



# Incidence and Costs of Multifetal Pregnancies in Andalusia (2000–2010)

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In the past 50 years the incidence of multiple pregnancies has increased dramatically due almost exclusively to two factors: delayed childbearing and assisted reproductive techniques. In this paper we analyze the variations in the incidence of multiple gestations in Andalusia, one of the biggest administrative regions in Spain, over the last decade. Assisted reproduction techniques are very often evaluated only in terms of implantation and pregnancy rates per cycle, ignoring everything related to complications of multiple births, prematurity or economic overload. The rate of twins in Andalusia has increased from 10.9 per thousand in 2000 to 16.2 per thousand in 2009. The rate of triplet births has also increased in recent years. After a decline in 2003, motivated by promulgation of the first Human Assisted Reproduction Law, there was an increase after a second law came into effect in 2006. Health care spending attributable to the excess of multiple pregnancies reported in the decade 2000–2010 may have been much higher than €25 million.

■ **Keywords:** multiple pregnancy, assisted reproduction, economic cost

Simultaneous development in the uterus of two or more fetuses is a normal phenomenon in lower mammals but it is rare in humans. Evolutionary adaptation of the maternal organism is aimed at developing a single fetus, therefore multiple pregnancy, although not strictly pathological, represents a deviation from the norm and in some extent a phylogenetic regression. If we consider that the first hominid species with human reproduction patterns appeared 2.5 million years ago, we can assume that the increased number of multifetal pregnancies observed in the last 50 years will have some biological price. In this sense Keith (1995) wondered 30 years ago if maternal and neonatal risks posed by iatrogenic multiple pregnancy were justified.

Multiple pregnancies increase first trimester symptoms such as nausea, headache, dizziness, and cramps. Hyperemesis gravidarum, threatened abortion, gestational hypertension, gestational diabetes, anemia, venous insufficiency, and sciatic pains, are also more frequent. Hypervolume in the final months produces palpitations, persistent constipation and frequent urination, edema and vascular compression in the legs and vulva, and dyspnea. Maternal weight gain in multiple pregnancies is higher than in singleton pregnancies, by an average of about 20 kilograms (Blickstein & Keith, 2003).

The occurrence of maternal complications such as preeclampsia, diabetes, premature rupture of membranes, or anemia increases with the number of fetuses (Conde-Agudelo et al., 2000; Elliot, 2005). The risk of maternal death is 3.6 times more common in multiple gestations (20.8 versus 5.8), independent of race and socio-cultural status (MacKay et al., 2006).

From a psychological point of view, multiple births are also a source of couple destabilization and social disruption in relationships. Such situations cause stress, depression and frequent mood swings. The studies published to date suggest that these problems are presented in one out of every three to four families. Postpartum depression is 40% more probable in cases of multiple pregnancies (Yoonjoung, 2009).

The most common complication of multifetal pregnancies is preterm birth (Chauhan et al., 2010). Birth occurs before 37 weeks in 50% of twin pregnancies and in 99% of triplet pregnancies, resulting in increased perinatal

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morbidity and mortality. The risk of cerebral palsy is four times more common in twins than in singletons (Pharoah, 2005). The probability of dying in the first year of life due to prematurity is seven times higher in the case of twin pregnancies. The proportion of low birthweight is also up to seven times higher.

In the past 50 years the incidence of multiple pregnancies has increased due almost exclusively to two factors: delayed childbearing and assisted reproductive techniques (Blondel & Karminski, 2002; Eriksson & Fellman, 2007). Age is housed as an independent risk factor (Fellman & Erikson, 2009) for natural multiple pregnancies. The probability of conceiving more than one fetus increases between the ages of 35 and 39 and declines thereafter, except among the black population where an increasing trend is observed after that age (Hardin et al., 2009). In these populations higher levels of endogenous FSH cause multiple ovulations and consequently multiple pregnancies.

On the other hand, for some women, artificial reproduction techniques (ART) are the only possibility of conceiving, so that treatments in assisted reproduction centres include high doses of FSH to allow the development of more than one egg per cycle, or intrauterine transfer of more than one embryo simultaneously, in order to increase the chances of pregnancy in a cycle of ovarian stimulation.

Results of ART are very often evaluated only in terms of implantation rates and pregnancy rates per cycle, ignoring everything related to pregnancy and multiple birth complications, prematurity of newborns, or economic or psychological overload, which appeared when several children were born simultaneously.

We provide an obstetric vision of the economic consequences of ART as a main etiologic factor for multiple pregnancies in Andalusia.

## Materials and Methods

Andalusia is one of the biggest administrative regions in Spain. It occupies the southern part of the country, with a population over eight million residents. It is divided into eight administrative provinces (Almería, Cádiz, Córdoba, Granada, Huelva, Jaén, Málaga and Seville). We consulted the Statistical Institute of Andalusia to find the data for total deliveries and newborns in Andalusian provinces per year. For information concerning the number of multiple births occurred in the region by year and by province, we have consulted Andalusian Health Central Services Minimum Basic Data Set (MBDS; Andalusia Health Service).

We have also consulted the latest update of National Health Service Case-Mix (Diagnoses Related Groups: DRG; Statistics Portal of NHS, 2008) to estimate economic costs for multiple births. Costs of DRG have been obtained regularly since 1997 with the information on hospital costs from cost accounting systems and clinical data on the discharges of patients in a representative

sample of hospitals of the National Health System. We have also reviewed national and regional benefits related to multiple births under the Ministry of Labour and Immigration and the Equality and Social Welfare Council of the Andalusian Government.

## Results

In the period between January 2000 and December 2009, 887,802 births were registered in Andalusia, with a total of 900,336 newborns. Table 1 shows the total number of births and newborns occurring by province and year.

In last decade 11,917 twin deliveries and 572 triplets have been registered, which means 13.4 twin deliveries per 1,000 and 6.4 triplets per 10,000. Twin birth rates in Andalusia show a progressive increase from 10.9 per 1,000 in 2000 to 16.2 per 1,000 in 2009. Triplet births rate decreased after 2002 (9.1 per 10,000), stabilizing around six per 10,000 (see Tables 2 and 3).

The duration of twin pregnancies has been stable in recent years with an average of 35.4 weeks. We have observed some differences among provinces. Jaén is the Andalusian province where twin pregnancies have a longer duration (36.2 weeks), and Málaga is the province where the average length is lower (34.8 weeks). The average length of triplet pregnancies was 32.1 weeks (33.2 weeks in Seville at the highest and 31.4 weeks in Granada at the lowest). The mean maternal age was 31.5 years for the twin pregnancy group and 32.2 for triplets, increasing over the period 2000–2010.

All multiple gestations require antepartum hospitalization. Hospital admission for twin pregnancies averaged 2.8 days (4.2–1.5) before labor and 4.9 days afterwards (4.3–6.5). Triplet pregnancies averaged 9.8 days for antepartum hospital admission (17.1 to 2.9 days) and 7.6 postpartum (9.6 to 6 days). The cesarean section rate is high in twin pregnancies (over 50%). Although some series consider the possibility of vaginal delivery in triplet pregnancies, in our environment, cesarean section is performed in all cases. Costs of DRG published by National Health Service are summarized in Tables 4 and 5. In most favourable situation for twins brought up in a vaginal delivery in the averaged week in Andalusia (35–36 weeks) we can calculate costs related to childbirth and neonatal care:

Vaginal twin birth

$$\text{DRG } 372 + 2 \times (\text{DRG } 620) = \text{€}1422 + (2 \times [\text{€}1782.59]) = \text{€}4,987.18$$

On the other hand, in triplet pregnancies without extra hospital admissions, delivered around the average 33–34 weeks, we can calculate costs related to cesarean section and neonatal care:

Triplet cesarean birth

$$\text{DRG } 651 + 3 \times (\text{DRG } 613) = \text{€}3905.88 + (3 \times [\text{€}9987.5]) = \text{€}33,868.38$$

**TABLE 1**  
Number of Deliveries and Newborns in Each Andalusian Province

Year	AL	CA	CO	GR	HU	J	MA	SE	TOTAL
2000									
Deliveries	5,979	12,644	7,969	8,872	4,747	6,698	13,886	19,395	80,190
Newborns	6,061	12,772	8,048	8,965	4,803	6,768	14,035	19,578	81,030
2001									
Deliveries	6,416	12,771	7,841	8,851	4,818	6,367	14,284	19,274	80,622
Newborns	6,487	12,894	7,947	8,942	4,890	6,427	14,419	19,458	81,464
2002									
Deliveries	6,357	12,881	7,818	8,574	4,916	6,439	14,610	19,617	81,212
Newborns	6,460	13,026	7,924	8,698	4,987	6,522	14,817	19,852	82,286
2003									
Deliveries	6,567	13,368	8,163	9,107	5,125	6,603	15,816	20,433	85,182
Newborns	6,683	13,531	8,259	9,222	5,194	6,682	16,038	20,722	86,331
2004									
Deliveries	7,408	13,852	8,112	9,477	5,137	6,674	16,590	21,063	88,313
Newborns	7,520	14,062	8,197	9,594	5,212	6,746	16,816	21,368	89,515
2005									
Deliveries	7,665	14,332	8,236	9,733	5,369	6,510	17,178	21,922	90,945
Newborns	7,803	14,530	8,355	9,872	5,462	6,602	17,394	22,268	92,286
2006									
Deliveries	8,297	14,554	8,523	10,035	5,510	6,809	17,847	22,740	94,315
Newborns	8,414	14,766	8,629	10,174	5,619	6,891	18,121	23,157	95,771
2007									
Deliveries	8,322	14,293	8,295	10,413	5,676	6,655	18,160	23,103	94,917
Newborns	8,451	14,492	8,402	10,545	5,784	6,723	18,462	23,533	96,392
2008									
Deliveries	8,974	14,350	8,661	10,574	6,010	7,011	18,774	24,796	99,150
Newborns	9,101	14,531	8,763	10,684	6,129	7,108	19,098	25,269	100,683
2009									
Deliveries	8,304	13,825	8,249	9,689	5,720	6,527	17,535	23,107	92,956
Newborns	8,453	14,036	8,380	9,813	5,818	6,614	17,879	23,603	94,578
TOTAL									
Deliveries	74,289	136,870	81,867	95,325	53,028	66,293	164,680	215,450	887,802
Newborns	75,415	138,640	82,904	96,509	53,898	67,083	167,079	218,808	900,336

Note: AL: Almería. CA: Cádiz. CO: Córdoba. GR: Granada. HU: Huelva. J: Jaén. MA: Málaga. SE: Seville.

The economic burden of multiple gestations (Callahan et al., 1994) is not limited to perinatal care. Disbursements made by the government with grants and subsidies are clearly insufficient to cover the costs that the birth of several children at once involve, but from an economic analysis viewpoint it is considerable if the fact that most multiple gestations originate from iatrogenic situations is taken into account. The main incentives are detailed in Table 6. The Spanish Government Economic Benefit for Multiples Births is a single payment provision. Since 2003, women with children under three years old can also reduce the amount of the tax differential on income by up to €1,200 per year per child, or opt for an advance payment of €100 per month. Also, from July 2007 to December 2010, another Spanish Government contribution was introduced, in the order of €2,500 per newborn (Government of Spain, 2007). The Andalusian Council provides another grant for multiple births, to be paid as an annual sum for the first three years after birth, which is limited by women's incomes (Government of Andalusia, 2002). With these grants, by the end of the third year after delivery, some families would have received more than

€20,000 for twins and nearly €35,000 for triplets from public funds.

We have observed over the last decade a rate of 13.4 twin births per thousand, equal to one twin birth every 72 births. If the twin rate had remained stable at 10.7 per thousand as described by Fuster et al. (2010), in the period

**TABLE 2**  
Total Number of Twin and Triplet Pregnancies Per Year (2000–2010)

Year	Twins	Rate (per 1,000)	Triplets	Rate (per 10,000)
2000	874	10.9	55	6.8
2001	896	11.2	59	7.3
2002	1,049	13.0	74	9.1
2003	1,131	13.3	56	6.6
2004	1,125	12.7	59	6.7
2005	1,222	13.4	55	6
2006	1,297	13.7	51	5.4
2007	1,364	14.4	46	4.8
2008	1,451	14.6	56	5.6
2009	1,508	16.2	61	6.6
Total	11,917	13.4	572	6.4

Note: Rates are reported as per 1,000 in twins and per 10,000 in triplets.

**TABLE 3**  
Number of Twin and Triplet Births Registered by Province (2000–2010)

Province	Twins	Rate (per 1,000)	Triplets	Rate (per 10,000)
Almeria	1,123	15.1	34	4.6
Cadiz	1,680	12.3	74	5.4
Cordoba	952	11.6	47	5.7
Granada	1,257	13.2	53	5.5
Huelva	797	15.0	28	5.3
Jaen	847	12.8	41	6.1
Malaga	2,374	14.4	153	9.3
Seville	2,887	13.4	142	6.6
Total Andalusia	11,917	1.4	572	6.4

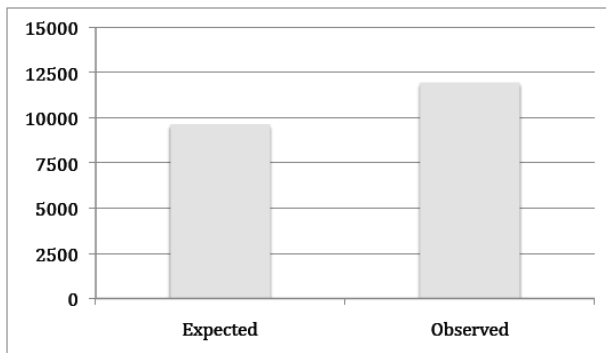
Note: Rates are reported as per 1,000 in twins and per 10,000 in triplets.

**TABLE 4**  
Cost of Obstetric Diagnosis Related Groups (DRG) in Multiple Pregnancies

Diagnosis related group (DRG)	Costs (euro)
373. Vaginal delivery without complications	1,422.61
372. Vaginal delivery with complications	1,679.97
371. Cesarean without complications	2,741.00
370. Cesarean with complications	3,036.43
651. High risk cesarean without complications	3,905.68
650. High risk cesarean with complications	4,980.22

**TABLE 5**  
Costs of Neonatal Diagnosis Related Groups (DRG) in Multiple Pregnancies

Birth	Mean birthweight	Diagnosis related Group (DRG)	Cost DRG (euro)
Twins	2000 to 2499 g	620: Newborn with birthweight between 2000 and 2499 g, without surgical pathologies	1782.59
Triplet	1500 to 1999 g	613: Newborn with birthweight between 1500 and 1999 g, without surgical pathologies	9987.50



**FIGURE 1**  
Number of expected\* and observed twin births in Andalusia (2000–2010; according to rates described by Fuster and Helling-Zeleny’s law).

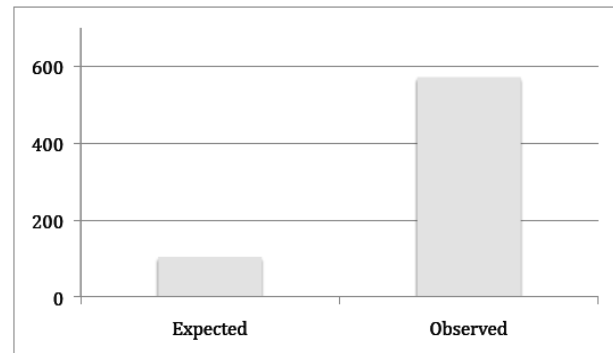
2000–2010 we would have found 9,650 twin births instead of the 11,950 registered. On the other hand we have found a rate of 6.4 triplet pregnancies per 10,000, corresponding to one triplet birth every 1,515 births (Figures 1 and 2). If we calculate the triplet pregnancy rate using the Helling and Zeleny biological approach (Twins:  $1/N$ ; Triplets  $1/N^2 \exp 2$ ), according to trends described by Fuster et al. (2010), in first half of 20th century we would have expected a triplet pregnancy every 8,464 births ( $1/92 \exp 2$ ), so that in last decade, 2000–2010, we would have expected 105 triplet pregnancies in Andalusia, instead of the 572 registered, which means an increase of 500% above expectations (Figures 1 and 2).

The differences described above between observed and expected cases of multiple pregnancies amount to 2,300 twins and 467 triplets. The economic burden of the increasing rates of multiple pregnancies can be calculated, as shown in Table 7.

**Discussion**

In our daily duties as gynecologists in one of the greatest maternity hospitals in our country, our attention is increasingly drawn to the growing number of multiple pregnancies that are attended every year. The analysis of data presented in this article shows that it is not a subjective impression derived from a selection bias. As it has been recently noted by Fuster et al. (2010), Andalusia is a Spanish region with a demonstrated higher rate of twin pregnancy.

By analyzing the fluctuations experienced by the rate of multifetal pregnancies in the last decade, we found in most provinces an increased number of multifetal births in 2001 and 2002, which declined in 2004. In 2004, the first *Spanish Assisted Human Reproduction Law* (Government of Spain, 2003) came into force. This law established limitations in producing a maximum of three oocytes in each reproductive cycle. It limited the number of embryos transferred in each cycle to three, in order to reduce the number of multiple births. Then in 2006, a new



**FIGURE 2**  
Number of expected\* and observed triplet births in Andalusia (2000–2010; according to rates described by Fuster and Helling-Zeleny’s law).

**TABLE 6**

## Main Grants and Subsidies for Multiple Births in Andalusia

	Twins		Triplets	
Spanish Social Security (S.M.I. 2010: €633.3)	Multiple delivery	4 × S.M.I.	Multiple delivery	8 × S.M.I.
Spanish Tax Agency	Grant at birth	2 × €2,500	Grant at birth	3 × €2,500
	Tax deduction: (2 × €1200) / year, 3 years		Tax deduction: (3 × €1200) / year, 3 Years	
Andalusian Government (limit for families with 2 members: 4.8 times S.M.I.*)	Multiple delivery	2 × €1,200 / year (3 years)	'Multiple Delivery'	3 × €1,200 / year (3 years)
Total cost (at the end of third year)		€21,932		€34,164

Note: \* S.M.I.: minimum interprofessional wage

**TABLE 7**

## Overcost Arising From Excessive Multiple Pregnancies Registered in the Last Decade in Andalusia (Cesarean Rate of 50% for Twins)

Birth	Excess (Observed – Expected)	Unit cost	Overcost 2000–2010
Twins	2,300	€4,987.18	€11,470,514
Triplets	467	€33,868.38	€15,816,533
		Total	€27,287,047

**TABLE 8**

## Number of Embryos Transferred Per Cycle in IVF Treatments in Spain

Number of embryos transferred	Frequency
1	14.2%
2	63.2%
3	22.8%

Note: Data obtained from Spanish Fertility Society, 2008.

*Spanish Human Assisted Reproduction Law* (Government of Spain, 2006) came into effect. This law maintained the limit of three embryos per transfer in IVF, but changed the approach of limiting the production of oocytes in each cycle, as it regulated embryos cryopreservation and its use for research purposes. The rising rates of triplet pregnancies found in all provinces in 2008 and 2009, except for Málaga and Jaén, is extremely striking.

The results observed in our study are consistent with the Spanish Fertility Society's (2008) latest annual report in which one single embryo was transferred in only 14.2% of cycles (Table 8). It is clear the role of ART is a primary etiologic factor for multiple pregnancies, and is therefore in the interest of fertility centers to prevent its occurrence. Commercial interests in private centers and economic interests of the pharmaceutical industry make it very difficult to consider the biological, economic, social, and psychological costs related to multiple pregnancies, transferring multiple embryos and hyperstimulating ovarian cycles. Given the extraordinary consequences of these procedures and the lack of a fluid communication between ART specialists and obstetricians, medical societies should promote new regulations. When a multiple pregnancy is

detected, the obstetrician is usually the one who has to warn future parents about physical, social, psychological and economic consequences due to multiple pregnancies. However, such information should have already been given to women prior to ART.

Approaches such as official promotion of single-embryo transfer (SET) or compulsory and systematic registration of final perinatal outcomes after ART in fertility centres should be taken into account. SET in IVF is being used in some countries, and the results in terms of rate of pregnancy are not so different. These protocols involve the use of lower doses of FSH in ovarian stimulation, and require the development of refined techniques of cryopreservation in order to consider, if necessary, multiple transfers of a single embryo (Maheshwari et al., 2011; Pandian et al., 2009).

The costs stated above impact almost entirely on the Andalusian Public Health System as in most cases multiple births are handled in public hospitals, even in cases of private ART pregnancies. Costs related to prenatal care or hospital admissions before delivery have not been included due to their high variability.

## Conclusions

Multiple pregnancies are a source of medical complications for mothers and newborns. They are also a source of psychological maladjustment, destabilization of the family and generate a significant economic burden. The economic cost of multiple pregnancies might be 10 to 30 times the cost of a single IVF cycle, their main etiologic factor.

We have identified an increasing rate of multiple pregnancies in Andalusia in the last decade. After declining in 2003, motivated by the promulgation of first *Human Assisted Reproduction Law*, there was a rise following the effect of a second human ART law in 2006. We can describe the incidence of multiple pregnancies in terms of epidemiological health alert. It is necessary to develop clinical protocols for single-embryo transfer and legislative tools in order to reduce maternal morbidity and perinatal mortality and disability resulting from the prematurity that multiples generate. Opportunity costs are not negligible. Health care expenditure attributable to the excess

multiple pregnancies reported in the decade 2000–2010 could have been much higher than 25 million euros.

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