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Obstetrical Implications in Multiple Pregnancies

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Abstract. In the present study 90 multiple pregnancies were examined. These were subdivided on the basis of the number of embryos involved (74 twins, 10 triplets, 6 quintuplets) and on whether they were followed at our clinic for the entire pregnancy or not. In each group we analysed certain variables, calculating the respective mean values and standard deviations. We used the ANOVA test to discriminate the eventual differences in the means of the variables analysed, operating a $p<0.05$ significance value. In addition, significant differences were analysed by the test of Contrasts (Scheffe F-test). The concept that emerged from the data investigated is that careful management of these pregnancies, carried out in high-level structures, can reduce the incidence of complications on both the maternal and fetal side and thus prevent "minimal brain damage" in the newborn.

Key words: Twinning, Multiple pregnancies, Triplets, Quadruplets, Quintuplets, Preterm delivery.

INTRODUCTION

Twinning is not a pathological condition in itself but because of the associated increase in maternal and fetal morbidity it must be considered a condition at increased risk.

Defects in the closure of the neural tube and labio-palatine clefts are the more common malformations found among multiple births which, when considered globally, constitute a population at risk for congenital anomalies [1]. In fact, the incidence of malformations among dizygotic twins does not differ significantly from that among singletons (on average, between 2-4% of births); in contrast, among monozygotic twins it is 2.7 times higher [8]. Severe anomalies, such as conjoined or amorphous fetuses, are less frequently found in twins than in triplet or other higher order multiples.

In monozygotic gestations there is a greater risk of anastomosis occurring between

the fetal circulations. This can cause such a disparity in the haematic flow as to create a nutritional imbalance. Extreme cases of this kind present, in the early stages, acardius of one twin and, in the later stages, episodes of twin-to-twin transfusion with oedema and polyhydramnios in the "receiving" twin and anaemia associated with oligoamnios and underdevelopment in the "donating" cotwin [3].

In addition to the genetic risk factors, the clinical complications characteristic of this type of pregnancy must also be considered [6,7]. For example, according to current literature, the incidence of preterm delivery in multifetal pregnancies is 50%, ie. twelve times greater than in singleton pregnancies. The highest risk period is between 26 and 32 weeks' gestation, hence, preventive measures such as bed rest, cerclage and tocolytic treatment are called on to avert such an occurrence [4].

Another complication of these pregnancies is when the demise of one of the fetuses occurs [4,5]. When this happens in early pregnancy, major problems do not exist as the dead fetus is soon absorbed. If, on the other hand, it occurs in the more advanced stages then there is a greater risk of pathological consequences for the surviving fetus eg. hypoxia or thromboembolism leading to encephalomalacia and ischaemic renal damage. On the maternal side, the most severe risk encountered is disseminated intravascular coagulation (DIC), therefore, regular coagulation controls are a must.

MATERIALS AND METHODS

From 1987 to 1993 we observed 90 multifetal gestations which we divided into three groups:

Group 1, 74 (82.2%) twin pregnancies
Group 2, 10 (11.1%) triplet pregnancies
Group 3, 6 (6.7%) quintuplet pregnancies

The average age of the patients was 31.3 years (SD ± 4,7).

Of these pregnancies 41.1% were spontaneous, 8.3% resulted from pharmaco-induced ovulation and the remaining 50% occurred following assisted fecundation programmes.

From the obstetrical anamnesis, parity in the first group was, on average, 0,25 (SD ± 0.55) and in the second group 0,5 (SD ± 0.7), while the number of previous abortions was 0,4 (SD ± 0.75) in the first group, 0,1 (SD ± 0.31) in the second group and 0,6 (SD ± 0.55) in the third.

In these 3 groups we analysed some variables (Tab. 1) calculating their respective means and standard deviations. In addition, we used the ANOVA test to discriminate eventual mean differences of the variables analysed within the three groups, applying a $p < 0.05$ significance value. Significant differences were then analysed by the Contrasts test, or Scheffe F-test (Tab. 2).

The 90 pregnancies observed were further divided into group A and group B. Group A, contained the 49 cases (54.4%) observed by us from the early stages and therefore monitored throughout the entire pregnancy and group B the remaining 41 cases (45.6%) who arrived at our clinic in the later stages either because complications had arisen or,

Table 1 - Means and Standard Deviations in Groups 1, 2 and 3

Variable	Group 1		Group 2		Group 3	
	Mean	DS	Mean	DS	Mean	DS
Age	31.541	4.866	28.9	4.557	32.667	1.366
Parity	0.257	0.55	0.5	0.707	0	0
Previous Abortion	0405	0.757	0.1	0.316	0.5	0.548
Spontaneous Pregnancy	0.5	0.503	0	0	0	0
Induced Pregnancy	0.473	0.503	0.7	0.483	0.5	0.548
Induced Ovulation	0.027	0.163	0.3	0.483	0.5	0.508
Fullterm Delivery	0.23	0.424	0.1	0.316	0	0
Preterm Delivery	0.676	0.471	0.6	0.516	0.667	0.516
Abortion	0.095	0.295	0.3	0.483	0.333	0.516
Spontaneous Delivery	0.284	0.454	0.4	0.516	0.167	0.408
Caesarean Section	0.716	0.454	0.6	0.516	0.833	0.408
Normal Growth	0.622	0.488	0.8	0.422	1	0
IUGR	0.311	0.466	0.2	0.422	0	0
Oligo/polyhydramnios	0.176	0.383	0	0	0	0
TTS	0.135	0.344	0	0	0	0
Abnormal Doppler Veloc.	0.135	0.344	0	0	0	0
Congenital Anom.	0.095	0.295	0.1	0.316	0	0
Weight 1	2038.9	819.8	1521	762.53	1276.67	666.556
Weight 2	1958.06	847.3	1489	870.94	1223.33	671.615
Weight 3			1382.2	698.34	831	320.866
Weight 4					1091	508.974
Weight 5					861.25	474.77
Monoc. Monoa	0.081	0.275	0	0	0	0
Monoc. Dia.	0.351	0.481	0.2	0.422	0.167	0.408
Dic. Dia.	0.586	0.499	0.8	0.422	0.833	0.408
Cerclage	0.081	0.275	0.8	0.422	1	0
First Trimester Bleed	0.257	0.44	0.4	0.516	0.667	0.516
Premature Onset of Labor	0.635	0.485	0.6	0.516	0.667	0.516
PROM	0.054	0.228	0	0	0	0
Abruptio Placentae	0.041	0.199	0	0	0	0
Pregnancy-induced Hypertension	0.081	0.275	0	0	0	0

otherwise, to avail of specialized labour/delivery assistance. These two groups also underwent the ANOVA test for the same variables (Tab. 3).

RESULTS

In the total group observed we had 20% fullterm deliveries, 66.7% preterm deliveries and 13.3% abortions. Overall, 28% were spontaneous (including the abortions) and the

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Table 2 - ANOVA Test and Contrast Test between Groups 1, 2 and 3

Variable	F Test	P	Significance
Age	1.65	0.197	n.s.
Parity	1.6	0.208	n.s.
Previous Abortion	0.9	0.409	n.s.
Spontaneous Pregnancy	7.73	0.0008	Signif.
Induced Pregnancy	0.9	0.412	n.s.
Induced Ovulation	13.67	0.0001	Signif.
Fullterm Delivery	1.26	0.288	n.s.
Preterm Delivery	0.11	0.896	n.s.
Abortion	2.8	0.066	n.s.
Spontaneous Delivery	0.51	0.601	n.s.
Caesarean Section	0.51	0.601	n.s.
Normal Growth	2.28	0.108	n.s.
IUGR	1.51	0.227	n.s.
Oligo/polyhydramnios	1.65	0.198	n.s.
TTS	1.21	0.0004	Signif.
Abnormal Doppler Veloc.	1.21	0.0004	Signif.
Congenital Anom.	0.31	0.736	n.s.
Weight 1	3.93	0.023	Signif.
Weight 2	1.18	0.046	Signif.
Monoc. Monoa.	0.68	0.508	n.s.
Monoc. Dia.	0.81	0.45	n.s.
Dic. Dia.	1.68	0.193	n.s.
Cerclage	51.62	0.0001	Signif.
First Trimester Bleed	2.55	0.084	n.s.
Premature onset of Labor	0.03	0.963	n.s.
PROM	0.44	0.644	n.s.
Abruptio Placentae	0.31	0.722	n.s.
Pregnancy-induced Hypertension	0.25	0.777	n.s.

Contrast Scheffe-Test

Variable	Group with Signif. Diff.	
Spontaneous Pregnancy	GR1/GR2	GR1/GR3
Induced Ovulation	GR1/GR2	GR1/GR3
TTS	GR1/GR2	GR1/GR3
Abnormal Doppler Veloc.	GR1/GR2	GR1/GR3
Weight 1		GR1/GR3
Weight 2		GR1/GR3
Cerclage	GR1/GR2	GR1/GR3

Table 3 - ANOVA Test between Groups A and B

Variable	F Test	P	Significance
Age	18.091	0.0001	Signif.
Parity	3.821	0.05	Signif.
Previous Abortion	0.201	0.656	n.s.
Spontaneous Pregnancy	48.481	0.0001	Signif.
Induced Pregnancy	39.741	0.0001	n.s.
Induced Ovulation	0.225	0.636	n.s.
Fullterm Delivery	5.111	0.026	Signif.
Preterm Delivery	1.424	0.236	n.s.
Abortion	0.901	0.345	n.s.
Spontaneous Delivery	2.176	0.144	n.s.
Caesarean Section	2.176	0.144	n.s.
Normal Growth	5.988	0.016	Signif.
IUGR	1.514	0.222	n.s.
Oligo/polyhydramnios	3.491	0.065	n.s.
TTS	0.935	0.336	n.s.
Abnormal Doppler Veloc.	2.732	0.102	n.s.
Congenital Anom.	0.068	0.794	n.s.
Weight 1	0.749	0.389	n.s.
Weight 2	0.272	0.603	n.s.
Weight 3	0.206	0.658	n.s.
Weight 4	0.866	0.421	n.s.
Weight 5	1.342	0.366	n.s.
Monoc.-Monoa	3.772	0.055	n.s.
Monoc.-Dia.	0.647	0.423	n.s.
Dic.-Dia.	3.141	0.079	n.s.
Cerclage	15.001	0.0002	Signif.
First Trimester Bleed	0.607	0.438	n.s.
Premature onset of labor	0.787	0.377	n.s.
PROM	1.454	0.231	n.s.
Abruptio Placentae	2.614	0.109	n.s.
Pregnancy-induced Hypertension	1.487	0.226	n.s.

remaining 72% were delivered by caesarean section. As regards maternal complications we had: 28.8% with threatened abortion, 8% with preeclampsia, 3.3% with detachment of a normally inserted placenta, 4.4% with premature rupture of the membranes and 63.3% with threatened preterm delivery. On the fetal side, congenital anomalies were found in 8.8% of the cases; regular fetal growth in 65.5%; intrauterine growth retardation (IUGR) in 26.6%; alterations in the amniotic fluid of 13.3%; flowmeter alterations in 11.1%, and feto-fetal transfusion syndrome in 11.1%.

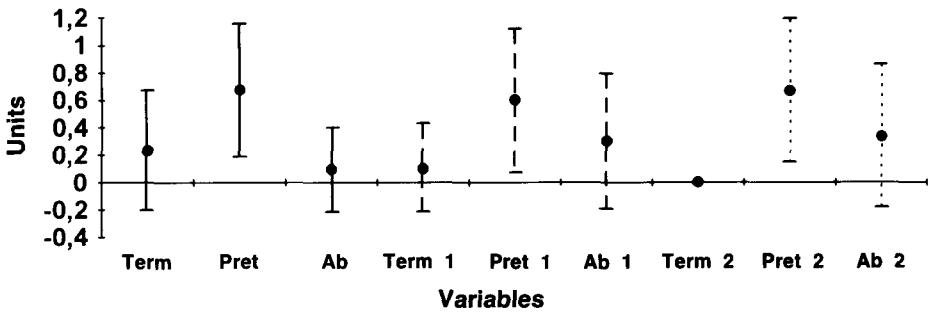

Fig. 1. Means and Standard Deviations of Fullterm and Preterm Delivery and of Abortion in Groups 1, 2 and 3.

[Term = Fullterm delivery Group 1; Pret = Preterm delivery Group 1; Ab = Abortion Group 1; Term 1 = Fullterm delivery Group 2; Pret 1 = Preterm delivery Group 2; Ab 1 = Abortion Group 2; Term 2 = Fullterm delivery Group 3; Pret 2 = Preterm delivery Group 3; Ab 2 = Abortion Group 3.]

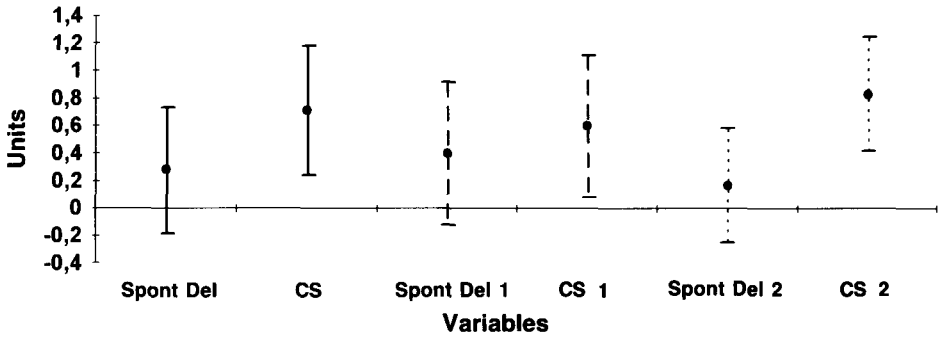

Fig. 2. Means and Standard Deviations of Spontaneous Delivery and Caesarean Section in Groups 1, 2 and 3.

[Spont Del = Spontaneous delivery Group 1; CS = Caesarean section Group 1; Spont Del 1 = Spontaneous delivery Group 2; CS 1 = Caesarean section Group 2; Spont Del 2 = Spontaneous delivery Group 3; CS 2 = Caesarean section Group 3.

The means and standard deviations of the variables analysed in the 3 patient groups (twins, triplets, and quintuplets) are shown in Tab. 1. The most representative variables were also recorded graphically (Figs. 1-4). Table 2 shows the results of the ANOVA test (by number of fetuses) with reference variables, and also the results of the Contrasts Scheffe F-test. Comparing the three groups, only some variables were significant. For example, the number of spontaneous maternities and pharmaco-induced ovulations have significantly different mean values in each of the three groups. It can be seen, in fact, from the Contrasts test and from Fig. 5 (obtained by the means and standard deviations) that the mean value for spontaneous maternities is high in group 1 while it is non-existent in the other two groups; the opposite occurs as regards induced ovulation.

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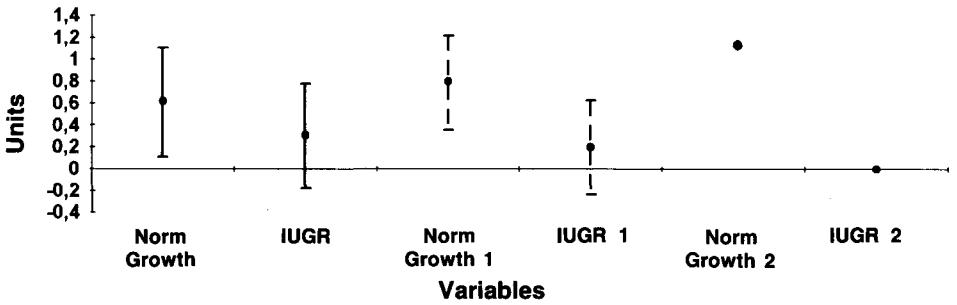

Fig. 3. Means and Standard Deviations of Normal Growth and IUGR in Groups 1, 2 and 3.

[Norm Growth = Normal growth in Group 1; IUGR = IUGR in Group 1; Norm Growth 1 = Normal growth in Group 2; IUGR 1 = IUGR in Group 2; Norm Growth 2 = Normal growth in Group 3; IUGR 2 = IUGR in Group 3.]

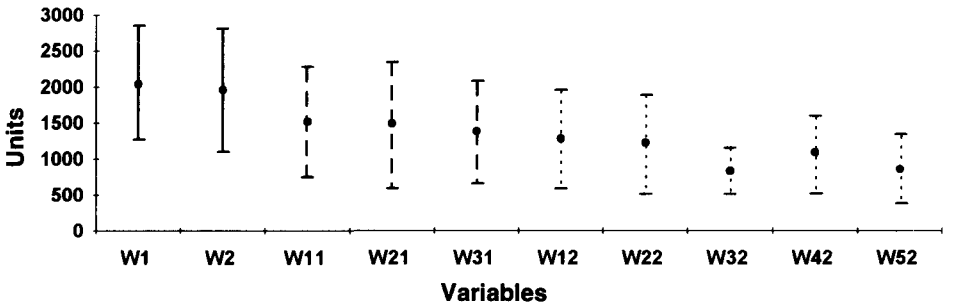

Fig. 4. Means and Standard Deviations of Birthweights in Groups 1, 2 and 3.

[W1 = Weight of first twin Group 1; W2 = Weight of second twin Group 1; W11 = Weight of first twin Group 2; W21 = Weight of second twin Group 2; W31 = Weight of third twin Group 2; W12 = Weight of first twin Group 3; W22 = Weight of second twin Group 3; W32 = Weight of third twin Group 3; W42 = Weight of fourth twin Group 3; W52 = Weight of fifth twin Group 3.]

Other significant variables were the twin-to-twin transfusion syndrome and flowmeter changes. The twin-to-twin transfusion syndrome is typical of monochorionic gestations. We had no such cases in groups 2 or 3, so therefore the mean values obtained refer solely to group 1.

For birthweights of the first and second twin within the three groups, a significance value for the Contrasts test is found among the twin and quintuplet pregnancies only. There is, however, a Contrasts significance among the three groups in relation to cerclage. This is because we carry out cerclage as a standard preventive measure in multifetal pregnancies, whereas, for twins it is usually only carried out in cases of verified cervical incompetence.

The results of the ANOVA test in groups A and B were significant for the following variables: age, parity, spontaneous maternity, induced pregnancy, fullterm delivery, regular fetal growth and cervico-isthmic cerclage (Tab. 3).

The mean parity in group B at 0.39 was clearly higher than in group A (0.163) and

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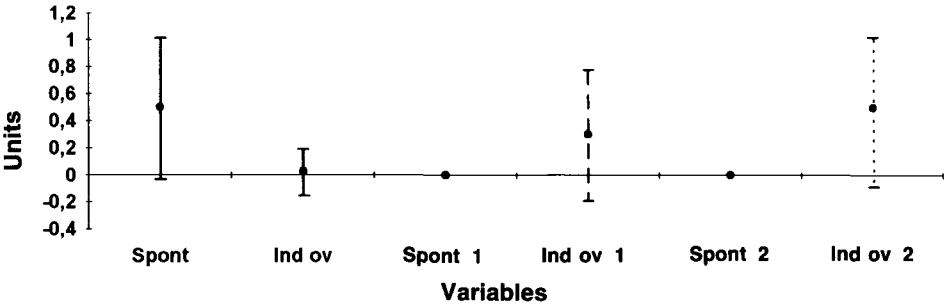

Fig. 5. Means and Standard Deviations of Spontaneous Pregnancy and Induced Ovulation in Groups 1, 2 and 3.

[Spont = Spontaneous pregnancy Group 1; Ind ov = Induced ovulation Group 1; Spont 1 = Spontaneous pregnancy Group 2; Ind ov 1 = Induced ovulation Group 2; Spont 2 = Spontaneous pregnancy Group 3; Ind ov 2 = Induced ovulation Group 3.]

the spontaneous pregnancy mean was also higher in group B (0.73) compared to group A (0.14). Obviously, the inverse is observed in the mean for the induced pregnancy variable ie. group B = 0.19 vs group A = 0.75. This may be due to the fact that many of the pregnancies followed through by us had resulted from assisted fecundation programmes.

Another point worth noting is the significant difference in the means relating to the fullterm variable in both groups (group B, m = 0.09 vs. group A, m = 0.28). The mean for regular fetal growth is also higher in group A (m = 0.77) than in group B (m = 0.53). The last significance value of note relates to the variable, cervico-isthmic cerclage. In group B the mean is 0.049 and in group A 0.362. Again, this difference can be attributed to the greater number of multifetal gestations pertaining to group A.

DISCUSSION AND CONCLUSIONS

The prevention of preterm delivery, with its many associated consequences for the newborn, constitutes one of the fundamental objectives in the management of multiple pregnancies. A "super-specialistic" handling of these gestations can greatly reduce the incidence of serious complications. This conclusive fact is clearly supported by the greater number of fullterm births obtained in group A who were monitored throughout their entire pregnancy at our clinic, compared to group B who only arrived to us in the more advanced stages. Moreover, it bears even greater importance in view of the fact that group A had 9 of the 10 triplet pregnancies and 5 of the 6 quintuplet pregnancies under examination. Group B was mostly made up of twin pregnancies which are obviously at less risk for preterm delivery than multifetal pregnancies. In any event, conscientious obstetrical management of these pregnancies offers a greater possibility for a successful outcome which, in turn, reduces the incidence of disease risk on both the maternal and fetal fronts.

The first important issue in the management of a multifetal pregnancy is its early diagnosis as such. Besides the most obvious virtue, that is, the identification of the number of embryos involved, it also provides for the early differentiation between monodiamniotic and mono-dichorionic gestations. The acquisition of such information is quite important because it greatly enhances the awareness of the various complications associated with and most likely to occur in the given gestation types. For example, twin-to-twin transfusion syndrome is more frequent in monochorionic-diamniotic twins (15% vs. 7.15%) [3]. In addition, early ultrasonographic examination allows for abortions occurring in the earlier stages of gestation to be identified.

Subsequent check-ups permit the early disclosure of congenital anomalies which, in our study, had an overall presence of 8.8%. The specific malformations involved were: one case of anencephaly with rachischisis and thoraco-gastroschisis; the others included cases of intestinal obstruction, lower urinary tract obstruction, omphalocele, isolated anencephaly and, lastly, trisomy 21 associated hydrops.

The prevention of disease risk is, by necessity, associated with the allround well-being of the mother and fetus(es) throughout pregnancy. It would, in fact, be rather limited thinking to consider that pharmacological intervention alone can prevent complications, such as preterm delivery, from arising. It is essential, therefore, that the following general criteria is enacted for the prevention of such a condition and that the patient is well-informed of the situation so that her full cooperation is forthcoming:

- Careful evaluation of the presence of cervico-isthmic incompetence in twin pregnancies and the performance of cerclage where necessary. This type of intervention should be performed as a preventive measure in all multifetal pregnancies.
- Restriction in working activity and increased rest. We deem it opportune to advise this, although no definite data on its beneficial effects actually exists.
- Oral administration of tocolytics on reduction of the uterine excitability threshold.
- Immediate hospitalization if symptoms and characteristics of preterm delivery are diagnosed and, even more so, if maternal and/or fetal complications are present.
- Hospitalization of all multifetal gestations from the 28th week in order to carry out prophylactic treatment against respiratory distress syndrome (RDS).

There is no one opinion on the best method of delivery. In fullterm twin gestations, the choice is usually made on the basis of fetal presentation. However, bearing in mind the related prematurity aspect, the most favoured, from a timing and procedural point of view, is abdominal section. In this manner, the newborn are furnished with an excellent "visiting card" to assist them in adapting to the initial impact of extrauterine life.

In our study, the obstetrical complications encountered were preeclampsia (8.8%), detachment of a normally inserted placenta (3.3%), premature rupture of the membranes (4.4%) and threatened preterm delivery (63.3%). Nonetheless, it should be noted that the percentage of disease was inferior to that reported in the literature. This improved result was not due to any magic formula, but to the constant, qualified management throughout the various stages of the pregnancies by medical and para-medical staff.

Among the feto-neonatal complications which occured were: IUGR (26.6%), alternation in the amniotic fluid (13.3%), flowmeter alterations (11.1%) and twin-to-twin transfusion syndrome (11.1%). In this regard, it should be noted that biophysical monitoring (biometric controls, Doppler-flowmeter controls, and cardiotocography etc.) to-

gether with preventive measures for RDS and treatment of complications in twin-to-twin transfusion syndrome all contributed to the low incidence of feto-neonatal pathology.

The average birthweights were: first twin 1938g (SD 824), second twin 2022g (SD 1625), third twin 1245g (SD 590), fourth twin 1238g (SD 387) and fifth twin 981g (SD 409). In the group of patients followed by us a significantly more regular fetal growth was recorded than in the group who were not followed at our clinic (group A, $m = 0.77$ vs group B, $m = 0.53$).

One very evident concept emerging from examination of the data set forth is the need for continued improvement in the diagnostic, therapeutic and propaedeutic procedures relating to multiple pregnancy. We aim to pursue this objective in order to consolidate the figures already recorded for the various categories at risk examined and to further prevent minimal brain damage from emerging in the neonatal follow-ups of multifetal pregnancies.

A first step in this direction could be the revaluation of ovarian stimulation programmes through drug therapy and a more specific indication of the average number of ova to be re-implanted in the uterus, based on the number of successful pregnancies obtained in more recent years. Guidance and information on this matter should be obtained from the various teams who carry out assisted fecundation programmes. All in all, this is not a particularly daring proposal if one considers that a Bioethics Commission already exists in Italy. This body is supported and validly represented by colleagues, experts in the various sectors, who could conscientiously integrate the points outlined above as part of their own control programme.

I should like to leave you with one reflection: the thought of having a child can spark-off a 'maturity crisis' either in the individual or the couple; the passing from the status of 'being' a child to 'having' a child. When this uncomfortable condition is multiplied in its expression, consideration must be given to the greater difficulty encountered in re-balancing the marasmus of interferring elements, like tension and fear, which can cause the pregnancy to be lived in an irrational state of anxiety. Such a state can culminate in the total upheaval of one's interpretation of what is best for his/her own interests and so when, in addition to this confused state, health problems arise a parent or parents are often led to make obligatory choices.

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