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Original Article *Özgün Araştırma*

A COMPARATIVE STUDY: HOW WERE CLINICAL RESEARCH ACTIVITIES AFFECTED IN THE FIRST YEAR OF THE PANDEMIC COMPARED TO THE PREVIOUS YEAR?

Karşılaştırmalı Bir Araştırma: Önceki Yıla Kıyasla Pandeminin İlk Yılında Klinik Araştırma Faaliyetleri Nasıl Etkilendi?

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ABSTRACT

Objective: The main purpose of this study is to determine how clinical research activities in a Clinical Research Center in Ankara are affected by the Covid-19 pandemic.

Material and Methods: In the study, we compared clinical trial activities before the pandemic (March 2019-February 2020) and during the pandemic (March 2020-February 2021) for two 12-month time periods. Data were collected from site coordinators, with strict attention to the confidentiality of volunteer data. Data were grouped as the number of studies newly initiated, closed, and closed to enrollment; number of scheduled, unscheduled, delayed, missed, and telephone visits according to study protocols; number of new patients screened, screening failures, new patients enrolled in studies, number of patients who dropped out for various reasons and the number of direct or online monitoring visits.

Results: According to our study, while the number of newly opened clinical trials during the pandemic period was adversely affected, clinical trial patient visits were carried out successfully despite delays. Compared to the pre-pandemic period, an increase was observed in the number of patients newly screened and enrolled in clinical trials and also in the number of patients excluded from the study, while a decrease was observed in the number of screening failures. It was seen that there was a shift towards online methods in monitoring visits made during the pandemic period.

Conclusion: While clinical research centers around the world were adversely affected during the pandemic period, it was observed that the clinical research activities in the center where we conducted the study were carried out successfully despite the setbacks.

***Keywords**: Clinical trials, covid-19 pandemic, oncology hospital, cancer, clinical research center*

ÖZ

Amaç: Bu çalışmanın amacı, Ankara'da bulunan bir Klinik Araştırma Merkezi'ndeki klinik araştırma faaliyetlerinin Covid-19 pandemisinden nasıl etkilendiğini belirlemektir.

Gereç ve Yöntemler: Çalışmada, pandemi öncesi (Mart 2019-Şubat 2020) ve pandemi sırasında (Mart 2020-Şubat 2021) klinik araştırma faaliyetlerini 12 aylık iki zaman dilimini karşılaştırdık. Veriler, gönüllü verilerinin gizliliğine dikkat edilerek saha koordinatörlerinden alındı ve yeni başlatılan, kapatılan ve hasta alımına kapanan çalıma sayısı; çalışma protokollerine göre planlı, plansız, gecikmeli, yapılmayan ve telefonla yapılan hasta vizitlerinin sayısı; taranan yeni hasta sayısı, tarama başarısızlıkları, çalışmalara kaydedilen yeni hasta ve çeşitli nedenlerle çalışmadan ayrılan hasta sayısı; doğrudan veya çevrimiçi izleme vizitlerinin sayısı şeklinde gruplandırıldı.

Bulgular: Çalışmamıza göre pandemi döneminde yeni açılan klinik araştırmaların sayısı olumsuz etkilenirken, klinik araştırma hasta ziyaretleri gecikmelere rağmen başarıyla gerçekleştirildi. Pandemi öncesi döneme göre tarama sayısı, klinik araştırmalara alınan hasta sayısı ve çalışma dışı bırakılan hasta sayısında artış, tarama başarısızlığında ise azalma gözlendi. Pandemi döneminde yapılan izleme ziyaretlerinde online yöntemlere doğru bir kayma olduğu görüldü.

Sonuç: Pandemi döneminde dünya genelinde klinik araştırma merkezleri olumsuz etkilenirken, çalışmayı yürüttüğümüz merkezdeki klinik araştırma faaliyetlerinin aksiliklere rağmen başarıyla yürütüldüğü gözlemlendi.

***Anahtar Kelimeler**: Klinik araştırmalar, covid-19 pandemisi, onkoloji hastanesi, kanser, klinik araştırma merkezi*

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INTRODUCTION

Covid-19 has spread rapidly since the first case was reported in Wuhan, China in December 2019 and it was announced as a pandemic by the World Health Organization (WHO) on March 11, 2020. The first case in Turkey was reported on the same day (1,2). The virus has rapidly spread around the world, as of 18 January 2022, more than 340 million infected people, including more than 5 million deaths were reported, according to WHO (3).

In Turkey, the majority of public or private hospitals were announced as Pandemic Hospitals with a Ministry of Health (MoH) decree on 20 March 2020. "Pandemic Hospital" was formally defined as a hospital in which the diagnostic and treatment processes are carried out for patients with a definitive diagnosis of Covid-19 infections. A guide document was published by the MoH designated that a definitive diagnosis of Covid-19 infection can be made by two infectious diseases and clinical microbiology specialists or chest disease, internal medicine and/or a third level adult intensive care unit specialist (4).

During the Covid-19 Pandemic, the hospital where we conducted this study was declared a "clean hospital" and in this context, all patients diagnosed with Covid-19 in this hospital were quarantined and immediately transferred to the pandemic hospitals.

The hospital has Clinical Research Center along with a separate Phase I clinic since 2017. There were 46 different clinical trials going on at the hospital at the start of the pandemic. With the declaration of a clean hospital during the pandemic period, clinical studies could be continued despite various disruptions. In this study we planned to investigate the effects of the pandemic in clinical trial center activities.

MATERIALS AND METHODS

The ethics approval of the study was obtained from the hospital's Ethics Committee (University of the Health Sciences Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Clinical Research Ethics Committee, date: 27.05.2020; issue number: 2020-07/713.), with the study protocol presented.

The first case of Covid-19 in Turkey, which was approved both with clinical signs and laboratory tests, was seen in March 2020. For comparisons, the period between March 2019-Feb 2020 (pre-pandemic period) and the period between March 2020 and February 2021 (pandemic period) were selected.

This study is a retrospective chart review study. We recorded the number of studies newly initiated, closed, and closed to enrollment; number of scheduled, unscheduled, delayed, missed, and telephone visits according to study protocols; number of new patients screened, screening failures, new patients enrolled in studies, number of patients who dropped out for various reasons and the number of direct or online monitoring visits. These data were obtained from site coordinators assigned for clinical research studies. We definitely followed the confidentiality of the research. Descriptive statistical analysis methods were implemented and results were expressed as number and percentage changes.

RESULTS

During the pre-pandemic period, there were 46 clinical studies being conducted, consisting of mostly Phase III studies. Although, 10 new studies were initiated in the pandemic period (47.36% decrease), 19 studies were started in the pre-pandemic period. While the number of closed studies in the prepandemic period was 5, 6 studies were closed during the pandemic period with an increase of 20%. However, due to low recording/non-registration, there were 6 recruitment closed studies in the pre-pandemic period and only 2 recruitment closed studies in the pandemic period (66% decrease) (Graph 1).

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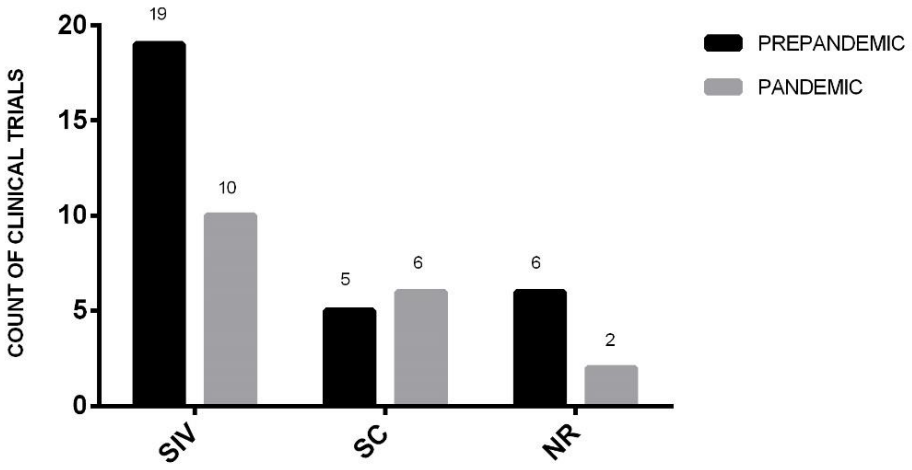
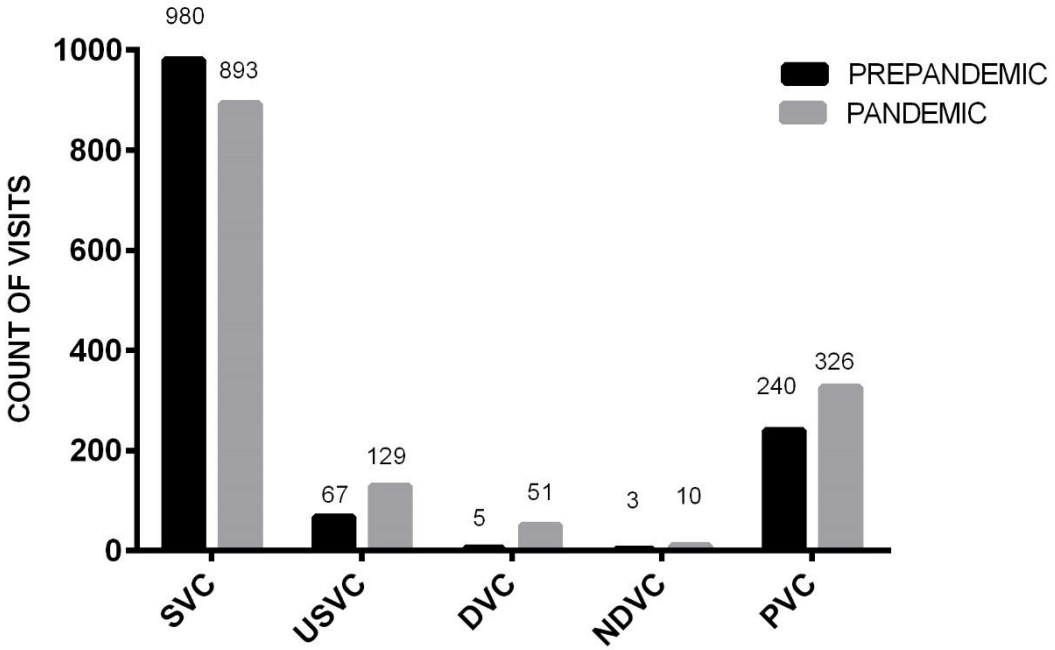


SIV: Site Initiation Visit, SC: Site Closure, NR: Not Recruiting trials

Graph 1: Status of pandemic clinical trials at the selected center

Compared to the prepandemic period, according to study protocols, scheduled visits decreased by 8.8% during the pandemic period, while unscheduled visits, often due to adverse events, increased by 92%. Delayed visits increased by about 9 times and the number of unmade visits increased by about 2.3 times. On the other hand, a 35% increase in the number of phone calls was observed (Graph 2).



SVC: Scheduled Visit Count, USVC: Unscheduled Visit Count, DVC: Delayed Visit Count, NDVC: Not Done Visit Count, PVC: Phone Visit Count

Graph 2: Comparison of clinical trial visits

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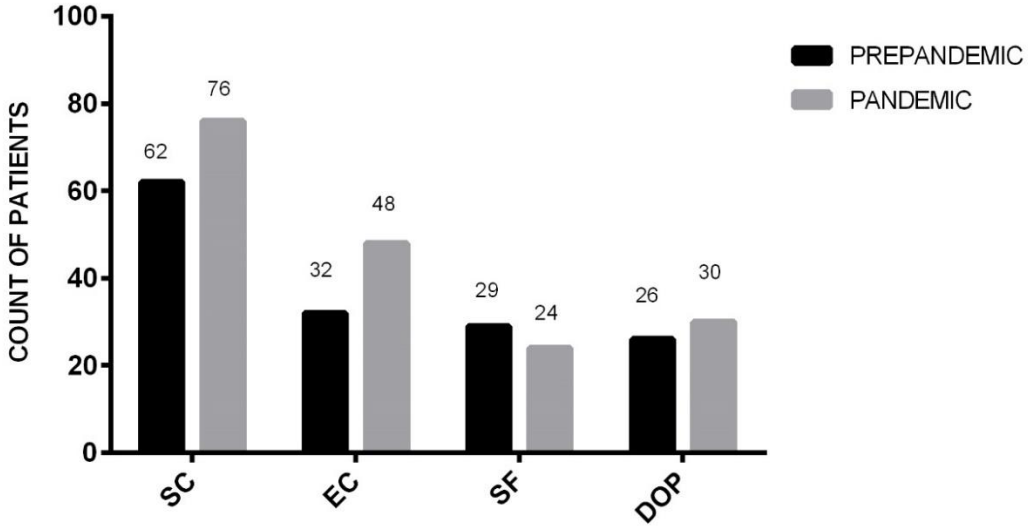
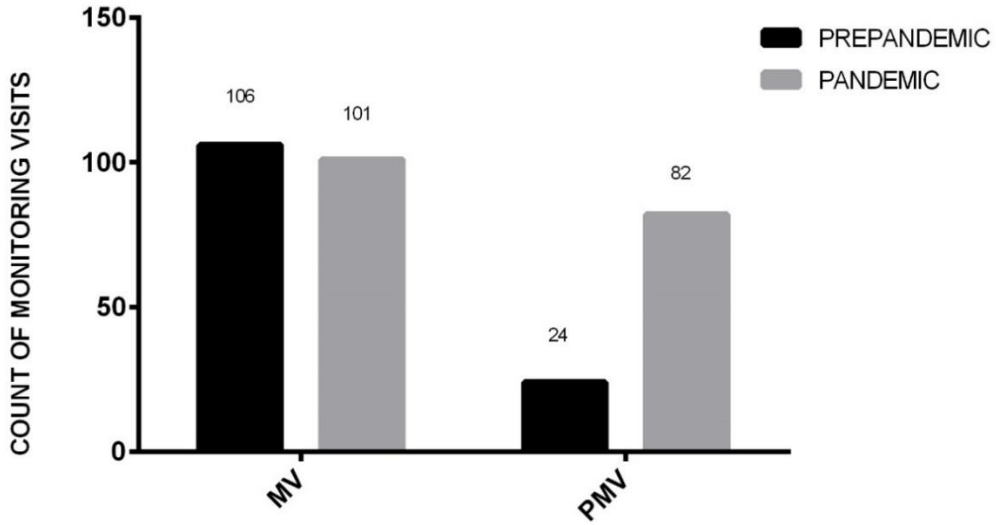
An increase of 22.5% was seen in the number of new patient screenings and 50% increase in the number of enrolled patients compared to prepandemic period. A reduction of 17% was observed in the number of screening failures during the pandemic period. In the pandemic period, the number of patients excluded from the study increased slightly by 15% because of various reasons (Graph 3).

Regular monitoring visits performed by the sponsors or legal representatives of sponsors (CRO) decreased by 5% during the pandemic period, and compared to the pre-pandemic period, the number of telephone or online monitoring visits increased by 241% (Graph 4).



SC: Count of New Patient Screening, EC: New Patient Enrollment Count, SF: Screen Failure, DOP: Drop-out Patient (Out of Trial Patient)

Graph 3: Comparison of the center's recruitment activities



MV: Monitoring Visit, PMV: Phone Monitorisation Visit

Graph 4: Comparison of monitoring activities

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DISCUSSION

Phase studies are a significant part of the new drug development process. The economic size of the global clinical research market has reached 44.3 billion USD in 2020 and is expected to grow by 5.7% annually from 2021 to 2028 (5). Turkey is a country which has performed 3575 active clinical studies (1.2% of worldwide) as of 28 February 2019 (6).

Clinical Pharmaceutical Research is assumed to be one of the sectors that will be adversely affected during the pandemic. The FDA announced that there may be difficulties in conducting clinical trials due to Covid-19 contamination for field personnel or study patients, as well as quarantine conditions, center closures, travel restrictions, dificulties in the supply chain for the investigational product (7). The following factors may also negatively contribute to the obstacles observed. The sources of health systems have been almost entirely allocated to the pandemic struggle at this time. Most of healthcare professionals have focused mainly on increasing daily activities due to the pandemic rather than clinical research. Pharmaceutical companies have allocated their energies and resources into vaccine and pharmaceuticals for Covid-19, and at this point, they have been encouraged by governments. Therefore, many non-Covid-19 clinical trials have been postponed, and previously started studies have been ceased.

Analysis of data on “ClinicalTrials.gov” indicates that more than 200 interventional oncology studies were suspended as a result of COVID-19 in March and April 2020 (8). Many study centers were closed during the pandemic period. Patients' interest in clinical trials has also decreased. International Medidata Solutions, an organization serving worldwide electronic clinical research data, published an analysis at September 2020 with data from 5222 studies, 198120 study sites. According to this report, there is a 10% and 20% reduction in new patients entering to trials per center in July and August 2020 compared to the pre-Covid baseline from 11 months of 2019 data (9).

Due to the regulations such as travel restrictions and curfews applied during the outbreak, the number of admissions to hospitals decreased and this led to a decrease in the recruitment of new patients to clinical trials globally. This reduction is observed in the number of new patient screenings and the number of new patients enrolled in trials. However, in the center where we conducted this study, compared to the pre-pandemic period, there was a 22.58% increase in the number of new patient screenings and a 50% increase in the new patient enrollment during the pandemic period. It is also noteworthy that there was a small decrease (-17.24%) in the number of the screening failures. But there was a slight increase (15.38%) in the number of patients who were excluded from the study, either voluntarily or for other reasons including death. This relative goodness in screening and enrollment of new patients will provide an advantage to this center compared to other centers in conducting clinical research activities.

As can be understood from the figures, the current clinical trials have been successfully carried out in this center despite many difficulties. Compared to the previous period, a slight reduction (8.87%) in the total number of scheduled visits observed. During clinical studies, it may be necessary to make unscheduled visits to patients at dates not specified in the protocols, mostly due to adverse events. Compared to the prepandemic period, an increase of 92% was observed in the number of unplanned visits during the pandemic period. Among the reasons for this increase, the clinical trial patients being infected with Covid-19 may be a factor. The number of delayed visits increased by about 10 times (5 to 51). There was a 233% increment (3 to 10) in the number of visits that cannot be performed. These are considered to be due to travel restrictions and are not considered to be specific to the hospital. Despite the difficulties of pandemic period, visits could be made even though there were delays.

Monitoring activities by CRO's (Contracted Research Organisation) on behalf of the sponsor are implemented

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by visiting the center or by telephone/online methods to check the quality of clinical trial data. In the center where we conducted this study, although monitoring visits were mostly made with direct center visits in the pre-pandemic period, an increase of 241% was seen in telephone/online methods in the pandemic period. There was no remarkable difference in direct visits to the center.

In conclusion, the pressure on non-Covid-19 clinical drug trials is estimated to continue as long as the Covid-19 threat continues. The continuation of clinical studies without being affected by the pandemic and the success of patient's treatment and visits have made this center one step ahead of other centers in the world. The clinical research center aims to eliminate the damage, caused by the acute impacts of the pandemic by increasing the medium- and long-term activities of this center.

Conflict of Interest: There were no potential conflicts of interest to be declared by the authors in this study.

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Researchers' Contribution Rate Statement: Concept/Design: RSŞ; Analysis/Interpretation: RSŞ, HK; Data Collection: RSŞ, HK; Writer: RSŞ, HK; Critical Review: RSŞ, HK; Supervision: RSŞ, HK.

Ethics Committe Aproval: University of the Health Sciences Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital Clinical Research Ethics Committee, date: 27.05.2020; issue number: 2020-07/713.

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