EFFECTIVENESS OF ACTIVE ADVERSE DRUG REACTION SURVEILLANCE FOR FIRST-LINE ANTI-TUBERCULOSIS DRUGS AT HAI PHONG LUNG HOSPITAL

Tran Thi Ngan[1*], Hoang Anh Vu[2], Nguyen Thi Thu Phuong[1]

ABSTRACT

Background: Adverse drug reactions (ADRs) related to first-line anti-tuberculosis (TB) drugs remain a major challenge, potentially affecting treatment adherence and outcomes. In many settings, ADR surveillance relies mainly on passive reporting, which may lead to under-detection. ***Objectives:*** To evaluate the effectiveness of pharmacist-led active ADR surveillance for first-line anti-TB drugs at Hai Phong Lung Hospital. ***Methods:*** A longitudinal before–after study compared passive ADR reporting (January 2023–November 2024) with pharmacist-led active surveillance (December 2024–May 2025) among hospitalized TB patients. Outcomes included ADR reporting frequency, ADR report quality, and the proportion of potentially preventable ADRs. Interrupted time series (ITS) analysis was used to assess changes following implementation. ***Results:*** During the passive surveillance phase, 130 ADR reports were recorded from 9,459 inpatient medical records, compared with 190 reports from 2,971 inpatient medical records during active surveillance. Implementation of pharmacist-led active surveillance was associated with a significant increase in ADR reporting from 1.40 to 6.32 ADRs per 100 inpatient records. Interrupted time series analysis demonstrated a significant immediate increase in the ADR reporting rate, corresponding to approximately 5.12 additional ADR reports per 100 inpatient records ($\beta = 5.12$; $p < 0.001$). The mean ADR report quality score improved from 0.84 to 0.99, with a significant immediate increase after the intervention ($\beta = 0.14$; $p < 0.001$) and a significant increasing post-intervention trend ($p = 0.001$). The proportion of potentially preventable ADRs decreased from 14.62% to 10.52%, with a significant decreasing trend during the post-intervention period ($\beta = -3.99$; $p = 0.002$), corresponding to an average reduction of approximately 4 percentage points per month. ***Conclusions:*** Pharmacist-led active ADR surveillance significantly improved ADR reporting frequency and quality and reduced potentially preventable ADRs in hospitalized TB patients, supporting its role in enhancing medication safety in TB treatment settings.

Keywords: *adverse drug reactions; anti-tuberculosis drugs; active surveillance; clinical pharmacist.*

I. INTRODUCTION

Tuberculosis (TB) remains one of the leading infectious diseases imposing a significant public health burden worldwide and in Vietnam. According to the World Health Organization (WHO), an estimated 10.7 million new TB cases were reported globally in 2024, with Vietnam ranking among the 30 countries with the highest TB burden worldwide (1). One of the major challenges in TB treatment is the management and prevention of adverse drug reactions (ADRs) associated with anti-tuberculosis medications, particularly hepatotoxicity, gastrointestinal disturbances, cutaneous reactions, visual impairment, and peripheral neuropathy related to first-line anti-TB drugs. The reported incidence of ADRs during tuberculosis treatment varies widely, ranging from 8% to 85%, depending on patient characteristics, treatment regimens, and monitoring methods (2, 3). These ADRs may compromise drug tolerability and treatment adherence, leading to treatment interruption or premature discontinuation, reduced therapeutic effectiveness, and an increased risk of drug-resistant TB. Therefore, ADR surveillance in TB treatment is a critical component of national TB control strategies, aiming to ensure medication safety and improve the therapy outcomes (4). However, in many healthcare settings, ADR surveillance still relies predominantly on voluntary reporting systems (passive surveillance), which often lead to underreporting, particularly for mild to moderate ADRs that nonetheless have a significant impact on treatment adherence. Active ADR surveillance enables early detection, systematic assessment, and timely intervention for adverse drug reactions, thereby reducing the risk of serious drug-related events and improving patient adherence to TB treatment (5).

[1] *Faculty of Pharmacy, Hai Phong University of Medicine and Pharmacy, Hai Phong, Vietnam*
[2] *Department of Pharmacy, Hai Phong Lung Hospital, Hai Phong, Vietnam*
Responsible person: Tran Thi Ngan
Email: ttngan@hpmu.edu.vn
Date of receipt: 22.1.2026
Date of scientific judgment: 12.3.2026
Reviewed date: 23.4.2026

Hai Phong Lung Hospital is a leading specialized center for tuberculosis diagnosis and treatment in Hai Phong city and the Northern coastal region of Vietnam, with a large number of hospitalized tuberculosis patients annually. A pharmacist-led active ADR surveillance model has been implemented at the hospital with the potential to improve medication safety; however, its effectiveness has not been systematically evaluated. Therefore, this study aimed to assess the effectiveness of active ADR surveillance for first-line anti-tuberculosis drugs at Hai Phong Lung Hospital between December 2024 and May 2025. The findings are expected to provide evidence to support the implementation and standardization of active ADR surveillance in tuberculosis care in Vietnam.

II. METHODS

Study design and setting

A longitudinal before–after study was conducted at Hai Phong Lung Hospital, Vietnam. Two surveillance phases were compared: a passive ADR surveillance phase from January 2023 to November 2024 and an active pharmacist-led ADR surveillance phase from December 2024 to May 2025.

Study population

The study included ADR reports related to first-line anti-TB drugs (rifampicin, isoniazid, pyrazinamide, ethambutol, and streptomycin). During the passive phase, all ADR reports routinely submitted to the hospital pharmacy department were included. During the active phase, hospitalized patients receiving at least one first-line anti-TB drug for at least 24 hours were monitored for ADRs.

Active ADR surveillance intervention

Active surveillance was conducted by a clinical pharmacist across inpatient TB wards. Activities included weekly participation in clinical ward rounds, systematic review of medical records, monitoring of laboratory results, and direct interviews with patients, caregivers, and healthcare staff to identify suspected ADRs. Pharmacist recommendations were provided to physicians when clinically significant or potentially preventable ADRs were identified.

Assessment of ADRs

The causal relationship between drugs and ADRs was assessed using the Naranjo algorithm, the quality of ADR reports was evaluated using the VigiGrade completeness score developed by the WHO Collaborating Centre for International Drug Monitoring, the preventability of ADRs was assessed using the WHO preventability criteria (5). All assessments were conducted independently by trained pharmacists, with consensus reached through discussion when discrepancies occurred.

Outcome measures

Primary outcomes included the frequency of ADR reports, quality scores of ADR reports, and the proportion of potentially preventable ADRs.

Statistical analysis

Data were analyzed using Microsoft Excel 2016 and R software version 4.3.1. Statistical analyses were performed using Microsoft Excel and R software. The effectiveness of active surveillance was evaluated using interrupted time series (ITS) analysis with segmented regression models. For ADR reporting frequency and ADR report quality score, segmented linear regression with Newey–West heteroskedasticity- and autocorrelation-consistent standard errors was applied. For the proportion of potentially preventable ADRs, segmented regression was conducted on monthly proportions (%), with results expressed as absolute percentage-point changes; a binomial segmented regression using counts was performed as a sensitivity analysis. All statistical tests were two-sided, and p-values < 0.05 were considered statistically significant.

Ethical considerations

The study protocol was reviewed and approved by the Scientific and Training Committee of Hai Phong University of Medicine and Pharmacy, as well as the Scientific and Technical Council of Hai Phong Lung Hospital.

III. RESULTS

A total of 130 ADR reports were recorded from 9,459 inpatient medical records during the passive surveillance phase, whereas 190 ADR reports were identified from 2,971 inpatient medical records during the active surveillance phase. The effectiveness of active surveillance was evaluated based on three main criteria: (1) the number and rate of ADR reports, (2) the quality score of ADR reports, and (3) the proportion of potentially preventable ADRs.

Effect of active surveillance on the number of ADR reports

The effect of active surveillance on ADR reporting frequency is summarized in Figure 1 and Table 1. The mean ADR reporting rate increased markedly from 1.40 ADR reports per 100 inpatient records during the passive surveillance period to 6.32 ADR reports per 100 inpatient records during the active surveillance period. Interrupted time series analysis demonstrated a statistically significant immediate increase in the ADR reporting rate following implementation of active surveillance, corresponding to approximately 5.12 additional ADR reports per 100 inpatient records (β = 5.12; 95% CI 3.64–6.60; p < 0.001). The pre-intervention trend showed a slight but non-significant increase (β = 0.04; p = 0.094), and no statistically significant change in the post-intervention monthly trend was observed during the six-month follow-up period (β = −0.22; p = 0.383).

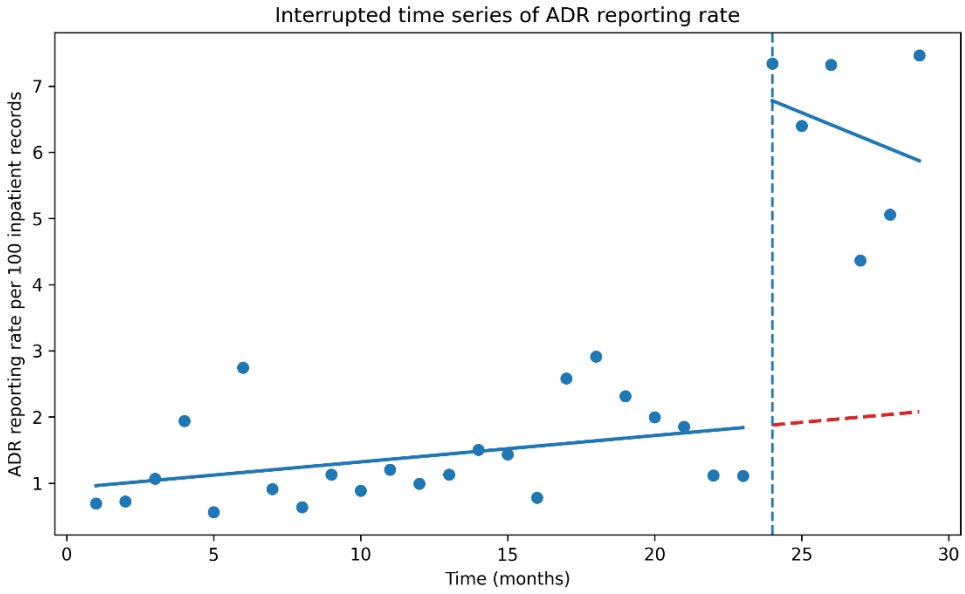

Figure 1. Interrupted time series of ADR reporting rate from January 2023 to May 2025. Dots represent monthly ADR reporting rates. Solid lines indicate the observed trends before and after the intervention, while the red dashed line represents the counterfactual trend assuming no intervention. The vertical dashed line indicates the start of active surveillance in November 2024.

Table 1. Segmented interrupted time series analysis of ADR reporting rate following implementation of active surveillance

Model component	Regression coefficient, β (SE*)	95% CI	p-value†	Clinical interpretation
Baseline monthly trend (pre-intervention)	0.040 (0.023)	−0.005-0.085	0.094	ADR reporting rate showed a non-significant increasing trend before the intervention.
Immediate change after implementation of active surveillance (Nov 2024)	**5.122 (0.756)**	**3.641-6.603**	**<0.001**	Immediate and statistically significant increase in ADR reporting rate after active surveillance was implemented.
Change in monthly trend after implementation	−0.221 (0.250)	−0.711-0.268	0.383	No statistically significant change in the post-intervention monthly trend.

** SE: Newey–West heteroskedasticity- and autocorrelation-consistent standard errors.*

† p-values correspond to Newey–West robust inference.

Effect of active surveillance on the quality of ADR reports

The effect of active surveillance on ADR report quality is summarized in Figure 2 and Table 2. The mean quality score of ADR reports increased markedly from 0.84 during the passive surveillance period to 0.99 during the active surveillance period, indicating near-complete reporting after implementation of active surveillance. Interrupted time series analysis demonstrated a statistically significant immediate improvement in the mean ADR report quality score (β = 0.14; 95% CI 0.13–0.15; p < 0.001). No significant change was observed in the pre-intervention trend, whereas a modest but statistically significant increasing trend in ADR report quality was observed during the post-intervention period (p = 0.001).

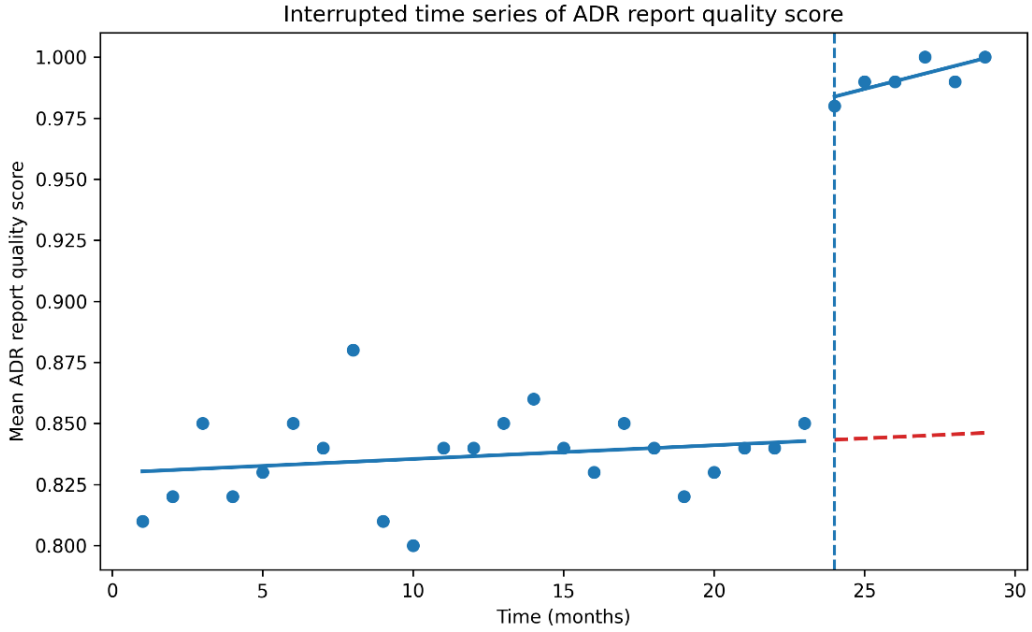

Figure 2. Interrupted time series of ADR report quality score from January 2023 to May 2025. Dots represent the monthly mean ADR report quality scores. Solid blue lines indicate the observed trends before and after the intervention, while the red dashed line represents the counterfactual trend assuming no intervention. The vertical dashed line indicates the start of active surveillance in November 2024.

Table 2. Segmented interrupted time series analysis of ADR report quality score

Model component	Regression coefficient, β (SE*)	95% CI	p-value†	Clinical interpretation
Baseline monthly trend (pre-intervention)	0.0006 (0.0005)	−0.0003 - 0.0014	0.200	No significant change in ADR report quality before the intervention.
Immediate change after implementation of active surveillance (Nov 2024)	**0.138 (0.006)**	**0.127 - 0.149**	**<0.001**	Immediate and significant improvement in ADR report quality after active surveillance.
Change in monthly trend after implementation	**0.0026 (0.0008)**	**0.001 - 0.004**	**0.001**	Significant increasing trend in ADR report quality during the post-intervention period.

** **SE:** Newey–West heteroskedasticity- and autocorrelation-consistent standard errors. † p-values correspond to Newey–West robust inference.*

Effect of active surveillance on the proportion of potentially preventable of ADR reports

The effect of active surveillance on the proportion of potentially preventable ADRs is summarized in Figure 3 and Table 3. The proportion of potentially preventable ADRs decreased significantly after pharmacist-led active surveillance, with the mean proportion declining from 14.62% during the passive surveillance period to 10.52% during the active surveillance period. Interrupted time series analysis did not show a statistically significant immediate change at the start of active surveillance (p = 0.303); however, a significant decreasing trend was observed during the post-intervention period (β = −3.99; 95% CI −6.57 to −1.41; p = 0.002), corresponding to an average reduction of approximately 4 percentage points per month.

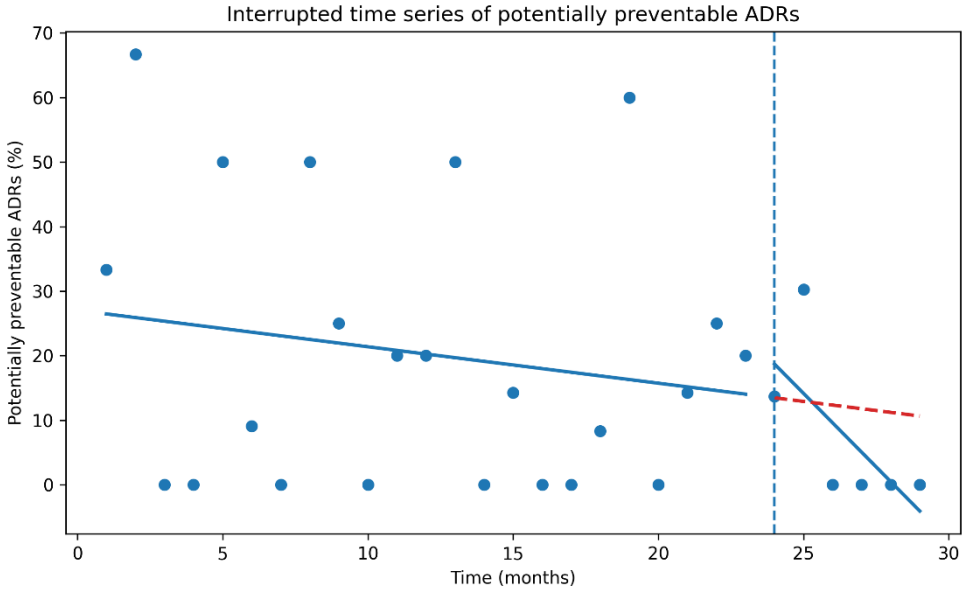

Figure 3. Interrupted time series of potentially preventable ADRs from January 2023 to May 2025. Dots represent the monthly proportion of potentially preventable ADRs. Solid blue lines indicate the observed trends before and after the intervention, while the red dashed line represents the counterfactual trend assuming no intervention. The vertical dashed line indicates the start of pharmacist-led active surveillance in November 2024.

Table 3. Segmented interrupted time series analysis of potentially preventable ADRs (%) following implementation of active surveillance

Model component	Regression coefficient, β (SE*)	95% CI	p-value†	Clinical interpretation
Baseline monthly trend (pre-intervention)	−0.565 (0.598)	−1.737-0.608	0.345	No significant change in the proportion of potentially preventable ADRs before the intervention.
Immediate change after implementation of active surveillance (Nov 2024)	9.210 (8.941)	−8.314-26.733	0.303	No statistically significant immediate change at the start of active surveillance.
Change in monthly trend after implementation	**−3.987 (1.317)**	**−6.568-−1.407**	**0.002**	Significant decreasing trend in potentially preventable ADRs during the post-intervention period (approximately 4 percentage points decrease per month).

** SE: Newey–West heteroskedasticity- and autocorrelation-consistent standard errors.*

† p-values correspond to Newey–West robust inference.

IV. DISCUSSION

This study evaluated the effectiveness of pharmacist-led active ADR surveillance in the treatment of tuberculosis with first-line anti-tuberculosis drugs at Hai Phong Lung Hospital using three key criteria: the number of ADR reports, the quality of ADR reports, and the proportion of potentially preventable ADRs. The findings demonstrated that active ADR surveillance resulted in substantial improvements, particularly a marked immediate increase in both the quantity and quality of ADR reports following implementation, while also contributing to a reduction in the proportion of potentially preventable ADRs. Notably, to the best of our knowledge, this is the first study in Vietnam to implement a pharmacist-led active ADR surveillance model for first-line anti-tuberculosis drugs in a specialized hospital setting and to evaluate its effectiveness using interrupted time series (ITS) analysis. The application of ITS analysis enabled quantification of both the immediate impact of the intervention and subsequent temporal trends, thereby providing robust evidence of the real-world impact of active ADR surveillance in clinical practice.

The number of ADR reports increased significantly immediately after implementation of pharmacist-led active surveillance, highlighting the important role of clinical pharmacists in detecting and documenting ADRs in settings where routine surveillance largely relies on voluntary reporting by physicians and nurses. This finding is consistent with previous study showing that active surveillance and clinical pharmacy interventions substantially increase the detection of ADRs related to anti-tuberculosis drugs compared with spontaneous reporting alone (6). In this study, several ADRs identified during the active surveillance period were detected through abnormal laboratory findings, such as elevated liver enzymes and increased uric acid levels, which were not captured during the passive surveillance phase, indicating that active surveillance expands the scope of ADR detection. However, no statistically significant long-term trend change in ADR reporting was observed after the intervention, which may be attributable to the relatively short post-intervention follow-up period (six months) and a potential initial intervention effect. These findings suggest that sustained effectiveness of active ADR surveillance requires integration with continuous training, regular feedback, and standardized ADR reporting procedures.

In addition to increasing the number of ADR reports, this study demonstrated a statistically significant improvement in the quality of ADR reporting following the intervention. The mean ADR report quality score increased from 0.84 during the passive surveillance period to 0.99 during the active surveillance period, and interrupted time series analysis showed an immediate post-intervention increase of 0.138 points. These findings indicate that active ADR surveillance not only facilitates the detection of more ADRs but also enhances the completeness and accuracy of information included in ADR reports. This improvement has important clinical implications, as the quality of ADR reports directly affects the assessment of causality, severity, and the formulation of appropriate risk management strategies. In passive surveillance systems, ADR reports often lack critical information such as suspected and concomitant medications, the temporal relationship between drug exposure and ADR onset, clinical course after drug withdrawal, and relevant laboratory findings (7). The direct involvement of pharmacists in ADR surveillance, detection, and report completion likely mitigated these limitations, thereby contributing to the observed improvement in ADR report quality.

One notable finding of this study was the significant reduction in the proportion of potentially preventable ADRs following implementation of active surveillance, with the mean proportion decreasing from 14.62% during the passive surveillance period to 10.52% during the active surveillance period. Notably, no potentially preventable ADRs were recorded during the final four months of active surveillance. Although interrupted time series analysis did not demonstrate a statistically significant immediate level change at the start of the intervention, a significant decreasing trend was observed during the post-intervention period, indicating a sustained reduction in potentially preventable ADRs over time. Most preventable ADRs identified in this study were

gastrointestinal events, such as nausea and diarrhea, commonly associated with combination regimens containing rifampicin, isoniazid, and pyrazinamide. Pharmacist-led interventions primarily focused on counseling patients on modifying dosing schedules to reduce gastrointestinal adverse effects. These interventions are simple, low-cost, and clinically effective, contributing to improved drug tolerability and treatment adherence. This finding is consistent with previous studies reporting that a substantial proportion of ADRs in tuberculosis treatment are preventable through optimization of medication use, close monitoring, and patient education (8).

The findings of this study underscore the important role of clinical pharmacists in ADR surveillance, particularly in tuberculosis treatment, which involves multidrug regimens and prolonged treatment duration. Implementation of active ADR surveillance not only increased the quantity and quality of ADR reports but also contributed to a reduction in the proportion of potentially preventable ADRs through timely clinical pharmacy interventions. However, this study has several limitations. The post-intervention follow-up period was relatively short, which may not fully capture the long-term impact of active ADR surveillance. In addition, the study was conducted at a single specialized hospital, and the findings may not be generalizable to other healthcare settings. Further studies with longer follow-up periods and implementation across multiple healthcare facilities are warranted to confirm the sustainability and scalability of this pharmacist-led active ADR surveillance model.

V. CONCLUSIONS

Active ADR surveillance led by clinical pharmacists improved ADR detection, reporting quality, and prevention of avoidable ADRs in hospitalized TB patients. This approach represents a feasible and effective strategy to enhance medication safety in TB treatment in Vietnam.

ACKNOWLEDGEMENTS

The authors thank Hai Phong Lung Hospital and Hai Phong University of Medicine and Pharmacy for supporting this study.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. **Global Programme on Tuberculosis and Lung Health (GTB).** Global tuberculosis report 2025. World Health Organization; 2025.
2. **Singh A, Prasad R, Balasubramanian V, Gupta N, Gupta P.** Prevalence of adverse drug reaction with first-line drugs among patients treated for pulmonary tuberculosis. Clinical Epidemiology and Global Health. 2015 2015/01/01/;3:S80-S90.
3. **Marie Joyce Jorge, Christian Bernard Esporlas, Marie Louise Emille Largoza, Rosally Zamora.** Adverse Drug Events from First-Line Anti-tuberculosis Drugs in a Tertiary Medical Center. European Medical Journal. 2024;9(4):113-9.
4. **Thủ tướng Chính phủ.** Quyết định số 374/QĐ-TTg về Phê duyệt Chiến lược quốc gia phòng, chống lao đến năm 2020 và tầm nhìn đến năm 2030. 2014.
5. **Bộ trưởng Bộ Y tế.** Quyết định số 29/QĐ-BYT về Hướng dẫn giám sát phản ứng có hại của thuốc (ADR) tại các cơ sở khám bệnh, chữa bệnh. 2022.
6. **Lan T, Wang H, Li X, Yin H, Shao D, Jiang Y, et al.** The effect of clinical pharmacists' intervention in adverse drug reaction reporting: a retrospective analysis with a 9-year interrupted time series. BMC health services research. 2022 Jul 19;22(1):925. PubMed PMID: 35854263. PMCID: PMC9295299. Epub 2022/07/20. eng.
7. **Ngân TT, Linh HDP, Phương NTT.** Phân tích hoạt động báo cáo phản ứng có hại của thuốc (ADR) tại bệnh viện Đa khoa Quốc tế Hải Phòng năm 2023. Y học Việt Nam. 2024;545 (số đặc biệt):4-52.
8. **Hareesh Kumar R, Lalitha Krishnappa, Pavithra Cheluvaraj, Radhika K, Akshata J S, Somasekhar M.** Adverse Drug Reactions During Intensive Phase of Treatment Among Multi- Drug Resistant Tuberculosis Cases Registered at a DR-TB Centre of Southern India. African Journal of Biomedical Research. 2024 09/20;27(1S):1667-73.