

## Research Article

# Congenital malformations in multiple births

Sharada B. Menasinkai<sup>1\*</sup>, Dakshayani K. R.<sup>1</sup>, M. A. Chiniwar<sup>2</sup>

<sup>1</sup>Department of Anatomy, Mysore Medical College and Research Institute, Mysore, Karnataka, India

<sup>2</sup>Department of Obstetrics and Gynecology, Mysore Medical College and Research Institute, Mysore, Karnataka, India

**Received:** 7 June 2013

**Accepted:** 14 June 2013

### \*Correspondence:

Dr. Sharada B. Menasinkai

E-mail: drsharadabm@gmail.com

© 2013 Menasinkai SB et al. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Objective:** The present study was done to know and compare the incidence of congenital malformations in singleton and multiple births in our hospital & compare with other studies.

**Methods:** A retrospective study done by collecting the data from parturition register from Jan 2008 to Dec 2011 (4yrs) from Cheluvamba Hospital attached to Mysore Medical College and Research Institute. Total number of the live births, still births, and abortions > 20 wks were collected. Details of multiple births such as maternal age, gestational age, sex & birth weight of the babies, U/S reports and congenital anomalies (CA) were noted.

**Results:** The total number of singleton births were 48700 and number of babies who had congenital malformations were 235 (48.25/10,000 births). Total number of multiple births were 579 including 10 triplets and number of babies who had CA were 11 (189.98/10,000 births,  $P < 0.0001$ ). In the present study sex of the babies were noted in all multiple births and zygosity could not be recorded. Among 579 multiple births 404 were of the Same Sex (SS) and 165 were of Opposite Sex (OS) in twins and 6 were of the same sex and 4 were of opposite sex in triplets. According to Weinberg formula 50% of same sex (SS) twins are monozygotic and 50% are dizygotic twins. Among the 11 babies with CA, 4 monozygotic twins had anomalies related to twinning such as Acardia with TRAP sequence (3 twins), and Thoracophagus (1 twin). 5 babies had CNS anomalies, 1 with cystic hygroma, 1 baby with multiple system affected.

**Conclusion:** The incidence of birth defects is more in multiple births and especially in monozygotic twins. In the present days increase in twinning rate due to advanced maternal age, hereditary factors and use of ovulation inducing drugs, which results in premature and low birth wt babies associated with poor lung maturity.

**Keywords:** Zygosity, Acardia with TRAP sequence, Thoracophagus, Cystic hygroma, MZ, DZ

### INTRODUCTION

Congenital malformations are major source of pediatric morbidity and mortality. Despite their clinical importance nothing is known of their etiology, only a handful of genetic and environmental determinants of birth defects have been clearly defined, accounting for only a small portion of all birth defects. Congenital malformations are more common in twins than singleton births. All twin pairs have a relatively similar intrauterine environment. Monozygotic (MZ) twins are identical genetically, but

Dizygotic (DZ) twins are no more similar genetically than other siblings. Congenital malformations are more common in monozygotic twins than DZ twins.<sup>1</sup>

Incidence of twinning is 1 in 80 in all pregnancies in UK. MZ twinning occurs in 1 in 300 births in all population, and DZ twinning occurs in 1 in 100 to 500 pregnancies. Late division >2 wks after conception can result in conjoint twins, 1 in 50,000 pregnancies. Increase in DZ twinning is due to advanced maternal age, positive family history of multiple births and use of ovulation inducing drugs.<sup>2</sup>

Previous studies inconsistently suggest that there may be an association between birth defects and multiple births. Children from multiple births who had birth defects were generally preterm, low birth wt and poor lung maturity. In most of the multiple births, only one child was born with birth defects (81% twins, 71% triplets).<sup>3</sup>

## METHODS

A study was done to compare the incidence of congenital malformations in singletons and multiple births. Data collected from Cheluvamba Hospital parturition records from Jan 2008 to Dec 2011 (4 yrs). It is a teaching hospital attached to Mysore Medical College and Research Institute. The data includes details of babies such as weight & sex of all the live births, still births and abortions >20 wks was recorded. In babies with congenital anomalies details of U/S reports, and pediatrician opinion was recorded.

## RESULTS

Total births were 49279 (235 multiple births) and babies with CA were 246 (11 among multiple births).

**Table 1: Showing the incidence of congenital anomalies in singleton and multiple births.**

Births	Number	number of babies with CA	Incidence /10,000 births
No of Singleton births	48700	235	48.25
No of multiple births	579 (10 triplets)	11 (2 triplets)	189.98
Total	49279	246	49.35

Chi Square test = 23.14, P< 0.0001.

The incidence of congenital anomalies in multiple births is 3 to 4 times higher than that of singleton births and is statistically significant. The rate of multiple births has remained same.

The zygosity was not determined in the majority of the multiple births. To estimate the proportion of monozygotic (MZ) and dizygotic (DZ) twins, we have utilized the Weinberg formula. All twin pairs are classified as same sex (SS) or opposite sex (OS). All opposite sex twin pairs are DZ whereas, 50% of same sex twin pairs are MZ and 50% are DZ.<sup>1</sup> So among total 579 twins in the present study 404 were same sex twins, and 165 were opposite sex twins. There were 10 triplets, 6 of same sex and 4 opposite sex. So 374 were DZ twins and 205 were MZ twins. Zygosity is important as congenital anomalies are more frequent among MZ twins.

2 Acardiac twins (photo 1& 2) and 1 conjoint twin (photo 3) were sent to Dept of Anatomy for autopsy.

**Table 2: Showing the details of the multiple births.**

Zygosity				
Twins	SS	404	Monozygotic twins	205
Twins	OS	165	Dizygotic twins	374
Triplets	SS	6		
Triplets	OS	4		

**Table 3: Congenital malformations in multiple births.**

Sl no	Congenital anomaly	Number of babies	Sex of the baby	Zygosity
1	Associated with twinning			
	Acardia with TRAP sequence	3	2 M pairs, 1 F	MZ
	Conjoint twin	1	1 F pair	MZ
2	Central nervous system			
	NTD	3	3 F	2 SS, 1 DZ
	Encephalocele	2	2 M	2 DZ
3	Others			
	Cystic Hygroma	1	1 M	1 DZ
4	Multiple system involved			
	Exomphalos, ambiguous sex, imperforate anus	1	Ambiguous sex	1 of triplet DZ
	Total	11 babies	5 M, 5 F, 1 ambiguous sex	

## DISCUSSION

Despite the lack of zygosity determination some interesting inferences could be made regarding Congenital Anomalies (CA) in SS and OS twins. Anomalies associated with twinning were substantially elevated in SS twins, whereas CA in OS twins were similar as in singleton births suggesting an increased risk is limited to SS twins. The data on occurrence of malformations among births during 4 yrs duration in our

hospital is presented here. The present data is smaller when compared with international studies.



**Photograph 1: Acardiac twin.**



**Photograph 2: Acardiac twin.**



**Photograph 3: Thoracophagus**

Methods Data were abstracted from UK population based Northern Multiple Pregnancy Register and Northern Congenital Abnormality Survey, 1998-2004 (6 yrs), by Pharoah PO et al.<sup>4</sup> Among 3311 twin conceptions both conceptuses were lost at <16 wks gestation in 67 and one in 142 conceptions. Of the 142 singleton survivors, 2 died in infancy, 2 were terminated for CA and 11 of the 138 had CA. 4265 babies with birth defects among 206,914 singleton births (206.1/10,000), and 197 among 5948 twins (331.2/10,000). Significant increase in the risk of birth defects among survivors of multiple conceptions.

**Table 4: Showing the comparison of CA with International studies.**

Authors	No of single births	No of babies with C A	Incidence/ 10,000 births	No of multiple births	No of babies with C A	Incidence /10,000 births
Pharoa et al	206914	4265	206.1	5948	197	331.2
Sipek et al	1,312,930	-	436	42448	-	598.38
Zhang et al	537593	-	266.97	7425	-	444.16
Glinianiaet al	147655	-	238.2	2329	-	405.8
Present study	48700	235	48.25	597	11	189.98

P.E. Doyle et al<sup>5</sup> reported an analysis of malformation rates in singleton and twin births using National Survey of births in England and Wales in 1979-1980 and 1982-1985. Number of singleton births were, 3,789,821 and total malformations 95510 and rate of incidence

252/10,000 births. There were 75844 twin births with total malformations were 1925 and incidence was 253.8/10,000 births. Incidence were calculated by number of malformations which were reported more in singleton births than in twins, where as rates in twins

were adjusted for maternal age by indirect standardization using the singleton rates as standard.

An analysis of occurrence of birth defects from single and twin pregnancies in the Czech Republic in 1994-2007 (13 yrs) reported by Sipek A et al<sup>6</sup>, there were 1,312,930 singleton births with incidence of birth defects 436 and 42448 twin births with incidence of birth defects 598.38 per 10,000 births respectively. There was increase in twin rate from 2.33% in 1997 to 4.17% in 2004. Zhang XH et al<sup>7</sup> reported a data obtained during 2007-2009, from hospital based birth defects surveillance system. There were 537593 singletons with incidence of CA 266.97/10,000 and 7425 multiple births (7303 twins & 122 triplets) and the incidence of birth defects was 444.16/10,000 births.

Glinianaia et al<sup>8</sup> reported an analysis of Northern multiple pregnancy Register and Northern congenital abnormality survey during 1998-2002 (4 yrs). There were 147655 singleton births with incidence of CA, 238.2/10,000 and 2329 twins with incidence of CA 405.8/10,000 births. Li SJ et al<sup>3</sup> analysed a data from Virginia Birth Defects Registry (VaCARES) during 1989-98. The incidence was 482.3 in singletons, 922 in twins and 1300 in triplets, quadruplets and above 2222.2 per 10,000 births. All these studies show higher incidence of CA compared with present study, probably due to accuracy of diagnosis and proper documentation of the statistics related to single/multiple births and congenital anomalies.

**Table 5: Showing the comparison of incidence of congenital anomalies in single and multiple births.**

Authors	Singleton births	No of babies with CA	Incidence of CA /10,000 births	Multiple births	No of babies with CA	Incidence of CA /10,000 births
Amar T et al	9262	171	184.6	62	2	322.5
Zamon T, Wal	28361	748	261	620	23	371
Nazer et al	48663	-	1720	448	-	3520
Present study	48700	235	48.28	579	11	189.98

Present study is comparable with studies reported by Amar T et al, Zamon T, Waland Nazer T et al.

Amar Taksande et al<sup>9</sup> reported a study from rural Medical College Hospital in central India. Among the 9262 singleton births 177 babies and 2 of the 62 pairs had congenital anomalies. Nazer J et al<sup>10</sup> reported a data from Hospital of University of Chile. There were 48663 singleton deliveries and incidence of CA 1720/10,000 births. There were 448 multiple births, incidence of CA 3520/10,000 births. Incidence of CA reported here is very high compared with present study.

Zamon T et al<sup>11</sup> reported prevalence of congenital anomalies in Pomeranian District, a data from Polish Register of Congenital Anomalies. There were 28361 singleton births with 748 babies with CA. Among the 620 multiple births 23 babies had congenital anomalies. Incidence of CA was 2.61% Singletons and 3.71% in multiple births.

Considering twin associated anomalies there were 4 cases in the present study, 3 acardiac twins and 1 thoracophagus. Epidemiological survey of CA in twins reported by Myrianthopoulos N C<sup>12</sup> in a small sample of 1195 twins with 219 babies with CA (18.33%) and 1 pair had conjoint twin. Nazer J et al<sup>10</sup> reported 4 pairs Siamese newborn malformations typical of MZ twins. 1 Acardiac

fetus with TRAP sequence, 1 fetus papiraceous, 2 hydroencephaly. Priyanka Gupta et al<sup>13</sup> reported 1 acardiac twin among 9 CA seen in 133 twins. In Japan Yoko Imaizumi<sup>14</sup> reported 112 conjoint twins during 1979-85, 60% were females. Tang Y et al<sup>15</sup> reported 122 conjoint twins among 4,282,536 births during 1996-2004 in China. Incidence of conjoint twin appears to be very high in China.

Anomalies affecting CNS are more in twin births as well as, singleton births. In the present study there were 5 babies of CNS anomalies (3 NTD, 2 others). According to Peter M et al<sup>1</sup> incidence of hydrocephaly was 16.39/10,000 and 8.2/10,000 in other CNS anomalies. Priyanka Gupta et al<sup>13</sup> reported 1 baby with Hydrolethrus syndrome (hydrocephalus, cleft lip and palate). According to Glinianaia et al<sup>8</sup> incidence of anencephaly and hydrocephalus was more than spina bifida in twin births.

Ghanashyam Das et al<sup>16</sup> reported a case of DZ twins with myelomeningocele which is a rare occurrence. Review of literature has revealed a large study of 96000 live births with congenital malformations only 3 pairs of twins were concordant for spina bifida. Studies implicating that twinning and neural tube defects may have common genetic and environmental factors. It was observed that upper neural tube defects were associated with excess twinning of MZ type or same sex DZ twins. In familial



association of neural tube defects with same sex DZ twins, delayed fertilisation has been implicated. Delayed fertilisation results on over ripe ova which lack cohesion and hence splitting of zygote. Similarly neural tube defects can be caused by lack of cohesion of neurulating cells.

Among the twins prevalence of spina bifida and myelomeningocele is reported to be less than singletons, with concordance rate of about 5.1% for MZ twins. Anencephaly was more frequent among same sex pairs than opposite sex pairs and singletons<sup>4</sup>. Twinning in neural tube defect may have common genetic or environmental factor.

In the present study total number of multiple births were less when compared to singleton births, where as congenital anomalies were less in both. The present study includes births more than 20 wks, live births and still births. The probable reason could be many multiple births end up in early abortions, (<16 wks). This Hospital is catering services to most of the rural pregnant women. The decrease in incidence of multiple births may be attributed to less use of ovulation inducing drugs. Most of the pregnant women were admitted as an emergency and may not have done ultrasonography.

Data from the population based study reported by Peter M et al<sup>1</sup> from Metropolitan Atlanta Congenital Defects Program (MACDP), show that the overall rate of malformed infants, as well as the incidence of several specific defects, is higher for twins than singletons. This elevated risk appears limited to same sex twins and is probably related to monozygosity. Among 4490 reported twinszygosity was not recorded and Weinberg formula applied and 50% of SS twins are DZ and 50% SS twins are MZ. PDA & TOF were more frequent in twins than singleton births.

In a study analysed by Hardin J et al<sup>17</sup>, a data from California Birth Defects Monitoring Program and vital statistics birth and fetal death records during 1983-2003 (10 yrs), the prevalence of cardiovascular defects in twins and singletons. There were 4858255 singleton births with 14078 babies with CHD. Among 54602 twins 628 babies had CHD. Increased prevalence was observed in twins compared to singletons in all 16 categories (ICD 10). Like sexed twin as a proxy of MZ twin has an increased prevalence of cardiovascular defects compared with unlike sexed twin. There were no babies with CHD in the present study.

Among the incidence of musculoskeletal anomalies (MSK) there is increase in positional foot defects due to uterine compression in multiple births. According to Peter et al<sup>1</sup> incidence of club foot was 28.69/10,000. The incidence of MSK anomalies reported by Sipek et al<sup>6</sup> is 90.93/10,000. Priyanka Gupta et al<sup>13</sup> reported 4 club foot out of 9 babies with C A. According Doyale PE et al<sup>5</sup> study musculoskeletal anomalies were less common. In

the present study there were no babies with musculoskeletal anomalies.

## CONCLUSION

There is higher incidence of birth defects among same sex twins compared to opposite sex and singleton births. Congenital anomalies associated with twinning such as, Acardiac twin with TRAP sequence and Conjoint twins are common with MZ twins, having higher risk of mortality and morbidity. Frequency of chromosomal anomalies in multiple births are same or less than singleton births.

## ACKNOWLEDGMENTS

We are thankful to the Hospital authorities for allowing us to collect the data from Medical Record Dept. We thank Dr. Mangala S., Asst Prof., Rajarajeshwari Medical College Bangalore and Dr. Seema Deepak, Assoc. Prof. M.M.C. & R.I. Mysore for the photographs of the two acardiac twins.

## REFERENCES

1. Peter M. Layde, J. David Erickson, Arthur Falek, Brian J. McCarthy. Congenital Malformations in Twins. *Am J Hum Genet* 1980;32:69-78.
2. Robert F. Mueller, Ian D. Young. Emery's Elements of Medical Genetics, Edinburgh Churchill Livingstone Harcourt Publishers Limited 2001. Developmental genetics 93-4.
3. Li SJ, Ford N, Meister K, Bodurtha J. Increased risk of birth defects among children from multiple births. *Birth Defects Res A Clin Mol Teratol* 2003;67:879-85.
4. Pharoah PO, Glinianaia SV, Rankin J. Congenital anomalies in multiple births after early loss of conceptus. *Hum Reprod* 2008;24:726-31.
5. Doyle PE, Beral V, Botting B, Wale CJ. Congenital malformations in twins in England and Wales. *Journal of Epidemiology and Community Health* 1990;45:43-8.
6. Sipek A, Gregor V, Horacek J, Stembera Z, Sipek, Klaschka J, et al. Birth defects incidence in children from single and twin pregnancies in Czech Republic - current data. *Ceska Gynkol* 2009;74:369-82.
7. Zhang XH, Qiu LO, Huang JP. Risk of birth defects increased in multiple births. *Birth Defects Res A Clin Mol Teratol* 2011;91:34-8.
8. Glinianaia S V, Rankin J and Wright C. Congenital anomalies in twins: A Register based study. *Human Reproduction* 2008;23:1306-11.
9. Amar Taksande, Krishna Vilhekar, Pushpa Chaturvedi and Manish Jain. Congenital Malformations at Birth in Central India: A rural Medical College Hospital based data. *Indian J of Human Genetics* 2010;16:159-63.

10. Nazer J, Cifuents L, Bazzan M. Congenital malformations in twins. *Rev Med Chil* 1999;127:158-64.
11. Zamon T, Wal. Prevalence and forms of Congenital Anomalies in twins born in Pomeranian District during the period from 1-07-1997 to 31-12-1998, Polish Register of congenital Anomalies. *Acta Genet Med Gemellol (Roma)* 1998;47(3-4):255-9.
12. Myrianthopoulos NC. Congenital malformations in twins: Epidemiologic Survey. *Birth defects Orig Artic Ser* 1975;11:1-19.
13. Gupta P, Faridi MM, Dev G. Congenital Malformations in Twins: Effect of Chorionicity and Zygosity. *Indian Pediatr* 2010;47:343-4.
14. Yoko Imaizume. Studies on birth defects and Twins in Japan. *Congenital Anomalies* 1990;30:69-78.
15. Tang Y, Zhu J, Zhou GX, Dal L, Wang YP, Liang J. An Epidemiological study on conjoined twins in China, from 1996-2004. *Zhonghua Yufang Yixue Zazhi* 41(Suppl. S):146-9.
16. Ghanshyam Das, Anju Aggarwal and M.M.A. Faridi. Dizygotic Twins with Myelomeningocele. *Indian Pediatr* 2003;70:265-7.
17. Hardin J, Carmichael SL, Selvin S, Lammer EJ, Shaw GM. Increased prevalence of Cardiovascular defects among 56,709 California twin pairs. *Am J Med Genet A* 2009;149A:877-86.

DOI: 10.5455/2320-6012.ijrms20130809

**Cite this article as:** Menasinkai SB, Dakshayani KR, Chiniwar MA. Congenital malformations in multiple births. *Int J Res Med Sci* 2013;1:xx-xx.