Background pregnancy rates in an infertile population

Norbert Gleicher\textsuperscript{1,3}, Burton VanderLaan\textsuperscript{2}, Donna Pratt\textsuperscript{1} and Vishvanath Karande\textsuperscript{1}

\textsuperscript{1}Center for Human Reproduction and the Foundation for Reproductive Medicine and \textsuperscript{2}Blue Cross Blue Shield of Illinois, Chicago, Illinois, USA

The objective of this cohort study was to determine the true spontaneous background pregnancy rate in an infertile population. A total of 9079 treatment months in infertile couples with infertility of at least 1 year's duration were recorded in a medical school affiliated infertility setting. Results indicated that the spontaneous clinical pregnancy rate in an infertile population was 2.02\% per inactive treatment month, resulting in a cumulative rate after 12 months of 19.9\%. It was concluded that couples with a history of infertility have a low but significant background pregnancy rate, which needs to be considered alongside the effectiveness of various treatment modalities.

\textit{Key words:} background rate/secundity/infertility/pregnancy rate

\section*{Introduction}

We have recently embarked on an investigation of various treatment protocols for infertility in an attempt to define the quickest and most cost-effective clinical approach towards different clinical problems. In contrast to many other areas in medicine, where similar efforts are underway, infertility lends itself to such investigations with relative ease since the desired outcome, namely pregnancy, represents a well defined endpoint. Consequently, the success of various treatment modalities can be defined as either a clinical pregnancy or delivery rate per treatment cycle.

Such a definition, however, ignores the fact that even obviously infertile patient populations experience a spontaneous pregnancy rate. The literature contains fairly extensive references to this phenomenon (Menken et al., 1986; Mosher and Pratt, 1990; Collins et al., 1995). Most studies addressing this point, however, usually define spontaneous pregnancy rates only in specific subpopulations of infertility patients. Alternatively, data on general patient populations waiting to enter infertility treatment have just undergone a hysterosalpingography (HSG). Such gynaecoradiological procedures are known to result independently in a small spontaneous pregnancy rate (Gleicher et al., 1992). A woman who underwent an HSG in a clomiphene citrate cycle might therefore conceive either because of clomiphene citrate or because of the gynaecoradiological procedure. Analysis of currently published data would interpret any HSG-related pregnancy success in a clomiphene citrate cycle as being a consequence of the drug treatment, while in studies of untreated patients or patient populations waiting for infertility treatment, such pregnancies would simply be missed.

True spontaneous background pregnancy rates should therefore be evaluated in patient populations under active evaluation or treatment by a provider of infertility care. At the same time such couples under study should not, at the time of observation, be in an active treatment cycle. The study reported here was designed to evaluate the spontaneous background pregnancy rate in such a patient population.

\section*{Materials and methods}

The Center for Human Reproduction (CHR), Chicago, IL, USA, received 1016 new infertility couples in 1994. The CHR provided a total of 9079 treatment months to these couples, as represented by ovulation induction cycles, cycles of pituitary down-regulation with gonadotrophin-releasing hormone analogues (GnRHa), cycles of assisted reproductive technologies and cycles with no administration of cycle-controlling medications.

For the purpose of this study 5541 treatment months were identified during which women either underwent no cycle stimulation and no cycle monitoring, passive cycle monitoring (of natural cycles where as far as could be determined, no action was taken in response to monitoring) only, or were on GnRHa suppression. These patients were considered to be the appropriate controls in determining spontaneous background pregnancy rates. This represented 61\% of total treatment months during 1994.

The CHR maintains a fully computerized data bank system, which generates monthly outcome reports on every treatment month, whether under active cycle stimulation or not. The data reported here represent the cumulative 1994 experience from this data bank. No treatment cycles were disqualified from analysis.
A clinical pregnancy was defined as a pregnancy which, at minimum, reached the stage of a gestational sac by vaginal ultrasound examination. All couples admitted to the CHR for infertility treatment fulfilled standard criteria for the diagnosis of infertility (Jones and Toner, 1993), which included a minimum duration of 1 year of reported infertility.

Results

A total of 112 clinical pregnancies occurred in 5541 treatment months amongst the control population, resulting in a spontaneous background pregnancy rate of 2.02% (confidence interval 1.2-3.4% per month). In all, 18 pregnancies occurred in 410 GnRHa down-regulated treatment cycles, resulting in a pregnancy rate of 4.39% for these patients. The remaining 5131 treatment months, involving couples with either no cycle monitoring at all or only cycle monitoring without cycle stimulation, therefore resulted in only 94 clinical pregnancies, for a monthly pregnancy rate of 1.83%.

In order to exclude the possibility of a skewed overall patient selection within the CHR, the same calculations were also made for a subgroup of CHR patients who were mandated to receive all of their infertility care at the CHR (Pratt et al., 1995). During the same study period of 1994, these managed care patients experienced 67 clinical pregnancies out of a total of 5250 treatment months and 3032 control months (57.8%), for a background pregnancy rate of 2.21%. Neither the proportion of control months (relative to the total) nor the rate of spontaneous background pregnancies per month differed significantly in this subgroup from the rest of the patient population, thus validating the assumption that the total CHR population of infertility patients does reflect a randomly referred infertility population.

Discussion

Collins et al. (1995) recently reported that the cumulative rate of conception leading to live birth was approximately 14.3% at 12 months in 28125 months of untreated observation in infertile couples. Assuming an approximate 2% monthly conception rate, as the data reported here suggest, it is possible to calculate an approximate 19.9% cumulative clinical conception rate after 12 months for our patient population. Allowing for an expected miscarriage rate of ~15% amongst clinical pregnancies (Stirrat, 1992), one can therefore anticipate a birth rate of ~16.9%.

As was noted above, it is not surprising that our pregnancy rates slightly exceed those reported by Collins et al. (1995). Not only did our control patients probably receive more interventions (and therefore treatment potentially contributing towards conception), but Collins et al.’s (1995) study also had to deal with the fact that some patients were lost to follow-up. It is actually much more surprising how similar the outcomes between these two studies are, considering the difference in methodology and, more importantly, the difference in patient populations. Collins et al. (1995) analysed a multicentre study, which automatically suggests a possibly heterogeneous patient population. In contrast, our study presents data from only one treatment centre, and therefore probably represents a more uniform approach towards infertility treatment.

The fact that, despite such methodological differences, the suggested (in the case of Collins et al., 1995) and observed (in our case) background pregnancy rates for infertility populations are so similar, suggests that these data are valid. This has obvious potential importance as we embark on defining cost-effective treatment options in infertility.

Specifically, this means that the so-called ‘success rates’ for any treatment option in an unselected infertile patient population should be reduced by ~2% per treatment month. Obviously, treatment options are currently not being chosen in unselected fashion. However, if cost-effective treatment options are to be determined, then precisely such unselected, prospectively randomized studies of different treatment options will have to be conducted in the near future. Whether clomiphene citrate will then result in, for example, a 7 or 9% clinical pregnancy rate as a first-line medication for the treatment of infertile couples may have considerable fiscal significance.

Lastly, it is important to note that neither the study of Collins et al. (1995) nor ours precludes the possibility of significantly different background pregnancy rates in other infertility populations, especially if they are not randomly chosen. Collins et al. (1995), in fact, also conclusively demonstrated that the chance of conception varied amongst patients with different infertility aetiologies. Differences can also be expected based on the age of patients and on their ovarian reserve (Scott et al., 1995). It therefore seems of the utmost importance that providers of infertility care maintain statistics on their spontaneous background pregnancy rates. Without such information they will not be able to assess the true effects of their various treatments.

References


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