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Review Article

The Effect of Twin Birth on Neonatal and Infant Mortality Rates: A Systematic Review

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Abstract

Background and aims: Twin birth may account for higher mortality rates in infants and neonates. To investigate the potential relationship between twin birth and infant and neonatal mortality rates (NMRs), a systematic review was conducted.

Methods: To gather the evidence for the relationship between twin birth and its potential effect on mortality during infancy and neonatal periods, a systematic review was conducted. The most important used databases were PubMed, Google Scholar, Web of Science, Scopus, ProQuest, Cochrane and Springer. Then, the databases were searched by appropriate keywords. After reviewing and evaluating the collected studies, trends in the different countries were compared.

Results: A total of 13 790 related studies were found, of which 128 studies were selected in the first step. The studies which were not related to the subject, in addition to repetitive studies, were excluded from the search in the second step based on inclusion and exclusion criteria by reviewing the abstract and, in some cases, the full article. Finally, 7 studies entered the last step.

Conclusion: This study showed that the mortality could be higher among twins than among non-twins, especially among boys.

Keywords: Twin, Twin birth, Infant mortality rate, Neonatal mortality rate, Monogamy pregnancy

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Introduction

Over the last decades, the incidence rate of multiple pregnancies has increased substantially due to older maternal age and the broader use of assisted reproduction techniques.[1] Multiple pregnancies can be considered as high-risk pregnancies with potential undesirable pregnancy outcomes as well as further complications, especially in childhood compared to the singletons.[2] Monozygotic twins may have a higher risk of fetal death, prenatal mortality and infant mortality rates than heterozygotic twins based on case reports and hospital-based case series,[3] which is about 4 to 6 times higher in twins than in singletons.[4] Moreover, there are many differences between twin and singleton pregnancies from many physiologic and pathologic perspectives; these differences make twins more vulnerable to environmental damage, both inside and outside of the mother's uterus .[5] In addition, twins are expected to experience a higher risk of harmful birth outcomes than singletons. Furthermore, the stillbirth and neonatal mortality rates could also be about 4 times and 5 to 7 times higher in twins than in singletons, respectively.[6] It would be worth to mention that fetal mortality rate is defined as a spontaneous intra-uterine death that is delivered after 28 completed weeks of pregnancy,[3] neonatal mortality rate (NMR) is the death of any live-born infant within 28 days of his/her birth based on the World Health Organization's (WHO's) standard definition, and infant mortality rate (IMR) is defined as the death of any live-born infant about 365 days after his/her birth.[7]

The increase in multiple pregnancies may be accompanied by an enhancement of preterm birth; moreover, women who have had the multiple births could prefer to choose cesarean section more than others.[8] In addition, one of the reasons for twin death could be the premature birth as well as limited embryonic growth in the mother's uterus.[9] Twins may account for about 10% of all prenatal mortality, which might be exclusively due to premature births. Furthermore, various studies have shown that twins may have a lower Apgar score,

the lower cardiac parameters and lower incidence of bleeding in the abdominal cavity; in addition, the rate of respiratory stress and necessity for intubation in the hospital may be much higher among them.[10] Multiple pregnancies could be associated with a higher risk of low birth weight (LBW) with potential long-term and chronic consequences; there are also disorders such as cerebral palsy and sudden death syndrome.[11] For instance, the prevalence of cerebral palsy might be between 7 and 12 per 1000 infant survivors in twins compared to 1 to 2 in singletons. In addition, monozygotic twins might be at a higher risk of cerebral palsy than heterozygotic twins.[3] Race may also affect twin pregnancies, which may be related to LBW and fetus, neonatal and IMRs. For example, in the United States, mortality rates were higher in black twins than in white twins.[5] The other reasons of death among twin births might be the sudden death syndrome; in addition, they may have attention deficit, hyperactivity disorder and delays in physical growth with potential increase in intensive care.[11]

It should be noted that while the rate of monozygotic twins, which is common all over the world, fluctuates between 3 and 5 per 1000 pregnancies, the rate of heterozygotic twins may be varied from 1.3 in Japan to 49 in Nigeria per 1000 pregnancies, even before the assisted reproductive techniques.[12] Although a small percentage of births in the United States and the United Kingdom are multiple births (about 3%), they may have more adverse effects which account for 16% of deaths in the UK.[13] Moreover, since 1998, the incidence of triple pregnancy has declined in England and Wales as well as Japan; therefore, the annual number of triplet pregnancies has been decreased gradually from 337 in 1195 to 246, 219, 181 and 157 pregnancies in 2005, 2006, 2007, 2008 and 2009, respectively.[12] Because of the relatively higher mortality in twins compared to singletons, the identification of the potential factors affecting deaths and investigation and discovery of the effective interventions leading to the reduction of death rates among twins are the main aims of this article.

Methods

In this systematic review, the articles published until January 2018 about twins, neonatal and infant mortality and their relationships were searched. Different databases were used for the study. At first, most popular databases were used including PubMed, Google Scholar, Web of Science and Scopus as well as Science Direct, ProQuest, Cochrane and Springer. The keywords were "infant mortality", "infant death", "neonatal mortality", "neonatal death", "twin mortality", "twin death", "Twin AND Infant AND Neonatal mortality/death" and "Twin infant neonatal mortality", "Twin AND infant mortality rate", "Twin AND Neonatal mortality rate" and "Twin AND neonatal and infant mortality rate". Figure 1 shows the results of this search.

Inclusion and Exclusion Criteria

The twins who have died in the neonatal period (in the first month of life) or in infancy (in the first year after birth) met the inclusion criteria. The desired outcome for searching was neonatal and infant mortality. In the terms of time, the articles published from 1996 to 2016 were selected. After detailed studying of 128 studies, the articles with little relevance to the subject were reviewed again, and then 18 articles remained. The full texts of these articles were studied again. After selecting the articles, their qualitative assessment was measured by STROBE checklist according to the criteria such as relevance to the topic, the responsiveness of the study to the research question and the quality of the articles.

Finally, 7 articles related to the research topic entered the final phase of the study. Table 1 shows the details of the final studies.

A data extraction table (in excel format) was used to collect the required data from the final articles containing information such as the title of the article, authors name, year of publication, location of the study, the age of study population, type of study, and so on.

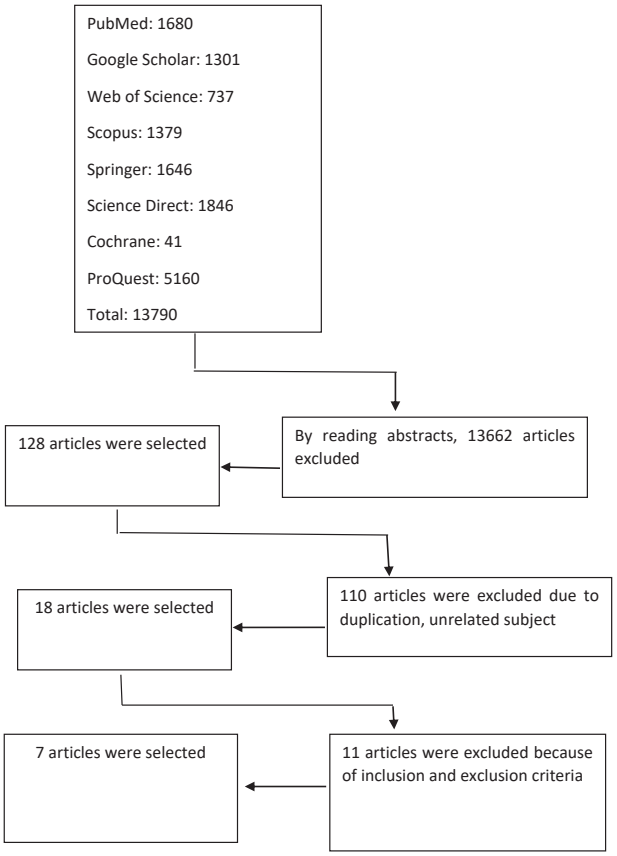

Figure 1. Search Results Details.

Table 1. The Final Articles Entered the Study

Author, Year	Country	Type of Study	Age Group	Quality of Study
Dunn A,[13] 1996	England	Trend	Newborns and infants	Good
Jaffar S,[14] 1998	Gambia	Trend	Newborns and infants	Medium
Alam N,[15] 2007	Bangladesh	Trend	Infants	Good
Burgess JL,[16] 2014	USA	Retrospective cohort study	Newborns	Good
Getahun D,[8] 2014	USA	Trend	Newborns and infants	Good
Smith LK,[17] 2014	England	Trend	Newborns	Good
Miyahara R,[18] 2016	Gambia	Trend	Newborns and infants	Good

Results

In this study, the trends of mortality in twins during the neonatal period and infancy in the United Kingdom, the United States, Gambia and Bangladesh were compared and investigated. The comparison of trends showed that in the past, the most important causes of death in newborns and infants were contagious diseases; however, with the advancement of medical and health situation, mortality from infectious diseases have been reduced, and other causes such as sudden death syndrome, cerebral palsy, complications of the placental abruption, hypoxia in the uterus and congenital anomalies have been more prevalent. On the other hand, in the countries like the Gambia, an African country, the problem of communicable diseases is still the main causes of death in neonatal period and infancy in twins. For example, a study conducted between 1989 and 1993 in the Gambia showed the statistics of stillbirth and live births in neonatal and postnatal periods in twins (Table 2). It can be seen in Table 2 that the mortality rate was higher in the early neonatal period than in the late neonatal and postneonatal period. In addition, the neonatal and IMRs were higher in twin boys than in twin girls.

The causes of twin mortality in this country are shown in Figure 2. It can be seen that 44.9% of the causes of neonatal mortality in the Gambia were unknown, and the causes associated with contagious diseases were: malaria disease (0.9 %), sepsis (7.5%), tetanus (3.7%), and various causes (32.7%), gastroenteritis (0.9%), and reasons that they do not agree on, was 7.5%. The reasons for post-neonatal mortality are shown in the above diagram as well.[14,18]

In Bangladesh, as a developing country, the mortality rate of multiple births between 1975 and 2002 is shown in Table 3.[15] The number of deaths of multiple births

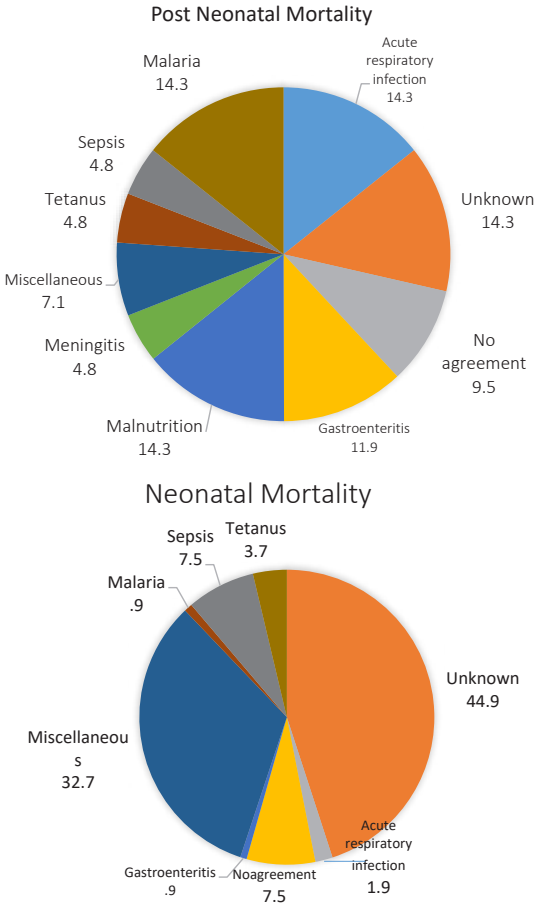

Figure 2. Causes of Death Among Neonatal and Post-Neonatal Twins

Table 2. Mortality Rates of Gambian Twins in Both Genders from 1989 to 1993

	Boys	Girls
Early neonatal mortality rate	142.9	90.9
Late neonatal mortality rate	57.7	37.4
Post-neonatal mortality rate	60.4	72.2

has decreased from 1975 to 2002, which may be due to the improvement of the health services and progress in medical sciences. In addition, the neonatal and infant mortality rates in twin boys were more than twin girls.[14,18]

The factors related to the death of multiple births in Bangladesh are shown in Table 4. The factors associated with the infant and neonatal mortality in twins were gender, mother's age during pregnancy, birth order, the birth interval with the previous child, mother's education level, household asset quintile, parent's religion and the type of health care services. The most related factor was the first birth order with an odds ratio of 1.6 and the least was maternal education with the odds ratio of 0.27 for Grade X.[15]

Table 3. Neonatal and Infant Mortality Rates Among Twin Birth Cohorts in Bangladesh from 1975 to 2002

Infant Birth Cohort	IMR Per 1000 Live Births (N)	Neonatal Birth Cohort	NMR Per 1000 Live Births (N)
1975-1984	485.4(615)	1975-1984	364.8(472)
1985-1994	475.1(620)	1985-1994	338.3(456)
1995-2002	355.9(294)	1995-2002	363.3(228)

Table 4. Factors Related to Twin Deaths in Bangladesh From 1975 to 2002

Newborns			Infants		
Risk Factors		**Rate Per 1000 Live Birth (the Number of Death)**	**Risk Factors**		**Rate Per 1000 Live Birth (the Number of Death)**
Gender	Male	441.3 (752)	Gender	Male	346.4(603)
	Female	458.7(777)		Female	313(553)
Maternal age	<20	594.1(180)	Maternal age	<20	493.6(155)
	29-20	454(839)		29-20	326.5(625)
	39-30	409.7(458)		39-30	294.9(338)
	40 +	403.1(52)		40 +	(38) 283.6
Live birth order	1	574.1(93)	Live birth order	1	458.8(78)
	4-2	459.7(771)		4-2	346.2(603)
	5 +	426.6(665)		5 +	297.6(475)
Birth interval	<24 months	(224) 557.2	Birth interval	<24 months	445.8(185)
	24–35 months	481.1(357)		24–35 months	331.6(251)
	36–59 months	378.3(370)		36–59 months	270.9(272)
	60 + months	358.2(144)		60 + months	244(102)
	Unknown	478.3(341)		Unknown	360.2(268)
Maternal education	None	471.4(973)	Maternal education	None	343.6(728)
	Grade I–IV	487.7(198)		Grade I–IV	356.6(148)
	Grade V	406(177)		Grade V	309.1(140)
	Grade VI–IX	363.3(113)		Grade VI–IX	268.7(90)
	Grade X+	18)216.9)		Grade X+	131(11)
	Unknown	510.2(50)		Unknown	382.4(39)
Household asset quintile	Lowest	496.7(302)	Household asset quintile	Lowest	366.6(228)
	Second	407.3(309)		Second	332.3(223)
	Middle	477.5(308)		Middle	358.4(238)
	Fourth	407.3(292)		Fourth	290.5(215)
	Highest	421.4(276)		Highest	327(222)
	Unknown	362.1(42)		Unknown	227.3(30)
Parents' religion	Muslims	441.2(1178)	Parents' religion	Muslims	320.2(884)
	Hindus	482.1(351)		Hindus	364.1(272)
Type of health services	Government	480.3(901)	Type of health services	Government	351.8(685)
	Private	412.6(628)		Private	301.7(477)

In a study carried out during1995-1996 and 2005-2006, the statistics were compared with each other.[8] In the United States, because of advanced medical and health services, other causes have also been studied. The causes of twin death can be attributed to factors such as congenital malformations, complications of pregnancy, respiratory distress syndrome, spinal and neurological complications, intrauterine hypoxia, infection and other causes. The most common reasons for the neonatal death in twins was due to the other causes and the least was contagious diseases because of the advanced medical and health services. Furthermore, there was a correlation between the maternal age and the NMR in twins (Figure 3). Twins who were born at the 34th week of pregnancy may have a higher mortality rate and by increasing gestational age, twin mortality could be significantly reduced.

In England and Wales, the trend of mortality in twins has declined (Table 6). The number of neonatal deaths in twin has gradually decreased from 1997 to 2008 which follows the pattern of developed countries and the number of twins birth has increased.[13,17]

Conclusion

The main aim of this article was to investigate whether

Table 5. Causes of Death Among American Twin Neonates Born during 1995-96 and 2005-2006[8]

	Neonatal Deaths 1995–1996		Neonatal Deaths 2005–2006	
	Rate	N	Rate	N
Congenital anomalies	605	3	608	2.2
Maternal complications of pregnancy	583	2.8	711	2.6
Respiratory distress syndrome	542	2.5	379	1.4
Complications of placenta/cord/membranes	381	1.8	395	1.4
Intrauterine hypoxia	59	.30	86	.30
Infection	170	.70	326	1.2
Other causes	2304	12	3051	11.1
Total	4644	23.1	5556	20.2

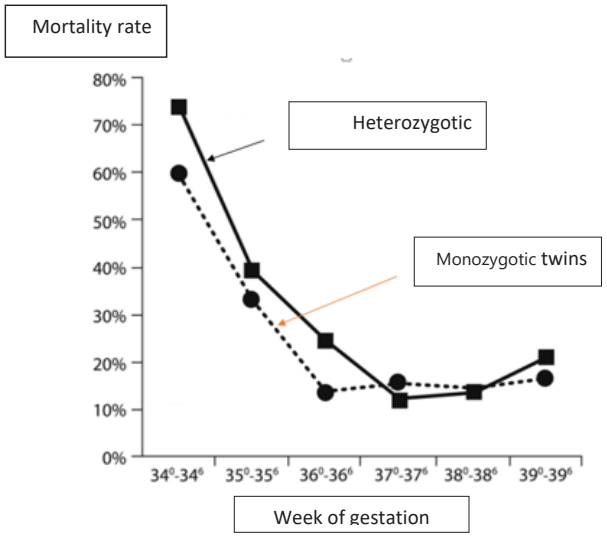

Figure 3. Comparison of Monozygotic and Heterozygotic Twins.[16]

Table 6. Neonatal Mortality Rates in England and Wales from 1997 to 2008

Year of Birth	Number	Rate in 1000 Live Birth
2000-1997	1222	187.4
2004-2001	1098	164.4
2008-2005	1164	152.7

there is any relationship between twin birth and infant and NMRs. By searching several databases, the comparison of trends in developed and developing countries has been conducted.

The findings of this study showed that the birth of twins has increased because of the advancement in the sciences, especially in developed countries over time. The trends showed that in the past, the most common causes of mortality of newborns and infants were infectious illnesses; however, with the advancement of medical and health technologies, mortality from communicable diseases have been decreased and the causes of twin death could be due to other causes such as premature birth, sudden death syndrome, neuropathic paralysis, complications of placenta, hypoxia in the uterus and congenital anomalies increased.[8] However, in developing countries such as South Africa, some communicable diseases like tetanus, malaria, gastroenteritis, blood infections, malnutrition and LBW could still be the leading causes of death. In these countries, there is no systematic study of the causes due to the poor levels of medical and health services.[14]

In developed countries, the number of twin pregnancies has increased, which is particularly notable over the past two decades. This might be due to the growth of in vitro fertilization in women. In fact, according to official statistics in 2000, about 7% of twin pregnancies are associated with assisted reproductive technology (ART). On the other hand, because of the use of cesarean section for delivery, the number of the premature births has been increased, which may in turn increase the number of twin deaths.[8]

Furthermore, the study of trends in developed countries showed that women who have lower socioeconomic status and lived in deprived areas, were less likely to have twin pregnancies, especially women over the age of 35.[13]

Ultimately, this study showed that the mortality rates in twins would be greater than in singletons, with higher rates among boys than girls.[14,15]

Ethical Approval

Not applicable.

Conflict of Interest Disclosures

None.

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