

## Frequency of Multiple Gestations in Kohat

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### ABSTRACT

**Objectives:** To determine the frequency of multiple gestations in Kohat City.

**Study Design:** Retrospective longitudinal study.

**Place and Duration of Study:** Labour Room and Neonatal Intensive Care Unit (NICU), Combined Military Hospital, Kohat Pakistan, from Jan 2019 to Dec 2020.

**Methodology:** We included 5285 women delivered at Combined Military Hospital, Kohat Pakistan, during our study period. Basic data were collected from medical record files, and further information was gathered through telephonic interviews with the patients. The frequency of multiple gestations was calculated and compared with local and international statistics.

**Results:** Out of 5285 deliveries during the study period, there were significant twin pregnancies 156(2.95%) and triplet pregnancies 11(0.21%). 167(3.16%) multiple deliveries were managed at our centre. Further probing showed that 109(65.3%) women used induction medication from registered medical practitioners or quakes/ spiritual healers to get pregnant.

**Conclusions:** Multiple gestations and the use of induction therapy are much higher in Kohat compared to other parts of the country.

**Keywords:** Assisted reproductive therapy, Fertility medicines, Fertility treatment, Multiple gestations, Ovulation induction.

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### INTRODUCTION

Twin pregnancy is considered high-risk because peri-natal mortality and morbidity in twins are higher than in singletons, mainly caused by low birth weight and prematurity.<sup>1</sup> Twins and triplets naturally occur in approximately 1 in 80 and 1 in 8000 pregnancies in the United States.<sup>2,3</sup> The incidence of spontaneous twins varies by country. The incidence of twins is lower in Japan and higher in Nigeria. Multiple pregnancies comprise an increasing proportion of the total pregnancies in the developed world due to older maternal age at childbirth and the extensive use of fertility treatments.<sup>4,5</sup> In countries where the rate of multiple gestations is high, up to 50 percent of twin pregnancies and 75 percent of triplet pregnancies occur due to fertility treatment.<sup>6</sup> Multiple gestations are rising in developed countries, with twins accounting for 3.4% of all births.<sup>7-9</sup> Multiple gestations are lower in developing and developing countries, generally 2-3% of all births. In a local study conducted in the Khairpur area of Sind, Pakistan, the frequency of twin gestation was 1.15%.<sup>10</sup> We observed a higher rate of multiple pregnancies in the Kohat region of KPK compared to other parts of the country, so we decided to collect the data and reasons behind these multiple gestations so

that local statistics could be formulated. More studies can further strengthen these local statistics and might be a reason to refine local clinical practices. We hypothesized that the desire to have more children in quick succession leads to practices causing multiple gestations in this area. The anxiety of not having children soon after marriage leads to the use of therapies and medicines from registered practitioners or spiritual healers and results in multiple pregnancies.

### METHODOLOGY

This retrospective longitudinal study was carried out at the NICU, Labour Rooms and Operation Theatre, Combined Military Hospital, Kohat Pakistan, from January 2019 to December 2020. All pregnant women presenting with multiple gestations to Combined Military Hospital, Kohat Pakistan, were included in the study by consecutive non-probability sampling. The sample size was calculated using the World Health Organization sample size calculator, taking a 95% confidence level, the absolute precision as 0.05, and the anticipated population proportion was 0.04.<sup>11</sup> Thus minimum sample size calculated was 60 but to increase the power of the study, we decided to collect the data for two years. Thus 167 cases of multiple gestations were included in the study. A total of 5285 medical records were included in the study.

**Inclusion Criteria:** All multiple gestation women who delivered after the age of viability (24 completed weeks

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of gestation), were included in the study. The multiple in-utero pregnancies and patients who used simple assisted reproductive techniques like ovulation induction were also included in the study.

**Exclusion Criteria:** All pregnant women who delivered before 24 completed weeks of gestational age, women with the history of in-vitro fertilization, ectopic pregnancies or other assisted reproductive techniques except ovulation induction were excluded from the study.

Out of all the delivered women, the frequency of multiple deliveries was calculated by analyzing birth records and NICU proforma attached to mothers' medical records. Detailed analysis of medical records was conducted, and any missing information was gathered by calling patients on the phone number available on the admission slip. Patients' consent was also obtained by phone call. Data was collected through a structured proforma. Confidentiality of the patient records was maintained.

Statistical Package for the Social Sciences (SPSS) version 19:00 was used for data analysis. Mean and standard deviation were calculated for quantitative data like maternal age, gestational age and newborn's birth weight. Frequency and percentage were calculated for categorical (qualitative) variables like ethnicity, gravidity, mode of delivery, newborns' gender, number of fetus and use of ovulation induction. The chi-square test was applied and the  $p$ -value  $\leq 0.05$  was considered significant.

### RESULTS

A total of 5285 patients were delivered at Combined Military Hospital, Kohat Pakistan, during the study period. Out of these a significant number 156 (2.95%) were twin pregnancies and 11(0.21%) were triplet pregnancies. A total of 167(3.16%) multiple deliveries were managed at our centre. Out of 5285 patients, 3453(65.34%) families were locals, and 1832(34.66%) families were settlers from other parts of Pakistan. In locals, the incidence of multiple gestations was even higher, with 124(3.6%) compared to settlers 43(2.35%). Further probing showed that 109(65.3%) patients had used some form of medicine to get pregnant, either from a registered medical practitioner or from quacks. Using iron, multivitamins, and folic acid was not considered a positive history for medicines. The mean maternal age was  $27.3 \pm 4.72$  years, the mean gestational age was  $34.15 \pm 1.85$  weeks, and the mean birth weight of neonates was  $1.87 \pm 0.44$  Kg (Table-I), of

all multiple gestations, 124(74.25%) mothers were locals and 43(25.75%) were outsiders.

**Table-I: Mean Maternal age, Gestational Age and Birth weight of the study population (n=167)**

| Study Parameters       | Mean $\pm$ SD                                  |
|------------------------|--|
| Maternal Age           | 27.30 $\pm$ 4.70 Years (Range: 18 to 40 years) |
| Gestational Age        | 34.10 $\pm$ 1.85 weeks (Range: 29 to 39 weeks) |
| Infants Average Weight | 1.87 $\pm$ 0.44 Kgs (Range: 0.9 to 3.15 Kgs)   |

Most mothers had multiple gestations in first gravidity 41(24.6%), second gravidity 38(22.8%) and third gestation 41(24.6%), 120(71.9%) mothers had multiple pregnancies in the first three gestations. Most women were delivered by LSCS 114(68.3%) while, 52(31.1%) women were delivered vaginally and only one woman delivered her first baby vaginally. There was a significant causal association between the use of medicines and the heterogeneous gender of fetuses ( $p < 0.001$ ). 156(93.4%) mothers delivered twins, and 11(6.6%) mothers gave birth to triplets. The association of use of fertility treatment was established based on patients' residence (ethnicity), gravidity and gender of newborns (Table-II).

### DISCUSSION

We all know that in Pakistan, quacks are using the same pharmaceutical products used by registered practitioners, but they mask the taste and colour of medicines by crushing them and mixing them with herbs. Therefore, we presumed that all those women who got medicines from quacks had taken fertility treatments. The affordability of the local population and the desire of people to have more children has led to these practices. In this study, the frequency of multiple gestations is much higher than reported in other parts of the country. It is a fact that developing nations have a lower incidence of multiple gestations because of less maternal age and less incidence of primary and secondary infertility; another reason is the lack of access to and affordability of fertility treatments in developing countries. In rural Sindh incidence of twin gestation was 1.15%, whereas, in our study, it was 2.95%.<sup>11</sup> A study conducted in Lady Reading Hospital Peshawar also showed results similar to ours, with an incidence of 3.2%. The higher incidence seems similar in that both Lady Reading Hospital and Combined Military Hospital, Kohat Pakistan, are referral hospitals of their respective areas and have huge dependent populations.<sup>12</sup> Both hospitals have better patient care capabilities than the other hospitals in the area, so all complicated and high-risk pregnancies are

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**Table-II: Multiple Gestations and Use of Fertility Treatment (n=167)**

| Parameters         |           |             | Use of Medications for Ovulation Induction |            |         |
|--------------------|-----------|-------------|--|------------|---------|
|                    |           |             | Yes  | No         | p-Value |
| Total              |           | 167(100%)   | 109 (65.3%)                                | 58 (34.7%) |         |
| Residence          | Locals    | 124(74.25%) | 94(56.3%)                                  | 30(18%)    | <0.001  |
|                    | Outsiders | 43(25.75%)  | 28(16.8%)                                  | 15(8.9%)   |         |
| Gender of Neonates | Male      | 54(32.3%)   | 24(14.37%)                                 | 30(18%)    | <0.001  |
|                    | Female    | 42(25.2%)   | 29(17.36%)                                 | 13(7.8%)   |         |
|                    | Mix       | 71(42.5%)   | 56(33.5%)                                  | 15(9%)     |         |
| Gravidity          | 1         | 41(24.6%)   | 33(19.8%)                                  | 8(4.8%)    | <0.001  |
|                    | 2         | 38(22.75%)  | 37(22.2%)                                  | 1(0.6%)    |         |
|                    | 3         | 41(24.6%)   | 26(13.2%)                                  | 15(8.9%)   |         |
|                    | 4         | 16(9.6%)    | 9(5.4%)                                    | 7(4.2%)    |         |
|                    | 5         | 12(7.2%)    | 3(1.8%)                                    | 9(5.4%)    |         |
|                    | 6         | 11(6.6%)    | 1(0.6%)                                    | 10(6%)     |         |
|                    | 7         | 4(2.4%)     | 0  | 4(2.4%)    |         |
|                    | 8         | 3(1.8%)     | 0  | 3(1.8%)    |         |
|                    | 9         | 1(0.6%)     | 0  | 1(0.6%)    |         |

referred to these hospitals, including multiple gestations. We hypothesized that there must be a role of ovulation induction therapies in the higher incidence of multiple gestations in this belt of the KPK province of Pakistan that is 72.5% of women took some medicine to help get pregnant compared to local study where the use of ovulation induction was only 16%.<sup>12</sup> Compared to the study of Lady Reading Hospital, our dependent population was either more afforded or entitled to receive free consultations and treatment, so the use of ovulation induction therapies was the highest ever reported ( $p < 0.001$ ). Out of 167 women, 35 (21%) women gave a clear history of use of ovulation induction from a registered practitioner. Another reason can be racial, which is again evident that the incidence of multiple gestations was higher in locals and lower in settlers ( $p < 0.05$ ). We also concluded that even advanced maternal age was not a reason to have multiple pregnancies, and even young women had multiple gestations. Most women had multiple gestations in the first, second or third pregnancy, contrary to the general concept that grand multiparity increases the incidence of multiple gestations. On the contrary, we hypothesise that most multiple gestations occurred due to ovulation induction.<sup>13</sup> In our study, 68.3% deliveries were carried by LSCS which was at par with local studies,<sup>12</sup> but much lower than an Iranian study where 96.3% of deliveries were done by LSCS.<sup>14</sup>

The frequency of twin pregnancies in industrialized countries has increased steadily over the past twenty years. The most important cause of multiple gestations is the increased usage of fertility treatment, assisted reproductive techniques (ART), and the ageing of the mothers.<sup>15-17</sup> Increasing maternal age has

decreased the chances of spontaneous conception, and many women require fertility treatment. The twin pregnancy rate in America has increased by about 75% from 1980 to 2009. A similar increase has also been reported in Western Europe and other countries.<sup>18,19</sup> The dizygotic twin rate varies in different countries and different factors such as race (10–40 per 1,000 births in blacks, 7–10 per 1,000 births in whites, and approximately 3 per 1,000 births in Asians), maternal age (the frequency has risen with increasing maternal age  $\geq 40$  years), heredity, the number of labours and the usage of ART.<sup>16,20</sup> The incidence of monozygotic twins is constant worldwide, at approximately four per 1,000 births. Naturally occurring triplet births occur in approximately 1 per 7,000–10,000 births; meanwhile, naturally occurring quadruplet births occur in approximately 1 per 600,000 births. Multiple gestations are considered high-risk because of their higher morbidity and mortality rates among mothers and neonates. Gestational age and newborn weight at birth are the most important independent predictors of neonates' morbidity/mortality and complications associated with twin birth.<sup>21</sup> The results of studies showed that the usage of ART in women of older ages was more likely, and therefore, their likelihood of multiple births increased.<sup>22-24</sup>

This study raised a red flag on the excessive use of ovulation induction in the community; when patients were asked, they told us that LHV had advised them to take medicines on the second day of the menstrual cycle. These Hakeem, LHVs or quacks do not know how much burden they are putting on the healthcare system. This study has pointed out an alarming situation only in this region of Pakistan

which should be a warning sign for district health administration. Through this study, we request that the city and health administrators they should take early and prompt action to stop such practices.

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### LIMITATION OF STUDY

Patients' lack of medical knowledge, the certainty of drug names and the exact nature of the drug which patients had used could not be ascertained.

### CONCLUSION

Despite the high risk to mothers and chances of complications to babies, people still use fertility treatment whether indicated or not. Social and peer pressure compels couples to use these medications, and the lack of awareness of patients has enhanced the magnitude of the problem into a pandemic in this region of Pakistan. We need to curtail such practices to ensure the health of mothers and neonates.

**Conflict of Interest:** None.

### Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MR & FY: Study design, data analysis, critical review, drafting the manuscript, critical review, approval of the final version to be published.

SA & SG: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

BS & R: Drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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