Medication-Related Challenges in Lower Middle-Income Countries of Asia: A Review of Four Countries and Recommendations for Improvement

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ABSTRACT
Background: It has been estimated that more than half of all medicines over the world are prescribed, dispensed or sold inappropriately.
Objectives: This review aims to describe medication-related challenges in four Lower Middle-Income Countries (LMIC) of Asia.
Methods: A review of electronic databases such as google scholar, ScienceDirect and PubMed was performed to identify studies related to medication safety in LMIC.
Results: The study results revealed that there is a lack of medication safety literature in most of the countries. Available literature reported that the prevalence of medication errors is very high, medications are dispensed by pharmacy technicians, hospital pharmacy services are offered only in contemporary hospitals and hospital drug information services are not widely implemented and there is a lack of e-health implementation. Among medication errors, unclear handwriting due to paper prescribing and incomplete prescription were common. Majority of medication errors and adverse drug event were unreported due to punitive culture, fear of litigation, lack of support from hospital management and incapacity to detect adverse events.
Conclusion: Medication safety is a major challenge facing LMIC. This study recommended several strategies to improve medication-related challenges in LMIC.

Keywords: Medication-Related Challenges, Middle-Income Countries, Asia.

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INTRODUCTION
Medication safety defined as freedom from preventable errors is a mutual and significant health priority (1-4). In recent years many organizations such as the World Health Organization (WHO)(5) and the Institute of Safe Medication Practices (ISMP) have advocated for medication safety (6). Multiple factors are involved in safe use of medication such as human errors, professional practice, the product, the environment and the culture. Medication errors have financial and clinical impact on patients and may cause mortality.

The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) defined medication errors as "Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer"(7). Medication errors lead to no less than one death every day and harm approximately 1.3 million people yearly in the United States(8). The occurrence in LMIC are expected to be the same, however the impact on patient safety is considered much worse compared to high income countries. A systematic review of medication errors in Southeast Asian countries reported that medication administration errors (15.2%-88.6%) were the most common type of errors followed by dispensing errors (14%-34.7%), prescribing errors (7%-35.4%) and preparation errors and transcribing errors (15%-70%)(9). There is a lack of review studies from LMIC on medication safety issues, particularly from Asia. Therefore, this review was thought to add to the existing literature and recommend strategies to improve medication safety in selected LMICs.

METHODOLOGY
Search strategy
Studies performed in four Asian LMIC were reviewed. The World Bank list of economies (June 2020) was used to classify countries by income level(10). Only studies published in English language were included.

Search terms
The following words were used "Lower and Middle Income" "LMIC" and country names "Pakistan, India, Bhutan, Bangladesh, Bhutan". Boolean terms such as ("AND" OR") were used. Key words were medication safety, medication errors (s), adverse drug event (s), adverse drug reaction (s), prescribing error (s), dispensing error (s), administration error(s).

Inclusion/exclusion criteria
No limitation was imposed on publication year. Case reports, reviews, letters to the editor, commentary and conference proceeding were excluded.

RESULTS AND DISCUSSION
Pakistan (population 222,011,185)(11)
Country Profile
Pakistan covers an area of 796,100 Km2 located in South Asia and share boarder with India, Iran, China and Afghanistan. Pakistan is one of the most populous countries in the world. The World Bank classified Pakistan as LMIC(10). The gross national income per capita was 4000 US dollar in 2015. The total expenditure on health per capita in 2014 was 129 US dollars and the total expenditure on health was 2.6% of GDP(12).

Healthcare system
An electronic health record to improve the quality of healthcare has been implemented fully or partially by few hospitals in Pakistan(13). Physicians, pharmacists and nurses have shown full compliance with the CPOE (13). A specialized 180 beds tertiary care hospital in Lahor had implemented an integrated and fully functional hospital information system since 2012 (14). Some private hospitals has got Joint Commission International accreditation and reported to provide safe and high quality healthcare to patients (15).

**Medication-related challenges**

Several studies were conducted to detect medication errors at different stages of medication use process. The highest incidence of medication errors reported were prescribing errors 95.6%(16) and administration errors 74.4%(17). Handwritten prescription contain missing data such as patient address, diagnosis, age, gender, weight, however hospitals that implemented electronic system reported that important information such as age, gender, prescriber’s signatures were found in all electronic prescriptions(18, 19). Prescribing errors were also reduced with the use of electronic prescribing system in a public hospital (20).

Due to the shortage of pharmacists and weak pharmacy laws in Pakistan, community pharmacy is taken by nonprofessionally qualified personnel. This had a negative impact on the quality of the services provided in the community pharmacy (21).

The causes of medication errors were associated with lack of knowledge, non-compliance with policies and procedures, human factors such illegible handwriting and lack of drugs (22).

**Bangladesh (population of 165,111,698)(11)**

**Country profile**

Bangladesh is a LMIC (10) and one of the highly populous countries in South East Asia with an area of 147,570 square km and a population of 165,111,698(11). The gross income per capita in 2013 was 2000 US dollars. The country’s total expenditure on health was 2.8% of Gross Domestic Product (GDP) in 2014. Under-five mortality rate is high at 41/1,000 live births (2013), as well as the maternal mortality ratio (MMR), which is at 170/100,000 live births (2013).

**Healthcare system**

The four key healthcare sectors in Bangladesh are the government, private sector, Non-Governmental Organizations (NGOs) and donor agencies. The NGOs provide a preventive and basic care to the unserved population. The public and private sectors are regulated by the Ministry of Health and Family Welfare. There are more than 678 public hospitals and 1005 non-governmental hospitals in Bangladesh(23). However, providing a safe and good quality health care to the poor people is still the biggest challenge facing the country. There is lack of e-health implementation in Bangladesh due to many challenges including poor internet services and lack of funding (24). There is also a lack of medication safety services in Bangladesh. Hospital pharmacy as a department is offered only in very few hospitals in Bangladesh. Typically, hospitals in Bangladesh do not have hospital pharmacy but retail drug stores are used instead. In the drug stores pharmacy technicians would often dispense prescribed medications. Nevertheless, hospital pharmacy as a department is offered only in modern private hospitals which are usually very expensive and not used by majority of the population. Hospital pharmacy activities offered include Pharmacy and Therapeutic Committee, Unit Dose System or floor stock system, Ward pharmacists reviewing patients’ prescriptions and providing counseling and one pharmacist in each ward or only in Intensive Care Unit (ICU) and nephrology units providing therapeutic recommendations to the physicians. There is no separate Drug Information Department; however, ward pharmacists provide drug-related information to patients and health care professionals in few private hospitals.

**Medication-related challenges**

Few studies were conducted in Bangladesh to explore medication safety challenges. A cross-sectional study conducted in a 450 beds teaching hospital, reviewed 200 handwritten prescriptions and identified 692 (3.46 per prescription) medication prescribing errors(25). The most common medication error identified were unclear name due to ambiguous handwriting, strength of medicine not mentioned, strength of medicine not stated for drugs marketed in various strengths and drug-drug interactions. A review of 300 patients prescriptions in three outpatient clinics located in three different cities reported prescription errors such as missing patients gender (64.33%), dosage regimen (28%), dose (20%), age (17.67%), dosage form (12.67%), prescriber signature (10.67%), name (5%), date of prescription (4%) and illegible handwriting (46%)(26).

Interventions to improve medication safety in Bangladesh hospitals were carried out in a private hospital in Dhaka. The hospital has reduced the rate of medication errors to 2.45% by adapting certain medication safety strategies including routine review of prescriptions by nurses or pharmacists with more emphasis on prescriptions containing High Alert Medications(27). Medication reconciliation and discussion of medication errors during committee meeting were the other intervention used. However, these improvements were faced by certain challenges such as underreporting of medication errors by healthcare professionals and lack of leadership for the initiative.

**India (Population 1,380,683,255)(11)**

**Country profile**

India is a LMIC(10) and the second most populous country in the world with a population of 1.3 billion people. The gross income per capita in 2013 was 5000 US dollars. The country’s total expenditure on health was 4.7% of Goss Domestic Product (GDP) in 2014. Under-five mortality rate is high at 53/1,000 live births (2013), as well as the maternal mortality ratio (MMR), which is at 190/100,000 live births (2013).

**Healthcare system**

Health care is provided through public and private sectors. The public hospitals facilities include teaching hospitals, referral hospitals, dispensaries, primary health centers, sub centers and health posts. The private sector is preferable by majority of the population in urban and rural areas because of the poor quality of care in the public sectors. Hospital pharmacy services to promote medication safety practice are not in place not only in public hospitals, but also in private hospitals which are considered the best quality medical care in India. The structure of hospital pharmacy services in the majority of public hospitals in India is divided into drug distribution department, drug stores, dispensing pharmacy and quality control department. There is a lack of services such as drug and therapeutic committee, medication safety officers and medication errors reporting systems. At the state level there are more than nine drug information centers, however there are lack of drug information centers in the hospitals level. Clinical pharmacy services involving active participation of pharmacists in physician rounds and review patient’s treatment charts especially in critical units are available in few hospitals in India.

**Medication-related challenges**

Several studies have been conducted to investigate several medication safety issues. A prospective observational study
including 304 patients from three medical wards of a teaching hospital reported that 34% of the patients had at least one medication error. The most common type of medication errors were drug-drug interactions (68.25%), incorrect dosing intervals (12%), and dosing errors (9.5%) (28). Antimicrobial agents, cardiovascular agents, gastrointestinal agents and central nervous system agents were the most common medications involved in medication errors. Predictors of medication errors were older age and increased number of medications prescribed. A cross-sectional study of 175 clinicians and 60 nurses reported that 87% to 89% of the respondents witnessed one or more adverse events. Barriers for not reporting adverse events include punitive culture fear of litigation, lack of support from hospital management, inability to detect adverse events (29). A one-year prospective observational study of a clinical pharmacist intervention conducted in medical, surgical and intensive care units of a 750 beds tertiary care hospital revealed that clinical pharmacists made 986 interventions. These interventions included medication errors (42.6%), drug choice problem (15.4%), drug-drug interactions (15.1%), dosing errors (4.8%), drug duplications (4.6%) and adverse drug reactions (ADRs) (3.8%) (30). The prevalence of dispensing errors in a tertiary teaching hospital was found to be 4.8% (31). Dispensing the wrong medicine (43.1%) was most commonly due to LASA medications names, wrong dosage (21.8%) and wrong strength (10.4%). A study conducted at a tertiary care hospital identified 160 dispensing errors in 12,340 prescriptions (32). Dispensing errors occurred most frequently between 11 am to 3 pm. Dispensing errors occurred mostly at prescription filling and were higher in hospital pharmacy compared to outpatient pharmacy. The top dispensing errors identified were omission (31.9%), wrong quantity (28.15), wrong drug (9.4%) and wrong strength (5.6%).

**Bhutan (Population 773,798) (11)**

**Country Profile**
The Kingdom of Bhutan is a LMIC (10) and a land-locked mountainous country with an area of 38,394 km² and a population of 775,000 (2015) and 37% of the population live in rural areas. The gross national income per capita is 7000 US dollars. The total expenditure on health as % of GDP is 3.6% (as of 2014). The under-five mortality rate is 36 per 1,000 live births (as of 2013) and the maternal mortality ratio is 120 per 100,000 live births (as of 2013).

**Healthcare system system**
Healthcare services are provided free of charge not only to the country nationals but also to visitors and tourists and this has been anchored in the country’s constitution. There are 20 districts and 201 sub-districts in Bhutan and health care is delivered through 31 hospitals and 178 basic health unit clinics and 654 outreach clinics. There is a shortage of pharmacists and physicians in Bhutan. Jigme Dorji Wangchuck National Referral Hospital (JDWNRH) which is the main referral hospital in the country has only two pharmacists and 15 pharmacy technicians. The ratio of doctors and nurses to population is very low (2 doctors and 8 nurses per 10,000 population) (33). There was no medical college in Bhutan until 2012 when the University of Medical Sciences of Bhutan was established. The university has faculty of traditional medicines, faculty of nursing and faculty of medicine.

**Medication Safety challenges**
Bhutan is known as ‘Land of Medicinal Herbs’ by the ancient, therefore traditional herbal medicines are widely used by the general public. Traditional and herbal products of Bhutan are even exported to neighboring countries. There is one hospital and 15 traditional medicine units in Thimphu, the capital city of Bhutan. The National Institute of Traditional Medicine conducts quality control tests on herbal products and raw materials as well as research to develop new products. The Drug Regulatory Authority (DRA) of Bhutan was established in 2004 to regulate human and veterinary medicines. The DRA staff consists of few pharmacists, pharmacy technicians and general staff. A voluntary ADRs reporting form is available that can be printed from the DRA website and filled and sent to the Nation Pharmacovigilance Center.

There is a lack of studies about medication safety in Bhutan. Drug and therapeutic committee exists only in the National Referral Hospital (JDWNRH) (34). In 2016 a study reported that pharmacists had better knowledge about ADRs and reporting than physicians and nurses whereas, tradition medicine practitioners had the lowest ADRs knowledge score (35). A more recent study published in 2018 reported that interviews with healthcare professionals to explore the knowledge, perceptions and experiences of patient safety revealed several patient safety issues (36). Errors identified by the interviewees included, administering the wrong drugs to the wrong patient, administering expired drugs, wrong drug dose, continuation of drugs for longer periods than necessary and drug omissions. ‘Irrational’ use of drugs was also common, and the use of antibiotics to treat non-bacterial infections or viral conditions (36).

**Recommendations to improve medication safety in LMIC**
- Moving from paper-based prescriptions to electronic prescription is highly beneficial in preventing medication errors commonly seen in LMIC such as the incomplete medication orders, illegible medication orders, use of prohibited abbreviation and missing important demographic information such as age, medical record number and prescribers signature.
- Pharmacists should carefully review all prescriptions before dispensing and when necessary, double check with the prescribing physician when a prescribing error has been identified.
- Effective medication reconciliation by pharmacists could prevent many types of errors such as omission, therapeutic duplications, dosing errors and drug-drug interactions.
- Procedures for preventing medication administration errors should be in place and strongly enforced.
- Healthcare systems policies and procedures that enable the identification, reporting and application of changes to prevent medication errors are crucial in promoting patient safety.
- Spread the culture that all healthcare professionals should admit their mistakes in order to prevent further patient harm and develop strategies of how to prevent future errors.
- Medication safety challenges should be seen as opportunities to improve practice and should be top priority of healthcare policy makers.

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