Medical Products for Cardiovascular Disease Management in Nepal: a needs assessment study

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ABSTRACT

Background

Medical Products and Technologies is a key component of the health system. Quality medicines and efficient management of the medical products can secure effective cardiovascular diseases management.

Objective

To collate information and identify strengths, weaknesses, opportunities and threats (SWOT) associated with medical products and technology component for cardiovascular disease management in Nepal.

Method

This study is a part of a larger rapid assessment of Nepal's health system for cardiovascular disease management and based on The Health System Assessment Approach: A How-To Manual (USAID). The authors conducted a desk review of documents related to the WHO "medical product and technology" building block component and key informant interviews using a pre-tested interview protocol. The first eight interviews were transcribed verbatim and analysed inductively to generate a codebook; and the remaining, transcribed and deductively coded based on the codebook. Findings were categorised into relevant topical area and SWOT components.

Result

Nepal has laws and provisions for medicine regulation, pharmacovigilance, post marketing surveillance, registration and licensing provisions for pharmacy industries/outlets, essential medicine lists and national formulary. These provisions also apply to medicines used for cardiovascular diseases. The challenge however, is the lack of effective implementation and monitoring, due to shortages of technical workforce and state of art information and technologies. Information on pharmaceutical expenditures for cardiovascular disease management is scarce; there are no standard national level guidelines that are consistently used to manage cardiovascular diseases in health facilities.

Conclusion

There are limited provisions and information on medical products for cardiovascular disease management in Nepal, and a need to strengthen existing provisions for medicine regulations and surveillance.

KEY WORDS

Cardiovascular Disease, Health System, Medicines, Medical Products, Nepal

INTRODUCTION

Sustained supply of, and cost-effective access to, medicines and medical products is vital for the smooth functioning of a health system. Any gap in the 'medical products and technology' component has the potential to jeopardise the overall health sector efficiency; the component, therefore, should be closely examined.[1] Medicines and medical products are indispensable to effective disease management, including the management of cardiovascular diseases (CVDs). CVDs remain one of the major causes of disability and deaths worldwide.[2] Over three quarters of CVD-related deaths occur in low- and middle-income countries.[3] CVDs accounted for 26.9% of total deaths and 12.8% of total Disability Adjusted Life Years (DALYs) in Nepal.[3] Whilst shortages of specialised and trained CVD workforce, lack of easy accessibility to tertiary level care and facilities for CVD and inadequate attention towards the prevention and health promotion aspect for CVD management have been identified as challenges for effective management of CVDs, specific information on the availability of resources to prevent and manage CVDs in Nepal remains sparse.[4] There is an urgent need to systematically assess the needs for, and gaps in, medicines and medical products situations- the infrastructure, availability and regulation- to effectively respond to the growing burden of CVDs. This study aims to collate information on medical products and technologies for CVD management in Nepal; and to identify the strengths, weaknesses, opportunities and threats (SWOT) in the area of medical products and technology used for managing CVDs.

The work presented here is a part of a larger rapid assessment of Nepal's health system steered by a national level task force co-chaired by the Chairman of Nepal Health Research Council (NHRC) and the Dean of Kathmandu University School of Medical Sciences (Principal Investigator of the Study).[5] Medical products and technology sub-committee led this study. The findings of the larger trial focusing on health system gaps have been published elsewhere.[6]

METHODS

This is a cross-sectional need assessment study guided by the United States Agency for International Development (USAID) "The Health System Assessment Approach: A How-To Manual", Version 2.0 (HSAA).[1] Assessment protocols were developed for each of the six building blocks of the - World Health Organization (WHO) health system framework (2012), namely: leadership and governance, health financing, health service delivery, human resources for health, health information management systems, and medical products and technologies. This study was guided by the protocol developed for the 'medical products and technology' component.

The Ethical Approval Board of the NHRC approved the study (Reg. no. 176/2018).

Data collection method, primarily involved: I) Desk Review and II) Key Informant Interviews (KIIs). The methods focused on gathering information on 34 indicators under eight topical areas related to the Medical Product and Technology Component (for CVDs) based on the HSAA, and exploring strengths, weakness, opportunities and threats pertaining to the medical product and technology component.[1] We also conducted a stakeholders' meeting, collected feedback on study design and protocol; the feedback received were included in the proforma.[5] Data collection (desk review and the interviews) was conducted between February - September 2019. Key information was updated as relevant and available.

I. Desk Review: The authors performed a desk review of relevant national laws, regulations, policies, reports and documents.[7-34]

II. Key informant interviews: We conducted KIIs with 12 key stakeholders engaged in national level control and governance of the medical products:

- 3 representatives from Department of Drug Administration (DDA)
- 4 representatives from Department of Health Services (DoHS) including logistic management information section and procurement section
- 1 representative from Consumers Right Investigation Forums
- 1 representative from Association of Pharmaceutical Producers of Nepal (APPON)
- 1 representative from Nepal Chemists and Druggists Association (NCDA)
- 1 representative from Academia, Department of Pharmacy
- 1 representative from National Medicine Laboratory (NML)

The KIIs were guided by a pre-tested semi-structured interview protocol. Participants were informed about the study and interviews were conducted after obtaining written informed consent from the participants. The interviews were audio-recorded with the permission from the participants. The recordings were stored in laptops secured by a password.

For data management and analysis, the authors organized the information extracted from the desk review alongside the topical areas and respective key indicators.

Similarly, all KIIs were transcribed verbatim (in Nepali language). To maintain anonymity, we replaced any names (or, other identifying information) by alphanumeric codes and stored the transcripts' paper copies in safe lockers only accessible to the research team.

A codebook was developed inductively using the first eight interviews by two independent coders (agreement:

89%). The rest were then coded deductively based on the codebook. A few new themes that emerged were added to the codebook. We categorised the codes into four categories- strengths, weakness, opportunities and threats (SWOT) as appropriate. Relevant codes were translated to English language. Specific information related to the topical areas and indicators gathered were included in the relevant sections.

Findings are presented for each topical area and indicator, and SWOT categories. Information on each indicator for each topical area is presented in tables. The result section is divided into five sections, each section covering two topical areas, followed by the SWOT analysis.

RESULTS

Pharmaceutical Expenses and Financing

National level data on expenditure on pharmaceuticals for CVDs is unavailable. Medical products are primarily financed through out-of-pocket (OOP) expenditure (Table 1).

Regulation and Selection of Pharmaceuticals

The National Medicine Policy (NMP) and the Drug Act 1978 are the key documents setting provisions for medicine regulation in Nepal. DDA, the national regulatory authority, is responsible for enforcement of the Drug Act 1978. Nepal has a National List of Essential Medicine (NLEM) to guide medicine selection processes. Regulation of medicines for CVDs are covered by these acts/policies; and, there are no separate and exclusive provisions for CVD medicines or other medical products (Table 2).

Procurement, Storage and Distribution

Public procurement of pharmaceuticals is guided by the Public Procurement Act 2007.[22] Whilst competitive bidding is the primary method of procurement in the public sector, the private sector procures medicine directly from wholesalers/retailers.[23] Provisions for medicine storage, such as cold chains, exist; however, effective storage is challenged by ineffective monitoring and lack of technical workforce to deal with lapses in the established facilities. Lack of proper storage for medicines/raw materials at entry ports, such as airports is a problem (Table 3).

Availability, access and appropriate use of medicines

Easy access to medical products in Nepal is challenged by geography; and medicine stock out is common. National level data on the availability and stock-out of CVD medications is unavailable. The tracer medicine list in Nepal does not contain any CVD medicine (Table 4).

Strengths, Weakness, Opportunities and Threats (SWOT) analysis

Nepal's constitutions, medicine related laws, regulations and guidelines set a strong foundation for medicine

Table 1. Pharmaceutical Expenses and Financing related information (Topical Area A & H)

Topical Area A: Standard Indicators	
Indicator	**Findings**
Total expenditure on pharmaceuticals (%Total expenditure on health)	~ 32.9%[*◊] [total expenditure on pharmaceuticals is ~4.46% of estimated Current Health Expenditure (CHE)[*◊]][7]
Total expenditure on pharmaceuticals (per capita at average exchange rate) in US$	~ US$16.13[8] **<u>According to Nepal National Health Account 7:</u>** [*]CHE: estimated at NPR 141.46 billion (US$ 1,409,060,000) (Fiscal Year (F/Y) 2015/016) [◊]Total Health Expenditure (THE): ~NPR 151.16 (USD 1.43) billion [**]Per capita THE was NPR 5216 (US$ 49) in the year 2015/016
Government expenditure on pharmaceuticals for CVD (per capita) in US$	Data not available
Private expenditure on pharmaceuticals (per capita at average exchange rate) in US$	Data not available
Topical Area H: Financing of Medical Products	
Proportion of annual national expenditure on medicines financed by government budget, donors, charities, and private patients (through OOP payments)	Pharmaceutical expenditure is primarily financed by household OOP direct payment. Nationally, over 3/4th of the total OOP spending is made on pharmaceuticals and medical goods.[7] Total expenditure on pharmaceuticals through prepayment schemes such as insurance, government and external funding is low.[7] For F/Y 2018/019, > 3 billion rupees was spent on medicine purchases, of which ~50% was estimated to be sourced by the government of Nepal (GoN).[8] ● Estimated expenditure for medicine purchases: $124, 440,000 (NRs. 3,95,41,00,000) ● Government of Nepal: $17, 26, 300 (NRs. 1,95,41,00,000) ● Grants: $ 17, 460, 200 (NRs. 1,95,79,00,000) Post federalization, the government has decentralized medicine purchase processes to the provincial and local level. For 2018/019, the functional expenditure for medical products, appliance and equipment was estimated at 0.85% of the total estimated functional expenditure for health segregated as 1.12% out of 66% estimated functional expenditure for health in federal and 1.83% out of 6.22% in provincial level.[8] "Now it is a bit different; due to low budget here (at the center).... budget has been allocated to every province, (budget) has gone to the province and then province sends it to the hospitals and district hospitals, there is more budget at provincial level than here. So here the (central) budget was low from this year, even the procurement is low." (-Management Division (DoHS) representative)

Existence of a system to recover the cost of pharmaceuticals dispensed in MoHP facilities	No robust system is in place to recover the cost of pharmaceuticals dispensed in MoHP facilities. For expired drugs, the government analyses the quantity and related cost; and suppliers replace the drugs damaged before their shelf life. "In case of expiry, we analyse them, the quantity and cost of expired drugs are estimated. We have a contract where, if the quality of drugs gets damaged before shelf life, suppliers replace them." (-Management Division (DoHS) representative) Similarly, medicine prices remain largely unregulated. While there is a cost evaluation committee for medicine cost determination at the Department of Drug Administration (DDA) (- DDA representative), and medicine price regulation has been tried before, the process was reported challenging. Multiple factors, including lack of consistent and scientific government mechanisms, prescribers' and publics' preference for 'brand' influence medicine cost regulation. "treatment expenses of a person increases when there is brand preference." (-Academia representative) Regulating costs was perceived necessary to reduce overall treatment cost. "In order to reduce costs of treatment, it is very important to limit the price (of medicines). Price limit should be done. It is because if doctors or retailers demand high commission, medicine companies suddenly increase the price, due to high commission demand. Due to which there is unlimited increase in the medicine prices. Hence, there should be a price limit for medicines. For brands." (-Consumer Rights Investigation Forum representative)
Out-of-pocket expenditure for health on CVD medicines	There is no national level estimation of OOP expenditure incurred particularly for CVD related medicines and medical products. Nonetheless, the OOP for healthcare in general and for pharmaceuticals in particular is high; OOP spending is estimated at NPR 78,427 million (55.4% of CHE & 51.9% of THE) - 63% of this expenditure is incurred for 'medicines and medical goods' (2015/016).[7] OOP expenditure made at private health facilities is estimated to be as high as 80% of total expenditure made at all kinds of the hospitals. Disease-wise, almost 2/3rd of the total OOP are spent on NCDs.[7]

regulation, including, medicine production, sale and distribution; this strong framework is the key strength for the Medical products and Technology component. The DDA is guided by the mission to ensure that medications are safe, effective and of expected quality. Provisions for PV and PMS have been established. The major weakness, however, is the lack of effective implementation of these acts, policies and guidelines, and monitoring of how these guidelines and available resources are being used in practice.

Table 2. Provisions for regulation and selection of pharmaceuticals (Topical Area B & C)

Topical Area B: Pharmaceutical policy, laws and regulations	
Indicator	**Findings**
Existence of a NMP or other government document that sets objectives & strategies for pharmaceutical sector for CVDs	Nepal's Constitution, the NMP 2007 and the Drug Act 1978, along with rules, regulations and committees set by the act sets the mission, objectives and strategies for the pharmaceutical sector in Nepal and apply equally to private and public sectors.[9-14] There are no acts or policies exclusively for CVD medications.
Existence of a comprehensive pharmaceutical law	Drug Act 1978 (last updated in 2000) and the regulations and rules under this act set a comprehensive mechanism for medicine regulation in Nepal.
Existence of a National Drug Regulatory Authority responsible for the promulgation and enforcement of regulations	The DDA is the National Drug Authority responsible for enforcement of the Drugs Act. It aims to: prevent drugs misuse/ abuse, dissemination of false or misleading information about efficacy and use of drugs, and to control the production, marketing, distribution, export and import, storage, and utilization of those drugs.[15] It is a quasi-judicial body financed by the GoN under the Ministry of Health and Population (MoHP). National Medicines Laboratory (NML) is the public medicine laboratory and works closely with the DDA in medicine regulation.
Existence of Pharmaceutical Registration of Drugs	Drug Registration Regulations/ Rules 1981 guides the registration of medicines (including medicines for CVDs), the licensing of wholesalers/ retailers and approval for establishing pharmaceutical industries. Medicines for use in Nepal should be registered for production (by national manufacturers), sale, import and export; similarly, medicine outlets should be licensed; and manufacturers seeking to establish the pharmaceutical industry should obtain approval- all from the DDA.[10] Licenses/ certificates issued are usually valid for 2 years. Despite regulatory mechanisms in place, unregistered and counterfeit (imitation or fraudulent) medicines- enter in "bags" and through porous borders bypassing the formal check mechanisms. "Unregistered medicines are a very big challenge. Previously they were not usually seen in the market... if we talk about these unregistered and counterfeit medicines, there were no such issues, this open border and us not being able to regulate is the reason. Unregistered drugs are there in the market." (-NML representative)

Existence of Post Marketing Surveillance (PMS)	DDA, together with NML conducts PMS of medicines. PMS, however, is not extensive due to lack of infrastructural and human resource capacity at NML.
Existence of Pharmacovigilance (PV)	The DDA operates as the national PV centre in liaison with the WHO collaborating Centre for International Drug Monitoring, Uppsala, Sweden since July 2006. There are 12 regional PV centres which collect and report ADRs to the national centre via 'Vigiflow' (an online program).[35] The Adverse Drugs Reactions (ADR) reporting mechanism is "spontaneous"; there is no system for active surveillance and reporting. (-DDA representative)
Mechanisms exist for licensing, inspection and control	DDA is responsible for inspection, licensing and control of pharmaceuticals. DDA conducts the monitoring of the medicine outlets (guided by Code on Sales-Distribution of Drugs 2015), pharmaceutical industries (routine inspection by the DDA and WHO-GMP Inspection as directed by the MoHP) and private laboratories (guided by Codes on Distribution of Drugs 2015).[17] Drug Investigation and Inspection Rules, 1983 guides the inspection and control of medicines; Medicine Registration Guidance (issued under Drug Registration Regulation) outlines the detailed provisions.[13] DDA generates reports of inspections and enforcements, as and when conducted (statistics about compliance and enforcement are not made available to the public). Drug Donation guidelines guide the quality of donated drugs in Nepal.[18]
Topical Area C: Selection of Pharmaceuticals	
Existence of NLEM	NLEM was first published in 1992 (revised six times since; current version: NLEM 2021).
Evidence of an active national committee responsible for managing the process of maintaining NLEM	A draft committee (mostly consisting of pharmacists from DDA) coordinates and drafts the NLEM. The main committee (involving people from the government health departments, such as the MoHP, DoHS, Nepal Medical Council and the WHO) provides technical guidance. Opinions are also sought from expert groups (for example, therapeutic experts, such as clinicians and other stakeholders.[19]
Total number of pharmaceuticals on NLEM	NLEM 2021 has listed 398 medicines including 32 different "cardiovascular medicines''.[19,20] Government provides 70 medicines, including cardiovascular (CV) medicines - Aspirin, Adrenaline, Atenolol, Amlodipine, Digoxin, Hydrochlorothiazide, Furosemide for free.[19,20] The government also plans to add Enalapril and Atorvastatin to the free medicine list.[19-21] Medicines in NLEM are listed using INN (International Nonproprietary Names).[19,20] The free essential medicines are distributed based on the level of care. "Till now looking at the infrastructures and resources of the government, hospitals are said to have 70 medical items for free, likewise 58 at primary health care centres and 38 items for free in the health posts." (-Management Division (DoHS) representative) CVD medicines like Atenolol & Furosemide (tablets) and adrenaline injections are available for free at all the levels- Tertiary level (Hospitals), Primary healthcare centres (PHCs) and Health posts; whereas Furosemide injections are available at tertiary level and PHCs. Aspirin, hydrochlorothiazide, Amlodipine and Digoxin tablets are available only at tertiary centres. Atropine (injection)- a medicine frequently used for CVDs is also included in the free drug list (albeit not categorised under 'cardiovascular medicines' in NLEM.)

"There is Nepal's constitution, then drug act, then consumer act and numerous regulations in the present context. Now the public health service act has been introduced. These four (acts) can provide full protection… but there is not even a 10% achievement." (-Consumers Rights Investigation Forum representative)

Important programs such as PV and PMS, although functional, are inadequate to produce effective outcomes. Nepal's PV program is perceived to be in its "infancy" stage, "not very effective" and "with no real output/impact". Its contribution to the international database and reporting is perceived minimal.

"Centre has not been sending adequate (PV) reports. It is not good in the global scenario as well…… There were only 220 in a year. Only a total of 900 something is reported in a period of 13 years. So it's not very effective." (-DDA representative)

Similarly, despite provisions for NLEM and NNF, their use is perceived limited. For example, the use of NLEM is limited to public procurement of free essential medicines. The assessment of if and how NLEM and Formulary is used by different sectors is lacking.

"many do not even know about the essential drug list…… even the physicians do not know about it. (-DDA representative)

Lack of adequate human resources to carry out the regulatory functions, criteria for selecting medicine distributors and quarantine facilities to handle medicines

Table 3. Procurement, Storage and Distribution of pharmaceuticals (Topical Area D & E)

Topical Area D: Procurement	
Indicator	**Findings**
Existence of formal SOPs for conducting procurement of pharmaceuticals	Public Procurement of pharmaceuticals in Nepal is guided by Public Procurement Act and Regulation, 2007, enforced by the Public Procurement Monitoring Office (PPMO) and applies to public procurement of all goods (including medical products).[22,24,25] The Procurement Section of the Management Division at DoHS, MoHP is responsible for public sector procurement.
Use of international non-proprietary name for MOH procurement	MoHP uses INN to procure medicines.
Percentage of procurements or purchases according to plan	The Logistic Management Division (LMD) procured 34 essential medicines (including 2 CVD medicine) in FY 2074/75.[26] According to a representative from the Logistic Management Information Section at DoHS, LMD did not procure any CVD equipment in the year 2017/18. As per consolidated procurement plan, 2017, 80% of procurement completed within the planned timeline.[27] The exact value of emergency procurement of pharmaceuticals for the past 2 years is unavailable. Except for some particular situations requiring a bulk of medicine at once, minimal emergency procurement was reported. "In the last two years, there hasn't been much emergency procurement. Sometimes there are specific situations, like, recently we have been trying this… there was a demand for vaccines for Hajj travellers. They needed it urgently; because it was needed urgently, we may call it an emergency. Such a process has been initiated." (-Management Division (DoHS) representative) Lead time for public procurement process generally ranges between 90-120 days.
Percentage of MOH pharmaceuticals procured through competitive bids	Government procures medicines primarily through a competitive bidding process. "About 70 to 80% of medicines are procured through a competitive bidding process. Through competitive bidding, medicines are procured in reduced price" (-Management Division (DoHS) representative) Medicines and medical equipment needs are mostly met through imports. Public procurement process was perceived as cumbersome to the national manufacturers. "the (public procurement) system is not robust enough that people will go and participate, it is very hurdlesome. It is very challenging not only because every manufacturer is (expected) to provide medicines at a low price, we are even ready to provide the medicines at low cost. But the public procurement itself is full of hurdles like technical barriers and so many others. It is so cumbersome that no one wants to go and participate." (-APPON representative)
Procurement pre-or-post qualification for suppliers and products	LMD performs pre-shipment inspection of all medicines before it leaves the manufacturer's premises. Inspection includes review of manufacturer's internal quality control documents, laboratory tests of random samples to ensure compliance with the specifications. Post-shipment inspection is a part of the receipt procedure by warehouse personnel.[28]
Pharmaceuticals procured based on reliable estimates	Estimation of medicines for public procurement considers multiple criteria, for example, past and current fiscal year product consumption, morbidity data, program consideration, user's demand or targeted health service user's population, particular program expansion plan, medical product's availability or stock out data and expired or surplus condition data.[29] The electronic- logistic management information system (e-LMIS) has greatly facilitated the procurement process. LMD procures some specific categories of medicines based on the program's demand. "Let's talk about any vaccine, when we talk about vaccines it is related to the work of the Family Welfare Division, there is a vaccine division. And the vaccine division decides which type of vaccine will be used, how much is needed in the country, to how many children etc." (-Management Division (DoHS) representative)
Private sector procurement processes	Private Sector procures medicines directly from the wholesalers and retailers. Most private sectors (private hospitals & pharmacies) employ direct procurement methods.[36] "It is obviously different in the private sector… Public Procurement Act need not be followed. They procure based on their need and comfort, but I guess the principle of procurement is the same everywhere. They also want medicines at low prices and good quality. They also care about quality like everyone else and also low prices. I think they design their own procurement accordingly." (-Management Division (DoHS) representative) "Manufacturers manufacture the products and supply them to importers. They provide them to their importers throughout the country and the importers provide them to the wholesalers after setting a certain margin. Wholesalers also set a margin and provide the products to the retailers." (-NCDA Representative)
Topical Area E: Storage and Distribution	
Value of inventory loss over 12 months of cardiovascular drugs	The total value of inventory loss over 12 months of CVD medicines is not known. Some degree of loss due to medicine expiry was reported. Lack of compliance to the standard protocol was perceived as a cause for loss due to medicine expiry. "At the facility level or dispensing level, if they do not follow Standard Treatment Protocol (STP) the medicines are not going to be used or cleared out. Now no one has been following it so, this new issue has come up…although few of them may be following it. Since so many of them are not following it, there are so many commodities still in stock which may later go into expiry if left undistributed" (-Management Division (DoHS) representative)
Percentage of deliveries or pick-ups according to plan for CVDs	Data not available

and raw materials at the port of entry, such as airports are additional weaknesses in the system.

"Actually, it's been 25 years since I have opened the pharmacy, they (authorities) have visited only two times (for inspection). We told them many times but every time they say that they do not have human resources." (-NCDA representative)

Existence of refrigeration units with functional temperature controls at each level of the distribution system	A cold chain network is maintained by the Department of Logistics Management, MoHP to support medicine storage. There are five regional cold chains, one central storage facility and two sub cold chain stores. At the district level, public health offices have small cold chain storage facilities. Effective cold chain supply is, however, challenged by the lack of technical workforce to maintain cold chain equipment. "Refrigeration technicians are insufficient, at provinces ... among 7, only 5 provinces have technicians, and they are not experienced. Now at the province or district or healthpost, even if only a refrigerator is damaged, a technician is to be sent from the central level..and it takes months ….and years…" (-Management Division (DoHS) representative) There is no evidence to prove that all medicine outlets- wholesalers and retailers- have cold-storage facilities. Medicines' quality was perceived to deteriorate after leaving the "safe manufacturing premises", due to substandard storage practices at medicine outlets. Many medicines distributors in Nepal are not technical persons, and hence are not necessarily aware about the sensitivity of the appropriate storage conditions required for pharmaceuticals. "Just like good dispensing practice, good storage practice is also equally important. I would rank the storage practice two out of ten, due to which even though medicines produced by X (name of company) itself is well manufactured, very well tested but when we check the medicines after 3 months, it loses all its potency and the product may fail after 3 months if the storage temperature has not been maintained. If we go look at the national level medicine storage, it looks completely like a dumping site, and no one wants to participate in that." (- APPON representative)

Table 4. Medicine availability, access and appropriate use (Topical Area: F & G)

Topical Area F: Availability and Access to Quality Products	
Indicator	**Findings**
Percentage of a set of unexpired tracer items if available	Out of 18 medicines in the tracer medicines list none are 'cardiovascular medicines'. Availability of tracer medicines is poor and their stock-out is frequent. According to the National Health Facility Survey 2015, only an average of 0.8% of all tracer items were available in public facilities at a time.[30] Store inventory data reveals that more than half of the free drugs were out of stock at least one time in a year. Stock out was most common in district hospitals and in health facilities (HFs) in the Mountain regions. District hospitals, Health Posts, PHCs and the then Sub Health Posts reported stock out of at least one free essential drug in a year at 100, 64, 60 and 53% respectively. Similarly, based on ecological region, data shows highest stock out of free drugs at least one time in a year at 80% in mountain regions, followed by Terai and Hilly (52 and 43%) regions.[31] Of the free drugs stocked out, 72.7% were stocked out for one quarter, 18.2% in two quarters and rest 9.1% round the year.[31] By items of free drugs, less than 5% of HFs had 69.3% of the free drugs stocked out, 5-10% had 20.9% of the free drugs stocked out and 11-15% of the HFs had 4.8 % of the free drugs stocked out.[31]
Percentage of households more than 5/10/20 Km from health facility/ pharmacy to dispense essential medicines for CVDs	While the data on distance of households from HFs/pharmacy to dispense essential medicines for CVDs is not available; as of 2015/016, 34.5%, 39.9% and 25.3% of the households in Mountain region were reported to be at a distance of <30 minutes, 30-60 minutes and >60 minutes from the nearest health facility. Similarly, 39.4%, 42.1% and 17.4% in Hill region and 61.5%, 35.3% and 3.1% in Terai region were reported to be at a distance of <30 minutes, 30-60 minutes and >60 minutes respectively.[32]
Existence of licensing provisions or incentives for private wholesalers and retailers for CVDs	Licensing provisions exist for private wholesalers and retailers. DDA provides products' manufacturing and marketing license to the drug industries. Periodic renewal is required.
Topical Area G: Appropriate Use	
SOPs, national and international guidelines for dispensing and counselling of CVD Drugs	Drug Category Rules 1986 categorizes drugs into three categories: Class A ("ka") (narcotics and poisonous substances), Class B (Antibiotics, hormones and others) and Class C (Over the counter medicines). It provides specific prescribing and dispensing guidelines for each category.[14] Most CVD medicines are categorized under Class B; and these medicines, according to the Drug Act should be sold only on the doctors' prescription and be dispensed by a pharmacist or pharmacy professional only or in their presence.[33] At the national level, Nepalese National Formulary (NNF) 2018 (previous editions: 1997, 2010) provides information on medicines (including drugs acting on the cardiovascular system) and their dosage forms available.[34] The use of NNF is perceived to be limited. DDA has recently inaugurated a mobile app version to increase the utilization of NNF. The National Good Pharmacy Practice Guideline 2005 was drafted to guide pharmacies in basic medications dispensing and counselling; however, if, and to what extent this has been implemented remains unknown.[37]
Functioning mechanisms to improve the prescribing and dispensing practices of CVD drugs	To promote appropriate use of medicines at the organization level, hospitals need to establish a Drug and Therapeutics Committee (DTC), mandated by the 'Hospital Pharmacy Guideline 2072'.[38] DTC should make medicine related decisions; and conduct review meetings every two months. However, there is no data on its implementation. Number of hospitals with DTC, and how useful and active this committee has been remains to be investigated. Although prescribing using INN is recommended by the NMP, many prescribers prescribe medicines using brand names.

"Now, we don't have any specific criteria (for selection of medicine distributors), but we choose distributors based on mutual understanding; and distributors are not very trained-personnel in the country." (-APPON representative)

"if the company has claimed it is a medicine kept in a sensitive condition, it should be checked, in the same condition it has to be opened and checked, but that condition is not maintained there, for medicines, we call it quarantine, due to lack of maintenance of those stuffs it happens. They open it in normal temperature, in this temperature they, even this temperature is not maintained at least AC is maintained here." (-APPON representative)

National therapeutic guides with standardized treatments for common CVDs	No functioning national therapeutic guide with standardized treatments for common CVDs are available. While general practice is to follow the international guidelines as relevant; Nepal is yet to formally endorse international guidelines for dispensing and counselling of medicines for CVD. Also, no evidence is available on how international guidelines are being used at an individual or institutional level. Guidelines availability for NCD services in Nepal is "consistently low".[30] Few facilities (~1%) offering services for CVDs have guidelines for NCD diagnosis and management. There is no provision of guidelines on CVDs in public health facilities.[30] Nationally endorsed and implemented training curriculum for CVD management for healthcare professionals including doctors, nurses and pharmacists is not available. Such training, where available, is specific to organizations. The frequency and curriculum of these trainings is a subject of separate research.
Treatment guidelines used for pre- and in-service training of health personnel in both public and private sector	The Nepal Chemist and Druggist Association (NCDA), in order to promote appropriate medicine use, provides training to the retailers registered with the Association. Pharmacists' involvement and role in medicine dispensing and counseling while still minimal at the community level, the pharmacy services are slowly gaining recognition at the hospital level. At the community level, appropriate use of CVD medications is a challenge not only because of low health and medicine related awareness amongst the general public, but also due to the lack of effective services for CVDs and NCDs from community pharmacies. There is a need to strengthen the pharmacy services at the community level to promote appropriate medicine use. "Our other belief is if we have 40 friends (interested in opening a pharmacy) then why not include them? Let's bring them as well. Let's provide training to them and let them open a pharmacy. Without training, if they keep a pharmacy without registration, they will bring shame and keep selling unnecessary medicines in the country." (-NCDA representative)

Lack of data on availability of CVD medicines, their use and expenditure is a major weakness that can impact, not only the management, but the planning processes.

On the other hand, having a Health Technology and Medical Product (HTP) Directive drafted and ready to use is an opportunity; however, that medical products, apart from the medicines, are not currently regulated under consistent national guidelines is a major threat.[39] The plans to decentralize the medicine regulatory activities and procurement processes, in the federal context, has been viewed as an opportunity to effectively expand the regulatory measures across the country; nonetheless, there are confusions with regards to the roles in the Federal System.

The SWOT identified for the WHO medical product and technology component is listed in Table 5.

DISCUSSION

Medical products and technologies- one of the six key components of the WHO health system building block- lie central to the management of the CVDs. Our assessment has highlighted the lack of, and the need for, CVD specific data on medicines and medical products in Nepal. CVD medicines, along with other medicines are regulated through the DDA; there are no separate provisions exclusively for CVD related products. Whilst laws, regulations and guidelines to regulate medicines and to guide safe and appropriate medicine use are in place, effective implementation is a problem. The nation's regulatory body- the DDA- is constrained by shortages of technically qualified human resources as well as recent technologies. Furthermore, there is no national level regulation in operation to regulate medical equipment and technologies.

Twenty seven percent of CHE was spent on CVD in 2015/2016.[7] However, how much of this is spent on CVD related pharmaceuticals and medical devices is not recorded. A study estimating costs for CVD risk-based management at a PHC in Nepal reported that medicines constitute the highest additional (disaggregated) annual costs (80%) for CVD risk management.[40] Yet another area where information is highly scarce is the private sector. There is no data on how much the private sector spends or earns, on and from, CVD related pharmaceuticals and devices. Estimating and regulating private sector expenses is crucial to make better decisions on overall CVD management. In Nepal, people usually pay OOP for their treatment; the impact of costs can be staggering and impact CVD management.[7,41] Despite medicine related laws and policies being applicable to both the private and public sector, monitoring and regulatory mechanisms primarily focus on public sectors. Effective public-private partnership can play a vital role in CVD management in resource limited settings like Nepal; therefore, understanding how both (and, others) sectors are contributing to disease management quantitatively and qualitatively is necessary.[42]

The growing burden of CVDs in Nepal is not appropriately reflected in, and addressed by, the NLEM.[3] Despite the significant financial burden imposed by CVD management, only nine 'medicines for cardiovascular disease' in the NLEM are considered for inclusion in the free drug list.[40] Furthermore, lack of any CVD medications in the tracer list indicates that CVD medicines are not necessarily and routinely 'traced' for their availability. This suggests a need for regular update of the free essential medicine list; and also, provision to include CVD medicine in the tracer list for routine inspection.

Nepal has ample provisions, laws/acts and mechanisms in place to guide the regulation of medicines. For a developing country with a struggling health system having these frameworks in place indicates the country's effort

Table 5. SWOT related to the Medical Product and Technology component

Strengths

1) Frameworks in place
1.1. Policies & Regulations: NMP, Drugs Act & Regulation in operation
1.2. Active National Regulatory body- DDA
1.3. Existence of Post-Marketing Surveillance
1.4. Existence of Pharmacovigilance System
1.5. Quality/regulatory requirements for how medicines are manufactured and distributed
●Existence of a system for pharmaceutical registrations for drugs
● Mechanisms in place for licensing, inspection and control
*International standards for quality considerations (for example, WHO GMP Criteria and Good Pharmacy Practice (GPP) guidelines
1.6. Resources to guide medicine selection and use
● National Essential Medicine List
● Nepalese National Formulary
● Evidence- based drugs preference
1.7. Act/ Regulation to guide Public Procurement Process
2. The LMIS (and e-LMIS) guiding public procurement process helping in;
● Systematic stock verification
● Forecasting stock
● Systematic Reporting and Feedback
3. Decentralization efforts (local levels being strengthened):
● Allocations of budget for medicine purchase at provincial level and local level
● New structure being developed
4. Increasing technology and capacity of the local medicine manufacturers

Opportunities

1. Health Technology Product and Medical Device Directive 2074
2. Decentralization efforts (local levels being strengthened):
● Allocations of budget for medicine purchase at provincial level and local level
● New structure being developed
● Decentralised public procurement
● Storage facilities being developed at local level
3. Provisions encouraging/mandating hospital pharmacy services (eg., hospital pharmacy guidelines available)
4. Provision encouraging/mandating Drugs and Therapeutics Committee in hospitals
● Increased recognition of pharmacy services (at hospital level)
5. Update of pharmacy curriculum; and strengthen pharmacies – to make better information transfer between community pharmacy professionals and patients

Weaknesses

1. Lack of proper implementation of policies, guidelines and acts
2. Shortages of human resources/ technical capacity
● For rigorous inspection/ control activities
● Quality assurance activities
● To deal with 'new/novel' issues of different 'technical' nature
● To strengthen Pharmacovigilance activities
Lack of competent and effective pharmacy manpower at the community level
3. PV System is not very effective - no real output
4. Product Registration moreover based on paper/document validation (possibility of fraud)
● No system in existence for bioavailability and bioequivalence testing of medications
5. Lack of study/data on:
● CVD related pharmaceuticals, uses, and expenditure
● Private sector procurement, private expenditure
● How resources such as the NLEM and NNF are being utilized
6. Lack of effective participation of the local manufacturers in the public Procurement of Essential medicines
● Reliance on import
7. Substandard Storage Practices/ Facilities
● Loopholes in vaccine storage and cold chain maintenance
● Shortage of technical manpower for cold- chain maintenance
● Issues with cold chain equipment maintenance
● No effective regulation of how medicines are stored at distributor/ retailer level
● Lack of storage and quarantine facilities for medicines at port of entry (eg. airport).
8. Medicine stock out, even for essential/free medicine is reported
● Tracer medicine list does not include any CVD medication
9. Priority to Competitive bidding- more emphasis on 'low' cost (rather than quality)

Threats

1. Lack of effective services for CVDs and NCDs from community pharmacies (Community pharmacies not competent enough to deal with the complexities associated with CVDs and co-morbidities)
2. Low health and medicine related awareness amongst the general public (low health-literacy)
3. No stringent regulation of medical devices, equipment and health technology products (apart from medications) at present
4. Ambiguity in policies/Grey areas
* for example, Nutraceuticals – being regulated by food/ but used as 'medicines'
5. Inadequate information on mechanisms for selection of medicines outside NLEM
6. Lack of clarity on the roles and functions of organizations and workforce in the Federal System- leading to confusions.

to streamline the regulations of medicine and medical products to promote safe medicine related practices. The flip side, however, is the lack of timely update of these laws/ policies, effective implementation of policies and programs and their monitoring. A primary example of this lack of timely enactment of policies and their implementation is the Health Technology and Products (HTP) Directive 2074.[39] The directive, although drafted and approved in 2074, is yet to be implemented. Currently there is no national level guideline that regulates the monitoring of such medical devices. While the development of the HTP Directive is a step in the right direction; there has been a tremendous delay. Bringing the directive to effect and establishing a system to monitor the quality of medical devices and other health technology products, is urgently needed. Lack of effective implementation (and monitoring) of legal policies and guidelines is also indicated by the non-compliance of the legislative provisions set for different pharmaceutical sectors. For example, not only are many pharmacies operating without license, the 'registered' retail and wholesale pharmacies often comply inadequately to the legislative requirements. A study found that registered pharmacies are inadequate (and, often poor) in the physical premises' requirement.[43]

There is a pressing need to strengthen the PV and PMS activities for safe medicine use practices such as timely withdrawal (or alterations) of medicine(s) possible- whether it is from a regimen for a specific patient due to adverse effects or from the market due to lack of safety/ quality- and minimize harm. The pharmacovigilance reporting has been poor; the DDA website reports that the national database contains about 547 ADR reports.[35] Additionally, how the reported ADRs are 'processed' (apart from feeding into the system and passing to Uppsala Monitoring Centre) is not clear. ADR reporting in Nepal is 'spontaneous' and therefore relies on the individual motivation of the practitioners at the regional centres.

Effective reporting can be hampered by other health priorities and challenges such as remote location and poor telecommunication services and low numbers and level of education of health professionals.[44] Studies have also shown limited awareness amongst the healthcare providers about pharmacovigilance reporting.[45,46] For effective reporting and outcome, PV should include active reporting from all sectors of the healthcare system-patients, doctors, nurses, pharmacists and traditional practitioners.[47] Furthermore, collected PV data are not classified and disseminated for wider use therefore, exactly what percentage of these ADRs are due to medicines used in CVD management is not known on the national level. Nonetheless, a study conducted at KIST Medical College showed that 31.27% of the adverse drug reactions were due to antihypertensive drugs.[48] International study estimates the incidence of fatal adverse drug reactions to be around 5% among the hospitalized patients accounting 3% of death.[49]

Our assessment has particularly highlighted the shortages of, and the need for additional and upgraded, workforce, equipment and technology, and appropriate medicine storage facilities. There is an overall shortage of pharmacy professionals in Nepal; the density of pharmacists per 10000 population is reported at 0.9.[50] The number of registered pharmacies in Nepal - reported at 29058 - is significantly more than the existing pharmacy workforce.[51] This has raised questions over appropriate supervision of pharmaceutical services, the quality of medicine dispensing practices, and, thereby medicine use at the community level.[52] Similarly, effective regulation and testing of medicine is impacted by lack of human resources and state of the art technologies.

Over 11 thousand registered medicines and 'special permission' medicines place a huge burden on NML for medicine testing, PMS activities amidst the lack of human and technical resources.[51,53] A large proportion of the medicines are imported; and 80-90% of them are imported from India and third-world countries.[54] Quality assessments of imported medicines often are based on the documents submitted by the manufacturers; Nepal is more vulnerable to data-falsification by the foreign manufacturers, as the regulatory mechanisms are not as robust. There is evidence to suggest that medicines in Nepali markets fail to comply with analytical standards.[55]

Lack of proper medicine storage facilities and practices is speculated to impact medicine quality. Decent medicine storage facilities are lacking in provincial and local level health facilities. Lack of effective medicine storage and quarantine facilities, particularly, at the import junctions, such as the airport and especially for 'sensitive' products in Nepal was highlighted in our assessment.

Assessment of medical products and technology components as part of the health system assessment conducted in other resource limited settings such as Kenya and Nigeria show similar issues.[56,57] For example, gaps in the lack of implementation of policies and regulations, high OOP expenditure for pharmaceuticals, feeble regulatory mechanisms and unregistered pharmacies have been reported.[56,57] In developed countries such as Canada and the Netherlands, strong public financing and insurance schemes protect people from the staggering impact of pharmaceutical cost burden.[58,59]

Strengths and limitations

Need assessment is an essential first step to effective planning, policy making and to develop strategies for disease management. By taking that first step, this study has laid the foundation and paved a way to address the gaps in medical products and technology components for better management of CVDs. In addition to extensive review of literature, stakeholders closely interacting with the component have been involved in the assessment and assessment has been conducted using the standard WHO manual; the study thus involves a strong multidimensional analysis of the component.

The study is not free from limitations. The main limitation is our inability to verify all data obtained through KII respondents. Although the possibility was addressed by providing the participants a list of the statistics we would seek from them in advance, this has been influenced by time limitations and is subject to memory lapses and reporting bias. Furthermore, we could not access all needed records on site. Another limitation is despite efforts, information on medical technology and equipment could not be extensively collected. The findings are more inclined towards 'medicines' than medical 'equipment'. Additionally, interviews were conducted with stakeholders based in Kathmandu; although they oversaw medicine regulation activities at the national level, this study may not be representative of the changing scenario at provincial and local level. Lastly, because our key stakeholders were mostly government representatives, detailed assessment of provisions and regulations pertaining to the private sector has not been possible.

CONCLUSION

There is a general lack of information on medical products specific to CVDs. Paucity of data related to the private sector makes it difficult to precisely estimate medicine expenditure, community level medicine regulation and use of medical products. The need assessment has highlighted the shortage of technical workforce and guidelines for CVD management and the need for upgrading technologies and facilities, such as the medicine storage facilities. Our study has highlighted an urgent need to:

- strengthen technical and human resource capacity of the DDA and the NML;
- generate national level evidence on availability, utilization and expenditures of CVD related pharmaceuticals; and,

research on how the current provisions for medicine regulation and use are utilised;

● ameliorate the processes of monitoring implementation of provisions mandated by acts, policies and guidelines;

● address the gaps in medicine storage and distribution; for example, by developing quarantine facilities at the point of entry and warehouse specifications for medicine storage, and routine monitoring of medicine storage at medicine outlets;

● develop and implement disease specific national level guidelines for CVD management.

● routinely train the workforce at all levels for effective management of CVDs. For this, develop training guidelines and provisions that can be consistently implemented across different healthcare settings of the country.

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