

## Outcome in twin gestations: A prospective observational study

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### ABSTRACT

**Background:** Incidence of twinning has increased due to the widespread use of assisted reproductive techniques. Twin gestation is associated with many maternal, fetal, and neonatal complications. **Objective:** The objective of the study is to study the fetal and neonatal complications and outcome of twin pregnancies. **Materials and Methods:** This is a prospective observational study conducted in a tertiary referral neonatal intensive care unit. 50 consecutive pairs of twins were recruited at the time of admission of the mother to the labor ward. Demographic details of the mother and of the infants were recorded. The outcome of the pregnancy was noted, and the live born infants were followed during the hospital stay and then up till 6 months of corrected gestational age. **Results:** Incidence of prematurity was 60%. Moderate to severe discordancy was identified in 17 (34%) pairs of twins and 43% infants were born small for gestational age (SGA). Intrauterine Fetal Death was noted in 6 out of 54 infants with discordant growth and 1 out of 46 infants with concordant growth ( $p=0.046$ ). The overall mortality in our study was 13.9%. Mortality in SGA infants was 23% and 6% in appropriate for gestational age infants ( $p=0.036$ ). **Conclusion:** Twinning is associated with high incidence of prematurity, growth discordance, congenital anomalies, intrauterine fetal death, and neonatal mortality.

**Key words:** Congenital anomalies, Growth discordance, Intrauterine fetal death, Neonatal mortality, Prematurity, Twins

The incidence of multiple pregnancies has shown a significant increase over the past decades due to the widespread use of assisted reproduction techniques. In the United States, twin births account for 3.4% of live births and over 96% of multiple births [1]. In Asian population, the rates of twinning are <9 per thousand, and in the African population, it is as high as 44.9 per 1000 [2,3]. Apart from the ethnicity, maternal age is the most important non-genetic factor influencing the twinning rate. Rao noted significant effect of maternal age and parity on twinning in a sample of 10,916 pregnant women. Younger mothers exhibited high rate of twinning in higher parities, and older mothers exhibited high rates of twinning in the low parities [4].

Twin gestation is associated with many maternal, fetal and neonatal complications and it is a challenge to both obstetricians and neonatologist. The major complication of twinning is prematurity and increased mortality. Before 34 weeks of gestation, incidence of preterm delivery is significantly high in twins as compared to singletons, and this may explain the significantly increased infant mortality seen in this group [5]. Ghai and Vidyasagar in their study noted that although twins constitute up to 2.6% of all newborns, they account for 12.2% of preterm births and 15.4% of neonatal death [6].

Other complications in twins include intrauterine growth restriction, fetal growth discordance, intrauterine fetal death (IUFD), and congenital malformations. Fetal growth discordance

means the percentage of weight difference between the twins, in relation to the bigger twin and may be mild (<15%), moderate (15-30%), or severe (>30%). Congenital anomalies include structural defects that share a common origin with the twinning process, vascular disruption syndromes and deformations. Glinianaia et al. in their population-based data on multiple pregnancies found that incidence of congenital anomalies in twins was 40.5 per 1000 twins versus 23.8 per 1000 singletons. The prevalence of congenital anomalies in monochorionic (MC) twins (63.3 per 1000) was nearly twice that in dichorionic (DC), (34.3 per 1000) [7]. Long-term studies of twins have reported adverse neurodevelopmental outcomes especially in MC twins. Since we have a high incidence of twins, we planned to undertake this study to assess the morbidity and mortality in twins after birth and to assess the growth and neurodevelopmental outcome at 6 months of age.

### MATERIALS AND METHODS

This was a prospective observational study conducted in a tertiary referral neonatal intensive care unit in a teaching hospital after obtaining approval from the Institutional Ethics Committee. 50 consecutive pairs of twins were recruited at the time of admission of the mother to the labor ward after obtaining written consent. Demographic details of the mother were noted. Demographic details of the infants were recorded with respect

to gestational age and growth parameters. The outcome of the pregnancy was noted, and the live born infants were followed up during the hospital stay. Complications and treatment details of the infants were recorded. The infants were then followed up till 6 months of corrected gestational age (CGA) to assess growth (weight, length, and head circumference) and development Infant Neonatal International Battery (INFANIB).

## RESULTS

About 50 pairs of twins were delivered between June 2015 and September 2015. A total number of infants delivered during this period was 1967. The incidence of twin pregnancy was 25.4 per 1000 live births. Out of these 100 infants, 93 survived. Incidence of IUFD was 7%. IUFD was noted in 6 out of 54 infants with growth discordance while same was 1 out of 46 infants with concordant growth and the difference was statistically significant,  $p=0.04$ .

Out of the 50 pairs of twins, 36 were DC (72%), and 14 were MC (28%). Incidence of prematurity was 60%. Moderate to severe growth discordancy, defined as 15-30% and >30% discrepancy of the weight of the bigger twin, respectively, was identified in 34% of the twins. Overall, mortality was 13.9%. Mortality in small for gestational age (SGA) versus appropriate for gestational age (AGA) was 23% versus 6% which was significant ( $p=0.036$ ). Neonatal demographic data and mortality are given in Table 1.

Respiratory distress syndrome (RDS) was present in 19.3% twins and 13.9% required surfactant therapy while respiratory support was needed in 22.5% cases. Congenital anomalies were found in 7 infants as shown in Table 2. Neurodevelopmental assessment with INFANIB on follow-up at 6 months showed that 78.5% twins were normal, 19.65% had transient abnormality, and only 1 was abnormal (Table 3). On follow-up at 6 months of CGA, only 26.7% were exclusively on breastfeeding, 41% were receiving mixed feeding, and 32.1% were exclusively on top milk.

## DISCUSSION

A total of 50 pairs of twins were enrolled in our study. Out of these, 93 survived. The incidence of twin pregnancy in our center was 25.4 per 1000 live births. This incidence is less than that reported by Chauhan et al. in the United States (32 per 1000) and Akinboro et al. in Nigeria (46.5 per 1000) [3,8]. This difference in twinning rates among countries is due to variation in dizygotic twinning, in which two zygotes are formed from two separately fertilized eggs. Maternal factors - such as genetic predisposition, advanced age, and increased parity - play a significant role in dizygotic twinning. Assisted reproductive techniques too are associated with high incidence of dizygotic twinning. Monozygotic twinning, in which two zygotes are formed from 1 ovum, occurs at a relatively constant rate of 3.5-4 per 1000 births across human populations.

In our study, women between 21 and 30 years of age constituted 76% of the women delivering twins. Primigravida and 2<sup>nd</sup> gravida constituted 78% of the women delivering twins. This observation

**Table 1: Neonatal demographic data and mortality**

Gestational age	Number of infants	Mortality (%)
<28	2	3 (72.1)
28-31.6	10	5 (26.3)
32-36.6	18	3 (8.8)
>37	20	2 (5.2)
Birth weight		
<1	5	4 (80)
1-1499	24	6 (25)
1500-1999	22	1 (4.5)
2-2499	33	1 (4.5)
>2.5	9	1 (4.5)
Weight status		
SGA	43	10 (23)
AGA	50	3 (6)

SGA: Small for gestational age, AGA: Appropriate for gestational age

**Table 2: Neonatal morbidity**

Morbidity	n (%)
Resuscitation	8 (8.6)
RDS	18 (19.3)
Surfactant	13 (13.9)
Respiratory support	21 (22.5)
Fetal growth discordance	
Mild	6 (12)
Moderate	13 (26)
Severe	4 (8)
Congenital malformation	7
Conjoined twins	1
Penile hypospadias	1
Ectopic kidney	1
Tracheoesophageal fistula	1
Syndactyly	1
CTEV	2

RDS: Respiratory distress syndrome, CTEV: Congenital talipes equino varus

in our study is different from previously reported data. Rao noted that younger mothers exhibited high rate of twinning in higher parities and older mothers exhibited high rates of twinning in the low parities [4]. Although maternal age and parity are highly correlated with twinning, the effects are independent of each other [9,10]. Out of the 50 pairs of twins, 36 were DC (72%), and 14 were MC (28%). These data are similar to previously reported incidence by Assunção et al., who noted 60.5% of the twins were DC and 37.6% was MC [11].

In our study, 60% of the twins were preterm (<37 weeks) and 12% twins were <32 weeks. This finding is similar to the incidence reported in other studies. Joseph et al. in their study demonstrated that 58% of twins delivered before 37 weeks and 11.9% before 34 weeks [12]. Prematurity is the single highest complication of twinning. In our study, we found mortality rate of 72.1% in twins <28 weeks and 26.3% in twins 28-31.6 weeks, which was related to the complications of prematurity. This compares well with some studies which have reported that prematurity accounts for

**Table 3: Follow-up at 6 months CGA (n=56)**

Feeding pattern	n (%)
Exclusive breastfeed	15 (26.7)
Mixed feeds	23 (41)
Top feed	18 (32.1)
Illnesses	
Pneumonia	6 (10.7)
Diarrhea	10 (17.8)
INFANIB	
Normal	44 (78.5)
Transient	11 (19.6)
Abnormal	1 (1.7)
Weight (centile)	
<10 <sup>th</sup>	31 (55.3)
>10 <sup>th</sup>	25 (44.6)
Length (centile)	
<10 <sup>th</sup>	19 (33.9)
>10 <sup>th</sup>	37 (66.07)
Head circumference (centile)	
<10 <sup>th</sup>	9 (16)
>10 <sup>th</sup>	47 (83.9)

INFAIB: Infant Neonatal International Battery, CGA: Corrected gestational age

60-80% of the deaths in twin infants [13,14]. Overall, mortality was high in our study (13.9%). This is much higher than that noted by Doyle (2.7%) among twins born in England and Wales in 1991 [15]. The common causes of death in our study included intraventricular hemorrhage, RDS, pulmonary hemorrhage, and perinatal asphyxia. Mortality in SGA versus AGA twins was 23% versus 6% which was significant with a  $p=0.036$ .

In our study, IUFD was noted in 6 out of 54 twins with growth discordance and 1 out of 46 twins with concordant growth, and the difference was statistically significant ( $p=0.046$ ). A high incidence of IUFD has been noted by Mahony et al. who studied 1094 twin pairs and concluded that twin pregnancies complicated by growth restriction or growth discordance were associated with a high risk of IUFD, particularly in MC twins. The incidence of IUFD in MC twin pregnancies was three times that in DC pregnancies (3.9% vs. 1.3%)  $p<0.001$  [16,17]. Since our sample size was small, we could not identify any effect of chorionicity on fetal death.

Common morbidities in twins were RDS, perinatal asphyxia, and growth discordance. Moderate to severe growth discordancy was identified in 34% of twins as against 11.9% reported by Nassar et al. [18]. Furthermore, 8 out of 13 deaths were seen in neonates with discordant growth. Miller et al. identified risk factors for divergent growth and categorized them as maternal, fetal, or placental [19]. We did not study the placental details, which may be one of the contributing factors for high incidence of growth discordance noted. Although there is extensive research on the increased morbidity and mortality rates in discordant twins, there are no guidelines on how to manage them optimally. In our study, 43% of the twins were SGA which is much higher than previously reported incidence. This may be

due to the higher incidence of growth discordance in our study population.

Incidence of malformation noted in our study was high (7%) which included 1 case of conjoined twin, 1 case of tracheoesophageal fistula and deformations like congenital talipes equinovarus. Many studies have documented a high incidence if congenital anomalies included cardiovascular, central nervous system, genitourinary and musculoskeletal anomalies. Incidence of twin specific congenital anomalies, like twin to twin transfusion syndrome, acardiac twins and twin reversed arterial perfusion sequence is low compared to other systemic malformations [7,20].

On follow-up at 6 months of CGA, only 26.7% were exclusively on breastfeeding, 41% were receiving mixed feeding, and 32.1% were exclusively on top milk. Thus, we need to focus on ensuring that mothers with twins get adequate support for lactation. Childhood illnesses such as diarrhea (10 infants) and pneumonia (6 infants) were common in these infants, which may be related to lack of breastfeeding rather than to twinning. Neuromotor assessment in the study population was found to be overwhelmingly normal except one abnormal score on INFANIB. Studies have found increased risk of death or neurodevelopmental impairment for extremely low birth weight (ELBW) twins when compared with the singleton ELBW infants [21]. Goyena et al. found gestation and growth discordance as the important factors influencing neurodevelopment [22]. These studies indicate that there is a small but significant influence of growth restriction on neurodevelopment.

## CONCLUSION

Twinning is associated with fetal and neonatal complications of prematurity, growth discordance, increased perinatal and neonatal mortality. Further, adequately powered research is required to study the long-term neurodevelopmental outcome.

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