

## RATIONAL PRESCRIPTION & USE: A SNAPSHOT OF THE EVIDENCE FROM PAKISTAN AND EMERGING CONCERNS

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### ABSTRACT

**Introduction:** Irrational drug use remains globally common and there is a lack of country level synthesis for strategizing policy actions in Pakistan.

**Methodology:** We conducted a scoping review of available peer reviewed and grey literature on prescribing patterns and drug dispensing in Pakistan to identify emerging concerns.

**Results:** There is excessive drug use in Pakistan compared to the average for LMICs with inappropriate prescribing, high use of injections and antibiotics, choice of more expensive drugs, inadequate dispensing and weak community pharmacy. Policy concerns include excessive drug registration, poor enforcement of essential drug lists and standard management protocols, open access of industry to health providers, and lack of private sector regulation.

**Conclusion and Policy Recommendations:** Review of evidence demonstrates deviance from rational use in the areas of medicine prescription, dispensing and self-medication, and low impact of existing policy measures. Quality of research needs to be improved focusing on standardized national surveys, consumer related formative research, and interventional research.

Rational drug use is a neglected area in Pakistan requiring policy measures at multiple levels of health system and continued and simultaneous investment in standardized research.

**Keywords:** Rational Drug Use, Pakistan, Review

### INTRODUCTION

Essential medicines, as defined by WHO, are those that satisfy the health care needs of the majority of the population [1]. The concept of "essential drugs" was introduced by WHO in 1975, followed by the first model Essential Drug List in 1977 and institutionalization of essential drugs as one of the eight components of primary health care in 1978 [2]. Irrational drug use is a common problem in Eastern Mediterranean and South Asian countries despite resource constraint for drugs [3; 4]. Irrational use may involve prescription of unnecessary number of medications, the use of injections where oral prescriptions are available, inadequate dosage or use over an inadequate period of time, use of antimicrobials for non-bacterial infection, the choice of higher cost over available lower cost therapeutic options, and inappropriate self-medication by patients [5].

It is estimated that half of all medicines globally are inappropriately prescribed, dispensed or sold [6]. However much of the evidence is fragmented and there is a dearth of national level synthesis on rational drug use. Such synthesis is pertinent to promote effective policies, drug regulation, clear clinical guidance and patient awareness. We attempted to provide a synthesis of existing evidence on irrational prescriptions and dispensing in Pakistan. A scoping review was conducted to collate existing evidence on in Pakistan and identify emerging concerns.

### METHODS

Our purpose was to landscape the evidence rather than a systematic sifting of evidence given that scientifically rigorous literature is thin in this area. The research was part of a larger exploratory study on Access to Medicines in Pakistan. The objective was to i) review existing literature relating to rational drug use; and ii) identify emerging policy concerns and research priorities.

We conducted a desk review of electronic databases looking into peer reviewed and grey literature on the six parameters of irrational drug use as defined by WHO. A search was made on Pubmed, Cochrane, Cinahal WHOLIS, ELDIS and Google Scholar using MESH terms "Irrational drug use Pakistan", "Drug dispensing Pakistan", "Essential Drugs Pakistan" and "Injection use Pakistan". Primary research and reviews supported by research data and published 1990 onwards were included while bio-efficacy studies and commentary articles were excluded. Our search yielded a total of 2176 titles from which 184 abstracts were shortlisted for review and 27 full texts were uploaded into EndNote (Figure 1). These comprised of 25 peer reviewed publications and 2 from grey literature. Yielded titles, abstracts and full texts were sifted by 2 researchers for identification of relevant studies and information was extracted into thematic grids. Quality filters were not applied to studies retrieved.

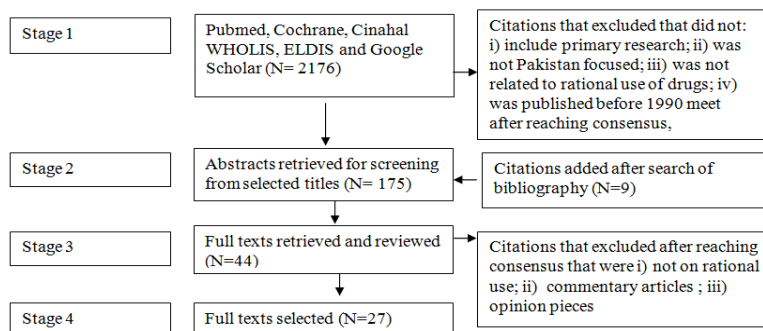


Fig. 1: Desk Review Process

## RESULTS

The largest volume of literature was related to prescribing practices (n=20) while there was lesser data on rational dispensing and storage (n=5) and self-medications (n=4). Studies reported results from different regions of Pakistan and included findings from urban

and rural areas. National large scale surveys were few with most studies having a local flavor and variation in sample from 25 to 3000 recipients. Methodologies also tended to vary across the studies. We present here a summary of findings. Table 1 presents comparison of Pakistan specific data to averages for LMICs.

**Table 1: Rational Drug Use Indicators: Comparison of Pakistan and LMIC**

Sr. No	Pakistan	Pakistan	LMICs
1.	Drugs per prescription	3 or >†	2.39†
2.	Drugs per prescription public sector	2.77#	
3.	Drugs per prescription private sector	4.51*	
4.	Antibiotics prescribed per patient encounter	70%†/ 52%#	45%†
5.	Injections prescribed per patient encounter	60%†/14.7%#	23%†
6.	Medicines prescribed from formulary	50%π	71.7 %
7.	Facilities having national formulary	20%#	78%†
8.	Medications prescribed by brand names	88%*	40%†
9.	Mean dispensing time	38 sec#	105 sec†
10.	Mean consultation time	1.8-9 minutes#	4 minutes †
11.	Self-medication of antibiotics	6-11%‡	

Source: † WHO: The World Medicines Situation; 2004.

#Networks: EDSP Baseline Survey Report; 2002.

\*Das N, Prescribing practices of consultants at Karachi, Pakistan.2001

†WHO: The World Medicines Situation; 2004. / #Networks: EDSP Baseline Survey Report; 2002

π Das N, Prescribing practices of consultants at Karachi, Pakistan. 2001, Najmi:Prescribing practices: an overview of three teaching hospitals in Pakistan. 1998,

#Hafeez A, Prescription and dispensing practices in public sector health facilities in Pakistan: 2004, Network: EDSP Baseline Survey Report; 2002

‡Haider & Thaver: implication for primary health care strategies. 1995, Sturm: Over-the-counter availability of antimicrobial agents, self-medication and patterns of resistance in Karachi, Pakistan. 1997

#Hafeez A: Prescription and dispensing practices in public sector health facilities in Pakistan: 2004, Nizami SQ: Drug prescribing practices of general practitioners and paediatricians for childhood diarrhoea in Karachi, Pakistan. 1996, / Networks: EDSP Baseline Survey Report; 2002.

### Excessive prescription of drugs

The average number of drugs prescribed per patient is 3 or more in Pakistan as compared to an average of 2-3 in LMICs [5] (Table 1). The use of medicine is significantly higher in private sector with an average of 4.1 medicines per prescription as compared to 2.7 in public sector (p<0.001)[7]. Similar results are reported by other studies with an average of 4.5 for private sector [8] and 2.77 for public sector [9], and would be even higher in both sectors if drugs per patient were computed. Within the public sector, there is little difference between medicines per prescription at frontline health facilities (2.75) and Teaching Hospitals (2.79)[10] underscoring the need for efficiency in prescriptions at frontline health facilities. Although a National Essential Drug List (EDL) exists, its availability was seen in one out of five public sector facilities [9]. The Compliance of medicines prescribed with EDL is reported to be only 50% in private sector [8] but is relatively higher at 80% in public sector teaching hospitals [11].

### Antibiotic overuse

Antibiotic overuse is one of the main reasons for excessive prescription with antibiotics prescribed in 70% of patient encounters in Pakistan as compared to 45% in LMICs [5]. Prescription rate is significantly higher for antibiotics (62%) and injections (48%) amongst GPs as compared to public sector with rates of 54% and 22% respectively (p < 0.001) [7]. Even within the public sector there is tendency to prescribe more costly antibiotics. A study reported 70% of prescriptions bypassing lower cost antibiotic alternatives at teaching hospitals [12] and another study reported use of 3<sup>rd</sup> generation (28%) and 1<sup>st</sup> generation (24%) Cephalosporins as leading antibiotics for surgical procedures with least use of macrolides [13].

### Excessive use of injections

Pakistan has one of the highest rate of injection usage with over 60% patient encounters involving an injection as compared to 60% in

LMICs [5]. Studies have reported up to 57% of patient encounters involving injections in public sector [12] and 25% in private sector [8]. Use of intravenous infusions is also significantly high in the private sector with 11% of GP prescriptions involving intravenous infusion compared with 1% for public providers (p < 0.001) [7]. Preference for injection usage is higher amongst general practitioners in rural areas (53%) as compared to urban areas (28%) while safe injection handling and disposal practices are weaker in rural areas [14; 15]. Insufficient quantities of syringes, use of multi dose vials for medications and lack of disposal boxes have been reported from health facilities leading to risky usage [16].

### Inappropriate use - communicable diseases

Prescription practices even for common endemic diseases frequently deviate from standard protocols. Treatment pattern for upper respiratory tract infections showed antibiotics being prescribed in an alarming 89% of prescriptions despite most such infections being self-limiting in nature [17]. Analysis of childhood diarrhea management showed that there was sub-optimal prescription of ORS and overuse of antibiotics. Only 53% of GPs and 61% of specialists prescribed ORS in more than 50% of encounters, while 50% of GPs and 66% of specialists prescribed antimicrobials with interestingly no significant difference between GPs and specialist [18]. Another study comparing across the public and private sectors showed GPs prescribing anti-diarrheals more frequently than doctors working in the public sector (p < 0.01). Management of tuberculosis also showed frequent variation from the recommended treatment. Only 3.4% GPs had knowledge of all DOTS components, 35% able to correctly prescribe drugs, dose and duration for initial phase and 30% for continuation phase of the therapy [19; 20]

### Inappropriate use - non communicable diseases

Drug prescribing patterns for chronic diseases also need significant rationalization. Appropriate therapy for hypertension is initiated by

only 35% of practitioners, thiazide diuretics internationally recommended as first line regimen are rarely prescribed (4.2%) and sedatives commonly used either as first-line medication for lowering BP (23.8%) or in combination with antihypertensive agents (45%) [21]. A study on diabetes management reports that insulin therapy was advised in combination with gluco-corticosteroids, thiazide diuretics, and propranolol, which are contraindicated due to drug interactions [22]. Yet another study on mental health reports that the treatment for psychiatric illnesses did not correlate to diagnosis in 25% of cases and doses of drugs were inappropriate in 31% prescriptions [11]. Overuse of steroids has been reported for arthritis and fairly high proportion of patients (38%) reported side effects [23].

#### Drug Dispensing and Storage

Provision of patient information needs improvement across health care providers and dispensers. Survey of public sector facilities found mean consultation time of only 1.79 minutes insufficient to give proper advice on medicine usage [10]. Lengthier times have been reported in private sector however yet insufficient for proper advice. Mean consultation time of 3 minutes by GPs and 9 minutes by pediatricians was reported for childhood diarrhea with instruction for ORS use was given in only 6% of encounters by GPs and 8.4% of encounters by pediatricians [18]. Dispensing time in the public sector has been reported as 38 seconds across a range of facilities, none of the dispensers wore gloves while dispensing, only 11% of drugs dispensed were adequately labeled and only 12% of cases a duplicate record of prescription was maintained at health facility [10]. Manual for procedures was available in only 5% of public sector facilities, refrigerators were working in 60% and temperature control was present in 24% [19].

#### Community Pharmacies

There are 45000-50000 pharmacies and medical stores in Pakistan [24], one of the highest numbers in LMICs. The large number of drug outlets makes regulatory checks difficult. A survey of drug outlets shows that only 12% of drug dispensers were pharmacologically trained and merely 35% had secondary school qualification [25]. Knowledge of correct dosages for common infections was poor with only 24% knowing proper administration of ORS, 21% suggesting anti-diarrheal preparation for childhood diarrhea, and 60% knowing the correct dose for amoxicillin [25]. Existing regulatory checks are aimed at quality of drug products but there is little regulation of quality of retail outlet. Proportion of pharmacies meeting licensing requirements was only 19.3%, qualified staff was present in only 22% pharmacies, only 10% had a temperature monitoring device and 4% had back-up power supply for refrigerators against frequent power outages [24].

#### Self-Prescription

Self-medication is reportedly widespread in Pakistan, however there are few studies that capture the magnitude of self-medication. In a household survey examining health seeking behavior for childhood illnesses, self-medication with antibiotics was seen in 11% of cases and with anti-diarrheals and anti-emetics in 11% of cases (11%) [26]. Another household survey within the general population found 6% rate of antibiotic self-medication [27]. However these figures are nearly two decades old and require updating. Self-medication is also common amongst the youth. A study on college students found a third of non-medical students reporting self-medication and 55.3% of medical students mostly belonging to 1st and 3rd year of medical college prescribe medicines independently [28;29].

#### Branded Use and Marketing Issues

88% of medicines are prescribed by brand names that in Pakistan [8] as compared to an average of 40% in LMICs [5]. Attending sponsored CME events and accepting funding for travel for educational symposia was associated with increased prescription rates of the sponsor's medications [30]. Another study critically analyzing claims from drug promotional brochures showed that 18% of advertisements were unjustifiable of which 32% was exaggerated, 21% ambiguous, 26% false and 21% controversial [31].

Yet another study reported that only 26% request information provided in educational brochures only received a response and only 15% of responses met the WHO criteria for optimal drug information [32].

#### DISCUSSION

Irrational drug use has been highlighted as a serious concern across LMICs but there is a dearth of national level synthesis [5]. We attempted to collate evidence on rational drug use in Pakistan by conducting a review of available published and grey literature on extent of the problem in Pakistan. Our focus was on rational use including prescriptions, dispensing, storage and patient usage of medicines. We did not report on availability issues which are the subject of a related larger study on access to medicines.

Although an Essential Medicines Program was established in Pakistan in the 1970s, our review indicates that irrational use continues to be widely prevalent. Prescription of medicines and injections is higher in Pakistan compared to the average for LMICs, mainly driven up high level of antibiotic usage. As shown in table 1, average number of medicines prescribed per prescription is 3 or more in Pakistan and some studies indicate it to be 4.5 in private sector. Whereas on contrary a study conducted in Chennai, India at a tertiary care hospital on antibiotics use concluded that average of 2.07 (Mean  $\pm$  SD 2.07 $\pm$ 0.9) drugs were prescribed per prescription [33].

Prescription Medicines are inappropriately prescribed even for endemic diseases despite existence of national disease control program and standard management protocols. Even though a national essential drug list exists, compliance with it is low across the sector. Prescribing predominantly follows brand names, and low cost options are frequently overlooked in favor of costlier medicines even in public sector facilities. Mean consultation time and medicine dispensation time is insufficient for patient advice on usage medicines, and safety and storage parameters for dispensing are inadequate. Irrational use is more marked in the private sector and in rural areas. Community pharmacy is also weak with under-equipped drug outlets, excessive access to over the counter drugs and insufficient attention to safety measures during dispensing. Evidence suggests that self-medication with antibiotics is commonly practiced by 6-11% of the population. Prescribing related and community usage issues relate to irrational use have been highlighted by recent studies from India, Iran, Lebanon, Lao and Thailand [4; 3; 34; 35].

Implications of excessive inappropriate drug use in Pakistan are already evident in Pakistan. Medicines consume the largest share (56%) of household out-of-pocket payments [36] and are driven up by excessive prescriptions and brand medications in addition to supply and pricing issues. Population based resistance to frontline antibiotics including ampicillin, cotrimoxazole, chloramphenicol and erythromycin was documented nearly two decades ago [27] and there is high incidence of multi-drug resistance-TB strains in Pakistan [37]. Moreover, overuse of injections has been conclusively linked to relatively high burden of Hepatitis B and C infection in Pakistan [38].

Policy measures globally have typically focused on the essential drug list and standard management guidelines and with a concentration on the public sector, overlooking the private sector [39]. In Pakistan, policy concerns (Figure 2) need to go be wider to address contributors of irrational drug use in with integrated action at multiple tiers of the health system. First, there is excessive registration of drugs in Pakistan with approximately 50,000 registered drugs [40], one of the highest numbers in LMICs. Many of the registered products are unnecessary, being variations in brand names and dosages. Although detailed procedures exist for drug product registration [41] weak adherence has encouraged a market monopoly with loose control [42]. De-registration is rare and even when applied its impact has been diluted by black marketing channels and continued physician prescriptions [43]. Second, while a national essential drug list has been in place since 1994 [40] and standard protocols of management are well developed, attention is needed on better enforcement strategies. Third, the private sector,

which has higher levels of inappropriate use and is the major provider of care, is poorly regulated and has few opportunities for government supported continuous medical education. Quackery is reported to be widespread but there is lack of database differentiating between licensed and un-licensed providers. Fourth, inappropriate advertisement claims and unrestricted access to medical practitioners have been linked with irrational prescribing.

The Pakistan Medical and Dental Council's ordinance on relationship between the industry and registered doctors and dentists is vague at best [44]. Finally, weak community pharmacy with proliferation of sub-standard drug outlets and largely unrestricted access to over the counter drugs further compounds the problem. These policy concerns need to be holistically addressed across pharmaceutical policy as well as health systems reforms.

**Fig. 2: Priority Policy and Research Concerns:**

Policy Concerns	Research Concerns
Adherence to EDL and standard management protocols	Periodic surveys of providers and drug outlets
Patient instructions, dispensing and storage of drugs	Reporting on standardized methods and indicators
Brand name prescriptions and unrestricted access of industry to providers	Differentiating licensed from unlicensed providers
Regulation of drugs retail outlets	Consumer demand and accountability
Self medication and unrestricted access to drugs	Best practice lessons from interventional research

Methodological challenges also need to be systematically addressed for rational drug use (Figure 2). While there were a number of studies on irrational use these generally lacked standardization, were local rather than national in scope and needed regular update. Efforts need to be directed towards development of national standard standardized databases to monitor rational drug consumption involving periodic drug surveys across health facilities, community pharmacies and communities, as practiced in established economies [45]. This argument is in line with findings in a study on antibiotic therapy for pneumonia in a rural healthcare center in India, where it was found that the present guidelines in standard textbooks for the treatment of pneumonia was giving a varied range of guidelines for treating in Out Patient Department basis and for treatment in the ward. This phenomenon is exposing unnecessarily mild cases of pneumonia to the similar treatment as given in severe case [46].

International indicators, standards and methodologies to provide benchmarks across countries are available developed by the International Working Group for Drug Statistics Methodology and the International Network for the Rational Use of Drugs [47; 48]. Supplementary research is also required in mapping of private sector inclusive of qualified providers, informal providers, and shadow pharmacies. These need to be accompanied by formative research looking into consumer demand, health-seeking preferences, and patient accountability which has been less well explored in comparison to quantitative concerns. Finally, there is less published in terms of successful interventions [39] and compilation of lessons learnt is needed for promotion of rational use at policy, supply, provider and consumer levels.

While rational drug use is an old agenda in Pakistan amongst the academic circles, policy and programmatic enforcement measures as well research rigour needs strengthening. Integration is needed across health systems and pharmaceutical policy research at all levels.

#### CONCLUSION

A collation of existing evidence in Pakistan shows deviation from rational use across medicine prescription, dispensing and self-medication, and low impact of existing policy measures. Policy investment is needed in regulation of drugs to reduce unnecessary proliferation and prescribing, and strengthening quality parameters at provider and community pharmacy. Investment is also needed in standardized surveys on rational use, formative research on consumer demand, and collation of successes policy ventures.

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