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RESEARCH ARTICLE

Improving Safety in Rheumatology Patients by Closing Pre-screening Laboratory Care Gaps with Rheumatologist-Pharmacist Co-management

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ABSTRACT

Objective: To close laboratory screening care gaps via rheumatology-pharmacy co-management in patients starting disease-modifying antirheumatic drugs.

Methods: Laboratory data were obtained from patients who started disease-modifying antirheumatic drugs (DMARDs) during the pre-and post-intervention periods. The intervention consisted of a rheumatology-pharmacy collaborative screening with guideline-driven DMARD protocol for hepatitis B, hepatitis C, and tuberculosis. The care gap closure for patients starting any type of DMARDs such as a conventional synthetic disease-modifying antirheumatic drug (csDMARD), a biologic disease-modifying antirheumatic drug (bDMARD), or a targeted synthetic disease-modifying antirheumatic drug (tsDMARD), was defined as meeting hepatitis screening completion. The care gap closure for patients starting a bDMARD or tsDMARD alone was defined as meeting both the hepatitis and tuberculosis screening completion. The Chi square method was used for the statistical analysis of the data comparing laboratory screening rates of rheumatologists' pre-intervention versus rheumatologist-pharmacist co-management post-intervention. Post-intervention, subgroup analysis of laboratory screening rates among rheumatologists alone versus rheumatologist-pharmacist co-management was also performed.

Results: During the 30-month period 6/1/2019 to 11/30/2021, hepatitis screening for patients on DMARDs improved from 77% with rheumatologists alone to 82% with co-management post-intervention (P=0.005), whereas hepatitis/tuberculosis screening for patients on bDMARDs/tsDMARDs improved from 75% to 85% respectively (P=0.005). In post-intervention subgroup analysis, hepatitis screening for patients on DMARDs improved from 80% with rheumatologists alone to 95% with co-management(P=0.00), whereas hepatitis/tuberculosis screening for patients on bDMARDs/tsDMARDs improved from 83% to 94% respectively (P=0.033).

Conclusion: By integrating clinical pharmacists into our rheumatology clinic, we significantly improved hepatitis and tuberculosis laboratory screening in our immunosuppressed rheumatic population.

Implications: Rheumatologists can consider integrating clinical pharmacists into their practices to improve patient safety by closing laboratory screening care gaps in the immunosuppressed rheumatic population.

Keywords: conventional synthetic, or biologic or targeted synthetic disease-modifying antirheumatic drugs, Hepatitis B virus, Hepatitis C virus, Tuberculosis, Immunosuppressive agents, rheumatologist-pharmacist co-management.

Data Availability: Population level data is available in the tables 1 and 2 included in this manuscript. Patient level data is restricted for patient confidentiality, legal and ethical concerns.

Introduction:

Patients with autoimmune rheumatic diseases, such as rheumatoid arthritis or other connective tissue diseases experience immune dysregulation and have an increased risk of potent infections. In addition, a considerable number of patients followed by rheumatologists are on immunosuppressive DMARDs for the management of their chronic immune-mediated diseases, lowering their ability to fight infections. The susceptibility of any infection may be higher than two-fold in these immunosuppressed patients when compared to the general population.[1]

There is a significant risk of reactivation of viral hepatitis and latent tuberculosis (TB) in rheumatic patients undergoing treatment with DMARDs. The risk of viral hepatitis reactivation has been recognized in patients with chronic or prior exposure of hepatitis who are treated with any DMARDs, while reactivation of the latent TB has primarily been reported in patients who are treated with bDMARDs or tsDMARDs. Inconsistent laboratory screening for hepatitis or TB in these individuals can lead to significant infection burden and increased morbidity.[2,3]

Patients with rheumatic diseases have an upward prevalence of 38% for hepatitis B virus (HBV) infection and 14% for hepatitis C virus (HCV) infection, and once on immunosuppressive therapy the risk of reactivation can increase up to 75% and 39% respectively.[4] Among patients with latent TB, progression to active disease occurs in up to 10% of patients and initiating anti-Tumor Necrosis Factor (aTNF) therapy multiplies this risk ten-fold.[5] If high-risk patients are screened and treated accordingly, these infections can be avoided.

The Centers for Disease Control and Prevention and expert rheumatologists recommend that rheumatic patients be screened for HBV and HCV before the initiation of DMARD therapy.[6-8] In addition, the American College of Rheumatology recommends screening for TB via either Purified Protein Derivative (PPD) or QuantiFERON-TB Gold prior to the initiation of bDMARDs and tsDMARDs.[9] Lastly in 2022, the European League Against Rheumatism advised screening and prophylaxis for opportunistic infections including but not limited to HBV, HCV and TB in all patients with autoimmune inflammatory rheumatic diseases.[10] Given these recommendations, standardization of laboratory screening for opportunistic infections should be considered for all immune patients starting DMARDs.

There is concern that a screening laboratory care gap exists in our rheumatic patients who start new DMARDs. By 2040, the number of adults diagnosed with arthritis in the US is projected to increase by 49% to 78.4 million.[11] The American College of Rheumatology Workforce Study in 2015 projected that by 2030, adult rheumatology providers will decline by 25% full time equivalent with the subsequent demand exceeding the provider supply by 102%.[12] In addition, new requirements are being placed on physicians on a regular basis by insurance companies, electronic health records, and health care systems. The ability of the rheumatology field to continue to deliver exceptional care is facing significant challenges in the setting of an increased aging population with arthritis, rheumatologist shortages, and physician workload.[13]

In the current environment, it is necessary to seek innovative care deliveries within the healthcare system.[14] In order to improve laboratory screening in this new clinical era and safely care for the rheumatic patient, clinical rheumatology pharmacists were embedded in our rheumatology department and guideline-driven rheumatologist-pharmacist co-management protocols were devised. With this rheumatologist-pharmacist collaboration, we aimed to identify and close infectious screening laboratory care gaps among our rheumatic population who started new DMARD therapy.

Methods:

Laboratory data were extracted from our electronic health record (EHR) of adult rheumatic patients with completed rheumatology visits from 1/1/2019 to 11/30/2021 who started a new DMARD. During the baseline period of 1/1/2019 – 5/31/2020, laboratory screening was managed by rheumatologists alone. During the study intervention period of 6/1/2020 – 11/30/2021, laboratory screening was managed by the rheumatologist-pharmacist co-management protocol for patients who opted to enroll in it. The medication screening protocol was designed by the combined efforts of the rheumatology-pharmacy team. The rheumatology pharmacists were trained on the American College of Rheumatology guidelines and laboratory screening protocol by a group of clinical rheumatologists.

The protocol included guideline driven criteria for infection screening prior to starting a new DMARD. New DMARD therapy consisted of either a csDMARD, bDMARD, or tsDMARD. Hepatitis and TB laboratory screenings were counted as present if there was documentation of these completed

laboratories in the patient's chart at any time prior to the DMARD initiation or up to one month after.

Hepatitis screening care gap closure for all patients who started a new DMARD was defined as meeting the laboratory screening criteria for both HBV (Hepatitis B surface antigen and Hepatitis B core antibody, at least Immunoglobulin M) and HCV (Hepatitis C antibody or hepatitis C Ribonucleic acid quantitative test). The percentages of HBV and HCV screened patients who started a new DMARD were calculated, respectively. The care gap closure for rheumatic patients who started a new bDMARD or tsDMARD was defined as meeting both screening laboratory components: hepatitis (HBV and HCV) and TB testing. The percentages of HBV, HCV, and TB screened patients were calculated, respectively. The Chi square method was used for the statistical analysis of the data comparison pre- and post-intervention.

Subgroup analyses were performed comparing laboratory screening of patients managed by rheumatologists alone versus rheumatologist-pharmacist co-management during the same post-intervention time frame. The care gap closure rates for screening laboratories of patients who started DMARDs were captured. Subgroup analysis was calculated using the Chi square method.

At the initiation of our project, the study was reviewed and approved for exemption by Geisinger Institutional Review Board.

Results:

During the 30-month period, hepatitis care gap closure rates for patients who started new DMARDs were examined at baseline between 6/1/2019 - 5/31/2020 in 720 patients screened by rheumatologists alone and post-intervention between 6/1/2020 -11/30/2021 in 1076 patients screened by rheumatologist-pharmacist co-management (Table 1). HBV and HCV screening for new DMARDs increased from 79% and 83% at baseline to 86% (P=0.0004) and 87% (P=0.0109) post-intervention, respectively. The care gap closure rates for total hepatitis (HBV and HCV) screening in all patients who started new DMARDs increased from 77% at baseline to 82% (P=0.005) post-intervention (Table 1). During the same baseline and post-intervention time intervals as mentioned above, the care gap closure rates for hepatitis/TB screening for patients who started a new bDMARD or tsDMARD were examined at baseline in 443 patients screened by rheumatologists alone and post-intervention in 482 patients screened by rheumatologist-pharmacist co-management. HBV and HCV screening increased from 84% and 85% at baseline to 90% (P=0.008) and 91% (P=0.01) post-intervention, respectively. TB screening increased from 89% at baseline to 95% (P=0.002) post-intervention whereas the average care gap closure for combined hepatitis/TB screening increased from 75% at baseline to 85% (P=0.0005) post-intervention (Table 1).

Table 1. Screening laboratories of patients who started a new DMARD or a new bDMARD/tsDMARD at baseline with rheumatologists alone versus post-intervention with rheumatologist-pharmacist co-management.

Pre-screen laboratories	Time frame	% Hepatitis B screening completed	% Hepatitis C screening completed	% TB screening completed	% screening care gap closure
All New DMARDS					
Pre-intervention: rheumatologist management	6/1/2019 – 5/31/2020	571/720 (79%)	595/720 (83%)	N/A	551/720 (77%)
Post-intervention: rheumatologist-pharmacists co-management	6/1/2020 – 11/30/2021	921/1076 (86%)	936/1076 (87%)	N/A	882/1076 (82%)
P-value		0.0004	0.0109	N/A	0.005
bDMARDs/tsDMARDs alone					
Pre-intervention: rheumatologist management	6/1/2019 – 5/31/2020	372/443 (84%)	378/443 (85%)	395/443 (89%)	334/443 (75%)
Post-intervention: rheumatologist-pharmacist co-management	6/1/2020 – 11/30/2021	433/482 (90%)	437/482 (91%)	456/482 (95%)	408/482 (85%)
P-value		0.008	0.01	0.002	0.0005

bDMARD: biologic disease modifying anti-rheumatic drug; DMARD: disease modifying anti-rheumatic drug; TB: tuberculosis (PPD or QuantiFERON-TB Gold); tsDMARD: targeted synthetic disease modifying anti-rheumatic Drugs.

Subgroup analysis of the post-intervention period between 6/1/2020 -11/30/2021 concomitantly compared laboratory screening rates between rheumatologist's alone vs rheumatologist-pharmacist protocolized co-management (Table 2). The hepatitis care gap closure rates for patients who started a new DMARD were examined in 921 patients screened by rheumatologists alone and 155 patients screened by rheumatologist-pharmacist co-management. HBV and HCV screening percentages by rheumatologists alone were 84% and 85% compared with screening percentages by rheumatologist-pharmacist co-management of 95% (P=0.0001) and 97% (P=0.00003), respectively. The total hepatitis care gap closure rates were 80% for rheumatologists versus 95% (P=0.000) for rheumatologist-pharmacist co-management (Table 2). The care gap closure rates for hepatitis/TB screening for patients who started a new bDMARD or tsDMARD were examined in 419 patients screened by rheumatologists alone and in 63 patients screened by rheumatologist-pharmacist co-management. The rheumatologists' screening rates were 89% for HBV and 89% for HCV when compared with rheumatologist-pharmacist co-management screening rates of 98% (P=0.016) and 98% P=0.023) respectively. Rheumatologists' screening rates for TB were 95% compared with rheumatologist-pharmacist co-management screening rates of 95% (P=0.81). The average care gap closure rates for hepatitis/TB screening were 83% for rheumatologists alone compared to 94% (P=0.033) for rheumatologist-pharmacist co-management post-intervention (Table 2).

Table 2. Post-intervention subgroup comparison of care gap closures of patients who started a new DMARD or a new bDMARD/tsDMARD with rheumatologists alone vs rheumatologist-pharmacist co-management.

Pre-screen laboratories Post-intervention	Time frame	% Hepatitis B screening completed	% Hepatitis C screening completed	% TB screening completed	% Screening care gap closure
All New DMARDS					
Post-intervention: rheumatologist management	6/1/2020 – 11/30/2021	773/921 (84%)	785/921 (85%)	N/A	735/921 (80%)
Post-intervention: rheumatologist-pharmacists co-management	6/1/2020 – 11/30/2021	148/155 (95%)	151/155 (97%)	N/A	147/155 (95%)
P-value		0.0001	0.00003	N/A	0.000
bDMARDs/tsDMARDs alone					
Post-intervention: rheumatologist management	6/1/2020 – 11/30/2021	371/419 (89%)	375/419 (89%)	396/419 (95%)	349/419 (83%)
Post-intervention: rheumatologist-pharmacists co-management	6/1/2020 – 11/30/2021	62/63 (98%)	62/63 (98%)	60/63 (95%)	59/63 (94%)
P-value		0.016	0.023	0.81	0.033

bDMARD: biologic disease modifying anti-rheumatic drug; DMARD: disease modifying anti-rheumatic drug; TB: tuberculosis (PPD or QuantiFERON-TB Gold); tsDMARD: targeted synthetic disease modifying anti-rheumatic Drugs.

Discussion:

This study showed that HBV and HCV screening rates significantly improved in the rheumatic population who started new DMARDs and were co-managed by the rheumatologist-pharmacist team. Similarly, HBV, HCV, and TB screening rates significantly improved in rheumatic individuals who started new bDMARDs or tsDMARDs and were co-managed. Furthermore, in the post-intervention subgroup analysis, when comparing usual care with rheumatologists alone versus the co-managed care, HBV and HCV screening rates in patients who started new DMARDs were significantly higher in the co-managed group. TB screening rates were similar between rheumatologist managed patients and the co-managed patients starting a new bDMARD or tsDMARD.

There was a significant screening improvement with co-managed care in all metrics except for tuberculosis screening which was similar among the two groups in the post-intervention sub-analysis. This similarity may be attributed to a possible

Hawthorne effect in patients managed by the rheumatologists alone after the introduction of guideline driven protocols among the rheumatologist-pharmacist co-management team. These protocols were available to all clinicians in the department which may have contributed to a modification in the rheumatologists' behavior. (TB screening completion of 95% was achieved in both rheumatologists alone and co-managed patients, post-intervention P=0.81).

Our data suggests that a care gap existed in all screening laboratories for patients who started a new DMARD when managed by rheumatologists alone. With the introduction of rheumatologist-pharmacist co-management to our rheumatology department, HBV and HCV screening rates for new DMARD patients and HBV, HCV, and TB screening rates for new bDMARDs or tsDMARDs patients were significantly improved. Additionally, the overall care gap closure rates for screening laboratories significantly increased in our newly immunosuppressed rheumatic population. Through the implementation of the clinical pharmacist into the rheumatology team, and the use of specialized guideline-driven protocols, we significantly narrowed the infectious laboratory care gaps across all fronts.

Avoiding harm to patients from the care intended to help them is essential, but difficult to achieve in the current environment of insufficient rheumatology staff and overwhelming patient care responsibilities. The integration of clinical pharmacists into our team introduced collaborative teamwork and shared responsibility in a safe expert-driven patient management setting. Our partnership helped us start a new healthcare delivery model which is safe and effective.

Since the initiation of our study, the rheumatology clinical pharmacists have expanded their patient co-management services to include roles in medication education, medication refills, and initiation of pre-authorization requests. This was achieved by carefully designed guideline driven medication criteria protocols in conjunction with pharmacist training of rheumatic medications and diseases. In turn, this new care model has allowed the rheumatologists to spend more time with the patients and decrease the clinical in-basket physician workload burden.[15]

To our knowledge, this is one of the first rheumatology programs in the United States and worldwide to implement such a partnership with mechanisms in place to ensure all pre-screening infectious laboratories are completed with data pre- and post-intervention. Kaiser Permanente reported creating an alert system in their infusion orders via their multidisciplinary team of physicians and pharmacists to identify HBV infections in patients on anti-CD20 therapeutics, however no further data are available.[16]

In our study, we describe the implementation of pharmacists in the care of acutely flaring rheumatic patients, while Chew et al. described a model of care where advanced practitioners including pharmacists were involved in the routine monitoring of chronic medications of rheumatic conditions such as gout, stable rheumatoid arthritis or seronegative spondyloarthropathy in the Singapore General Hospital.[14] In Chew's study, pharmacists with DMARD prescribing ability primarily co-managed chronic stable patients but reviewed with the rheumatologist as the need arose. Both patients and physicians were satisfied by the process.[14] Implementation of pharmacists in other medical specialties has demonstrated improved medication adherence, hypertension and hyperlipidemia care, and reduced hospitalizations for congestive heart failure.[17,18] To our understanding, this type of unique multidisciplinary care is still novel in the rheumatology setting.

One limitation of our study is that we did not directly measure the patient or rheumatologist satisfaction with the rheumatologist-pharmacist collaboration. Furthermore, there may have been an initial personal bias among some rheumatologists about entrusting patient care to another healthcare professional. However, the data from our rheumatologists from a previous study by Rottmann et al., which looked at DMARD refills by pharmacists, suggested that rheumatologists reported positive feedback from their patients and became personally engaged in the collaborative work with the pharmacists.[15] Additionally, in their study, no adverse events were reported by patients or rheumatologists during the co-management. They adopted a standardized approach to care, with the development of a protocol and pre-authorization smartset to build a trusting collaborative multidisciplinary team, working toward providing safer patient care. [15]

Another limitation was that there was no randomization of patients to the physician alone versus rheumatologist-pharmacist co-management arm during the intervention phase, relying rather on the rheumatologist requesting the co-management which generated a self-selection element. Despite the possibility of a Hawthorne effect, laboratory screening and care gap closures remained significantly higher in the rheumatologist-pharmacist

co-managed group compared to rheumatologists' group during the same time frame.

Today, we are one step closer to fulfilling one of the aims of the framework set forth by the Institute of Medicine: providing safer care for our rheumatic population.[19] We achieved this with the implementation of rheumatology pharmacists to our team. This novel approach to patient care has proven successful and has great potential for reproducibility and spread of pharmacist integration through different medical institutions and rheumatology teams.

Conflicts of Interest: The authors have no conflicts of interest to disclose.

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