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Mucus observations in the fertile window: a better predictor of conception than timing of intercourse

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BACKGROUND: Intercourse results in a pregnancy essentially only if it occurs during the 6-day fertile interval ending on the day of ovulation. The strong association between timing of intercourse within this interval and the probability of conception typically is attributed to limited sperm and egg life times. METHODS: A total of 782 women recruited from natural family planning centres in Europe contributed prospective data on 7288 menstrual cycles. Daily records of intercourse, basal body temperature and vaginal discharge of cervical mucus were collected. Probabilities of conception were estimated according to the timing of intercourse relative to ovulation and a 1–4 score of mucus quality. RESULTS: There was a strong increasing trend in the day-specific probabilities of pregnancy with increases in the mucus score. Adjusting for the mucus score, the day-specific probabilities had limited variability across the fertile interval. CONCLUSIONS: Changes in mucus quality across the fertile interval predict the observed pattern in the day-specific probabilities of conception. To maximize the likelihood of conception, intercourse should occur on days with optimal mucus quality, as observed in vaginal discharge, regardless of the exact timing relative to ovulation.

Key words: Bayesian analysis/cervical mucus/day-specific pregnancy probabilities/menstrual cycle/ovulation

Introduction

Intercourse is unlikely to result in a conception unless it occurs during the 6-day fertile interval ending on the day of ovulation (Wilcox *et al*., 1995; Dunson *et al*., 1999). The start of the fertile interval generally corresponds to a significant rise in estrogen levels, which results in the secretion of estrogenic cervical mucus and characteristic changes in vaginal discharge (Billings *et al*., 1972; Insler *et al*., 1972; Katz *et al*., 1997). Although monitoring of these changes has long been used as a marker of the fertile interval (Billings *et al*., 1989; World Health Organization, 1983; Dorairaj, 1991; Hilgers and Stanford, 1998; Sinai *et al*., 1999), the extent to which mucus characteristics predict the day-specific probabilities of conception within the fertile interval is not known.

Because properties of cervical mucus determine whether sperm will be capable of survival and transport to the ovum (Moghissi, 1973; Yudin *et al*., 1989; Katz, 1991; Kunz *et al*., 1997), we hypothesize that mucus characteristics on the day of intercourse provide a clinically important predictor of the probability of conception independent of the timing relative to ovulation. In particular, consistent with the well known role of estrogenic mucus in enhancing progressive sperm motility (Eriksen *et al*., 1998) and allowing for penetration, storage and transport of normal spermatozoa (Odeblad, 1968, 1997; Menarguez *et al*., 2003), we anticipate that the day-specific probabilities of conception will increase progressively with a ranking of the fertility of the mucus.

Using data from the European Study of Daily Fecundability (Colombo and Masarotto, 2000), we estimate the day-specific probabilities of conception according to both the timing of sexual intercourse relative to ovulation and a 1–4 ranking of the fertility of the mucus. Our data provide additional information not available in the World Heath Organization (1983) study evaluating the use of vulvar mucus observations in estimating the fertile interval. Because the WHO study did not have a mucus-independent marker of ovulation day, the data cannot be used to address our hypotheses. In addition, the WHO study had problems with under-reporting of intercourse (Trussell and Grummer-Strawn, 1991).

Table I. Classification of mucus symptoms from vaginal discharge

Mucus score	Feeling	Appearance
1	Dry, rough and itchy or nothing felt	Nothing seen
2	Damp	Nothing seen
3	Damp	Mucus is thick, creamy, whitish, yellowish, or sticky
4	Wet, slippery, smooth	Mucus is transparent, like raw egg white, Stretchy/elastic, liquid, watery, or reddish

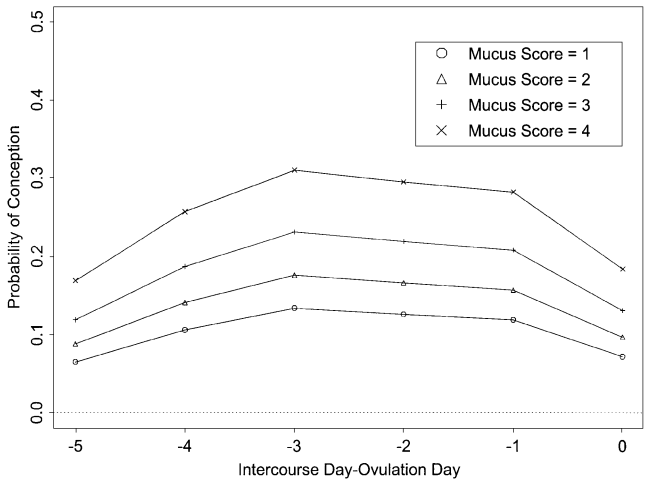

Figure 1. Estimated probability of pregnancy with a single act of intercourse in the fertile interval conditional on mucus observations.

Materials and methods

Description of study design and data

The European Study of Daily Fecundability is a prospective cohort study conducted to determine the daily probability of conception on each cycle day relative to ovulation for healthy women in their reproductive years. From 1992 to 1996, 782 women were recruited from seven European centres providing services in fertility awareness and natural family planning (NFP). Women enrolled were experienced in NFP, married or in a stable heterosexual relationship, 18–40 years of age, had at least one menses after cessation of breastfeeding or delivery (if applicable), and were not currently taking hormonal medication or drugs affecting fertility. In addition, neither partner could have a history of fertility problems, and couples were required not to use barriers or spermicide generally. Additional details on the inclusion and exclusion criteria, the demographics of the cohort, and other study methods and initial results have been published elsewhere (Colombo and Masarotto, 2000).

Women kept daily records of basal body temperature (BBT), cervical mucus symptoms and intercourse. The daily mucus observations were classified according to Table I, ranging from a score of 1 (no discharge and dry) to 4 (transparent, stretchy, slippery). This 1–4 mucus scoring system is designed to summarize a wide variety of different mucus characteristics in a way that is predictive of the presence of fertile-type estrogenic mucus, which is characterized by a high score. If a discharge exhibited mixed characteristics, or if a woman observed multiple types of mucus through the course of the day, the highest matching category was chosen to assign the score. A primary goal of this study is to assess directly the extent to which the different levels of the mucus score predict a real difference in the conception probability.

The BBT data are used as a mucus-independent marker to estimate the day of ovulation within each menstrual cycle using the three over six rule (Marshall, 1968) to identify the last day of hypothermia as described by Colombo and Masarotto (2000). Previous research suggested that a BBT-based estimate of the ovulation day has a high probability of being within 1 day of the true ovulation day, and that estimates of day-specific conception probabilities based on BBT are very similar to those based on estimating ovulation through urinary hormonal assays (Dunson *et al*., 1999) or ultrasound (Gnoth *et al*., 1996*)*. A comparison of multiple markers of ovulation with the ultrasound-determined day of ovulation indicated that the last day of hypothermia, while not perfect, is an accurate marker of ovulation day (Ecochard *et al*., 2001).

In a previous analysis of these data, Dunson *et al*. (2002) found that nearly all pregnancies occurred from intercourse that took place in the 6-day window ending with the BBT-determined day of ovulation. This 6-day period was considered to be the fertile interval, and days outside this period were not taken into consideration. Cycles were excluded from the analysis if there were insufficient BBT data to determine the ovulation day, if there were no reported intercourse acts during the fertile interval, or if there was a day within the fertile interval on which intercourse occurred but mucus information was missing. Out of 6724 menstrual cycles of data with 487 pregnancies, 1473 cycles remained in the analysis, with 353 pregnancies. For the purposes of this study, pregnancy is defined as either an ongoing pregnancy of at least 60 days from the last menses or a clinically identified spontaneous abortion within 60 days of the last menses.

Bayesian statistical analysis approach

Modelling and estimation of pregnancy probabilities were carried out using a Bayesian hierarchical modelling approach (Dunson, 2001). This involves choosing prior distributions for unknown parameters in a statistical model based on previous information and updating this information with the data in the study to obtain posterior distributions, which represent the current state of knowledge about the unknown parameters. We base our inferences on summaries of the posterior distribution, including posterior means, 95% credible intervals and posterior probabilities.

We estimated the probability that intercourse would result in pregnancy on each of the days in the 6-day interval ending on the day of ovulation. In a cycle where intercourse occurred on more than one day during the fertile period, it is impossible to determine which act resulted in the pregnancy. Following Barrett and Marshall (1969), Wilcox *et al*. (1995), Dunson *et al*. (2002) and Stanford *et al*. (2003) among others, we use a statistical model that allows for the incorporation of information from cycles where multiple intercourse acts occurred. Since most women contributed more than one cycle to the data, the model was also designed to account for within-woman dependency. The analyses presented in this article are based on the methods of Dunson and Stanford (2003).

Results

There was clear evidence of an increasing trend in the pregnancy probability with increases in the mucus score after adjusting for the timing and frequency of intercourse relative to

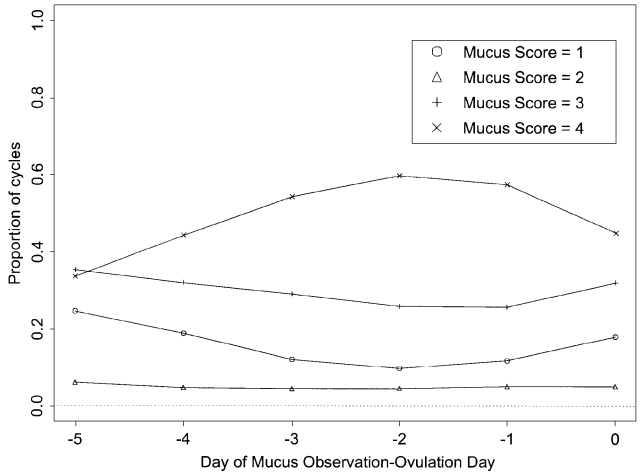

Figure 2. Proportion of cycles with each mucus score on each day in the fertile interval

the BBT-identified ovulation day. In particular, the posterior probability of no effect of mucus on the pregnancy probability was <0.01. The significant trend was attributable to a steady increase in the pregnancy probability with each unit increase in the mucus score. Specifically, the posterior probability of an increase in the pregnancy probability in going from a mucus score of 1 to 2 was 0.95, while the corresponding probabilities in going from scores of 2 to 3 and from 3 to 4 were 0.97 and >0.99, respectively.

This relationship is demonstrated in Figure 1, which shows the estimated day-specific pregnancy probabilities for the four mucus types. The day of lowest fertility was 5 days before ovulation, and the day of highest fertility was 3 days before ovulation. The difference in pregnancy probability between these two days ranged from 0.06 to 0.14, depending on mucus quality, while the difference in pregnancy probability attributable to increasing the mucus score from 1 to 4 ranged from 0.1 to 0.18. Thus the gain in pregnancy probability attributable to an increase from the lowest to highest mucus score is generally higher than the gain attributable to having intercourse 3 days before ovulation instead of 5 days before ovulation. Intercourse on any day in the 6-day window where the mucus is type 4 has a pregnancy probability that is $\geqslant$0.17, while the pregnancy probability does not exceed 0.13 on days with no secretions (mucus score = 1). Within the fertile window, the type of mucus observed on the day of intercourse is more predictive of conception than the timing relative to ovulation.

Figure 2 shows the distribution of the reported mucus scores according to timing within the fertile interval. On each day, type 4 mucus is the most common, with the largest proportion occurring 2 days before ovulation, which is also the day on which the smallest proportion of cycles had no vaginal discharge (type 1 mucus). It is important to note that each of the days had a substantial proportion of women in each of the mucus categories. Although fewer women reported type 2 mucus and that proportion remained essentially constant across the fertile window, there was a significant difference in the pregnancy probabilities between type 2 mucus and the other categories.

Discussion

Regardless of the timing of intercourse relative to ovulation, pregnancy probabilities are highest when observations indicate the presence of the most fertile-type estrogenic mucus. In particular, the highest conception probability when there is no observed discharge, occurring 2 days before ovulation, is lower than the conception probability on any day in the 6-day interval when most fertile-type mucus is present. These results provide direct evidence that mucus plays a role in fertility that is more important than its previously identified role as a marker of the fertile window of the menstrual cycle. Observations of the most fertile-type mucus are probable throughout the fertile window, but are most prevalent 2 days before the estimated ovulation day.

Previous estimates of pregnancy probabilities on days relative to ovulation did not account for daily observations of the quality of mucus, though researchers have identified increased conception probabilities on days when secretions were observed compared with no secretions (Dunson *et al*., 2001) and in cycles with high mucus scores averaged over the fertile window (Stanford *et al*., 2003). Our study demonstrates that the quality of mucus explains most of the relationship between the pregnancy probability and the timing of intercourse relative to ovulation. It is remarkable that even a rough categorization of mucus on a scale of 1–4, based on a woman's own observations (Table I), explained more of the variability in the day-specific probabilities of pregnancy than could be attributed to timing of intercourse relative to ovulation.

Our results have important clinical implications. Because vulvar observations of cervical mucus predict not only the fertile days of the cycle but also the probabilities of conception within the fertile interval, monitoring of mucus provides additional information not provided by other methods for identifying the fertile interval. In particular, methods based on cycle monitoring by daily vaginal ultrasound and/or urinary LH detection are not informative about the probability of conception at a particularly time in the fertile interval within an ovulatory cycle. In addition, such monitoring is expensive and inconvenient and can miss the beginning of the fertile interval and even the most fertile days. Many women already rely on their own calculations to predict ovulation, often obtaining estimates different from results of ultrasound or LH detection (Gnoth *et al*., 2002). Hence, monitoring of mucus provides a useful clinical marker of days with high conception probabilities.

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