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REVIEW ARTICLE

# Outcomes for patients with Guillain-Barré syndrome requiring mechanical ventilation: a literature review

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**Abstract**
*Background* This is a literature review of outcomes for patients with Guillain-Barré Syndrome (GBS) who require admission to the intensive care unit for mechanical ventilation. Respiratory distress is the leading cause of death in the acute phase, and occurs in about 25 % of patients.
*Aims* The aim of this review is to compile, analyse, and summarise the most relevant literature looking at outcomes for Guillain-Barré (GB) patients requiring admission to the intensive care unit and mechanical ventilation.
*Methods* A PubMed and Google-Scholar literature search was performed using the key words 'Guillain-Barré, Outcomes, Mechanical Ventilation, Prognosis, Mortality, ICU. All 7 papers from the years 2000–2014 which assessed outcomes for GBS patients requiring mechanical ventilation were included, and critically analysed.
*Results* The parameters recorded by these studies looked at mortality, disability, length of hospitalisation, and complications. The mortality of GB patients requiring mechanical ventilation varied from 8.3 to 20 %, Disability was primarily measured by the GBS disability scale. One study deemed that a score of 0–1 was a positive outcome, and found that slightly over half 53.8 % of the patients fulfilled that criteria. Over half of the mechanically ventilated patients were required to be admitted for over 3 weeks. Complications during ICU admission are common, with bed-sores (40 %), pneumonia (30.2 %) and sepsis (17.4) being the most frequently encountered in one study.
*Conclusion* Accurate data are limited by the fact that these studies are retrospective, often covering long periods in the past. Larger, more recent, prospective, multi-centre studies will be required.

**Keywords** Mortality · disability · Guillain-Barré · outcome · Intensive care · Mechanical ventilation

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## Background and aims

A recent article published in Nature by Bianca van den Berg et al., described Guillain-Barré syndrome (GBS) as 'potentially life-threatening post infectious disease characterised by rapidly progressive, symmetrical weakness of the extremities' [1].

The clinical profile and characteristic CSF findings of Guillain-Barré syndrome were first described by Landry in 1859 [2]. In 1916 Guillain, Barré, and Strohl re-established this picture, observing that they could differentiate this form of neuropathy from poliomyelitis from ether a raised concentration of protein with a normal cell count in the CSF, or from albuminocytological dissociation. In the modern day, our clinical diagnosis of Guillain-Barré syndrome is still very much in line with the early observations of these neurologists, with the hallmarks of GBS being a combination of rapidly progressive symmetrical weakness in the limbs with or without sensory disturbances, hyporeflexia or areflexia, in the absence of a CSF cellular reaction [3].

In the majority of GBS studies, infection in the upper respiratory tract or gastrointestinal tract predominate, producing symptoms of fever (52 %), cough (48 %), sore throat (39 %), nasal discharge (30 %), and diarrhoea (27 %), although many other types of infections have been reported [3].

Respiratory insufficiency occurs in approximately one out of every four patients (25 %), and these patients may require ICU admission and mechanical ventilation [1]. Outcome for these patients is likely to be worse. During their time in intensive care, these patients are vulnerable to a number of life threatening complications. A recent study conducted by Rajat et al. in 2007 involving 76 patients, listed the following complications as 'serious ICU complications' encountered by GBS patients in their study: pneumonia, sepsis; severe dysrhythmia; ileus/bowel perforation; deep vein thrombosis; pulmonary embolism; gastrointestinal haemorrhage; pseudomembranous colitis; and complications of tracheostomy. Two-thirds of patients in this study had at least one of these 'serious ICU complications' and one-quarter of patients in this study had three or more serious complications. These complications contribute significantly to the mortality and morbidity of patients suffering from GBS [4].

The aim of this study is to provide a concise review of the outcomes for GBS patients requiring mechanical ventilation.

## Methods

Relevant literature pertaining to the outcomes of GBS patients requiring mechanical ventilation, were identified using PubMed and Google Scholar searches with the keywords 'Guillain-Barré, Outcomes, Mechanical Ventilation, Prognosis, Mortality, ICU'. A total of 7 papers found in this search aimed to assess outcomes for these patients and these were all included. Only papers published since the beginning of the year 2000 were used to analyse outcomes. Supplementary papers were consulted for general discussion, reference, and additional information. The following parameters were analysed by one or more of the papers in this study to assess outcome: Mortality, recovery of ambulation, Length of hospital stay, complications, GBS disability scale (Hughes), Barthel index (BI), EuroQuol-5D (EQ-5D) and Fatigue Severity Scale.

## Results

### Mortality

Mortality was the only outcome parameter that was common to all 7 of the papers. The overall mortality rate in these studies varied from 8.3 to 20 %.

The lowest mortality was recorded by Azim et al. (2013), for their study entitled 'Outcome of mechanical ventilation in patients of Guillain-Barré syndrome: An audit from a tertiary care centre' [5] This study looked at 86 mechanically ventilated patients. All patients with Guillain-Barré syndrome who required admission to ICU and mechanical ventilation for 7 consecutive years were included in this study. The average patient age was 32.4 (±18.12) years. 82 % of patients in their study were male. The deaths of the patients in this study were due to complications of ICU admission and Mechanical ventilation, including ventilator acquired pneumonia (VAP) and sepsis [5].

The highest mortality rate (20 %) was recorded by Fletcher et al. (2000) for their study entitled 'Long-term outcome in patients with Guillain-Barré syndrome requiring mechanical ventilation' [6]. All 60 patients with GBS that required admission to a single intensive care unit for mechanical ventilation between 1976 and 1996 were included in this study.

The higher mortality in this study (20 vs 8.3 %) at first glance would appear to have some relation to the fact this is a much older study, published 13 years before Azim et al.'s study. In 2008 the Journal of clinical neuromuscular disease published 'National trends in hospital outcomes among patients with Guillain-Barré syndrome requiring mechanical ventilation'. In this article Souayah et al. compare data from 1992 to 2002 to assess if outcome for these patients has evolved in a decade of progress in healthcare [7]. Before 2002 the majority of new treatment modalities for Guillain-Barré syndrome were not available. By 2002 many strategies for the treatment of GBS existed, including immunotherapies and specialised intensive care units [8, 9]. Contrary to what we would have expected, improved and altered clinical strategies over those 10 years are not reciprocated in mortality rates, length of hospitalisation, or hospital charges their study. The mortality of patients in 2002 was 11.1 % whereas in 1992 it was 7.6 %. It is important also to note that this is the largest study included in this review, with accurate data taken from the US 'National Inpatient Sample', which contains data from approximately '5–8 million hospital stays' [7]. Although there is no evidence of improvement in the 10 years of this study, this does not mean that there were not improvements made during the period of Fletcher DD et al.'s study, from 1976 to 1996.

The second highest mortality rate of the 7 papers that were included in this review was recorded by Witsch et al. (2013) in their paper 'Long-term outcome in patients with Guillain-Barré syndrome requiring mechanical ventilation'. This paper looked at 110 GB patients requiring mechanical ventilation from the years 1999–2010, and they found a long-term mortality rate of 13.6 % as well as an in hospital mortality of 5.5 %. [10] These mortality rates are vastly lower than Fletcher et al.'s 20 % mortality and are more in keeping with the other studies in this review. When Fletcher DD et al.'s 20 % mortality is contextualised with this paper as well as the other 5 more recent papers in this study; it becomes likely this 20 % mortality rate is outdated.

Other mortalities reported by studies in this review include 12.1 % by Netto et al. (2011) in 273 patients between 1984 and 2007 [11]; 10.4 % in a separate study by Netto AB et al. (2011) in 173 patients between 1997 and 2007 [12]; and finally Köhrmann et al. (2009) reported and age related mortality in which there was a 41 % mortality in those patients older than 65, and 7 % in those under 65, in a study group of just 32 patients [13].

In addition to measuring mortality, Netto AB. et al. identify features associated with poor prognosis. 'Independent risk factors determining mortality were found to be elderly age group, autonomic dysfunction, pulmonary complications on logistic regression analysis, whereas hypokalemia and bleeding from any site were found to be the risk factors on univariate analysis' [12].

This mortality figures should be considered alongside the generally accepted mortality of patients with Guillain-Barré syndrome (GBS), which has varied widely with rates between 1 and 18 % [11].

In Fletcher et al's study (2000), at the time of maximal recovery, 81 % of the patients that had a poor outcome had required mechanical ventilation, with mortality related to GBS accounting for over 50 % of the patients with a poor outcome by this point' [6].

## Disability

Disability was measured by four studies using the GBS disability scale (Hughes scale) which measures disability as follows [14]:

| | Guillain-Barré disability scale (Hughes) |
|---|---|
| 0 | Healthy |
| 1 | Minor symptoms and signs of neuropathy but capable of manual work/running |
| 2 | Able to walk with a stick (5m across open space), incapable of manual work/running |
| 3 | Able to walk with a stick, applicance, or support (5m across an open space) |
| 4 | Confined to bed of chair bound |
| 5 | Requiring assisted ventilation at any time during either day or night |
| 6 | Death |

Netto et al. (2011) Looked at Hughes scale score (HS) at the time of discharge for 152 patients. They found that 47 (30.9 %) patients were ambulant with or without support at this point, meaning that they had a Hughes Score of 3 of less [12]. The reason that this number appears quite low is that outcome was measured at the time of discharge, rather than at the point of maximal recovery.

Fletcher et al. (2000) defined a good outcome as 'ability to ambulate without assistance' [6]. They determined functional disability and predictors of outcome at 1 year and at maximal recovery, rather than at the time of discharge as in the case of Netto et al. (2011) [6, 12]. Fletcher et al.'s (2000) study found that in the 60 mechanically ventilated patients in their study 79 % eventually regained independent ambulation. And 19 % of patients improved at least one functional grade beyond 1 year [6].

Witsch et al. (2013) determined disability not only by using the Hughes scale, but also by using the Barthel index (BI), EuroQuol-5D (EQ-5D) and Fatigue Severity Scale. They deemed that a favourable outcome was a GBS disability score of 0–1, 1 year or longer after admission, and found that in 110 mechanically ventilated patients, 53.8 % fulfilled this criteria. 73.7 % of survivors had no or mild disability (BI 90-100). Using the five dimensions of the EQ-5D, they found that 50.6 % stated no mobility impairments, 58.4 % stated no self-care impairments, 36.4 % stated no usual activity limitations, 36.4 % stated no pain, and 50.6 stated no anxiety or depression. 30.4 % of patients suffered from a sever fatigue syndrome [10].

Kohrmann et al. (2009) tried to correlate age with functional outcome. They found that once elderly patients have survived the early, most critical period, recovery was often as good as younger patients (80 % good outcome vs. 86 %), in a patient group of 32.

Netto et al.'s study (2011) identify the following as risk factors for a low Hughes scale score (≤3) and good functional outcome at discharge: 'younger age, presence of bulbar symptoms, less severe weakness at presentation, slower evolution of symptoms over more than 3 days, demyelinating neuropathy on electrophysiological studies, absence of sepsis, hypokalemia, and nutritional complications' [12] Witsch et al. (2013) found significant correlations of outcome with age, type of therapy, and number of immunoglobulin courses [10].

### Length of hospitalisation

Some studies used length of hospital stay as an outcome parameter. The largest study included in our review was by Souayah et al. (2008). They give the mean length of hospital stays for two different years; 1992 and 2002, for 754 and 994 patients, respectively. The found that the average length of hospitalisation in 1992 was 40.3 ± 36.3 days, where as in 2002 it was longer at 52.6 ± 23.3 days [7].

Azim et al. (2013) looked at both the length of hospitalisation as well as the length of ventilation as outcome parameters. They found that over half of the patients in their study (51.1 %) required a stay of >3 weeks. They defined prolonged mechanical ventilation as >2 weeks, and found that this applied to 64 % of patients. Owing to an extended of period of time spent in ICU many patients require a tracheostomy. Tracheostomy was required in 85 % of patients in this study [5].

### Complications

Although the complications of ICU admission and mechanical ventilation are themselves reflected by the mortality of patients, they can be analysed in on their own as outcome parameters. This was done by Azim et al. (2013). The most common complication in their study was bed sores, which was encountered by 40 % of patients. This was followed by ventilator associated pneumonia (VAP) in 30.2 % of patients. 17.4 % developed sepsis and 7 developed UTI [5]. Tracheostomy is often considered as a strategy to reduce the incidence of ventilator acquired pneumonia [15]. Patient turning, special mattresses, and special skin care products, can be used in the prevention of pressure ulcers [16].

### Additional

As well as the 7 papers that were included in this review which look specifically at outcomes for patients with GBS that require mechanical ventilation, there are many papers that look at outcomes for patients with GBS as a whole. One particular paper by González-Suárez et al. (2013), is worthy of mention. Although this paper looks at outcomes for patients with GBS as a whole, 17 % of patients in this study required mechanical ventilation. This study identified some possible predictors of poor outcome in patients with GBS, and found that mechanical ventilation was one of these predictors, showing greater numbers of sequels at discharge. A trend to associate with greater deficits was seen in the follow-up; however, the results were not statistically significant. Other possible poor outcome predictors in the study included age over 55. Patients older than 55 years were the most affected at the admission, with greater deficits at discharge. These deficits were measured using the GBS disability scale. Cranial nerve involvement was also related with greater deficits at discharge. Finally, they suggest that there is a trend for worse prognosis in patients with axonal lesions in conduction studies. Having said this, although these associations are true for GBS patients as a whole, they may not prove true for mechanically ventilated patients in particular, as only 17 % of the patients in this study of 106 patients were mechanically ventilated [17].

## Conclusion

The main drawback of all of the studies included in this review is that they are retrospective. The oldest study in this review is by Fletcher et al. (2000) [4]. Although published in the twenty-first century this study contains data going as far back as 1976. This of course makes it less likely that the results of their study accurately represent the true outcomes for Guillain-Barré patients today. Because of the scarcity of Guillain-Barré patients that require mechanical ventilation, many of the studies span a large period of time to increase the amount of patients in their study. Netto et al.'s study (2011) for example, spans the period of 1984–2007. Although this is a recent publication with some recent data included, the majority of the information is from the twentieth century [11]. It is likely that the patients at the end period of this study received different treatment from the GB patients at the start of the study [8, 9].

One of the difficulties of collating data for 'disability' as an outcome is that different studies measure disability at different points. Netto et al. measured disability at discharge, whereas Fletcher DD. Et al. measured it at 1 year and at maximal recovery [6, 11].

Each paper in this review must be individually read to fully appreciate their differences and conclusions. It is impossible to assume that the methods of each of the studies will be equal. One such variable that exists between the different studies is in the treatment of these patients. In Azim et al.'s study (2013) for example, not all of the patients received intravenous immunoglobulin (IVIGs) [5], which have a known benefit in treatment, [18] due to financial restrictions. Plasma exchange is another option in the treatment of Guillain-Barré. Recovery time has been shown to decrease by 50 % with the use of plasma exchange over the course of 10 days. This works by eliminating immune complexes, autoantibodies, and cytotoxins from the blood. There is a slight risk of relapse; however, in most cases this helps to speed recovery without causing harm [19]. Fortunately for our review, it does not matter if patients received plasma exchange or IVIGs, as the efficacy of plasma exchange is equal to that of IVIGs [18].

In summary accurate data will be best achieved by more recent prospective studies using larger cohorts of patients from various institutions, with all patients ideally receiving comparable levels of medical therapy within the intensive care unit.

**Compliance with ethical standards**

**Conflict of interest** None to declare.

**Ethical approval** This article does not contain any studies with human participants performed by any of the authors.

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