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Decline in semen parameters from 2000 to 2016 among Bangladeshi men attending a tertiary care hospital

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Introduction

The objective of this study was to analyze longitudinal changes in sperm parameters of Bangladeshi men. We hypothesized that semen parameters declined for this population. Methods: We retrospectively analyzed semen data from men aged 18-44 years who sought care for general sperm quality or updates on fertility status at an infertility clinic in Dhaka, Bangladesh, from January 2000 to June 2016 (n = 13,853). Samples with incomplete data were excluded (n = 143). The WHO normal criteria and semen analysis procedures were used to evaluate parameters of the remaining 13,810 specimens. Samples with missing values on sperm concentration (n = 1,817) were excluded from concentration analyses. Age and duration of abstinence at testing were recorded and adjusted for. Data were imported into SAS® 9.4 statistical software. Temporal significance was investigated using one-way ANOVA for mobility parameters and Chi-square test for raw concentration. Logistic regression analysis defined the effects of confounders on azoospermia and raw concentration, while median regression modeling adjusted confounders for concentration, total motility, and rapid linear (RL) motility. Results: Age distribution was significantly correlated with annual parameter changes (concentration, total motility, and RL motility P < 0.0001). Adjusted total motility and RL motility declined by 20% from their maximum values to end of the study (P < 0.0001). Raw concentration lacked clear trends and was unaffected by adjustment. Azoospermia increased by 18% between the 2000-2010 and 2011-2016 participants (odds ratio = 0.16 [0.14–0.16]). Conclusion: In agreement with the hypothesis, Bangladesh males attending this clinic have experienced decline in semen parameters (total motility and RL motility) and increased frequency of azoospermia.

Changes in sperm quality indicators – sperm count, percentage of sperm mobility, sperm density, and normal sperm morphology – have been explored globally over the last two to three decades.[1] Longitudinal and cross-sectional studies in Israel showed that the average sperm parameters in the nation have dropped over the last 25 years, with significant decrease of total motile sperm counts per ejaculate and percentage motility.[2] A retrospective analysis of semen in men in Western Europe revealed a significant decrease in sperm motility and increase in immotile sperm from 1977 to 1995.[4] Another study highlighted Japan and Denmark as having the lowest semen indicators in the world. This study, as well as a review on all sperm-density studies done from 1994 to 1998, concluded that while geographical location of nations may result in regional disparities for semen quality, parameters have declined for overall and in both regions.[5][6]

While semen data are available for most of the global communities, South-East Asian countries lack research studies. A 2007 study conducted by the infertility unit at the Bangladesh Sheikh Mujib Medical University found that about 62% of couples attending the infertility unit faced primary infertility, while 38% experienced secondary infertility. Semen analysis results from this study indicated that among the male partner, oligospermia, or sperm concentration of <20 × 106 sperm/mL, caused the highest infertility in 33.5% of cases.[7][8] In 2010, an estimated 3 million Bangladesh couples were subfertile; and for 60% of those couples, the male partner was responsible.[9]

The objective of this study was to analyze changes in semen quality of a subset of the Bangladeshi male population attending an infertility clinic between 2000 and 2016. Through this study, we hope to evaluate whether there is an observable decline of semen parameters in Bangladesh males, as determined by trends recorded for mobility, morphology, and concentration. Based on trends observed in the global community, we hypothesized that there is a temporal decline in semen parameters for the study population.

Materials and Methods

The Ethical Review Committee of the Diabetic Association of Bangladesh approved the protocol of this study (Memo no: BADAS-ERC/REC/16/0019). Participants were required to provide signed consent for their analysis results to be included in the study database and received signed analysis reports for their personal records.

Study population and participants

Data collection for this study was conducted in the Centre for Assisted Reproduction (CARE) at the Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders (BIRDEM) from January 2000 to June 2016. CARE is one of the largest infertility clinics in Bangladesh and a major clinic for infertility referrals. A majority of patients at CARE reside in Dhaka, Bangladesh, but services are also provided to patients from other regions in the country and those visiting from overseas.

The overall study population consisted of 13,853 participants. A total of 143 participants were excluded from analysis due to incomplete data. 6,787 datasets did not have quantitative sperm concentration values and were excluded from raw concentration analyses. Data is not available for 2006 and thus data from 2000 to 2005 and 2007 to June 2016 is included.

Semen analysis procedures and calculations

All semen analyses were conducted by a single laboratory technician who used the same type of laboratory materials for the entire duration of the study. The methods used for semen analysis are outlined in the WHO’s Laboratory Manual for Examination and Processing of Human Semen.[4] Participants provided semen samples through masturbation or intercourse at the on-site masturbatorium. 3–5 days of abstinence before sampling was advised, and duration was recorded. Samples were liquefied for 30 min and then gently mixed before 2–3 drops were extracted. Drops were loaded onto a Makler counting chamber (0.01 mm × 0.01 mm grid) and observed under a phase-contrast microscope at ×10 magnification. The laboratory technician determined morphology by adjusting the microscopic view to a higher magnification so that physical characteristics of the spermatozoa were visible. The count of sperm that were not in the normal tadpole shape or swim abnormally were considered to have abnormal morphology. The percentage of sperm with abnormal morphology was estimated based on the magnification of the grid, proportional to the overall 10 × 10 Makler chamber grid.

Statistical analysis

The dataset (n = 13,810) was imported from an electronic database into SAS® 9.4 statistical software (Cary, North Carolina) for analysis. Because normally tested semen parameters can be severely skewed, median (interquartile range) was reported for parameter baseline. Age, duration of abstinence, and liquefaction were reported as mean ± standard deviation. Significance of differences between annual means and medians were found through parametric one-way ANOVA tests, while raw concentration significance was determined through Chi-square distribution analysis. P < 0.05 was considered statistically significant. Patients with missing quantitative concentration data or incomplete records (n = 1,817) were excluded from the logistic-regression analyses of this variable. To adjust for confounding, concentration, morphology, and RL motility were adjusted by median age of patients at the time of testing and median duration of abstinence before testing through median regression modeling.

Baseline sperm characteristics, age, and duration of abstinence of the study population (n = 13,810) are shown in Table 1. The average age of participants was 35.4 ± 6.6 years, and age distribution was significantly correlated with annual parameter changes (P < 0.0001) [Table 1]. Duration of abstinence (P = 0.05) and liquefaction (P = 0.07) remained unchanged in annual comparisons, both averaging around 3.2 ± 0.8 days and 1.0 ± 0.8, respectively. All semen parameters (concentration, total motility, RL motility, and normal morphology) appeared to vary...
Our study shows that for Bangladesh men, there has been a decline in total motility and RL motility on semen analysis from 2000 to 2016, and the trends and magnitude of decline are more evident upon adjusting for age and duration of abstinence. The incidence of azoospermia also increased when adjusted for age and duration of abstinence.

Interestingly, the overall frequency of normozoospermia increased upon adjusting for the WHO 2010 concentration diagnosis. Although findings do not indicate that the actual frequency of fertile males increased, the criteria changed from ≥20 × 10⁶/mL to >15 × 10⁶/mL, and this may be solely responsible for the shift in normozoospermia because more participants qualified for the former criteria. There is no established threshold between the WHO 1999 and 2010 parameters, frequencies can change depending on the cutoff used which makes it difficult to assess whether the laboratory technician’s classification of oligozoospermia versus normozoospermia is consistent over time. Although consistently reported by a single technician, measurement bias also exists where human error affects accuracy of semen parameter readings. The longevity of data collection provides strength to this study and show that studies of this nature are feasible despite Bangladesh being a low-resource setting. Moreover, semen analysis readings and methodology should be consistent because the analyses were conducted by a single observer who used the same type of laboratory materials for the entire duration of the study.

Conversely, several improvements were needed in the study design and dataset. Although it was previously described that normozoospermia and acrospermia increased with time, characterization of the diagnoses was limited by the absence of raw concentration readings for all of these data, if these data were available, the qualifications for oligozoospermia stratification could be described more accurately. It is also important to note that sample size did not remain consistent throughout the study. There was a fluctuation of participants during the second half of the study. Therefore, the increase in frequency of acrospermia may have offset the expected decrease in normozoospermia. Moreover, there appeared to be a lack of consistency between 2000 and 2004, which may or may not be associated with the reduced sample size compared to post-2008 data. Association could be explained for the decrease in diagnosis because the parameters would not have been affected by the WHO criteria until 2010, but sample size is not a conclusive factor because none of the factors other than motility showed associated.

Among the correlated dataset, outliers who do not reside in Dhaka or have drastically different life course exposures are not eliminated. Therefore, the effect of confounding due to influential risk factors (i.e. exposure to toxins, preexisting health conditions, environmental factors, and drug use) is not clear. All the study participants were from a single clinic, thus limiting generalizability of our results. Moreover, we were unable to follow single participants over time and determine whether multiple datasets represented a single participant due to a lack of patient identifiers. Significant measurement bias exists where the WHO 2010 semen parameters have been deemed unreliable from emerging studies because they are determined by the world population at large, thus potentially not providing a true measure for the burden of infertility as differentially regional.[10] An absence of raw concentration counts for 618 participants makes it difficult to assess whether the laboratory technician's classification of oligozoospermia versus normozoospermia is consistent over time. Although consistently reported by a single technician, measurement bias also exists where human error affects accuracy of semen parameter readings.

This study provides a rationale for conducting observational studies on male infertility in the context of Bangladesh and neighboring South Asian countries. As we established the trend of decline in motility and RL motility in acrospermia in a clinic population, the next step might be to determine whether this is also true for the overall population and evaluate the reasons for trends. Controlled studies tracking life course exposure of males in Bangladesh that are supplemented with extensive patient history, semen data, lifestyle factors, and effects of xenobiotics on reproductive hormones would help describe how the burden of male infertility may be reduced and prevented. There is a need for global action to solidify an understanding of declining semen holistically in order to combat specific causes for the propensity of future generations. Moreover, improvement of the WHO parameters to provide a clearer definition for male infertility as varied for context would improve treatment regimens of male partners significantly.

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There are no conflicts of interest.

References