
Stillbirth Pattern in an Isolated Mediterranean Population: La Alpujarra, Spain

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Abstract This study attempted to analyze the effect of several factors on the stillbirth pattern in a relatively isolated rural population, La Alpujarra (Spain), during the first half of the 20th century. The study was a retrospective analysis from a total sample of 2199 births to 525 mothers, allowing for birth year of mother, maternal age, parental inbreeding, family size, birth order, sex, single/twin delivery, and birth interval. Binomial probability distribution of stillbirths provided no evidence for any significantly increased risk in relation to family size. Analysis of covariance (ANCOVA) of stillbirth risk in affected families indicated a significant effect for sex of the child, parental consanguinity, and birth year of mother. Logistic regression showed increased risk in twin delivery and pregnancy order one, but not for birth order other than one. Multivariate analysis of variance (MANOVA) testing for differences between affected and unaffected families supported a temporal decrease of stillbirths during the period studied. Although the birth interval average was significantly shorter in affected families ($p < 0.0001$), this association did not hold, in a more detailed analysis, for individual intervals in these families ($p = 0.20$). There was no significant effect of maternal age on stillbirths in the whole sample or limited to first pregnancies. These results suggest that birth order one and twin delivery were the main determinants of the stillbirth pattern in La Alpujarra. Furthermore, our data indicate that the decline in stillbirth rate began before medical facilities for perinatal care became available, which was not until after 1950. The temporal decrease in stillbirth rates may therefore be related to an increasing social attention to deliveries rather than to prenatal care medical facilities.

Perinatal mortality, a term coined by Peller (1948) to include late fetal and early neonatal deaths, constitutes an aspect of population reproductive health that has long been investigated in epidemiological and biodemographic studies. Perinatal

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mortality represents a segment of prereproductive mortality that, along with other demographic variables such as fertility, has been classically investigated as a valuable indicator of biological fitness of human groups. The distribution of perinatal mortality rates indicates an interesting geographical and temporal variation throughout the 20th century. At present, the most important between-population crude rate differences correspond mainly to those between developed and developing countries, possibly because of differentials in socioeconomic factors and medical facilities (see, for example, Murrells et al. 1985; Saksena and Srivastava 1980), but other reasons cannot be excluded (Petridou et al. 1996; Coory 1998). In many cases, the risk of perinatal mortality has been found to be associated with different biological and social-demographic factors (Forbes and Pickering 1985; Kiely et al. 1986; Swenson and Harper 1979), pointing to possible population-specific patterns that depend on ecological and social peculiarities. From a temporal perspective, the sharp decline in prereproductive mortality related to the demographic transition experienced in most areas of the industrialized world during the 20th century has also influenced perinatal mortality rates (Teitelbaum 1975; Terrenato et al. 1979). The considerable improvements in socioeconomic conditions and the quantity and quality of pre- and postnatal care have led to a drastic reduction of mortality during infancy and childhood. However, despite all efforts, perinatal losses have not similarly decreased in frequency. In particular, the stillbirth rate has constituted a progressively increasing percentage of total mortality in the prereproductive period and is now generally considered to be the most relevant mortality *fraction* from the point of view of natural selection (Ulizzi et al. 1979; Ulizzi et al. 1998).

Recent suggestions for altering the definition of perinatal mortality have been taken into account, and modified, in specifying the limits of this study. The more widely used classifications of perinatal mortality distinguish between stillbirths (including fetal losses at 28 completed weeks of gestation until birth) and neonatal deaths (those occurring from birth to 6–8 days following). As for the lower limit, although recent proposals suggest registering as stillbirths those fetal deaths at 24 to 27 completed weeks of gestation as a more efficient definition for perinatal care (Cartlidge and Stewart 1995; Alberman et al. 1997), here, as in most studies, the classical limit is considered according to the characteristics of the collected data (see below). The upper limit was established to be within 24 hours after birth, in order to minimize potential biases associated with the recalled data used; besides, most neonatal mortality is attributed to perinatally related events (Cartlidge and Stewart 1995).

Little is known about the clinical causes of stillbirth mortality. Only recently have data on cause and time of death of stillbirth been available in a few developed countries. Among the most frequently mentioned causes are asphyxial conditions; congenital anomalies; complications of the placenta, cord, and membranes; low birth weight; and fetal immaturity. It has been estimated that placental pathologic conditions are responsible for around one-third of stillbirths; however, the causes of stillbirth are many and varied, and usually a remarkable

proportion (more than one-third) remain unexplained (Incerpi et al. 1998). On the other hand, studies of stillbirth determinants have described a set of maternal, child, pregnancy, and ecological factors that might play a role in affecting fetal and neonatal survival in different population groups. Maternal age, birth order, child sex, multiple births, as well as several ecological variables, have been found among the most relevant determinants (see, for example, Pastore et al. 1997; Waldhoer et al. 1996; Petridou et al. 1996; Raymond et al. 1994). The clinical mediators associating these factors with stillbirth are still unexplained, however.

Based on retrospective data from the first half of the 20th century, this paper examines the effects of several biodemographic factors on the risk of unsuccessful termination of pregnancy due to stillbirth in La Alta Alpujarra Oriental (286.4 km²). This area is located in the easternmost part of La Alpujarra region (2000 km²), on the eastern side of the Sierra Nevada range, which lies in the southeast Iberian Peninsula. It is inhabited by a rural Mediterranean population (8734.9 average inhabitants for the period 1900–1950) that is mainly devoted to small-holding farming. It is scattered among small villages in different valleys at an altitude of about 1000 m. Access is difficult and was especially so before roads were constructed between 1940 and 1960. Previous demographic studies conducted on this geographically and culturally isolated population indicate an average endogamy rate of 92.54%, along with considerable emigration to industrialized regions causing a marked decline in the population size, similar to many other Spanish rural populations (Luna 1984a, 1984b). Data on mortality and fertility for the period under consideration reveal a substantial decrease in mortality. The persistence of high fertility rates, however, shows that the demographic transition was not completed before 1950 (Luna and Moral 1990; Luna and Fuster 1990). The present results on determinants of stillbirth pattern should contribute to the demographic information available on La Alta Alpujarra Oriental as an approach to the biological fitness of this population. Furthermore, because of the geographical and cultural similarities among many Mediterranean regions, these results could likely be generalized to include other rural Mediterranean groups before demographic transition was completed.

Materials and Methods

Data used in this paper proceed from a sample of the reproductive records obtained from resident families in La Alta Alpujarra Oriental (for details see Luna et al. 1997). Only reproductive histories corresponding to complete families were selected for this study. Complete families are defined as those of a finite size with mothers beyond the reproductive age (45 years). In our study, only mothers whose last delivery occurred before 1950 were selected; hence, most were more than 45 years of age at the time data were collected (1978). Only very few women under 45 years of age (but close to 45) were included because they were dowerers, and, according to Luna and Fuster (1999), the extramarital fertility in this region was null during the period studied. Data were obtained by personal inter-

views. In all cases more than one family member was interviewed and the information given was matched to that in the "*Libro de Familia*" (an official Spanish document of the family unit), to minimize the recall bias. From selected families, the following variables were available: birth date of mother, marriage date, maternal age, parental inbreeding, family size, parity (birth order), sex of newborn, twin/single delivery, and birth interval (period between two consecutive deliveries, measured in months).

In this paper, no distinction between perinatal mortality and stillbirth was made. According to the usual methods, stillbirths were defined as all newborns who died during delivery, abortions following 7 or 8 months of gestation, and live births not living longer than 24 hours. All stillbirths registered, except for two fetal deaths in the eighth gestational month, had died during delivery or a few hours after delivery. The stillbirth rate has been defined as the number of stillbirths for 1000 registered deliveries. The information collected was stored in two files, one corresponding to deliveries (Mortin1.sta, with 2199 births), and the other to families (Mortin2.sta, with 525 mothers). The analysis of these data was used to define the Alpujarran stillbirth pattern during the first half of the 20th century.

The dependence of stillbirth occurrence in relation to family size only was tested by χ^2 . The possible regulating action of parental inbreeding and newborn sex on stillbirth risk was measured through an analysis of covariance (ANCOVA) test. In this test, the dependent variable is stillbirth rate in families with a dead newborn (Vox-Cox transformed), the factor is parental inbreeding, and the covariate is male percentage at delivery. According to values F coefficient, couples were classified into only two categories, consanguineous ($F \geq 1/256$) and non-consanguineous (the rest), due to the low number of related couples. The parity and twinning effects were analyzed by a logistic regression. The mean maternal age effect was assessed by two methods: (1) by a regression, to determine significant association between maternal age and stillbirth rate; and (2) through a logistic regression, to evaluate this same effect at first deliveries, due to the particular importance of mortality in the case of a firstborn.

Finally, the secular decrease of stillbirth was approached by regression analysis between maternal birth date and stillbirth rate in the 525 families. The joint effect of this secular change, beginning reproductive age of women and reproductive pace of couples, was evaluated through a multivariate analysis of variance (MANOVA) test by comparing maternal birth date, marital age of mothers, family size, and average birth interval. In families with a loss, the birth interval effect on stillbirth risk was analyzed by a logistic regression.

Results

In the first half of the 20th century, the selected Alpujarran mothers had 2199 deliveries, 117 of which were stillbirths. The average family size was 4.19 children and the stillbirth rate was 53.21 born dead for 1000 deliveries (Table 1). In 439 complete families (83.62%) no stillbirths were present, and in almost half

Table 1. Family Distribution of Stillbirth According to Family Size in the Alpujarra Population

Family Size	Total Families	Families with <i>n</i> Stillbirths				Total Stillbirths		Stillbirth Rate (No./1000)	No. of Families Firstborn Dead
		<i>n</i> =0	<i>n</i> =1	<i>n</i> =2	<i>n</i> =3	Obs.	Exp.		
1	21	21	0	—	—	0	1.12	0	0
2	99	90	9	0	—	9	10.53	45.45	3
3	117	106	6	4	1	17	18.67	48.43	10
4	86	72	11	3	0	17	18.30	49.42	5
5	84	64	17	1	2	25	22.35	59.52	10
6	46	33	8	3	2	20	14.68	72.46	7
7	29	22	5	1	1	10	10.80	49.26	2
8	19	16	1	1	1	6	8.09	39.47	1
9	12	7	2	3	0	8	5.75	74.07	3
10	8	5	3	0	0	3	4.26	37.50	0
11	3	2	0	1	0	2	1.76	60.61	1
13	1	1	0	0	0	0	0.69	0	0
Totals	525	439	62	17	7	117	117	53.21	42

(42) of the remaining 86 families the stillbirths were firstborns. No family with more than three stillbirths was found.

As for the effect of family size, the observed and random expected number of stillbirths did not show significant differences ($\chi^2 = 5.00$, df [degrees of freedom] = 8, $p = 0.76$; extreme classes were grouped due to low frequencies). These results indicate that the stillbirth frequency rises according to the sibship size, as expected. Consequently, the family size does not have any significant effect on the stillbirth rate.

In the 86 families with stillbirths, an ANCOVA test on mortality rate (dependent variable; Vox-Cox transformed) in relation to parental inbreeding (factor) and sibship male percentage was carried out. The results show a positive correlation between stillbirth rate and male percentage ($F_{1,83} = 6.09$, $R^2 = 6.84\%$, $r = 0.262$, $p = 0.016$; Figure 1), which is not modified by different values of parental inbreeding ($F_{1,82} = 0.98$, $p = 0.33$). This suggests that boys have a greater stillbirth probability than girls. On the other hand, stillbirth rate in the 12 consanguineous families was significantly lower than that observed in the 74 nonconsanguineous families (adjusted average: 21.53 vs. 32.13%; $F_{1,83} = 4.46$, $p = 0.038$). This result indicates that in consanguineous couples stillbirth risk of children is reduced.

In the families, maternal birth date and stillbirth rate were negatively correlated ($F_{1,523} = 5.84$, $R^2 = 11.0\%$, $r = -0.105$, $p = 0.016$), suggesting that the Alpujarra stillbirth rates experienced a secular decrease during the first half of the 20th century.

From birth data, the relationships between stillbirth rate (dependent variable) and parity, firstborn, and twinning (independent variables), measured by lo-

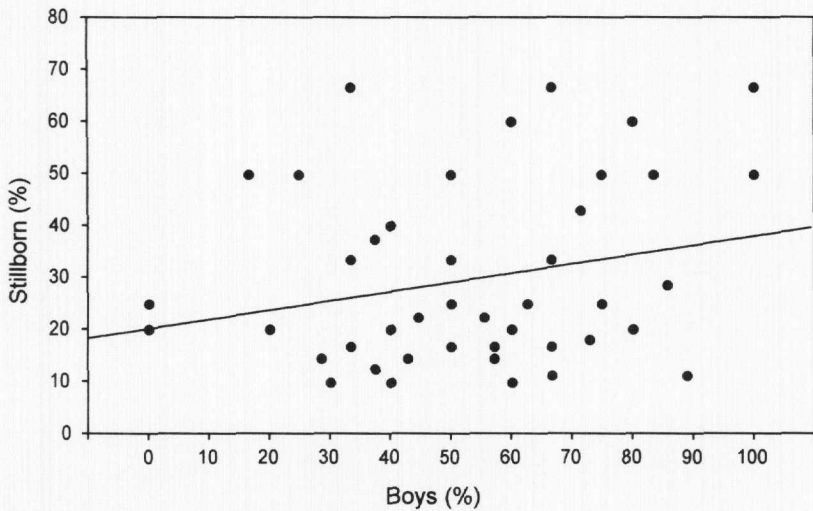


Figure 1. Stillbirth rate and percentage of male stillborn in families with stillbirths.

Table 2. Logistic Regression Results between Stillbirth and Parity, Firstborn, and Twinning

Variable	Effect	t_{2195}	p
Parity	0.055	0.87	0.38
Firstborn	0.88	3.24	0.001
Twinning	1.11	2.65	0.008

gistic regression, showed a significant effect ($\chi^2 = 18.45$, $df = 3$, $p = 0.0003$, 94.8% of cases assigned correctly). However, the individual effect of each variable was different (Table 2). The 2147 children of single deliveries had a lower death rate than the 52 twins corresponding to 26 deliveries (50.28 vs. 134.62). Similarly, the 530 firstborn children (there were five twinning and firstborn deliveries) had a greater death probability than their subsequent siblings (83.02 vs. 42.52). However, the birth order after the first delivery had no significant effect on stillbirth risk.

A family analysis showed that mean maternal age does not have any significant effect on stillbirth rate (regression: $F_{1,523} = 1.56$, $r = 0.055$, $p = 0.21$), nor firstborn mortality rate (logistic regression: $\chi^2 = 0.34$, $df = 1$, effect = 0.021, $p = 0.55$).

In all families examined, the effects of maternal birth date, marital age of women, family size, and average birth interval were compared (Table 3). Results

Table 3. Results of the MANOVA Analysis: Average Values of Maternal Birth Date, Marital Age of Women, Family Size, and Birth Interval in Families with and without Stillbirths

Variable	Families with Stillbirths	Families without Stillbirths	$F_{1,1644}$	p
Maternal birthdate	1918.97	1922.29	27.82	< 0.0001
Marital age (years)	23.70	23.72	0.013	0.91
Family size	6.27	5.38	41.87	< 0.0001
Birth interval (months)	37.31	43.32	15.06	< 0.0001

Wilks's lambda = 0.963, $R^2 = 3.7\%$, $p < 0.0001$.

indicate that: (1) generally, mothers with stillbirths were born before mothers without losses, corroborating the secular decrease of Alpujarran stillbirths; (2) marriage age of mothers does not show any differential effect on death risk of children; (3) again, families with stillbirths showed larger family size (one more son) than families without losses; and (4) on average, families with stillbirths had shorter birth intervals than families without stillbirths (Figure 2). This fact could

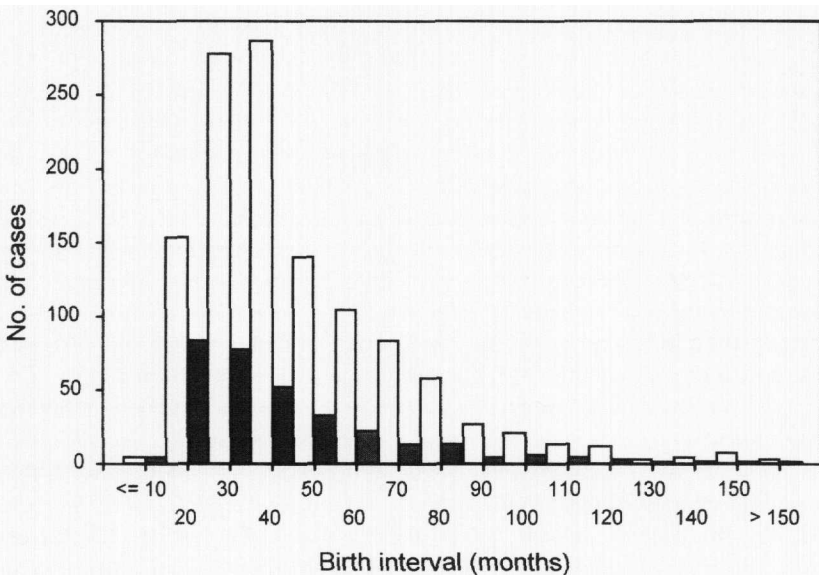


Figure 2. Birth interval frequencies in families without stillbirths (white bars) and families with at least one stillborn (ruled bars).

be explained by a reduced lactation period when the newborn dies at delivery. However, a more detailed analysis in families with stillbirths shows that the birth interval preceding a stillbirth does not significantly differ from that preceding a live birth (39.66 months vs. 36.62 months; logistic regression: $\chi^2 = 0.15$, $df = 1$, effect = 0.085, $p = 0.70$).

Discussion

In general, during the first half of the 20th century Alpujarra stillbirth rates appear statistically independent of female fertility as expressed by the number of deliveries in complete families. However, it must be taken into account that our sample had no women with only one pregnancy resulting in stillbirth (Table 1), and that the proportion of women whose last delivery corresponded to stillbirth was very low. This may be the result of behavior influencing birth control, e.g., couples initially having a stillbirth that then resort to recurrent pregnancies. From a general point of view, it is probable, as indicated by Gualteri et al. (1985), that specific family factors (e.g., pathology, maternal-fetal incompatibilities, and other biological and/or cultural features) could affect the risk of stillbirth in particular cases, but not in a significant way at the population level, as it appears in our sample from La Alpujarra.

From our data, the stillbirth pattern in the population of La Alpujarra could be summarized as being the result of four main risk factors: social/sanitary, mechanical, biological/genetic, and demographic determinants. There are marked differences between the Alpujarra stillbirth rate (53.21 deaths per 1000 deliveries, in the 525 complete families) and the general Spanish population rate during the same period (23.8 per 1000 in 1900; 26.3 per 1000 in 1915, and 9.03 per 1000 in 1946; INE, 1990). It is reasonable to assume that the virtual absence of obstetric and other medical care facilities in La Alpujarra is responsible for a significant number of stillbirths due to complications of gestation, delivery, and environmental influences. For the same reason, rates of around 50 deaths per 1000 deliveries are found in several developing regions of India and Bangladesh (Saksena and Srivasta 1980; Mostafa et al. 1991). These rates contrast with those reported for developed countries, as well as with those for developed regions of Spain (5.48–7.20 in Catalonia; Ramis 1992) or in the neighboring Andalusian provinces of Almería (6.86 per 1000 in 1979) and Granada (5.36 per 1000 in 1979).

The social and sanitary improvements observed in human populations over time, especially in western countries, clearly explain the gradual decrease of mortality risk at delivery. La Alpujarra, in spite of its traditional geographical and reproductive isolation (Luna 1984a), has also experienced a decrease in stillbirths. However, this decrease is less likely connected to improvements in sanitation both because of the endogenous character of most stillbirths and because major improvements in public health facilities did not occur in the area studied until the late 1950s. The decrease in mortality risk at delivery observed in La Alpujarra is

more likely the result of social and educational changes, such as women's awareness of their reproductive function. This modest decrease in mortality risk at delivery over time agrees with data on infant mortality in the same population (Luna and Moral 1990).

The increased risk observed for twin deliveries and among primiparous mothers could indicate mechanical hindrances (size of uterus, size of birth canal), independent of other health problems and reproductive anomalies. The significant increase in the risk of mortality in twin deliveries is consistent with other studies (Bulmer 1970; Casper et al. 1994). This association can be explained by fetal competition for uterine space along with fetal age, causing an important risk factor for mortality either at the time of delivery or in late abortions, as also observed in our population (Luna et al. 1997). Similarly, primiparous mothers exhibited a higher risk of stillbirth than multiparous mothers, as in many other prospective and retrospective surveys (Bakketeig and Hofman 1979; Mostafa et al. 1991; Yudkin and Baras 1983). This finding can also suggest an increased mechanical risk associated with a smaller birth canal in primiparous mothers, since the order of births following the first delivery had no effect on stillbirth probability, an effect that was investigated and shown to have no significant results.

As for biological factors, this study shows that both parental inbreeding and sex of children affect death risk. The smaller stillbirth risk observed in La Alpujarra among related parents coincides with a lower abortion rate obtained in this and other populations (Luna et al. 1997; Goldschmidt et al. 1961; Freire-Maia et al. 1961; Reddy and Rao 1978; Reddy 1992). Some authors have suggested that as a result of higher genetic homogeneity between parents, parental consanguinity reduces the frequency of maternal-fetal incompatibilities (Philippe 1974; Reddy 1985). Particularly, it is known that ABO and RH incompatibilities can induce losses at different stages of pregnancy (Cohen and Sayre 1968; Gualteri et al. 1985). Most likely, this higher genetic homogeneity among relatives could explain the low rates found both for stillbirth and abortion in Alpujarra. In this context, our results may be compatible with the hypothesis that deleterious recessive genes were operational only in late neonatal lifetimes, a finding confirmed in several population studies (Reddy and Rao 1978; Frasier 1962; Roberts and Bonné 1973). However, other studies on stillbirth in India show no differences in death risk at delivery (Devi et al. 1981). These results pose a question about the possible influence of consanguinity on stillbirth risk.

Regarding sex incidence, our results indicate that there is higher male than female mortality risk during delivery, a difference that characterizes human populations in general and the Alpujarran population in particular (Luna 1984a). This differential mortality has been observed since the first stages of postpartum life (Curtis and McDonald 1991; Sathar 1985; Harpending and Pennington 1991; Swenson 1981; Swenson et al. 1993), though the differences tend to decrease with age according to the progressive decrease of death risk during growth (Edmonston 1983).

Concerning demographic determinants, we analyzed incidence of birth in-

terval, maternal age, and parity. In relation to this last factor, as already mentioned, stillbirth risk is significantly higher for firstborns than for subsequent siblings. In about half the families with stillbirths (48.84%) in our study, the stillbirth was the first parity. Relatively higher stillbirth rates associated with the first parity have been described in several populations (e.g., Saksena and Srivastava 1980; Swenson 1981; Mostafa et al. 1991; Forbes and Pickering 1985). In contrast to results of other studies, however, our results do not show perinatal loss regularly increasing with parity order (Saksena and Srivastava 1980; Casterline 1989; Kallan 1992).

In human populations, a significant decrease of abortion risk associated with long birth intervals has been described, because long intervals determine better intrauterine fetal growth (Casterline 1989; Kallan 1992). Sometimes this influence is extended until delivery, according to other surveys (Swenson 1981; Boerma et al. 1984; Mostafa et al. 1991). The decreased risk of abortion is ascribed to a competitive effect between pregnancy and lactation (Williams 1968-69), in which ovum implantation is hindered because the necessary endometrial regulation is absent (Vilee 1960). In fact, in mammalian vermin, Hafez and Ishibashi (1965) have proven a lag of ovum implantation when fertilization occurs but the mother is in a period of lactation. However, interaction between regulatory factors is very complex and can determine, as Williams (1968-69) observed in England, Scotland, and Wales, an increase in stillbirth rate in deliveries with very large intervals. Our results suggest that the possible effect of birth interval is very weak at the moment of delivery. The smaller average birth interval found in Alpujarra mothers with stillbirths is not a risk factor for this mortality, but is a consequence of the reduction of lactation when stillbirths occurred.

As for maternal age, biological explanations for increased risk in older mothers include reduced uterine blood flow to the placenta, hypertension problems, and genetically defective fetuses that are more frequent among older mothers (e.g., Casterline 1989; Kallan 1992; Resseguie 1974). However, in contrast to other studies (e.g., Saksena and Srivastava 1980; Mostafa et al. 1991; Forbes and Pickering 1985; Keily et al. 1986), our results do not reveal any such association in La Alpujarra regarding either children or firstborn. This lack of relationship is also in contrast to the well-demonstrated influence of maternal age on spontaneous abortion risk in the same population (Luna et al. 1997). We conclude that the effects of maternal age on prereproductive mortality decrease during the course of the pregnancy. Hence, at the moment of delivery, this influence could be very insignificant, and for this reason it might be not detected in La Alpujarra, perhaps due to data shortage.

In summary, this study showed that the stillbirth pattern in La Alpujarra between 1900 and 1950 was significantly determined by mechanical risk factors associated mainly with first deliveries, twin deliveries, and to a lesser extent by parental inbreeding and sex of children. Over the period studied, a clear trend towards decreasing stillbirth rates could be related to social and educational changes. From the results of this study, the apparently low stillbirth pattern based

on provincial values (because there are no data available on the present Alpujarran population) could be interpreted as the result of obstetric improvements for reducing risk associated mainly with first deliveries.

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