

Assessment of the Relationship between Recurrent High-risk Pregnancy and Mothers' Previous Experience of Having an Infant Admitted to a Neonatal Intensive Care Unit

Sedigheh Hantoosh Zadeh (MD)¹, Mamak Shariat (MD)², Zahra Farahani (MSc)^{3*}, Padideh Dehghan (MD)⁴, Rodabeh Mansory (MD)⁵, Nasrin Chegini (MD)⁵, Freshteh Amini (BS)⁶

¹ Professor, Department of Perinatology, School of Medicine, Tehran University Medical of Sciences, Tehran, Iran

² Associate Professor, Maternal, Fetal & Neonatal Research Center, Tehran University of Medical Sciences, Tehran, Iran

³ MSc of Physiology, Maternal, Fetal & Neonatal Research Center, Tehran University Medical of Sciences, Tehran, Iran

⁴ Medical Doctor, Breastfeeding Research Center, Tehran University of Medical Sciences, Tehran, Iran

⁵ Medical Doctor, Department of Midwifery, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

⁶ BSc of Midwifery, Department of Midwifery, School of Nursing and Midwifery, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO	ABSTRACT
<p><i>Article type:</i> Original article</p>	<p>Background & aim: High-risk pregnancies increase the risk of Intensive Care Unit (ICU) and Neonatal Intensive Care Unit (NICU) admission in mothers and their newborns. In this study, we aimed to identify the association between the recurrence of high-risk pregnancy and mothers' previous experience of having an infant admitted to NICU.</p> <p>Methods: We performed a cohort, retrospective study to compare subsequent pregnancy outcomes among 232 control subjects and 200 female cases with a previous experience of having a newborn requiring NICU admission due to intrauterine growth retardation, preeclampsia, preterm birth, premature rupture of membranes, and asphyxia. The information about the prevalence of subsequent high-risk pregnancies was gathered via phone calls.</p> <p>Results: As the results indicated, heparin, progesterone, and aspirin were more frequently administered in the case group during subsequent pregnancies, compared to the control group ($P<0.001$). Also, pregnancy-induced hypertension, preeclampsia, preterm labor, and gestational diabetes mellitus were more frequent in the case group, compared to the control group ($P<0.05$).</p> <p>Conclusion: There was a positive correlation between recurrent high-risk pregnancy and previous experience of having a newborn requiring NICU admission. As the results indicated, mothers in the case group were at a higher risk for preeclampsia, preterm labor, and gestational diabetes mellitus, compared to the control group. Therefore, earlier diagnosis, prompt treatment, and prevention should be taken into account by physicians.</p>
<p><i>Article History:</i> Received: 28-Sep-2014 Accepted: 14-Nov-2014</p>	
<p><i>Key words:</i> Diabetes Gestational High-risk Intensive care unit Neonatal</p>	

► Please cite this paper as:

Hantoosh Zadeh S, Shariat M, Farahani Z, Dehghan P, Mansory R, Chegini N, Amini F. Assessment of the Relationship between Recurrent High-risk Pregnancy and Mothers' Previous Experience of Having an Infant Admitted to a Neonatal Intensive Care Unit. Journal of Midwifery and Reproductive Health. 2015; 3(1): 293-297. DOI: 10.22038/jmrh.2015.3585

Introduction

High-risk pregnancy refers to a pregnancy associated with increased risk of neonatal mortality and morbidity. About 10-20% of pregnancies may be terminated or complicated by abortion, stillbirth, fetal malformation, intrauterine growth restriction (IUGR), preterm labor, preeclampsia, and gestational diabetes

mellitus (GDM).

Half of prenatal deaths occur due to high-risk pregnancies (1). Mothers with a poor obstetric history, resulting in neonatal NICU admission, are at a higher risk for future complicated pregnancies. Brahman et al. indicated that women with a prior history of preeclampsia and adverse maternal/prenatal outcomes are prone to the recurrence of these conditions (2). Also,

* Corresponding author: Zahra Farahani, MSc of Physiology, Maternal, Fetal & Neonatal Research Center, Tehran University Medical of Sciences, Tehran, Iran. E-mail: fetuspapyurus@gmail.com

McCowan reported that mothers with a prior history of miscarriage or those with small-for-gestational-age (SGA) infants were at a higher risk of bearing SGA newborns in subsequent pregnancies (3).

Kristensen et al. indicated that preterm delivery may be repeated 5 times or more in subsequent pregnancies (4). A positive history of GDM and type 2 DM can also significantly affect neonatal morbidity and NICU admission. Preterm delivery and NICU admission more than 24 hours are more frequent in mothers with GDM. In fact, NICU admission has been reported in 29% of GDM cases and 40% of type 2 DM pregnancies (5-7). Villar et al. also revealed that most mothers with an IUGR infant had given birth to a low-birth-weight neonate in their previous pregnancies (8).

There is no doubt that early detection of complicated pregnancies may prevent further maternal and neonatal morbidities. Physicians' awareness about the patients' prior medical history and previous pregnancy outcomes is a great help for the management of subsequent pregnancies. This study was performed with the aim to identify the association between the recurrence of high-risk pregnancy and mothers' previous experience of having a newborn admitted to NICU.

Materials & Methods

This retrospective, cohort study was carried out at Vali-Asr Hospital in 2009-2011. The target population consisted of 435 mothers and the participants were divided into 2 groups: 1) the case group with a previous experience of having an infant admitted to NICU due to preeclampsia, GDM, preterm labor, premature rupture of membranes (PROM), and asphyxia, and 2) the control group without such experiences.

Medical records were selected sequentially and mothers' data were recorded in a questionnaire by an expert midwife. Then, the information about the prevalence of subsequent high-risk pregnancies was gathered via phone calls. Three mothers from the case group were excluded due to other concurrent complications, lack of consent, missing data, and lack of access to phone numbers.

Finally, we analyzed the collected data and compared the subsequent pregnancy outcomes

between the case and control groups. For quantitative variables, the frequency was reported as mean \pm SD, and the relationship between variables was assessed by student's t-test. For qualitative variables, frequency was expressed as number/percentage and the relationships between variables were analyzed by Chi-square; odds ratio was calculated when applicable (CI= 95%). SPSS version 15 was used for data analysis. P-value < 0.05 was considered statistically significant (power=80%).

This study was approved by the Medical Ethics Committee and was in accordance with the Declaration of Helsinki. Informed consents were obtained from the participants before entering the study. Patients' data were kept confidential and no intervention was performed in our study. Also, no extra costs were imposed on the participants.

Results

The target population included 232 control mothers and 200 women in the case group. Demographic data and prior history of PROM, cesarean section, pregnancy-induced hypertension (PIH), IUGR, and GDM in the two groups are shown in Table 1. Subsequent complicated

Table 1. Comparison of demographic data in the two groups and previous pregnancy-related complications

Variables	Case group	Control group	P-value
Weight gain (Mean \pm SD)	11.80 \pm 6.127	9.91 \pm 5.401	0.001
Pregnancy interval (Mean \pm SD)	5.47 \pm 3.942	6.72 \pm 4.085	0.001
Gravidity (Mean \pm SD)	3.11 \pm 1.331	2.96 \pm 1.194	0.194
Abortion (Mean \pm SD)	.52 \pm 1.027	43 \pm .865	0.329
Intrauterine fetal death (Mean \pm SD)	.38 \pm .692	.13 \pm .462	0.0001
Cesarean section N (%)	97(56)	70(41)	0.005
Preterm PROM* N (%)	33(16)	0	0.0001
PIH** N (%)	63(21.5)	2 (0.9)	0.0001
GDM*** N (%)	23(11.5)	1 (0.5)	0.0001
IUGR**** N (%)	8(4)	0	0.003

Table 2. Comparison of recent pregnancy outcomes in the two groups

Complications	Case N (%)	Control N (%)	B	SE	P-value	OR	CI=95% (lower band-Upper band)
PIH	42(21)	26(11)	0.350	0.354	.0006	1.817	1.121-2.945
Preeclampsia	49(24.5)	35(15)	0.576	0.324	.015	2.096	1.232-3.565
GDM	47(23.5)	36(16)	0.486	0.254	.031	1.664	1.027-2.697
IUGR	13(5.5)	7(3.5)	-0.493	0.494	.292	0.60	0.23-1.55
Preterm PROM	42(18)	36(18)	-0.256	0.264	.960	0.98	0.60-1.61
Preterm birth	29(12.5)	39(19.5)	0.636	0.279	.049	1.687	1.000-2.847

Table 3. Comparison of drug administration for preventing pregnancy-related complications in the two groups

Drug administration	Case N (%)	Control N (%)	P-value
Progesterone	30(15)	12 (5)	0.0001
Heparin	17 (8.5)	15(6.5)	0.0001
Aspirin	35(17.5)	15(6.5)	0.0001

pregnancies with hypertension, preeclampsia, preterm labor, and GDM were more frequently reported in the case group ($P < 0.05$) (Table 2). Compared to the control group, heparin, progesterone, and aspirin were more frequently administered in the case group during subsequent pregnancies in order to prevent obstetric complications ($P < 0.0001$) (Table 3).

No differences were observed between the two groups in terms of receiving prenatal care in previous and subsequent pregnancies ($P = 0.57$, $P = 0.11$). Overall, 95% and 96% of subjects in the case ($n = 190$) and control ($n = 223$) groups received prenatal care during subsequent pregnancies, respectively. On the other hand, 94.5% ($n = 189$) and 90% ($n = 208$) of subjects in the case and control groups had received prenatal care for their previous pregnancies, respectively. Both groups received supplements during pregnancies.

Discussion

In this prospective investigation, we found that mothers with a previous experience of having a baby hospitalized in NICU had a higher risk of subsequent complicated pregnancies. Physicians should be aware of the associated risk factors in order to manage predictable problems in subsequent pregnancies. This management not only improves health care

quality and safety but also reduces the costs imposed on health care systems.

Based on the obtained results, hypertension and preeclampsia in subsequent pregnancies were more common in the case group, which may be related to the recurrence of thrombophilia or placental dysfunction. Our results were consistent with the findings of Wikstrom and colleagues. They showed that mothers with a prior history of preterm preeclampsia, resulting in stillbirth or SGA birth, more often experienced successive high-risk pregnancies due to abnormal placentation (9).

The consequences of poor placentation in the mother and fetus lead to iatrogenic preterm delivery and neonatal mortality and morbidity. Defects in myometrial spiral artery and reduction in uterine artery blood flow may be involved in the pathophysiology of preeclampsia (10). In accordance with our results, Furuya et al. also indicated the role of genetic maternal predisposing factors in the pathophysiology of abnormal placentation in pregnancy-induced hypertension, which resulted in complications such as IUGR in subsequent pregnancies (11).

In addition, GDM and preterm labor were more common in our case group, compared to the control group. In fact, pregnancies, complicated by GDM, increase the rate of IUGR birth and NICU admission (6). Moreover, previous GDM-complicated pregnancies increase the risk of subsequent GDM (12, 13); the risk of recurrent GDM in subsequent pregnancies is reported in up to 70% of cases (14).

In the present study, preterm delivery, which was more frequent in subsequent pregnancies of the case group, might have occurred due to untreated genitourinary tract infections. Our results were compatible with previous reports that showed that genitourinary tract infection increases the risk of preterm labor in subsequent

pregnancies. In fact, mothers with susceptibility to genital infections (or chronic genital infections) could be at a greater risk of preterm labor (4, 15).

In this study, mothers in the case group received more progesterone, heparin, and aspirin, compared to the control group. In fact, progesterone level could be a marker of placental function. It seems that placental dysfunction results in preterm labor, and IUGR and PROM in previous pregnancies might re-occur in subsequent pregnancies, along with other clinical complications, which lead to abortion or preterm labor pain. However, progesterone administration may decline the risk of such problems.

Our findings were consistent with those obtained by Krymko and colleagues. They showed that in 140 mothers with a prior history of preterm labor and neonatal NICU admission, the rates of abortion and preterm delivery in subsequent pregnancies were higher than those reported in mothers without such experiences. They also pointed the role of progesterone administration in obtaining better pregnancy outcomes (4).

Besides, the effect of thrombophilia during pregnancy (e.g., resulting in severe preeclampsia and placental abruption) may be relieved by aspirin and heparin administration. Silver confirmed the role of heparin in decreasing neonatal mortality risk. Bramham also indicated that heparin and aspirin administration in mothers with a positive history of preeclampsia and neonatal NICU admission decreased the risk of preeclampsia in subsequent pregnancies (2).

We also found that the majority of mothers in both groups had received prenatal care. Therefore, safe health care programs should be implemented for mothers during the prenatal period in our country, particularly in Tehran.

Unfortunately, in the current study, we only evaluated some associated complications. Therefore, other problems such as oligo- or polyhydramnios and urinary tract infections should be assessed in future studies. We also did not evaluate the role of some demographic factors such as maternal age, gestational age, and parity, which might have influenced the findings.

Conclusion

There was a positive correlation between recurrent high-risk pregnancy and previous

experience of having an infant admitted to NICU. In fact, mothers with such experiences were at a higher risk. Therefore, prevention, early diagnosis, and prompt treatment should be considered by physicians.

Conflicts of interest

Authors declared no conflicts of interest.

References

1. Kilpatrick S, Garite T. High-Risk Pregnancy Care, Research, and Education for Over 35 Years. Society of Maternal Fetal medicine and the SMFM Foundation. 2011; 1:32.
2. Bramham K, Briley A, Seed P, Poston L, Shennan AH, Chappell L. Adverse maternal and perinatal outcomes in women with previous preeclampsia: a prospective study. *American Journal of Obstetrics & Gynecology* 2011; 204(6): 512-e1.
3. McCowan L, Horgan R. Risk factors for small for gestational age infants. *Best Practice & Research Clinical Obstetrics and Gynaecology*. 2009; 23: 779-793.
4. Krymko H, Bashiri A, Smolin A, Sheiner E, Bar-David J, Shoham-Vardi I, et al. Risk factors for recurrent preterm delivery. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2004; 113(2): 160-163.
5. Watson D, Rowan J, Neale L, Battin M. Admission to NICU following pregnancies complicated by gestational or type 2 diabetes. *Australian and New Zealand Journal of Obstetrics and Gynaecology*. 2003; 43(6):429-432.
6. Capula C, Chiefari E, Vero A, Arcidiacono B, Iritano S, Puccio L, et al. Gestational Diabetes Mellitus: Screening and Outcomes in Southern Italian Pregnant Women. *ISRN Endocrinology*. 2013; 2013: 387495.
7. Tomić V, Petrović O, Crnčević Orlić Ž, Mandić V. Gestational diabetes and pregnancy outcome - do we have right diagnostic criteria? *The Journal of Maternal-Fetal & Neonatal Medicine*. 2013; 26(9): 854-859.
8. Villar J, Carroli G, Wojdyla D, Abalos E, Giordano D, Ba'aqeel H, et al. Preeclampsia, gestational hypertension and intrauterine growth restriction, related or independent conditions? *American Journal of Obstetrics and Gynecology*. 2006; 194(4): 921-031.
9. Wikström A, Stephansson O, Cnattingius S. Previous preeclampsia and risks of adverse outcomes in subsequent non preeclamptic pregnancies. *American Journal of Obstetrics & Gynecology*. 2011; 204(2):148e1-e6.
10. Spencer N, Carr DJ, David AL. Treatment of poor placentation and the prevention of associated adverse outcomes - what does the future hold?

- Prenatal Diagnosis. 2014; 1-30.
11. Furuya M, Ishida J, Aoki I, Fukamizu A. Pathophysiology of placentation abnormalities in pregnancy-induced hypertension. *Vascular Health and Risk Management*. 2008; 4(6):1301-1313.
 12. Getahun D, Fassett MJ, Jacobsen SJ. Gestational diabetes: risk of recurrence in subsequent pregnancies. *American Journal of Obstetrics and Gynecology*. 2010; 203(5):467-e1.
 13. Kim C, Berger DK, Chamany S. Recurrence of gestational diabetes mellitus: a systematic review. *Diabetes Care*. 2007; 30(5):1314-1319.
 14. Bottalico JN. Recurrent Gestational Diabetes: Risk Factors, Diagnosis, Management, and Implications. *Seminars in Perinatology*. 2007; 31(3): 176–184.
 15. Buchmayer S, Sparen P, Cattingius S. Previous pregnancy loss; risks related to severity of preterm delivery. *American Journal of Obstetrics and Gynecology*. 2004;191(4):1225-1231.