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Risk Factors for Twinning with Special Reference to Chorionicity – A Hospital Based Study

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Abstract
Background: *The rise in the incidence of twin pregnancies all over the world is not only due to assisted reproductive techniques but also due to various other risk factors. Twin pregnancy is associated with increased risk of maternal and fetal complications which in turn increases financial, emotional and social cost to the twins themselves and their families.*
Materials and Methods: *A clinical non-interventional 'nested' case control study was conducted in a tertiary care centre over a period of 1 year. To study the risk factors, all the required data were collected by personal interview of mothers.*
Results: *Nearly one third of twins were monochorionic twins. Dichorionic twins were found to be more in higher socio-economic groups, maternal age > 25 years, advanced parity and infertility treatment, especially ovulation induction with clomiphene citrate.*
Conclusions: *Epidemiological studies on twins helps us in better understanding the phenomenon of childbirth.*
Key Words: *Chorionicity, Monochorionic, Dichorionic, Twins.*

Introduction

Studies on multiple pregnancy are fundamental to the scientific understanding of the role of nature and nurture[1]. Yet surprisingly, up to now, we have had a very incomplete picture of the number of twins around the world. Only for highly developed countries with good birth registrations, reliable national information on the incidence of twinning and the changes therein over time is available. Information from developing regions is scarce or lacking all together. [2]

Twin gestations are associated with increased risk of maternal and neonatal complications, both in the developed as well as developing countries. While multiples represent only 3% of all the deliveries, they are responsible for 13% of preterm births, 21% of low birth weight infants and 11% of neonatal deaths.[3,4] It is also associated with significant maternal morbidity and mortality.[5] The incidence of twins is increasing globally and occurs in 1/80 pregnancies. This increase is not only due to rise in

ARTprocedures,but also due to changing trends towards delayed childbearing.[6,7] Therefore, determining the magnitude of problemand identifying the risk factors are crucial for possible prevention and better interventions.

Materials and Methods

This was a clinical,non-interventional prospective 'nested' case controlstudyconducted in a tertiary care hospital over a period of one year.There were a total of 15,310 deliveries during the study period, of which, 232 were twin pregnancies. All the 232 cases of twins admitted to the hospital and delivered here were enrolled in the study. The twins were divided into two groups - Monochorionic (MC) and Dichorionic (DC) based on chorionicity. Chorionicity was determined by ultrasound taken in the first and second trimesters and were confirmed by placental examination postnatally. Detailed history was taken from the mother inorder to identify the risk factors associated with twinning.These patients were followed up till delivery.The risk factors under consideration were age, parity,religion, socioeconomic status, family history of twinning, infertility treatment, use of OCP's, which were analyzed on the basis of chorionicity.

Statistical method used for analysis was chi-square test and students testwherever appropriate.P<0.05 was taken as significant.Data entry was done using Microsoft excel and analysis done using SPSS.Consent was obtained from the patients included in the study.Institutional Ethics Committee clearance was also obtained.

Results

Incidence of twins

There were a total of 15,310 deliveries during the 1 year study period.The total number of twins during this period was 232.The incidence of twins in the present study was found to be 15.1 %. The incidence of DC twins were 9.92 and that of MC twins were 5.2.

Type of twins (Table 1)

Table 1

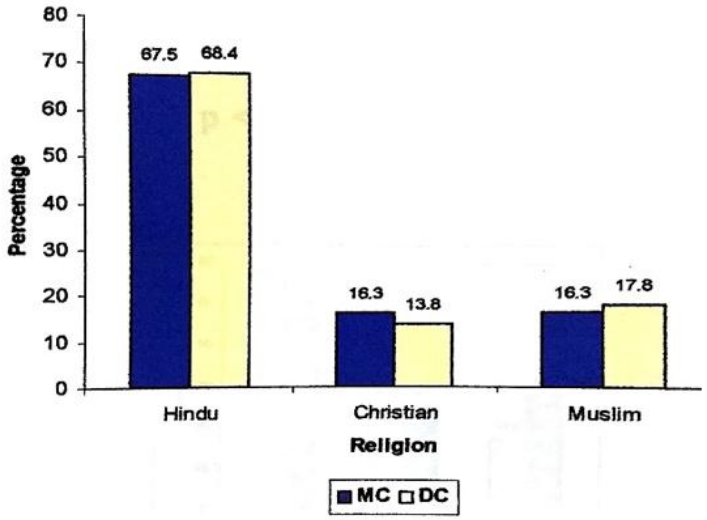
Type	Number	%
MCMA	12	5.17
MCDA	68	29.3
DCDA	152	65.5
Total	232	100

Nearly one-third of twins were Monochorionic.

Religion

Distribution according to religion.(fig: 1)

Fig 1



x^2=0.288 p value- not significant

Religion and religious practices were not found to significantly influence chorionicity.

Socioeconomic status(table 2)

Table 2

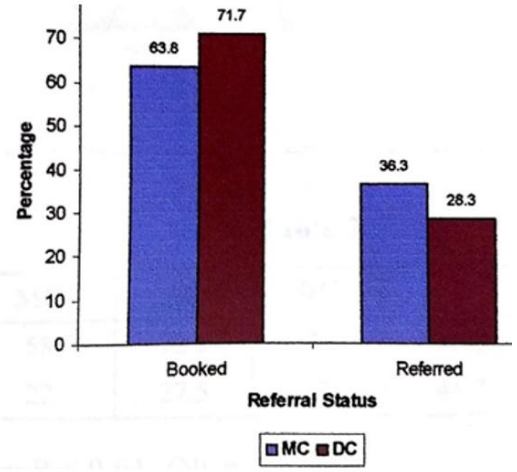
SES	Monochorionic		Dichorionic		Total twins	
	Number	%	Number	%	Number	%
Low	45	56.3	71	46.7	116	50
Middle	21	26.3	38	25	59	25.4
High	14	17.5	43	28.3	57	24.6
Total	**80**	**100**	**152**	**100**	**232**	**100**

x^2=4.050 p< 0.05 OR= 1.983

Dichorionicity was found to be higher in high socioeconomic group and the finding was statistically significant.

Referral status (fig: 2)

Fig 2

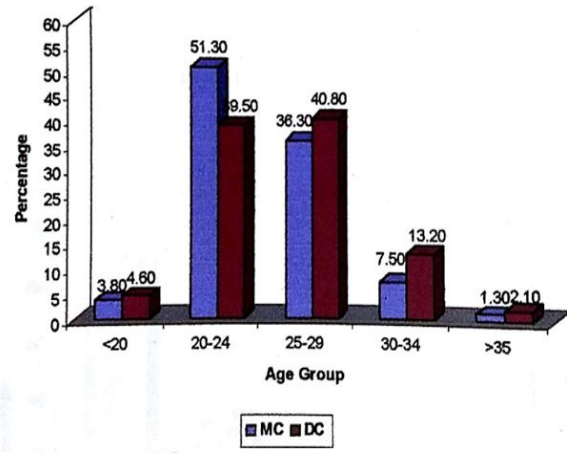


x^2=3.153 P==NOT significant

Referrals were more for monochorionic twins to tertiary centre in view of increased complications and poor perinatal outcome.

Maternal Age(fig: 3)

Fig 3



x^2=6.559 p<0.01 OR= 2.134

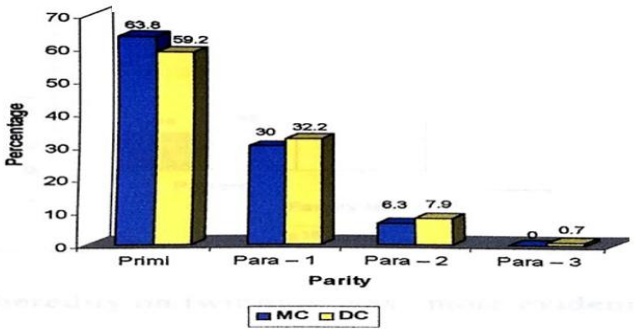
Mean maternal age for Monochorionic twins = 24.4,

Mean maternal age for Dichorionic twins= 25.5

Risk of dichorionicity was found to increase with maternal age and the association was found to be significant.

Parity (fig: 4)

Fig 4

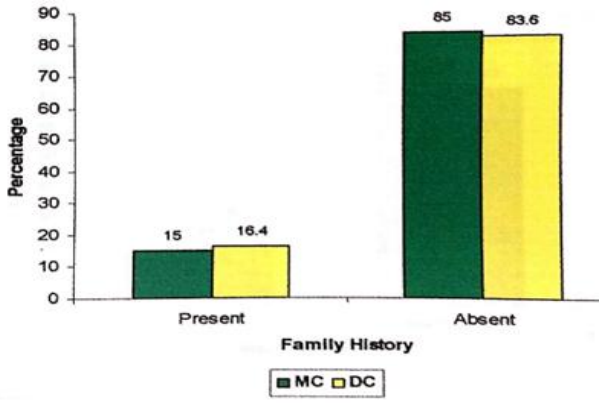


x^2= 0.453 p<0.05 OR=1.811

Risk of dichorionicity was found to increase with parity

Family history of twins(fig: 5)

Fig 5

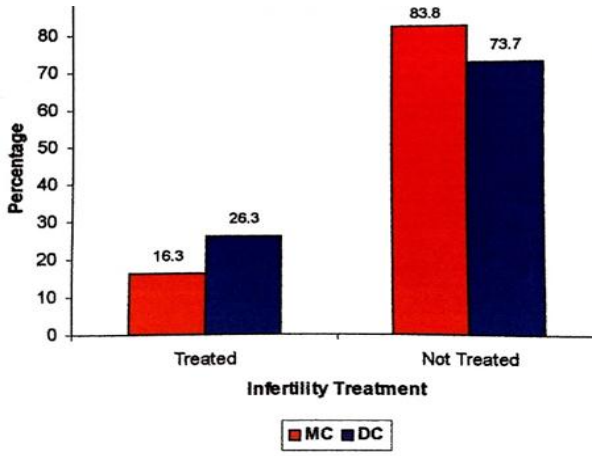


x^2=0.082 p>0.05 OR=1.896

15.9% of twins had history of multiple pregnancy in their family. It was comparable between monochorionic and dichorionic twins.

Infertility treatment (fig: 6)

Fig 6



x^2= 0.082 p< 0.05 OR= 1.896

Incidence of dichorionic twinning was more than monochorionic twinning among infertilty treated couples.

Ovulation induction (table 3)

Table 3

Drugs	Monochorionic		Dichorionic		Total twins	
	Number	%	Number	%	Number	%
No treatment	66	82.5	110	72.4	176	75.9
Clomiphene	9 5	11.3 6.3	34 2	22.4	43 7	18.5 3
Letrozole	-	-	6	1.3	6	2.6
Gonadotrophins				4		
Total	**80**	**100**	**152**	**100**	**232**	**100**

56 patients were given ovulation induction with various protocols. Clomiphene citrate was the most commonly used drug for ovulation induction. There were more of dichorionic twins with clomiphene and the finding was statistically significant.

The significant risk factors (table 4)

Table 4

PARAMETER	P value	OR	x^2
Socio-Economic Status	< 0.05	1.983	4.050
Parity	< 0.05	1.811	0.453
Maternal Age	< 0.01	2.134	6.559
Infertility treatment	< 0.05	1.896	0.082

Discussion

1.**Types of twins**

In the present study, there were 12 cases of MCMA twins (5.17%), 68 cases of MCDA (29.3%) and 152 cases of DCDA (65. 5%). The ratio between MC:DC being 34.4 : 65.5. Previous studies in the hospital in 1986 showed a ratio of MC: DC of 38.6 :61.4.

2.**Incidence of twins**

The Incidence of twins in SAT hospital in the 1 year period was 15.1%.Previous studies in the same hospital showed an incidence of 13.6%(1986) and 16% (1994). Population based studies from India, Bangladesh, Nepal and Kyrgyzstan have twinning rates below 9 per 1000[2].Smits et al[2] observed that the average of the national twinning rates in the 76 countries was 13.1 per 1000 or one twin birth in 76.3 births. This figure is close to the average rate of spontaneous twinning mentioned in the present study.

The incidence of DC twins were 9.92 and that of MC twins were 5.2. Monozygotic twinning is thought to occur at a relatively constant rate of 3.5–4 per 1000 births across human populations.[1]The higher twinning rate, especially of MC twins observed in the present study compared to the national average is perhaps due to the nature of our centre, being a tertiary referral hospital.

3.**Age**

In the present study, maximum number of MC twins were in the younger age group of 20-24(51.3%) and DC twinning was more in the 25-29 years age group(40. 8%).Mean age for MC twins was 24.4 and the mean age for DC twins was 25.5. Advanced maternal age has been found to be the most significant risk factor for DC twinning in the present study and the finding is similar to other reported statistics.[2]Previous studies done in the hospital showed a maximum incidence in 20-24 year age group (1986) and 26-30 years (1994). This change is probably due to the changing trends in marital age and more Family planning acceptance.

Studies by Bakare et al[8] showed increased incidence of twinning with advanced maternal age. Keith L[9]showed twinning rates rose steeply to peak between 30-34 years falling afterwards but rising again after 40. Guttmacher[10] noted highest twin frequency at about 40 years and that this was limited to dizygotic twins. According to studies by Jewell and Lynch[11,12] multiple births occur more frequently among older mothers even without use of fertility enhancing therapies.

4.**Religion**

Majority of MC (67.5%) as well as DC (68.4%) twins were Hindus. This may be because they constituted the majority (68. 1%).Religionand religious practices were not shown to influence

chorionicity. Studies have shown that racial factors may affect dizygotic twinning, but the rate of monochorionic twinning was found to be remarkably similar throughout the world.

5.**Socioeconomic status**

Both MC and DC twin pregnancies were found to be higher in the low socio-economic group(56.3% and 46.7% respectively). This may be because about 50% of the study population came under the low socio-economic group.In the present study, dichorionicity was associated with the higher socioeconomic groupwhen compared to MC and the association was found to be statistically significant.This can be explained by the influence of better nutrition or increased incidence of infertility treatment leading to dizygotic twinning in the higher Socioeconomic group.

Our finding is similar to studies by Tilahunetal[13]and Ananth CV[14] who also found out high twinning rate in relation to higher socioeconomic group in their respective studies.

6.**Referral status**

Majority of the MC(63.8%) and (71.7%) of DC twin pregnancies were booked in SAT. Multiple pregnancy and chorionicity is detected in the first trimester itself, which reflects in early referrals and booking in first trimester itself, to SATH, being a tertiary care centre. Referrals were more for MC twins (35%) compared to dichorionic (28.3%). This may be related to higher incidence of complications in MC twins.

7.**Parity**

The number of MC &DC twins were more among primis (63.8% & 59.2% respectively). Risk of DC twinning was found to increase with increase in parity, compared to MC twins, the risk being 1.81 times (OR-1.81) and the association was statistically significant. Compared to previous studies by Indianauthors, it is seen that the incidence of higher age groups and grand multiparas have come down drastically. This is due to limitation of family size and FP gaining acceptance.

Ghai & Vidyasagar[15] identified a twinnning rate of 21.3/1000 among primis as compared to 26/1000 among multis.Increased parity has been associated with increased incidence of twins in studies by Korsak VS and MusiliF.[16,17]

8.**Family history of twins**

In females with family history of twins, the risk of DC twinning (16.4%) was found to be slightly higher than MC twins(15%).The risk was 1. 9 times, but the association was not found to be statistically significant.

Studies by Tilahun[13]identified family history as risk factor for dizygotic twinning. Obiechina[18] in his studies has confirmed this finding.

Family history of twinning increases the chance of having twins, but the family history of the mother is a more important determinant than that of thefather. InBulmersanalysis[19]of twins,1 out of 25 (4%) of their mothers was alsotwin, but only 1/60(1.7%) of their fathers was a twin. In the present study, such an assosciation was not found.

9.**Infertility treatment**

In the present study, the incidence of twinning following treatment for infertility was 22.8%. The incidence was only 4% in studies conducted in the hospital in 1986 which clearly shows that problems related to infertility and hence its treatment, is on the rise. The risk of dizygotic twinning was more (26.3%) compared to monozygotic twinning (16.3%) following infertility treatment, the rise being 1.9 times, but the association was not found to be significant.

Derom & colleagues[20] found an alarming increase in both MC and DC twinning as aresult of ovulation induction.A study done in USA in 2006[19]found that assisted reproductive technology accounted for 18% of all the twins since 1970.

10.**Ovulation induction**

Clomiphene citrate was the most frequently used drug for ovulation induction. Other methods used were letrozole, gonadotrophins and IUI.

11.**Oral contraceptive use**

Therisk of twinning following cessation of OCP was found to be higher in dichorionic (5.3% as compared to MC, 3.8%).Tilahun et al[11] in their studies have found strong association between twinning and use of OCP**.**

Conclusion

From the present study, it has been found that nearly one third of twins were monochorionic twins. Dichorionic twins were found to be more in higher socio-economic groups, maternal age> 25 years, advanced parity and infertility treatment, especially ovulation induction with clomiphene citrate. Religious influences and family history were comparable in both monochorionic and dichorionic twinning. Early identification of twinning from the risk factors will help early diagnosis so that complications can be picked up earlier and managed.

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