

## ORIGINAL ARTICLES

# The rates of spontaneous abortion declined: a retrospective cohort study from an industrialized area in Italy, 1996-2010

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## ABSTRACT

**Background:** Spontaneous abortions (SA) were analyzed in an industrialized Italian region over a 15-year period to evaluate time trends. Retrospective cohort study.

**Methods:** Since 1991, in Lombardy a standard form has been used to register all discharges from public or private hospitals. This study analyzed the Lombardy Region registry of hospital admissions in 1996–2010. Using the hospital discharge register, SA-related crude admission rates per 100 pregnancies in women aged 15 to 50 years, residing in Lombardy, were computed; age- and nationality-adjusted rates were also calculated. SA cases were identified searching the database for the ICD-9 codes for SA. SA rates/100 pregnancies (livebirths+SAs+induced abortions/2) in strata of age and calendar year were computed. Poisson regression analysis was used to test trends over time.

**Results:** The crude SA rate was 10.72/100 pregnancies in 1996 and 10.45 in 2010. The corresponding age-standardized rate was 9.21. SA frequency was 4-5 times higher in women aged  $\geq 40$  years in comparison to women aged  $< 20$  years. Age-adjusted SA rates decreased, over time, in non native Italian women.

**Conclusions:** In this population, living in an industrialized area, SA frequency/100 pregnancies has slightly declined during the last 15 years.

**Key Words:** Spontaneous abortion, Temporal trends, Frequency, Time trend, Gender medicine

## 1. INTRODUCTION

Spontaneous abortion (SA) is a common adverse outcome of pregnancy. Several epidemiological and laboratory studies have linked the frequency of SA with exposure to environmental factors such as air pollution<sup>[1]</sup> and smoking.<sup>[2-4]</sup>

These pollutants affect the reproductive outcome of pregnancy immediately when they become prevalent contaminants in a specific area or they are banned. An analysis of SA temporal trends in specific geographic areas can be useful to evaluate whether new factors that can affect the outcome of

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pregnancy negatively had a significant presence in a specific geographic area. Along the same line, the ban of specific pollutants (*e.g.* smoking) may affect the frequency of SA, as it seems to be affecting the rate of preterm births.<sup>[5]</sup>

Frequency of SA may also be affected by several factors such as maternal age<sup>[6]</sup> or the use (or lack thereof) of certain assisted reproduction techniques (ART) in the clinical practice, factors that are markedly changed in the last decades.<sup>[7]</sup> Information on SA trends in different populations is scant in the literature<sup>[1,8]</sup>

In this paper we have analyzed the temporal trends of SA in Lombardy, a highly industrialized area, over the 1996-2010 period.

## 2. METHODS

A standard form is used to register all discharges from public or private hospitals in Lombardy. Among other data, information on hospital, patient age and nationality are reported. We have obtained the data for the 1996-2010 period; since 1996, data on hospital admissions that lasted less than 24 hours long were also recorded.

SA cases were identified searching for codes 632, 634.X (X=1 to 9) of the International Classification of Diseases Ninth Revision (ICD-9). The denominator for estimating frequency of SA was the total number of pregnancies including births, SA and induced abortions (IA)/2, as suggested

by Susser,<sup>[9]</sup> to avoid distortion due to high rates of induced abortion in population. Since the frequency of IA vary greatly between ad within populations, this correction is needed to restore the comparability of SA rates.

These numbers were obtained from the same database. SA Rates per 100 pregnancies in strata of age and nationality (native Italian/not native Italian) were computed. Rates were standardized for age (in quinquennia) and woman's nationality (native Italian/non-native Italian) by the direct method, using the 2010 cases as standard. Poisson regression models, with calendar-year fitted as a continuous variable, were used to evaluate any linear trends in rates over the study period between 1996 and 2010. SA rates and trend tests were calculated for age groups.

## 3. RESULTS

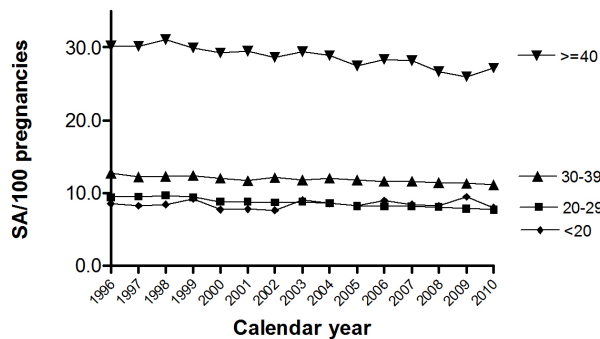
The total number of pregnancies in the 1996-2010 period was 1,777,011 and SA-related hospital admissions were 188,233.

Table 1 shows the crude and standardized SA rates per 100 pregnancies in strata of calendar year and nationality. The crude SA rate was 11.91/100 pregnancies in 1996 and 11.34 in 2010. When considering the age standardized rates by nationality, in 1996 the age-adjusted rate was 14.04 in native Italian women and 11.43 in non native Italian ones. In both groups, these rates, tested with Poisson's regression model, tended to decrease, being 11.75 and 10.19 respectively in 2010 ( $P<.0001$ ).

**Table 1.** SA rates/100 pregnancies (births+SA+induced abortions/2), crude, age-adjusted and age- and nationality-adjusted; 1996-2010, Lombardy, Italy

Calendar year	Certified number of SA	Rate/100 pregnancies Crude	Rate/100 pregnancies Age-adjusted: Native Italian	Rate/100 pregnancies Age-adjusted: non Native Italian	Rate/100 pregnancies Age- and nationality-adjusted
1996	11,627	11.91	14.04	11.43	13.36
1997	11,540	11.75	13.76	11.66	13.21
1998	11,877	11.94	13.81	11.66	13.25
1999	12,154	11.97	13.69	11.75	13.18
2000	12,101	11.51	13.25	10.54	12.54
2001	12,047	11.42	12.95	10.56	12.33
2002	12,416	11.68	13.11	10.61	12.46
2003	12,719	11.64	12.91	10.67	12.33
2004	13,164	11.81	12.92	11.17	12.46
2005	12,855	11.59	12.60	10.53	12.06
2006	13,224	11.62	12.51	10.42	11.97
2007	13,257	11.66	12.28	11.16	11.99
2008	13,279	11.47	12.01	10.66	11.66
2009	13,104	11.34	11.85	10.40	11.48
2010	12,869	11.34	11.75	10.19	11.34

The age-nationality-adjusted estimates also declined between 1996 and 2010 ( $P < .0001$ ). A significant time trend was detected by means of Poisson regression model, adjusting for age and nationality ( $P < .0001$ ). The SA rates increased with age (see Figure 1), but declined in all age classes ( $P < .0001$ ), with the exception of the youngest women (aged less than 20 years,  $P > .05$ ).



**Figure 1.** Age- and nationality-adjusted SA rates/100 pregnancies (births+SA+induced abortions/2), by age class among women residing in Lombardy, 1996-2010

#### 4. DISCUSSION

The general results of this study showed that SA frequency/100 pregnancies has slightly declined during the last 15 years.

Before discussing the results, some potential limitations should be considered.

In Lombardy all hospital admissions in private and public hospitals are registered by law in an administrative regional data base, therefore our data should be considered totally representative of the cases of SA admitted in hospital in the region.

It is possible that some cases could be treated conservatively (*i.e.* wait and see) in outpatient centers. This mode of treatment should be more common in the recent years, if at all, since early diagnosis of SA increased. This potential bias should tend to underestimate the frequency of SA. With regard to the quality of diagnosis, for administrative reasons, all medical records are reviewed, and the diagnoses confirmed by local medical officers. It has been suggested that analysis of SA trends based on administrative records may underestimate the frequency of SA, however this effect seems to be constant over time.<sup>[10]</sup>

There is a methodological issue regarding the competing risk of IA: SA rates in populations in which IA is frequent tend to be lower. For this reason, we adjusted the number of IAs in the denominator, as suggested by several authors.<sup>[9, 11, 12]</sup>

In Italy, SA rates increased between 1980 and 1995,<sup>[6]</sup> probably because of older maternal age and changes in the environment. From 1995 to 2006, the crude SA rates (SA/livebirth) did not show any significant increase.<sup>[13]</sup> However, the initial apparent rise was, at least in part, due to women becoming more aware of early spontaneous abortion, as also suggested by Lang and Nuevo-Chiquero.<sup>[8]</sup>

In the interpretation of these findings, some potential confounders should be considered.

Age is the main risk for SA. In this population, SA frequency was 4-5 times higher in women aged over 40 than in those aged < 20 throughout the whole studied period (1996-2010), which is consistent with the literature.<sup>[6, 14]</sup> In younger women we did not find any significant change, whereas in women aged more than 20 years (more likely to be having a planned pregnancy) a declining SA trend was observed. Overall age-adjusted rates tended to decrease, though in Lombardy, in the same period, the mean age at birth increased from 30.6 in 1996 to 31.5 in 2008.<sup>[15]</sup> Similar results have been found in other European populations, as in Denmark,<sup>[16]</sup> where a prospective register linkage study found that fetal loss is high in women in their late 30s or older, irrespective of reproductive history. In a Swedish register study,<sup>[17]</sup> rising mean age at pregnancy of women only partially accounted for the SA increase seen in 1983-2003; the authors suggested several possible explanation, among which more sensitive urine pregnancy tests and gynecologic examinations by ultrasound.

An increased SA risk has been inconsistently reported after the introduction of ART. In Lombardy the frequency of ART has been increasing over the last 15 years: the estimated number of ART cycles was 849/million inhabitants in 2005 and 998/million inhabitants in 2008; more than 25% of ART procedures are performed in women aged  $\geq 40$  years.<sup>[18]</sup> However we did not observed any increase in SA frequency in women aged 30-39 or  $\geq 40$  years, thus supporting that no effect on SA risk exists, at least at a population level.

Smoking is a well recognized risk factor for spontaneous abortion.<sup>[2, 3, 19]</sup> The prevalence of women smokers in fertile age has not changed substantially over the last decades in Italy and in Lombardy.<sup>[20]</sup> However, women planning a pregnancy or seeking advice during pregnancy are strongly advised to quit smoking: about 90% follow this advice, though most relapse after delivery.<sup>[21]</sup> Even secondhand tobacco smoke had been suggested as a risk factor for miscarriage: a recent cross-sectional analysis of data from the Women's Health Initiative<sup>[22]</sup> found that high level of lifetime secondhand smoke exposure significantly increased the risk estimate for SA. It has been suggested that tobacco control legislation

may affect reproductive health.<sup>[5]</sup> This sample may offer the opportunity to analyze the effect of these laws, from a population prospective. In Italy smoke-free legislation was promulgated in 2003 and became effective in 2005. We did not observe any drop of SA rates after 2005, but it is possible that the slow decline was, at least partially, due to a new attitude towards smoking in public places already adopted before the smoking ban. Since the early 2000s many hospitals, public offices, restaurants and cinemas had banned smoking or had separate rooms for smokers and non smokers. In fact, a Health Ministry directive<sup>[23]</sup> regulated the matter, indicating that smoking was banned in most public places. So the effect of less exposure to passive smoke if any, should already be present before 2005.

Another interesting finding of this analysis is the observation that non-native Italian women have a lower SA risk than native Italian women. This may be due to the fact that healthy young women are more likely to migrate than non healthy ones, though generally health conditions are worse in non native women than in native ones. Moreover, the pregnancy awareness and therefore SA at early stage may be lower in this group of women, leading to an underestimate of the SA rate.<sup>[8]</sup>

In Lombardy the proportion of deliveries from foreign res-

idents increased from 5.3% in 1996 to 24.2% in 2008.<sup>[13]</sup> This increasing proportion may also explain part of the lower rates observed in the later calendar period in the age-adjusted SA rates. However, the age-adjusted rates by country of origin declined over the 1996-2010 period in native Italian as well as in the non native Italian group.

In conclusion, this analysis shows that in Lombardy, Italy, Southern Europe, notwithstanding the increasing age at delivery, SA rates were declining over the 1996-2010 period. This finding is important, as it shows that in an industrialized area, the risk of SA seemed not affected by potential introduction of new pollutants.

## CONFLICTS OF INTEREST DISCLOSURE

The Authors declare no conflict of interest.

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