

Research Article

# A Comparison of Perinatal Outcomes in Multiple Pregnancies: Assisted Versus Spontaneous Conception: A Cross-Sectional Study

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## Abstract

**Objective:** To investigate the difference in perinatal and delivery outcomes in multiple pregnancies, depending on mode of conception.

**Design:** An observational cross sectional study.

**Setting:** Homerton University Hospital NHS Foundation Trust, a University Hospital in London.

**Sample:** All multiple pregnancies delivered at the hospital between the inclusive years 2009-2012 were reviewed with a total of 341 pregnancies included.

**Methods:** Maternal demographics and perinatal outcomes including mortality rates, were collected on all participants.

**Main outcome measures:** Maternal demographics including age and length of postnatal hospital stay, pregnancy outcomes including mode of delivery, and perinatal outcomes including mortality rates.

**Results:** Women who conceived naturally were significantly younger ( $30.42 \pm 5.98$  years) than those conceived through assisted treatment ( $34.24 \pm 5.73$  years;  $p < 0.05$ ). Babies conceived through assisted treatment were born at a significantly lower gestational age ( $33.81 \pm 4.05$  weeks) than those conceived spontaneously ( $34.81 \pm 3.55$  weeks;  $p < 0.05$ ). The average birth weight was significantly lower in those conceived by assisted treatment as compared to those conceived naturally. More naturally conceiving women delivered by spontaneous vaginal delivery (23.9%) as compared to those conceived by assisted treatment (9.2%,  $p < 0.05$ ).

**Conclusions:** Comparable perinatal mortality rates are seen between twins conceived naturally and those conceived by assisted reproductive technology; however significantly lower gestational age, birth weight and vaginal delivery rates were seen in pregnancies conceived by assisted treatment.

**Keywords:** Multiple pregnancies; Twins; Assisted reproductive therapy; ART

## Introduction

There is ongoing discussion regarding the outcome of pregnancies following assisted conception. With regards to multiple pregnancies, more frequent in assisted conception cohorts, there is a particular variability in data regarding neonatal and maternal outcomes.

A 2004 systematic review and a large 2008 study both stated that in cases of twin pregnancy following assisted conception that the perinatal mortality is significantly lower, when compared with those spontaneously conceived [1,2]. Furthermore, a review found an increased level of antenatal complications in assisted-conception twin pregnancies, but only to a level that had limited impact on the morbidity and mortality of an individual pregnancy [3]. In contrast to this, a more recent 2015 study demonstrated an increased risk of adverse neonatal outcomes including stillbirth, low gestational weight, sepsis and low Apgar score in twins conceived by assisted reproductive technology (ART) [4]. However, the confounding influence of preterm birth had not been extrapolated in this particular study. Preterm birth in itself is an independent risk factor for additional adverse neonatal outcomes and is seen in greater frequency in the ART pregnancy population [4,5]. These findings are supported by 2015 meta-analysis demonstrating higher rates of preterm birth associated with increased rates of premature rupture of membranes in ART pregnancies [6].

Thus, there is no consensus when individual papers are reviewed with regards to assisted conception twins and perinatal outcome, with some demonstrating no association with preterm and low birth weight

[7,8], and others reporting increased risk [9-11]. Other studies have concluded twins conceived by assisted methods have similar obstetric and neonatal outcomes [12-14].

Two review papers in 2009 and 2011 studied the risks of assisted conception on obstetric outcomes. They both found that there was an increased caesarean section rate for assisted conception twins when compared with those spontaneously conceived [15,16]. A recent study further identified an association of ART pregnancies with pre-eclampsia, placental abruption, placenta praevia and obstructed labour [17]. These associations may provide additional reasoning as to why there is an increased caesarian section incidence in the ART population, beyond the association with higher socioeconomic status [17].

The study objective of this study is to add weight to the evidence surrounding assisted-conception multiple pregnancies, with a particular focus on perinatal outcome and delivery method.

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## Methods

This is an observational cross sectional study, carried out at a single UK University hospital. Data was collected from eligible participants who delivered multiple births following assisted conception methods and compared with the control group with multiple births who had conceived spontaneously. Maternal details were collected regarding age and any assisted reproductive therapy required. Data from the pregnancy was collected with gestational age at birth and birth weight. Length of stay in hospital for the baby was also included.

The statistical analysis was performed using the statistical package for social sciences (SPSS V22.0). Independent t-tests were conducted when data was normally distributed; to compare the above parameters between naturally conceived pregnancies and those conceived with assisted techniques. For data not normally distributed the non-parametric, Mann Whitney test was used. Chi-squared tests were used to compare treatment, live birth rate and delivery method.

## Results

All multiple pregnancies delivered at the Homerton University Hospital NHS Foundation Trust between the inclusive years 2009-2012 were reviewed with a total of 341 pregnancies included (330 twin and 11 triplet pregnancies). This included pregnancies conceived by assisted techniques (38.4%) and naturally (61.6%).

The mean maternal age of all women was 31.8 years. An independent t-test revealed naturally conceived pregnancies were significantly ( $t = -5.84, p < 0.05$ ) younger ( $30.42 \pm 5.98$  years) than those conceived through assisted treatment ( $34.24 \pm 5.73$  years), as shown in Table 1. There was no statistical difference in the ethnicity of each group.

The mean gestation for all women was 34.5 weeks ( $\pm 3.67$ ) and the average birth weight was 2.15 kg ( $\pm 0.67$ ). A significant difference ( $t = 2.34, p < 0.01$ ) was found in the gestational age at delivery between babies conceived naturally ( $34.81 \pm 3.55$  weeks) and those conceived through assisted treatment ( $33.81 \pm 4.05$  weeks). This difference remained significant when adjusted for maternal age.

The average birth weight was also found to be significantly ( $t = 2.862, p < 0.01$ ) lower in those conceived by assisted treatment ( $1996 \pm 723$  grams) as compared to those conceived naturally ( $2215 \pm 666$  grams).

The average neonatal length of hospital admission was longer for those conceived by assisted treatment ( $15.1 \pm 19.5$  days) compared with those conceived naturally ( $12.3 \pm 18.6$  days) ( $p < 0.05$ , Mann-Whitney). A Chi-square test for independence (with Yates Continuity Correction) indicated no significant association between method of conception and live birth rate, ( $p = 0.26$ ).

The mode of delivery depending on method of conception was analyzed using multiple Chi-squared tests. Fewer women delivered by emergency or elective caesarian section when conceived naturally

(33.5 and 29.2% respectively,  $p < 0.01$ ) compared with those conceiving with assisted treatment (37.4 and 41.2% respectively,  $p < 0.01$ ). More spontaneously conceived pregnancies (23.9%) delivered by spontaneous vaginal delivery as compared to those conceived by assisted treatment (9.2%,  $p < 0.01$ ).

All the above results included both the triplet and twin pregnancies, however the differences were still significant when adjusted to include either only twin or triplet births.

## Discussion

### Main findings

Our results showed that pregnancies conceived from assisted treatments are born one week earlier than those conceived naturally. It logically leads from this that these babies weigh approximately 220 grams less and have increased lengths of stay of 3 days. There was no significant difference in the perinatal mortality between the two groups.

### Strengths

This study adds to the growing evidence surrounding the outcome of multiple pregnancies, depending on their conception methods. Studying the mode of delivery and maternal outcomes allows an interesting insight into the patient and physician attitude.

### Limitations

This paper was limited in not including data on chronicity or more details surrounding the indications for decisions made regarding delivery method.

### Interpretation

The results are in line with other studies that highlight a significant difference in perinatal outcome depending on mode of conception [9-11]. Despite lower birth weight in ART neonates, no significant difference in the perinatal mortality between the two groups was identified, which supports results from previous recent studies [12-14,18].

The differences in the mode of delivery raise an interesting discussion. It may be explained by both physicians and mothers having a different attitude, depending on whether they had conceived using assisted fertility treatments or not. This view is supported by a 2013 paper, which concluded that clinicians had differing views on invasive prenatal testing depending on the method of conception [19]. It showed that clinicians were 3.2 times less likely to recommend amniocentesis for pregnancies conceived from assisted treatment than for a spontaneous pregnancy [19]. Furthermore there are likely demonstrable differences between the socioeconomic status of the two groups: an independent predictor of improved perinatal outcomes [17].

The results in our paper showed that pregnancies conceived by assisted techniques were more likely to be delivered by elective caesarian section than naturally conceived pregnancies, a view supported by previous studies [15,19]. If an elective caesarian section was not opted for then assisted conception multiple pregnancies were more likely to deliver by emergency Caesarean section rather than vaginally. This finding may suggest that pregnancies were seen as "more precious" if the couple had required fertility treatment to conceive. This view is supported by a 2005 study that found obstetricians to be more likely to recommend Caesarean section as the method of delivery if the couple had undergone fertility treatment [20]. The authors in this paper challenge this standpoint, stating that ultimately all pregnancies should be viewed in the same light and considered equally 'precious'.

	Natural conception	Assisted reproductive therapy conception
Maternal age (years)	30.42 $\pm$ 5.98	34.24 $\pm$ 5.73
Gestational age (weeks)	34.81 $\pm$ 3.55	33.81 $\pm$ 4.05
Birth weight (grams)	2215 $\pm$ 666	1996 $\pm$ 723
Length of stay in hospital (days)	12.3 $\pm$ 18.6	15.1 $\pm$ 19.5

**Table 1:** Comparison of maternal age, gestational age, birth weight and length of hospital stay between twins conceived by natural conception and assisted reproductive technology (ART).

## Conclusion

This study adds to the growing pool of evidence regarding outcome of multiple pregnancies depending on method of conception. Although studies have been conflicting in the past, this may highlight differences in physician opinion on intervention and attitude towards antenatal care depending on whether the couple had required fertility treatment or not. It may also reflect the huge amount of 'converse' confounding factors present, in particular: differences in chorionicity between multiple pregnancies conceived spontaneously, which have a higher incidence of monozygotic twins compared to assisted-conception. This, in addition to higher socioeconomic status, may in turn attenuate the negative effects of lower birth weight, increased risk of pre-term labour and maternal age on overall perinatal outcomes [21]. Refining research methods to adjust for these discrepancies will likely help to identify whether mode of conception represents an independent variable on perinatal outcomes. There is consensus however, that twins have poorer outcomes compared to singleton births. Reducing the multiple birth rates following assisted conception treatments remains the priority.

## Contribution to Authorship

Husain S, Homburg R, Dooley W and Lonsdale S designed the study. Dooley W, Lonsdale S and Diamantopoulos A collected the data. Dooley W, Lonsdale S, Diamantopoulos A and Homburg R wrote the manuscript. Dilgil M performed the statistical analysis. Husain S, Gudi A and Shah A critically reviewed the study design and manuscript.

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