SPONTANEOUS ABORTION OVER TIME: COMPARING OCCURRENCE IN TWO COHORTS OF WOMEN A GENERATION APART

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A prospective study of menstrual cycles and reproductive outcomes has been in progress since 1935. Data from this study are used to describe the risk of spontaneous abortion in two time periods 26 years apart. Out of the total of 3889 women who have enrolled in this study, two cohorts of women are selected for analysis: cohort one consists of 2070 university students who entered the study in 1935-1944, and cohort two consists of 1375 students a generation later, 1961-1970. Cohort one has contributed 2408 pregnancies, and cohort two, 1493 pregnancies. Overall spontaneous abortion risk for the two cohorts is 16.9% and 13.1%, respectively. However age-specific risks of spontaneous abortion do not differ for the two groups, nor is there a difference in the gestational duration of spontaneously aborted pregnancies.

abortion (miscarriage); prospective studies

Spontaneous abortion has been regarded in at least two recent public health controversies as crucial evidence in assessing possible hazards to humans (1, 2). This reflects a growing scientific interest in early fetal loss as a health index. Theoretical papers by Stein and her colleagues (3, 4) have justified and further stimulated the use of spontaneous abortion as a major outcome measure in epidemiologic investigations.

Despite this interest, the basic epidemiologic features of spontaneous abortion remain obscure. The problems of measuring spontaneous abortion risk are formidable (5), and only a handful of large-scale epidemiologic studies of spontaneous abortion have ever been reported. None of these has been repeated or sustained over a long enough period to provide data about possible changes over time. This paper describes a longitudinal study of menstrual and reproductive events, and examines in particular the occurrence of spontaneous abortion in two similar groups of women a generation apart.

MATERIALS AND METHODS

The data to be presented here are from a prospective study which has been in continuous operation since 1935, and is known as the Menstruation and Reproduction History Study (MRH). This project was started by one of us (A.E.T.) to test the hypothesis that the length of normal menstrual cycles varies like other biologic phenomena, rather than occurring regularly every 28 days. To test this
hypothesis, freshmen women at the University of Minnesota were invited to participate in a study in which they were to record the first and last day of each menstrual period on a calendar card. On the reverse of the card the women were instructed to list any events which might have disrupted their cycle, such as trauma, illness, or pregnancy. These women were instructed not to record events from memory. If a flow period was not recorded at the time it occurred, the card was to be left blank, with the reason for that blank noted on the reverse side. Supplementary information such as marital status or pregnancy outcome was collected in a brief annual report. (More complete descriptions of this study may be found in Treloar et al. (6, 7).)

Between 1935 and 1939, 1984 women volunteered for this study. Fifty-seven per cent of these women continued to contribute data after college, and nearly 40 per cent of the original group continued to provide data until their menstrual periods ceased. Twenty-six years later, a second cohort of women was again enlisted from freshmen women at the University of Minnesota; 1276 women volunteered for the study between 1961 and 1965, of whom 63 per cent are still participating. Additional volunteers have been accepted into the study at other times. These women were usually relatives or friends of participants. They include several hundred daughters of the original cohort, and 15 granddaughters.

A total of 3889 women have enrolled in this study since 1935, of whom virtually all are white, middle-class, and college educated. These women have contributed data on nearly a half-million menstrual cycles, which have demonstrated that menstrual cycle length has considerable variability (6).

In the course of recording these menstrual cycles, participants have also reported several thousand pregnancies. The event of pregnancy is determined in this study simply by a woman's report of her pregnancy, regardless of how it was diagnosed. Spontaneous abortions are defined as those reported pregnancies which terminate within 20 weeks of the previous menstrual period. All pregnancies and spontaneous abortions known to the participants presumably have been included in these data, unless the fact of a pregnancy has deliberately been withheld. Out of 4877 reported pregnancies, 18 ectopic pregnancies and 63 pregnancies ending in induced abortion have been excluded from analysis; 450 pregnancies were also excluded for lack of a date for the previous menstrual period. In effect, this excludes all pregnancies reported on the annual questionnaire but not on the menstrual calendar card. The remaining 4346 pregnancies, 89 per cent of the original group, were analyzed. Of these pregnancies, 685 or 15.8 per cent ended in spontaneous abortion.

In order to address the question of possible changes in spontaneous abortion risk over time, two cohorts of pregnancies have been extracted from all eligible pregnancies. The first cohort consists of 2408 pregnancies occurring to women who enrolled in the study during its first decade, 1935–1944. The second cohort consists of 1493 pregnancies occurring to women who enrolled in the study a generation later, in the decade 1961–1970. These two cohorts include 90 per cent of all eligible pregnancies in the study.

RESULTS

Of the 2408 pregnancies occurring in cohort one, 406 or 16.9 per cent ended in spontaneous abortion. In cohort two, only 196 or 13.1 per cent of the 1493 pregnancies ended in spontaneous abortion. However, this comparison of crude spontaneous abortion risk does not consider differences in maternal age. Cohort one includes pregnancies at the older maternal ages when risk is highest, while the women in cohort two are still in their mid-
Figure 1. Occurrence of spontaneous abortion, by maternal age: Menstruation and Reproduction History Study, in progress since 1935.

Table 1

Mean gestational lengths of pregnancies ending in spontaneous abortion, by cohort and maternal age

<table>
<thead>
<tr>
<th>Maternal age</th>
<th>20-24</th>
<th>25-29</th>
<th>30-34</th>
<th>35-39</th>
<th>40-44</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort one</td>
<td>8.6</td>
<td>9.4</td>
<td>9.2</td>
<td>9.1</td>
<td>9.7</td>
<td>9.2*</td>
</tr>
<tr>
<td>(n = 35)</td>
<td>(n = 101)</td>
<td>(n = 120)</td>
<td>(n = 85)</td>
<td>(n = 46)</td>
<td>(n = 387)</td>
<td></td>
</tr>
<tr>
<td>Cohort two</td>
<td>8.4</td>
<td>9.8</td>
<td>9.3</td>
<td>9.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 36)</td>
<td>(n = 95)</td>
<td></td>
<td>(n = 66)</td>
<td></td>
<td></td>
<td>(n = 197)</td>
</tr>
</tbody>
</table>

* Cohort means not significantly different (p > 0.50).

Finally, the two cohorts are compared by the mean gestational age of the fetus at the time of spontaneous abortion. The mean lengths of pregnancies ending in spontaneous abortion are not significantly different for the two cohorts, either in the aggregate, or within each age-specific stratum (table 1). Mean gestational length is 9.2 weeks in cohort one and 9.4 weeks in cohort two.

Discussion

What began as a study of menstrual cycles has resulted in a prospective description of the lifetime reproductive experience of a group of women. While the

to late-thirties. A comparison of age-specific risks for the two cohorts shows no differences in spontaneous abortion between the two groups (figure 1).

Pregnancy order (gravidity) may influence the risk of spontaneous abortion independently of maternal age (8). Thus, a group difference in gravidity might affect a comparison of the abortion risk in the two groups. However, the two cohorts in the Menstruation and Reproduction History Study are practically identical in their age-specific gravidity. That is, the timing of pregnancies among women who bore children is very similar in these two groups of women.
Menstruation and Reproduction History Study (MRH) provides useful data, there are several problems with these data. First, this study was not specifically designed for the purpose of describing pregnancy outcomes. In particular, the format of questions on the annual medical report regarding pregnancy outcome has been modified several times over the years. However, the menstrual calendar card, and not the annual report, is the main source of data regarding pregnancies. Descriptions of pregnancy as recorded on the menstrual calendar card are unambiguous in nearly all cases. The most serious ambiguity occurs around 1971–1973, when abortion laws were being liberalized. During that period, there are 16 reports of “abortion” which cannot be distinguished, either by calendar card information or medical report, as “spontaneous” or “induced.” (After 1973, a specific item on induced abortions was added to the annual report form.) Abortions which could not be clearly identified as induced have been coded as spontaneous, which may add misclassified abortions to the pool of spontaneous abortions. Even if we assume these 16 abortions are misclassifications, the findings presented above are not changed.

Selection bias may intrude in at least two ways. One is through incomplete record-keeping. Most women have some gaps in their records, ranging from weeks to years. Ninety-six per cent of the participants have records more than half complete, but only 60 per cent of the women have records more than 95 per cent complete. However, women with incomplete records do not otherwise appear different in their menstrual histories from women with complete records. Selection bias may also result from the various lengths of time women have stayed in the study.

The possibility of selection bias might have been restricted by analyzing only those data from women with the most complete records. However, we have been reassured of the usefulness of the complete data set by the following observations: 1) the patterns of attrition and non-response are similar for the two cohorts to be compared; and 2) the overall patterns of spontaneous abortion observed in the complete data set are consistent with the observations of other large epidemiologic studies (discussed below).

There is no conclusive way to determine whether illegally induced abortions have been disguised as spontaneous in these data, which is a problem in nearly any study of spontaneous abortion. In this study, however, a woman does have the opportunity to conceal an induced abortion simply by leaving the record blank or by withdrawing from the program. Thus, there may be less motivation here than in other study designs to misrepresent an induced abortion as “spontaneous.”

The self-reported, prospective design of the MRH study is unique among descriptions of spontaneous abortion. Most studies depend either on women’s recall of previous abortions, or on the prospective registration of pregnant women. In order to relate the MRH data to data collected by more usual methods, they are compared with data from a well-known study of women enrolled in a prepaid medical care plan (New York Health Insurance Program, or HIP), as reported by Shapiro and colleagues (9, 10). The study is chosen for comparison because:

1) The HIP study is the only example of a cohort design (in this case reconstructed) for which published data are available regarding the exact gestational week at termination.

2) The distribution of maternal ages is nearly identical in the two studies, which removes maternal age as a potential confounder.

3) The HIP study defines spontaneous abortion by strict criteria, including medical documentation, in contrast to the MRH study which relies only on the woman’s report of a spontaneous abortion.
FIGURE 2. Maternal-age-specific risk of spontaneous abortion, the Menstruation and Reproductive History (MRH) and the New York Health Insurance Program (HIP) studies.

FIGURE 3. Occurrence of spontaneous abortion as a percentage of surviving pregnancies at each gestational age, the Menstruation and Reproductive History (MRH) and the New York Health Insurance Program (HIP) studies.

This provides the opportunity to compare the effect which very different operational definitions of spontaneous abortion might have on the observed occurrence.

The HIP study does not provide separate data for race. About 14 per cent of the women in that study are black, while women enrolled in the MRH study are drawn from a student population almost completely white.

The overall occurrence of spontaneous abortion (less than 20 weeks of gestation) in the HIP study is 11.4 per cent, compared to 15.8 per cent for all eligible pregnancies in the MRH study. This apparent higher risk in the MRH group is present at each maternal age (figure 2).

When the frequency of spontaneous abortion is plotted by gestational age, it is apparent that the MRH study includes a
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larger number of early abortions (figure 3). The risk of abortion at gestational ages above eight weeks is similar for the two groups, while the excess of abortions at eight weeks and earlier accounts for practically the entire excess in the MRH group. The higher risk for women in the MRH study seems to be a result of its higher detection of early spontaneous abortion. This suggests that women do not usually see their doctor for a pregnancy or spontaneous abortion before eight weeks of gestation (that is, before their second missed menstrual period), while after that time, most abortions known to women are also medically documented. Despite the fact that these two studies describe two different groups of women by two different methods, there seems to be concordance between self-reported and medically documented risk of abortion after eight weeks of gestation.

Data collected by the MRH study has permitted a comparison of the risk of spontaneous abortion in two similar groups of women a generation apart. When controlling for maternal age, there is no apparent difference in risk between the two groups, and thus no apparent change in risk over time. This observation marks a distinction between early and late fetal loss. Late fetal mortality (stillbirth) has declined steadily in the United States in recent decades (11). The contrast between these two time trends may indicate major differences in the etiologic factors affecting early and late fetal mortality.

References