Critical Demographic Changes among Sperm Donation Recipients Over Three Decades

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ABSTRACT **Background:** Sperm banks initially focused on providing sperm donation (SD) to heterosexual couples grappling with severe male infertility. Notable advancements in fertility treatments and sociological trends have broadened the scope of SD toward single women and same sex female couples.

Objectives: To evaluate SD recipient characteristics over the last three decades in Israel according to demographic parameters.

Methods: This retrospective cohort study included 5489 women who received SD between January 1992 and December 2021 from a tertiary referral center. We divided the overall period into six groups of five years each. A comparison of demographic characteristics of women who received SD in different periods was performed according to age at the beginning of the treatment, marital status (single women and same sex female couples, heterosexual couples), and ethnic origin.

Results: The average age of women who received SD was 37.02 ± 5.36 years. The average patient age rose from 35.08 years in 1992–1997 to 37.43 years in 2017–2021 (*P*-value < 0.01). The use of SD was more common among single women and same sex female couples compared to heterosexual couples in later years. Regarding single and same sex female couple, the percentage of SD recipients increased radically from 33% to 88.1% (*P*-value < 0.01).

Conclusions: Modern sperm banks treat older patients in non-heterosexual relationships. These trends encompass not only medical implications (e.g., in vitro fertilization vs. intrauterine insemination) but also delve into the personal and sociological impact experienced by both patients and offspring.

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KEY WORDS: ethnic origin, single mothers, sperm bank, sperm donation, women received donated sperm

The availability of donor gametes provides individuals and couples who otherwise may not be able to conceive with an opportunity to build a family [1]. The use of sperm and oocyte donation services has increased over the past several decades [2,3]. Worldwide social changes over several decades have been investigated extensively in a multitude of studies in diverse population groups. Focusing on egg donation, in addition to clinical importance, egg donor cycles enable optimal assessment of any paternal impact on the embryonic genome [4]. Focusing on sperm donation (SD), the rise of single women or same sex lesbian families changed fundamental demands of sperm banks. From a secret process aimed at supplying sperm to heterosexual couples experiencing severe male infertility with limited medical evaluation of sperm donors [5], the modern era is characterized by open public discussion about novel topics such as offspring number limitation per donor and donor identity disclosure vs. anonymity preservation [5]. Parallel medical breakthroughs in the field of genetic testing and screening [6] combined with global male fertility deterioration [7] have made sperm bank considerations throughout the process of sperm donor selection sophisticated than ever.

Surprisingly, despite the increase of single women and same sex lesbian families among SD recipients, the scientific comparisons between different SD recipients are limited. Arocho et al. [8] reported that nearly 500,000 women utilized SD in the United States between 2015 and 2017, a substantial increase from the 170,000 recorded in 1995. The National Longitudinal Lesbian Family Study initiated in 1986 [9] supplied important research regarding lesbian couples, their opportunities for SD, the psychological implication of their children [10]. The strong impact of family type (single women, same sex couple, and heterosexual couples) on an offspring's desire to know their donor [11] have been investigated as well, reflecting higher tendency toward establishing such

relationships, especially among single women in contrast to heterosexual couples. Yet, comparison of family types over time, which enable scientific investigation of sociological trends, remains lacking.

Perspectives toward SD are also influenced by cultural and religious considerations. Religious and conservative patients who often favor of a traditional heterosexual family are prone to negative perceptions toward SD. Fortier [12] noted similar hesitation toward gamete donation among monotheism beliefs regardless of specific religion. Homburg and colleagues [13] reported that similarities rather than differences seemed to dominate in the attitudes of the orthodox Catholic, Hindu, Jewish, and Muslim beliefs and doctrines. Initial perceptions among recipients may impact their application for SD in various ways, such as age at start of application and donor selection. Israeli society is marked by ethnic and religious diversity, with a significant emphasis on reproduction and childbirth. Rabbinical instructions according to Halacha (traditional rabbinical Jewish law) focus on married women and still refrain from acknowledging the growing number of non-married donor insemination patients [14]. Therefore, investigation of demographic trends according to ethnic, cultural, and religious background on Israeli society may be relevant for other countries as well.

In this study, we examined demographic trends over three decades at a single sperm bank (SB). We investigated patient age, marital status, and ethnic background to assess evolution of these parameters during a long follow-up of 30 years.

PATIENTS AND METHODS

The long-term follow-up of this retrospective study included all women older than 18 years of age who received SD at the Shamir Medical Center Sperm Bank between January 1992 and December 2021. Shamir Medical Center is a tertiary medical center that provides fertility services, including SD, to a large population living in the central region of Israel. Thus, our study was based on nonselective population data.

In the 1990s, changes were introduced in the artificial insemination process due to increasing concerns about the transmission of human immunodeficiency virus (HIV) through semen. As a result, the use of fresh semen from donors was prohibited, and frozen semen from accredited sperm banks became the only approved method for artificial insemination. We started our research in 1992 because significant changes were implemented in the artificial insemination process, primarily driven by increasing concerns about HIV transmission through semen donation [15].

Data from this retrospective study were collected from electronic medical records. Data included the woman's age at the beginning of treatment, family status, and ethnic origin. Overall, ethnic origin was divided into seven subgroups: Ashkenazi Jews, Sephardi Jews, combinations, Balkan Jews, Ethiopian Jews, others, and ethnic minorities.

Patients were grouped into 5-year cohorts of the study period, which included six eras of SD treatment: 1992–1996, 1997–2001, 2002–2006, 2007–2011, 2012–2016, and 2017–2021. Analysis focused on patient demographic characteristics at the beginning of treatment. We analyzed women who received SD according to each of the following parameters: age (patient age at the beginning of treatment), family status (heterosexual relationship, single woman, or same sex relationship), and ethnic origin (seven subgroups). These comparisons enabled us to isolate subgroups of each parameter.

We focused on patients who utilized SD throughout the follow-up period. The study did not consider the frequency of each woman's SD requests. Each patient was considered as one participant in the study, regardless of whether she underwent one or multiple donations.

Categorical variables were described as frequencies and percentage, age was listed as mean ± standard deviation. Analysis of variance (ANOVA) was used to compare age among period categories and chi-square test was used to compare categorical variables. The Bonferroni method was applied to control multiple comparisons of the post-hoc test.

All statistical tests were 2 sided, and $P < 0.05$ was considered statistically significant. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 28 (SPSS, IBM Corp, Armonk, NY, USA).

The study was approved by the local institutional review board. Informed consent was not required.

RESULTS

The study included 5489 women who received donated sperm between January 1992 and December 2021. The entire time frame was subdivided into six intervals, each spanning five years: 1992–1996 (228 patients, 4.2%), 1997–2001 (464 patients, 8.5%), 2002–2006 (702 pa-

Table 1. *P*-values of recipient age calculated by repetitive comparisons

	1992–1996	1997–2001	2002–2006	2007–2011	2012–2016
1997–2001	1.000	–	–	–	–
2002–2006	0.000	0.006	–	–	–
2007–2011	0.000	0.000	1.000	–	–
2012–2016	0.000	0.000	1.000	1.000	–
2017–2021	0.000	0.000	0.363	1.000	1.000

Figure 1. Recipients age trend over 30 years of follow-up

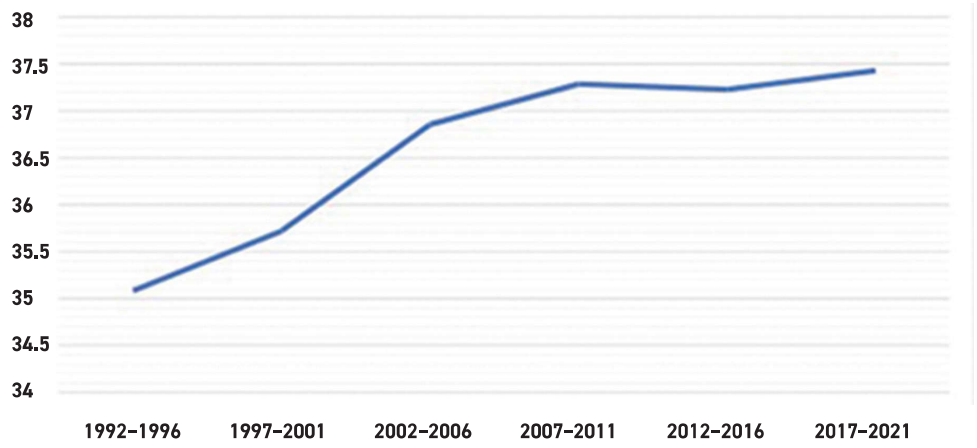
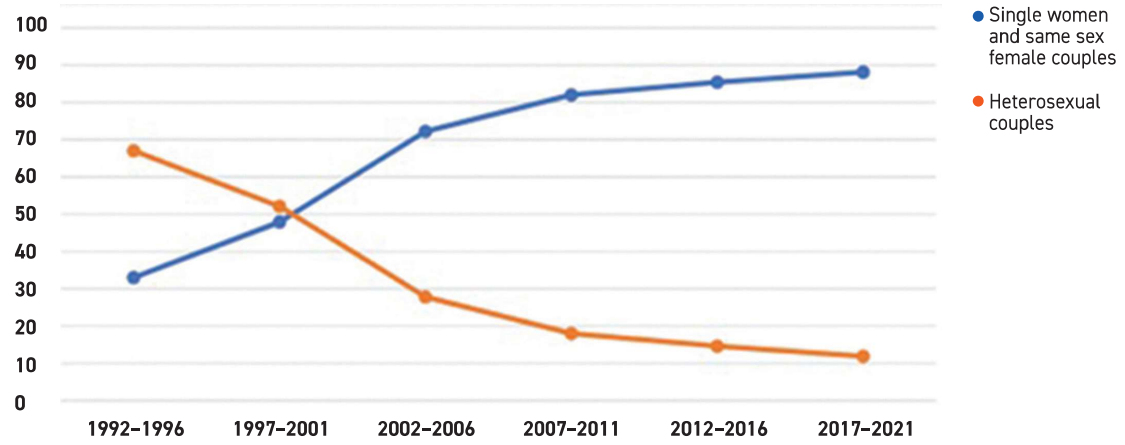


Figure 2. Marital status

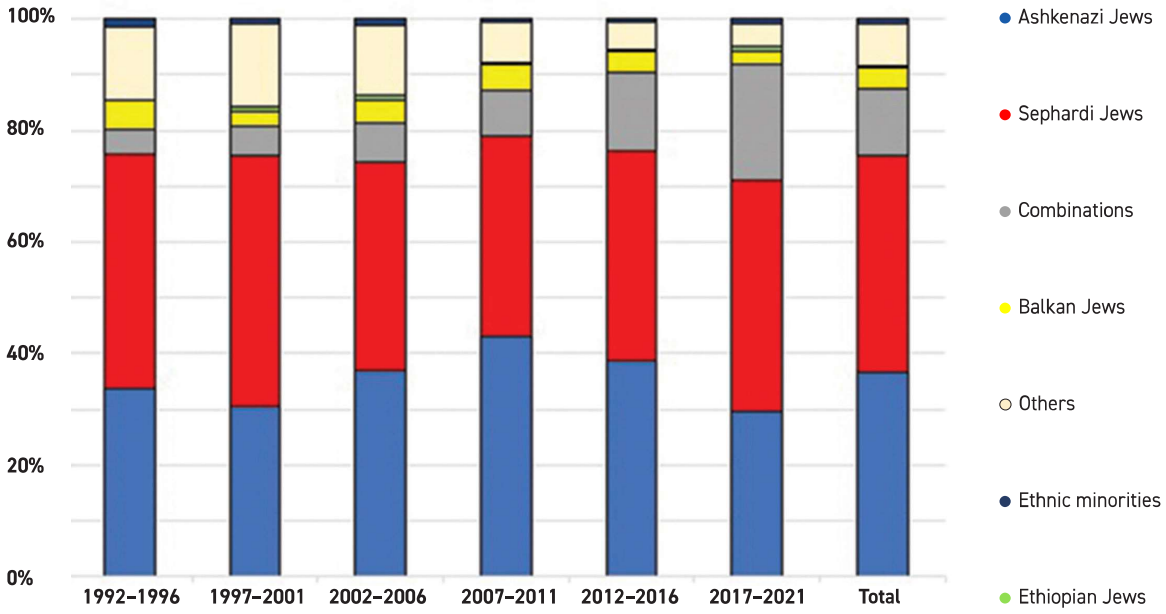


tients, 12.8%), 2007–2011 (1482 patients, 27%), 2012–2016 (1439 patients, 26.2%), and 2017–2021 (1174 patients, 21.4%).

The division into six groups of five years each of the study period demonstrates the following data regarding the patient's age in years: 1992–1996 (35.1 ± 6.55), 1997–2001 (35.7 ± 6.6), 2002–2006 (36.9 ± 5.7), 2007–2011 (37.3 ± 4.9), 2012–2016 (37.2 ± 4.9), and 2017–2021 (37.4 ± 5.2). Repetitive comparisons revealed a significant shift between 1997–2001 and 2002–2006 [Figure 1, Table 1].

Focusing on marital status, a comprehensive significant trend was demonstrated throughout the study period.

Figure 3. Distribution by ethnic origin of groups by treatment, 5-year intervals



While between 1992–1996 two-thirds of recipients had heterosexual relationships, the same was true only for 11.9% of patients between 2017–2021 [Figure 2]. Repetitive comparisons found a significant difference (*P*-value < 0.05) on each comparison, except two comparisons of 2012–2016 to 2007–2011 and 2017–2021 periods (both *P*-value > 0.05).

The leading ethnic origin was Sephardi Jews (38.8%), followed by Ashkenazi Jews (36.7%), combinations (11.9%), others (7.6%), Balkan Jews (3.7%), ethnic minorities (0.7%), and Ethiopian Jews (0.5%). Ethnic background remained stable throughout the study period without significant differences [Figure 3].

Data spanning from 2008 to 2019 revealed that approximately 65% of patients opted for Jewish sperm from Israel, while roughly 35% chose non-Jewish donor sperm from abroad. In recent years a discernible preference for non-Jewish sperm donors from abroad has been noted. The utilization of Jewish donors from Israel now stands on par with that of non-Jewish donors from abroad.

Data collected from 1998 to 2021 revealed that among the women included in the study, 8007 cases (34.1%) involved sperm donations for intrauterine insemination, while 15,429 cases (65.9%) utilized sperm donations for in vitro fertilization procedures.

DISCUSSION

The current study included over 5400 patients who received SD over three decades. The characteristics of patients who currently apply for SD are dramatically different from those of women who applied during the early years of the sperm bank, which emphasizes dramatic social trends. Almost 90% of current patients were not in heterosexual relationship. While our study focused mainly on social trends, medical changes also impacted the routine practices of sperm banks. Consequently, combined medical and social changes, which frequently conflict, resulted in enormous challenges.

An obvious implication of the current study related to patient age at the time of the fertility treatment as well as fertility and obstetric outcome. Age is a crucial factor in fertility outcome, and individuals who are considering starting a family should be aware of the potential impact of age on their chances of conception. By the age of 35, the chances to conceive decline progressively [16]. Our study showed a significant increase in maternal age over the years from 35.08 years of age in 1992–1996 to 37.43 years of age in 2017–2021.

Focusing on family status, we found a dramatic increase in the use of SD over time by single women and same sex couples compared to heterosexual couples. Ad-

vances in fertility treatment have made it easier and more accessible for single women to conceive using donor sperm [5]. The trend of increasing use of SD among single women may have also been influenced by changing societal norms and attitudes toward single parenthood. As society becomes more accepting of non-traditional family structures, more single and lesbian women may feel comfortable choosing to start a family on their own [17]. The similarity of ethnic origin with our patients during the follow-up period suggested that these sociological trends were uniform within Israeli society.

Sperm banks face a substantial gap between donor supply and demand. While we demonstrated a rapidly growing population of single women and lesbian couples applying for SD, we also emphasized the growing demand to limit birthrate per donor, which resulted in a decline of available donors [18]. Moreover, medical standards of top-rated semen analysis and comprehensive genetic tests reduced the rate of accepted candidates [18]. Second, the fact that the vast majority of SD originate from non-heterosexual relationships emphasizes the dilemma regarding the offspring's desire to know their biological father versus the sperm bank's obligation to maintain the donor's anonymity [19].

Our research has several noteworthy strengths that significantly bolster its overall quality and impact. First, the study included a substantial sample size, encompassing a significant number of patients. This extensive and diverse data set provided robust statistical power, allowing for more reliable and comprehensive analyses. Second, a key strength lies in the wealth of information gathered from a single tertiary medical center. This focused approach ensured the consistency and reliability of the data, which originated from a single source with standardized practices and protocols. Throughout our research, we strived to present a unique perspective on demographic changes among SD recipients and included a thoughtful analysis of the subject matter.

The current study has several limitations. We did not include information regarding fertility outcome. This information is especially important for assessing the consequences of the increase in SD recipient age over the years, which negatively affects the reproductive outcomes [16]. The retrospective design of the study was another limitation. Our data were generated from a single tertiary medical center that provided services only to the Israeli population, which was characterized by high fertility treatment rates and young childbearing age, although the mean age of SD recipients was higher than the average population. Last, we did not distinguish between single women and those in a lesbian relationship since the awareness for the latter group was limited during the first decade of the follow up. Still, the current results emphasize the dramatic decline of heterosexual couples, which is an important contribution to the literature.

CONCLUSIONS

To the best of our knowledge, this is the longest follow-up study to reflect dramatic sociological changes among sperm donation recipients. Sperm banks have made significant strides since their establishment in the early 20th century. Initially, sperm banks were established to help heterosexual couples who were struggling with infertility. However, with changing societal norms and attitudes toward non-heterosexual relationships, sperm banks have evolved to serve a broader population, including older patients in non-heterosexual relationships. These trends encompass not only medical implications but also personal and sociological aspects that influence patients and offspring.

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Capsule

Putting BCR and TCR sequences on the map

Although current spatial transcriptomics technologies can locate gene expression within tissues, they are unable to map full-length B cell receptor (BCR) and T cell receptor (TCR) sequences in this context. **Engblom** and co-authors developed a method called spatial transcriptomics for variable, diversity, and joining sequences (Spatial VDJ), which spatially annotates full-length immunoglobulin and T cell antigen receptor transcripts in frozen human tissue sections. This approach, which also resolves whole transcriptomes and tissue morphology, results in high-fidelity mapping and spatial lineage tracing of B and T cell clones in both human lymphoid and tumor tissues. This technology has the potential to advance our understanding of lymphocyte spatial dynamics in various clinically relevant phenomena such as infection, vaccination, and cancer.

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Capsule

Autoimmune amelogenesis imperfecta in patients with APS-1 and celiac disease

Ameloblasts are specialized epithelial cells in the jaw that have an indispensable role in tooth enamel formation (amelogenesis). Amelogenesis depends on multiple ameloblast-derived proteins that function as a scaffold for hydroxyapatite crystals. The loss of function of ameloblast-derived proteins results in a group of rare congenital disorders called amelogenesis imperfecta. Defects in enamel formation are also found in patients with autoimmune polyglandular syndrome type-1 (APS-1) caused by AIRE deficiency, and in patients diagnosed with celiac disease. However, the underlying mechanisms remain unclear. **Gruper** and co-authors showed that the majority of patients with APS-1 and celiac disease developed autoantibodies (mostly of the IgA isotype) against ameloblast-specific proteins, the expression of which is induced by AIRE in the thymus. This situation results in a breakdown of central tolerance and subsequent generation of corresponding autoantibodies that interfere with enamel formation. However, in celiac disease, the generation of such autoantibodies seems to be driven by a breakdown of peripheral tolerance to intestinal antigens that are also expressed in enamel tissue. Both conditions are examples of a previously unidentified type of IgA-dependent autoimmune disorder that is called autoimmune amelogenesis imperfecta.

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