RÉSUMÉ

Diminution de la qualité du sperme chez les hommes consultés pour l’infertilité de couple dans la République de Moldova

Introduction. Environ 15% des couples cherchent un traitement médical pour l’infertilité le facteur masculin étant impliqué dans 50% des cas environ. Les analyses du sperme sont utilisées comme facteur pronostique et thérapeutique afin d’évaluer le potentiel de la fertilité masculine.

L’objectif de l’étude était d’évaluer les tendances régionales de la qualité du sperme chez les partenaires masculins des couples confrontés à l’infertilité, afin d’identifier l’état actuel des influences du facteur masculin à l’infertilité dans notre pays.

Matériaux et méthodes. On a réalisé une étude rétrospective sur 5767 patients ayant effectué une analyse du sperme entre 2012 et 2020. Tous les échantillons de sperme ont été prélevés après une période d’abstinence recommandée de 3 à 5 jours. L’analyse du sperme a été effectuée conformément au Manuel de laboratoire de l’OMS pour l’examen et le traitement du sperme humain, 5e édition, 2010. La régression linéaire a été utilisée pour examiner les tendances sur les années en tous les paramètres de sperme.

RÉSULTATS. Des tendances décroissantes ont été significatives dans tous les paramètres de sperme : volume de sperme (1,1% par an); concentration en spermatozoïdes (3,2% par an); nombre total de spermatozoïdes; et les autres paramètres de sperme.

ABSTRACT

Introduction. About 15% of the couples seek medical treatment for infertility, the male factor being involved in about 50% of cases. Semen analyses are used as prognostic and treatment factor in assessing the potential for male fertility.

The objective of the study was to evaluate the regional tendencies of the semen quality in male partners of couples facing infertility, to identify the status of the contributions of male factor to infertility in the Republic of Moldova.

Materials and methods. We performed a retrospective study on 5767 patients who performed semen’s analysis between 2012-2020. All semen samples have been collected after a recommended period of sexual abstinence of 3 to 5 days. Semen analysis was performed according to the World Health Organization (WHO) Laboratory Manual for the Examination and Processing of Human Semen, 5th edition, 2010. Linear regression was used to examine trends over time in all semen parameters.

Results. Declining trends were significant in all semen parameters: semen volume (1.1% per year); sperm concentration (3.2% per year); total sperm number

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INTRODUCTION

Worldwide it is estimated that approximately 15% of couples at reproductive age experience infertility, the male factor being involved in about 50% of cases\(^1,2\). According to the World Health Organization (WHO), the diagnosis of infertility with the involvement of the male factor is established when the results of the repeated analysis of the sperm are below the normal values established by the WHO. The quality and quantity of semen are used as an indirect factor in assessing the potential for male fertility. According to specialist sources, semen analysis remains the most useful and fundamental investigation, with a sensitivity of 89.6%, being able to detect 9 out of 10 men with a genuine infertility problem\(^3\). It is also considered a milestone in the assessment of the infertile partner and helps to define the severity of male factor infertility\(^4\).

The evaluation of sperm parameters in men is of individual interest for couples who have difficulty conceiving. According to the results of the sperm analyses values, it can be confirmed that the male factor influencing fertility was excluded in the first stage, providing prognostic information, and identifying opportunities for therapeutic interventions. This interest is also argued at the population level, to identify possible temporal or geographical differences in male fertility\(^5\). Semen analyses is a test that assesses the formation and maturity of sperm that provides a perspective not only on sperm production (number), but also on sperm quality (motility, morphology). It also provides information on the functional status of the seminiferous tubules, epididymis, and accessory sex glands, and its results are often taken as a surrogate measure of a man’s ability to conceive. Assessing male fertility potential by sperm analysis remains the basic clinical tool\(^6,7\).

THE OBJECTIVE OF THE STUDY was to evaluate the regional tendencies of semen quality in men of infertile relationships who were under investigation for couple infertility and attended reproductive clinic for routine semen analysis, to identify the status of the contributions of male factor to infertility in our country.

MATERIALS AND METHODS

We performed a retrospective study between 2012–2020 in the Republic of Moldova, covering all male partners of infertile couples who performed semen analysis. A total of \(n=5767\) patients have been evaluated: \(n=200\) in 2012; \(n=703\) in 2013; \(n=852\) in 2014; \(n=794\) in 2015; \(n=703\) in 2016; \(n=685\) in 2017; \(n=630\) in 2018; \(n=640\) in 2019 and \(n=560\) patients in 2020. The mean age in the studied group was \(37.4 ± 6.3\) (SD) years. Semen evaluation for all subjects was routinely performed during the infertility workup.

Semen samples were collected by masturbation into sterile plastic containers in the laboratory, after a recommended period of sexual abstinence of 3 to 5 days. The semen analysis was performed by...
the computerized method on the automated analyser SQA IIC-P (Medical Electronic Systems, USA). Semen analysis was performed according to the WHO Laboratory Manual for the Examination and Processing of Human Semen, 5th edition, 2010.

The data have been analysed using SPSS statistical computer software (22.0; SPSS Inc) and Microsoft Office Excel. Linear regression was used to examine trends over time in semen parameters: sperm concentration; motility; morphology and vitality. An analysis of variance (ANOVA) test was carried out to see if there were any overall differences in the means of sperm parameters, for each year of the period 2012 to 2020 and for medians (ANOVA according to Kruskal Wallis). The study was carried out in accordance with the protocol No 48 of April 12, 2018, which was approved by the Research Ethic Board of State University of Medicine and Pharmaceutics „Nicolaie Testemitanu”, Chisinau, Republic of Moldova.

RESULTS

Data on semen samples from a total of n=5767 men were available for analysis. Age, volume, sperm concentration, sperm motility, normal forms and vitality had normal distributions. The mean age of the patients was 37.4±6.3 (SD) years (CI 95%: 37.3-37.6; median: 37) (Figure 1).

Descriptive statistics, means ANOVA and medians ANOVA according to Kruskall Wallis test results data for each sperm parameters for each year from 2012 to 2020 are listed in Tables 1, 2, 3. For all the sperm parameters, statistically significant differences were found between the years.

The mean value for total semen volume was 2.9±1.1 mL, (95% CI: 2.8–2.9; median 2.9). Overtime, the mean volume decreased significantly from 3.0±1.2 mL in 2012 to 2.7 ± 1.0 mL in 2020, with an average rate of decrease of the mean volume of 1.1% per year. Linear regression to examine changes in volume trend over time was performed by the model: Semen volume = 3.5 -0.04 * Year, (R2 = 0.015; F = 43.5; p = 0.000), with average annual decrease of 0.04 mL (p = 0.000) (Table 1, Figure 2 a, b).

The mean pH during the study period was 7.8±0.2 (95% CI: 7.82-7.83; median: 7.8). The average in these years fluctuated between 7.79 and 7.85. The analysis of the means (ANOVA: F = 10.8; p = 0.000) signals the existence of statistically significant differences between years, but it is not possible to identify a trend, a fact confirmed by a regression model without statistical significance (F = 0.002; p = 1.000) (Table 1, Figure 2 c, d).

Decreases in mean sperm concentration were observed over the study period (from 48.6±38.1 million/mL to 34.7±29.1 million/mL), with an average rate of decrease of the mean 3.2% per year. The mean

![Figure 1. Distribution of male partners of infertile couples who performed semen analysis by age](image-url)
Figure 2. Box plot and linear regression for: a, b volume; c, d pH; e, f sperm concentration; g, h total sperm number, period 2012-2020
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Total sperm concentration was 39.0±33.3 million/mL, (95% CI: 38.2–39.9; median: 29). The mean annual decrease in sperm concentration is 2.2 million/mL (p = 0.000), according to the model: Sperm concentration = 75.1-2.2 * Year, (R² = 0.025; F = 146.6; p = 0.001) (Table 1, Figure 2 e, f).

The evaluation of the mean of the total sperm number in the sample indicates 112.1±109.3 million/ejaculate (95% CI: 109.2-114.9; median: 74.5) during 2012-2020. Overtime, the mean total sperm number declines from 142.5±125.9 million/ejaculate to 93.4±88.1 million/ejaculate, the annual decrease rate being 3.8%. Model: total sperm number = 241.2-8.0 * Year (R² = 0.029; F = 174.9; p = 0.000) showing that the average annual decrease is 8.0 million/ejaculate (p = 0.000) (Table 1, Figure 2 g, h).

The total mean for the progressive motility was 31.1±18.4 (%) (95% CI: 30.6–31.6; median: 32) with annual decrease rate 1.9%, from 35.3±20.2% to 29.4±16.7%. Linear regression model: progressive motility = 47.6-1.02 * Year (R² = 0.017; F = 100.9; p = 0.000) (Table 2, Figure 3 a, b).

The decline in the mean concentration of motile sperm was from 25.2±27.5 million/mL to 16.6±23.1 million/mL, annual rate of decrease is 3.6%. The total mean concentration of motile sperm during

Table 1. Results of volume, pH, sperm concentration and total sperm number, years 2012-2020

| Years | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | Total |
|-------|------|------|------|------|------|------|------|------|------|-------|
| **Abs. no** | 200 | 703 | 852 | 794 | 703 | 685 | 630 | 640 | 560 | 5767 |
| **Volume, (mL)** | 3.0 | 3.2 | 2.9 | 2.8 | 2.8 | 2.9 | 2.8 | 2.8 | 2.7 | 2.9 |
| Mean | 3.0 | 3.2 | 2.9 | 2.8 | 2.8 | 2.9 | 2.8 | 2.8 | 2.7 | 2.9 |
| Standard deviation | 1.2 | 1.3 | 1.2 | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 | 1.0 | 1.1 |
| **pH** | 7.8 | 7.8 | 7.9 | 7.8 | 7.8 | 7.9 | 7.8 | 7.8 | 7.8 | 7.8 |
| Mean | 7.8 | 7.8 | 7.9 | 7.8 | 7.8 | 7.9 | 7.8 | 7.8 | 7.8 | 7.8 |
| Standard deviation | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| **Sperm concentration (million/mL)** | 48.6 | 49.9 | 43.2 | 41.7 | 41.7 | 36.3 | 33.4 | 33.6 | 33.6 | 34.7 |
| Mean | 48.6 | 49.9 | 43.2 | 41.7 | 41.7 | 36.3 | 33.4 | 33.6 | 33.6 | 34.7 |
| Standard deviation | 38.1 | 37.0 | 34.0 | 34.8 | 34.8 | 31.7 | 29.2 | 32.5 | 29.7 | 29.1 |
| **Total sperm number (million /ejaculate)** | 142.5 | 157.2 | 125.1 | 115.8 | 100.5 | 96.2 | 93.8 | 95.0 | 95.0 | 112.1 |
| Mean | 142.5 | 157.2 | 125.1 | 115.8 | 100.5 | 96.2 | 93.8 | 95.0 | 95.0 | 112.1 |
| Standard deviation | 125.9 | 133.9 | 114.9 | 113.6 | 97.8 | 95.5 | 96.4 | 95.7 | 88.1 | 109.3 |
| CI 95% | 124.9 | 147.3 | 117.4 | 107.9 | 93.3 | 89.0 | 86.2 | 87.6 | 86.1 | 109.2 |
| CI 95%+ | 160.0 | 167.1 | 132.8 | 123.7 | 107.8 | 103.3 | 101.3 | 102.5 | 100.8 | 114.9 |
| Median | 110.5 | 125.4 | 87.5 | 77.9 | 67.5 | 62.1 | 59.5 | 64.0 | 66.5 | 74.5 |
| Percentile 25 | 39.3 | 45.0 | 30.6 | 25.2 | 24.0 | 25.3 | 22.0 | 24.4 | 27.2 | 27.2 |
| Percentile 75 | 231.6 | 242.5 | 198.4 | 180.6 | 155.2 | 136.4 | 136.3 | 139.5 | 136.2 | 168.0 |

* Year (R² = 0.029; F = 174.9; p = 0.000) showing that the average annual decrease is 8.0 million/ejaculate (p = 0.000) (Table 1, Figure 2 g, h).

The total mean for the progressive motility was 31.1±18.4 (%) (95% CI: 30.6–31.6; median: 32) with annual decrease rate 1.9%, from (35.3±20.2% to 29.4±16.7%). Linear regression model: progressive motility = 47.6-1.02 * Year (R² = 0.017; F = 100.9; p = 0.000) (Table 2, Figure 3 a, b).

The decline in the mean concentration of motile sperm was from 25.2±27.5 million/mL to 16.6±23.1 million/mL, annual rate of decrease is 3.6%. The total mean concentration of motile sperm during
Figure 3. Box plot and linear regression for: a, b progressive motility; c, d concentration of motile sperm; e, f total number of motile sperm; g, h motility index
The study period was 18.5±23.2 million/mL (95% CI: 17.9–19.1; median: 8.9). Linear regression resulted in the model: Motile sperm concentration = 39.7-1.3 * Year (R² = 0.019; F = 114.8; p = 0.000), with an average annual decrease of 1.3 million/mL (p = 0.000) (Table 2, Figure 3 c, d).

The evaluation of the mean of the total number of motile sperm in the sample showed 51.4± 66.1 million/ejaculate (95% CI: 49.7-53.1; median: 22.6), annual rate decrease 4.7%. The concentration of functional sperm recorded a total mean of 10.6±15.1 million/mL (95% CI: 10.2-11.0; median: 2.9). By model: functional sperm concentration = 25.5-0.9 * Year (R² = 0.02; F = 120.6; p = 0.000). The analysis of this model shows that the average annual decrease is 0.9 million/mL (p = 0.000) (Table 3, Figure 4 a, b).

### Table 2. Sperm motility results of men from infertile couples between 2012-2020

| Years | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | Total |
|-------|------|------|------|------|------|------|------|------|------|-------|
| Abs. no | 200 | 703 | 852 | 794 | 703 | 685 | 630 | 640 | 560 | 5767 |
| Progressive motility (%) | | | | | | | | | | |
| Mean | 35.3 | 36.3 | 32.9 | 32.2 | 30.0 | 28.6 | 28.1 | 28.6 | 29.4 | 31.1 |
| Standard deviation | 20.2 | 19.5 | 19.1 | 18.9 | 17.8 | 16.9 | 17.8 | 17.0 | 16.7 | 18.3 |
| CI 95%- | 32.5 | 34.9 | 31.7 | 30.9 | 28.7 | 27.3 | 26.7 | 27.3 | 28.0 | 30.6 |
| CI 95%+ | 38.2 | 37.7 | 34.2 | 33.5 | 31.3 | 29.9 | 29.5 | 29.9 | 30.8 | 31.6 |
| Median | 39.0 | 39.0 | 35.0 | 33.0 | 30.0 | 28.0 | 26.0 | 27.5 | 28.0 | 32.0 |
| Percentile 25 | 15.5 | 20.0 | 15.0 | 15.0 | 14.0 | 13.0 | 12.0 | 13.0 | 14.0 | 14.0 |
| Percentile 75 | 52.0 | 52.0 | 49.0 | 49.0 | 45.0 | 43.0 | 43.0 | 43.0 | 46.0 | 46.0 |
| Concentration of motile sperm (million/mL) | | | | | | | | | | |
| Mean | 25.2 | 24.8 | 20.6 | 19.9 | 16.8 | 14.6 | 14.6 | 14.6 | 16.6 | 18.4 |
| Standard deviation | 27.5 | 24.7 | 21.8 | 22.9 | 21.1 | 18.5 | 21.5 | 18.6 | 23.1 | 22.1 |
| CI 95%- | 21.5 | 23.0 | 19.1 | 18.4 | 15.3 | 13.2 | 13.7 | 13.2 | 14.9 | 17.9 |
| CI 95%+ | 29.6 | 26.7 | 22.0 | 21.7 | 18.7 | 16.1 | 17.1 | 16.3 | 19.2 | 19.1 |
| Median | 29.6 | 26.7 | 22.0 | 21.7 | 18.7 | 16.1 | 17.1 | 16.3 | 19.2 | 19.1 |
| Percentile 25 | 15.9 | 17.6 | 12.6 | 9.5 | 7.8 | 7.0 | 7.2 | 5.8 | 6.7 | 7.8 |
| Percentile 75 | 45.0 | 40.5 | 36.4 | 35.2 | 32.0 | 28.3 | 28.0 | 22.3 | 23.5 | 24.6 |
| Total number of motile sperm (million/ejaculate) | | | | | | | | | | |
| Mean | 70.3 | 77.8 | 58.6 | 54.9 | 44.8 | 40.5 | 41.0 | 40.7 | 40.3 | 51.3 |
| Standard deviation | 77.1 | 84.7 | 68.1 | 68.3 | 58.4 | 54.4 | 58.4 | 56.2 | 52.4 | 65.7 |
| CI 95%- | 59.5 | 71.7 | 54.0 | 50.2 | 40.4 | 36.4 | 36.4 | 36.3 | 36.0 | 49.7 |
| CI 95%+ | 81.0 | 84.5 | 63.2 | 59.8 | 49.1 | 44.6 | 45.6 | 45.1 | 44.7 | 53.1 |
| Median | 45.0 | 51.1 | 29.7 | 23.7 | 19.8 | 17.2 | 14.8 | 17.1 | 20.1 | 22.6 |
| Percentile 25 | 6.4 | 9.3 | 4.5 | 3.4 | 3.2 | 3.3 | 2.7 | 3.4 | 3.7 | 3.7 |
| Percentile 75 | 121.6 | 120.3 | 94.2 | 88.7 | 68.3 | 57.9 | 53.7 | 56.0 | 58.1 | 78.4 |
| Motility index | | | | | | | | | | |
| Mean | 130.8 | 135.0 | 117.6 | 113.8 | 101.5 | 92.6 | 92.6 | 91.9 | 92.0 | 106.7 |
| Standard deviation | 102.5 | 99.4 | 91.6 | 93.3 | 84.2 | 77.3 | 83.9 | 78.0 | 75.1 | 88.3 |
| CI 95%- | 116.5 | 127.6 | 111.4 | 107.3 | 95.3 | 86.8 | 86.0 | 85.8 | 85.8 | 104.4 |
| CI 95%+ | 145.1 | 142.4 | 123.7 | 120.3 | 107.8 | 98.4 | 99.2 | 97.9 | 98.3 | 108.9 |
| Median | 110 | 116 | 89.5 | 79 | 74 | 69 | 64 | 66.5 | 68 | 76 |
| Percentile 25 | 33.5 | 51.0 | 37.5 | 34.0 | 35.0 | 32.0 | 26.0 | 32.0 | 33.0 | 34.0 |
| Percentile 75 | 210 | 212 | 196 | 190 | 160 | 136 | 132 | 138 | 134 | 172 |
Figure 4. Box plot and linear regression for: a, b concentration of functional sperm; c, d total number of functional sperm; e, f sperm morphology; g, h vitality
The total mean of total number of functional sperm is 29.6±44.3 million/ejaculate (95% CI: 28.4-30.7; median: 8.4). The average annual rate of decrease in the mean total number of functional sperm is 5.2% from 42.2±52.1 million/ejaculate to 22.5±35.3 million/ejaculate. The model: total number of functional sperm = 79.4-3.1 * Year (R² = 0.027; F = 158.0; p = 0.000) with the average annual decrease 3.1 million in the ejaculate (p = 0.000) (Table 3, Figure 4 c, d).

The mean percentage of sperm with normal forms during the study period was 22.1±12.3 (%), (95% CI: 21.7-22.4; median 20), annual decline rate 1.8% from 24.6±14% to 20.7±12%. The model: normal forms = 32.7-0.7 * Year (R² = 0.017; F = 96.0; p = 0.000) (Table 3, Figure 4 e, f).

In the study period, the mean percentage of vitality was 46.7±38.4 (%) (95% CI: 45.7-47.7; median: 35). Annually, the percentage of live sperm decreased from 58±36 (%) to 30±34 (%), the mean rate of decrease being 5.5% per year. The model: percentage of viable sperm = 108.3-3.8 * Year (R² = 0.054; F = 330.5; p = 0.000), the average annual decrease 3.8 (%) (p = 0.000) (Table 3, Figure 4 g, h).

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### Table 3. Results of functionality, viability, and normal forms of sperm, 2012-2020

| Years | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 | 2019 | 2020 | Total |
|-------|------|------|------|------|------|------|------|------|------|-------|
| Abs. no | 200 | 703 | 852 | 794 | 703 | 685 | 630 | 640 | 560 | 5767 |
| Concentration of functional sperm (million/mL) | 15.5 | 15.1 | 12.0 | 11.8 | 9.5 | 8.1 | 8.5 | 8.3 | 9.1 | 10.6 |
| Standard deviation | 18.4 | 18.1 | 15.1 | 15.9 | 14.0 | 12.6 | 13.7 | 13.0 | 14.4 | 15.1 |
| CI 95% | 12.9 | 13.8 | 11.0 | 10.7 | 8.4 | 7.1 | 7.4 | 7.2 | 7.9 | 10.2 |
| CI 95%+ | 18.1 | 16.4 | 13.0 | 13.0 | 10.5 | 9.0 | 9.6 | 9.3 | 10.3 | 11.0 |
| Median | 10.0 | 7.5 | 4.4 | 3.4 | 2.6 | 2.5 | 2.2 | 2.4 | 2.8 | 2.9 |
The model: normal forms = 32.7-0.7 * Year (R² = 0.017; F = 96.0; p = 0.000) (Table 3, Figure 4 e, f).

| Total number of functional sperm (million/ejaculate) | 42.0 | 46.1 | 34.1 | 32.4 | 25.1 | 21.9 | 23.6 | 22.6 | 22.5 | 29.5 |
| Standard deviation | 52.1 | 57.6 | 45.5 | 45.8 | 38.8 | 33.9 | 39.7 | 36.5 | 35.5 | 43.8 |
| CI 95% | 34.7 | 42.1 | 31.0 | 29.2 | 22.2 | 19.4 | 20.5 | 19.8 | 19.5 | 28.4 |
| CI 95%+ | 49.3 | 50.9 | 37.1 | 35.8 | 28.0 | 24.5 | 26.7 | 25.4 | 25.4 | 30.7 |
| Median | 18.8 | 22.2 | 11.3 | 8.8 | 7.3 | 6.4 | 6.1 | 6.7 | 7.5 | 8.4 |
The model: percentage of viable sperm = 108.3-3.8 * Year (R² = 0.054; F = 330.5; p = 0.000), the average annual decrease 3.8 (%) (p = 0.000) (Table 3, Figure 4 g, h).

| Normal forms (sperm morphology %) | 24.6 | 25.2 | 23.1 | 22.8 | 21.6 | 20.6 | 20.2 | 20.3 | 20.7 | 22.0 |
| Standard deviation | 14.0 | 13.0 | 12.4 | 12.2 | 11.6 | 10.8 | 11.8 | 11.2 | 10.8 | 12.0 |
| CI 95% | 22.7 | 24.3 | 22.3 | 21.9 | 20.8 | 19.8 | 19.3 | 19.5 | 19.8 | 21.8 |
| CI 95%+ | 26.6 | 26.3 | 24.0 | 23.6 | 22.5 | 21.6 | 21.2 | 21.3 | 21.7 | 22.4 |
| Median | 23.0 | 26.0 | 22.0 | 20.0 | 19.0 | 19.0 | 19.0 | 19.0 | 19.0 | 20.0 |
The model: percentage of viable sperm = 108.3-3.8 * Year (R² = 0.054; F = 330.5; p = 0.000), the average annual decrease 3.8 (%) (p = 0.000) (Table 3, Figure 4 g, h).

| Vitality (%) | 24.6 | 25.2 | 23.1 | 22.8 | 21.6 | 20.6 | 20.2 | 20.3 | 20.7 | 22.0 |
| Standard deviation | 14.0 | 13.0 | 12.4 | 12.2 | 11.6 | 10.8 | 11.8 | 11.2 | 10.8 | 12.0 |
| CI 95% | 22.7 | 24.3 | 22.3 | 21.9 | 20.8 | 19.8 | 19.3 | 19.5 | 19.8 | 21.8 |
| CI 95%+ | 26.6 | 26.3 | 24.0 | 23.6 | 22.5 | 21.6 | 21.2 | 21.3 | 21.7 | 22.4 |
| Median | 23.0 | 26.0 | 22.0 | 20.0 | 19.0 | 19.0 | 19.0 | 19.0 | 19.0 | 20.0 |
DISCUSSION

Over the years, numerous studies have been published, where semen analysis has been a key tool for assessing the trend in male infertility. The analysis of data from the literature indicates that the quality and quantity of semen are steadily declining, which highlights an alarming phenomenon of declining male fertility. This has been illustrated by several studies in many parts of the world which argue that men’s reproductive health has been declining rapidly in recent years, with some variations in some geographical regions.

A study carried out in Finland from 1998 to 2006 found a decrease in the quality of semen in the general population. Another study conducted in southern Tunisia over a 12-year period on a sample of 2,940 men in infertile relationships also concluded a decline in semen quality. Furthermore, a study conducted in France between 1988 and 2007 at the Reproductive Biology Laboratory of the University Hospital of Marseille, which included the semen analysis of 10,932 male partners of infertile couples, concluded that the entire population showed trends in decrease in sperm concentration (1.5% per year), total sperm count (1.6% per year), total motility (0.4% per year), rapid motility (5.5% per year) and normal morphology (2.2% per year). According to a study conducted by our team in 2018, the abnormal quality of semen was found in 59.8% of male partners of couples facing infertility, the incidence increases from 50% in 2012 to 66.3% in 2018. A study carried out by Rolland et al. over a 17-year period in France, among a sample of 26,609 partners of totally infertile women undergoing Assisted Reproductive Technology (ART) procedures demonstrated a continuous decrease in semen concentration of 1.9% per year and a significant decrease in the percentage with morphologically normal forms.

Our results of the analysis of sperm parameters in the male population (n = 5767) of the Republic of Moldova who face infertility in couples are the same to other specialized studies and show that the quantity and quality of semen decline significantly in the study period 2012-2020. Decline trends were significant in all semen parameters: semen volume, sperm concentration, total sperm number, progressive motility, concentration of motile sperm, total number of motile sperm, concentration of functional sperm, total number of functional sperm, normal forms, and vitality.

The topic of declining male fertility remains controversial, the potential etiologic factors leading to decreased sperm quality are still not fully elucidated. Multiple factors have been shown to have correlative associations in these idiopathic sperm abnormalities such as oxidative stress, unknown genetic and epigenetic abnormalities and endocrine disruption through environmental pollution.

CONCLUSIONS

Our results indicate that the quality and quantity of semen are steadily declining in the population of men consulted for couple infertility in the Republic of Moldova from 2012 to 2020. The analysis of the regional tendencies of the semen parameters are necessary and can be considered an indirect factor in evaluating the status in male fertility. In the future, it is necessary to carry out various research studies to find out the major causes that lead to the decrease of quality and quantity of semen. This is an indication necessitating to focus on the management and preventive program for male infertility.

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- Conceptualization, S.R. and M.S.; methodology, S.R.; software, V.M.; validation, S.R.; formal analysis, S.R.; investigation, V.M.; resources, S.R. and M.S.; writing—original draft preparation, S.R.; writing—review and editing, S.R., M.S., V.M.; visualization, S.R. and M.S.; supervision, V.M.; project administration. All the authors have read and agreed with the final version of the article.

Compliance with Ethics Requirements:
- “The authors declare no conflict of interest regarding this article”
- “The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study”
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- None

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