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CLINICAL PHARMACY RESEARCH REPORT

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Evaluation of virologic suppression rates during the COVID-19 pandemic with outpatient interdisciplinary HIV care

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Abstract

Introduction: The Coronavirus Disease 2019 (COVID-19) pandemic has presented social distancing challenges leading healthcare systems to adapt and utilize telemedicine platforms more than ever before. Reducing patient exposure to COVID-19 became a primary concern, especially for populations at an increased risk for severe illness, such as human immunodeficiency virus (HIV) positive patients.

Objectives: The primary objective of this study was to measure the impact of pharmacy services including telehealth through the percentage of virologically suppressed patients (HIV ribonucleic acid [RNA] < 200 copies/mL) during the pre-COVID and post-COVID time periods. Secondary objectives included the percentage of patients with undetectable viral loads (HIV RNA < 20 copies/mL), percentage of patients with cluster of differentiation 4 (CD4) cell counts greater than 200 cells/mm^3, and changes in CD4 cell counts and percentages pre-COVID and post-COVID.

Methods: This was a retrospective chart review at a single center HIV primary care clinic in Brooklyn, NY evaluating electronic medical records (EMRs) of 211 HIV-positive patients. Pre-COVID was defined as 1 year prior to March 13, 2020, and post-COVID was defined as March 13 to July 20, 2020.

Results: Viral load suppression rates for pre and post-COVID were 88.6% and 85.3%, respectively (P = .28). Undetectable viral load rates for pre and post-COVID were approximately 81.5% and 74.4% (P = .096). Mean CD4 cell counts and percentages were 617 cells/mm^3 and 29% for pre-COVID, and 460 cells/mm^3 and 22% for post-COVID. CD4 cell counts greater than 200 cells/mm^3 pre-COVID and post-COVID was 92.6% and 78.3%, respectively (P = .001).

Conclusion: Utilization of pharmacy services including telehealth, may allow clinical pharmacists to collaboratively provide remote services without jeopardizing patient outcomes. Larger studies are needed to confirm these findings, and display the long-term impact and satisfaction of these services.

KEYWORDS
adherence, collaborative practice, medication management, telehealth

1 | INTRODUCTION

On March 13, 2020, the United States declared the Coronavirus Disease 2019 (COVID-19) a national emergency. Since November 2020, COVID-19 has been confirmed in over 102 million cases worldwide,[1] with 25 million confirmed cases in the US.[2] A respiratory infection that can be spread from person to person, COVID-19 may present with a range of mild to severe symptoms including fever, cough and shortness of breath. Individuals at a heightened risk are believed to be older adults and those with preexisting underlying comorbidities such as cardiovascular disease, diabetes, and respiratory illnesses.[3] The Centers for Disease Control identified people living with Human Immunodeficiency Virus (PLWH) as a population that may be at an increased risk for severe illness from COVID-19 compared with those of the general population.[4,5] Data regarding the actual disease risk among PLWH is lacking. D'Souza et al distributed a telephone survey to asses symptom and testing prevalence to 3411 patients, of whom 61% were human immunodeficiency virus (HIV)-positive. Symptoms were similar among HIV-positive and negative patients; however, a higher percentage of PLWH tested positive for COVID.[6] These data differs from other reports displaying PLWH have similar positivity rates.[7] PLWH are a unique population with uncertain and conflicting data regarding their risks for COVID-19 making it critical for healthcare professionals to truly understand how the HIV epidemic and COVID-19 pandemic comingle and affect one another.

A syndemic occurs when two or more epidemics interact synergistically to produce an increased burden of disease.[8] The coexistence of the global COVID-19 pandemic and HIV/acquired immunodeficiency syndrome (AIDS) epidemic mutually enhance vulnerability which can significantly affect the overall health of a population.[4] Of those infected with HIV in the United States, nearly half are 50 years of age or older.[4,9] Although older patients living with HIV have the potential threat of negative outcomes due to COVID-19, it is believed younger HIV-positive individuals are also at risk following the recent data displaying the vulnerability of populations aged 18-49 years.[4] In addition, immunocompromised HIV-positive individuals with lower CD4 cell counts, unsuppressed HIV RNA viral loads, and/or the presence of other comorbidities may be at an even greater risk of infection and complications. Aside from health complications, PLWH can also be confronted with further challenges including mental health, substance abuse, and societal stigmas creating a complex syndemic when occurring simultaneously with COVID-19.[10] In order to ensure optimal health outcomes and maintain viral load suppression rates during this global pandemic in PLWH, it is critical to prevent lapses in care, and ensure adherence to antiretroviral therapy (ART). Viral load suppression is both an individual and public health concern as patients on ART with undetectable viral loads preserve their health and significantly reduce the risk of transmitting the virus along with other opportunistic infections.

Amidst the pandemic, telehealth provided a platform for patients to navigate the health system and access routine care while reducing their exposure.[11] Telemedicine technologies provide a useful approach in managing the needs of patients with chronic illnesses during COVID-19, while remote. The Brooklyn Hospital Center (TBHC) is home to the Program for AIDS Treatment and Health (PATH) Center, a New York State Designated AIDS Center with two locations, one at the main campus and one off-site. The PATH Center is federally funded by the Ryan White Program serving close to 1000 HIV-positive patients. The majority of patients are insured through Medicaid (55%) with approximately 1% of patients receiving AIDS Drug Assistance Program (ADAP). Within the clinic, patients are able to establish care with an infectious disease physician and are seen by an interdisciplinary team including a clinical pharmacist. Patients who may prefer one-on-one visits are able to be seen by one of the physician assistants or nurse practitioners. As of January 2020, approximately 45% of patients were seen in the interdisciplinary model and 55% in the one-on-one format. Interdisciplinary clinic occurs Monday to Friday with pharmacotherapy clinic having three sessions per week. During interdisciplinary clinic, medical residents see the patients first. Once the residents have completed their visit, the infectious disease physician, clinical pharmacist (including pharmacy residents), and students then round into each clinic room. The medical resident presents the patient to the team, and from there the team discusses and agrees on a treatment plan. The clinical pharmacist in the room focuses on medication reconciliation, patient assessment, clinically significant drug-drug interactions, and chronic disease state management, in addition to e-prescribing medications to the patient's pharmacy. Commonly, patients with uncontrolled chronic disease states seen in interdisciplinary clinic are referred to pharmacotherapy clinic for further management.

After COVID-19 was declared a national emergency, the PATH Center transitioned to mainly virtual visits with the goal to ensure continuity and optional care while preventing lapses in medication adherence, specifically with ART. As an interdisciplinary clinic, clinical pharmacists play a critical role in patient care through collaborative drug therapy management. Pharmacotherapy visits and medication management was completely transitioned to telemedicine for the first time. This study describes the steps taken by the clinical pharmacists at the PATH Center during the COVID-19 pandemic in a joint effort with physicians, nurses, and case workers to manage patients remotely, and evaluates the impact on patient outcomes.

2 | METHODS

This was a retrospective, single center chart review evaluating electronic medical records (EMRs) of 211 HIV-positive patients who required ART renewals or follow-up during the pandemic. Patients were included in this study if they were older than 18 years of age with a diagnosis of HIV, had established care with an infectious disease provider in clinic and seen in the interdisciplinary model, and had a medication request placed. Data collected from the EMR system included the number of audio-only or audiovisual visits with a provider and/or clinical pharmacist, ART regimen, HIV RNA, and CD4 cell counts with percentages. Pre-COVID was defined as 1 year prior to March 13, 2020, and post-COVID was defined as March 13 to July

TABLE 1 Baseline Characteristics

Characteristic	Pre-COVID (n = 211)	Post-COVID (n = 164)
Age (years), mean	53 ± 11.8	53 ± 11.8
Male, n (%)	120 (56.9)	94 (57.3)
Race or ethnicity, n (%)		
Black Or African-American	162 (76.8)	124 (75.6)
White	22 (10.4)	16 (9.8)
Other	16 (7.6)	14 (8.5)
Unknown/Declined	11 (5.2)	10 (6.1)
ART regimen n (%)[a]		
Bictegravir/FTC/TAF	95 (45.2)	69 (42.3)
Darunavir/cobi/FTC/TAF	11 (5.2)	7 (4.3)
Dolutegravir/ABC/3TC	8 (3.8)	6 (3.7)
Dolutegravir + FTC/TAF	9 (4.2)	7 (4.3)
Dolutegravir/rilpivirine	10 (4.8)	7 (4.3)
Elvitegravir/cobi/FTC/TAF	38 (18.1)	29 (17.8)
Rilpivirine/FTC/TAF	20 (9.5)	15 (9.2)
Other	20 (9.5)	23 (14.1)

[a]Due to 1 elite controller not on ART, pre-COVID (n = 210) and post-COVID (n = 163).
Abbreviations: 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; cobi, cobicistat; FTC, emtricitabine; TAF, tenofovir alafenamide.

20, 2020. The time frames were relative to the date a national emergency was declared in the United States and the clinic transitioned to mainly telehealth services. Data was analyzed using descriptive statistics, chi-squared tests, and *t*-tests. Institutional review board approval was deemed unnecessary by the institution.

On and after March 13, 2020, several clinical interventions were implemented at the PATH Center to allow for a streamlined transition from in-person visits to virtual services. For medication authorizations, the nursing staff would forward refill requests to the clinical pharmacists through EPIC, the electronic medical record used by the PATH center. An EPIC inbox was created at the beginning of the pandemic allowing the PATH Center pharmacists to have access to one centralized inbox. Under a collaborative practice agreement (CPA) previously implemented, the clinical pharmacists would then review the patient chart, perform medication reconciliation, order and assess labs, provide recommendations, and e-prescribe medication. When needed, interventions were discussed with the provider and all encounters were documented within the EMR. Patients who required additional management of chronic disease states such as hypertension, hyperlipidemia, diabetes mellitus, and anticoagulation were either managed in the virtual interdisciplinary visit or referred for a virtual pharmacotherapy visit. For telehealth or telephone encounters, Signal and Google Voice were used at the beginning of the pandemic which then transitioned to Doximity by May 2020. With Doximity, the clinic was able to use iPhones, iPads, Android devices, or a computer to connect with patients on a secure platform for telehealth visits. Clinical pharmacists utilized an accepted "incident-to" physician billing model, based on a facility fee, with a 99 212 level, or problem-focused visit. For Medicare Fee for Service, these video visit rates equal that of a face-to-face visit; however, this is not the same for all payers. For telephone visits using audio-only technology, the pharmacists billed evaluation and management (E/M) codes of 99 441 (5-10 minutes), 99 442 (11-20 minutes), and 99 443 (21-30 minutes). Generally, billing for audio-only telephone visits were completed at a level 1 or 2 (99 441 and 99 442). For all telehealth visits, time spent with each patient and patient's understanding of a billable visit was documented in the EMR.

The primary objective of this study was to measure the impact of pharmacy services including telehealth through HIV RNA suppression rates (HIV RNA < 200 copies/mL) in HIV-positive patients managed at the PATH Center during the periods of pre-COVID and post-COVID. Secondary objectives included the percentage of patients with undetectable viral loads (HIV RNA < 20 copies/mL), percentage of patients with CD4 cell counts greater than 200 cells/mm^3, and changes in CD4 cell counts and percentages pre-COVID and post-COVID.

3 | RESULTS

There was a total of 211 patients with medication refill requests sent to the clinical pharmacists with the majority of patients being Black or African American (76.77%) having a mean age of 53 years and identifying as male (57%). All patients included did have prescription coverage with the majority being federally insured through Medicaid. Overall, patients were being managed on an Integrase inhibitor (INSTI)-based antiretroviral regimen (81.9%) with 45.2% on bictegravir, 18.6% on dolutegravir, and 18.1% on elvitegravir, respectively. Additional baseline characteristics can be found in Table 1.

HIV-RNA laboratory values were obtained for all patients pre-COVID (*n* = 211) and 164 patients post-COVID based on clinic COVID practices. Of the patients in the study, 187 patients pre-COVID (88.6%) and 140 patients post-COVID (85.3%) were virologically suppressed with HIV RNA less than 200 copies/mL ($P = .35$). The number of patients with an undetectable viral load, or HIV RNA less than 20 copies/mL, was 172 (81.5%) pre-COVID and 122 (74.4%) post-COVID ($P = .096$), indicating no statistical significance. Lymphocyte panels were available for 203 pre-COVID and only 69 post-COVID as these labs are obtained less in practice. Mean CD4 cell counts and percentages were approximately 617 cells/mm^3 and 29% for pre-COVID, and 460 cells/mm^3 and 22% for post-COVID. CD4 cell counts greater than 200 cells/mm^3 pre-COVID and post-COVID was 92.6% and 78.3%, respectively ($P = .001$). Pre-COVID and post-COVID clinical outcomes are displayed in Table 2. Of the 211 patients, 50% had one or more telehealth visits with either a PATH Center physician and/or clinical pharmacist.

TABLE 2 Clinical outcomes

Primary outcome	Pre-COVID (n = 211)	Post-COVID (n = 164)	*P*-value
HIV RNA <200 copies/mL, n (%)	187 (88.6)	140 (85.4)	.35
Secondary OUTCOMES	Pre-COVID (n = 203)	Post-COVID (n = 69)	*P*-value
HIV RNA <20 copies/mL, n (%)	172 (81.5)	122 (74.4)	.096
CD4 cell count >200 cells/mm^3, n (%)	188 (92.6)	54 (78.3)	.001
CD4 cell count (cells/mm^3), mean	617	460	.0004
CD4 cell count (cells/mm^3), median	582	373	
CD4 cell count (%), mean	28.5	24	.0233
CD4 cell count (%), median	29	22	

When medication refill requests were submitted, the clinical pharmacists would perform thorough medication reconciliations and chart reviews, and order and assess laboratory work when appropriate in order to send electronic prescriptions and/or provide recommendations to the provider. This was done for all 211 patients. As the clinic is composed of close to 1000 patients with approximately 45% being seen in the interdisciplinary model, 211 is not the total number of patients. It is likely that the remainder of patients had a sufficient supply of medication, including ART, as stable patients are commonly prescribed a 3-month supply. For refill authorizations, patients were frequently contacted by the clinical pharmacists to assess adherence and determine if laboratory work was needed or feasible. In general, laboratory work was only required for patients who had a recent history of ART non-adherence or detectable viral loads. The pharmacists entered a telephone and/or order-only encounter into EPIC for all 211 medication refill requests. For patients who completed audio-only or audiovisual telehealth visits, the patient care process was implemented through the established CPA. During interdisciplinary or pharmacotherapy visits, the clinical pharmacists would collect or verify any necessary information including but not limited to medication list and health/social histories, perform assessments, and develop and implement a patient-specific drug therapy plan.

4 | DISCUSSION

In March of 2020, The Department of Health and Human Services (DHHS) released interim guidance for COVID-19 in PLWH, which has been periodically updated throughout the pandemic. This guidance states that telehealth services can replace face-to-face encounters for nonurgent care and adherence counseling, which was encouraged at the PATH Center. In addition, PLWH that are stable with suppressed viral loads should have routine in-person visits postponed to the extent possible.[12] This study highlights the potential impact of pharmacy services including telehealth on maintaining HIV RNA suppression rates.

Although the DHHS guidance states that any planned switch in ART should be delayed, the clinical pharmacists at the PATH Center were able to collaboratively and safely transition regimens through the utilization of telehealth services without negatively impacting viral load suppression. This was not common practice and was done usually in the setting of safety and/or efficacy concerns. Additionally, as the guidance recommended postponing clinic visits when appropriate, patients were asked to present in-person to the clinic only if laboratory work was needed. It should be noted that post-COVID lab work likely occurred after an interaction with either a provider or clinical pharmacist as orders needed to placed following a patient assessment to determine the necessity. Generally, CD4 counts are obtained less frequently than viral loads at 3-12 months intervals depending on duration of viral load suppression and previous CD4 counts. Optional monitoring of CD4 count can be considered in those patients who have a CD4 count greater than 500 cells/mm^3 with consistently undetectable viral loads for at least 2 years.[13] Patients who had a lymphocyte panel obtained during the post-COVID time period were more likely to have uncontrolled or newly controlled HIV and therefore lower CD4 counts. This is evidenced in our findings by the lower number of lymphocyte panels obtained post-COVID, and the statistically significant differences in CD4 cell counts and percentages when comparing pre-COVID and post-COVID periods.

Spinelli et al preformed a similar study were the investigators evaluated viral suppression rates after telemedicine was instituted due to shelter-in-place mandates in San Francisco. In comparison to pre-COVID-19, viral load suppression rates had a considerable decrease. The odds of viral nonsuppression increased by 31% during the pandemic despite telemedicine visits. The investigators stated that while telehealth visits offer patient convenience, it may result in less access to clinic-based social support services. Within this study, 16% of patients were homeless and were found to have higher odds of unsuppressed viral loads during the pandemic.[14] Although differing from our study results, the coexistence of the COVID-19 pandemic and HIV/AIDS epidemic is being highlighted revealing the increased in disease burden PLWH are likely experiencing.

Limitations of this study include being retrospective and single-centered, having a short follow-up time period, and having a decreased number of patients included in the post-COVID analysis. The long-term impacts of HIV management may not have been captured as post-COVID data were only collected between March and July 2020. If a patient had their ART modified during the study, the impact of this change may not have been observed. Also, mainly patients with uncontrolled HIV or a recent history of nonadherence

were required to present for laboratory work. When appropriate, stable patients had their follow-up visits and laboratory work extended to a later date. Because of this, the post-COVID numbers are less than pre-COVID. When discussing limitations, it is important to mention availability of technology. The PATH Center mainly cares for an underserved population with patients having a potential lack of access to the necessary technology, such as smartphones and internet connection, for virtual visits hindering the utilization of telehealth services, specifically audiovisual. It should be noted that the majority of visits were able to be completed using audiovisual technology.

In addition, the lack of data regarding chronic disease states management other than HIV was identified as a limitation. This is mainly due to the clinic requiring patients to present for laboratory work only when medically necessary in an attempt to limit patient exposure. It should also be noted that post-COVID viral loads were not taken in retrospect to the telehealth visit(s), but likely after an interaction with a clinical pharmacist after the refill request was received and patient was assessed. Due to the interdisciplinary nature of the clinic, televisits were done by a provider and/or pharmacist limiting the ability to solely measure the impact of the pharmacist. Although visits were done by either a provider, pharmacist, or both, all 211 refill authorizations were completed by the pharmacists. The thorough chart reviews and constant communication required for authorizations is believed to have impacted patient adherence and suppression rates; however, there is a lack of objective data to confirm. Approximately half of the patients requesting refills completed a telehealth visit by a provider and/or pharmacists. It is likely that a portion of the patients who did not complete a televisit were relatively stable and had their visit extended to a later date. The continuity of care achieved and maintenance of viral load suppression rates allowed this vulnerable population to potentially have a reduction in risk factors associated with complications of respiratory or opportunistic infections.

This study provided evidence that pharmacy services including telehealth may be an option to collaboratively manage PLWH in order to maintain virologic suppression rates when in-person visits are not feasible or safe. It is believed that the refill authorizations performed by the clinical pharmacists, which included adherence assessments, prevented gaps in medication use and likely contributed to the non-statistical difference in viral loads pre-COVID and post-COVID. Beyond the pandemic, remote services can be an alternative for stable HIV-positive patients as a supplement to in-person visits. Access to resources will need to be addressed to ensure all patients eligible for virtual visits have the opportunity.

Utilization of pharmacy services including telehealth may allow clinical pharmacists to collaboratively provide remote services without jeopardizing patient outcomes. The results from this study display the potential interdisciplinary role clinical pharmacists have in maintaining viral load suppression rates in PLWH through virtual services. Larger, future studies are needed to confirm these findings, and display the long-term impact and satisfaction of these services.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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