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Araştırma Makalesi/Research Article

Analysis of Late Preterm Births: Are There any Differences Among Etiologic Subgroups in Terms of Neonatal Outcomes?*

Geç Preterm Doğumların Analizi: Yenidoğan Sonuçları Açısından Etyolojik Altgruplar Arasında Farklılıklar Var mı?

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Aim: To evaluate the neonatal outcomes of late preterm births (LBPs) according to etiologic subgroups and to evaluate if there is any association between birth indication and neonatal morbidity in late preterm births.

Material and Method: Singleton pregnancies delivered between $34^{0/7}$–$36^{6/7}$ weeks (34 weeks and 36 weeks 6 days of pregnancy) during a 3-year period at a tertiary care university hospital were studied. Indications for delivery were classified as either spontaneous or inducted with medical indication. Inducted with medical indication LPBs were categorized as either evidence-based (EB) (eg. severe preeclampsia/eclampsia, HELLP syndrome, abnormal fetal test, placenta previa or placental abruption with vaginal bleeding, and unstable/worsening medical conditions) or non evidence-based (NEB) (mild preeclampsia, intrauterine growth restriction with normal fetal test, oligohydramnios with normal fetal test, and mild/stable medical conditions).

Results: There were 179 LPBs; 118 (66%) spontaneous and 61 (34%) inducted with medical indication. 76% of spontaneous LPBs were preterm labor with intact membranes and 24% were premature preterm rupture of membranes. 52% of inducted with medical indication LPBs were EB and 48% were NEB. The frequencies of neonatal intensive care unit (NICU) admissions were similar between the groups. The only significant difference among indications was infection rates in NICU (7% in the spontaneous *vs.* 33% in the inducted with medical indication group; *P*<0.001). Women with NEB deliveries were significantly older (31,6 vs. 27,9; *P*=0,010). NICU admission rates were significantly higher in the EB group, when compared to the NEB group (40% vs. 7%; *P*=,003)

Conclusion: Inducted with medical indication LPBs consist of almost one third of all LPBs and accompany high rates of neonatal infections. Also among inducted with medical indication LPBs, neonatal morbidity is higher in cases with EB indications, when compared with the NEB subgroup.

Key Words: ***Late Preterm Births, Iatrogenic, Spontaneous***

Amaç: Geç preterm doğumların etyolojik subgruplara göre yenidoğan sonuçlarının analizi ve geç preterm doğumlarda doğum endikasyonu ve yenidoğan morbiditesi arasında ilişki olup olmadığının değerlendirilmesi.

Gereç ve Yöntem: Bir üniversite hastanesinde meydana gelen $34^{0/7}$–$36^{6/7}$ hafta arası (34 hafta ve 36 hafta 6 gün gebelikler) doğumlar 3 yıllık bir süre için incelendi. Doğum endikasyonları spontan ve tıbbi endikasyonla indüklenen doğumlar olarak sınıflandırıldı. Tıbbi endikasyonla indüklenen geç preterm doğumlar kanıta dayalı olan (ciddi preeklampsi, eklampsi, HELLP Sendromu, anormal fetal test, plasenta previa, kanamayla birlikte plasenta dekolmanı, stabil olmayan kötüye giden tıbbi durumlar) ve kanıta dayalı olmayan (hafif preeklampsi, normal fetal testlere eşlik eden intrauterin gelişme geriliği, normal fetal testlere eşlik eden oligohidramnioz, hafif stabil tıbbi durumlar) endikasyonlar olarak değerlendirildi.

Bulgular: Toplam geç preterm doğum sayısı 179 olarak bulundu. 118'i spontan, 61'i tıbbi endikasyonla indüklenen doğumlardı. Spontan geç preterm doğumların %76'sında membranların intakt, %24'ünde ise rüptüre olduğu bulundu. Tıbbi endikasyonla indüklenen geç preterm doğumların %52'si kanıta dayalı endikasyon ile doğurtulurken, %48'i ise kanıta dayalı olmayan endikasyonlar ile doğurtuldu. Yenidoğan yoğun bakım ihtiyacı her 2 grupta da benzerdi. Yenidoğan yoğun bakıma yatış endikasyonları arasında tek anlamlı fark enfeksiyon oranlarında izlendi (%7 spontan grup, %33 tıbbi endikasyonla indüklenen grup p<0,001). Kanıta Dayalı Olmayan doğum grubundaki kadınlar, Kanıta Dayalı grubundaki kadınlara gore anlamlı olarak daha yaşlı olarak hesaplandı (31.6 vs. 27.9; p=0,01) . Yenidoğan yoğun bakım yatış oranları kanıta dayalı olan grupta anlamlı olarak daha yüksekti. (40% vs. 7% p=0.003)

Sonuç: tıbbi endikasyonla indüklenen geç preterm doğumlar olguların 1/3 ünü oluşturmakta ve yüksek neonatal enfeksiyon oranına sahip olarak izlendi. Aynı şekilde neonatal morbiditenin de kanıta dayalı grupta daha yüksek olduğu görülmüştür.

Anahtar Sözcükler: ***Geç Preterm Doğum, İyatrojenik, Spontan***

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Preterm birth is delivery before 37th gestational week and late preterm birth (LPB) is defined as delivery between $34^{0/7}$ and $36^{6/7}$ weeks of gestation (1). Late preterm births constitute a significant portion of preterm births and the incidence in the United States has been reported as 8.1% (2,3). Although many of them are not considered a high-risk category, late

preterm new-borns have a significant burden to society due to increased rates of short and long-term morbidity and mortality (4). Spontaneous preterm birth and premature rupture of membranes are the most common reasons of LPBs (5). However, a considerable amount of them are inducted births (5). Inducted with medical indication LPBs are categorized as either evidence-based (EB) (eg. severe preeclampsia/ eclampsia, HELLP syndrome {hemolysis, elevated liver enzyme levels, and low platelet levels}, abnormal fetal testing, placenta previa or abruptio placenta with vaginal bleeding, and unstable/worsening medical conditions) or non evidence-based (NEB) (mild preeclampsia, intrauterine growth restriction with normal fetal testing, oligohydramnios with normal fetal testing, and mild/stable medical conditions) (6).

Late preterm births are associated with increased respiratory distress syndrome, transient tachypnea of newborn, and requirement for ventilatory support as well as intraventricular hemorrhage, necrotizing enterocolitis, sepsis, hyperbilirubinemia and feeding difficulties. Not only morbidity is higher in these cases, but also late preterm newborns were found to be under increased risk for mortality compared to their term counterparts (3). Therefore, substantial morbidity and mortality associated with LPBs necessitate a better understanding of this entity and identification of risk factors. Thereby, developing more effective management modalities can be feasible.

The aim of the present study was to evaluate the neonatal outcomes of late preterm births according to etiologic subgroups and to evaluate if there is any association with birth indication and neonatal morbidity in late preterm births.

Material and methods

This retrospective study was conducted in a university based tertiary care hospital in accordance with the principles of the Declaration of Helsinki and approved by the Institutional Review Board of university. Records of all singleton pregnancies delivered between $34^{0/7}$ and $36^{6/7}$ gestational weeks between January 2011 and December 2013 in the department of obstetrics and gynecology were reviewed. Indications for delivery were classified as either spontaneous or inducted with medical indication as described in the literature. Inducted with medical indication LPBs were categorized as either EB (eg, severe preeclampsia/eclampsia, HELLP syndrome, abnormal fetal testing, placenta previa or abruptio placenta with vaginal bleeding, and unstable/ worsening medical conditions) or NEB (mild preeclampsia, intrauterine growth restriction with normal fetal testing, oligohydramnios with normal fetal testing, and mild/stable medical conditions) (6).

Data were analyzed using the Statistical Package for Social Sciences 20.0 for Windows (*SPSS Inc., Chicago, IL*). Parametric tests (Independent-samples t-test and posthoc Tukey test) were applied to data of normal distribution and non-parametric tests (Mann–Whiney U-test and Kruskal-Wallis Test) were used for data of questionably normal distribution. Continuous data were presented as either mean±standard deviation or median-interquartile range (minimum-maximum). All differences associated with a chance probability of 0.05 or less were considered statistically significant.

Results

There were 179 late preterm births, of which 118 (66%) spontaneous and 61 (34%) inducted with medical indication. Seventy six percent of spontaneous LPBs were preterm labor with intact membranes and 24% were premature preterm rupture of membranes. Of inducted with medical indication LPBs, 52% had EB indications and 48% occurred in conjunction with NEB indications. The frequencies of neonatal intensive care unit (NICU) admission were same (24.5%) in both groups. The only significant difference among indications was infection rates in NICU (7% in the spontaneous *vs.* 33% in the inducted with medical indication group; $P<0.001$). Also, admission rates for NICU were remarkably higher in the EB group compared to the NEB group (40% *vs.* 7%, respectively; p=0.003).

Discussion

The aim of the current study was to analyse the neonatal outcomes of LPBs with spontaneous and medical indications. Our results indicated that infection rates were higher in iatrogenic LPBs and admission for NICU was higher in the LPBs occurring due to inducted with evidence based medical indications.

In spite of the recent decline in rates of LPBs, incidence and subsequent consequences still remain a substantial concern. It has been postulated that infants with LPB are under risk for suboptimal long-term outcomes, therefore timely assessment and long-term follow-up are essential. Identification of individuals under risk and providing educational facilities on these topics is crucial in alleviation of the burdens due to LPBs (7).

For LPBs, instability of temperature and respiratory distress syndrome may be detected during perinatal hospitalization or conditions like hyperbilirubinemia and feeding difficulties can necessitate readmission (7). Hence, motivation and efforts are increased to lower the frequency of LPBs and to achieve more acceptable rates of morbidity and mortality.

The indication for intensive care unit stay for the LP newborn is determined with respect to the clinical risk factors or disease. Moreover, factors that affect the decision to admit the LP newborn to a NICU include the level of care facilities available, preferences of the provider and practice of the institution according to gestational age or birth weight thresholds (8,9).

However, there is lack of data for reduction of LPB rates in the current evidence based knowledge. No bulletins or committee reports exist on the

steps to be taken and multiple complex causes underlying LPBs make the situation more challenging. Complexity and heterogeneity of underlying causes, establishing a simple preventive strategy is impossible. Hopefully, reports indicate that despite the fact that rates of preterm birth and LPBs are increased, perinatal mortality rate is decreased for LPBs (10).

Intensive care requirements of late preterm infants are reported higher than term infants (11). A study by Raju et al. (12) showed a NICU admission rate of 51% in LP infants. In our study, rate of need for NICU was found to be 24.5%. In this aspect, there was no difference between spontaneous and inducted with medical indication groups.

Owing to the immature immune system and defense mechanisms in preterm infants, they are more vulnerable to infections. Infection rate in late preterm infants has been reported as high as 15% in the literature (13). In our study, infection rates were 7% in the spontaneous and 33% in the iatrogenic groups. Neonatal infection rate in inducted with medical indication group seems to be higher than that reported in the literature. Gyamfi-Bannerman et al. (4) reported that of the 2693 late preterm deliveries, 32.3% (872/2693) were iatrogenic; 56.7% were delivered for NEB indications. Neonates in the EB group were more likely to be admitted to the NICU (56.0% *vs.* 31.0%, $p<0.001$). In our study NICU admission rates were significantly higher in the EB group, too. It is noteworthy that EB indications are more likely to constitute risk factors for NICU admission in our series. In this retrospective study, we found that 48% and 52% of all late preterm births occurred due to NEB and EB indications, respectively. Our results demonstrated that the modes of delivery were not different between the groups. In recent literature, Morais et al. (14) have reported that delivery indications of 524 late preterm births due to NEB and EB causes were 25% and 75%, respectively.

Main limitations of this study are retrospective design and relatively small sample size. Differences in participant characteristics, roles of confounding factors such as environment, metabolism and ethnicity, definition of terms such as 'evidence based' and 'non-evidence based' and restrictions attributed to methodology must be remembered during interpretation of our results.

To conclude, findings of the present study imply that iatrogenic LPBs comprise approximately one third of all LPBs and are accompanied with high rates of neonatal infection. Among inducted with medical indication LPBs, neonatal morbidity is higher in cases with EB indications compared to patients with NEB indications.

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