Temporal and geospatial trends in male factor infertility with assisted reproductive technology in the United States from 1999–2010

Anobel Y. Odisho, M.D., M.P.H.,[a] Ajay K. Nangia, M.B.B.S.,[b] Patricia P. Katz, Ph.D.,[a,c] and James F. Smith, M.D., M.S.[a,d]

[a] Department of Urology, University of California, San Francisco, San Francisco, California; [b] Department of Urology, University of Kansas Medical Center, Kansas City, Kansas; [c] Department of Medicine and Institute for Health Policy Studies, University of California, San Francisco, San Francisco, California; and [d] Department of Obstetrics, Gynecology, and Reproductive Sciences and Institute for Health Policy, University of California, San Francisco, San Francisco, California

Objective: To estimate the prevalence of male factor infertility diagnosis within the context of assisted reproductive technology (ART) clinics and its geographic and temporal distribution from 1999–2010.
Design: Population study based on patients presenting for care at ART centers.
Setting: Clinics providing ART services.
Patient(s): All male patients seeking infertility care at ART clinics.
Intervention(s): Data were obtained from the Centers for Disease Control and Prevention, analyzed, geocoded, and mapped.
Main Outcome Measure(s): Prevalence of male factor infertility diagnosis in a couple seeking infertility care.
Result(s): Between 1999 and 2010, 1,057,402 cycles of ART using nonfrozen, nondonor eggs were performed, increasing from 62,809 cycles in 1999 to 99,289 cycles in 2010. Nationwide in ART clinics, the period prevalence of isolated male factor infertility was 17.1% and the prevalence of overall male factor infertility diagnoses was 34.6%. The highest prevalence was reported in New Mexico (56.4%) and lowest in Mississippi (24.2%).
Conclusion(s): The prevalence of male factor infertility diagnosis varies significantly by time and space within the United States, whereas its overall prevalence has remained remarkably stable. This study provides the spatial analytic framework for future research to explore factors associated with male factor infertility.
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Key Words: Male factor infertility, prevalence, geospatial mapping, GIS, health services

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Significant social and demographic shifts in the United States, combined with improved IVF techniques, have led to increased interest in and utilization of assisted reproductive technology (ART). Men and women continue to postpone marriage, with a current median age of first marriage at 25.8 years for women and 28.3 years for men (1). The mean maternal age at first childbirth has increased, and the percentage of births to women more than 40 years has more than doubled, from 1.2%–2.8%, in the past 20 years (2–4). Although knowledge of female infertility prevalence allows clinicians and researchers to examine underlying causes for these changes, the prevalence and distribution of male factor infertility, thought to be present in 40%–50% of infertile couples, remains poorly understood (5–7).

Survey-based measures of the prevalence of male factor infertility have shown that 7.5% of men in the United States report seeking help for infertility, and of those that sought care, 18.1% reported clinician-diagnosed male-related infertility (8). More than 1.1 million men sought fertility care in 2002 (9) and there were 131–172 physician visits per 100,000 insured men for infertility care between 1994 and 2006 (10, 11). National estimates, using data from the National Survey of Family

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Reprint requests: James F. Smith, M.D., M.S., Department of Urology, University of California, San Francisco, San Francisco, California 94143-1695 (E-mail: smithjf@urology.ucsf.edu).

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Growth, suggest that the prevalence of male factor infertility was approximately 12% in 2002 (12). At present, however, no study has estimated the geographic distribution of a male factor infertility diagnosis in the United States at the national and regional levels or explored changes in male factor infertility diagnoses over time.

The objective of our study was to characterize longitudinal and geographic trends in the diagnosis of male infertility within the context of ART clinics in the United States during a 12-year period and to identify regions or time periods of high or low levels of male factor infertility.

MATERIALS AND METHODS

Data Preparation

As a result of the Fertility Clinic Success Rate and Certification Act passed in 1992 (13), the data from all ART cycles performed in US fertility clinics are reported to the Centers for Disease Control and Prevention National ART Surveillance System. The National ART Surveillance System reports data for 95% of ART clinics. Annual infertility diagnoses data at the clinic level were obtained from the Centers for Disease Control and Prevention (14). Institutional Review Board approval was not required for this analysis of publicly available, deidentified, and aggregated data. Because clinic names were not standardized over time (the same clinic was reported over time using varying abbreviations, punctuation, and spellings), we used text clustering algorithms in Open Refine, a free open-source text, and data processing platform (15, 16). This was manually verified based on clinic names and their medical directors. Clinic addresses were obtained from the Centers for Disease Control and Prevention. Data and missing fields were updated with double-data entry using Amazon Mechanical Turk (Amazon.com, Inc.) (17). Mechanical Turk allows for simple, repetitive human tasks to be assigned to a distributed workforce. Using this service allowed for rapid, high quality duplicate data entry for a low cost.

Geographic Analysis

Geocoding, the process by which street addresses are converted into longitude and latitude coordinates, was performed using the *R* statistical computing environment (18) and the *ggmap* package (19) with the Google Maps API (20). Using the clinic longitude and latitude and the *spatial* package (21), clinics were overlaid on state and county maps obtained from the US Census TIGER/Line system (22) and Hospital Referral Region (HRR) maps obtained from the Dartmouth Atlas of Health Care (23). The HRRs are geographic areas developed by the Dartmouth Atlas of Health Care to represent markets for tertiary medical care delivery. The HRRs have been used in a number of settings to account for variations in healthcare access, utilization, and outcomes (24–26). This is a widely used health policy tool, more accurate than mapping purely along arbitrary political boundaries that do not reflect the distribution and utilization of healthcare resources.

Data Visualization

Shaded matrix graphs, similar to gene microarray heat maps, were generated using *R*. They allowed for clear visual representation of more than 600 data points and concisely displayed changes in male factor infertility prevalence over time. Choropleth maps, thematic maps with shading representing a calculated variable, were generated using QGIS, an open-source Geographic Information System platform (27).

Outcome Measure

The prevalence of male factor infertility at ART clinics, defined as any abnormal semen parameter or sperm functional assay, was reported annually by each clinic, and for analysis was weighted by the number of nondonor, nonfrozen ART cycles performed by the clinic in that year. Clinics were the baseline unit of analysis, which were aggregated to state levels. Means were weighted based on proportional contribution of each clinic based on cycles performed in that state during the cumulative time period 1999–2010, as shown:

$$\sum r_i \times \frac{cycles_i}{cycles_s}$$

where i = clinic; r_i = rate of male infertility as reported at each individual clinic; $cycles_i$ = number of IVF cycles performed at that clinic; and $cycles_s$ = cumulative number of IVF cycles performed in each state from 1999–2010.

Isolated male infertility was defined as a diagnosis of male factor infertility without concomitant female factor infertility. Total male infertility was defined as any male factor infertility, either isolated or in the presence of female factor infertility. Data were aggregated to the state and HRR levels for analysis and mapping.

RESULTS

The number of ART clinics in the United States increased from 367 in 1999 to 440 in 2010, representing a 19.9% increase (4.6% annual average). By 2010 only three states (Maine, Montana, and Wyoming) lacked an ART clinic. During this time period, 1,057,402 nondonor, nonfrozen cycles were performed, increasing from 62,809 in 1999 to 99,289 by 2010—a 58.1% increase (Table 1). The number of annual cycles peaked at 102,924 in 2008, with a slow decline through 2010.

The mean annual prevalence of isolated male factor infertility as diagnosed at all ART clinics was 16.9%–17.5% in the years between 1999 and 2010, with an overall mean of 17.1%. Despite stability in the overall prevalence of male factor infertility, there was high variability at the state and HRR levels. Analysis by geographic region showed little significant variation in the diagnosis of isolated male factor infertility. Isolated male factor infertility was reported in 17.9% of men presenting to ART clinics in the Midwest, 16.8% in the Northeast, 17.1% in the South, and 16.9% in the West (SD 8.0%–9.8%).

State-level analysis (Table 2) revealed high variability in isolated male factor infertility diagnoses. Utah (26.9%), Minnesota (25.4%), Wisconsin (24.6%), New Hampshire (24.2%), and Vermont (23.2%) had the highest proportion of isolated male factor infertility diagnosed at ART clinics, whereas Alabama (10.3%), Mississippi (11.3%), West Virginia (11.9%), Georgia (12.3%), and New Mexico (12.6%) had the