



## Original Article



## Outcome of Low Molecular Weight Heparin Use in Pregnant Women with Oligohydramnios at A Tertiary Care Hospital

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## ARTICLE INFO

**Keywords:**

Oligohydramnios, Low Molecular Weight Heparin, Outcomes, Maternal Risks

**How to Cite:**Tabassum, S., Tarin, A. U., Suman, F., Nawaz, N., Rao, S. A., & Mukhtar, H. (2025). Outcome of Low Molecular Weight Heparin Use in Pregnant Women with Oligohydramnios at A Tertiary Care Hospital: Heparin Use in Pregnant Women with Oligohydramnios. *Pakistan Journal of Health Sciences*, 6(3), 48-52. <https://doi.org/10.54393/pjhs.v6i3.2832>**\*Corresponding Author:**Shagufta Tabassum  
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## ABSTRACT

Oligohydramnios refers to an antenatal condition in which the amniotic fluid volume is abnormally low and has poor fetal consequences. This research strives to elaborate on the convoluted connections between oligohydramnios and the associated maternal and fetal risks.

**Objectives:** To find out the frequency of pregnancy outcomes in pregnant women with oligohydramnios using low molecular weight heparin (LMWH). **Methods:** The prospective cohort study was conducted at the Obstetrics Department of Nishtar Hospital, Pakistan from November 2024 to January 2025. One hundred and twenty-two women fulfilling the inclusion criteria were included. Patients were given 40 mg LMWH subcutaneously once a day. The patients were followed till delivery to determine outcomes including live birth, preterm delivery, weight at birth, admission to the Neonatal Intensive Care Unit (NICU) and pre-eclampsia. SPSS version 26.0 was employed to analyze the data. **Results:** Out of 122 participants, 120 (98.4%) resulted in live births while 2 (1.6%) were intra-uterine deaths. Among all births, 21 (17.2%) were delivered preterm while 101 (82.8%) were delivered at term. 108 (88.5) weighed >2.5 kg. Among 120 live births, 23 (19.2%) were admitted to the NICU for observation or treatment. **Conclusions:** It was concluded that the study results support the use of LMWH in oligohydramnios as a proportion of adverse perinatal outcomes was low in our study. LMWH was found to be efficacious, authentic and safe in oligohydramnios to achieve desired clinical outcomes and decrease the burden of associated morbidities and mortalities in the targeted population.

## INTRODUCTION

Amniotic fluid is a water-like substance surrounding the developing fetus. It is present in the amniotic sac which starts forming about 12 days' post-conception. Its composition includes water, nutrients, enzymes, hormones and antibodies [1]. The amniotic fluid serves many functions for the growing fetus. It acts as a cushion and saves the fetus from any injury and umbilical cord compression. It keeps the fetus at a constant temperature and allows it to move around in the womb. It also helps the development of bones, muscles and other organs along with providing nutrients, hormones and antibodies to the growing fetus [2]. The amniotic fluid equilibrium is sustained by the virtue of balance of production (lung fluid and urine) and resorption (swallowing and intra-membranous flow). The amount of amniotic fluid increases

exponentially with the development of the fetus, reaches its peak around the gestational age of 34 weeks and starts to decline thereafter [3]. The normal amount of amniotic fluid is a reassurance of normal function of the placenta and is considered the most important among fetal well-being tests [4]. The reduced amount of amniotic fluid may be an indicator of an underlying pathology including placental insufficiency, congenital anomaly or ruptured membranes. Oligohydramnios is also a frequent finding in a hypertensive woman with intrauterine growth restriction, especially in cases of pre-eclampsia [5]. The abnormal amount of amniotic fluid can interfere with the development and growth of the fetus. The decrease in amniotic fluid volume increases the incidence of preterm delivery, low birth weight and perinatal mortality [6]. The



frequency of major congenital abnormalities, low birth weight and intra-uterine growth restriction also increases exponentially with decreasing amniotic fluid volumes<sup>5</sup>. Oligohydramnios has also a strong association with pre-eclampsia. The ultrasound is the best practical method to assess amniotic fluid volume. There are various formulas for amniotic fluid volume calculation. The preferred method is amniotic fluid index (AFI), though some use a single deepest pocket to assess liquor volume. To calculate AFI, the uterus is divided into four quadrants. The largest fluid pocket free of umbilical cord or fetal parts in each quadrant is considered and their anteroposterior diameters are summed up. The AFI in the range of 7 to 25 cm is appraised as normal. The term oligohydramnios is used when AFI is <5cm [7]. Worldwide, oligohydramnios is observed in 1-5% of antenatal patients [8]. In Pakistan, oligohydramnios has been estimated to be observed in 3% of pregnancies [9]. Traditionally, aspirin has been used along with hydration to improve amniotic fluid volume. However, the prophylactic use of heparin has proven very beneficial in conditions like recurrent miscarriages, anti-phospholipid syndrome and thrombophilia as regards perinatal outcomes [10]. It has also been used in cases of oligohydramnios with promising results regarding live birth, birth weight and maturity of fetus [11]. LMWH is now appreciated as superior to unfractionated heparin as the chances of allergic reactions, hemorrhagic disorders, thrombocytopenia, and osteoporosis are less likely with its use [12]. Also, no teratogenic side effects have been attributed to its use. LMWH in oligohydramnios acts by enhancing anti-thrombin activity and inhibiting certain coagulation factors, particularly factor Xa. It thus reduces the risk of blood clots and the resultant increased placental blood flow improves oxygen and nutrient delivery to the fetus. The enhanced placental blood flow also maintains normal fetal kidney blood supply resulting in normal fetal urine production and improvement of amniotic fluid volume. Very few local studies have been conducted to evaluate the role of LMWH in oligohydramnios and almost all of them have compared Aspirin and LMWH in oligohydramnios. None of them have evaluated the role of LMWH in addition to standard Aspirin treatment. The study results produce a beneficial database of the local population as we commonly observe pregnant ladies with low amniotic fluid index in our daily routine. The results help clinicians anticipate such adverse perinatal outcomes for timely diagnosis and proper management to reduce perinatal morbidity and mortality. If proven effective, LMWH could provide a targeted therapeutic option, improving pregnancy outcomes in patients with oligohydramnios.

This study aims to determine the frequency of pregnancy outcomes in antenatal patients having oligohydramnios with the use of low molecular weight heparin.

## METHODS

A prospective cohort study was conducted after ethical review Board of Nishtar Medical University granted ethical clearance vide reference letter number 18981/NMU. The study spanned from November 2024 to January 2025. WHO calculator was used to calculate the sample size by the formula:  $n = z^2pq / d^2$ . Where  $z=1.96$ ,  $p=8.69\%$  [7] (Frequency of pre-eclampsia with low AFI),  $q=100-p$  and  $d=5\%$ . This sample size was 122 pregnant ladies with oligohydramnios. The pregnant ladies having singleton pregnancy with AFI <5 cm at or after 28 weeks were included. Those having fetal anomalies or diabetes mellitus were not included. Eligible patients were enrolled using a purposive sampling technique, ensuring that each participant received a comprehensive explanation of the study's procedures and written informed consent was ensured from each of them. They were also ensured about the fact that there was no risk involved to the patient while participating in this study. Confidentiality protocols were strictly observed for both medical and non-medical information. After registration, ultrasonography of the participants was carried out. The patients with low AFI (<5 cm) were recruited for pregnancy outcomes till delivery. Standard treatment with 75 mg Aspirin was given to all patients. Patients were also given 40 mg low molecular weight heparin subcutaneously once a day. The patients were advised of weekly follow-up visits. At each visit, fetal biometry, amniotic fluid volume and umbilical artery Doppler studies were performed. All the observations were made by a designated team of consultant radiologists at our institution to ensure uniformity and consistency. Patients were followed till delivery to determine outcomes including live birth, preterm delivery, neonatal weight, admission to NICU and pre-eclampsia. All information was noted in a formulated data collection sheet which included the following: demographic data, parity, gestational age at presentation, BMI, blood pressure and ultrasound report. Follow-up ultrasounds were documented on it. Neonatal outcomes encompassed living status, maturity of the baby, birth weight and admission of the baby to NICU. SPSS version 26.0 was employed to analyze the data. For numerical data like patient age, parity, BMI, and gestational age, mean and standard deviation were calculated. However, for outcomes, frequencies and percentages were tabulated. Normality tests were conducted using the statistical software SPSS. When  $p>0.05$ , the null hypothesis was accepted, and data were normally distributed. Control of effect modifiers like age, obesity, parity and gestational age was made possible by making stratified tables. Post-stratification chi-square test was applied to see their effect on the outcome.

## RESULTS

In this study, 122 patients fulfilling the inclusion criteria were recruited. The mean maternal age was  $26.75 \pm 4.44$  years. 102 (83.7%) were 15-30 years of age while 20 (16.3%) were 31-40 years old. Twenty (16.4%) were primigravidas, 77 (63.1%) had 1-4 kids while 25 (20.5%) had 5 or more kids. The mean BMI was 27.39. About 89 (73%) had normal BMI while 33 (27%) were obese. The mean gestational age at presentation was 32.67 weeks. Out of 122, 47 (38.5%) presented at 28-32 weeks of gestation while 75 (61.5%) presented after 32 weeks of gestation (Table 1).

**Table 1:** Characteristics of Demographics of study participants

| Variables                       | Minimum | Maximum | Mean $\pm$ SD    |
|---------------------------------|---------|---------|------------------|
| Age                             | 18      | 38      | 26.75 $\pm$ 4.44 |
| BMI                             | 21      | 38      | 27.39 $\pm$ 4.69 |
| Parity                          | 1       | 9       | 3.90 $\pm$ 2.26  |
| Gestational Age at Presentation | 28      | 35      | 32.67 $\pm$ 1.81 |

Out of 122 participants, 9 (7.4%) had pre-eclampsia while the majority remained normotensive. Among all conceptions, 120 (98.4%) resulted in live births while 2 (1.6%) were intra-uterine deaths. Among all births, 5 (4.1%) were delivered at 32-35 weeks, 16 (13.1%) at 36 weeks while the rest 101 (82.8%) were delivered at term. As regards birth weight, the vast majority weighed  $>2.5$  kg. Among 120 live births, 23 (19.2%) were admitted to the NICU for observation or treatment (Table 2).

**Table 2:** Outcomes after LMWH Usage in Patients with Oligohydramnios

| Outcomes                 | Yes n=122 (%age) | No n=122 (%age) | p-value  |
|--------------------------|------------------|-----------------|----------|
| Pre-Eclampsia            | 9 (7.4)          | 113 (92.6)      | $<0.001$ |
| Live Birth               | 120 (98.4)       | 2 (1.6)         | $<0.001$ |
| Newborn Weight $>2.5$ Kg | 108 (88.5)       | 14 (11.5)       | 0.036    |
| Term Delivery            | 101 (82.8)       | 21 (17.2)       | $<0.001$ |
| NICU Admission           | 23 (19.2)        | 97 (80.8)       | 0.002    |

Multinomial logistic regression was applied to calculate the odds of live birth after adjusting age and other factors (Table 3).

**Table 3:** Stratification of Live Birth in Association with Age, Parity, Gestational Age and BMI

| Characteristics                 | Subgroups  | n (%)      | p-value  |
|---------------------------------|------------|------------|----------|
| Age                             | 15-30      | 100 (83.3) | $<0.001$ |
|                                 | 30-40      | 20 (16.7)  |          |
| Parity                          | Zero       | 20 (16.7)  | 0.965    |
|                                 | 1-4        | 37 (30.8)  |          |
|                                 | 5 Or More  | 63 (52.5)  |          |
| Gestational Age at Presentation | 28-32      | 47 (39.2)  | 0.830    |
|                                 | 33-36      | 73 (60.8)  |          |
| BMI                             | $<24.9$    | 51 (42.5)  | 0.070    |
|                                 | 25 Or More | 69 (57.5)  |          |

An independent sample t-test or ANOVA was applied to analyze differences among groups. Our analysis demonstrated a statistically significant association between maternal age and live birth outcomes ( $p < 0.001$ ). Women aged 15-30 years had a higher proportion of live births compared to those aged 30-40 years. Parity did not show a significant association with live birth rates ( $p = 0.965$ ). Gestational age at presentation did not show a significant difference in live birth rates ( $p = 0.830$ ). Pregnant women who presented between 28-32 weeks and 33-36 weeks had similar outcomes. The analysis showed a near-significant association between BMI and live birth outcomes ( $p = 0.070$ ). While this result did not reach statistical significance, it suggests that higher BMI may contribute to adverse pregnancy outcomes in women with oligohydramnios receiving LMWH.

## DISCUSSION

An adequate amniotic fluid volume constitutes the most important component of a normal pregnancy, as it plays the role of protective cushion for the fetus, prevents umbilical cord compression, and contributes to fetal lung development. Oligohydramnios (AFI  $<5$  cm) is associated with serious risks to fetal well-being. The most important and common causes of maternal and fetal mortality and morbidity are pre-eclampsia and fetal growth restriction. Both of these have oligohydramnios as the accompanying feature. Our study comprised 122 pregnant ladies having oligohydramnios at or onward 28 weeks of gestation. The mean maternal age was 26.75 years which is near that calculated by Twesigomwe et al., in Uganda [13]. Mushtaq et al., also found similar (27.86%) results in a study conducted in Pakistan [14]. The mean BMI of pregnant ladies in this study was 27.39. Out of these, 27% had a BMI of more than 30 kg/m<sup>2</sup>. Our results regarding obesity and oligohydramnios are the same as those reached by Mushtaq et al., from Pakistan [14]. This narrates that obesity has no association with oligohydramnios. The same was concluded by Bistervels et al., [15]. Amniotic fluid can be reduced in both obese as well as normal-weight mothers. The gravidity in our study ranged from 1-9. The same was observed by Mohammed and his colleague from Iraq [16]. The mean parity in our study was found to be 3.90. Nearly 20 (16.4%) were primigravidas, 25 (20.5%) were grand multiparas having 5 or more kids and 77 (63%) had 1-4 kids. Our results are proximate to those reached by Bakhsh et al., from Saudi Arabia where 24.9% were primigravidas and 75.1% were multigravidas [17]. The significant association with maternal age underscores the importance of close monitoring in older pregnant women. While parity and gestational age at presentation were not significant predictors, the trend observed with BMI highlights the need for weight management and nutritional counselling in pregnant women at risk for oligohydramnios.

The main outcome of our study was to find out the frequency of pregnancy outcomes in antenatal patients having oligohydramnios with the use of low molecular weight heparin. Regarding maternal outcomes, 7.4% of the participants developed pre-eclampsia. However, it was calculated as 8.69% in the study by Zaman *et al.*, [18]. The slightly high rate of pre-eclampsia in the later study may be due to the fact it was a private hospital study, where patients of the middle and upper class present and usually have chronic hypertension as a result of their eating habits and lifestyle. The metabolic changes induced by pregnancy lead to superimposed pre-eclampsia in such patients. Among 122 births, there were two intra-uterine deaths while the vast majority (98.6%) were live births. Results concluded live births in 93.33% of their cases. The high live birth rate in our study strongly supports the beneficial effects of LMWH in cases with oligohydramnios. Not only live births were more registered but the overall health status of newborns was also much better. In our study, term delivery was achieved in 82.8% of the cases and 17.2% were preterm deliveries. The high rate of preterm delivery in our study can be explained by the high BMI of most of our participants as 57.5% of them were either overweight or obese. Zullino *et al.*, also found a strong association between preterm delivery and increased BMI [19]. Another explanation for this high preterm delivery rate is the grand multiparity as most participants already had more than 5 kids. Cruz-Lemini *et al.*, found a strong association between grand multiparity and preterm delivery [20]. In a study by Chen *et al.*, 22.2% of babies were delivered preterm [21]. This difference can be explained by the fact that in developed countries, the neonatal facilities are very advanced and the babies are born relatively preterm with very good survival prognosis and the fetal risks of oligohydramnios with the continuing pregnancy are thus avoided. In the current study, 108 (88.5%) newborns had weight more than 2.5 kg at the time of birth. It again reflects the promising results of LMWH as regards fetal outcome. In our study, 19.2 % of newborns were admitted to NICU for various reasons like low APGAR scores, and respiratory problems. In a similar study conducted by Iftikhar *et al.*, 18.3% of babies were admitted to the NICU. However, the admission to NICU was relatively higher (28.6%) in a similar study in Pakistan [22]. Sultana *et al.*, had a similar study with 28.9% admissions to NICU [23]. This difference can be explicated by the fact that the latter study was organized at a semi-government hospital where extra precautions are followed and newborns are kept in NICU for even observation.

## CONCLUSIONS

It was concluded that the use of low molecular weight heparin (LMWH) in pregnant women with oligohydramnios

is effective and safe, leading to favourable pregnancy outcomes. The frequency of adverse perinatal events, including pre-eclampsia, intrauterine death, preterm birth, low birth weight, and NICU admissions, was low in our study. These results support the use of LMWH as a beneficial intervention to improve perinatal outcomes and reduce associated maternal and neonatal complications in this population.

## Authors Contribution

Conceptualization: ST

Methodology: NN, HM

Formal analysis: AUT, FS

Writing review and editing: ST, SAR

All authors have read and agreed to the published version of the manuscript

## Conflicts of Interest

All the authors declare no conflict of interest.

## Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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