Andrology in the Era of COVID

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Abstract

Objective: The last year has represented a challenging time for andrology laboratories due to the COVID-19 pandemic. Public health guidelines and government regulations intended to reduce the spread of COVID-19 caused a shift in patient practices across healthcare. They impacted the infertility laboratory by changing where and how semen samples are collected. The current study compared the quality of semen being collected for routine semen analysis (SA), and therapeutic IUI cycles, comparing the first year of the pandemic with the previous twelve-month period in a regional fertility center.

Materials and Methods: Institutional rules, public health guidelines, and government regulations required the majority (> 98%) of semen samples collected at a regional fertility center to be collected off-site starting March 18th, 2020. The center serves a catchment basin of approximately 300 miles in diameter, meaning some patients might travel for 1-2 hrs to deliver samples collected at home or have to make other arrangements for a collection location closer to the laboratory. To determine the impact of the delay in processing and other factors, such as stress, on semen quality, the center conducted a study comparing the standard semen parameters in two arms. The COVID-19 arm were patients seen from March 18th, 2020 to March 17th, 2021, and they were compared to the Pre-COVID-19 arm, who were seen from March 18th, 2019 to March 17th, 2020. Semen Analysis parameters analyzed for all samples included volume, concentration/mL, motility, morphology, total concentration, and total motile concentration. IUI samples were also analyzed for post-wash total concentration and total motile concentration. Resulting Data were compared using student's T-test.

Results: A total of 423 SA and 378 IUI records were compared. As expected, off-site collection significantly increased the time from collection to completion of the procedure ($P < 0.001$). Numerous semen parameters of the standard semen analysis were 10-20% lower in the pandemic year when collecting off-site than the same parameter in the 12 months before the pandemic when on-site collection was used. Focusing on IUI data, the average processing time from collection to finish increased 26 to 48 mins ($p < 0.006$). Average Total motile sperm has decreased from 49 to 42 million (14%; $P < 0.05$) between groups. Pregnancy data is pending.

Conclusion: The pandemic has presented challenges to all reproductive centers. The challenges appear to have had a negative effect on the overall semen quality of patients. While it is unclear how much of an impact delays in processing have, the data is highly suggestive they impact patient treatment.

Impact Statement: While delivery of reproductive health care continued during the pandemic, changes in public health guidelines and governmental regulations have impacted patient care, thereby causing a reduction in semen quality. Public health officials and practices may need to reevaluate how semen samples are collected for diagnostics and treatment to mitigate this reduction in quality while maintaining the overall health of patients and staff.

Introduction

Pandemics have happened repeatedly throughout the centuries, the most famous being the bubonic plague pandemic, often called the Black Death, which raged across Eurasia, Europe, and northern Africa from 1346 to 1353. An estimated 75 to 200 million people died during the Black Death. Unfortunately, in modern times societies are not free of pandemics. There were five pandemics in the 20th and 21st centuries (Table 1), the most famous of which was the 1918 Spanish Flu Pandemic. The Spanish Flu Pandemic was caused by the H1N1 Influenza virus and killed 50 million people.

Health authorities became aware of a cluster of patients with pneumonia of unknown origins on December 31st, 2019, in Wuhan, China. Seven days later, on January 7th, the cause was identified as a coronavirus temporarily named 2019-nCoV. By January 30th, the World Health Organization (WHO) declared the outbreak a public health emergency of international concern (PHEIC). At that time, there were 98 cases and no deaths in 18 countries outside China. In February 2020, 2019-nCoV was officially named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), also known as COVID-19. By March 11th, 2020, the WHO declared COVID-19 a pandemic. By then, it had already caused 118,000 confirmed cases in 114 countries and 4291 deaths. COVID-19 is caused by one of seven coronaviruses known to infect humans. Four cause mild respiratory symptoms are considered some of the viruses that cause the common cold. However, SARS-CoV, MERS-CoV, and SARS-CoV-2 cause severe respiratory symptoms with significant morbidity and mortality for patients (Table 2).

The COVID-19 virus is easily transmissible and moderately fatal, allowing the virus to spread quickly from person to person. World wide there have been 219 million cases as of October 7th, 2021, and 4.51 million deaths. The symptoms of COVID-19 are highly variable but commonly include fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, and diarrhea. A significant portion of patients who contract COVID-19 may not show any symptomology at all, while others may deteriorate quickly. It is also common for patients with COVID-19 to suffer symptoms for weeks or months, even after recovery, and have been dubbed long haulers.

The first case of COVID-19 in the U.S. was identified in Washington state on January 19th, 2020. As of October 7th, 2021 there have been 44.1 million cases of COVID-19 in the U.S. and 709,000 deaths. In Texas, there have been 4.4 million cases and 67,056 deaths attributed to COVID-19. In Lubbock County, Texas, there have been 64,369 cases of COVID-19 and 857 deaths.

The first case of COVID-19 was reported in Lubbock, Texas, on March 17th, 2019 immediately after Texas Tech University System began a rapid depopulation of students, staff, and faculty from their facilities. At Texas Tech University Health Sciences Center, all non-essential surgeries were stopped, including surgeries associated with infertility treatments (Figure 1). The collection room for male patients to collect semen samples at the infertility laboratory was closed. No patients were allowed to receive semen analysis or other assisted reproductive technology (ART) procedures. Laboratory procedures were allowed to resume by May 1st, 2020, but only with at-home collection of semen samples. While students were allowed to return to campus on August 1st, 2020, the lab was not permitted to resume on-site collection on a very limited basis until March 15th, 2021, almost a year after in-laboratory collections were stopped.

History of Pandemics since 1918

20th Century

- 1918 – Spanish Flu
  - H1N1 Influenza Virus
  - 50 Million Deaths Worldwide
- 1957 – Asian Flu
  - H2N2 Influenza Virus
  - 1.5 Million Deaths Worldwide
- 1968 – Hong Kong Flu
  - H3N2 Influenza Virus
  - 1 Million Deaths Worldwide

21st Century

- 2009 – Swine Flu
  - H1N1 Influenza Virus
  - 284,000 Deaths Worldwide
- 2020 – COVID-19
  - Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
  - 4.51 Million Deaths Worldwide as of October 7th 2021

Table 1: The pandemics of the 20th and 21st centuries, note that until the 2020 COVID-19 pandemic the last four pandemics were caused by influenza viruses.

Coronaviruses that Infect Humans

Mild Respiratory Symptoms

- HcoV-229E – 1966
  - Genera-Lineage – α
  - Aminopeptidase N (CD13)
  - Bats → Camelids → Human
- HcoV-OC43 – 1967
  - Genera-Lineage – β-A
  - 9-Oacetylated sialic acid (SA)
  - Rodents → Cattle → Humans
- HcoV-NL63 – 2004
  - Genera-Lineage – α
  - ACE2
  - Bats → Unknown → Humans
- HcoV-NL63 – 2004
  - Genera-Lineage – α
  - 9-Oacetylated sialic acid (SA)
  - Rodents → Unknown → Humans

Severe Respiratory Symptoms

- SARS-CoV – 2003
  - Genera-Lineage – β-B
  - ACE2
  - Bats → Masked Palm Civets → Human
- MERS-CoV – 2012
  - Genera-Lineage – β-C
  - DPP4
  - Bats → Dromedary Camels → Human
- SARS-CoV-2 – 2019
  - Genera-Lineage – β-B
  - ACE2
  - Bats → Pangolin? → Human

Table 2: There are seven coronaviruses that infect humans. Four cause mild respiratory symptoms while three cause severe acute respiratory symptoms. Outlined above are the names, genetic lineage, target receptor and zoonotic vectors of coronaviruses known to infect humans.

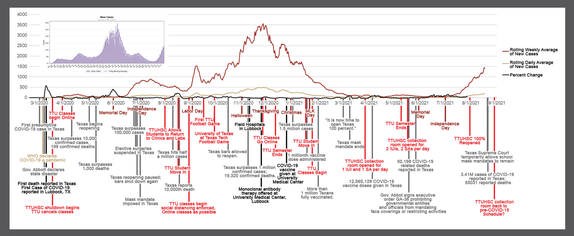

Figure 1: A timeline of significant COVID-19 related events compared to the weekly average infection rate curves for Lubbock County. Inset in the figure is the CDC weekly average infection rate curve for the US, notice that Lubbock County's curve closely follows the national curve though with a few unique disturbances. Note that this graph is only through August 15th, 2021.

	2019	2020	% change	P Value
Collection Time to Processing Completion	27.4	50.6	84.7%	< 0.001
Number of IUI's (n)	237	194	-17.60%	

Figure 2: Time to collection increased by 84.7% with the implementation of at-home semen collection for patients seeking infertility evaluation and treatment, including intrauterine insemination patients.

	2019	2020	% change	P Value
Number of IUI's (n)	237	194	-17.60%	
Motility	47.4	41.6	-12.2%	0.068
Total Count	262.4	217.9	-17.0%	0.071
Total Motile	150	115.5	-23.0%	0.054
Post-Wash Motility	54.8	49.8	-9.1%	0.072
Post-Wash Total Count	179.3	173.8	-3.1%	0.671
Post-Wash Total Motile	107.2	100.2	-6.5%	0.112
Post-Processing Recovery Rate	71.5%	86.8%	21.4%	< 0.01

Figure 4: There was a numerical difference in average motility, total count and total motile count pre- and post-wash in patients seeking treatment in 2019 versus 2020. It is well known that motility and total motile count are impacted by time from collection to processing.

	2019	2020	% change	P Value
Number of IUI's (n)	237	194	-17.60%	
Volume	2.8	2.8	0.0%	0.970
Progression	86	81.6	-5.1%	0.621
Concentration	86.5	84.4	-2.4%	0.874
Post-Wash Volume	0.5	0.5	0.0%	0.999
Post-Wash Progression	95.8	90.2	-5.8%	0.098
Post-Wash Concentration	362.9	357.7	-1.4%	0.743

Figure 3: As expected, semen parameters that are not affected by time, such as concentration, volume or progression were not different in patients seeking treatment in 2019 or 2020

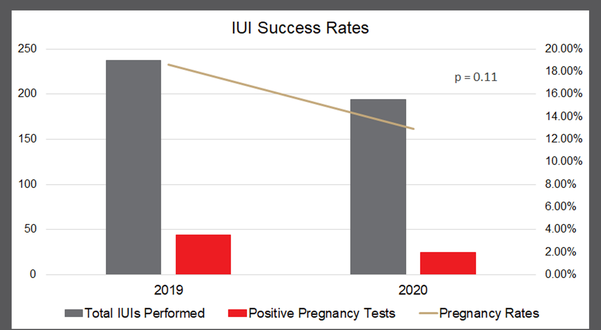

Figure 5: While not statistically significant there is a numerical difference of 28.5% between patients who sought IUI in 2019 and 2020, this change is likely caused to the extended time between collection and processing. The pregnancy rate dropped from 18.6% in 2019 to 12.9% in 2020, historically in this practice the IUI pregnancy rate is 16-18%.

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Introduction Cont.

It is well known that as the time between semen collection and processing grows longer, semen parameters, such as motility and forward progression, will decline. Therefore, a semen sample should be processed within one hour of collection to preserve the sample's quality under standard procedures. However, during the COVID-19 pandemic, infertility clinics were forced to suspend operations or allow patients to collect at home, causing the time between collection and processing to increase. The present study aims to examine the effect of this increased time to processing on patients seeking IUI as treatment for infertility in a regional fertility center.

Materials and Methods

IRB approved Retrospective Chart Review

- Inclusion criteria
  - IUI procedure performed at Texas Tech University Health Sciences Center in 2019 and 2020
- Exclusion criteria
  - All other ART procedures
  - IUI procedures performed in other years
- Statistical Analysis
  - student's t test
  - Chi Square

Treatment Arms

2019 – 3/2019-3/2020
- Semen Collection at the Lab
- 237 IUIs
  - Data Collected
    - Semen Parameters
    - Time to Processing
    - IUI Outcome

2020 – 3/2020-3/2021
- Semen Collection at Home
- 194 IUIs
  - Data Collected
    - Semen Parameters
    - Time to Processing
    - IUI Outcome

Results

1. Time to processing was significantly longer with at home collection P>0.001 (Figure 2)
2. All semen parameters were numerically decreased (Figure 3 & 4) Semen parameters that are not affected by time to processing such as pre- and post-wash volume, pre- and post-wash concentration were not different regardless of collection location (Figure 3)
3. While not significant due to insufficient numbers, all parameters that are associated with fertilizing ability of sperm were approaching significance (Figure 4)
4. Unexpectedly, the post wash recover improved by 21% from 2019 to 2020 (P>0.001, Figure 4), this is possibly due to a change in personnel or increased time for the sample to liquify before processing.
5. While not statistically significant, there was a numerical difference in the number of IUIs performed between 2019 and 2020 (Figure 5)
6. There was a numerical difference in the pregnancy rate from 2019 to 2020. In 2020 the pregnancy rate dropped 28.5% to 12.9%, in 2019 the pregnancy rate was 18.6% (P>0.11, Figure 5). The historic pregnancy rate at this practice is 16-18%

Conclusions

- At home collection increases time from collection to processing
  - All semen parameters numerically lower in patients collecting at home
  - There was evidence of increased sperm damage in samples collected at home
- Pregnancy rate numerically lower
  - Fewer patients – potentially due to patients choosing to not seek treatment during the uncertainty of the COVID-19 pandemic.
  - Historic pregnancy rate is consistent year to year

Conflict-of-Interest

LP and SP wish to disclose a conflict-ofinterest with Reproductive Solutions, they are both stockholders and scientific advisors to the company. A conflict-of-interest management plan is filed with and monitored by the TTUHSC Conflict of Interest in Research Committee (COIRC) and the TTUHSC Research Integrity Office (RIO).