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# Comparison of Sperm Deformity Indexes between Patients who have and have not Experienced COVID-19

COVİD-19 Geçiren ve Geçirmeyen Hastaların Sperm Deformite İndeks Değerlerinin Karşılaştırılması

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***ABSTRACT***

***Objective:*** *Ever since its identification in December 2019, the novel coronavirus SARS-CoV-2 has rapidly disseminated worldwide, giving rise to the COVID-19 (coronavirus disease-19) pandemic. The male reproductive system is susceptible to the effects of COVID-19, leading to potential alterations in semen parameters. In this study, we conducted a comparison between patients who have previously contracted COVID-19 and those who have not, specifically focusing on the sperm deformity index (SDI) as a parameter for assessing sperm morphology.*

***Material and Method:*** *134 patients over the age of 18 who applied to Hospital Andrology Laboratory between 29 November 2022 and 29 December 2022 were included in the study. Of these, 44 were patients who have had Covid-19, and 90 were patients who have not had COVID-19. These patients were compared in terms of SDI parameter and other semen parameters (ejaculate volume, sperm concentration, total sperm count, total motility, progressive motility and percentage of normal morphology sperm). The calculation of the SDI was performed by dividing the total number of observed deformities by the total count of sperm.*

***Results:*** *A noteworthy distinction was observed in the SDI values between the two groups, with a statistically significant difference (p<0.001). There were no statistically significant differences found in terms of other semen parameters between the groups (p>0.05).*

***Conclusion:*** *SDI, one of the semen parameters, was found to be significantly different in both groups. Further comprehensive studies are warranted to thoroughly investigate the impact of COVID-19 on semen parameters.*

***ÖZET***

***Amaç:*** *Yeni koronavirüs SARS-CoV-2, Aralık 2019'da tanımlanmasından bu yana hızla dünya çapında yayılmış ve COVID-19 (koronavirüs hastalığı-19) salgınına yol açmıştır. Erkek üreme sistemi, COVİD-19'un etkilerine karşı hassastır ve bu durum semen parametrelerinde potansiyel değişikliklere yol açabilmektedir. Bu çalışmada, özellikle sperm morfolojisini değerlendirmeye yönelik bir parametre olan sperm deformite indeksi'ne (SDI) odaklanarak, daha önce COVİD-19'a geçirmiş ve geçirmemiş hastalar arasında bir karşılaştırma yaptık.*

***Gereç ve Yöntem:*** *Çalışmaya 29 Kasım 2022 ile 29 Aralık 2022 tarihleri arasında Adana Şehir Hastanesi Üremeye Yardımcı Tedavi Merkezi'ne başvuran 18 yaş üstü 134 hasta dahil edildi. Bunlardan 44'ü COVID-19 geçirip iyileşen, 90'ı ise COVID-19 geçirmeyen hastalardı. Bu hastalar SDI parametresi ve diğer semen parametreleri (ejakülat hacmi, sperm konsantrasyonu, toplam sperm sayısı, toplam hareketlilik, ilerleyici hareketlilik ve normal morfolojiye sahip sperm yüzdesi) açısından karşılaştırıldı. SDI hesaplanması, gözlenen toplam deformite sayısının toplam sperm sayısına bölünmesiyle yapıldı.*

***Bulgular:*** *Her iki grup arasında SDI değerlerinde istatistiksel olarak anlamlı farkla dikkat çekici bir farklılık gözlendi (p<0,001). Gruplar arasında diğer semen parametreleri açısından istatistiksel olarak anlamlı farklılık saptanmadı (p>0,05).*

***Sonuç:*** *Semen parametrelerinden SDI'nın her iki grupta da anlamlı olarak farklı olduğu görüldü. COVID-19'un semen parametreleri üzerindeki etkisini kapsamlı bir şekilde araştırmak için daha kapsamlı çalışmalara ihtiyaç vardır.*

***Keywords:***
*Sperm deformity index*
*COVID-19*
*Semen parameters*

***Anahtar Kelimeler:***
*Sperm deformitesi indeksi*
*COVİD-19*
*Semen parametreleri*

## INTRODUCTION

In 2019, COVID-19, which emerged in the city of Wuhan, China, caused significant changes in various fields such as education, health, and economy, and it has affected the whole world. In the context of combating COVID-19, vaccine studies have been conducted worldwide, and research on the effects of the virus on human systems has also been accelerated (1). Currently, the coronavirus family, consisting of 30 members, represents the largest group of positive-sense single-stranded RNA viruses. Angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) receptors play an important role in the transmission of SARS-CoV-2. These receptors are co-expressed in the testis and male genital tract. This observation strongly suggests the high probability of the virus specifically targeting the

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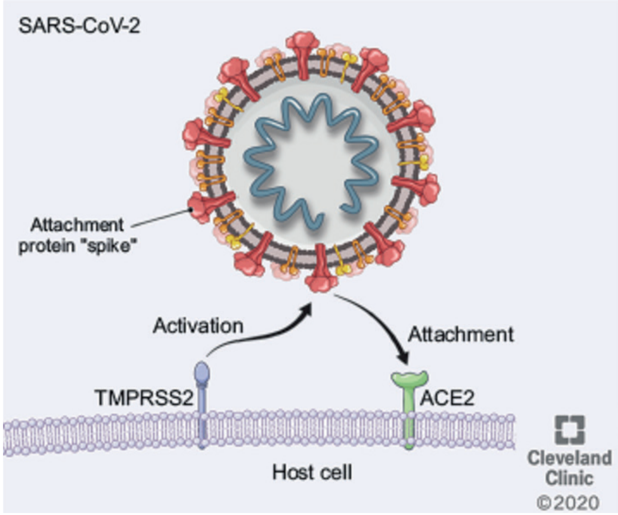


**Figure 1:** Cellular entry mechanism. Severe acute respiratory syndrome-coronaviruse-2 (SARS-CoV-2) infection is mediated by the binding between viral spike proteins and angiotensin I converting enzyme 2 (ACE2) cellular receptor, and the further proteolytic cleavage and activation of spike proteins by the transmembrane protease serine 2 (TMPRSS2) (5).

testis and male genital system during infection (Figure 1). Numerous studies have reported that more than 25 different viruses can enter human semen and potentially have harmful effects on spermatozoa and male fertility. Examples of such viruses include HSV (Herpes Simplex Virus) and HIV (Human Immunodeficiency Virus). The question of whether SARS-CoV-2 has similar effects in males continues to be an important research question that has not been definitively answered in preliminary studies (2-5). Semen analysis is considered a fundamental component of male fertility assessment, and guidelines established by the World Health Organization (WHO) form the basis for standardizing procedures and establishing global reference values. Routine evaluation of male fertility typically includes assessing sperm count, motility, and morphology in ejaculated semen. The incidence of morphological abnormalities in spermatozoa has been comprehensively described using indices such as the sperm deformity index (SDI), teratozoospermia index (TZI), or multiple anomaly index (MAI). These indices provide valuable measurements for evaluating the structural integrity and abnormalities of sperm cells. The SDI is calculated by dividing the total number of morphological anomalies in sperms by the total number of sperm analyzed, including both normal and abnormal sperm (6-8). The SDI represents a new approach to expressing sperm morphological parameters. Its absolute value represents the balance between the prevalence of spermatozoa with multiple structural deformities and the proportion of spermatozoa exhibiting normal morphology in a specific semen sample. Compared to both the percentage of normal sperm morphology and the multiple anomaly index, the SDI is a more reliable predictor of the outcome of in vitro oocyte fertilization. This emphasizes the importance of SDI as a valuable parameter for evaluating the fertilization potential of spermatozoa in assisted reproductive techniques. Studies have shown that SDI is associated with the fertilization rate in traditional IVF procedures (9,10). In this study, we investigated a previously underexplored topic by comparing the sperm deformity indices of patients who have and have not experienced COVID-19.

## MATERIAL AND METHODS

Before starting our study, we obtained the necessary permissions from the Adana City Training and Research Hospital Ethics Committee (Meeting Number: 125, Decision Number: 2528). Our retrospective study included male patients who applied to the Adana City Training and Research Hospital Assisted Reproduction Unit for sperm analysis between November 29, 2022, and December 29, 2022. Patients under 18 years of age and those who could not provide a sperm sample through masturbation were excluded from the study. Information about whether the patients have previously had COVID-19 was obtained from the medical history form (patient files), and the patients were grouped accordingly. According to this grouping, 44 patients have previously had COVID-19, while 90 patients have not. A total of 134 patients were included in this study for analysis and review. Information on how long ago the patients have COVID-19 has obtained from the patient files. This period varied between 23±11 months. Data on ejaculate volume, sperm concentration, total sperm count, total motility, progressive motility, percentage of sperm with normal morphology, and SDI values were collected from the semen analysis report forms of the included patients. These parameters were evaluated to assess the characteristics of the semen samples. The two groups were compared based on the above-mentioned parameters according to the World Health Organization's 2021 Semen Analysis Criteria. These criteria include a minimum ejaculate volume of ≥ 1.4 ml, sperm concentration of ≥ 16 million/ml, total motility of ≥ 42%, progressive motility of ≥ 30%, and percentage of sperm with normal morphology of ≥ 4%. By applying these criteria, a comparative analysis was conducted to evaluate whether there was any difference between the two groups in terms of semen characteristics. SDI values were obtained by dividing the total number of observed deformities in a SperMac-stained slide at 1000x (100 x 10) magnification by the total number of spermatozoa. This calculation provided a quantitative measure of the proportion of deformities in the analyzed sperm population. The deformities shown in Table 1 were used as the basis for morphology assessment (7). Statistical analyses were performed using IBM SPSS Statistics 25 software package. After conducting a normality analysis of the data, various statistical techniques were used to interpret the data. The normal distribution of the data was measured using normality tests (Kolmogorov-Smirnov test, Shapiro-Wilk test). Additionally, measures of skewness and kurtosis, arithmetic mean, mode, median values, and histograms were considered. This included creating frequency tables to summarize categorical variables, calculating descriptive statistics to describe the central tendency and variability of continuous variables, and using parametric (Independent Samples t-test) and non-parametric tests (Mann-Whitney U test) depending on the nature of the variables. In our study, ejaculate volume,

**Table 1:** Classification of sperm morphology (7).

| Location | Normal (ideal/typical) appearance | Abnormal |
|---|---|---|
| **Head** | The head should be smooth, regularly contoured and generally oval in shape. There should be a well-defined acrosomal region comprising 40–70% of the head area (96). The acrosomal region should contain no large vacuoles, and not more than two small vacuoles, which should not occupy more than one fifth of the sperm head. The post-acrosomal region should not contain any vacuoles. | • acrosome less than 40% or larger than 70% of a normal head area, or<br>• length-to-width ratio less than 1.5 (round) or larger than 2 (elongated), or<br>• shape: pyriform (pear shaped), amorphous, asymmetrical, or non-oval shape in the apical part, or<br>• vacuoles constitute more than one fifth of the head area or located in the post-acrosomal area, or<br>• double heads, or<br>• any combinations |
| **Midpiece** | The midpiece should be slender, regular and about the same length as the sperm head. The major axis of the midpiece should be aligned with | • irregular shape, or<br>• thin or thick, or<br>• asymmetrical or angled insertion at head, or<br>• sharply bent, or<br>• any combinations |
| **Tail** | The principal piece should have a uniform calibre along its length, be thinner than the midpiece and be approximately 45 µm long (about 10 times the head length). It may be looped back on itself, provided there is no sharp angulation indicative of a broken flagellum. | • sharply angulated bends, or<br>• smooth hairpin bends, or<br>• coiled, or<br>• short (broken), or<br>• irregular width, or<br>• multiple tails, or<br>• any combinations |
| **Cytoplasmic residue** | Cytoplasmic droplets (less than one third of a normal sperm head size) are normal. | • residual cytoplasm is considered an anomaly only when it exceeds one third of normal sperm head size |

sperm concentration, total motility, progressive motility, percentage of sperm with normal morphology, and SDI values were expressed as continuous variables. A p-value < 0.05 was considered statistically significant.

**RESULTS**

In our study, we found no statistically significant difference ($p>0.05$) in terms of ejaculate volume, sperm concentration, total sperm count, total motility, progressive motility, and percentage of sperm with normal morphology between the group that have previously contracted COVID-19 and the group that have not, as indicated in Table 2. However, as shown in Table 2, we observed a significant difference in SDI values between the two groups ($p < 0.001$). This indicates that while there were no significant differences in traditional semen parameters, the SDI values reflected significant differences between the two groups.

**DISCUSSION**

In our study, no significant difference was found in terms of ejaculate volume between those who have and have not contracted COVID-19. However, Kurashova et al. (11) reported a significant difference in ejaculate volume between COVID-19 positive and negative groups. The difference between our study and Kurashova et al.'s could be explained by their smaller control group of 20 individuals. In a study by Rafiee et al. (12), significant differences were found in semen volume between pre-

**Table 2:** Analysis and statistical evaluation of sperm parameters and SDI values.

| Semen Parameters | Group of individuals who have had COVID-19. (Mean-SD) (n=44) | Group that have not had COVID-19 (Mean-SD) (n=90) | p value |
|---|---|---|---|
| **Volume (mL)** | 3.41-1.42 | 3.45–1.59 | 0.838 |
| **Concentration (Million/mL)** | 54.24-36.61 | 50.72-37.20 | 0.516 |
| **Total Sperm Count (Million)** | 179.02-134.42 | 165.1-137.02 | 0.436 |
| **Total Motility (%)** | 54.15-15.15 | 56.01-18.00 | 0.502 |
| **Progressive Motility(%)** | 44.93-16.17 | 46.40-20.11 | 0.65 |
| **Morphology (Normal)** | 2.36-1.95 | 2.22-1.35 | 0.694 |
| **Sperm Deformity Index** | 1.75-0.44 | 1.42-0.28 | 0.00 |

*a: The data did not follow a normal distribution. When comparing the measurement values of two independent groups with non-normally distributed data, the "Mann-Whitney U" test was used. A p-value less than 0.05 was considered a significant difference when comparing the independent variables between groups.*

*b: The data is normally distributed. The independent samples t-test was used to compare the independent variables in the samples. A p-value less than 0.05 was considered statistically significant.*

and post-disease COVID-19 positive patients. However, in their study, semen analysis was performed within 2 months after COVID-19 infection, whereas in our study, the patients have contracted COVID-19 a longer time ago. This longer duration might have allowed for the semen volume to recover. While COVID-19 might have an acute effect on semen volume reduction, the recovery process might not have a long-term impact.

In our study, no statistically significant difference was observed in sperm concentration between patients who have and have not contracted COVID-19. Li et al. (13) reported a significant decrease in sperm concentration when comparing COVID-19 positive patients with the control group. However, the number of cases in their study was not as high as in ours, and the semen samples in their study were obtained from autopsies. Guo et al. (14) investigated the impact of COVID-19 on semen parameters in men who have previously contracted and recovered from the disease. When compared with the control group, they noted a significant decrease in sperm concentration in patients who have experienced COVID-19. However, it was noteworthy that in some recovered patients, the sperm concentration in the second sample was significantly higher than in the first. This suggests that there might be temporary differences in sperm parameters among individuals who have had and recovered from COVID-19. From this, it is possible to conclude that COVID-19 might have an acute effect on reducing sperm concentration. Gharagozloo et al. (15) also mentioned the potential for recovery in sperm parameters after COVID-19 infection. The fact that the patients in our study have contracted COVID-19 a long time ago might have contributed to the lack of significant difference in sperm concentration compared to the group that did not have COVID-19. In our study, no significant difference was found in terms of total sperm count between the groups that have and have not experienced COVID-19. Guo et al. (16) reported that the total sperm count returned to normal levels within 32 days after diagnosis. Indeed, the dynamic nature of the recovery process and sperm parameters might have contributed to the lack of significant difference in total sperm count between the groups. Piroozmanesh et al. (17) found that the total sperm count was significantly lower in individuals who have experienced COVID-19 compared to those who have not. This could be attributed to the acute effect, as their study was conducted between COVID-19 positive (throat swab) and negative patients. However, our study included patients who have experienced and recovered from COVID-19. Koç et al. (18) demonstrated that COVID-19 significantly reduced both the total and progressive motility of sperm in individuals who contracted the infection. However, the limited number of patients and the study being conducted in Ankara, which may have a different population density and stress level compared to Adana, could explain the differences between their study and ours. Additionally, differences in the timing of semen analysis before and after COVID-19 infection could also affect the strength of their study. Ma et al. (19) reported in a limited study that semen parameters were normal in 8 out of 12 COVID-19 patients. Our study, especially in terms of sperm concentration, total motility, and progressive motility, is consistent with this study. In a study conducted by Temiz et al. (20), similar findings to our study were obtained regarding sperm concentration, total motility, and progressive motility in COVID-19 patients. Furthermore, Temiz et al. observed that sperm morphology was significantly lower in COVID-19 patients compared to the control group, highlighting another potential impact of COVID-19 on male fertility. The relationship with acute fever during the illness period is an interesting aspect that may require further research. However, the limited number of participants in the study and the presence of fever in the patients during their study could explain the differences between their study and ours. Our study is a retrospective study, and information about whether the patients who have recovered from COVID-19 had a fever during their illness could not be obtained. Gacci et al. (21) suggested in their study that the recovery of semen parameters in patients who have recovered from COVID-19 might be related to the severity of the disease. We could not find any studies in the literature that investigated the sperm deformity index value in COVID-19 patients, making our study unique in this regard. We found a significant difference in sperm deformity index values between patients who have and have not experienced COVID-19 ($p < 0.001$). An important finding of our study is that COVID-19 does not affect the normal morphology of sperm but increases the rate of abnormal morphology. This could be explained by the fact that COVID-19 does not cause a deterioration in normal morphology but increases the number of deformities in abnormal sperm. Aziz et al. (23) measured the amount of reactive oxygen species (ROS) in infertile patients and found that infertile patients with high ROS levels had lower SDI values. In our study, SARS-CoV-2 might have led to a significant decrease in SDI values in patients who have recovered from COVID-19 by increasing the amount of reactive oxygen species. Turner et al. (24) stated that ACE2 receptors in the testes have functions related to immunity, inflammation, and many other functions. SARS-CoV-2 might increase inflammation by binding to ACE2 receptors and increasing their numbers, potentially leading to sperm deformities.

There are some limitations to our study. The fact that information about whether patients have contracted COVID-19 was obtained from patient records relatively weakened the strength of our study. Additionally, the varying duration from COVID-19 infection to recovery among patients might have affected the semen parameters differently. This is another factor that restricted our study.

## CONCLUSION

SARS-CoV-2 can affect multiple systems in the body, including the male reproductive system. To deepen our understanding of the effects of COVID-19 on semen parameters and male reproductive health, more comprehensive studies are needed.

**Conflict of Interest:** No conflict of interest was declared by the authors.
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