



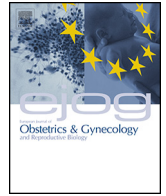
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Communication with fertility patients during the COVID-19 pandemic- let's talk about it

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ABSTRACT

Objective: To assess the impact of the COVID-19 pandemic on the activity of a tertiary fertility service and compare telemedicine and face-to-face meetings during this time.

Methods: This was a retrospective cohort study conducted in a university affiliated tertiary medical center. Included were patients scheduled for an appointment in the in-vitro fertilization (IVF) unit between March 18th and April 15th. A comparison was made between patients who chose telemedicine as opposed to face-to-face meetings. Additionally, the population of patients who chose to cancel their appointment was characterized. IVF cycle outcomes were additionally compared between the groups. **Results:** Overall, 90 IVF clinic appointments were scheduled during the study period. Thirty-four (37.8 %) patients chose to arrive to the clinic in spite of the COVID 19 pandemic and partial quarantine, 27 (30.0 %) patients chose to avoid in person meeting and scheduled a telemedicine appointment and 29 (32.2 %) patients cancelled their appointment. On comparison between patients who chose telemedicine vs. face-to-face meeting, the telemedicine group had lower prevalence of primary infertility (20.0 % vs. 47.1 %, $p = 0.037$) and higher rates of preimplantation genetic testing indication for in-vitro fertilization (48.2 % vs. 20.6 %, $p = 0.026$). Rate of a first-ever clinic visit was higher in patients that arrived for a face-to-face meeting, as compared to telemedicine encounter (55.9 % vs. 28.0 %, respectively; $p = 0.036$). Patients that opted to avoid attending the clinic or meeting via telemedicine had higher rates of medical comorbidities compared to patients who chose to attend their appointment (51.7 % vs. 29.5 %, $p = 0.016$). Rate of appointments that led to fresh or frozen-thawed embryo transfer and these transfers' outcomes (clinical pregnancy rate) were similar in the telemedicine and face-to-face meeting groups (72.2 % vs. 88.0 % and 30.8 % vs. 31.8 %, $p = 0.73$ and $p = 1.00$; respectively).

Conclusion: Telemedicine is a valuable tool for delivering fertility care during the COVID-19 pandemic. There is need to determine which patients will benefit most from this modality.

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Introduction

Countries all over the world are currently coping with an unprecedented outbreak of the novel coronavirus (COVID-19). Since its declaration by the World Health Organization (WHO) as a pandemic on March 11th, 2020 it has been spreading at an alarming rate raising need for swift action in the attempt of lowering infection rates.

Medical societies have taken the initiative and have published guidelines aiming to alleviate the burden from healthcare systems

worldwide. The modus operandi of these recommendations consists of postponing elective cases and limiting any non-urgent treatments. The American Society of Reproductive Medicine (ASRM) has joined this effort and on March 17th published recommendations calling for an immediate suspension of new treatment cycles aimed at achieving pregnancy. Furthermore, embryo transfers, elective surgeries and invasive diagnostic procedures were also mentioned as procedures which should be avoided at this time [1]. Currently, data regarding the effect of COVID-19 during pregnancy is equivocal with certain studies presenting no association between the two [2,3] while others describe increased risk of maternal and fetal complications [4,5].

Though not considered by the society as lifesaving, fertility treatments have unique characteristics which call for special consideration. For women with increased age and low ovarian reserve time is precious and the prospect of postponing treatment

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for an indefinite period of time may be detrimental. Moreover, almost in all cases of infertility, couples seeking fertility treatments are often under immense psychological and emotional stress with a substantial impact on quality of life [6]. These have encouraged fertility units worldwide to search for ways of continuing their service during these trying times.

On March 15th our in-vitro fertilization (IVF) unit cancelled all new cycles, however continued treating women who were currently in the process of controlled ovarian stimulation (COS) or frozen-thawed embryo transfer (FET) cycle. On the same day, couples were contacted by phone and offered to convert their upcoming visit to a telephone meeting. All surgical procedures were concluded by March 29th after which no elective procedures were performed.

In recent years telemedicine has shown great promise in its ability to substitute face-to-face encounters with similar clinical results [7]. The Covid-19 pandemic has encouraged healthcare providers to shift towards use of telemedicine at a rapid pace leading to questions regarding the suitability of this modality for treatment of patients suffering infertility.

The aim of this study was to assess the impact of the COVID-19 pandemic on our IVF services activity. In order to better understand the needs of our patients in this challenging period, we also aimed to compare the characteristics of couples who agreed to telemedicine encounter to those who chose a face-to-face meeting.

Methods

We conducted a retrospective cohort study at a single tertiary university teaching hospital. Included were patients scheduled for an appointment in the IVF unit between March 18th and April 15th, the time of COVID 19 epidemic in Israel with its consequent limitation of human activities.

On March 19th following restrictions which shutdown the education system and limited work in the public and private sector, the Israeli Ministry of Health imposed a complete quarantine with the exception of need to replenish provisions and medications. This de facto, limited all travel for non-essential purposes and was enforced judiciously by the police.

All patients scheduled for consultations during those dates were contacted via telephone and presented with 3 options – in-person meeting (with appropriate personal protective equipment

(PPE)), telephone appointment (telemedicine) or appointment cancellation with intent to reschedule the appointment when the pandemic condition will allow. Patients who chose the face-to-face meeting option arrived at our medical center for an appointment with a reproductive endocrinology and infertility (REI) specialist. Patients who preferred a meeting by telemedicine received an appointment which was set to the same time and date of their original appointment with the same physician. Telemedicine was performed via phone conversation without a video feed. The platform used included a telephone conversation during which electronic medical record software was utilized to process information gathered during the meeting. Following the encounter, women were able to send supplementary medical information needed via email.

Patients who chose to cancel their appointment were acknowledged that they will not be scheduled for an alternative appointment date at this time.

Patients' electronic medical records were evaluated. Information collected from medical records included demographic and general medical background data. Reproductive data was also collected and included years of infertility, type of infertility-primary or secondary, indication for IVF treatment including ovulation disorder, age related infertility, unexplained infertility, male factor infertility, genetic -Preimplantation Genetic Testing (PGT), fertility preservation or need of oocyte or sperm donation. Information regarding the appointment itself was also assessed, including the number of previous visits, was the patient scheduled an appointment for the patient's regular REI doctor or other attending REI and the meeting purpose (COS cycle planning, FET cycle planning or consultation with recommendations).

Additional data collected were appointment outcomes – referral to controlled ovarian stimulation, frozen-thawed cycle or fertility preservation and embryo transfer data and outcomes – embryo stage at transfer, number of transferred embryos and chemical and clinical pregnancy rates. As these pregnancies are still ongoing and some patients continued pregnancy follow-up in other medical centers- we were not able to report live birth data.

All parameters were compared between the two study groups-patients who participated in a telephone meeting and patients who arrived for an in-person meeting.

The study was approved by the Investigation Review Board of our Medical center (IRB number HMO 0313-20).

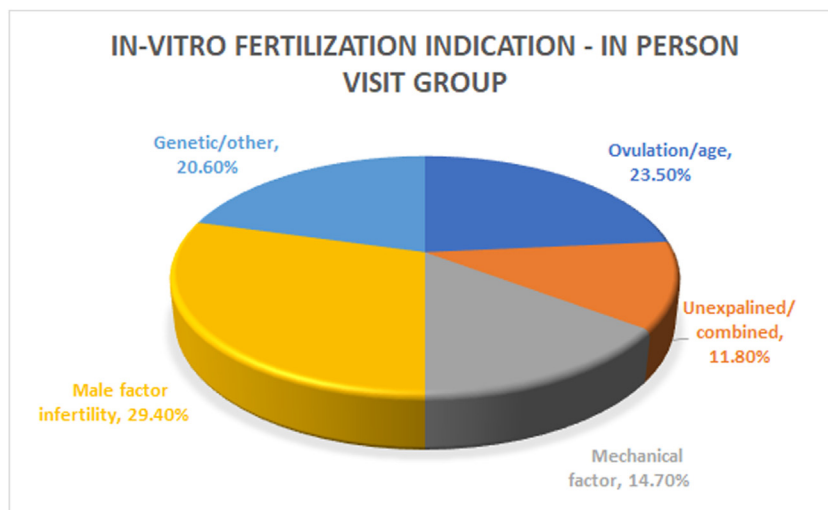


Fig. 1. Indications for In-vitro fertilization in the in -person visit group.

Statistical analysis

Student's T-test was performed to assess differences in continuous variables between the groups. The chi-square and Fischer exact tests were implemented for categorical variables. We report two-sided p values, with a value of <0.05 considered significant. All data analysis was performed using statistical software package SPSS 24.0 (SPSS Inc., Chicago, IL)

Results

Overall, 90 IVF clinic appointments were scheduled between March 18th and April 15th. Thirty-four (37.8 %) patients chose to arrive to the IVF clinic in spite of the partial quarantine and 27 (30.0 %) couples chose to avoid in person meeting and scheduled a telemedicine appointment. Twenty-nine (32.2 %) patients cancelled their appointment. The indication for IVF in the traditional face-to-face and telemedicine groups is presented in Figs. 1 and 2, demonstrating high rate of patients with a PGT indication for IVF in the telemedicine group.

Table 1 shows the general and reproductive background characteristics of the two study groups. Women's age, parity, years of infertility and comorbidities were similar. However, the telemedicine group had lower prevalence of primary infertility (20.0 % vs. 47.1 %, p = 0.037) and higher rates of PGT indication (rather than infertility) for IVF (48.2 % vs. 20.6 %, p = 0.026). Details regarding the appointment itself were additionally compared (Table 2), demonstrating similar distribution of appointment indication. Nevertheless, the rate of a first-ever IVF clinic visit was higher in patients that arrived for a face-to-face meeting, as compared to telemedicine encounter (55.9 % vs. 28.0 %, respectively; p = 0.036).

Population of patients that opted to avoid attending the clinic had a mean age of 35.3 years and an average of 3.1 years of infertility. Additionally, they had higher rates of medical comorbidities compared to patients who chose to attend their appointment (51.7 % vs. 29.5 %, p = 0.016). Primary infertility was also increased in this group but did not reach statistical significance (54.2 % vs. 35.6 %, p = 0.122). Main indication for IVF in this population was impaired ovulation and age-related infertility (29.2 %).

Analysis of appointment outcomes is presented in Table 3. Percentage of appointments that led to IVF cycles resulting in fresh

Table 1
Basic characteristics of the study population according to the type of clinic visit.

Parameter	Type of clinic visit		P value
	In-person	Telephone	
No. of patients	34	27	
Age	35.6±7.5 (36.5)	32.6±6.3 (32)	0.11
No. of children	0.7±1.0 (0)	0.6±0.6 (0)	0.67
Nulliparity	19/34 (55.9 %)	11/25 (44.0 %)	0.37
Comorbidity	10/34 (29.4 %)	8/27 (29.6 %)	0.99
Primary infertility	16/34 (47.1 %)	5/25 (20.0 %)	0.037
Genetic indication for IVF	7/34 (20.6 %)	13/27 (48.2 %)	0.026
Years of infertility	2.9±2.0 (2.8)	3.2±2.6 (2.8)	0.60

Data presented as mean±SD (median) or n/N (%).
Note: IVF, In-vitro fertilization.

Table 2
Appointment at the fertility clinic data according to type of visit.

Parameter	Type of clinic visit		P value
	In-person	Telephone	
No. of patients	34	27	
Regular physician	20/34 (58.8 %)	16/27 (59.3 %)	0.97
First visit at clinic	19/34 (55.9 %)	7/25 (28.0 %)	0.036
Appointment indication			0.14
First COS cycle	7/34 (20.6 %)	5/25 (20.0 %)	
Repeat COS/FET/consult	15/34 (44.1 %)	13/25 (52.0 %)	
Fertility preservation	6/34 (17.7 %)	7/25 (28.0 %)	
OD/sperm D	6/34 (17.7 %)	0	

Data presented as n/N (%).
Note: COS, controlled ovarian stimulation; FET, frozen-thawed embryo transfer; OD, oocyte donation; sperm D, sperm donation.

or frozen-thawed embryo transfer as well as the clinical pregnancy rate for these cycles were similar in the telemedicine and face-to-face meeting groups (72.2 % vs. 88.0 % and 30.8 % vs. 31.8 %, p = 0.73 and p = 1.00; respectively).

Discussion

The COVID-19 pandemic has changed the way medicine is being practiced worldwide. Healthcare systems have been forced to adapt quickly in order to successfully face the challenge of delivering high quality care while insuring a safe environment for healthcare workers and patients. In most hospitals, focus has been

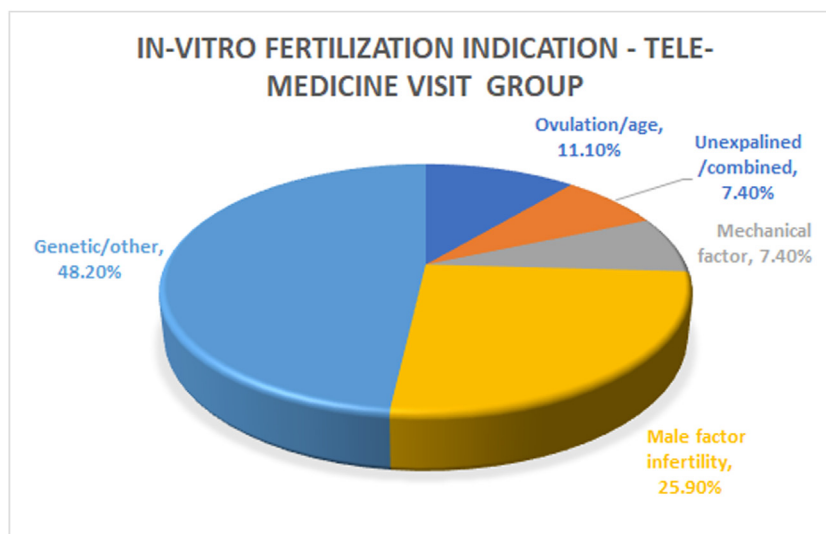


Fig. 2. Indications for In-vitro fertilization in telemedicine group.

Table 3
Appointment outcomes according to type of visit.

Parameter	Type of clinic visit		P value ^a
	In-person	Telephone	
No. of patients	34	27	
Referred to COS/FET cycle	25/34 (73.5%)	18/27 (66.7 %)	0.59
Embryo transfer	22/25 (88.0%)	13/18 (72.2 %)	0.73
Fertility preservation	1/25 (4.0%)	4/18 (22.2 %)	0.07
Cycle cancellation	2/25 (8.0%)	1/18 (5.6 %)	1.00
Embryo transfer data			
Fresh embryo transfer	11/22 (50.0 %)	5/13 (38.5 %)	0.51
Frozen embryo transfer	11/22 (50.0 %)	8/13 (61.5 %)	0.51
No. of embryos transferred	1(1)	2(1)	
Embryo stage at transfer			0.26
Cleavage stage	17/22 (77.3 %)	7/13 (53.8 %)	
Blastocyst	5/22 (22.7 %)	6/13 (46.2 %)	
Chemical pregnancy	8/22 (36.4 %)	4/13 (30.8 %)	1.00
Clinical pregnancy	7/22 (31.8 %)	4/13 (30.8 %)	1.00

Data presented as n/N (%) or Median (IQR).

Note: COS, controlled ovarian stimulation; FET, frozen-thawed embryo transfer.

^a Calculated using Fisher's exact test.

put on life-saving treatments while less urgent services have been cut-back substantially. Following restrictions implemented due to the rapid spread of COVID-19, our IVF clinic continued functioning while modifying its setting. This study provides an overview of the healthcare response with respect to ART treatments during the first and sudden phase of the COVID-19 pandemic. The telemedicine option investigated in this study, represents an adaptation aimed to allow maximal safety for both patients and healthcare providers while maintaining the availability of fertility clinics services and ART treatments

We found that approximately one third of the couples opted for telemedicine visit instead of an in-person meeting or visit cancellation. The telemedicine group had fewer cases of primary infertility and patients in that group were more likely to have attended the clinic for a repeat visit. We also found that the telemedicine group had higher rate of PGT indication for IVF treatment compared to the face-to-face group.

These differences reflect patients' consideration when proposed a telemedicine rather than a face-to-face meeting. Patients suffering from infertility in which the diagnosis is clear or has been established, are more prone to waive a face-to-face meeting under certain circumstances. In contrast, couples with primary infertility or when infertility factor is unknown, may believe that a face-to-face conversation is likely to contribute and affect their diagnosis or management. Moreover, the rate of appointments that led to fresh or frozen-thawed embryo transfer and these transfers' outcomes (clinical pregnancy rate) were similar in the telemedicine and face-to-face meeting groups. These results validate this option in selected cases, though larger studies are required to verify our findings.

Telemedicine has been shown to be advantageous in a wide array of medical disciplines [8–11]. While lacking the face-to-face meeting, telemedicine affords clear advantages such as patient convenience, ability to offer care in remote areas and to shorten waiting periods. Specifically, in the field of assisted reproduction, telemedicine has been implemented in monitoring ovarian stimulation in IVF cycles. Data presented in previous studies showed similar reproductive outcome with higher patient satisfaction and lower level of stress [12,13]. In another study, Hernández et al. report on a comparison between women undergoing face-to-face care and women assigned to telemedicine in a fertility clinic setting. Women in the telemedicine group had reduced time until first outpatient visit and time to initiation of treatment. No difference was observed with regard to pregnancy and complication rates [7]. Albeit these encouraging results,

telemedicine has yet to be utilized on a large scale in fertility clinics mostly due to suspicion shown by healthcare providers and lack of clear benefit.

The COVID-19 outbreak has accelerated the process of applying telemedicine in all medical fields as well as in the field of reproductive medicine. The immediate need to deliver medical care to populations under quarantine as well as the call for social distancing have made telemedicine a compelling option too beneficial to be overlooked.

Patients for whom it was their first visit chose more often a face-to-face visit as opposed to telemedicine. One explanation could be the personal nature of such an encounter during which the foundations are set for the physician-patient relationship. This fundamental aspect of delivering medical care may have an effect on treatment success through increased compliance and treatment continuity. Once patients were familiar with their caregivers, they were more inclined to undertake a telemedicine conference. This may help to ascertain cases in which telemedicine will be most beneficial and appropriate in the setting of an IVF clinic.

Women undergoing IVF treatment for genetic indications such as PGT may have specific characteristics which may render them suitable for use of telemedicine. Patients referred for such indications seldom have reproductive abnormalities which require further evaluation and often arrive with a specific diagnosis making them fitting for telemedicine visits.

Recent data suggests patients with comorbidities are more susceptible to complications following infection with COVID-19 [14,15]. This correlates with our finding that over 50 % of couples who cancelled their visit had medical comorbidities. We believe that such patients should be encouraged towards telemedicine visits during the near future so as to minimize their risk of infection.

Little is known regarding the activity of IVF clinics during the COVID-19 pandemic and this study provides a unique opportunity to evaluate current trends in this climate. The direct comparison between in-person and telemedicine groups may enable targeting of patients which would benefit from telemedicine. We also analyzed the less studied group of couples who canceled their visit focusing on factors which could explain their choice.

The main limitation of this study is its retrospective nature. Furthermore, though being an important tool for assessment of new service modalities, no patient satisfaction questionnaire was used. Data with respect to reason patients chose one type of visit setting over another was unavailable. We acknowledge the fact that the relatively small cohort limits the generalizability of our findings. Nevertheless, in this unique era, we believe that publishing available data on patient management is of interest.

Conclusion

We present our IVF clinic's experience during these unprecedented times while describing patient characteristics according to form of visit. The COVID-19 pandemic has forced us to face unparalleled challenges changing the way we deliver medical care. We hope these finding will enhance patient care in general and help to optimize the process of implementing telemedicine into clinical practice of reproductive medicine in particular, during these challenging times.

Author's contribution

GK and HC have contributed substantially to the conception and design of the study, analysis and interpretation of data and drafting and revising of the article. CM has contributed substantially to analysis and interpretation of data as well as drafting of the article. UD has contributed substantially to the analysis and interpretation

of data and drafting and revision of the article. ABM has contributed substantially to the acquisition, analysis and interpretation of data and drafting and revision of the article. All authors read and approved the final manuscript.

Ethics approval

The study was approved by the Human Research Ethics Committees of the Hadassah University hospital (IRB) and conforms to the provisions of the declaration of Helsinki.

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Transparency document

The [Transparency document](#) associated with this article can be found in the online version.

Declaration of Competing Interest

The authors report no declarations of interest.

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None.

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