

Epidemiology and Antenatal Complications of Twin Gestation: An 8-Year Review

Abdulaziz Al Mulhim, LM, JB, CAB (O& G)*

Objective: To determine the incidence, epidemiology and antenatal complications of twin gestation.

Setting: Department of Obstetrics and Gynecology, King Fahad University hospital, Al-Khobar, Saudi Arabia.

Subject and Design: Two-hundred and twenty-seven (227) patients with twin gestation that delivered over an 8 year period were studied. The control group comprised of two singleton deliveries that followed immediately after the twins. Patients were divided into three groups according to gestational age of the first, prenatal care and the total number of antenatal visits to the hospital.

Main outcome and result: The incidence of twin deliveries after 24 weeks gestation was ten per thousand. The majority of cases occurred in patients aged 20-30 years of parity 4 and above. There was a higher incidence of iron deficiency, anemia, pre-term labor, intrauterine growth retardation, pregnancy induced hypertension and intrauterine fetal death in the study group compared to the control.

Conclusion: Frequent prenatal visits, earlier diagnosis and management of several maternal complications would lower the incidence of perinatal morbidity and mortality. Early determination of zygosity is useful in establishing the prognostic categories of twin gestation. Further studies are needed to address the specific aspect of twin gestation in order to outline those areas for improvement of care in this challenging area of obstetrics.

Bahrain Med Bull 2001;23(2):56-60.

Twin gestations constitute less than 1% of all births, yet they are responsible for a disproportionate amount of the overall perinatal morbidity and mortality¹. Several studies have suggested that twin gestations impose greater demands on the maternal physiologic systems than do singleton pregnancies²⁻⁴. It is generally believed that an increased incidence of maternal complications in pregnancy is due to this burden on the adaptive capacity of the mothers. Although there is a large body of contemporary literature dealing with twin gestations, only a few reports have specifically focused on the incidence of maternal complications as they occur in twin gestations. Similarly, few reports have examined other factors, such as maternal age, zygosity or variation in prenatal care that might be related to the scope and magnitude of these maternal complications.

* Associate Professor and Consultant
Department of Obstetrics & Gynecology
College of Medicine, King Faisal University
Dammam, Saudi Arabia

The purpose of this study was to determine the incidence, epidemiology and antenatal complications of twin gestations seen at the King Fahad Hospital of the University, Al Khobar, Eastern Province, Saudi Arabia between January 1991 and December 1998.

METHODS

The case records of 227 patients with twin gestation that delivered during the period of study were reviewed. The control group comprised of two singleton deliveries that occurred immediately after a twin delivery giving a total of 454 patients.

Demographic data, past obstetric history of twins, mode of occurrence of the current pregnancy and antenatal complications during the index pregnancy were noted for the patients and control groups. In all cases, the diagnosis of twin gestations was based on clinical and ultrasound examinations. The patients with twins were divided into three groups based on the gestational age at the first prenatal care visit and the total number of visits as follows: Group 1 patients had prenatal care beginning before 24 weeks and had six or more prenatal clinic visits; Group 2 patients had prenatal care beginning after 24 weeks and had fewer than six prenatal clinic visits; Group 3 patients had no prenatal care during the pregnancy.

Facilities for cytogenetic and postmortem examinations were not available at the hospital. Statistical analysis was performed by means of the χ^2 test with Bonferroni correction for multiple comparisons and values of $P < 0.005$ were considered as significant by this method⁵.

RESULTS

The incidence of twin gestations of 24 or more weeks that delivered during the 8 year study period is shown in table 1. The incidence of twin gestation increased from 8/1000 in 1991 to 12/1000 in 1998 with an overall incidence of 10/1000 of all deliveries. Zygosity was successfully determined by placental pathology or fetal sex in 87% (197 patients). The overall incidence of dizygotic twins in this series was 66% (150 patients), monozygotic was 21% (47 patients) and 13% (30 patients) was undetermined.

Table 1. Incidence of twin gestation delivered after 24 weeks

	1991	1992	1993	1994	1995	1996	1997	1998	Total
Total mothers delivered	2706	2814	2830	2993	3128	3114	2514	2884	22983
Twin gestations	23	28	26	24	24	32	35	35	227
Percentage (%)	0.8	1.0	0.9	0.8	0.8	1.0	1.4	1.2	0.99

Table 2. Incidence of Twin in relation to age

<i>Age distribution (years)</i>	<i>Total patients delivered (No)</i>	<i>Patients with twin gestation (No)</i>	<i>%</i>
< 20	1500	26	1.7
20-25	6141	63	1.0
26-30	7228	63	0.9
31-35	4290	38	0.9
36-40	2321	23	1
>40	1276	14	1.1

*Range: 16-44 years**Mean 29 years*

A maternal family history for twin pregnancy among first or second degree relatives was present in 10% (23 patients) 8.3% (19) of these were from patients with dizygotic pregnancies. None of the patients had a previous twin pregnancy. Spontaneous twinning occurred in 38% (87 patients), invitro fertilization and embryo transfer resulted in 12% (27 cases) and fertility drugs were used in 50% (113 cases) of twin gestations. The age distribution of the patients ranged from 16-44 years with a median of 29 years (Table 2). Primigravidas represented 20% (45 patients) of the group with an age range of 16-41 years (mean age was 22 years). Multigravida patients ranged between 17 and 43 years (mean age was 27 years) (Table 3). Group 1 constituted 4.6% (104 patients) of our study group, Group 2 patients 25% (57 patients) and Group 3, 29% (66 patients).

Table 3. Incidence of Twin Gestations in Relation to Parity

<i>Parity</i>	<i>Total patients delivered (No)</i>	<i>Patients with Twin gestation (No)</i>	<i>%</i>
1	4028	23	0.6
2	3756	35	0.9
3	3700	35	0.9
4	3713	41	1.1
5	7559	93	1.2

Table 4 shows the incidence of common complications during pregnancy. The overall incidence of complications was 91% (206) in the study. This was significantly higher compared with the control group (33%). There was only a single antenatal complication in 75% and multiple complications in 25% of the patients with twin pregnancy.

Table 4. Antenatal Complications in Twin and Singleton Gestations (Control Group)

<i>Complication</i>	<i>Twin gestation</i> (<i>N</i> = 227)		<i>Singleton</i> (<i>N</i> =454)	
	<i>No</i>	<i>%</i>	<i>No</i>	<i>%</i>
Anemia	36	15.8	14	3.0*
Preterm labor	70	30.8	33	7.3*
Pregnancy induced hypertension	36	15.8	17	3.7*
Gestational diabetes mellitus	9	3.9	17	3.7
Antepartum hemorrhage	6	2.6	9	2.0
Fetal death	7	3.0	6	1.2*
Pyelonephritis	8	3.5	19	4.2
SPROM without labor	12	5.3	20	4.4
IUGR	22	10	14	3.0*

* statistically significant

PROM - Premature rupture of membrane

IUGR - intrauterine growth retardation

The most common complication, preterm labor (spontaneous onset of regular uterine contractions with progressive dilatation of the cervix before 37 weeks gestation) was nearly fourfold in twin gestations as compared with the singleton gestations (30.8% and 7.1% respectively). The incidence of induced hypertension (defined as a blood pressure of 140/90 mmHg or greater on two occasions 6 hours apart occurring after 20 weeks of gestation) was also significantly increased in twin gestation as compared with singleton ones (16.2% versus 3.7%). Intrauterine fetal death of one or both fetuses after 24 weeks gestational age occurred in 3% of twin gestation, a nearly threefold higher rate than in the singleton gestations (1.2%). Anemia [haemoglobin <10.0 g/dl] occurred in 16.2% of twin gestation, which was five times higher than in the control group (2.9%).

Intrauterine growth retardation [defined as fetal weight less than the tenth percentile for gestational age] occurred in 10% of twin gestation which was three times higher than singleton gestations (3%).

Other common complications like pyelonephritis (urine culture showing greater than 10^5 bacterial colonies per milliliter and maternal temperature of 38°C with costovertebral angle tenderness), gestational diabetes mellitus (two or more elevated serum glucose levels in a 3 hour, 100g glucose tolerance test after overnight fasting), spontaneous premature rupture of membranes (confirmed by aseptic speculum examination) and antepartum hemorrhage (vaginal bleeding after 24 weeks gestation) were not significantly higher in twin gestations than in singletons.

Table 5. Antenatal Complications in Relation to Zygosity

Complication	Dizygotic twins (N=150)		Monozygotic twins (N= 47)		Undetermined (N=30)	
	No	%	No	%	No	%
Anemia	24	16.0	8	17.0	4	13
Pre-term labor	48	32.0	17	36.1	5	16.6
Pregnancy induced hypertension	27	18	7	14.8	2	6.6
Gestational diabetes mellitus	6	3.3	1	2.1	3	10.0
Antepartum hemorrhage	4	2.6	1	2.1	1	2.1
Fetal death	4	2.6	2	4.2	1	2.1
Pyelonephritis	5	3.3	2	4.25	1	3.3
PROM without labor	8	5.3	2	4.25	2	6.7
IUGR	8	5.3	12	26	2	6.7*

* Statistically significant

PROM - Premature rupture of membranes

IUGR - intrauterine growth retardation

Table 5 shows the incidence of pregnancy complications in relation to the zygosity. Pregnancy induced hypertension was more common in dizygotic twin pregnancies. However this frequency did not achieve significance when corrected by the Bonferroni method. Intrauterine growth retardation, intrauterine fetal death and preterm labor were more common among monozygotic twin gestations.

Table 6. Antenatal complication in relation to prenatal care

Complication	Group 1 (N=104)		Group 2 (N=57)		Group 3 (N=66)	
	No	%	No	%	No	%
Anemia	8	7.6	11	19.2	17	25.7*
Pre-term labor	16	15.3	22	38.5	32	48.4*
Pregnancy induced hypertension	9	8.6	11	19.2	16	24.2*
Gestational diabetes mellitus	4	3.8	2	3.5	3	4.5
Antepartum hemorrhage	2	1.9	2	3.5	2	3.0
Fetal death	1	0.9	2	3.5	4	6.0
Pyelonephritis	5	4.8	1	1.7	2	3.0
PROM without labor	5	4.8	3	5.3	4	6.1
IUGR	5	5	5	9	12	18*

* Statistically significant

PROM: Premature rupture of membranes

IUGR- intrauterine growth retardation.

Table 6 shows the antenatal complications in the three groups of patients divided according to the prenatal care they received. Group 1 patients had the lowest incidence of complications. Group 2 patients had more complications than Group 1 except for pyelonephritis which was more frequent in Group 1. Group 3 patients had a significantly higher incidence of anemia, preterm labor, pregnancy induced hypertension, intrauterine fetal death and intrauterine growth retardation compared with group 1 patients.

DISCUSSION

The incidence of twinning varies widely throughout the world; the highest being reported in black populations, with Nigeria having a rate of 1 in 20 to 25 pregnancies^{2,3} and the lowest in Oriental populations⁴. In our study, there were 22,756 singleton gestations and 227 twin gestations during the study period giving an incidence of 1 in 100 pregnancies. The rate increased from 1991 to 1998 and this may be due to the increasing use of medications for ovulation induction and assisted methods for conception in the management of infertility. There were 140 (62%) twin gestations that resulted from ovulation induction and 27 of these from in-vitro fertilization and embryo transfer in the study. The remaining 87 (28%) cases were the result of spontaneous ovulation.

The rate of monozygotic twinning is fairly constant throughout the world at 3 to 5 per thousand deliveries² but in our study, the incidence was slightly lower (2 per thousand).

Monozygotic twinning is thought to be due to chance, unrelated to heredity resulting from a delay in implantation associated with nutritional, hypoxic or other stress². The incidence of dizygotic twinning ranges widely between 4 and 40 per 1,000 deliveries², with 6 per 1000 deliveries in our study. The zygosity could not be determined in 30 (13%) cases of twins in the series which can be studied using enzymatic markers or dermatoglyphics.

Cameron determined 8% out of 45 % of twins with undiagnosed zygoty using these markers⁶. The incidence of twinning is affected by a variety of maternal characteristics that include age, parity, genetic predisposition and the use of fertility drugs⁶.

The mean maternal age in the twins was 31 years as compared with 25 years for singletons. Most studies have found that the incidence of twinning increases with advancing maternal age up till 35 years after which the rates decline².

Maternal age is the only factor that may possibly affect rates of monozygotic twinning². Heuser et al found the incidence of monozygotic twins to be 3 per 1,000 in women less than 20 years of age, while among women over 40 it was 4.5 per 1,000⁷. This difference in the incidence is not as dramatic as that seen for dizygotic twinning, which increased from 2.5 per 1,000 in women 15-19 years of age to 11.5 per 1,000 in women 30-34 years of age⁸.

The twinning rate for primigravidas was 6 per 1,000 and 11 per 1,000 for multigravidas ($P < 0.0001$) in our study. Ghai and Vidyasagar found a rate of 21.3 per 1,000 among primigravidas as compared to 26 per 1,000 among multigravidas⁹.

The finding that twinning is more likely to occur among the higher parity patients has been shown to be independent of maternal age⁷. The issue of whether parity or gravidity is more influential in dizygotic twinning has not been fully examined. This may be true but, in our

study about 140 sets of twins were due to the use of fertility drugs and assisted methods of conception.

Maternal family history for twin gestation among the first or second degree relatives was obtained in 23 (10%) patients, 19 (83%) of them were from patients with dizygotic gestations. There is no evidence that the incidence of monozygotic twinning increases with a family history of twins, but increased dizygotic twinning rates do seem to be affected by maternal familial influences as shown in our study. Mothers of dizygotic twins have been found more likely to have recurrent twin gestation than women who never had a twin gestation before⁶. White and Wyshak found that 17% of women who were twins themselves gave birth to twins, as compared to 0.8% of women whose husbands were twins¹⁰. These rates, when compared to the general population twinning rate of 1.1% illustrate that familial tendencies seem to be restricted to the maternal side.

Pre-term labor was overwhelmingly the most frequent complication in the series. Our incidence frequencies conform with those of other series¹¹. We did not find a statistically significant correlation of preterm labor and zygosity.

The level of prenatal care has its benefits in patients with twin pregnancy as shown in our study, with lower rates of complications in patients with more frequent visits and early antenatal diagnosis. Some reports have suggested that bed rest and/or hospitalization increases the duration of gestation¹². As a policy, strict bed rest and prophylactic tocolytic therapy was neither enforced nor quantitated in our study, we cannot support or refute this contention. Our incidence of pregnancy induced hypertension in the series (16%) compares favorably with 15-40% reported in the literature¹³. We also found that dizygotic twins are at greater risk of pregnancy induced hypertension although it was not statistically significant. Pregnancy induced hypertension has been suspected of having an immunologic basis and as the antigenicity of each fetus in dizygotic twins is different it may have a bearing to this finding¹⁴. Alternatively, there may be a hereditary tendency for dizygotic gestations to develop pregnancy induced hypertension^{15,16}. Patients who received inadequate prenatal care had a higher incidence of pregnancy induced hypertension and also increased severity of the disease. The most likely explanation for this may be that the mild form of the condition remained undetected in these patients.

Intrauterine fetal death and intrauterine growth retardation were found to be more frequent in twin than in singleton pregnancy as reported by other authors^{17,18}. Unfortunately, autopsies were not performed in any of our cases, so that etiologies could not be analyzed. We found that zygosity was significantly related to the incidence of fetal death and intrauterine growth retardation with monozygotic gestations suffering greater losses^{19,20}. Other studies have also correlated placental membrane type to fetal death¹⁹. Monochorionic placentas are always monozygotic and such placentas usually have fetal vascular anastomosis, although frank twin-twin transfusion is rare. However, mechanisms other than Twin-Twin transfusion syndrome but, related to vascular communication, have been found to be associated with fetal death and intrauterine growth retardation in twins²¹. We also found that levels of prenatal care were related significantly and inversely to fetal death rate and intrauterine growth retardation. Fetal malformation was not studied in the series due to non-availability of autopsy. Other complications such as antepartum haemorrhage, gestational diabetes mellitus, spontaneous rupture of membranes and pyelonephritis were not significantly higher in twin gestations than singleton ones in the series.

CONCLUSION

Prenatal care and early diagnosis is clearly advantageous to the patients as all the complications were increased in Group 2, highest in Group 3, least in Group 1, and hence would have a great impact on reducing the occurrence and severity of certain complications. Frequent prenatal visits, earlier diagnosis and management of several maternal complications would lower the incidences of perinatal morbidity and mortality in the patient group. In addition, it seems that early determination of zygosity is useful in establishing the prognostic categories of twin gestation. Further studies are needed to address the specific aspect of twin gestation in order to outline those areas for improvement of care in this challenging area of Obstetrics.

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