Prescribing Trends and Rationality Analysis of Fixed-Dose Combinations: A Cross-Sectional Study in Bangladesh

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Abstracts

Background: Fixed-dose combinations (FDCs) are increasingly used in clinical practice to enhance therapeutic efficacy, reduce pill burden, and improve patient adherence. However, irrational prescribing of FDCs remains a significant concern, particularly in low- and middle-income countries such as Bangladesh, where regulatory oversight may be limited. Irrational FDCs can increase adverse drug reactions, financial burden, and contribute to antimicrobial resistance.

Objective: This study aimed to evaluate the prescribing trends and assess the rationality of FDCs in a tertiary care hospital in Bangladesh.

Methods: A cross-sectional observational study was conducted at the Department of Pharmacology, Community Based Medical College Hospital, Bangladesh, over a period of January to December 2025**,** including 89 randomly collected prescriptions from outpatient departments. Data on patient demographics, diagnosis, and prescribed FDCs were recorded using a structured form. Each FDC was classified as rational or irrational based on standard treatment guidelines, pharmacological compatibility, and recommendations from the WHO and the Bangladesh National Essential Medicines List. Data were analyzed using SPSS version 25, with descriptive statistics (frequency and percentage) and Chi-square tests to assess associations between diagnosis, demographics, and rationality. A p-value <0.05 was considered statistically significant.

Results: Among the 89 prescriptions, 61 (68.5%) contained at least one FDC. Of these, 34 (55.7%) were rational, while 27 (44.3%) were irrational. Amoxicillin + Clavulanic acid was the most frequently prescribed rational combination, and Ciprofloxacin + Tinidazole was the most common irrational combination. Chi-square analysis revealed a significant association between diagnosis and rationality ($\chi^2 = 9.82$, df = 3, p = 0.02), indicating higher rational FDC prescribing for infectious conditions compared to gastrointestinal or pain-related conditions.

Conclusion: While rational FDC prescribing is observed, a substantial proportion of prescriptions remain irrational, underscoring the need for stronger guideline enforcement, prescriber education, and awareness programs to promote safe and effective pharmacotherapy.

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Introduction

Fixed-dose combinations (FDCs) are pharmaceutical formulations that combine two or more active pharmacological agents in a single dosage form with a fixed ratio. These combinations have gained considerable importance in modern therapeutics due to their potential to enhance patient compliance, improve therapeutic outcomes, and reduce pill burden, particularly in the management of chronic and infectious diseases such as hypertension, diabetes mellitus, tuberculosis, and human immunodeficiency virus (HIV) infection.[1] The rationale for using FDCs is primarily based on pharmacological synergy. Drugs combined in an FDC often have complementary mechanisms of action, which may enhance efficacy while minimizing adverse effects compared to individual administration.[2] For instance, the combination of amoxicillin with clavulanic acid not only broadens the antibacterial spectrum but also reduces the risk of resistance, demonstrating the clinical utility of well-designed FDCs.[3] Furthermore, simplified regimens with fewer pills have been associated with improved adherence, particularly among patients on long-term therapy, the elderly, and individuals with multiple comorbidities.[4] Despite these clear benefits, the irrational use of FDCs has emerged as a significant global concern. Irrational FDCs are those combinations that are not supported by scientific evidence regarding efficacy, safety, or pharmacokinetic compatibility.[5] Such combinations may expose patients to unnecessary medications, increase the risk of adverse drug reactions, and escalate healthcare costs. Moreover, irrational FDCs, especially involving antibiotics, contribute to the emergence of antimicrobial resistance, which poses a major public health threat worldwide.[6] The problem of irrational FDC use is particularly prominent in low- and middle-income countries, including Bangladesh. Contributing factors include inadequate regulatory oversight, the availability of numerous over-the-counter drug combinations, and aggressive pharmaceutical marketing.[7] Prescribers may also lack up-to-date knowledge regarding evidence-based FDC use, leading to inappropriate prescription patterns. Studies in South Asia have reported that a large proportion of commercially available FDCs are not recommended in standard treatment guidelines and may pose significant health risks.[8] Evidence from various countries indicates a persistent problem of irrational prescribing. In India, for example, multiple studies have documented that a significant number of FDCs in the market lack scientific justification, and many were banned due to safety concerns.[9] Similarly, in Nepal, research has revealed widespread use of irrational FDCs, particularly in outpatient settings, highlighting the need for stricter enforcement of guidelines.[10] In the context of Bangladesh, although the National Essential Medicines List (NEML) includes a limited number of approved FDCs, irrational combinations are still widely available and prescribed, emphasizing the gap between regulatory policy and clinical practice.[11] The implications of irrational FDC prescribing extend beyond clinical safety. Patients may be subjected to unnecessary financial burden due to the cost of redundant or ineffective combinations. Additionally, healthcare providers face challenges in monitoring adverse effects, as it becomes difficult to attribute a side effect to a specific drug in a multi-drug combination.[5] Such practices can compromise the overall quality of care and patient trust in the healthcare system. While rational FDCs have documented advantages, such as improved compliance, synergistic efficacy, and reduced pill burden, there remains a need for systematic evaluation of prescribing patterns in clinical settings. Regular audits of FDC use can identify trends, highlight irrational combinations, and

inform policy interventions. Several global and regional guidelines, including those of the World Health Organization (WHO), recommend the use of FDCs only when supported by robust clinical evidence and when the combination offers therapeutic advantages over single-drug therapy. [10] Given the increasing reliance on FDCs in Bangladesh and the lack of comprehensive studies evaluating their rationality, there is a pressing need for research in this area. Assessing prescribing patterns, identifying the most commonly used combinations, and classifying them as rational or irrational will provide critical insights. Such evidence can guide prescribers, inform national policies, and promote rational drug use, thereby enhancing patient safety and treatment effectiveness. Therefore, the present study was undertaken to evaluate the prescribing trends and rationality of fixed-dose combinations in a tertiary care hospital in Bangladesh. By providing evidence on current practices, this research aims to contribute to the rational use of medications and support the development of guidelines that minimize risks associated with irrational drug combinations.

Objectives

General Objective:

- To evaluate the prescribing trends and rationality of fixed-dose combinations

Specific Objectives:

- To identify commonly prescribed FDCs
- To classify FDCs as rational or irrational
- To analyse demographic characteristics of patients receiving FDCs

Methods

This cross-sectional observational study was conducted at the Department of Pharmacology, Community Based Medical College Hospital, Bangladesh, over a period of January to December 2025. The study aimed to evaluate prescribing patterns and assess the rationality of fixed-dose combinations (FDCs) in routine clinical practice. A total of 89 prescriptions were randomly collected from outpatient departments to serve as the study sample. Only prescriptions containing at least one drug were included in the analysis, while incomplete or illegible prescriptions were excluded to ensure data accuracy. Data were recorded using a structured data collection form, which included patient demographic details such as age and gender, the primary diagnosis, and details of all prescribed drugs, with a particular focus on fixed-dose combinations. Each FDC was subsequently classified as either rational or irrational based on established treatment guidelines, pharmacological compatibility, and recommendations from the World Health Organization and the Bangladesh National Essential Medicines List. The collected data were entered into SPSS version 25 for statistical analysis. Descriptive statistics, including frequency and percentage, were used to summarize the findings. Additionally, the Chi-square test was applied, where appropriate, to explore associations between patient demographics, diagnosis, and the rationality of prescribed FDCs. A p-value of less than 0.05 was considered statistically significant. This methodological approach ensured a comprehensive and systematic assessment of prescribing trends and rationality in the selected hospital setting.

Results

Out of 89 prescriptions analyzed, 52 (58.4%) were from male patients and 37 (41.6%) from female patients. A total of 61 prescriptions (68.5%) contained at least one fixed-dose combination. Among these, 34 (55.7%) were classified as rational, while 27 (44.3%) were identified as irrational. The most commonly prescribed rational FDC was amoxicillin with clavulanic acid (18 cases), followed by

sulfamethoxazole with trimethoprim (10 cases). The most frequent irrational FDCs included ciprofloxacin with tinidazole (12 cases), ibuprofen with paracetamol (8 cases), and omeprazole with domperidone (7 cases). Chi-square analysis revealed a statistically significant association between diagnosis and the rationality of prescribed FDCs ($\chi^2 = 9.82$, df = 3, p = 0.02), indicating that patients with infectious diseases were more likely to receive rational combinations compared to those with pain/inflammation or gastrointestinal conditions. These findings highlight that while rational prescribing exists, a substantial proportion of irrational FDCs continues to be prescribed, emphasizing the need for targeted interventions and adherence to standard treatment guidelines.

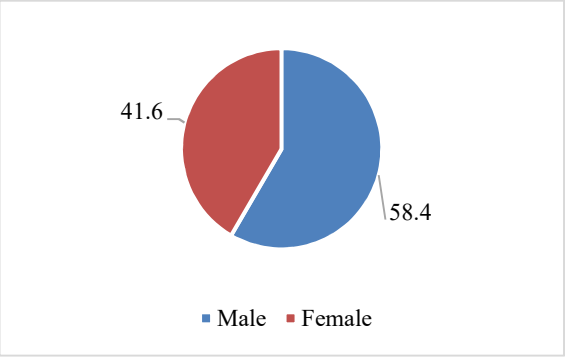

Figure 1. Distribution of Study Participants by Gender (n = 89)

Table I: Distribution of Prescriptions by Fixed-Dose Combination (FDC) Use (n = 89)

Category	Frequency (n)	Percentage (%)
Prescriptions containing FDC	61	68.5
Prescriptions without FDC	28	31.5

Table II: Distribution of Prescriptions by Rationality (n = 61)

Classification	Frequency (n)	Percentage (%)
Rational	34	55.7
Irrational	27	44.3

Table III: Frequency and Rationality Classification of Prescribed Fixed-Dose Combinations (FDCs)

FDC Name	Frequency (n)	Classification
Amoxicillin + Clavulanic acid	18	Rational
Sulfamethoxazole + Trimethoprim	10	Rational
Ciprofloxacin + Tinidazole	12	Irrational
Ibuprofen + Paracetamol	8	Irrational
Omeprazole + Domperidone	7	Irrational
Other FDCs	6	Mixed

Table IV: Diagnosis-wise Distribution of Rational and Irrational Prescriptions (n = 61)

Diagnosis	Rational n (%)	Irrational n (%)	Total n (%)	p-value
Infection	20 (66.7)	10 (33.3)	30 (100.0)	
Gastrointestinal	5 (38.5)	8 (61.5)	13 (100.0)	
Pain/Inflammation	3 (25.0)	9 (75.0)	12 (100.0)	0.02
Cardiovascular	6 (100.0)	0 (0.0)	6 (100.0)	
Total	34 (55.7)	27 (44.3)	61 (100.0)	

Discussion

The present cross-sectional analysis evaluated prescribing trends and the rationality of fixed-dose combinations (FDCs) in a tertiary care hospital in Bangladesh. The study revealed that 68.5% of the analyzed prescriptions contained at least one FDC, and of these, 55.7% were classified as rational while 44.3% were irrational, based on standard criteria. These findings reflect a mixed pattern of FDC prescribing practices, highlighting both appropriate and inappropriate use of combination medicines. FDCs are intended to simplify treatment regimens, enhance therapeutic efficacy, and improve patient adherence, especially in complex conditions that require multiple pharmacotherapies. Rational FDCs, such as the amoxicillin plus clavulanic acid combination observed frequently in this study, are evidenced to provide synergistic benefits by extending antimicrobial activity and reducing the likelihood of resistance when used appropriately.[11] This study's findings align with such rational applications in infectious disease management, where clinicians appear to prescribe evidence-based FDCs more frequently. However, irrational FDC use remains a pervasive concern, as seen in the substantial proportion (44.3%) of prescriptions flagged in this study. Irrational FDCs often lack scientific justification regarding pharmacodynamic and pharmacokinetic compatibility, dosage rationale, or proven therapeutic advantage. Published research has consistently documented the presence of such combinations in clinical practice. For instance, irrational FDCs were identified in FDCs marketed in South Asian pharmaceutical markets and were linked with adverse outcomes and therapeutic inefficacy.[12] Similarly, irrational antibiotic combinations without sufficient clinical evidence contribute to adverse drug reactions and accelerated antimicrobial resistance patterns.[13] The clinical impact of irrational FDCs is well documented. In observational studies, irrational FDC formulations were associated with increased adverse drug reactions compared to rational combinations.[14] Such risks underscore the potential harm when FDCs are prescribed without clear clinical justification or guideline support. This has significant public health implications in resource-limited settings where over-the-counter access and insufficient regulatory enforcement may compound irrational use. In this study, ciprofloxacin with tinidazole, ibuprofen with paracetamol, and omeprazole with domperidone were among the most frequently prescribed irrational combinations. These combinations may reflect habitual or empiric prescribing rather than evidence-based practice. For example, combining analgesics with different mechanisms of action may be justified in certain pain syndromes, but indiscriminate use without specific indication can increase the risk of adverse effects and complicate clinical management. Similarly, combining antibiotics without sensitivity data or without established efficacy increases the probability of antimicrobial resistance, which is a global health priority concern.[15] The significant association revealed by the Chi-square analysis between diagnosis and rationality of prescribed FDCs ($p = 0.02$) suggests that clinical context influences the likelihood of rational prescribing. Infectious disease cases showed higher rational FDC use compared to pain/inflammation or gastrointestinal conditions. This may reflect greater adherence to infectious disease treatment guidelines that advocate for specific evidence-based combinations. Conversely, conditions with less structured treatment algorithms may be susceptible to more empiric or unsupported combinations, leading to irrational prescriptions. Comparative studies support this observation. In Nepal, unregistered and irrational FDCs were

prevalent in local pharmaceutical markets, largely due to regulatory gaps and inadequate rational use policies.[16] Other cross-sectional investigations have also identified high proportions of irrational FDC prescribing and recommended strengthening regulatory oversight and prescriber education.[2] Similarly, studies assessing prescribing patterns in India report that many marketed FDCs lack therapeutic justification and are frequently prescribed despite guideline recommendations.[17] The persistence of irrational FDC use reflects multifactorial influences including pharmaceutical marketing practices, insufficient continuing medical education, and lack of access to up-to-date clinical guidelines. Health systems with limited prescribing audits are at risk of entrenched irrational practices. Comprehensive interventions are therefore required, encompassing regular audits of prescribing patterns, prescriber training programs, and integration of rational drug use principles into clinical guidelines. Strengthening institutional policies and national regulatory frameworks can further mitigate the spread of irrational combinations in clinical practice. Educational strategies targeting healthcare providers can improve knowledge and auditing of FDC use. A study assessing knowledge, attitude, and practice regarding FDC prescribing among resident doctors found significant gaps in awareness of rational combination use, suggesting that prescriber education is crucial to promoting rational prescribing behaviors.[18] Such educational efforts could be integrated within hospital postgraduate training and continuous medical education (CME) programs to reinforce evidence-based prescribing. The findings of this study are subject to certain limitations. As a single-centre study with a relatively small sample size, the generalizability of results to other regions or health settings may be limited. Additionally, the rationality classification was based on available guidelines and essential drug lists, which may not capture all nuances of clinical decision-making in complex cases. Future studies with larger, multicentre samples and inclusion of prescriber perspectives could deepen understanding of drivers of irrational FDC use and inform targeted interventions.

Conclusion

The study's results demonstrate that while rational FDC prescribing is present, a significant portion of prescriptions involves irrational combinations. Clinical context significantly influences rational prescribing, with infectious diseases showing more guideline-supported combinations. The persistence of irrational FDC use underscores the need for comprehensive strategies including regulatory oversight, prescriber education, and integration of evidence-based guidelines to promote rational pharmacotherapy and minimize associated risks.

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