Guillain–Barré syndrome in pregnancy

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Guillain–Barré syndrome (GBS) complicating pregnancy is a rare event. Reports before the mid-1980s suggested that GBS in pregnancy carries a high maternal morbidity and mortality. However, it is uncertain whether availability of active treatment such as plasmapheresis and intravenous immunoglobulin together with advancement in intensive care has improved maternal outcome. This review examines the maternal and fetal outcomes of GBS complicating pregnancy reported in the recent English literature.

Key words: Guillain–Barré syndrome, pregnancy

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Literature search

A literature search using PubMed, MEDLINE and EMBASE was conducted using the key words “Guillain–Barré,” “acute demyelinating polyradiculoneuropathy” and “pregnancy.” The bibliographies of each article and relevant review articles were examined to further identify potential reports. Because we aimed to review the maternal and fetal outcomes in recent years, we limited our search to articles published between 1986 and 2002.

We identified 23 case reports with 29 cases of GBS in pregnancy (2–24). In addition, we included an unreported case encountered in our unit in 2002 (case 30). Information regarding the etiological agents, specific treatments, need for ventilatory support, pregnancy outcomes, maternal outcomes and methods of analgesia/anesthesia were retrieved and evaluated.

Epidemiology of GBS in pregnancy

The incidence of GBS in the general population is around 0.75 to 2 in 100,000 per year (25), with increasing incidence with age (26). Cheng et al. (27), in a retrospective study of disease incidence in Swedish women, found no significant difference between pregnant women and the general population, with an age-adjusted rate ratio of 0.86 [95% confidence interval (CI) 0.52–1.53]. However, there appeared to be an increased incidence immediately postpartum, with a rate ratio...
The timing of disease onset in the three trimesters was examined among the reviewed cases (Table 1). Of the 30 cases, only four (13%) had onset in the first trimester, 14 (47%) in the second trimester, and 12 (40%) in the third trimester. These proportions of cases in the three trimesters were similar to those reported by Nelson and McLean (1) in 1985.

**Diagnosis and clinical presentation of GBS**

GBS is suspected when a patient presents with progressive motor weakness and areflexia – the only criteria that must be present for the diagnosis (28). Commonly, patients would have a history of upper respiratory tract infection (40%) or gastroenteritis (20%) within 4 weeks prior to onset of disease (26, 29). However, the clinical spectrum of GBS is wide. Other clinical features include sensory symptoms, cranial nerve involvement (most commonly facial palsy), autonomic dysfunction causing pulse and blood pressure changes, and respiratory failure – a major cause of morbidity and mortality (28).

Delay in presentation is a common feature. The duration from onset of symptoms to presentation was reported in 22 cases and it was longer than 1 week in 50% of them. This delay in presentation might be due to initial nonspecific symptoms that mimic physiological changes in pregnancy (13).

Laboratory and electrophysiological investigations can be useful in diagnosing GBS in both nonpregnant and pregnant patients, but neither of them is specific for the disease and they may not always be present. Albuminocytologic dissociation in cerebrospinal fluid with elevated protein content and a normal mononuclear leukocyte count (10/µm³) are common findings and are strongly suggestive of GBS (28). Typical features of nerve conduction studies will show evolving multifocal demyelinating polyneuropathy (25), although normal studies may be found in about 15% of cases (26). Magnetic resonance imaging has also been used recently for diagnostic purposes (30), although it is again a nonspecific test. Spinal nerve root, especially selective anterior root, enhancement with gadolinium on magnetic resonance imaging is suggestive of GBS (31).

**Infectious etiology and immunopathogenesis**

GBS results from abnormal immune responses directed towards the peripheral nerves. Reports from the nonpregnant population revealed that an antecedent infectious event could be identified in two-thirds of cases (32) and this was thought to be the trigger for the abnormal immune response (33). Molecular mimicry has been suggested as one of the explanations for GBS induced by certain infectious agents (30).

Among all known infectious agents, *Campylobacter jejuni* has been recognized recently as the most common pathogen associated with GBS in the nonpregnant population. Rees et al. (29) found that 26% of patients with GBS had serological evidence of *Campylobacter jejuni* infection, as compared to only 1% of age-matched controls. They also found that cases of GBS associated with preceding *Campylobacter jejuni* infection were characterized by axonal degeneration, slow recovery and more severe residual disability (29).

In the 30 reported cases of GBS in pregnancy, no case of *Campylobacter jejuni* infection was reported, although most case reports did not mention whether a specific test for this pathogen was performed.

Cytomegalovirus (CMV) has been found to be the second most common infectious agent associated with GBS in the nonpregnant population. It was reported in 13% of cases (34). GBS after CMV infections are characterized by initial severity with respiratory difficulties, delayed recovery, and severe sensory loss (35). Among the 30 pregnant cases reviewed, a specific pathogen was identified in 13 cases (Table 1). Nine cases had evidence of recent CMV infection and of these nine, five required ventilatory support (55%), one of whom died. One woman had a second-trimester miscarriage associated with CMV placentitis. Attempts to identify the causative infectious agent should be made in all cases of GBS complicating pregnancy because pathogens such as *Campylobacter jejuni* and CMV are associated with more severe disease and longer recovery. The identification of these agents can aid the estimation of disease progress, patient counseling and the planning of subsequent pregnancy management. Moreover, infection by pathogens such as CMV may also have significant implications for the developing fetus.

**Specific treatments for GBS and their use in pregnancy**

Randomized controlled trials showed that plasmapheresis is effective in treatment of GBS compared to supportive management (36,37), with shorter duration of mechanical ventilation and reduced time to full ambulation. Improved outcome was especially observed in those with plasmapheresis started within 2 weeks of symptom onset (38). Potential risks of plasmapheresis include hypotension, fluid overload, septicemia
and deranged clotting profile (39). The safety of plasmapheresis in pregnancy has been well documented in other conditions such as thrombotic thrombocytopenic purpura complicating pregnancy. The risks of complications of plasmapheresis were found to be similar between pregnant and nonpregnant patients (40).

Intravenous immunoglobulin (IVIG) has been used to treat GBS since the 1980s. IVIG has the advantages of low risk of complications and ease of application (34). IVIG and plasmapheresis were found to be equally effective in treatment of GBS (41). In pregnancy, the safety of use of IVIG has been established based on its use in treating conditions such as maternal idiopathic thrombocytopenia purpura and fetal alloimmune thrombocytopenia (42).

In the 30 cases reviewed, 22 cases received IVIG or plasmapheresis (Table I). Among women treated with plasmapheresis or IVIG, there was no report of any treatment-induced maternal or fetal complication. As IVIG does not involve significant alterations in blood volume, it might be a better choice for GBS complicating pregnancy.

Maternal and fetal outcomes in pregnancies complicated by GBS

In the 30 cases reported after 1985, ventilatory support was required in 10 women (33.3%). The duration of ventilatory support was reported in six cases, and ranged between 2 and 126 days. The availability of IVIG or plasmapheresis does not seem to be associated with a lower requirement in ventilatory support. This may be partly due to the long delay from onset of neurological symptoms to presentation and treatment (more than 1 week in half of the reported cases). Active treatment such as plasma exchange is reported to be more beneficial when started within 7 days after disease onset (38).

Fetal outcomes were reported in 27 cases (Table I). There were three terminations of pregnancies. After the termination of pregnancy, one woman remained bed-bound for 20 weeks (case 2), another had to stay in intensive care for 12 weeks and then had “a slow recovery” (case 25), and the third took 8 weeks to fully recover (case 29). This supported the previous observation that termination of pregnancy does not hasten the recovery of maternal disease nor improve maternal outcome (1). GBS on its own is therefore not an indication for termination of pregnancy.

There was one pregnancy that was complicated by missed abortion due to CMV placentitis (case 20). In the remaining 23 pregnancies, there was one case of fetal demise due to sudden maternal death (case 4). There was no neonatal death, giving a perinatal survival rate of 95.7%. Preterm deliveries occurred in eight cases (34.7%), of which three had spontaneous labor while five were iatrogenic preterm deliveries due to deterioration of maternal neurological condition (three cases) or preeclampsia (two cases).

There was one case (case 21) of neonatal GBS born to an affected mother. The baby required mechanical ventilation on day 12 of life, with flaccid paralysis of all limbs, absent deep tendon reflexes, and respiratory distress. The baby responded to IVIG treatment and recovered within 2 weeks. The authors suggested fetal nerve damage by maternal antibodies to CMV epitopes as the possible cause. This was the only case report of neonatal GBS resulting from maternal disease.

Management of GBS in pregnant women

A multidisciplinary approach involving the physicians and obstetricians is essential in the management of GBS in pregnant women. Apart from specific treatments such as IVIG or plasmapheresis mentioned earlier, attention should be paid to the identification and treatment of infective complications, prevention of venous thromboembolism, pain management, and the management of psychological distress resulting from the disease and anxiety towards the pregnancy.

The incidence of pulmonary embolism in nonpregnant GBS was reported to be between 1 and 13% (43). Prophylactic anticoagulation in the immobilized GBS patient is considered a standard management in most units (44). Even with prophylactic anticoagulation, Gaber et al. (44) still found a clinical deep venous thrombosis incidence of 7% and a pulmonary embolism incidence of 4%. They also found that the highest risk for deep vein thrombosis was during the first 12 weeks after the onset of symptoms. As pregnancy itself is also a strong risk factor for thromboembolism, prophylactic anticoagulation should be administered early in GBS pregnant women with poor mobility. Apart from pharmacological prophylaxis, physical measures such as pressure stockings, physiotherapy and early mobilization are also useful.

Nosocomial infection is an important complication of GBS patients. As many as 25% of GBS patients acquired pneumonia and 30% suffered from urinary tract infections (25). Because these infections tend to be more severe in pregnant women, early identification and treatment are desirable.
<table>
<thead>
<tr>
<th>Case</th>
<th>Gestation* (weeks)</th>
<th>Specific treatment</th>
<th>Ventilatory support</th>
<th>Pregnancy outcome</th>
<th>Maternal outcome</th>
<th>Neonatal outcome</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>Nil antenatally. Plasmapheresis postpartum</td>
<td>No</td>
<td>CS at 40 weeks for failure to progress in labor</td>
<td>Walked with frame 3.5 months after delivery</td>
<td>Unknown</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>14</td>
<td>Plasmapheresis</td>
<td>Yes</td>
<td>TOP at 16 weeks, reason not stated</td>
<td>Walked with sticks 5 months after admission</td>
<td>TOP</td>
<td>CMV</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>No</td>
<td>Yes</td>
<td>Preterm labor at 34 weeks with forces delivery while patient in coma</td>
<td>Exubated 30 days after delivery, no remaining deficit upon discharge</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>18</td>
<td>No</td>
<td>Yes</td>
<td>Maternal death at 25 weeks</td>
<td>Improved and discharged on day 39, Sudden death at home, probably due to tracheo-esophageal fistula</td>
<td>Died in utero</td>
<td>CMV</td>
</tr>
<tr>
<td>5</td>
<td>18</td>
<td>No</td>
<td>Yes</td>
<td>Spontaneous labor at 38 weeks, forces delivery</td>
<td>Off ventilator 6 days after delivery, unable to walk unaided upon discharge</td>
<td>Normal</td>
<td>CMV</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
<td>Plasmapheresis</td>
<td>Yes</td>
<td>CS at 37 weeks for unengaged head, septicemia, hemodynamic disturbances</td>
<td>“Floppy infant” syndrome due to maternal benzodiazepine use. Normal development at 9 months</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>8 before admission at term</td>
<td>No</td>
<td>No</td>
<td>Spontaneous labor at term. Emergency CS for previous classical CS</td>
<td>GBS symptoms already resolved 3 weeks before labor. Arrest during CS after succinylcholine. Successful resuscitation</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>26</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>PPROM at 33 weeks, CS for cord presentation</td>
<td>Almost complete recovery of functions by 30 weeks</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>9</td>
<td>26</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>IOL for preeclampsia, SVD at 36 weeks</td>
<td>Postpartum course uncomplicated. Normal</td>
<td>CMV</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>32</td>
<td>Nil antenatally. Plasmapheresis postpartum</td>
<td>No</td>
<td>CS at 35 weeks for preeclampsia</td>
<td>Continued to deteriorate after CS</td>
<td>Normal</td>
<td>CMV</td>
</tr>
<tr>
<td>11</td>
<td>16</td>
<td>Nil antenatally. Plasmapheresis postpartum</td>
<td>No</td>
<td>Not stated</td>
<td>Ambulatory 25 days after admission</td>
<td>Not stated</td>
<td>–</td>
</tr>
<tr>
<td>12</td>
<td>35</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>CS at 38 weeks for previous perinatal death</td>
<td>Slight proximal paresis of lower limbs on discharge 2 weeks later</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>13</td>
<td>36</td>
<td>Nil antenatally. Plasmapheresis postpartum</td>
<td>No</td>
<td>CS for rapid progression of neurological symptoms at 36 weeks</td>
<td>Only bilateral facial nerve palsy remained 6 weeks after CS</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>14</td>
<td>36</td>
<td>Nil antenatally. Plasmapheresis postpartum</td>
<td>Yes</td>
<td>CS at 36 weeks for deteriorating respiratory function</td>
<td>Continued to deteriorate postpartum, regained motor strength and discharged after 8 weeks</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>15</td>
<td>36</td>
<td>Nil antenatally.</td>
<td>No</td>
<td>CS at 36 weeks for deteriorating neurological condition</td>
<td>Deteriorated postpartum, requiring ICU care. Discharged 6 weeks later with only facial nerve palsy</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>16</td>
<td>35</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>CS at 38 weeks at patient’s request</td>
<td>Symptoms resolved postpartum, discharged 2 weeks later with mild proximal lower limb weakness</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>17</td>
<td>24</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>Preterm labor and SVD at 35 weeks</td>
<td>Complete resolution by 3 months postpartum</td>
<td>Normal</td>
<td>CMV</td>
</tr>
<tr>
<td>18</td>
<td>29</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>SVD at term</td>
<td>Good recovery at 37 weeks. Returned later in labor</td>
<td>Normal</td>
<td>Rubella</td>
</tr>
<tr>
<td>19</td>
<td>15</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>SVD at term</td>
<td>Normal power at 34 weeks</td>
<td>Normal</td>
<td>–</td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>Missed abortion at 20 weeks</td>
<td>Ambulatory 9 days after admission</td>
<td>Normal</td>
<td>CMV</td>
</tr>
<tr>
<td>21</td>
<td>29</td>
<td>IVIG with no improvement, then plasmapheresis</td>
<td>Yes</td>
<td>SVD at 38 weeks while patient tetraplegic and ventilated</td>
<td>Improved 4 months after onset</td>
<td>Affected by GBS, required mechanical ventilation day 12 after birth. Treated with IVIG, returned to normal after 14 days</td>
<td>CMV</td>
</tr>
</tbody>
</table>
Patients suffering from GBS may complain of neuritic pain and paresthesia, and suitable pain relief should be provided. Carbamezapine has been shown to be effective for the relief of muscle and neuritic pain in GBS patients in a placebo-controlled trial (45). In cases of severe pain, opioids may be needed. As carbamezapine is teratogenic, its use in early pregnancy should be avoided.

Mode of delivery

In the 23 women who progressed beyond the second trimester, cesarean sections were performed in 14 cases (61%) (Table I). In three women, cesarean section was performed for deterioration of maternal neurological condition. Vaginal delivery was achieved in nine cases, including one woman who was still tetraplegic and ventilated when spontaneous delivery occurred at 38 weeks (case 21). Indeed, the risk of complications such as thromboembolism and anesthetic risk is higher in mothers with GBS. Despite neurological deficits, impairment of uterine contraction activity was not observed in the cases reviewed, and the ability of normal vaginal delivery was demonstrated. Therefore, maternal GBS is not an indication for cesarean section and operative delivery should be reserved for obstetric indications only.

### Anesthesia and analgesia

The choice of labor analgesia and anesthesia for cesarean section should be considered carefully in the pregnant patient with GBS. Both regional and general anesthesia have potential additional risk in these women.

The main problem with general anesthesia in GBS is the use of succinylcholine, as postsynaptic receptor proliferation in these patients can lead to hyperkalemia during depolarization. Feldman (7) (case 7) reported a case of cardiac arrest due to hyperkalemia that occurred shortly after succinylcholine administration for general anesthesia. Autonomic instability in GBS patients may also pose problems during general anesthesia. However, no complication was reported in three other cases in which general anesthesia was used (cases 8, 10 and 25).

Concerns regarding GBS being triggered by the use of regional anesthesia were first raised by Steiner et al. in 1985 (46). The authors reported four cases of GBS occurring 1–2 weeks after epidural anesthesia (three for general surgery and one for delivery). It was postulated that the mechanical or chemical disturbance caused by the procedure might have triggered GBS in these patients. This remained an unproven hypothesis, as GBS is also known to have an increased occurrence postpartum and after surgery. Nevertheless, this report raised concern when administering analgesia or anesthesia in

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<table>
<thead>
<tr>
<th>Case No</th>
<th>Weeks Pregnant</th>
<th>Treatment</th>
<th>Mode of Delivery</th>
<th>Outcome</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 (18)</td>
<td>25</td>
<td>IVIG</td>
<td>SVD at 38 weeks</td>
<td>Improved after IVIG. Deteriorated again at 33 weeks, IVIG repeated. Almost complete recovery by 37 weeks</td>
<td>Normal</td>
</tr>
<tr>
<td>23 (19)</td>
<td>7</td>
<td>IVIG, then plasmapheresis</td>
<td>CS for genital warts at 38 weeks IOL for postterm. CS for failure to progress TOP at 9 weeks (in view of severe illness and CMV infection)</td>
<td>Weaned from ventilator 18 weeks after onset Required manual evacuation of rectum for severe constipation. Walked unaided at term Discharged from ICU after 86 days, slow recovery afterwards</td>
<td>Normal</td>
</tr>
<tr>
<td>24 (19)</td>
<td>24</td>
<td>No</td>
<td>No</td>
<td>Not stated</td>
<td>EBV</td>
</tr>
<tr>
<td>25 (20)</td>
<td>6</td>
<td>IVIG</td>
<td>Yes</td>
<td>TOP</td>
<td>CMV</td>
</tr>
<tr>
<td>26 (21)</td>
<td>15</td>
<td>IVIG</td>
<td>SVD at term</td>
<td>Discharged 21 days after admission Ambulatory at time of delivery</td>
<td>Normal</td>
</tr>
<tr>
<td>27 (22)</td>
<td>21</td>
<td>Plasmapheresis</td>
<td>No</td>
<td>CS for failure to progress in labor at term</td>
<td>Normal</td>
</tr>
<tr>
<td>28 (23)</td>
<td>27</td>
<td>IVIG</td>
<td>No</td>
<td>SVD at 37 weeks</td>
<td>Normal</td>
</tr>
<tr>
<td>29 (24)</td>
<td>4</td>
<td>Steroid and plasmapheresis</td>
<td>TOP at 18 weeks, reason not stated</td>
<td>No deficit 2 months later</td>
<td>TOP</td>
</tr>
<tr>
<td>30 (25)</td>
<td>20</td>
<td>IVIG</td>
<td>No</td>
<td>CS for brecch at 39 weeks</td>
<td>Discharged with minimal deficit at 33 weeks gestation at illness onset</td>
</tr>
</tbody>
</table>

CMV, cytomegalovirus; CS, cesarean section; EBV, Epstein–Barr virus; ICU, intensive care unit; IOL, induction of labor; PPROM, preterm prelabor rupture of membranes; SVD, spontaneous vaginal delivery; TOP, termination of pregnancy.
GBS patients for fear of triggering an exacerbation or recurrence. In the 30 cases we reviewed, five cases reported the use of regional anesthesia or analgesia (cases 1, 23, 24, 27 and 30), including four cases of epidurals and one case of combined spinal epidural. All procedures were uncomplicated without any worsening or relapse of neurological symptoms. We therefore consider that the benefit of regional anesthesia outweighs the theoretical risk in most circumstances. However, good documentation of the patient’s neurological deficit prior to regional anesthesia is important for future monitoring for deterioration, as well as for medico-legal reasons. Fear of paralysis or loss of sensation may also be a problem encountered by those who recover from GBS. Sympathetic counseling with clear explanations should be provided to avoid psychological distress.

Conclusion

Guillain–Barré syndrome is a rare neurological disease. Despite advances in GBS treatment and intensive care standards, morbidity of GBS complicating pregnancy remains high. Termination of pregnancy did not shorten disease duration or improve maternal outcome, and is not indicated for GBS. Early diagnosis and active treatment with the use of IVIG or plasmapheresis together with prevention of complications is the key to success in management of pregnant women with GBS.

References


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