



Factors Associated With Prognosis of Guillian Barre Syndrome

Thesis

Submitted for Partial Fulfillment of the Master
Degree in Neuro Psychiatry

By

May Ahmad Nasr Ashour

M.B.B.Ch, Faculty of Medicine, Ain Shams University

Under Supervisors

Prof. Dr. Naglaa Mohamed El Khayat

Professor of Neurology
Faculty of Medicine – Ain Shams University

Dr. Maha Aly Nada

Assistant Professor of Neurology
Faculty of Medicine – Ain Shams University

Dr. Heba Hamed El_ Sayed Afeefy

Lecturer of Neurology
Faculty of Medicine – Ain Shams University

**Faculty of Medicine
Ain Shams University
2018**

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لَسْبَحَانَكَ لَا نَعْلَمُ لَكَ
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢



ACKNOWLEDGEMENT

First of all, thanks to **Allah** whose magnificent help was the main factor in completing this work.

No words could express my deepest thanks and appreciation to **Prof. Dr. Naglaa Mohamed El Khayat**, Professor of Neurology, Faculty of Medicine, Ain Shams University, for inspiring me with the idea of this work. Her patience, precious advice and guidance enlightened my way throughout this work.

I want also to express my profound gratitude to **Dr. Maha Aly Nada**, Assistant Professor of Neurology, Faculty of Medicine, Ain Shams University, for her patience, valuable advice and continuous help in completing this work.

I am also deeply indebted to **Dr. Heba Hamed El_Sayed Afeefy**, Lecturer of Neurology, Faculty of Medicine, Ain Shams University, for her kind help, guidance, useful advices, continuous encouragement and support all through my entire work.

Finally, my deepest thanks to all my family and colleagues who helped me in the production of this work.

Contents

Subjects	Page
List of abbreviations.....	II
List of figures.....	III
List of tables.....	V
• Introduction	1
• Aim of the Work	5
• Review of Literature	
♦ Chapter (1): Guillain–Barré Syndrome.....	6
♦ Chapter (2): Neurophysiologic Studies in the Evaluation GBS	40
♦ Chapter (3): Predictors of Outcome in Guillain-Barré Syndrome.....	61
• Patients and Methods	79
• Results	84
• Discussion	123
• Summary	129
• Conclusion	131
• Recommendations	132
• Limitations in Our Study	133
• References	134
• Arabic Summary	

List of Abbreviations

AIDP	: Acute inflammatory demyelinating polyneuropathy
AMAN	: Acute motor axonal neuropathy
BBE	: Bickerstaff's brainstem encephalitis
CIDP	: Chronic inflammatory demyelinating polyradiculoneuropathy
CMAP	: Compound muscle action potential
CMV	: Cytomegalovirus
CNV	: Cranial nerve variants
CSWS	: Cerebral salt-wasting syndrome
GBS	: Guillain-Barré syndrome
IVIG	: Intravenous immunoglobulin
LOS	: Lipooligosaccharides
MFS	: Miller-Fisher syndrome
MUP	: Motor unit potential
NCS	: Nerve conduction study
PE	: Plasma exchange
QSART	: Quantitative sudomotor axon reflex test
SIADH	: Syndrome of inappropriate antidiuretic hormone
SNAP	: Sensory nerve action potential

List of Figures

<u>No.</u>	<u>Figure</u>	<u>Page</u>
<u>1</u>	Guillain-Barre Syndrome time course.	9
<u>2</u>	Major Guillain-Barré syndrome subtypes in which antibody-mediated effector pathways, including complement activation, cause glial or axonal membrane injury with consequent conduction failure.	15
<u>3</u>	Treatment approach for Guillain-Barre syndrome	31
<u>4</u>	Median motor (A) and sensory conduction (B study wave	44
<u>5</u>	Fibular (peroneal) motor conduction study showing amplitude, distal latency, and conduction velocity results typical and axonal neuropathy	50
<u>6</u>	Median motor conduction study showing distal latency and conduction results typical of an inherited demyelinating neuropathy	52
<u>7</u>	Ulnar motor study showing compound muscle action potential amplitude drop between the wrist and below elbow stimulus sites, distal latency prolongation, and conduction velocity slowing, all typical of an acquired demyelinating neuropathy	53
<u>8</u>	Summary of currently identified/suggested predictors of mechanical ventilation and of prognosis in GuillaineBarre´ syndrome	75

List of Figures

<u>No.</u>	<u>Figure</u>	<u>Page</u>
<u>9</u>	Flow chart.	84
<u>10</u>	Baseline NCS data.	90
<u>11</u>	Follow up NCS outcome.	94
<u>12</u>	Comparison between baseline and follow up disability score measurements in improved GBS patients.	105
<u>13</u>	Comparison between baseline and follow up albumin measurements in improved GBS patients.	106
<u>14</u>	Comparison between the 2 groups of patients regarding follow-up disability score assessments.	111
<u>15</u>	Comparison between the 2 groups of patients regarding follow-up albumin assessments.	112
<u>16</u>	Correlation between follow up disability score and baseline disability score.	115
<u>17</u>	Correlation between follow up disability score and baseline Na.	116
<u>18</u>	Correlation between follow up disability score and baseline albumin.	117
<u>19</u>	ROC curve of baseline disability score.	120
<u>20</u>	ROC curve of baseline Na level.	121
<u>21</u>	ROC curve of baseline albumin level.	121
<u>22</u>	ROC curve of baseline CSF protein level.	122

List of Tables

<u>No.</u>	<u>Table</u>	<u>Page</u>
<u>1</u>	Diagnostic criteria for Guillain-Barré syndrome.	24
<u>2</u>	Main likely predictors of prognosis in Guillain-Barré syndrome: derived from findings of prospective literature of studies including a majority of treated patients.	76
<u>3</u>	Socio-demographic data among 50 GBS patients	85
<u>4</u>	Baseline clinical data among 50 GBS patients	86
<u>5</u>	Baseline laboratory data among 50 GBS patients	88
<u>6</u>	Baseline CSF data among 50 GBS patients	89
<u>7</u>	Baseline NCS data among 50 GBS patients	90
<u>8</u>	Treatment data among 50 GBS patients	91
<u>9</u>	Follow up clinical and laboratory data among 50 GBS patients	92
<u>10</u>	Follow up NCS data among 50 GBS patients	93
<u>11</u>	Mortality outcome data among 50 GBS patients	95
<u>12</u>	Comparison between the 2 groups as regards socio-demographic data using Mann-Whitney's U and Chi square tests	96

List of Tables

<u>No.</u>	<u>Table</u>	<u>Page</u>
<u>13a</u>	Comparison between the 2 groups as regards Disability score (on admission) using Mann-Whitney's U.	97
<u>13b</u>	Comparison between the 2 groups as regards baseline clinical data using Chi square tests.	98
<u>14</u>	Comparison between the 2 groups as regards baseline laboratory data using Mann-Whitney's U test	100
<u>15</u>	Comparison between the 2 groups as regards baseline CSF data using Mann-Whitney's U and Chi square tests	101
<u>16</u>	Comparison between the 2 groups as regards baseline NCS data using Chi square test	102
<u>17</u>	Comparison between the 2 groups as regards treatment data using Chi square test	103
<u>18</u>	Comparison between improved group of patients as regards serial clinical and laboratory assessments	104
<u>19</u>	Comparison between improved group of patients as regards serial NCS assessments	107
<u>20</u>	Comparison between same or worsened group of patients as regards serial clinical and laboratory assessments	108
<u>21</u>	Comparison between same or worsened group of patients as regards serial NCS assessments	109

List of Tables

<u>No.</u>	<u>Table</u>	<u>Page</u>
<u>22</u>	Comparison between the 2 groups of patients as regards serial clinical and laboratory measurements using repeated measures ANOVA test	110
<u>23</u>	Multiple regression model for the Factors affecting follow up disability outcome (score) in all patients using Forward method	114
<u>24</u>	Logistic regression model for the Factors affecting NCS outcome (improved or worsened) in all patients using Forward method	118
<u>25</u>	Roc-curve of disability scoring system and some baseline laboratory markers to predict patients with NCS improvement (33) from patients without (7)	119

INTRODUCTION

Guillain-Barré syndrome (GBS) is a common neurological disorder that is characterized by symmetrical weakness of the limbs which reaches a maximum severity within 4 weeks (*Yuki et al., 2010*).

GBS occurs throughout the world with a median annual incidence of 1.3 cases per population of 100 000, with men being more frequently affected than women. GBS is considered to be an autoimmune disease triggered by a preceding bacterial or viral infection. *Campylobacter jejuni*, cytomegalovirus, Epstein-Barr virus and *Mycoplasma pneumoniae* are commonly identified antecedent pathogens (*Kuwabara et al., 2004*).

Although intravenous immunoglobulin (IVIG) and plasma exchange (PE) were proven to be effective treatment options for GBS (*Hughes et al., 2014*).

Many patients still have poor prognosis and sequelae such as decreased mobility, severe long-term fatigue syndrome and chronic pain (*Witsch et al., 2013*).

The reported mortality of GBS varies between 3% and 7% (*van den Berg et al., 2013*).

Typical GBS is an acute, predominantly motor neuropathy involving distal limb paresthesias, relatively symmetric leg weakness, and frequent hyporeflexia or areflexia. Recent study suggests that some patients with GBS had normal or hyperreflexia (*Kuwabara et al., 2002*).

According to a recent classification, Bickerstaff's brainstem encephalitis (BBE) can also be included into GBS variants (*Wakerley et al., 2014*). Also, previous reports from western countries showed that acute inflammatory demyelinating polyneuropathy (AIDP) is the most common subtype of GBS (*Mitsui et al., 2015*). However, the proportion of different subtypes of GBS and their prognosis varied significantly among different regions (*van Doorn et al., 2010*).

Patients with AIDP has significantly better outcome at 3 months follow up and 6months follow up than patients with acute motor axonal neuropathy (AMAN) and patients with BBE-GBS Prognosis of AMAN group and BBE-GBS group at 3 months follow up and 6 months follow up had no significant difference, prognosis of Miller-Fisher syndrome (MFS) group and that of cranial nerve variants (CNV) group at 6 months were both good, Previous studies have identified that high age, preceding diarrhea, and low Medical Research Council sum score (MRC sum score) are

independently associated with poor prognosis in GBS (*Walgaard et al., 2011*).

Hyponatremia is the most common disorder of electrolytes in clinical practice, occurring in up to 15- 30% of hospitalized patients (*Verbalis et al., 2007*).

Hyponatremia is defined as serum sodium concentration below 135 mmol/l at nadir, including mild hyponatremia (130-135 mmol/l), moderate hyponatremia (125-130 mmol/l), and severe hyponatremia (125 mmol/l). Hyponatremia is one of the most severe metabolic complications affecting patients with critical neurologic disease because even mild hyponatremia is associated with increased mortality, and rapid correction of chronic hyponatremia can cause severe neurologic deficits and death (*Waikar et al., 2009*).

Although the association between GBS and hyponatremia has been reported previously, the small sample sizes of these studies make it difficult to address the possible prognostic value of hyponatremia in GBS (*Saifudheen et al., 2011*).

It is reported that the main cause of hyponatremia in GBS is syndrome of inappropriate antidiuretic hormone (SIADH) (*Saifudheen et al., 2011*).

On the other hand, cerebral salt-wasting syndrome (CSWS) was also identified as the cause of hyponatremia in GBS case report (*Lenhard et al., 2011*).

Neurological disorders can stimulate the production of a high level of inflammation, resulting in an increase or decrease in acute phase reactants (*Mungan et al., 2014*).

Albumin is a late-reacting negative acute-phase protein (*Tsirpanlis et al., 2005*).

Hypoalbuminemia is common in patients with GBS, it decreases after the subacute period, and there is a negative correlation between albumin levels and GBS disability. The mean pre- and post-treatment serum albumin levels of the AIDP group were lower than those of the other groups. Such decreases in mean albumin levels in AIDP are thought to be mainly due to inflammation, hemodilution, or an acute phase response (*Hahn et al., 1998*).

AIM OF THE WORK

To study contributing factors that may affect poor and good prognosis of GBS cases.