International Journal of Women's Dermatology 3 (2017) S1–S5

Contents lists available at ScienceDirect

International Journal of Women's Dermatology

Retrospective evidence on outcomes and experiences of pregnancy and childbirth in epidermolysis bullosa in Australia and New Zealand☆,☆☆,★

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ARTICLE INFO

Article history:
Received 24 November 2014
Received in revised form 14 December 2014
Accepted 15 December 2014

Keywords:
Epidermolysis Bullosa
Pregnancy
Delivery
Childbirth
Anesthesia

ABSTRACT

Background: Pregnancy in epidermolysis bullosa (EB) has not been comprehensively studied.
Objective: We aimed to develop a foundational database, which could provide peri-obstetric advice in EB.
Methods: Survey questionnaires were sent to obstetricians, unaffected mothers of EB babies, and mothers with EB. Results were analyzed using chi-square, Fisher exact, and t-tests.
Results: Out of 1346 obstetricians surveyed, 195 responded, and only 14 had encountered EB. All recommended normal vaginal delivery (NVD), except for one elective Caesarean section (CS). We received responses from 75 unaffected mothers who had delivered EB babies. They had significantly more complications in their EB pregnancies compared to their non-EB pregnancies. A further 44 women with various types of EB who had given birth responded. Most delivered via NVD and had no significant increase in complications in both their EB and non-EB pregnancies. In both groups, there were no significant differences in blistering at birth in babies delivered via NVD and CS.
Conclusion: In conclusion, most patients with EB who are capable of giving birth do not have an increased risk for pregnancy-related complications and NVD appears to be safe. Awareness of this data amongst obstetricians and dermatologists should lead to improved quality of care for mothers and babies affected with EB.

Introduction

Ongoing research on various aspects of epidermolysis bullosa (EB) is currently underway. Most reports are focused on the molecular basis and classification of this disease. Diagnostic criteria and treatment options for this condition are constantly evolving, but little focus has been directed towards pregnancy and childbirth in these patients. There is a scarcity of literature available addressing this important issue, and this paper aims to fill that gap, and provide sound evidence and guidance for mothers who are pregnant with EB babies.

Milder forms of EB, such as EB simplex, often go undiagnosed: this could explain the relative lack of pregnancy cases reported. On the other hand, very few reports in the literature detail pregnancy and childbirth experiences of mothers and infants with more severe forms of EB, including junctional EB (JEB) and recessive dystrophic EB (RDEB). It does not always follow that all patients with severe forms of EB will have difficult pregnancies (Price and Katz, 1988).

The bulk of the available literature is mainly on prenatal diagnosis of severe forms of EB (EBS or JEB with pyloric atresia, Herlitz JEB, and RDEB) and its role in management decisions such as termination (D'Alessio et al., 2008; Marinkovich et al., 1995; Yan et al., 2007; Pfendner et al., 2003; Norup 1999). A survey performed in Denmark amongst obstetricians and pediatricians showed that in the case of newborns with severe EB, there was a strong consensus to withhold life-prolonging treatment, reflecting attitudes to EB (Norup 1999).

A patient with non-Herlitz JEB was reported who had two miscarriages prior to giving birth successfully via Cesarean section under epidural anesthesia (Price and Katz, 1988). A patient with RDEB in Germany had two vaginal deliveries resulting in healthy babies, with uncomplicated episiotomy wound healing, and no exacerbations of EB during her

☆ IRB Status: The study was approved by the South Eastern Sydney Local Health District Human Research Ethics Committee from October 2006 to July 2012.

☆☆ Disclosures: Partial support was provided by DebRA Australia, New Zealand, the Lord Mayor's Trust and the Caroline Quinn Trust Fund. The authors have no conflict of interest to declare.

★ This article is a reprint of a previously published article. For citation purposes, please use the original publication details; International Journal of Women's Dermatology 1 (2015) 26–30. DOI of original item: 10.1016/j.ijwd.2014.12.005.

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http://dx.doi.org/10.1016/j.ijwd.2017.02.002

pregnancy (Büscher et al., 1997). Another patient with RDEB had preterm labor at 36 weeks and premature rupture of membranes, yet delivered a healthy baby via Cesarean section (Bianca et al., 2003). In the French literature, there is a report of a patient with EBS who developed a herpetiform flare of EBS-DM during the first two months of her pregnancy (Diris et al., 2003). More recent reports include that of a patient with Kindler syndrome with vaginal stenosis who had a successful Cesarean delivery (Hayashi et al., 2007). The report most recently published is a case report of 11 pregnancies in three patients with recessive EB in Australia. One of the patients had non-Herlitz JEB and had delivered two unaffected babies via NVD eight years apart. The two other patients were sisters who both had generalized RDEB. One of them delivered three healthy unaffected babies via NVD, and the other delivered five unaffected babies via NVD. They all had no complications or flare of their EB during their pregnancies and the peripartum period (Choi et al., 2011). More recently, there has been a report of three more women, each with RDEB-intermediate (RDEB-I), all of whom had successful vaginal deliveries without major cutaneous or mucosal complications (Hanafusa et al., 2012). There is also an online patient information handout on pregnancy and childbirth in EB published by the Dystrophic EB Research Association (DEBRA) UK group in May 2006 which reports that women with EB have successfully had vaginal and Cesarean deliveries (Pillay, 2006).

Labor and delivery practices include airway management strategies, the role of regional anesthesia, and the use of nonadhesive tape and padding (i.e. Mepitel, Mepilex, Mepitac, Mepiform) as minor trauma may lead to severe lesions (Price and Katz, 1988; Pillay, 2006). Regional anesthesia has been used successfully in these patients. There are five reported cases that used either spinal or epidural anesthesia for Cesarean section, and epidural anesthesia for vaginal delivery without any ensuing complications (Baloch et al., 2008; Broster et al., 1987; Berryhill et al., 1978).

In view of this limited information, we designed a survey looking at the experiences of a large group of obstetricians, unaffected mothers who delivered babies with EB, and EB patients themselves who have delivered babies. We have developed a foundational database, and have developed recommendations on periobstetric advice in relation to EB.

Methods

This study was granted ethics approval by the South Eastern Sydney Local Health District Human Research Ethics Committee - Southern Sector on the 3rd of October, 2006 until July, 2012.

Questionnaires were sent out to three participant groups, namely obstetricians in Australia, unaffected mothers who had given birth to EB babies, and EB females who had given birth.

The list of obstetricians was obtained from the Royal Australian and New Zealand College of Obstetricians and Gynecologists (RANZCOG), whilst the list of EB patients and their parents was obtained from patients known to us, most of whom are in the Australasian EB Registry which is being maintained at St. George Hospital, Sydney, NSW, Australia (Kho et al., 2010). The appropriate questionnaires were mailed to these obstetricians and patients in the post with self-addressed envelopes. Some questionnaires were also handed out to member families of DEBRA Australia and New Zealand, new patient referrals seen at St. George Hospital, and patients attending EB clinics. All participants had given signed informed consents to participate in the study and share their data.

A substudy was also performed that looked into the percentage and locations of blisters, if any, in babies born with EB to unaffected mothers and those diagnosed with EB This was achieved by sending out further questionnaires with body maps to both groups of respondents.

The data was then collated and summarized over a period of 4.8 years (October 2006–August 2011). Statistical analysis was performed using chi-square tests, t-tests, and Fisher exact tests. The statistical program used was SigmaStat. Based on the results, peri-obstetric recommendations were made for EB patients and mothers giving birth to EB babies.

Results

Group 1: Data from obstetricians in Australia

The questionnaires were sent out in one batch to 1346 obstetricians in Australia, and 195 responded. Only 14 of the 195 obstetricians who responded had encountered mothers or babies born with EB. Their average number of years in practice was 17. Six of the 14 obstetricians attempted a literature search on EB in pregnancy and childbirth, but only three were successful in finding any articles on pregnancy in EB. Also, only four had coordinated the management of these patients with a dermatologist.

The 14 obstetricians all recommended normal vaginal delivery (NVD). However, one performed an elective Cesarean section (CS) at the patient's request which resulted in poor wound healing and a post-operative wound infection. Furthermore, 111 of the 195 obstetricians indicated the need to have information about EB available in antenatal clinics.

Group 2: Data from mothers without EB who had given birth to EB babies

We sent 122 survey questionnaires to EB-unaffected mothers who had given birth to at least one child with EB. Attempts were made to contact all non-responders, and they were re-sent the survey forms. We received 75 completed questionnaires out of the 110 mailed out (a 68% response rate or 75% response of those known to us). An additional 12 forms were returned, undelivered, owing to changes of address. These pertained to 176 pregnancies and 174 births, 84 (48%) of whom were affected by various types of EB: (35 with EBS, 14 with JEB, 19 with DDEB, and 17 with RDEB). There were 69 surveys from mothers in Australia and 6 from New Zealand. The age of respondents ranged from 19–78 (mean age of 46.2) and they had given birth to between one and four children, with an average of about two children in each family. A total of 43 out of the 75 mothers (57%) had children under 18 years of age. A summary of their characteristics is shown in Table I.

Most mothers with EB had normal vaginal deliveries without any ensuing complications. The ratio of NVD to CS was 4:1. Table II shows the modes of delivery of both EB-affected and EB-unaffected children whilst Table III shows the list of complications during pregnancy and delivery of both groups of babies from mothers who were unaffected by EB themselves. A chi-square analysis showed significantly more (approximately two-fold) complications in the pregnancies that delivered EB babies (22/84) as compared to EB-unaffected babies (11/90) ($p = .031$). Fisher's exact testing also revealed significantly more complications in EB babies delivered via CS (including emergency CS) as compared to NVD ($p < .001$).

Five cases of full-term babies not known to have EB in advance due to a lack of family history of EB were delivered using vacuum suction and/or forceps, resulting in skin being eroded from the babies' head, face and mouth areas; these babies were subsequently diagnosed with severe forms of EB. The first case was a baby with RDEB delivered via NVD and vacuum suction in which skin was removed from the baby's face and mouth. The second case was a baby with RDEB delivered via NVD and forceps, where skin was removed from non-facial parts of

Table I
Demographics of mothers with EB, and mothers without EB, who have given birth to EB babies.

	Number of mothers with EB	Number of mothers without EB
Number of mothers	44	75
Mean age and age range	45.1 (22-82)	46.2 (19-78)
Mothers from Australia	37	69
Mothers from New Zealand	7	6
Number of offspring	112	174
EB-affected babies	54	84
EB-unaffected babies	58	90

EB, epidermolysis bullosa.