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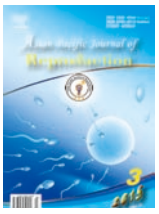

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Infant mortality in twin pregnancies following in-utero demise of the co-twin

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ABSTRACT

Objective: To assess whether conversion from twin to singleton pregnancy following the demise of a co-twin influences survival. **Methods:** This retrospective study compared the risk for neonatal, post-neonatal and infant death for converted co-twins versus unconverted co-twins using the US matched multiple file dataset for the period 1995-2000. We also examined the same risks for converted versus same-quantile co-twins, hazard ratios (*HR*) and 95% confidence intervals (*CI*) were computed using Cox Proportional Hazards models. **Results:** The risk for neonatal (*HR*=0.18, 95% *CI*: 0.09-0.34 and *HR*=0.69, 95% *CI*: 0.50- 0.96) and infant death (*HR*=0.22, 95% *CI*: 0.12-0.42 and *HR*=0.57, 95% *CI*: 0.42-0.77) were significantly lower for converted twins than for unconverted twins and same-quantile twins, respectively. For black compared to white, the risk for post-neonatal death increased by 89% (*HR*=1.89, 95% *CI*= 1.03, 3.48), and 79% (*HR*=1.79, 95% *CI*=1.53, 2.09) for converted *vs*. unconverted and converted *vs*. same-quantile, respectively. For converted black, the risk for neonatal death decreased by 17% (*HR*=0.83, 95% *CI*=0.73-0.93) as compared to unconverted. **Conclusions:** Risks for all mortality types were lower among converted co-twins than their unconverted or same-quantile counterparts. The lower neonatal and higher post-neonatal mortality among black require future research.

1. Introduction

Twin pregnancies are high-risk gestations with elevated perinatal mortality rates[1]. Twins, when compared with singletons, have a five-fold risk of fetal death, seven-fold elevated risk of neonatal death, and five-fold risk of infant death[2-4]. Twins also respond differently from singletons to interventions that are designed to lengthen the gestational age at birth[5-6]. Factors that impact fetal mortality risks include prenatal complications, maternal age, poor obstetric history and Assisted Reproductive Technology (ART) [1-6]. Twins face greater risks for low birth weight, preterm birth, long-term disability and early death than singletons[7].

Death of one of the twins in a multiple gestation can lead to severe complications in the surviving co-twin, especially in the second or third trimester[8]. The prognosis of the surviving twin in a dichorionic twin pregnancy is better than in a monochorionic twin gestation. The latter has more neurological complications such as neural tube defects, optic nerve hypoplasia, microcephaly, and hemorrhagic or hypoxic lesions of the white matter[9]. Other

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anomalies include bilateral renal cortical necrosis, unilateral absence of kidney, gastro intestinal tract atresia and hemifacial microsomia [9]. An important consequence of the demise of a co-twin is cerebral palsy in the surviving co-twin, which may be the result of prenatal damage arising from placental vascular anastomoses[10]. Fichera *et al* [9] also reported a greater risk of perinatal mortality for the surviving co-twin in monochorionic *vs.* dichorionic pregnancies following a single intra-uterine, second or third trimester death.

As a result of in-utero demise of a co-twin, a twin pregnancy may sometimes be converted into a singleton gestation[5]. In these cases, the growth and development of the surviving singleton co-twin depends on the adaptive response and physiological process in the remaining pregnancy period. Salihu *et al* studied the fetal programming switch process among surviving co-twins from a twin programming trajectory to that of a singleton during pregnancy[5].

It is well established that surviving co-twins have higher mortality rates than live-born twin pairs[11]. Surviving co-twins also bear a greater risk for later morbidity, including neuro-cognitive and behavioral problems[11–14]. It remains, however, unknown to what extent exposure to double programming in utero would impact subsequent morbidity and mortality of surviving co-twins. It will be interesting and useful to determine whether conversion to a singleton fetal programming pattern by surviving co-twins influences future survival. We are unaware of any twin study that has examined the contribution of double programming to early mortality among twins. Thus, the objective of this paper is to estimate the risk for neonatal, post-neonatal, and infant death among twins that were able to convert to singleton gestation as compared to those who do not within a large population-based sample of twins.

2. Materials and methods

The dataset from the "matched multiple birth file" prepared by the National Center for Health Statistics (NCHS), for the period 1995-2000, was used for this study. This dataset contains matched and linked data for multiple deliveries in the United States. The data files consist of individual records of live births and fetal deaths involving multiple deliveries. In the dataset, siblings were linked to their biological mothers through the use of a unique identifier. The primary outcomes of interest in this study were infant mortality (death of the infant from day 0 to day 364 after birth), neonatal mortality (death from day 0 to day 27 after birth) and post-neonatal mortality (death from day 28 to day 364 after birth).

Gestational age was determined as the time between the last menstrual period and the time of delivery of the baby (95% cases). When the menstrual estimate of gestational age was inconsistent with the birth weight (e.g. very low birth weight at term), a clinical estimate of gestational age on the vital records was used instead[15]. The precision of using the gestational age as noted on the US birth certificate has previously been validated[16]. The exposure of interest in this study is conversion to singleton programming in the surviving co-twin following the demise of the other twin. The concept of change or turning points was used in order to estimate the point periods in-utero at which the "switch" from a twin to a singleton fetal programming sequence might have occurred following the demise of a co-twin. In a previous study, we reported findings showing that a critical in-utero mass has to be attained by the surviving co-twin for successful conversion to a singleton path during pregnancy. In that pioneer study, it is reported that a critical mass and a specific gestational age (change point) need to be attained for the conversion from twin to singleton to take place. Results of the study showed that a critical mass (80th percentile of the gestational age-specific birth weight distribution for twins of same sex pairs and 70th percentile for opposite sex pairs) have to be attained by the surviving co-twin for successful conversion to a singleton path during pregnancy. The threshold (change point) for the conversion of the surviving co-twin to a singleton programming sequence was approximately at the 27th week of gestation. A surviving co-twin satisfying these conditions will be referred to as "converted twin" throughout this manuscript. Otherwise, we will refer to the surviving co-twin as an "unconverted twin".

We consider two comparison groups for our study. In the first case we compare the survival of converted twins *vs.* unconverted twins. In second case comparison of survival between converted twins and same-quantile twins (co-twins who reached the same quantile of the birthweight distribution at the same gestational age, but who could not switch to singleton programming because their co-twin also survived and was delivered alive) is considered.

We selected viable births (20–44 weeks of gestation) for both converted, as well as unconverted and same-quantile twins. We further categorized twin clusters into three groups based on the presence or absence of a stillbirth (defined as intra-uterine fetal demise at 20 weeks' gestation):

1. Group A: all members were live births
2. Group B: one member was a live birth and the other a stillbirth (surviving co-twin model)
3. Group C: Both members experienced a stillbirth

We excluded Group C from further analysis. In the first comparison converted *vs.* unconverted only Group B is considered. In the second comparison converted *vs.* same-quantile twins, both co-twins from Group B and co-twins from Group A who reached the same quantile of the birth weight distribution at the same gestational age, but who could not switch to singleton programming because their co-twin also survived and was delivered alive were considered. The selection pathway for the co-twins used in this analysis is given in detail in Figure 1.

Study variables included in this analysis comprised: day of birth and death, mode of delivery (cesarean or vaginal), pregnancy and labor complications, method of delivery, maternal socio-demographics (race, age, marital status, educational level) and maternal lifestyle factors (smoking) and infant characteristics (e.g.,

sex). Maternal race was defined as black, white and others; maternal age was grouped as less than 18 years, 18 to 34 years and 35 years. Maternal education level was categorized into two groups: less than 12 years of education and 12 years. The study also determined the occurrence of maternal medical complications among both groups. Maternal complications considered included anemia, preeclampsia, chronic hypertension, placental abruption, diabetes and placenta previa.

The rate of infant mortality was computed by dividing the total number of deaths by the total number of live births and multiplying the outcome by 1 000. *Chi*-square test was used to assess differences in proportions. The Cox proportional hazard model was employed to perform the survival analysis. We used the Cox proportional hazards regression model to derive adjusted hazard ratios after testing for non-violation of the proportionality assumption in each case. We confirmed this by plotting the log-negative-log of the Kaplan-Meier estimates of the survival function versus the log of time[17]. The resulting curves were found to be parallel, confirming the proportionality assumption. Adjusted hazard ratios were derived by loading all the variables that were considered to be potential confounders into the model. The Cox proportional hazard model is expressed as :

$$h(t) = h_0(t) \exp\{b_1x_1 + b_2x_2 + ... + b_px_p\}$$

where h(t) is the hazard function in which h0 (t) represents the baseline hazard; the covariates are (x_1, x_2 ..., x_p) whose effects are measured by the size of the individual coefficients (b_1, b_2, ...,b_p), and t is the survival time of infancy. The type 1 error rate was set at 5% for all tests of hypotheses. Analysis was conducted using R statistical software, version 3.0.2. This study was approved by the institutional review board at the University of South Florida.

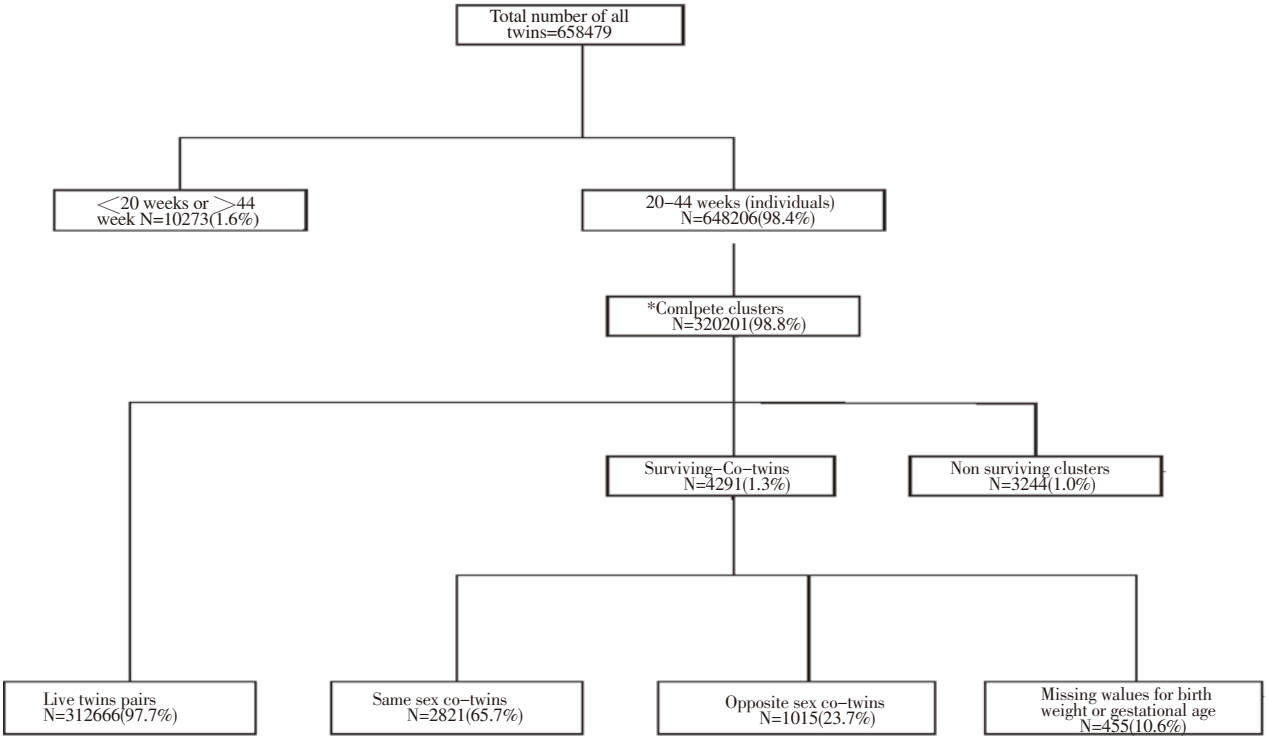

Figure 1. Flow chart for exclusion and inclusion criteria.
*Complete clusters or twin-pairs for which information on both was available

3. Results

For the first comparison: Converted *vs.* Unconverted, a total of 4 291 co-twins were analyzed. Of this 1 289 (30.04%) were co-twins converted to singleton while 3002 (69.96%) were unconverted and maintained the initial twin programming pattern. For the second comparison: Converted *vs*. Same-quantile twins, a total of 390 302 twins were analyzed. Of this number, 1 289 (0.33%) were co-twins converted to singleton while 389 013 (99.67%) were either unconverted co-twins that maintained the initial twin programming pattern or co-twins who reached the same quantile of the birth weight distribution at the same gestational age, but who could not switch to singleton programming because their co-twin also survived and was delivered alive. The frequencies of socio-demographic characteristics of the study population from the first comparison (converted vs unconverted) are summarized in Table 1. Around 80% of mothers were white, non-smokers and aged between 18 and 34 years. Mothers of converted twins were more likely than those of unconverted twins to be older, white, married and to have at least a high school education (Table 1). Mothers of unconverted twins were more likely than those of converted twins to smoke cigarettes

in pregnancy (P<0.001). Also from Table 1, labor complication does not show a significant difference between the two groups (P=0.247)

Infant mortality rates among converted versus unconverted birth (first comparison) are displayed in Table 2. Significant differences were observed in neonatal, post-neonatal and infant mortalities between the two groups. Neonatal mortality rate was lower for converted (3.18%) than for unconverted twins (31.77%) (P<0.0001). Rates of post-neonatal and infant death were also smaller among converted than for unconverted twins (postneonatal death: 0.39% for converted *vs*. 1.77% for unconverted twins, P<0.0001; infant death: 3.57% for converted *vs*. 33.54% for unconverted twins, P<0.0001).

Table 1

Socio-demographic characteristics, rates of pregnancy and labor complications of study populations United States, 1995-2000 comparing converted and unconverted twins (n=4291)[a].

Socio-demographic characteristics		Convertedc co-twin n (%)	Unconverted co-twin n (%)	P-value [b]
Mother's age	Less than 18 years	35(2.72)	138(4.60)	
	18 to 34 years	1 018(78.98)	2 510(83.61)	<0.001
	35 years	236(18.30)	354(11.79)	
Mother's race	White	1 038(80.53)	2 160(71.95)	
	Black	202(15.67)	723(24.08)	<0.001
	Others	49(3.80)	119(3.97)	
Infant sex	Male	662(51.36)	1 533(51.07)	0.887
	Female	627(48.64)	1 469(48.93)	
Mother's educational level	Less than 12 years	219(16.99)	657(21.89)	<0.001
	12 years or more	1 070(83.01)	2 345(78.11)	
Marital status	Married	964(74.79)	1 995(66.46)	<0.001
	Not married	325(25.21)	1 007(33.54)	
Mother's smoking	Yes	62(4.82)	287(9.56)	<0.001
	No	1 287(95.18)	2 715(80.44)	
Labor complications	Yes	91(7.06)	182(6.06)	0.247
	No	1 198(92.94)	2 820(93.94)	
Ceasarian delivery	Yes	454(35.22)	2 030(67.62)	<0.001
	No	835(64.78)	972(32.38)	

[a] Note: Only yes responses are reported. [b] Significant p-values are in bold font. P-values of 0.05 or less were considered significant. [c] converted means the pregnancy has changed from twin to singleton after demise of co-twin.

Table 2

Rates of neonatal, post-neonatal and infant mortality among twins (converted versus non converted twin births), United States, 1995-2000[a]

Rates per 1 000 live births n=4291	Converted co-twin n (%)	Unconverted co-twin n (%)	P-value [a]
Neonatal death (<28 days)	41(3.18)	954(31.77)	<0.001
Post-neonatal death (28-364 days)	5(0.39)	53(1.77)	<0.001
Infant death (0-364 days)	46(3.57)	1007(33.54)	<0.001

[a] Significant p-values are in bold font. P-values of 0.05 or less were considered significant.

Table 3 presents summary estimates for the adjusted hazard ratios for neonatal, post-neonatal and infant deaths in relation to types of twin programming for first comparison (converted versus unconverted) and selected medical risk factors. The risk for all types of mortality was reduced for converted as compared to unconverted twins [Adjusted hazard ratio, *HR* (95% confidence interval, *CI*) for neonatal death=0.18(0.09, 0.34), post-neonatal death=0.59(0.06, 5.28) and infant death=0.22(0.12, 0.40)]. Although lower, the reduced risk for post-neonatal death is not statistically significant. The most interesting factor associated with subsequent death of the surviving twin was mother's race. For infants of black mothers as compared to white mothers, the risk for post-neonatal death increased by 89% (*HR*=1.89, 95% *CI*=1.03, 3.48), while we see a borderline significance reduction for neonatal death by 10% (*HR*= 0.90, 95% *CI*=0.77, 1.05), and for infant death by 6% (*HR*=0.94, 95% *CI*=0.80, 1.09). We found no significant difference between white versus other (non-black or white races). We found also no statistically significant difference with respect to mother's age despite the hazard ratio being consistently lower for older mothers. Marital status and place of delivery also show no significant difference.

Compared to female babies, males were at 11% lower risk of neonatal death (*HR*=0.89, 95% *CI*=0.79, 1.00) and at 12% lower risk of infant death (*HR*=0.88, 95% *CI*=0.78, 0.99) but no significant difference for post-neonatal death (*HR*=0.86, 95% *CI*=0.40, 1.16). Babies delivered via cesarean section were at lower risk of neonatal death (*HR*=0.73, 95% *CI*=0.60, 0.89) and infant death (*HR*=0.75, 95% *CI*=0.62, 0.90) than those delivered by vaginal route. High maternal education decreased the risk of neonatal death (*HR*=0.78, 95% *CI*=0.67, 0.91) and infant death (*HR*=0.77, 95% *CI*=0.66, 0.90).

Summary estimates for the adjusted hazard ratios for neonatal, post-neonatal and infant deaths in relation to types of twin programming for second comparison (converted versus same-quantile twins) and selected medical risk factors are presented in Table 4. As was the case for the first comparison, the risk for all types of mortality was reduced

Table 3

Hazard ratios (95% *CI*) for predictors of infant mortality among Converted *vs.* Unconverteda surviving co-twins.

Parameters	Predictors	Neonatal death HR (CI) [b]	Post-neonatal death HR (CI) [b]	Infant death HR (CI) [b]
Twin to singleton conversion	Unconverted twin	1.00	1.00	1.00
	Converted twin	0.18(0.09, 0.34)	0.59 (0.06, 5.32)	0.22 (0.12, 0.40)
Maternal age	Less than 18 years	0.76(0.56, 1.01)	1.06 (0.33, 3.34)	0.77 (0.58, 1.02)
	18 to 34 years	1.00	1.00	1.00
	35 years or more	0.93 (0.75, 1.15)	0.92 (0.39, 2.18)	0.93 (0.75, 1.14)
Maternal race	Black	0.90 (0.77, 1.05)	1.89 (1.03, 3.48)	0.94 (0.80, 1.09)
	White	1.00	1.00	1.00
	Others	0.92(0.64, 1.32)	2.94(1.13, 7.63)	1.01(0.72, 1.41)
Infant sex	Male	0.89 (0.79, 1.00)	0.86 (0.40, 1.16)	0.88 (0.78, 0.99)
	Female	1.00	1.00	1.00
Marital status	Married	1.00	1.00	1.00
	Non married	1.01 (0.87, 1.17)	1.14 (0.62, 2.12)	1.01 (0.87, 1.17)
Place of delivery	Clinic	0.82 (0.52, 1.31)	0.83 (0.48, 1.43)	0.86 (0.54, 1.37)
	Not clinic	1.00	1.00	1.00
Type of delivery	Caesarean section	0.73 (0.60, 0.89)	1.00 (0.58, 1.73)	0.75 (0.62, 0.90)
	Vaginal birth	1.00	1.00	1.00
Complications	Yes	0.93 (0.69, 1.24)	1.01 (0.36, 2.82)	0.92 (0.70, 1.22)
	No	1.00	1.00	1.00
Maternal education level	More than 12 years	0.78(0.67, 0.91)	0.66(0.35,1.28)	0.77(0.66, 0.90)
	12 years or less	1.00	1.00	1.00
Gestational age		0.72(0.71, 0.73)	0.96(0.87, 1.05)	0.73(0.72, 0.74)
Birth weight		0.99(0.98, 0.999)	0.99(0.98, 0.999)	0.99(0.98, 0.999)

[a] Significant p-values are in bold font. *P*-values of 0.05 or less were considered significant. [b] *HR* = Hazard Ratios, *CI* = 95% Confidence Intervals.

for converted as compared to same-quantile twins [Adjusted hazard ratio, *HR* (95% confidence interval, *CI*) for neonatal death=0.69(0.50, 0.96), post-neonatal death=0.66(0.27, 1.58) and infant death=0.57(0.42, 0.77)]. Although lower, the reduced risk for post-neonatal death is not statistically significant. The race of the mother plays an important role. Compare to whites, the risk of post-neonatal death increased for both black (*HR*=1.79, 95% *CI*=1.53, 2.09) and Others: non-white or black (*HR*=1.73, 95% *CI*=1.29, 2.32). By contract, neonatal death decrease by 8% (*HR*=0.83, 95% *CI*= 0.73, 0.93) for blacks compared to whites.

Table 4

Hazard ratios (95% *CI*) for predictors of infant mortality among Converted co-twins *vs* Same-quantile co-twins[a].

Parameters	Predictors	Neonatal death HR (CI) [b]	Post-neonatal death HR (CI) [b]	Infant death HR (*CI*) [b]
Twin to singleton conversion	Same-quantile twin	1.00	1.00	1.00
	Converted twin	0.69(0.50, 0.96)	0.66 (0.27, 1.58)	0.57 (0.42, 0.77)
Maternal age	Less than 18 years	0.86(0.68, 1.09)	1.05 (0.74, 1.48)	0.82 (0.67, 0.99)
	18 to 34 years	1.00	1.00	1.00
	35 years or more	0.87 (0.74, 1.01)	0.71 (0.57, 0.89)	0.80 (0.71, 0.91)
Maternal race	Black	0.83 (0.73, 0.93)	1.79 (1.53, 2.09)	1.08 (0.98, 1.19)
	White	1.00	1.00	1.00
	Others	0.89(0.68,1.16)	1.73(1.29,2.32)	1.16(0.95, 1.42)
Infant sex	Male	0.93 (0.85, 1.02)	0.81 (0.71, 0.92)	0.89 (0.83, 0.96)
	Female	1.00	1.00	1.00
Marital status	Married	1.00	1.00	1.00
	Non married	0.93 (0.83, 1.04)	1.91 (1.64, 2.22)	1.17 (1.07, 1.28)
Place of delivery	Clinic	0.66 (0.45, 0.97)	0.50 (0.19, 1.34)	0.66 (0.46, 0.95)
	Not clinic	1.00	1.00	1.00
Type of delivery	Caesarean section	1.00 (0.89, 1.12)	1.15 (1.01, 1.32)	0.98 (0.90, 1.07)
	Vaginal birth	1.00	1.00	1.00
Complications	Yes	0.90 (0.74, 1.10)	1.12 (0.89, 1.42)	0.96 (0.83, 1.12)
	No	1.00	1.00	1.00
Maternal education level	More than 12 years	0.84(0.75,0.96)	0.61(0.52,0.71)	0.74(0.67,0.81)
	12 years or less	1.00	1.00	1.00
Gestational age		0.62(0.61,0.63)	0.86(0.84,0.88)	0.66(0.65,0.66)
Birth weight		0.99(0.98,0.999)	0.99(0.98,1.00)	0.99(0.98,1.00)

[a] Significant *P*-values are in bold font. *P*-values of 0.05 or less were considered significant. [b] *HR*=Hazard Ratios, *CI*=95% Confidence Intervals.

The risk for all types of mortality was reduced for male as compared to female twins [Adjusted hazard ratio, *HR* (95% confidence interval, *CI*) for neonatal death=0.93(0.85, 1.02), post-neonatal death=0.81(0.71, 0.92) and infant death=0.89(0.83, 0.96)]. Babies delivered via cesarean section were at higher risk of post-neonatal death (*HR*=1.15, 95% *CI*=1.01, 1.32) than those delivered by vaginal route. High maternal education decreased the risk of all type of mortality [neonatal death (*HR*=0.84, 95% *CI*=0.75, 0.96), post-neonatal death (*HR*=0.61, 95%*CI*=0.52, 0.71 and infant death (*HR*=0.74, 95% *CI*=0.67, 0.81)]. Deliveries in a clinic were associated with lower risk of neonatal death (*HR*=0.66, 95% *CI*= 0.45, 0.97) and infant death (*HR*=0.66, 95% *CI*=0.46, 0.95) as compared to those outside a clinic setting. Older mothers show a low risk of all types of infant death (neonatal, *HR*=0.87, 95% *CI*=0.74, post-neonatal, *HR*=0.71, 95% *CI*=0.57, 0.89, infant death, *HR*=0.80, 95% *CI*= 0.71, 0.91) as compare to younger mothers.

4. Discussion

The matched multiple birth file was used in this paper to study the impact of intrauterine demise of a co-twin on neonatal, post-neonatal and infant mortality of the surviving sibling. Findings from this study suggest that the death of the co-twin confers a survival advantage for the sibling, namely a lower risk of neonatal, post-neonatal, and infant death. To our knowledge this is the first study to report an advantage (in terms of survival through infancy) associated with conversion of a twin pregnancy to a singleton gestation.

Another significant finding of our analysis is the impact of maternal education on survival of surviving co-twins. Maternal education was inversely associated with the risk of death of the surviving co-twin. Offspring of mothers with more than 12 years of education had lower risk of neonatal, post-neonatal and infant death as compared to those born to women with 12 years or less of education. A surprised finding of our study is an increased risk of infant mortality among mothers between 18 to 34 years as to compared to age <18 years. Previous studies have shown that teenage pregnancies, in general, are associated with an increased risk of neonatal mortality[18, 19]. They reported that an increased risk may be linked to biological immaturity[20] although other factors might also play a role[21–22].

Despite multiple reports of increased mortality associated with complications in twin pregnancies[21–24]. For example, Spellacy *et al*. [25], found that twin pregnancies were complicated by elevated risk for hypertension, anemia and placental abruption. Our study did not find a significant association between mortality and complications (anemia, preeclampsia, hypertension, placental abruption, diabetes and previa).

This study confirms findings from previous researchers that twin infants born to black parents are at a higher risk of mortality when compared to their white counterparts[26, 27]. A two fold risk of post-neonatal death was observed in infants of black mothers as compared to white mothers. But in contract a low risk of neonatal is observed when converted twins are compared to same-quantile co-twins who reached the same quantile of the birth weight distribution at the same gestational age, but who could not switch to singleton programming because their co-twin also survived and was delivered alive. A decreased risk of neonatal, post-neonatal and infant mortality was observed for male offspring as compared to female. Our finding of an elevated risk of post-neonatal death in converted *vs* same-quantile twins comparison after the demise of a twin sibling is also in agreement with prior reports of cesarean delivery being a risk factor for singleton deaths, as a converted co-twin is now analogous to a singleton[28]. But in contrast a low risk is observed when converted are compared to unconverted only.

This paper shows that mothers' age plays an important role in the rates of conversion from twin to singleton pregnancy. Rates of conversion to singletons increased with increasing age. Mothers < 34 years old were more likely to deliver unconverted twin than converted twins. Those 35 or older had a greater likelihood of having converted than unconverted twins. This finding could explain the lower risk of all mortality types among surviving co-twins from mothers that were 35 years old, as conversion is associated with lower risk of death.

Our study has limitations. The findings in this study are only applicable to surviving co-twins of already viable twin pregnancies. The pregnancies included in this study were of 20 weeks of gestation. This selection excludes application of the findings to spontaneous partial fetal loss before attainment of viability. In addition, Assisted Reproduction Technology (ART) is responsible for approximately 16% of the twin pregnancies in the United States[29]. However, we are unable to comment on the generalizability of our findings to pregnancies conceived through ART, as the database used lacks that specific information. ART-related multifetal pregnancies are considerably more common among whites, and the elective surgical reduction in the number of growing fetuses may be associated with a worse prognosis of the surviving co-twin, therefore a potential confounding by elective fetal reduction by race is also possible. It is known that the prognosis of the surviving twin in a dichorionic twin pregnancy is better than in a monochorionic twin gestation[9]. Unfortunately we lack information

on whether the pregnancy is dichorionic or moochorionic.

A major strength of our study is the substantial sample size of the data used in our analysis. The data was extracted from over 600 000 surviving co-twin birth records, making it the largest population-based study on co-twin delivery. The use of a national population database also makes our outcome less likely to be influenced by selection bias and provides valuable and reliable information for future studies in surviving co-twin research.

This study shows that there are survival advantages for the surviving co-twin after the demise of the co-twin. Timely intervention before the 27th week of gestation and helping the fetus reach the critical mass needed for conversion can decrease the likelihood of death for the surviving co-twin. Also, identifying important protective factors and interventions that help in the conversion of the surviving co-twin can help in increasing its survival rate. More research is needed to understand factors associated with neonatal and infant mortality in twin pregnancies complicated by the death of one member of the twin pair.

Conflict of interest statement

We declare that we have no conflict of interest.

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