Changing trends of causative factors in antenatal mothers with bad obstetric history: a retrospective study

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ABSTRACT

Background: The death of an infant, in utero or after birth has been a devastating experience for parents and clinicians alike. Various efforts are being made to make an accurate diagnosis of such pregnancy losses at the earliest to prevent the emotional and physical stress that the woman undergoes. This study aims to assess the changing trends in risk factors and outcome of pregnancies in cases of bad obstetric history (BOH) and to identify the newly emerging maternal and fetal factors contributing to incidence of pregnancy loss.

Methods: This study is a retrospective analysis of antenatal women with BOH attending the obstetrics and gynecology OPD at Chettinad hospital. The study was conducted during a time period of 1 year (May 2019 to May 2020).

Results: The medical complications and underlying causes for BOH were analysed among the study group. Out of 41 women, 6 were diagnosed to have gestational diabetes mellitus (GDM), 8 were found to be hypertensive and 1 APLA positive. Neonatal mortality was encountered in 2 cases, attributing to Inborn error of metabolism. However, the cause for BOH remained unexplained in 3 individuals.

Conclusions: A full work-up can be initiated after two consecutive losses to identify and treat the various causes responsible for BOH. Lot of further studies and research are being conducted to unravel the mystery in these cases. Despite these efforts, the male factors contributing to recurrent pregnancy loss have remained largely unexplored.

Keywords: Pregnancy loss, Neonatal outcome, Inborn errors of metabolism, Mode of delivery
contributed to parental chromosomal abnormalities, anatomical causes contribute to 10%-15%, while other causes like endocrine-17-20%, antiphospholipid antibody syndrome to 15%-20%. However, the underlying cause remains unknown in 33% cases.

**Aim of the study**

The aim of the study was to assess the recent trends in risk factors and outcome of pregnancies in cases of BOH and to identify the various maternal and fetal factors contributing to incidence of pregnancy loss. The maternal factors contributing to pregnancy loss was analysed in terms of age, BMI, gravidity, parity, presence of conditions such as parental chromosomal anomalies, maternal thrombophilic disorders (APLA) structural uterine anomalies, hypothyroid, gestational diabetes mellitus, hypertension, premature rupture of membranes, antepartum haemorrhage, cervical incompetence, tuberculosis. The fetal outcomes of interest are prematurity, fetal anomalies (structural/chromosomal), intra uterine growth retardation (IUGR), inborn error of metabolism (IEM), stillbirth, mode of delivery, birth weight, fetal distress, meconium-stained liquor.

**METHODS**

This study is a retrospective analysis of antenatal women with BOH attending the obstetrics and gynecology outpatient department at Chettinad hospital. The study was conducted during a time period of 1 year (May 2019 to May 2020). The records of the patients satisfying the inclusion and exclusion criteria was obtained from the medical records department.

**Inclusion criteria**

Inclusion criteria for the study were ≥2 consecutive spontaneous abortions, ≥2 early neonatal deaths, ≥2 stillbirths, ≥2 intrauterine fetal deaths, ≥2 intrauterine growth retardation, ≥2 congenital anomalies in the fetus, and combination of any ≥ 2 of the above.

**Exclusion criteria**

Exclusion criteria for the study were-induced abortions, previous uneventful deliveries (vaginal/LSCS). After getting informed consent of participants included in the study telephonically and ethical committee approval. Based on the inclusion and exclusion criteria, 41 patients were included in the study. The medical complications and underlying causes for BOH were analysed among the study group. Fetal outcomes such as prematurity, Fetal anomalies (structural/chromosomal), Intra uterine growth retardation (IUGR), inborn error of metabolism (IEM), stillbirth, mode of delivery, birth weight, Fetal distress, Meconium-stained liquor were also analysed. All the above data were analysed using SPSS software.

**RESULTS**

In our study, nearly 67.3% of women belonged to age between 20-30 years, with a mean age of about 28.56±2.79 SD. The mean BMI of women included in the study was 23.2±2.07SD (Table 1).

Out of 41 women, 6 were diagnosed to have gestational diabetes mellitus (GDM), 8 were found to be hypertensive and 1 APLA positive. The cause for recurrent neonatal death was thought to be but on evaluation found to have been due to inborn errors of metabolism-isovaleric acidemia in one and fatty acid oxidation defect in another. However, the cause for BOH remained unexplained in 3 individuals (Table 2).

In our study, we found that 65% women delivered by caesarean section while 29.2% delivered vaginally and 0.04% by VBAC (Table 3 and 4).

Various fetal outcomes such as preterm delivery, IUGR, stillbirth, MSL, IUD and neonatal morbidities and mortalities were noted. The incidence of MSL was 31.7% while preterm delivery accounted for about 21.9%. Neonatal mortality was noted in 4.8% of the cases. However, 41.4% (n=17) had good fetal outcome (Table 5).

About 43.9% women were gravida 4, whereas 31.7%, 9.7%, 14.6% women were gravida 3,5 and 6 respectively. (Table 6).

**Table 1: Maternal factors.**

| Variables          | Mean  | SD (±) |
|--------------------|-------|--------|
| Age (years)        | 28.56 | 2.79   |
| BMI                | 23.2  | 2.07   |
| Parity             | 1.24  | 0.70   |
| Birth weight       | 2.88  | 0.48   |

**Table 2: Medical complications/underlying causes.**

| Medical complications/underlying causes | N  |
|----------------------------------------|----|
| APLA                                   | 1  |
| Hypothyroid                            | 8  |
| Tuberculosis (tb)                      | -  |
| Gestational diabetes mellitus (GDM)    | 6  |
| Pre-eclampsia                          | 8  |
| Lateal phase defect                    | -  |
| Hyperprolactinemia                     | -  |
| Parental chromosomal anomalies         | -  |
| Prelabour rupture of membranes (prom)  | 6  |
| Antepartum haemorrhage (APH)           | 1  |
| Malpresentation                        | 4  |
| Cervical incompetence                  | 2  |
| Inborn error of metabolism             | 2  |
| Unexplained                            | 3  |
Table 3: Mode of delivery.

| Mode of delivery | N  |
|------------------|----|
| LSC              |    |
| Overall          | 27 |
| Elective         | 9  |
| Emergency        | 18 |
| Vaginal delivery |    |
| Overall          | 12 |
| Normal vaginal delivery | 10 |
| Vacuum assisted  | 2  |
| Forceps          | -  |
| VBAC             | 2  |

Table 4: Indications for elective and emergency LSCS.

| Emergency LSCS | Indication | N  | Elective LSCS | Indication | N  |
|----------------|------------|----|---------------|------------|----|
| Failure to progress | 1 | Malpresentation | 2 |
| Fetal distress | 2 | BOH | 2 |
| Failed induction | 2 | Previous LSCS | 5 |
| APH             | 1 | Total | 9 |
| Previous LSCS | 5 |
| Multiple pregnancy | 1 |
| Pre-eclampsia | 2 |
| Malpresentation | 2 |
| Total          | 18 |

Table 5: Fetal outcome.

| Variables                  | N  | Percentage (%) |
|----------------------------|----|----------------|
| Preterm                    | 9  | 21.9           |
| IUGR                       | -  | -              |
| Stillbirth                 | -  | -              |
| Msd                        | 13 | 31.7           |
| Neonatal mortality and morbidity | 2 | 4.8 |
| IUD                        | -  | -              |

Table 6: Parity wise distribution.

| Parity | N  | Percentage (%) |
|--------|----|----------------|
| G1     | 13 | 31.7           |
| G2     | 18 | 43.9           |
| G3     | 4  | 9.7            |
| 2G5    | 6  | 14.6           |

DISCUSSION

The attempt to identify the underlying cause for recurrent pregnancy losses has led to revelation of contributing factor in about 40-50% of women. Even in couples where no underlying problem is found, the chances for a successful pregnancy can typically be in the 50-70% range.1

In our study, 7.3% of women had no underlying medical complication contributing to BOH. Anand et al showed that incidence of low-birth-weight baby was 4 times more among women with BOH.5 However in our study, 31.6% of babies born to mothers with BOH were low birth weight, the mean birth weight being 2.88±0.48 SD.

The incidence of gestational hypothyroidism leading to suboptimal obstetric outcomes is around 1%.6 Our study showed an increase in the incidence of gestational hypothyroidism of about 21.9%.

Deodhar et al and Surkan et al showed high incidence of hypertension in BOH group as also seen in our study (19.5%).8

2 out of 41 women had history of mid-trimester abortions in previous pregnancy strongly suggestive of cervical incompetence, hence prophylactic cervical encirle (McDonald suture) was done in these patients.

Previous studies by Hughes et al reported an increased incidence of gestational diabetes mellitus while we were unable to confirm such a finding in our study. (14.63%)9

Increase in BMI has led to higher incidence of peripartum complications such as preterm birth, caesarean delivery and GDM, however the mean BMI of our study group was around 23.2±2.07 SD.10

Antiphospholipid syndrome and APLA is now increasingly recognized as being an important cause of BOH leading to early miscarriages and thus emphasizing the need for antibody screening of women with pregnancy loss.11 The prevalence of APLA positivity in women with BOH is 10-46%.12 However, Incidence in our study was about 2.4%.

Further evaluation of neonatal death of unknown cause revealed the association between inborn errors of metabolism such as isovaleric acidemia and Fatty acid oxidation defect accounting to about 4.8% in our study. While Unrecognized metabolic disorders especially, remain a preventable cause of maternal and neonatal mortality and morbidity, recent studies have managed to fill the gap in literature, exploring the unanswered questions on the association between inborn errors of metabolism and pregnancy loss.13

In our study, 4 out of 41 women had malpresentation (9.7%), however only two among them had underlying uterine anomaly (uni-cornuate uterus and arcuate uterus).

About 21.9% women delivered <36 weeks of gestation (n=9) out of which 3 women delivered at 32-33 weeks of gestation. Premature rupture of membranes (PROM), a risk factor for preterm delivery and neonatal infections were noted in 17% of women.
Meconium-stained liquor (MSL) was reported in 31.7% (n=13) of newborns of which 6 newborns required resuscitation. However, the fetal outcome in our study group was found to be good.

In our study, we found that 65% women delivered by caesarean section while 29.2% delivered vaginally and 0.04% by VBAC. Out of the 65% women who underwent caesarean section, 33.3% were planned whereas 66.6% were emergency caesarean sections. Vaginal delivery was accomplished in 29.2% (n=12) of the women, however 2 among the 12 required vacuum assistance due to poor maternal effort.

In this study, only 30 (73.17%) women out of 41 were identified to have possible factors responsible for pregnancy losses. In 8 (19.5%), 7 women had PROM, 1 had APH, both being probable indirect causes for BOH, while the cause of recurrent pregnancy loss was unexplained in 3 (7.3%).

Limitations

Paternal factors which may attribute to the bad obstetric outcome could not be ruled out, since it is a retrospective study.

CONCLUSION

A full work-up can be initiated after two consecutive losses to identify and treat causes that include endocrine causes, APLA, uterine anomalies, balanced translocations etc. Implementation of lifestyle modification should go hand in hand. Inborn errors of metabolism should be considered in the diagnosis of any sick neonate along with common acquired causes to aid parents plan future pregnancy. Newer approaches such as preimplantation genetic diagnosis (PGD) followed by artificial reproductive technique (ART) may be done. In spite of various attempts to diagnose and treat the cause, almost half the cause of BOH remains unexplained. Lot of further studies and research are being conducted to unravel the mystery in these cases. Recent studies have revealed the role of paternally expressed genes in trophoblastic invasion and placental proliferation which may affect the pregnancy in early embryogenesis. Despite these efforts, the male factors contributing to Recurrent pregnancy loss have remained largely unexplored.

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