ASSESSMENT OF PERI-NEONATAL MORTALITY AND MORBIDITY RISK IN TWIN PREGNANCY

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Summary: A case control study on peri-neonatal mortality and morbidity rates in 154 twin pregnancies has been performed.

The mortality rates along with main neonatal morbidity factors were evaluated in relation to the birth weight and gestational age. The risk of death in peri-neonatal period was 17 times greater (relative risk 17.30) ($p < .00005$) in newborns weighing less than 2000 g and about 15 times (r.r. 14.53) ($p < .00005$) in twins born before 34th week of gestational age with respect to the controls. The Apgar score of the 2nd twin was lower than that of the 1st, both at 1′ ($p < .05$) and 5′ ($p < .025$).

The development of HMD was strongly influenced by the gestational age when less than 34th week (r.r. 15.89) ($p < .00005$).

No difference in incidence was found between the newborns with gestational age between 34-37 weeks and those at term.

The potential implications of these findings on obstetric and neonatologic treatment of LBW and VLBW twins was discussed.

INTRODUCTION

In spite of the progress made in the last twenty years in the fields of obstetrics and perinatology, twin pregnancies still represent an important and current problem due to the greater risk involved.

The perinatal mortality is from 3 to 7 times greater than that of single pregnancies [1, 2].

Although it is typical to find a higher incidence of congenital malformations in twin pregnancies, the most serious neonatological problems are due to prematurity and its complications [2].

The great part of the perinatal mortality and morbidity takes place in the group of newborns with a birth weight of less than 2500 g (LBW) independent of gestational age [1].

Intrapartum asphyxia is one of the major risks for LBW fetuses being a cause of elevated mortality as well as the possible cause of permanent neurological sequelae related to cerebral hemorrhage [3].

The obstetric and neonatologic factors which influence the prognosis of this group of neonates are current topics of discussion [1, 2, 3, 4].

We analyzed retrospectively all the twin deliveries during the 11 year period from 1973 to 1983 at the Obstetric and Gynecologic Department of the University of Pavia with the objective of identifying the categories of twin pregnancies at very high risk, looking for the factors which primarily influence perinatal mortality and morbidity.

MATERIAL AND METHODS

The records of 154 consecutive twin birth were analyzed.

For each case a series of maternal and fetal parameters were evaluated (maternal age and parity, gestational age and type of delivery), the Apgar score was constantly assigned by the neonatologist. The neonates were divided into classes according to weight and gestational age.

Each class was evaluated for perinatal mortality and its relative cause when known, and for the main factors of morbidity.

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Table 1. — *Delivery in twin pregnancies.*

	PRESENTATION			
	V-V	V-B	B-V	B-B
No. of cases	83	32	23	16

		No. of cases	%
TYPE OF DELIVERY:	Vaginal spontaneous	101	(65.6)
	* Vaginal operative	29	(18.8)
	Cesarean section (urgent 16 / elective 8)	24	(15.6)

* Vaginal operative	1st fetus	2nd fetus	both
v.e.	4	1	/
f.	2	2	2
b.e.	1	15	1
f.+b.e.	/	/	1
No. of cases	7	18	4

LEGEND:
v.: vertex
b.: breech
v.e.: vacuum extractor
f. : forceps
b.e.: breech extraction

Perinatal and neonatal mortality was defined according to the recommendations of FIGO [5].

The diagnoses of hyaline membrane disease (HMD), patent ductus arteriosus (PDA) and of necrotizing enterocolitis (NEC) were made by the Department of Neonatal Intensive Care according to the accepted clinical and instrumental standards.

Early and late neonatal morbidity and mortality were evaluated in relation to birth weight, gestational age, birth order and type of delivery.

Statistical analysis was performed in a "case control study".

The relative risk along with the 95% confidence interval was analyzed for each category with the "odds ratio" methodoly.

The risk was considered significant when it did not include the value of 1 with respect to the reference category within the confidence interval [6].

RESULTS

During the period considered there were 154 twin deliveries out of a total of 17438 pregnancies, equal to 0.88%, with an incidence of 1/112.

Maternal age varied from 18 to 42 years, with a mean age af 28.032±5.46; 60.4% of the patients were nulliparas.

The gestational age varied from 25 to 42 weeks of amenorrhea with a mean age of 36.227 ± 3.3 weeks; of the twin deliveries 93 (60.4%) were preterm births.

There were 130 (84.4%) births by vaginal delivery of which 101 (65.6%) were spontaneous and 29 (18.8%) were operative, and of these 7 apply to the first twin, 18 to the second, 4 to both.

Cesarean section was performed in 24 (15.6%) cases.

In the vaginal deliveries we observed that 76.6% of the presentation were vertex versus 23.3% which were breech, the later with greater incidence in the 2nd twin.

A summary of the types of deliveries is reported in table 1.

The mean weight was 2303 ± 557.22 g. There was no significant difference of birth weight between the first and the second twin.

176 (57.1%) new borns had a weight less than 2500 g (LBW).

Evaluating the data according to the criteria set by Lubchenco [7], 73 twins

Table 2. — *Perinatal mortatily (* intra-uterine fetal death)*

Cases no.	1	2	3	4	5	6*	7*
Sex	M	M	F	F	F	M	F
Weight in g	1250	1300	2500	2500	2200	1300	820
Apgar 1′ and 5′	9-7	5-4	4-3	4-4	5-4	/	/
Gestational age	24	33	39	39	29	40	39
Maternal age	36	28	34	34	29	34	36
Gestational A/W ratio	AGA	SGA	AGA	AGA	LGA	SGA	SGA
Type of delivery	B.v.d.	V.v.d.	C.S.	C.S.	B.v.d.	C.S.	V.v.d.
Birth order	1st	1st	1st	2nd	2nd	2nd	2nd
Neonatal pathology	m.m.	S.I.+ HMD	T.	T.	p.	/	/
Maternal gestational pathology	/	e.	f.	f.	p.e.	/	/
Post maternal pathology	m.o.	/	/	/	/	/	/

LEGEND = A/W: age/weight; v.d.: vaginal delivery; C.S.: cesarean section; B.: breech; V: vertex; m.m. multiple malformations; S.I. severe immaturity; e: epilepsy; p.e.: pre-eclampsia; f.: flebitis; m.o.: metroplastic operation; p.: prolapse of ombelical corde; T.: thoracopagus.

(23.7%) resulted to be small for gestational age (SGA).

There was no significant disparity in the distribution of sex.

In our study there were 18 deaths in the overall neonatal period (5.84%). The perinatal mortality was 2.27% while late neonatal mortality was 3.57%. Intra-uterine death of the fetus before the onset of labor occurred in 2 cases.

A summary of the perinatal mortality and late neonatal mortality is reported respectively in tables 2 and 3.

There was no significant difference between the mortality of the first and the second twin.

Table 3. — *Late neonatal mortality.*

Cases no.	1	2	3	4	5	6	7	8	9	10	11
Sex	M	M	F	F	F	M	F	F	F	M	M
Weight in g	940	950	1190	990	1500	1300	1650	1370	1500	950	1270
Apgar 1′ and 5′	7-7	6-5	6-6	5-4	5-5	5-6	7-7	6-6	5-7	7-7	8-6
Gestational age	28	28	30	33	33	33	36	33	32	29	30
Maternal age	26	26	18	22	22	28	26	24	32	31	22
Gestational A/W ratio	AGA	AGA	AGA	SGA	AGA	SGA	SGA	SGA	AGA	AGA	AGA
Type of delivery	V	B	V	B	C.S.	B	V	B	V	V	C.S.
Birth order	1st	2nd	2nd	1st	2nd	2nd	1st	1st	2nd	1st	1st
Neonatal pathology	HMD	S.I.+ NEC	HMD	HMD	S.I.+ HMD	HMD	NEC	HMD	NEC	S.I.+ HMD	PDA
Maternal gestational pathology	/	/	/	R.C.	E	E	/	M.S.	/	/	/

LEGEND = A/W: age/weight; HMD: hyaline membrane disease; S.I.: severe immaturity; NEC: necrotizing enterocolitis; R.C. renal calcoli; M.S.: monolateral salpingo-oophorectomy during the actual pregnancy; E.: eclampsia; PDA: patent ductus arteriosus.

Table 4. — *Perinatal and late neonatal mortality in relation to the maternal parameters - age, parity and gestational age.*

Maternal parameters	Number of pregnancies		Perinatal and late neonatal mortality	
	no.	%	no.	%
Age				
15 - 20	13	8.45	1	3.85
21 - 25	37	24.02	4	5.4
26 - 30	54	35.06	6	5.55
> 30	50	32.47	7	7
Parity				
0	93	60.4	12	6.45
1 - 2	54	35.1	5	4.6
> 2	7	4.5	1	7.1
Gestational age				
< 26 weeks	1	0.6	1	50
26-27 »	1	0.6	0	/
28-29 »	4	2.6	4	50
30-31 »	7	4.5	2	14.3
32-33 »	15	9.7	6	20
34-35 »	19	12.3	0	/
36-37 »	46	29.9	1	1.1
> 37 »	61	39.6	4	3.3

Maternal age and parity cannot in any way be correlated to the incidence of neonatal mortality (tab. 4).

Gestational age, on the contrary, strongly influences mortality when it is of less than 34 weeks of gestational age (g.a.) (23.21% vs 1.98%) (odds ratio 14.93) (95% confidence interval 6.65 and 45.85) ($p < .00005$).

No significant difference in mortality appeared between neonates with gestational age between 34 and 37 weeks with respect to those born at term. No correlation exists between sex of the twins, order of birth and mortality.

Correlating mortality with weight at birth (table 5), we observed that the risk of mortality is clearly increased (up to 17 times) and restricted to twins with a birth weight of less than 2000 g (18.75% vs 1.32%) (odds ratio 17.30) (95% confidence interval 7.16 and 65.63) ($p < .00005$).

We could not find any greater risk of mortality in twins whose birth weight was between 2000 and 2499 g with respect to those weighing 2500 g or more.

Table 5. — *Perinatal mortality in relation to sex, weight and birth order.*

Neonatal caracteristics	1st twin		2nd twin		Mortality			
	no.	%	no.	%	1st		2nd	
SEX								
M. no. 151 (49.03%)	76	50.3	75	49.7	5	6.57%	4	5.33%
F. no. 157 (50.97%)	78	49.7	79	50.3	4	5.20%	5	6.33%
WEIGHT IN G								
500 - 999	3	0.9	3	0.9	3	100.00%	2	66.66%
1000 - 1499	11	3.6	13	4.2	4	36.36%	3	23.1 %
1500 - 1999	24	7.8	26	8.4	1	4.16%	2	7.69%
2000 - 2499	54	17.5	42	13.6	—	— — —	1	2.38%
2500 - 2999	52	16.9	58	18.8	1	1.92%	1	1.72%
3000 - 3499	7	2.3	10	3.2	—	— — —	—	— — —
⩾ 3500	3	1.0	2	0.6	—	— — —	—	— — —
	154	50.0	164	50.0	9		9	

Table 6. — *Apgar-score at 1 and 5 minutes for the 1st and 2nd twin, respectively.*

	1 minute		5 minutes	
	≤7	8 - 10	≤7	8 - 10
1st twin	32	122	28	126
(154)	20.77%	79.23%	18.18%	81.82%
2nd twin	50	104	47	107
(154)	32.46%	67.54%	30.52%	69.48%

Table 7. — *Summary of the perinatal morbidity (the totals in parentheses refer to all the neonates of the respective weight classes at 27 days).*

Weight	Pathology	No. of cases	%
≤ 1999	HMD	7	10.9
(Total 80)	P.D.A.	5	7.8
	S.I.	5	7.8
	Sepsis	2	3.1
	NEC	1	1.6
		20	
2000-2499	P.D.A.	5	5.2
(Total 96)	Sepsis	4	4.2
	NEC	2	2.1
	HMD	3	3.1
	C.H.	1	1.0
		15	
⩾2500	NEC	3	2.3
(Total 132)	P.D.A.	2	1.5
	HMD	2	1.5
	S.I.	1	0.8
		8	

LEGEND: = S.I.: severe immaturity
C.H.: cerebral hemorrhage

Table 6 reports the values of the Apgar score at 1′ and 5′ referring to the 1st and 2nd twin. The 2nd twin more frequently presented a poor Agpar score (≤7) with respect to the 1st, both at 1′ (32.46% vs 26.23%) ($p<.05$) and at 5′ (30.52% vs 22.22%) ($p<.025$).

Table 7 illustrates the more frequent neonatal pathologies and their relation to birth weight.

HMD and PDA certainly represent the most important factors of morbidity. The development of HMD depends on birth weight, especially when less than 2000 g (odds ratio 4.46) (95% confidence interval 1.29 and 20.53) ($p<.03$).

No difference of incidence can be observed between the first and second twin.

HMD is almost entirely attributed to the group of twins whose gestational age is of less than 34 weeks (table 8); in this group of neonates the development of this pathology accounts for 16.07% of the morbidity vs 1.19% present in the group of neonates with a greater g.a. (odds ratio 15.89) (95% confidence interval 3.56 and 20.3) ($p<.00005$).

On the other hand, no difference is found between the neonates of a g.a. included between 34-37 weeks and those at term.

A late closure of the ductus arterious is strongly influenced by g.a., the neonates with a g.a. of less than 34 weeks present a risk up to 5 times greater with respect to those with a greater g.a. (10.71% vs 2.38%) (odds ratio 4.92) (95% confidence interval 1.24 and 27.88) ($p<.01$).

DISCUSSION

Considered in its whole perinatal mortality resulted lower in this investigation than the figures previously reported

Table 8. — *HMD and PDA in relation to gestational age.*

	GESTATIONAL AGE	
	< 34 W.	⩾ 34 W.
HMD	9/56	3/252
	16.07%	1.19%
PDA	6/56	6/252
	10.71%	2.38%

in the literature. In fact Medearis and coll. ([3]) report a perinatal mortality rate of 11.6% in 3594 twin pregnancies, while Keith and coll. ([4]), who collected data from 13 American hospitals in a period of 4 years, reported a mortality rate of 7.3% in 588 twin pregnancies.

A preterm delivery is a typical complication of twin pregnancies.

In fact, in this study, it was a complication in 60.4% of all deliveries, with a slightly higher frequency than reported by others authors ([1, 3, 4]).

18.18% of twins were born before 34 weeks of gestation, representing a very high risk category. The relationship between mortality and gestational age indicates that the mortality in neonates with a gestational age less than 34 weeks (23.2%) is at least 15 times greater than those with a higher g.a. This confirms that this group of newborns should be considered at very high mortality risk ([8, 9]).

To correctly evaluate perinatal mortality rate-weight relationship, the gestational age must be considered, to find SGA versus AGA (appropriate gestational age) newborns.

However, it is typical for many authors to evaluate perinatal mortality exclusively on the basis of weight.

This observation is supported by various studies in which the comparative evaluation of the effects of low birth weight and prematurity on mortality rates, demonstrate a predominance of the first factor ([10, 11]).

The risk of mortality was strongly increased (about 17 times) in the class of birth weights under 2000 g.

However, there were no significant differences in mortality in the classes of birth weight between 2000-2499 g and those higher.

Considering also the single pregnancies, McCormick ([10]) reports a neonatal mortality risk (0-27 days from birth) 40 times greater in the classes with weight less than 2500 g with respect to classes with higher weights. These two risks are not comparable because they were extracted from non-homogeneous categories and with different criteria.

The same authors reports an attributable risk of mortality in the neonatal period in the category of birth weight less than 2500 g of about 2/3. The attributable risk represents the proportion of all the neonatal deaths occuring in the category being discussed. Utilizing similar criteria to define neonatal mortality, the attributable risk for twins of weight less than 2500 g is equal to 7/8. This indicate that in the neonatal period 87.5% of all twin deaths occur in neonates of weight inferior to 2500 g as compared to about 66.7% in the global population.

We noted that there was no difference in the prognosis for neonates of weight between 2000-2499 g with respect to those of greater weights; this is of paramount importance considering that 31.2% of all twins belong to this weight category.

The incidence of morbidity in twin pregnancies is still superior with respect to single pregnancies.

At birth, asphyxia is of fundamental interest as a factor able to contribute to either mortality or to abnormal neurological development ([11, 12]).

It is well known that neurological sequelae are influenced both by low birth weight as well as eventual cerebral hemorrhage connected to intrapartum asphyxia ([11, 13, 14]).

Twin deliveries often present complications for the second twin who is more affected when its weight is less than 2000 g and delivered vaginally ([13]).

In this study the frequency of a poor Apgar is significantly higher in the 2nd twin as opposed to the 1st at both 1′ as well as at 5′.

When we considered only the second twin upon whom extraction breech was carried-out, the risk of fetal asphyxia, re-

presented by a poor Apgar score, is 8 times higher than that encountered by the 1st twin (odds ratio 8.17) (95% confidence interval 3.47 and 24.76) ($p < .001$). Obviously, many of the 2nd twin asphyxia represent the indication for extraction breech, rather than the consequence. Not withstanding these facts, the risks of breech extraction should be greatly emphasized, expecially whein the 2nd twin is LBW. Barret *et al.* [13] proposed a cesarean section in cases where neonatal weight can be extimated to be less than 1500 g, based upon retrospective data with stratification of weights for 198 twin pregnancies.

HMD develops in 15-20% of twins with birth weights <2500 g; the consequent mortality for this pathology is 20-40% [1, 2, 3, 4].

Since prematurity and LBW are prerogative of twin pregnancies, HMD is a primary problem. In this study, glucocorticoid prophylaxis was administrated in almost all of the pregnancies before the 34th week of gestational age. All the neonates affected by the disease need to be treated in a Neonatal Intensive Care Department.

The threshold value of g.a. for the developments of HMD resulted to be the 34th week of gestation. The risk in fact, is up to 16 times greater in twins of lower gestational age with respect to those with a higher g.a.

There is not significant difference in gestational ages between 34 and 37 weeks and above.

Even though fetal asphyxia is more frequent in the 2nd twin, the incidence of HMD in both 1st and 2nd fetus is the same.

This confirms the data of Kenney and coll. [15] which exclude the causal role of fetal asphyxia in HMD genesis during the neonatal period.

The relative risk of HMD is 4 times greater in the weight category less than 2000 g, even though, the frequency of the disease is already higher in neonates with weights <2500 g.

Considering these indications glucocorticoid administration would be limited to higher risk category, namely, preterms deliveries before 34th week in which the neonatal weight is estimated to be lower than 2500 g.

In the last 15 years have improved survival of neonates LBW and the increased use of artificial ventilation has permitted the survival and therefore the observed high frequency of neonates with a delayed closure of the ductus arteriosus.

The exact pathogenesis of this condition is unknown but the consequences affecting the neonates can be very serious (bronchopulmonary displasia) [16].

Our data demonstrate that this defect can be observed especially in twins of gestational ages less than 34 weeks (the relative risk is about 5 times greater with respect to older neonates).

These finding are in correlation with data of single pregnancies, where prematurity is the principal causative factor of this pathology [16].

CONCLUSIONS

Medical literature universally attributes the noteworthy decrease in perinatal mortality in the last 20 years to the advances in obstetrics and neonatology.

The decrease in mortality is primarily due to the increase in the survival of LBW neonates, represented for the most part by preterms [10, 11, 14, 17].

In single pregnancies the obstetric and neonatologic factors which improve the possibility of survival are relatively well defined. Although few results have been obtained in the prevention of LBW, their survival can be improved substantially by:

1) Early identification of factors indicating a pregnancy at high risk [11, 17, 18].

2) Increase of the numbers of C.S. in pregnancies with LBW fetuses and above all in those of VLBW. For the latter, a statistically higher survival rate has been demonstrated when born by C.S. ([18]).

3) Access to qualified units for neonatal intensive care ([17]).

4) The centralization of high risk cases towards III level perinatology centers ([17]).

For obvious reasons equally wide data does not exist regarding obstetric factors able to positively influence the survival rate in twin deliveries in as much as prematurity and LBW represent the rule.

Beyond the anomalies of presentation of the 1st twin which constitutes an indication for C.S.; the exact role that the type of delivery plays in the prognosis of twins weighing less than 2000 g is widely discussed ([11, 12, 19]).

In accordance with Barret and coll. ([13]) we retain opportune resorting to elective C.S. in preterm twin deliveries before 34th week of gestational age and/or when the estimated fetal weight is of about 1500 g (VLBW).

A serie of reasons supported the choice of VLBW as a cut-off category:

1) In this and in other studies ([1, 3, 4, 9]) about 70-80% of the perinatal mortality in the twin pregnancies is included in the category of g.a. less than 34 weeks and of weight less than 2000 g; a real improvement in the possibility of survival can be obtained only by lowering the mortality rate of this group.

2) In single pregnancies it has been demonstrated that there is a higher survival rate in the VLBW when born by C.S. ([18]).

3) It is apparent, to say the least, that the number of neonatal complications is greater in VLBW twins born by vaginal delivery ([13]).

4) Ecotomography provides the possibility of estimating the birth weight with an accuracy of ±20% in 95% of the cases ([20]).

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