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Factors Associated with Re-Admission and Mortality Rate in Low Birth Weight and Very Low Birth Weight Infant

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Abstract--- *Molecular evaluation of thrombophilia panel is one of the practical evaluations in recurrent miscarriage. Clotting and disruption in uterine placental circulatory system result in miscarriage, intrauterine growth retardation, and preeclampsia. In Iranian population, it is possible to identify new genetic disorders due to the high rate of kinship marriages and different gene storage. The present study was conducted with the aim of investigating the new mutations in the thrombophilia panel related to recurrent miscarriage. This is a case-control study. The research population consisted of the patients with recurrent miscarriage referred to Kamali Hospital in Karaj. A total of 100 women with recurrent miscarriage (at least 2 miscarriages) and 100 women with at least one successful pregnancy (more than 2 miscarriages) were selected through convenience sampling method. DNA amplification was performed by PCR. Mutation analysis was performed using chromes software, and then, it was analyzed by SPSS software. In the case group, 10 patients (10%) with PAI-1 homozygous gene (G / 4G4) and in the control group, 2 patients (2%) were PAI-1 homozygous gene (G / 4G4) were identified, and this difference was statistically significant. Moreover, 20 patients (20%) in the case group and 3 patients (3%) in the control group were positive in terms of MTHFR gene polymorphism, which the difference between two groups being statistically significant. The results of this study revealed that the presence of PAI-1 homozygous gene and MTHFR polymorphism gene increases the risk of recurrent miscarriage. Thus, thrombophilia panel screening is recommended in patients with recurrent miscarriage.*

Keywords--- *Gene Mutation, Thrombophilia Panel, Recurrent Miscarriage, PAI-1 Homozygous Gene, MTHFR Polymorphism.*

I. INTRODUCTION

Low birth weight (LBW) is a common problem in pediatric medicine, especially in developing countries, and is a strong predictor of immediate and future outcomes. The lower is the newborn's weight; the higher is the risk of mortality and long-term complications [1]. Moreover, many LBW infants develop neurological developmental deficits as well as learning and cognitive problems at 1-8 years of age [2, 3].

LBW is defined as a birth weight of less than 2500 g. A birth weight below 1500 and 1000 g is considered very low birth weight (VLBL) and extremely low birth weight (ELBW), respectively. This medical condition may be caused by several reasons like genetic, nutritional, and obstetric factors, premature delivery, and inappropriate fetal growth in the uterus resulting in an infant that is small for gestational age [4-7].

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The global prevalence of LBW is 15.5% with 96% of the cases occurring in developing countries, which could be due the socio-economic conditions and lifestyle of the mothers [5, 6]. Available reports suggest that half of the mortality in infants is due to LBW, birth asphyxia, respiratory problems, congenital malformations, and infection [7-9]. LBW infants are more prone to cerebral problems, impaired neurological development, respiratory diseases, and sudden infant death [10, 11]. Other consequences associated with LBW include the high costs of care that imposes heavy financial burdens on families, because these infants may frequently need hospitalization and special healthcare services. It is estimated the cost of care of these infants is 6 times higher than their normal weight counterparts [12-15].

Therefore, considering the high costs of care and the increased risk of hospital acquired infections, physical and mental problems of parents regarding adapting the parental role, there is an increased tendency towards early discharge of hospitalized infants, which may be associated with different outcomes [16, 17]. This tendency started years ago and has received an increasing attention ever since [18]. According to the WHO statistics, the mean discharge time has decreased by two days. Other advantages of early discharge are de medicalization of the postnatal care process and developing a strong parent-infant relationship [19-22]. Discharge criteria include appropriate breathing and sucking abilities and a stable temperature. However, the discharge weight is usually below 2000 g in premature infants. A weight of 1700-1800 g is a good criterion for discharge in European countries [23]. In countries like Iran, due to the limited capacity of hospitalization and more rapid discharge of LBW infants, they are discharged at 1500 g. considering the importance of this issue, this study was conducted to evaluate the mortality and re-hospitalization rates of these infants with an emphasis on discharge weight [24-26].

II. MATERIALS AND METHODS

Study Type

This cohort study was conducted in 96 infants with a discharge weight of below 1500 g and 96 infants with a discharge weight of 1500-2500 g in the intensive care units of Imam Ali and Kamali hospitals in Alborz province and met the inclusion criteria entered the study. The inclusion criteria were a weight of less than 2500 g and being ready for discharge. These infants were categorized to two groups of VLBW (discharge weight below 1500 g) and LBW (discharge weight between 1500-2500 g). The samples were assigned to two groups of below 1500 g (96 newborns) and above 1500 g (96 newborns).

These infants were followed up for mortality, risk factors, and re-hospitalization for up to three months after discharge. For this purpose, the researcher attended the hospitals every week and identified the infants that could be discharged. Then, their demographics were recorded in a questionnaire, including the gestational age, infant sex, family history, birth rank, and birth weight. Contact data were obtained from all parents to facilitate follow-up. Then, infant outcomes (mortality and re-hospitalization rates) were evaluated in both groups for up to three months after discharge and the results were compared at the third month post discharge.

Ethical Considerations

This study was approved by the Ethics Committee of Alborz University of Medical Sciences. The study objectives were explained to the parents of all hospitalized newborns and informed consent was obtained from them.

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III. RESULTS

One hundred and five infants (54.7%) were boys and 87 (45.3%) were girls. One hundred and twelve newborns (58.5%) were term infants, 108 (56.3%) were first-birth rank, and 41 (21.4%) had a positive family history of LBW.

According to (Table 1), the mortality rate of VLBW infants was higher compared to LBW infants (17.71% versus 7.29%, p=0.24). The re-hospitalization rate was also higher for VLBW infants (39.58% versus 23.96%, p=0.015).

Table 1: Comparison of Mortality Rate According Related Factor in Two Groups

Related factor		(***VLBW***)	***(LBW)***	***p-value***
Gender	girl	3(42.9%)	9(52.9%)	0.39*
	boy	4(57.1%)	8(47.1%)	
Gestational age	preterm	5(71.4%)	13(76.5%)	0.03*
	term	2(11.8%)	2(28.6%)	
	Post-term	2(11.8%)	0	
Birth rank	1	8(47.1%)	1(14.3%)	0.599*
	>1	9**(**52.9**%)**	6**(**85.8**. %)**	
Low birth weight history		3(17.6%)	3(42.9%)	0.4*
Mortality rate		17(17.71%)	7(7.29%)	0.02*

*chi-square

(Table 1) presents the effect of other risk factors or the infant mortality rate. Moreover, the re-hospitalization rate had no significant correlation with sex (p=0.187) and family history (p=0.424) while its correlation with gestational age (p=0.079) and birth rank (p=0.011) was significant (Table 2).

Table 2: Comparison of Re-hospitalized Rate According Related Factor in Two Groups

Related factor		***(VLBW)***	***(LBW)***	***p-value***
Gender	girl	18(47.4%)	11(47.8%)	0.187*
	boy	20(52.6%)	12(52.2%)	
Gestational age	preterm	23(60.5%)	12(52.2%)	0.079*
	term	6(15.8%)	10(43.5%)	
	Post-term	9(23.7%)	1(4.3%)	
Birth rank	1	21(55.3%)	7(30.4%)	0. 011*
	2	6(15.8%)	7(30.4%)	
	3and higher	11(28.9%)	9(39.2%)	
Low birth weight history		3(17.6%)	3(42.9%)	0.4*
Re-hospitalized rate		38(39.58%)	38(39.58%)	1*

*chi- square

The Receiver Operating Characteristics (ROC) curve analysis was applied to calculate the best discharge weight. According to the results, for LBW infants, the optimal discharge weight was 1620 g for mortality control with a sensitivity of 53.5% and a specificity of 77% (AUC=0.739, CI: 0.64-0.838) (Figure 1) and 1775 g for re-hospitalization control with a sensitivity of 48.2% and specificity of 83.3% (Figure 2).

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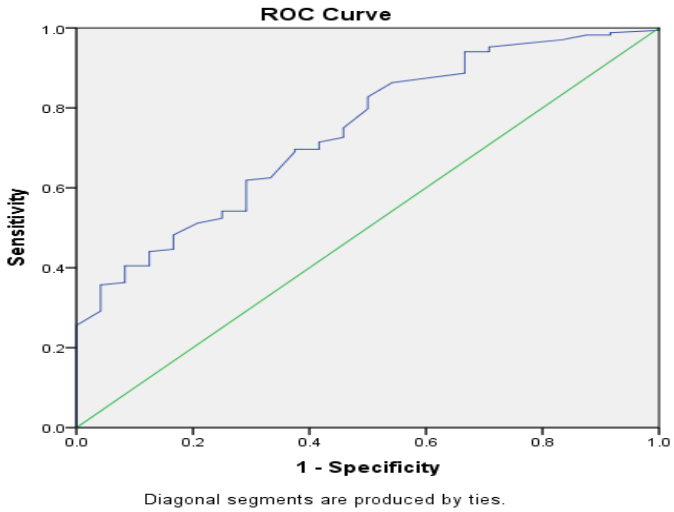

Figure 1: ROC Curve of Optimal Discharge Weight for Mortality Control

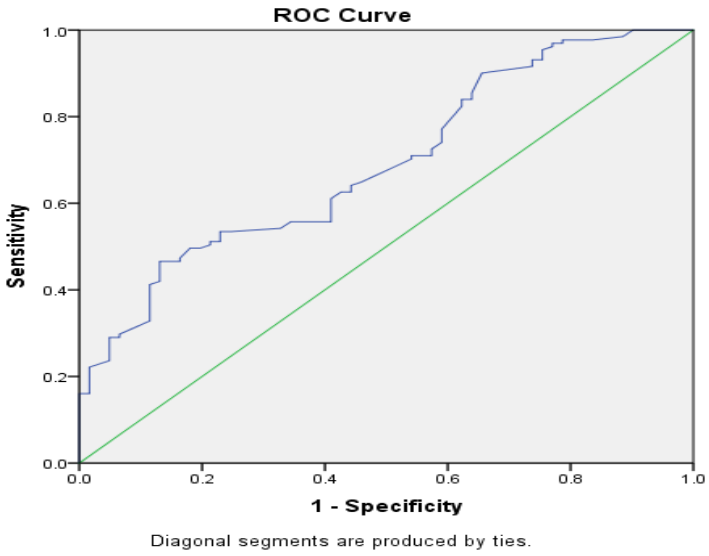

Figure 2: ROC Curve of Optimal Discharge Weight for Re-hospitalization Control

IV. DISCUSSION

In Iran, considering hospitalization limitations, LBW infants are discharged at 1500 g. The results of this study showed that due to the higher mortality and re-hospitalization rate of VLBW infants, discharge at 1500 g is not rational. The results of the current study were consistent with a study conducted by Ballot et al in 2016 that found a significant difference in the survival rate between LBW (92.1%) and VLBW infants (69.1%) (1). Many other studies also found that LBW and prematurity were predictors of infant mortality [27-29]. In the present study, being preterm correlated with infant mortality in both groups. Babaei et al [12, 30] reported a decrease in the last child's weight with an increase in the number of children; therefore, the infant mortality rate increased in relation to the birth rank. In the present study, birth rank had no significant effect on infant mortality while it increased the re-hospitalization rate [31, 32]. The reason for the increased re-hospitalization rate may be that parents are more sensitive to the

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symptoms of their first children, which could be due to lack of adequate experience and knowledge [33-36].

In a study by Dashti et al, re-hospitalization rate had a significant correlation with infant weight and gestational age; however, no significant relationship was found between sex and re-hospitalization rate [37]. The authors attributed these findings to lack of similar criteria for re-hospitalization; however, in the present study, the re-hospitalization criteria were similar in the two hospitals where the study was conducted [38, 39]. In the study by Dashti et al, about 40% of the infants were re-hospitalized within one month after discharge. Although this duration was 3 months in the present study, it is still a short period and can affect the outcomes, because the risk of re-hospitalization and mortality is still high until one year of age [40-43].

Glass et al found that the infant's sex was an important risk factor for the mortality rate, and reported that female infants had a better condition compared to male infants [44, 45].

Stichtenoth et al studied the increased risk of obstructive bronchitis in 1967 VLBW infants and found that male sex and birth rank were risk factors for this diseases and re-hospitalization [46, 47]. We found no relationship between the mortality and re-hospitalization rates and sex; however, more girls were hospitalized in the case group and more boys were hospitalized in the control group, and more girls were hospitalized in general. Nonetheless, the mortality and re-hospitalization rates were higher in VLBW infants in our study compared to other studies [48].

Although there is no general agreement on the appropriate discharge weight, Underwood et al found that weights below 1000 g were not recommended because they were associated with a re-hospitalization rate of 49% within 18 months of discharge [49]. According to the results of ROC curve analysis, weights above 1500 g, i.e. 1600-1800 g, are recommended to prevent infant mortality and re-hospitalization. Birth weight has a direct effect on the infant outcomes and is one of the priorities in neonatology. Other determinants of neonatal outcomes should be studied as well [50]. In a study showed the effects of short-term hospitalization of LBW infants. The authors believed that long-term hospitalization of LBW and VLBW infants exposed them to medical and mental consequence, and also results of study showed that a program based on education and personal support for the family to deliver healthcare services to the LBW infant was cost-effective and was associated with positive results [51]. Some other studies have also emphasized the role of training and support for the parents of LBW infants and their importance in neonate outcomes [52]. Therefore, more studies are required to evaluate training and supportive programs for delivering health services to LBW infants and their effects on the mortality rate and pediatric outcomes.

V. STUDY LIMITATIONS

In the hospitalized infants, there may be underlying conditions that are related to the infant's weight and therefore to the discharge weight and therefore complete matching was not possible. In addition, the follow-up time was limited to three months and studies with longer follow-ups, for at least 1 year, are recommended.

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