Country)	Age (Sex)	HAV IgM Ab		Interval (days)	clinical manifestations						Serum	CSF	GBSDS at nadir	Electrophysiology (Diagnosis)	Treatment	Outcome & Follow-Up
		Serum	CSF		Motor				Sensory	Reflex						
					Cranial Nerve Palsy	Limb										
						Upper		Lower								
						P	D	P	D							
														denervation potentials (AMSAN)		strength, and no sensory loss.
Shubhakaran et al. [45] (2019-India)	20 (M)	+	NR	10	VII	1/5	1/5	0	0	Normal	Absent	ALT = 310 AST = 680 ALP = 380 T.Bil = 13.4	Pr = 64.8 Glu = 64 Cells = 5	5	Reduced nerve conduction velocity, prolonged distal latencies and no F-wave response (Pure motor AIDP)	IVIG	Complete remission within 2 months.
Samadi et al. [46] (2019-Iran)	30 (M)	+	NR	12	Normal	↓↓	↓↓	↓↓	↓↓	NR	NR	ALT = 127 AST = 628 ALP = 298 T.Bil = 27	NR	4	AMAN	PP	Full neurological and muscular recovery observed in patient after 2-month follow-up.
Sami et al. [21] (2020-Morocco)	9 (M)	+	NR	8	Dysphagia	2/5	3/5	2/5	3/5	Paresthesia/ Reduced proprioception	Absent	ALT = 1330 AST = 1170	Pr = 77 Cells = 3	5	Absence of motor and sensory potentials in various nerves (AMSAN)	IVIG PP	After 10 months, only heaviness in the right lower limb remained as a sequela.
Kumar & Mohan [28] (2020-India)	19 (F)	+	NR	7	NR	3/5	3/5	3/5	3/5	NR	↓	↑ ALT ↑ AST T. Bil = 15	NR	3	Generalized motor axonal neuropathy (AMAN)	Supportive	One-month follow-up showed overall improved muscular strength and LFT.
López Ruiz et al. [56] (2020-Spain)	40 (M)	+	NR	NA	VII, Bulbar palsy	2/5	2/5	2/5	2/5	Paresthesia	Absent	ALT = 2277 AST = 1364 T.Bil = 6.3	Pr = 152 WBC = 10	5	Absence of F waves, evidence of sensory-motor demyelination in the extremities (AIDP)	IVIG PP	Overall improvement with persistent areflexia.
Mardani et al. [47] (2020-Iran)	35 (F)	+	NR	16	VII, Bulbar palsy	2/5	2/5	2/5	2/5	Paresthesia	Absent	ALT = 1080 AST = 1200 T.Bil = 8.9	Pr = 80 Glu = 63 No cells	4	Prolonged velocity in peripheral nerves with slightly decreased axonal amplitude (AIDP)	IVIG PP	Enhanced motor function and resolved facial paralysis by the third week.
Blecker & Ehtsham [59] (2021-USA)	53 (F)	+	NR	11	NR	4/5	4/5	3/5	3/5	Numbness/ Decreased sensation in her lower extremities	Absent	ALT = 46 AST = 40 ALP = 138	Pr = 72 WBC = 5	3	NR	IVIG	Overall improvement following immunotherapy.
Laursen et al. [60] (2021-USA)	59 (M)	+	NR	6	Normal	↓	↓	↓	↓	Numbness/ Tingling/ Decreased vibratory sense	Absent	NR	Pr = 68.8 Cells = 5	4	AIDP	IVIG	Normal gait and mild fingertip paresthesia five

(*continued on next page*)

Table 1 (*continued*)

Author (Year-Country)	Age (Sex)	HAV IgM Ab		Interval (days)	clinical manifestations						Serum	CSF	GBSDS at nadir	Electrophysiology (Diagnosis)	Treatment	Outcome & Follow-Up
					Motor				Sensory	Reflex						
		Serum	CSF		Cranial Nerve Palsy	Limb										
						Upper		Lower								
						P	D	P	D							
																months post-discharge.
Nemakayala et al. [61] (2021-USA)	65 (F)	+	NR	5	NR	↓	↓	↓	↓	Sensory changes of all extremities	NR	ALT = 3611 AST = 2353 T.Bil = 9	ACD	5	AIDP	IVIG	Normal respiration and liver function after nine days.
Semwal et al. [22] (2021-India)	5 (F)	+	NR	NA	NR	$\frac{2}{5}$	$\frac{2}{5}$	$\frac{2}{5}$	$\frac{2}{5}$	NR	Absent	↑ ALT ↑ AST ↑ T.Bil	ACD	4	Demyelinating neuropathy (AIDP)	IVIG	Overall improvement.
Hyeong-woo et al. [49] (2022-Korea)	53 (F)	+	NR	11	NR	$\frac{4}{5}$	$\frac{4}{5}$	$\frac{3}{5}$	$\frac{3}{5}$	Numbness	NR	ALT = 1690 AST = 4843 ALP = 150 T.Bil = 14.32	Pr = 39	3	Sensory-motor peripheral neuropathy due to diabetic neuropathy and demyelination (AIDP)	IVIG	Improved LFT and neurologic symptoms on day 31
Abubakar et al. [48] (2023-Indonesia)	22 (M)	+	NR	18	VII, Bulbar palsy	$\frac{4}{5}$	$\frac{3}{5}$	$\frac{4}{5}$	$\frac{4}{5}$	Normal	→	↑ ALT ↑ AST	Pr = 65 Cells = 5	3	AIDP	Supportive Physiotherapy	At the third-month follow-up, the patient exhibited normal gait and experienced overall improvement.
Aswanth et al. [23] (2023-India)	< 3 (F)	+	NR	26	NR	NR	NR	NR	NR	NR	Absent	ALT = 788 AST = 920 T.Bil = 7.95	NR	6	Conduction block in the left median motor and left tibial motor nerves with preserved distal latencies, CMAP and conduction velocity in all nerves with normal F wave latencies (AIDP)	Antibiotics IVIG PP CS	Expired after 40 days of hospitalization.

* In Age (Sex) column, F represents female and M represents male. Age is reported as years.
** Throughout the table, ↑, ↓, and → represent increase, decrease, and no change in the following quantitative measures, respectively.
*** In CSF column, protein and glucose levels are reported as mg/dl (Cell count, RBC and WBC are reported as the number of cells in milliliters).
**** In Serum column, AST, ALT, ALP are reported as IU/l and total bilirubin as mg/dl.
***** Time interval is defined as the number of days between the first presentations of HAV and GBS.
****** Upper limbs and lower limbs are categorized as P (proximal) and D (distal).
Abbreviations: NR: not reported, GBSDS: Guillain–Barré syndrome disability score, NL: normal, Pr: Protein; Glu: glucose, T Bil: total bilirubin, HAV: hepatitis A virus, AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, Ab: antibody, WBC: white blood cell, RBC: red blood cell, IVIG: intravenous immunoglobulin, LFT: liver function tests, CMAP: compound muscle action potential, SNAP: sensory nerve action potential, AIDP: acute inflammatory demyelinating polyneuropathy, AMAN: acute motor axonal neuropathy, AMSAN: acute motor sensory axonal neuropathy, PCB: pharyngeal-cervical-brachial, MFS: miller fisher syndrome, CSF: cerebrospinal fluid, PP: plasmapheresis, CS: corticosteroid, ACD: Albuminocytological dissociation.

Table 2
Risk of bias assessment of included studies using JBI critical appraisal tool.

Author (Year)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Yes (%)	Risk of bias
Johnston et al. [52] (1981)	✓	✓	✓	✓	×	✓	✓	✓	87.5	Low
Dunk et al. [53] (1982)	✓	✓	✓	✓	×	✓	✓	✓	87.5	Low
Igarashi et al. [29] (1983)	✓	✓	✓	✓	×	✓	?	✓	75	Low
Grover et al. [58] (1986)	✓	✓	✓	×	×	×	×	✓	50	Moderate
Marés-Segura et al. [54] (1986)	✓	✓	✓	✓	×	×	×	✓	62.5	Moderate
Ono et al. [30] (1994)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Brunschwig et al. [55] (1995)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Lee et al. [31] (1997)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Mihori et al. [32] (1998)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Azuri et al. [16] (1999)	✓	✓	×	✓	✓	✓	✓	✓	87.5	Low
Breuer et al. [33] (2001)	✓	✓	✓	×	✓	✓	✓	✓	87.5	Low
Ratnasari et al. [24] (2002)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Özışık et al. [34] (2002)	✓	×	✓	✓	✓	✓	✓	✓	87.5	Low
Kocabas and Yildizdas [17] (2004)	✓	✓	×	✓	✓	✓	✓	✓	87.5	Low
Gerenli et al. [18] (2004)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Comoglu et al. [35] (2006)	✓	✓	×	✓	✓	✓	✓	✓	87.5	Low
Chitambar et al. [25] (2006)	✓	×	✓	✓	✓	✓	✓	✓	87.5	Low
Kadanali et al. [19] (2006)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Bae et al. [36] (2007)	✓	✓	×	✓	✓	✓	✓	✓	87.5	Low
Kang et al. [37] (2007)	✓	×	×	✓	✓	✓	✓	✓	75	Low
Park et al. [38] (2008)	✓	✓	✓	✓	✓	✓	×	✓	87.5	Low
Thapa et al. [20] (2009)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Khan and Badshah [26] (2012)	✓	✓	?	✓	✓	×	✓	✓	75	Low
Jo et al. [39] (2013)	✓	✓	×	✓	✓	✓	✓	✓	87.5	Low
Sharma et al. [40] (2013)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Menon et al. [41] (2014)	✓	×	✓	✓	✓	✓	✓	✓	87.5	Low
Nomani et al. [42] (2015)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Patel et al. [43] (2015)	✓	✓	✓	×	✓	✓	✓	✓	87.5	Low
Roşculeţ et al. [57] (2016)	✓	×	?	×	✓	✓	✓	✓	62.5	Moderate
Baltadzhiev et al. [27] (2018)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Modi et al. [51] (2018)	✓	×	×	×	✓	✓	×	?	37.5	High
Saito et al. [44] (2018)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Chua et al. [50] (2018)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Shubhakaran et al. [45] (2019)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Samadi et al. [46] (2019)	✓	✓	×	?	✓	✓	✓	✓	75	Low
Sami et al. [21] (2020)	✓	✓	✓	×	✓	✓	✓	✓	87.5	Low
Kumar and Mohan [28] (2020)	✓	✓	×	×	×	?	✓	✓	50	Moderate
López et al. [56] (2020)	✓	✓	×	✓	✓	×	✓	✓	75	Low
Mardani et al. [47] (2020)	✓	✓	×	×	×	✓	✓	✓	62.5	Moderate
Blecker and Ehtsham [59] (2021)	✓	✓	×	×	✓	✓	✓	✓	75	Low
Laursen et al. [60] (2021)	✓	✓	×	×	✓	✓	✓	✓	75	Low
Nemakayala et al. [61] (2021)	✓	✓	×	?	✓	✓	✓	✓	75	Low
Semwal et al. [22] (2021)	✓	✓	×	×	×	×	×	✓	37.5	High
Hyeong-woo et al. [49] (2022)	✓	✓	×	×	?	✓	×	×	37.5	High
Abubakar et al. [48] (2023)	✓	✓	✓	✓	✓	✓	✓	✓	100	Low
Aswanth et al. [23] (2023)	✓	✓	×	✓	✓	✓	✓	✓	87.5	Low

Abbreviations: JBI: Joanna Briggs Institute, '✓' indicates yes, '×' indicates no and '?' indicates unclear.
Q1. Were patient's demographic characteristics clearly described? **Q2.** Was the patient's history clearly described and presented as a timeline? **Q3.** Was the current clinical condition of the patient on presentation clearly described? **Q4.** Were diagnostic tests or assessment methods and the results clearly described? **Q5.** Was the intervention(s) or treatment procedure(s) clearly described? **Q6.** Was the post-intervention clinical condition clearly described? **Q7.** Were adverse events (harms) or unanticipated events identified and described? **Q8.** Does the case report provide takeaway lessons?
The risk of bias was ranked as high when the study reached up to 49 % of "yes" scores, moderate when the study reached from 50 to 69 % of "yes" scores, and low when the study reached more than 70 % of "yes" scores.

nerve involvement was observed in 55.3 % of patients. Among these, 17 % presented exclusively with facial nerve palsy, 8.5 % exhibited solely bulbar palsy, and 29.8 % demonstrated both conditions. Sensory complications were documented in 53.2 % of the cases, 19.1 % of the cases showed no complications, and 27.7 % of the cases had no reported information on sensory outcomes. Most reported sensory complications were paresthesia, impaired joint position and vibratory distortions, respectively.

3.5. Laboratory findings

Elevations in ALT (ranging from normal to 8760 IU/l) and AST (ranging from normal to 11,700 IU/l) were observed in 93 % (41/44) and 92 % (36/39) of the cases that reported these values, respectively. Furthermore, total bilirubin ranged from normal to 85 mg/dl. All cases that reported the presence of HAV IgM antibody in serum and CSF yielded positive results. The CSF protein levels varied from normal to 760 mg/dl, with elevation observed in 78.6 % (33/42) of the reported cases. The WBC count ranged from 0 to 13 cells/μL and was within normal limits in 90 % (38/42) of the reported cases. Overall, albuminocytological dissociation was identified in 76.2 % (32/42) of cases that underwent CSF laboratory testing.

3.6. Nerve conduction findings

Among the 46 cases with available nerve conduction study details, 69.57 % met the electrophysiological criteria for AIDP, 15.22 % for AMSAN, 10.87 % for AMAN, 2.17 % for MFS, and 2.17 % for PCB subtypes.

3.7. Treatment and outcome

Of the patients, 42.7 % received IVIG, 12.7 % underwent plasmapheresis, 6.3 % were treated with corticosteroids, and 23.4 % recovered with supportive treatment alone, without IVIG, plasmapheresis, or corticosteroids. A combination therapy involving IVIG, plasmapheresis, and corticosteroids was administered in 14.9 % of the cases. Furthermore, 34.04 % of the patients required intubation and mechanical ventilation (GBSDS: 5). Out of the 47 cases, 46 patients survived, with only one fatality reported (GBSDS: 6) [23]. With the exception of the one fatal case, all other patients recovered within a timeframe ranging from one week to 18 months [23].

4. Discussion

In this review, we thoroughly examined the existing literature on the potential association between HAV infection and GBS. In the majority of cases studied, initial signs and symptoms of HAV infection preceded the onset of GBS symptoms. HAV infection was confirmed through clinical symptoms, abnormal hepatic laboratory results, and the presence of anti-HAV IgM antibodies in both serum and CSF. Additionally, most cases exhibited albuminocytological dissociation in their CSF analysis, a hallmark of GBS. Clinical manifestations, sensorimotor abnormalities, and EMG-NCV findings were all indicative of GBS in the subjects studied. The majority of cases had a GBS disability score ranging from 3 to 5, indicating significant severity, with patients being unable to walk without assistance and many being immobile. Some patients experienced even more severe distress, necessitating assisted ventilation. This highlights the substantial burden of the condition and suggests the need for early interventions to alleviate patient suffering.

Emerging evidence highlights a wide range of infections that can potentially trigger GBS, with *Campylobacter jejuni* being the most common, alongside other pathogens such as Zika virus, Epstein-Barr virus, influenza virus, and SARS-CoV-2 [62–66]. The proposed mechanism involves an autoimmune response, where the immune system mistakenly targets the peripheral nerves following exposure to these infectious agents, resulting in inflammation and myelin damage. The clinical presentation of postinfectious GBS closely resembles classic GBS, characterized by progressive muscle weakness, tingling sensations, and, in severe cases, paralysis. Symptoms typically begin in the lower limbs and ascend over time.

Hepatitis E and hepatitis A are common causes of liver disease, primarily transmitted through the fecal-oral route. For over a decade, an association has been found between prior infection with HEV and GBS [67]. Laboratory evidence of recent hepatitis E virus infection was found in 3–11 % of GBS cases [68–71]. While there have been reports linking hepatitis E to GBS, the connection between hepatitis A and GBS is less clear. Nevertheless, recent studies have suggested a potential link between GBS and recent HAV infection [11].

A possible mechanism is hypothesized to underlie this condition and is known as molecular mimicry, which assumes that structural similarities between HAV antigens and gangliosides on peripheral nerve cells trigger an autoimmune response. In this scenario, the immune system produces antibodies against HAV antigens that cross-react with gangliosides, leading to an inflammatory response. This response involves the activation of T-cells and macrophages, the release of pro-inflammatory cytokines, and subsequent damage and demyelination of peripheral nerves. Several cases in our study presented with positive serum anti-ganglioside antibodies [23,32,38], further strengthening this theory. The proposed mechanism is illustrated in Fig. 3.

Molecular mimicry is strongly supported as the mechanism underlying the association between GBS and *Campylobacter jejuni* infection. Research demonstrates that specific strains of *C. jejuni* express sialylated lipooligosaccharides (LOS) in their outer membrane, which structurally resemble human gangliosides, such as GM1 and GD1a found on peripheral nerves. This mimicry triggers the production of antibodies

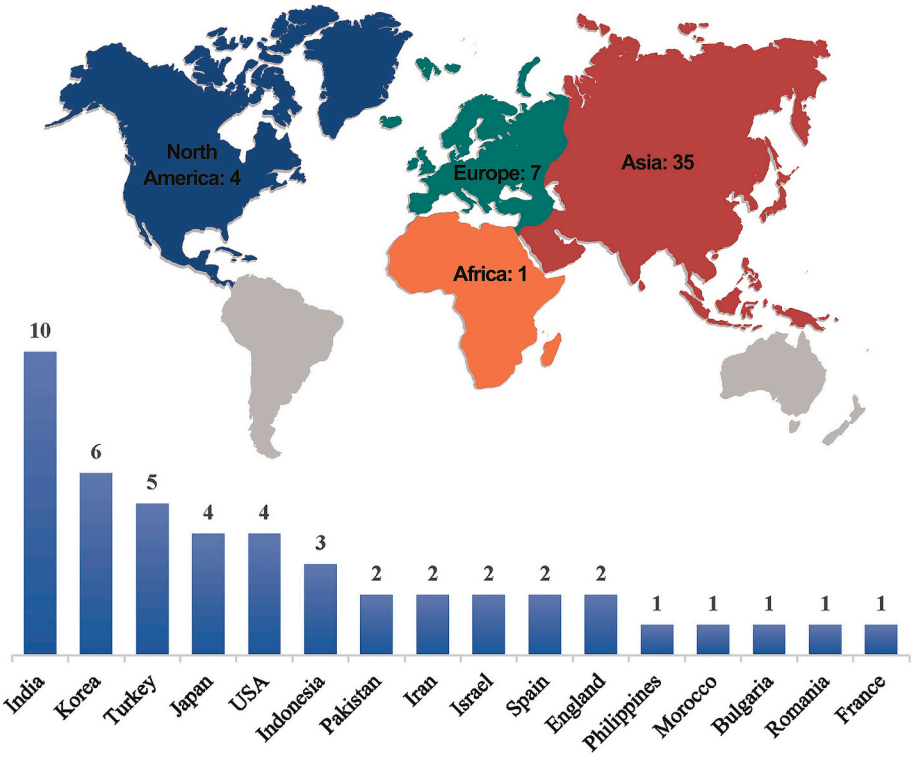

Fig. 3. Illustration of potential mechanism linking hepatitis A virus to Guillain-Barré Syndrome; (B) B-lymphocyte, (T) T-lymphocyte, (M) Macrophage. Molecular Mimicry: This mechanism suggests that structural similarities between HAV antigens and gangliosides on peripheral nerve cells lead to an autoimmune response. The immune system produces antibodies against HAV antigens, which cross-react with gangliosides, initiating an inflammatory response. This results in the activation of T-cells and macrophages, the release of pro-inflammatory cytokines, and subsequent damage and demyelination of peripheral nerves.

targeting the bacterial LOS during infection, which can cross-react with gangliosides in the peripheral nervous system due to their structural similarity [72,73]. The resulting immune-mediated damage to nerves is a hallmark of GBS, particularly in axonal subtypes like AMAN and AMSAN. In our study, we identified eight cases with positive anti-HAV IgM antibodies detected in their CSF. The interval between HAV infection and the onset of GBS symptoms ranged from 2 to 45 days, with a mean of 10.64 ± 7.84 days. This range is consistent with other post-infectious neuropathies, including those associated with *Campylobacter jejuni* and HEV, where immune-mediated damage typically occurs 1–4 weeks after the initial infection [12].

The common prodromal symptoms observed in cases included fever, malaise, and jaundice, consistent with acute hepatitis. Abnormal liver enzyme levels were a prominent feature, with marked elevations in AST and ALT serving as hallmark findings. For example, AST levels ranged from 237 IU/l to over 1500 IU/l, while ALT levels frequently exceeded 1000 IU/l in severe cases [58,61]. These pronounced symptoms were often accompanied by the neurological manifestations of GBS, such as muscle weakness, areflexia, and cranial nerve involvement, typically emerging within two weeks. This temporal association further strengthens the link between the two conditions. However, given the limited number of cases and supporting data, these findings are not conclusive, and further cellular and molecular investigations are necessary to elucidate the underlying mechanism.

Regarding the geographical distribution of cases, the majority were reported in Asia, followed by Europe, North America, and Africa. Hepatitis A virus is primarily transmitted through the fecal-oral route, which is more prevalent in countries with lower socioeconomic status. Developed countries in North America and Europe are expected to exhibit lower incidence rates of HAV infection. In Africa, the lower number of reported cases can be attributed to inadequate healthcare facilities for screening and limited academic resources for documenting and reporting these conditions. The geographic distribution of the studied cases is illustrated in Fig. 2.

Considering the potential association between these two conditions, it is assumed that enhancing global health standards and educating the public about the transmission pathways of HAV could help decrease the incidence of such cases. However, the exact molecular mechanisms underlying this condition have not yet been thoroughly investigated. Future studies are warranted to enhance our understanding of this association.

This study had some limitations. To ensure a homogeneous study, we aimed to include equal types of studies. Therefore, we excluded a few studies that had designs other than case reports. On the other hand, some of the included studies did not report sufficient amount of information and we had to exclude them from our review. Standard reporting of cases aligning with established guidelines (e.g., CARE) can increase the quality of available literature and ensure its clinical applicability. Lastly, the limited number of reports and cases included in this study prevent us from drawing definitive conclusions. Improved access to educational and healthcare facilities in underdeveloped countries could enhance the screening and documentation of cases, potentially leading to better global health outcomes and increased generalizability of future research.

In conclusion, this review highlights a potential association between HAV infection and GBS. The clinical presentation, serological findings, and electrophysiological data suggest that HAV might be linked to the development of GBS, potentially through mechanisms such as molecular mimicry. The predominance of cases in Asia and the correlation with HAV's fecal-oral transmission route emphasizes the need for heightened awareness and preventive measures, especially in regions with lower health standards. Despite the observed association, the precise mechanisms remain unclear, emphasizing the need for further research to elucidate the relationship between HAV and GBS.

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CRediT authorship contribution statement

Amirhosein Ghasemi: Writing – review & editing, Writing – original draft, Formal analysis. **Nima Broomand Lomer:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis. **Alia Saberi:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no conflict of interest.

Data availability statement

All data generated or analyzed during this study are included in this published article.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ensci.2025.100551.

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