

Short-term prognostic factors in Guillain-Barré syndrome: cohort study at the Hospital General de México

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Abstract

Introduction: Guillain-Barré syndrome (GBS) is the most frequent cause of acute flaccid paralysis. However, few studies have investigated short-term prognostic factors. **Objectives:** The objectives of the study were to describe the clinical characteristics of a sample of GBS patients treated at the General Hospital of Mexico and to identify the prognostic factors at discharge. **Methods:** A descriptive and analytical cohort study, including patients with GBS, was conducted from April 2020 to May 2022. Demographic information, comorbidities, clinical variants, neurophysiological alterations, modified Erasmus GBS Outcome Score (mEGOS) and Erasmus GBS Respiratory Insufficiency Score scales, etc., were collected. Functional recovery at discharge was measured with Hughes scales and Medical Research Council (MRC). A case-control analysis was performed among patients with good and poor functional recovery on discharge based on the Hughes scale. **Results:** Total sample was 69 patients: 74% men and 26% women, mean age: 43.7 ± 16.3 years; 38 (55%) patients presented classic variant, 22 pure motor variant (31%). Evolution time: 6.8 ± 6.7 days. Most common Hughes score at admission was 4 points ($n = 54$, 78%). 87% ($n = 60$) received plasmapheresis. 23 (33.3%) presented an axonal pattern and 46 (66.6%) demyelinating. On discharge, 31 patients had Hughes 3 or less (ambulatory) and 27 Hughes 4 or greater (non-ambulatory). When performing factor analysis, it was found that mEGOS, MRC, total lymphocytes, and creatine phosphokinase (CPK) were associated with the prognosis at discharge. **Conclusions:** The most frequent clinical variant was the classic (sensitive-motor) with demyelinating alteration; the factors related to better recovery at discharge were mEGOS, MRC on admission, total lymphocyte count, and serum CPK levels.

Keywords: Guillain Barré syndrome. Outcome. Modified Erasmus GBS outcome score. Mexico. Disability.

Introduction

Guillain-Barré syndrome (GBS) is a symmetric, ascending, immune-mediated polyradiculoneuropathy, generally preceded by an infectious process that can occur at any age¹⁻³. At present, GBS is the most common cause of acute flaccid paralysis in the world^{3,4}. Its incidence and severity increase with age, generally associated with axonal damage, greater involvement of cranial nerves, and

worse functional recovery³⁻⁵. It is estimated that the United States, Mexico, and Central America are countries with a high prevalence of GBS. In this sense, although there are no exact epidemiological reports, it is estimated that in Mexico, the prevalence is about 3.9/100 000 inhabitants (95% confidence interval: 3.1–4.9)⁵⁻⁸. Recent studies suggest an increase in the global prevalence of GBS, especially due to the SARS-CoV-2 pandemic and the mass vaccination used to combat it⁹.

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The main electro-clinical variants are acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN), and Miller Fisher syndrome^{1,2}. Recent evidence supports GBS as a spectrum disorder, that is to say, with geographical regional variations and significant clinical heterogeneity^{3,10}. Its clinical spectrum varies from mild to severe symptoms, with ascending and rapidly progressive weakness. At the most severe end of the spectrum, up to 30% of patients develop paralysis of all four extremities and respiratory failure, requiring mechanical ventilation (MV).¹ Cranial nerve involvement is a predictor of MV, and patients with AIDP have a higher risk of MV than those with the AMAN/AMSAN variants^{11,12}.

GBS represents a neurological emergency since, despite appropriate treatment, up to 20% of patients will be severely disabled, and approximately 5% will have a fatal outcome^{3,9,13}. Regardless of recent advances in the knowledge and care of GBS, it is reported that case fatality in Mexico reaches approximately 12%⁵. In 2019, México reported an incidence of 0.71 cases/100,000 people/year. The most common electrophysiological variant in México was AMAN, and its incidence has a seasonal distribution with a peak of axonal variants during the summer, while the AIDP variant was more frequent in winter, possibly associated with a higher incidence of respiratory infections⁵.

Approximately 40-70% of patients with GBS have a previous infection, the nature of which can influence the clinical phenotype, prognosis, and the electrophysiological subtype. *Campylobacter jejuni* and *Cytomegalovirus* are the most commonly isolated pathogens; the former explains the pathogenesis of AMAN, and the latter mainly for AIDP, which may also explain the seasonal distribution^{3,4}.

Multiple studies have identified several adverse prognostic factors in GBS. The most commonly reported are advanced age (> 70 years), orotracheal intubation, the need for MV, systemic infection, and the neutrophil-lymphocyte index, among others (Table 1)^{1,4,11,14-16}.

The previous studies on prognostic factors in GBS have investigated these factors at different times during the evolution of the disease, from 1 year to several months after the acute stage^{4,8}. Few studies report prognostic factors in the short term (at the time of hospital discharge). It is clear that these factors are also highly dependent on the type of population studied and the country^{3,8}. Identifying these short-term prognostic factors in GBS is of great importance for the clinical

Table 1. Main reported factors of poor functional prognosis in GBS

Variable	OR	CI 95%
Older age (over 70-years-old)	10.3	1.3-77
Ootracheal intubation	2.087	1.057-4.119
Mechanical ventilation	4.323	1.882-9.931
Axonal subtype	9.2	1.3-63.9
CMAP distal < 0.4	8.67	2.33-32.27
Neutrophil-lymphocyte index in < 60 years	1.36	1.05-1.76
> 9-day delay in initiating immunotherapy treatment	4.34	1.28-14.66

GBS: Guillain-Barré syndrome; CMAP: muscular component of the action potential with distal stimulation; OR: odds ratio; CI: confidence interval.

physician since it will allow timely interventions to obtain better functional results in these patients. For all of the above, the objective of the present investigation was to describe the clinical features of a cohort of patients with GBS treated at the General Hospital of Mexico (GHM) and to analyze the factors related to a better functional prognosis at hospital discharge.

Methods

A prospective, observational, descriptive, and analytical cohort study was carried out; all patients with a confirmed diagnosis of GBS who were admitted to the neurology service of GHM during the period from April 2020 to May 2022 were included in the study. Patients who met with the National Institute of Neurological Disorders and Stroke criteria for GBS at any Brighton level of certainty were included.¹⁷ Patients with incomplete information in the clinical record and those not hospitalized were excluded from the study. Demographic information, comorbidities, clinical variant, neurophysiological study, days of hospitalization, blood count, Erasmus Guillain-Barré Syndrome Outcome Score (mEGOS), and Erasmus GBS Respiratory Insufficiency Score (EGRIS) scales were collected. The degree of functional recovery at discharge was measured with the Hughes and Medical Research Council (MRC) scales for muscle strength. A case (Hughes 3 or less = ambulatory) and control (Hughes greater than 3 = non-ambulatory) type analysis was performed for the analysis of prognostic factors. In the statistical analysis, descriptive statistics were first used, and to compare the groups with good vs. poor functional recovery, the

Table 2. Clinical and sociodemographic features in total sample of GBS patients

Variable	Total sample (n = 69)	No.	%
Sex	Female	18	26.1
	Male	51	73.9
Age	Average: 43.7 years (SD: 16.3)		
Civil status	With couple Without couple	41 28	59.4 40.6
Residency	Mexico city Estado de México Other states	34 23 12	49.3 33.3 17.4
Comorbidities (number)	Average: 2 (SD: 1.06)		
History of diarrhea	Yes No	25 44	36.2 63.8
History of upper tract respiratory infection	Yes No	13 56	18.8 81.2
Clinical variant	Classic Pure motor Miller Fisher syndrome Faringo-cervicobraquial	39 22 7 1	56.5 31.9 10.5 1.4
Acute treatment	Plasmapheresis (number of sessions) Immunoglobulin Without immunotherapy	61 (3-5) 4 4	88.4 5.8 5.8
Evolution time at the beginning of treatment (days)	Average: 2.57 (SD: 2.07) (Median: 2)		
mEGOS score	7.12 (SD: 2.9)		
EGRIS score	4.23 (SD: 1.76)		
Axonal/Demyelinating variant	Axonal Demyelinating	23 46	33.3 66.7

SD: standard deviation; GBS: Guillain-Barré syndrome; EGRIS: Erasmus GBS respiratory insufficiency score; mEGOS: modified erasmus GBS outcome score.

following tests were used: Fisher's exact test, Chi-square, Mann Whitney U, or Student's T test, depending on the type of variable.

Results

The total sample was 69 patients: 74% men and 26% women. Average age \pm standard deviation (SD) was of 43.7 ± 16.3 years. 49 % of the patients were originally from Mexico City and 33% from Estado de México. Twenty-five patients (36 %) had a history of diarrhea. Regarding clinical variants, 55% patients presented the classic variant (sensory-motor), 31% pure motor variant and 10% presented Miller-Fisher variant (ataxia, ophthalmoplegia, and areflexia) and only one patient presented a pharyngo-cervicobrachial variant (Table 2). The mean evolution time from the onset of symptoms to time of hospital admission was 6.8 ± 6.7 days.

The average \pm SD Hughes scale score at admission was 3.85 ± 0.60 , and the most frequent Hughes scale category at admission was 4 points (78%), followed by 3 points (13%). Sixty-one patients (88%) received plasmapheresis, 4 (5.7%) received immunoglobulin as acute treatment, and 4 (5.7%) patients do not receive immunotherapy. In clinical neurophysiology studies, 66% (n = 46) showed a demyelinating pattern, and 33.3% presented an axonal pattern (n = 23). The average number of total days of hospitalization was 18.72 ± 9.4 . Complications (for example, urinary tract infections, pulmonary infections, cardiac arrhythmias, and hyponatremia) were observed in 16 (23%) of patients; 23% of the cases required management in the Intensive Care Unit (ICU), with the average number of days spent in the ICU being 8.4 ± 4.6 . Two patients died during hospitalization (2.8%), and only two patients had a history of SARS-CoV2 infection (2.8%). The summary

of laboratory variables and the initial and final scores of the scales are presented in **Tables 3 and 4**. As expected from the treatment with immunotherapy, a significant improvement was observed in the two functional outcome variables between the evaluations of admission versus discharge: Hughes ($p < 0.0003$) and MRC ($p = 0.0004$) (**Fig. 1**).

At discharge, only 58 patients were evaluated on the Hughes scale. 31 patients had Hughes 3 or lower (ambulatory or good recovery), and 27 had Hughes 4 or higher (non-ambulatory or bad recovery). When factor analysis was carried out, it was observed that the mEGOS scale, the MRC for muscle strength, total lymphocytes, and elevated creatine phosphokinase (CPK) were associated with a better prognosis at discharge (**Table 5**).

Discussion

To the best of our knowledge, no previous studies in Latin America describe prognostic factors at discharge from hospitalization of patients with GBS. The main focus of most studies is functional prognosis over longer periods, such as 3-6 months or a year. Unlike many other autoimmune disorders, GBS has been reported to be more common in men than in women. The male/female ratio in our study was higher (2.8:1) than reported in the international literature (1.5:1), with a 74% predominance of the male sex¹⁸.

This predominance of the male sex in GBS is well established in the literature, but apparently, in children and adolescents, this predominance is not consistent. Although the explanation for this predominance of the male sex is not fully clear, it has been proposed that there are different immune responses in both sexes to different non-protein antigens¹⁸.

In the present sample of patients, the average age was lower (43.7 years) than that reported in the International Guillain-Barré Syndrome Outcomes Study (IGOS) (51 years)^{13,16}; however, it is similar to reported in other studies carried out in México (46.6 years)¹, this may be due to multiple factors, but it is possible that exposure to infectious agents at younger age in our country explains a lower average age in our population compared to populations of Europe or the United States¹⁹.

According to the literature, up to 76% of patients with GBS have a history of an infectious disease, with *C. jejuni* diarrhea being the most commonly reported cause¹⁶. In our study, only 36% had a history of diarrhea before the onset of the clinical picture, without

Table 3. Laboratory characteristics in the total sample of patients with GBS

Variable	Average \pm SD
Total leukocytes	10 194 \pm 4551
Total neutrophils	6 215 \pm 3931
Total lymphocytes	2 188 \pm 3522
Neutrophil-to-lymphocyte ratio	6.66 \pm 12.17
Lactate dehydrogenase (U/L)	197.97 \pm 80.84
Creatine phosphokinase (U/L)	189.84 \pm 247.68
CSF: Proteins (mg/dL)	126.56 \pm 95.85
CSF: Leukocytes	2.95 \pm 4.37
CSF: Lymphocytes	1.07 \pm 1.30
CSF: Neutrophils	4.68 \pm 10.47

GBS: Guillain-Barré syndrome; CSF: cerebrospinal fluid; SD: standard deviation.

Table 4. Initial and final scores in Hughes and MRC scales in patients with GBS

Variable	Category	No.	%
Hughes scale at admission	0	0	0
Average: 3.85 \pm 0.60 (n = 69)	1	1	1.4
	2	1	1.4
	3	9	13.1
	4	54	78.3
	5	4	5.8
	6	0	0
Average MRC scale at admission (n = 69)	31.1 \pm 14.6		
Hughes scale at discharge	0	1	1.7
Average: 3.17 \pm 1.15 (n = 58)	1	5	8.6
	2	10	17.2
	3	16	27.6
	4	24	41.4
	5	0	0
	6	2	3.4
Average MRC scale at discharge (n = 58)	40.4 \pm 14.55		

GBS: Guillain-Barré syndrome; MRC: Medical Research Council scale for muscle strength.

finding a significant association between this infection and more severe forms of presentation, which differs from what has been reported in various studies. However, in our study, it was impossible to determine stool culture or polymerase chain reaction (rt-PCR) to confirm *C. jejuni* infection, which may explain the under-reporting of cases. On the other hand, it is noteworthy that only 2.8% of the cases had a documented

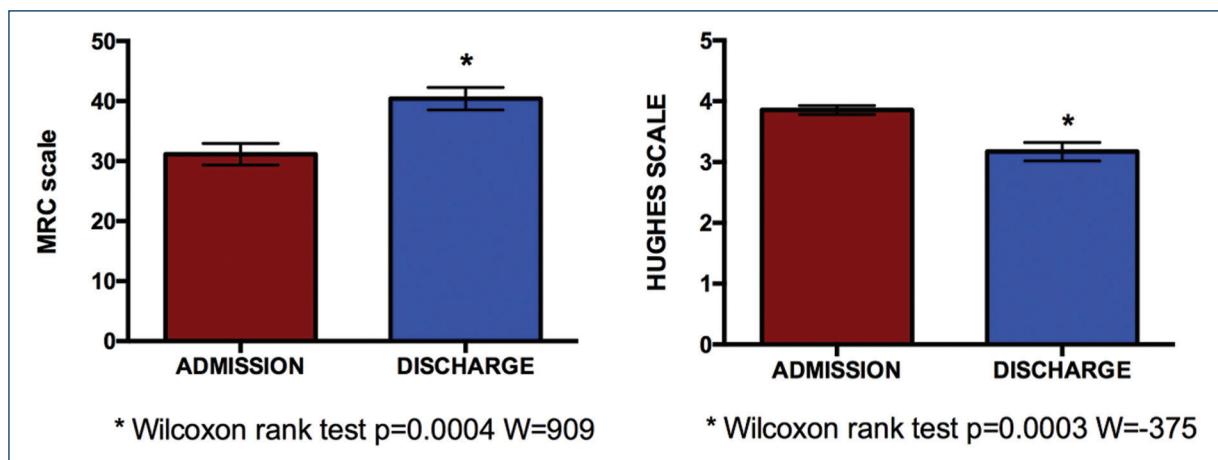


Figure 1. Effect of immunotherapy treatment. Baseline versus Endpoint MRC assessments for muscle strength and the Hughes scale. The bars represent the average \pm the Standard Error of the Mean. MRC: Medical Research Council.

SARS-CoV-2 infection; this is despite the fact that patient sampling was carried out during the first two years of the pandemic; however, more patients may have presented SARS-CoV-2 infection asymptotically or with minimal symptoms as has been previously reported²⁰.

The most common electrophysiological variant in our sample was AIDP (66%), being similar to what was reported in Europe and North America population²¹ and in contrast with what was previously reported in another study carried out in our country, where the AMAN variant was the most reported subtype (45.4%)¹.

This difference observed in our study concerning the electrophysiological variant may be because the study by López-Hernandez et al. was carried out in a neurological medical center, while our study is more representative of a general hospital population.¹ Despite this, both studies agree well on the frequency of clinical variants: sensory-motor in the first place (50%), followed by a pure motor (31%)¹.

In the present study, we found a high percentage (82.3%) of non-ambulatory patients at the time of hospital admission (Hughes 4 or higher); this percentage is higher than that observed in the IGOS study, where 76% of the patients were non-ambulatory at the time of greater severity of the disease²². We consider that these findings may be due to sample bias, given that only hospitalized patients were included in this study, while those with less severity were not hospitalized.

In studies carried out in developing countries, mortality (17%) is usually higher than in developed countries (5%), which is probably due to a higher proportion

of patients with axonal forms of GBS and less access and/or availability of mechanical respirators, intensive care facilities, and immunotherapy²³. In our study, 91.9% of patients received immunotherapy, which was higher than expected, according to international reports. The need to require ventilatory support and stay in intensive care (23%) was greater, in contrast to reports from developed countries (19%), but lower (30.6%) than in other studies carried out in Mexico,¹ in addition to observing low mortality in our study (2.8%).

Regarding the factors associated with functional prognosis at hospital discharge, in the present investigation, we found that ambulatory patients at discharge (Hughes < 3) had a significantly higher MRC score at admission. Likewise, ambulatory patients had a significantly lower mEGOS score on admission. Both results are expected, given that these evaluations have previously been reported to be significantly associated with functional prognosis in GBS²⁴. Similarly, significantly higher levels of total blood lymphocytes were observed in non-ambulatory patients at hospital discharge. In this sense, the previous studies have shown that the neutrophil-to-lymphocyte ratio (NLR) can represent a good inflammatory and prognostic marker in patients with several neurological diseases²⁵.

For example, one study investigated the relationship between the NLR measured on the day of admission and the subsequent motor deterioration in patients with GBS, finding an inverse and significant correlation between the NLR and the deterioration of motor function during the first 14 days in patients who did not receive immunotherapy²⁶. In another study, the Hughes score had a positive

Table 5. Results of the comparative analysis between patients with good versus poor functional recovery at discharge (ambulatory vs. non-ambulatory patients)

Variable	Hughes at admission 3 or less (ambulatory) (n = 31)	Hughes at discharge more than 3 (non- ambulatory) (n = 27)	Statistic test p-value
Sex			
Female	10	8	Fisher (p = 1.000)
Male	21	19	
Age	43.26 ± 18.2	43.96 ± 15.8	T test (p = 0.8688)
Civil status			
With couple	15	21	Fisher (p = 0.0305)
Whitout couple	16	6	
Residency			
Mexico City	12	15	Xi Cuadrada (p = 0.0650)
Estado de México	10	11	
Other states	9	1	
Comorbidities	0.86 ± 1.2	1.29 ± 1.1	Mann Whitney (p = 0.0802)
History of diarrhea			
Yes	11	10	Fisher (p = 1.000)
No	20	17	
History of upper tract respiratory infection			
Yes	6	6	Fisher (p = 0.896)
No	25	21	
Clinical variant			
Classic	18	15	Fisher (p = 0.3823)
Pure motor	7	11	
Miller Fisher Syndrome	6		
Faringocervico brachial		1	
Hughes at admission			
Category 1	1	0	Xi cuadrada (p = 0.4890)
Category 2	1	0	
Category 3	4	2	
Category 4	24	25	
Category 5	1	0	
Acute treatment			
Plasmapheresis	28	25	Xi cuadrada (p = 0.8921)
Immunoglobulin	2	1	
Without immunotherapy	1	1	
Evolution time at the beginning of treatment (days)	2.41 ± 1.8	2.11 ± 1.3	Mann Whitney (p = 0.8952)
MRC at admission	36.03 ± 13.42	27.85 ± 14.07	T test (p = 0.0287)
Modified Erasmus GBS outcome score	6.16 ± 2.9	7.88 ± 2.8	Mann -Whitney (p = 0.0314)
Erasmus GBS respiratory insufficiency score	3.79 ± 1.6	4.29 ± 1.8	T test (p = 0.2885)
Neurophysiological variant			
Axonal	8	13	Fisher (p = 0.1032)
Demyelinating	23	14	
Total leukocytes	17,676 ± 29,648	9656 ± 3796	Mann Whitney (p = 0.5278)
Total neutrophils	5727 ± 3681	6069 ± 2760	Mann Whitney (p = 0.6789)

(Continues)

Table 5. Results of the comparative analysis between patients with good versus poor functional recovery at discharge (ambulatory vs. non-ambulatory patients) (continued)

Variable	Hughes at admission 3 or less (ambulatory) (n = 31)	Hughes at discharge more than 3 (non- ambulatory) (n = 27)	Statistic test p-value
Total lymphocytes	1405 ± 1078	2228 ± 1261	Mann Whitney (p = 0.0057)
Neutrophil-to-lymphocyte ratio	6.211 ± 8.2	6.425 ± 15.7	Mann Whitney (p = 0.2365)
Lactate dehydrogenase (U/L)	198.8 ± 99.4	197.3 ± 62.4	T test (p = 0.9787)
Creatine phosphokinase (U/L)	185.3 ± 107.2	46.8 ± 20.29	Mann Whitney (p = 0.0462)
Days of evolution at the time of lumbar puncture	12.07 ± 8.0	9.46 ± 3.3	Mann Whitney (p = 0.8766)
CSF: Proteins	157.6 ± 116	105.6 ± 81.16	Mann Whitney (p = 0.4173)
CSF: Leukocytes	3.0 ± 4.7	3.23 ± 4.33	Mann Whitney (p = 0.8251)
CSF: Lymphocytes	1.032 ± 1.3	1.037 ± 1.25	Mann Whitney (p = 0.9397)
CSF: Neutrophils	2.96 ± 4.24	7.73 ± 16.	Mann Whitney (p = 0.27770)
Medical complications	Si: 6, No: 25	Si: 6, No: 21	Fisher (p = 1.000)
Stay in ICU (days)	8.25 ± 5.7	8.16 ± 3.4	Mann Whitney (p = 0.6028)
Hospitalization days	19 ± 9.36	18.70 ± 10.53	Mann Whitney (p = 0.7313)

GBS: Guillain-Barré syndrome; MRC: Medical Research Council scale for muscle strength; CSF: cerebrospinal fluid; ICU: intensive care unit.

correlation with NLR, and the MRC had a negative correlation with NLR²⁵. However, in our study, no association was observed between NLR and good recovery at discharge. However, it was observed with the total serum lymphocytes, which, in any case, suggests that the severity of GBS may be associated with a greater systemic inflammatory response²⁷. Other serum biomarkers that have been associated with a worse prognosis how: low albumin, increased immunoglobulin, and increased levels of neurofilaments light chain²⁸. Finally, it was observed that there were significantly higher levels of the serum CPK enzyme in patients with better functional recovery at discharge. This CPK elevation has already been reported in GBS in up to 16.7% of cases; however, its prognostic significance has yet to be fully understood, so it must be confirmed in subsequent studies²⁹.

The limitation of this study was that the number of patients was reduced, so it will be necessary to

increase the number in future studies. The sample has a selection bias since only patients requiring hospitalization due to their severity were included in the study. Likewise, it would be important to have long-term functional and quality-of-life evaluations of patients to establish whether short- and long-term prognostic markers are the same or different. Finally, it will also be important in future studies to have more information on the different parameters of neurophysiology studies and the antiganglioside antibody profile of patients.

Conclusions

The most frequently observed clinical variant of GBS was the classic variety (sensory-motor), and the most common electrophysiological variant was the demyelinating variety. A significant effect of immunotherapy treatment on functional status at hospital discharge was

corroborated. MRC at admission, mEGOS scale, total serum lymphocyte count, and CPK levels were associated with functional prognosis at hospital discharge.

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Conflicts of interest

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

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