Country Pharmaceutical Situation Based on World Health Organization Indicators: Evidence from an Upper-Middle Income Country

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Abstract:
Evaluating the performance of national authorities has a pivotal role in the development of evidence-based policymaking. Regarding the complexity of the pharmaceutical sector and its severe impacts on public health, Food and Drug Administrations' (FDA) performance should be evaluated at regular intervals. This study aims to depict a comprehensive picture of the Iranian pharmaceutical situation and its structural gaps. In this cross-sectional descriptive study, inspired by indicators proposed by the world health organization (WHO), a checklist was developed with six component topics and 239 indicators. These topics considered the existence and performance of six critical structures, including national drug policy (NDP), regulatory system, medicine supply system, medicine financing, production and trade, and rational use of drugs (RUD). Afterward, the translation validity and then face and content validity of the research tool was confirmed by relevant experts. The data were collected by referring to official documents, reports, and critical informants in the Iranian Food and Drug Administration (IRFDA). According to the WHO indicators, the scores for structures of IRFDA are 80% in NDP, 61.5% in the regulatory system, 64.7% in the medicines supply system, 84.8% in medicines financing, and 60% in production, and trade, and 71.7% in RUD. Considering the status of structures and processes, IRFDA should attempt to provide an action plan commensurate with the NDP. Besides, it should modify the regulations regarding its responsibilities and authorities, develop transparency and accountability in its offices, publish a national essential medicines list, and revise motivational and punitive policies to create RUD.

Keywords: Pharmaceutical Policy; Systems Analysis; World Health Organization; supply and distribution; Pharmaceutical Economics

1. Introduction

Evaluating the performance of national authorities has a pivotal role in the development of evidence-based policymaking in every country[1]. The main objective of such evaluations could be the structural investigation of a system or measuring its operational indicators. The measurement of operational indicators will be helpful if the structural assessment of the system is carried out in the first step. Given that the pharmaceutical sector's policies affect some indicators, such as people's access to high-quality medicines, patient safety, and Rational Use of Drugs (RUD) development, employing a systematic

method for the periodic evaluation of pharmaceutical systems takes on significance[2]. This assessment could present an image of the current status, show the gaps in the pharmaceutical system, and provide health policy-makers with an integrated map of the pharmaceutical system's inputs and outputs.

To this end, international organizations and developed countries have periodically designed various tools to regularly assess the structure and performance of pharmaceutical systems [3]. One of the most recognized tools in this field is the "World Health Organization" (WHO) operational package for assessing, monitoring and evaluating country pharmaceutical situations"[4].

Given the enjoyment? of a holistic approach, various countries have welcomed this tool warmly. This standard method investigates multiple countries' progress over time and allows researchers to compare various indicators in different regions with different facilities. According to the procedure provided by WHO, the evaluation of pharmaceutical sectors is conducted based on a hierarchical approach at three levels[4].

At the first level of this package, the indicators of pivotal structures and processes are assessed. In other words, the first-level indicators provide an overall assessment of every sector's current infrastructure and necessary procedures in a pharmaceutical system. These indicators are evaluated using unique checklists and compare the capacities of various sectors over time[4]. Furthermore, the results are likely to determine the country's capacity for implementing the pharmaceutical system' new policies. At the second level, by conducting a national survey, operational indicators, including access to essential medicines, affordability of medicines, and RUD based on clinical guidelines, are assessed[4]. Finally, more indicators are developed at the third level covering critical components of the pharmaceutical system such as medical supply management, medicine pricing, intellectual property rights, HIV/AIDS management, and regulatory capacity assessment[4]. Countries can use these indicators as a baseline assessment and follow-up studies depending on their capabilities and needs.

Based on the hierarchy explained above, the principal purpose of the present study is to conduct the 'first-level' assessment of the Iranian pharmaceutical system. Therefore, the structural status of the National Drug Policy (NDP), regulatory system, medicines supply system, medicines financing, production and trade, and RUD will be evaluated. Ultimately, this study depicts the Iranian pharmaceutical system's current situation and presents its structural gaps. It is worth noting that no integrated research has been conducted on the structural status of the Iranian pharmaceutical system.

2. Methods

In this cross-sectional descriptive study, inspired by indicators proposed by WHO[4], a checklist was developed with six component topics and 239 indicators. These topics include considering the existence and performance of six critical structures and processes, including the status of NDP, regulatory system, medicines supply system, medicines financing, production and trade, and RUD. Afterward, the translation validity and the face and content validity of the research tool were confirmed by pharmaceutical sector experts. The data were collected by referring to official documents, reports, and critical informants in Iranian Food and Drug Administration (IRFDA) from April to July 2019. In the following sections, the leading indicators of this study have been explained in brief:

2.1. National drug policy

NDP is a written master policy that creates the required integrity between pharmaceutical regulations and the health sector's guidelines, thereby providing a framework for future policymaking [5]. The principles of essential medicines list (EML) preparation, medicines financing and pricing, procurement and distribution of medicines, regulatory system, pharmacovigilance, RUD, and human resource development in the pharmaceutical sector are the main components of NDPs in various countries[5]. Moreover, this document helps harmonies the functions and strategies of all executive sectors, including public and private sectors.

2.2. Medicines regulatory system

This dimension includes planning regulatory framework in terms of regulatory authority, marketing authorization, licensing, regulatory inspection, control of narcotics, quality control, pharmacovigilance, counterfeit medicines, dispensing and prescribing, and promotion and advertising[4].

2.3. Medicines supply system

In this dimension, the availability and accessibility of essential medicines at various levels should be monitored. To this end, the regulatory body supervises medicines purchasing and distribution channels to assure the fulfillment of justice requirements in different geographical locations[4].

2.4. Medicines financing

The primary purpose of policymaking in this component is fair participation in medicines financing. The accessibility of medicines for all people is the best result of the policies made in this dimension[6]. Availability and affordability indicators are affected by three main issues, including "the amount of pharmaceutical public budget," "pricing policies," and "financial programs such as insurance policies and determining the level of out of pockets"[4].

2.5. Production and trade

The pharmaceutical industry is comprised of a wide range of capacities, including raw materials production, new drug development, product formulation, filling, and packaging. This dimension can be affected by pharmaceutical regulatory measures and the performance of health markets in the light of supportive laws such as intellectual property rights[4].

2.6. Rational use of drugs

harmaceutical policies can exert significant effects on the improvement of RUD. The key policies of this dimension include preparing the EML and standard treatment guidelines, encouraging generic drug prescription and usage, providing educational programs for health professionals and the community, and establishing pharmaceutical information centers[4].

To ensure the validity of the collected data, the data collectors received sufficient training about the data gathering methods and filling out the designed checklists[7]. To ensure the accuracy of the responses, the documents and evidence of each declared situation were reviewed as well.

3. Results and discussion

The results of the overall evaluation of IRFDA are provided in Table 1. Each of the six dimensions is analyzed in detail in the following parts.

This study evaluated Iran's pharmaceutical system's key processes and structure indicators. Based on the indicators proposed by WHO, the findings indicate that Iran's pharmaceutical system meets up to 70% (61.5-84.8) of a standard system's criteria in the six dimensions investigated.

Finally, to provide a broad overview of the structural status of Iran's pharmaceutical system, our findings were compared with those of other studies conducted in various countries, such as Finland, Austria, Argentina, The Netherlands, Switzerland, Portugal, Jordan, Iraq, Oman, and Saudi Arabia. Similarly, the present study's findings were compared with the results of review studies prepared by WHO, which investigated the same issues in 156 countries with different levels of income.

3.1. National drug policy

NDP is a master policy that tries to determine both short- and long-term goals, priorities of the pharmaceutical sector, and its main strategies in achieving such goals and priorities. Iranian NDP was first provided officially in 2006, then revised in 2017. The vision of each pharmaceutical sector has been depicted in detail in this document. However, there is no corresponding action plan to cover the responsibilities of managers and personnel, budget, and timetables. Moreover, the alignment of the NDP with other macro policies of the health system should be considered with clarity.

To begin with, the Iranian NDP does not have a corresponding action plan. However, in three-quarters of the other countries, NDPs have action plans compatible with national health regulations. Over the past five years, these plans have been updated in most high-income countries and less than half of low-income countries[(9)]. As table 2 demonstrates, Iran has considered the main headlines of a standard NDP, except for the "EML"[(10–19)].

Table 1. Overall score of IRFDA

	National drug policy	Regulatory system	Medicines supply system	Medicines financing	Production and trade	Rational use of drugs
Structural adaptation with WHO criteria (%)	80.0	61.5	64.7	84.8	60.0	71.7

Table 2. The country situation of NDP functions in Iran and other investigated countries

Functions	The function is considered in:	The function is not considered in:
Essential medicines list (EML) preparation (Number of medicines on EML)	AT(6000), AR(54), JO(680), IQ(1259), OM(650), SA(183)	FI, NL, CH, PT, IR
Medicines financing	All investigated countries	
Medicines pricing	FI, NL, CH, PT, AT, JO, IQ, OM, SA, IR	AR
Medicines Procurement	CH, PT, AT, AR, JO, IQ, OM, SA, IR	FI, NL
Medicines Distribution	All investigated countries	
Medicines Regulation	All investigated countries	
Pharmacovigilance	NL, CH, PT, AT, AR, JO, IQ, OM, SA, IR	FI
Rational use of medicines	All investigated countries	
Human Resource Development	CH, PT, AT, AR, JO, IQ, OM, SA, IR	FI, NL
Research	FI, NL, CH, PT, AT, AR, JO, IQ, SA, IR	OM
Monitoring and evaluation	NL, CH, PT, AT, AR, JO, IQ, OM, SA, IR	FI
Traditional Medicines	OM, SA, IR	Other countries

IR: Iran, FI: Finland, AT: Austria, AR: Argentina, NL: The Netherlands, CH: Switzerland, PT: Portugal, JO: Jordan, IQ: Iraq, OM: Oman, SA: Saudi Arabia

3.2. Medicines regulatory system

One of the significant structural prerequisites for the promotion of pharmaceutical policies in both private and public sectors is the presence of a legal framework, including the following subcategories:

3.2.1. Regulatory authority

Based on the "Medical, pharmaceutical, food and drinks law approved in 1955" and the subsequent amendments to that and the "Health Ministry Establishment Act," the IRFDA is responsible for monitoring pharmaceutical procedures. However, the laws mentioned above have not defined the scope of responsibilities and authorities of the IRFDA. The management of regulatory issues related to the pharmaceutical sector has also been assigned to the "IRFDA's General Directorate of Pharmaceutical and Narcotic Affairs." This affair is financed by the public budget and the proprietary revenues of IRFDA. The main decisions at the IRFDA are made in commissions whose reference is the law approved in 1955. Although the significant choices in the IRFDA are made in commissions, there is no systematic procedure to ensure transparency and accountability in their decision-making process, so stakeholders would not be informed about the reasons for the rejection of their request. However, they can protest against decisions made at relevant commissions.

The IRFDA is active in promoting both regional and international cooperation. For example, the IRFDA is an active member of the *pharmaceutical inspection cooperation scheme* (PIC/S) in unifying pharmaceutical inspection processes. Similarly, the IRFDA cooperates with the international conference on harmonization (ICH) in unifying pharmaceutical registration processes. The IRFDA's official website (www.fda.gov.ir) provides the public with information such as regulations and procedures, the specifications of the registered medicines, and the information about the licensed pharmaceutical companies. However, the information available on this website is updated at various intervals.

3.2.2. Marketing authorization

To issue a market authority, some rules and criteria must be met. According to an official announcement by the IRFDA, 11949 pharmaceutical licenses were issued until April 2019. These licenses are retrievable in the information system of this organization. The open part of the information is available to the public on the official website of the IRFDA.

In issuing a market authority, medicine registration can be conducted based on the applicant's request in all generic, brand, and branded-generic categories. Marketing authorization was granted by the "Legal Commission of Medicines Production and Import." Medicine registration is conducted based on reviewing the common technical document (CTD), testing the product sample, and inspecting production sites. Concerning the registration of imported medicines, it is also required a certificate of pharmaceutical product (CPP) be provided based on the format announced by WHO. According to this format, companies should give IRFDA the verifications of both product quality and product sales authorization in the original country.

3.2.3. Licensing

All manufacturers, distributors, importers, and pharmacies must obtain the licenses for their professional activities based on defined regulations and criteria, with the final decisions made by the *IRFDA's legal Commissions.*

3.2.4. Regulatory inspection

The compliance of manufacturing practices with standards of Iran's good manufacturing practice (GMP) is examined in the field through regulatory inspection. Inspection is conducted according to the national and international guidelines and written checklists at all levels of production, distribution, import, export, community, and hospital pharmacy services.

3.2.5. Supervision of narcotics

According to the existing regulations, such as the "Counter Narcotics Law approved in 2010", the IRFDA is in charge of monitoring and controlling narcotics. In addition, concerning their intermediate ingredients, the "Ministry of Industry, Mine, and Trade" and the IRFDA are in charge. Moreover, Iran is one of the signatories to international conventions on narcotics, psychotropic substances, and their intermediate ingredients, including the "Single Convention on Narcotic Drugs" in 1961 (about natural and synthetic narcotic drugs), the "Convention on Psychotropic Substances" in 1971 (about psychotropic substances, amphetamines, and *methamphetamines), and the "*UN Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances" in 1988 (about 26 reagent chemicals or industrial solutions used for producing narcotic and psychotropic drugs).

3.2.6. Quality control

The IRFDA's quality management system acts following the "quality bylaw." This manual is an official protocol to guarantee medicines' quality and preventive and corrective measures (when the results are inappropriate). Besides examining the companies' documents and conducting necessary inspections, medicines are tested at various levels of production and distribution. For instance, in post-marketing quality control (PMQC), sample testing is performed on the medication available in the market. In addition, further tests are done on the samples suspected of fraud or not meeting the required standards. The referral food and drug laboratory and IRFDA's trusted laboratories working as its contractors often do these tests. These tests are conducted by quality control laboratories located in other countries in rare cases. Imported medicines are subject to regulations similar to the locally produced medicines; in such cases, the documents are reviewed, and quality control tests are done for all locally produced, imported, and even donated medicines. If any medication do not have the required quality, they will not be eligible for granting marketing authorization. Furthermore, in case of identifying any health-threatening problems, such as severe adverse drug reactions (ADR), the defective products will be recalled and eradicated according to established guidelines. The information on recalled medicines is publicly available on the organization's official website.

3.2.7. Pharmacovigilance

The ADRs of all medicines and biological products are monitored at provincial and national levels by universities' ADR centers and the "ADR Center" of IRFDA in voluntary reports. This procedure includes the diagnosis of moderate and severe ADRs, evaluating them, discovering their causes, and controlling and preventing them. The ADRs of vaccines are regularly recorded by the health deputy of the Ministry of Health (MoH). Since Iran is a member of the WHO Program for International *Medicine Monitoring,* all these reports are delivered to the Uppsala Monitoring Center.

3.2.8. Counterfeit medicines

Identifying and fighting against counterfeit drugs are conducted based on the "Anti-Contraband and Foreign Currencies Smuggling Act" by the official representatives of the IRFDA at the "Iranian Administration for Anti-Contraband and Foreign Currencies Smuggling." To this end, pharmacies, distribution companies, herbal medicines stores, and health shops are inspected regularly. In addition, the IRFDA considers all reports received from various sources, including the reports released by other official authorities, vice-chancellors for food and drug in medical universities, specific reports by non-official research groups, reports released by non-governmental organizations (NGOs), and reports provided by the general public. In 2015, the IRFDA developed a medicine authenticity control system called TTAC (trace and track and authentication control) with the possibility of public access. Patients could ensure the authenticity of their medicines by checking the medicines' unique identifier (UID) in this system.

Dispensing and prescribing

According to the Iran Medical Council (IMC) regulations, the "MoH Establishment Act," and the law approved in 1955, the MoH grants the prescription authorization to the members of IMC. In addition to physicians, this license is also granted to some medical sciences graduates, such as midwives, according to a limited list of medicines. Prescribing based on medicines' generic names is not compulsory; however, it should be limited to the Iran drug list (IDL), and the national formulary. Furthermore, the prescriptions should be adapted to the hospital's formulary produced on a generic-name basis at public hospitals. Additionally, in both public and private pharmacies, pharmacists can use generic substitution. In this regard, some policies, such as eliminating insurance coverage of some brand medicines and imposing limitations on imported medicines with a local manufacturing type, encourage local pharmaceutical companies to produce medicines. Eventually, the establishment of pharmacies is subject to regulations introduced by the IRFDA as the "Regulations of Pharmacy Establishment." This regulation introduces the criteria for license holders and pharmacy location and facilities.

3.2.9. Promotion and advertising

The IRFDA and IMC are in charge of monitoring all pharmaceutical advertisements. According to the existing rules, the direct advertising of prescription and non-prescription medicines in public is not allowed. To control medicine advertisement, there are several regulations such as "the executive bylaw of advertisement for chemical and biological medicines" announced by IRFDA in 2015, "article 3 under the guideline on pharmaceutical products advertisement", "regulations on the advertisement of medicines, food products, beverages, cosmetics, and health products approved in 2007 by Iran Medical Council", and "article 5 under the law on medical, pharmaceutical, food and drinks, approved in 1955". The abovementioned regulations mainly emphasize on avoiding direct-to-consumer advertising and non-evidence-based claims.

Like other countries investigated, Iran enjoys a well-formed regulatory body. There is also a governmental budget for these regulatory bodies even though they have incomes from their professional activities. In terms of market authorities, just like in Iran, medicine registration is computerized in almost half of low-income countries and most middle-income and high-income countries. The "WHO certification scheme" is utilized for medicines registration in low-income countries, yet high-income countries use national models. Results have shown that its regulatory system becomes stronger upon an increase in a country's income [(9)].

Quality control tests and the registration of complications are conducted in Iran as well. These measures are often done in high-income countries. However, complications are registered in about half of low-income countries, and the quality control system is implemented in less than 70% of them[(9)]. In addition, the efficiency and safety of medicines are monitored after they enter the market in most high-income countries and two-thirds of other countries, such as Iran. Furthermore, there are regulations and programs for combating counterfeit drugs in most high-income countries and more than half of low-income countries(9)[(8)]. These programs are also available in Iran. According to Table 3, a comparative study on the status of the regulatory bodies in Iran and ten other countries indicated that the regulatory system in Iran is comprehensive and qualified, with all issues taken into account in other countries [(10–19)].

3.3. Medicines supply system

Generally speaking, the IRFDA is in charge of medicine supply supervision in Iran; however, routinely, no centralized purchasing is made on the national level, except in special cases, such as vaccines and AIDS and hepatitis medicines. The IRFDA makes centralized purchasing at the national or international level by calling for bids among registered medicines. Concerning medicines used in public health facilities, universities of medical sciences are in charge of medicines supply and procurement for both their hospitals and community pharmacies. In the matter of monopole producers for which no call for bids is published, negotiation with manufacturers is the common method of the price cut. In recent years, negotiations conducted by the IRFDA have resulted in the price reduction of over 295 imported medicines. Additionally, the WHO prequalification system is applied to supply the medicines for AIDS, malaria, tuberculosis, and vaccines. Ultimately, no group purchasing plan with other countries has been developed so far by the IRFDA and the MoH.

At first, like Iran, most countries adopt a combined approach to their medicine supply system, with the participation of public and private sectors. In 75% of low-income countries and 90% of middle-income and high-income countries, medicine procurement by the public sector is limited to their EML [(9)]. Hence, other medicines are provided mainly by private sectors and NGOs. However, given the lack of EML in Iran, the government is required to do its best to supply lots of medicines. Most Low-income countries supply medicines by calling for bids. However, this is conducted by direct negotiations with suppliers in high-income countries [(9)]. As already stated, both methods are adopted for medicines supply in Iran

Table 3. The country situation of regulatory functions

	FI	AT	AR	NL	CH	PT	JO	IQ	OM	SA	IR
Regulation	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Marketing authorization/ registration	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Inspection	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Quality control	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Market control	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓
Licensing	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓
Medicines advertising and promotion	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓
Clinical trials control	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✓
Pharmacovigilance	✓	✓	✗	✓	✓	✓	✓	✓	✓	✓	✓

FI: Finland, AT: Austria, AR: Argentina, NL: The Netherlands, CH: Switzerland, PT: Portugal, JO: Jordan, IQ: Iraq, OM: Oman, SA: Saudi Arabia, IR: Iran

3.4. Medicines financing

According to the information recorded in the Track and Trace Authentication Control (TTAC) system settled in IRFDA, approximately 1300 and 500 million euros were spent to supply pharmaceutical finish products and active pharmaceutical ingredients in 2017. Based on the Iranian national health policies, some medicines such as "Iron drop" for children under five years of age and "Iron and folic acid supplements" for pregnant women are provided free to fulfill their primary healthcare needs. In addition, antimalarial, anti-tuberculosis, anti-AIDS, anti-hepatitis drugs, and vaccines in national vaccination programs are supplied to the public by supportive governmental finances. In the same vein, the government funds the supply of expensive medicines for patients with refractory diseases, hemophilia, and thalassemia. Likewise, at the primary level of public healthcare, most services such as prescriptions and counseling, and pharmaceutical services are provided through supportive governmental finance. Although prescribers are not commonly allowed to dispense medicines, there is a limited list of medicines at primary healthcare centers prescribed and dispensed by either physicians or health workers, according to the guidelines.

Given the public insurance coverage in Iran, approximately 95% of the Iranians and 60-80% of medicines registered on the Iran Drug List (IDL) are covered by public and private medical insurance companies. This coverage is provided based on end-user prices, including tariffs, duties, and the profits of manufacturers, distribution companies, and pharmacies. Medicine prices are regularly updated on the websites of insurance companies and the IRFDA's website for public information. The vice-chancellors conduct regular inspections in public and private pharmacies for food and drug in medical universities to monitor medicines' prices. Moreover, pharmacies are required to write medicines prices on drug invoices.

Pharmaceutical pricing policies are more common in high-income countries. The monitoring system of medicine prices at pharmacies is implemented in Iran, most high-income countries, and one-third of low-income countries [(9)]. In most countries, regardless of their income status, several medicines are distributed free of charge under certain conditions for specific diseases and with public insurance coverage [(9)]. Over 50% of low-income and middle-income countries have insurance systems that cover the public sector's central portion of medicine costs. However, in all high-income countries, an insurance system covers most medications [(9)]. In Iran, most generic medicines are covered by the insurance system. Due to controlling induced demands, medicines' sales and distribution by prescribers and prescription by pharmacists and dispensers are prohibited in most countries. Medicines distribution by prescribers is possible in only a few countries. Likewise, in only a few countries, medicine sales incomes are used to pay prescribers' salaries [(9)]. This is practiced in Iran only for the first-level healthcare services at rural health centers for a limited list of medicines.

Levying customs tariffs and duties increases medicines' final price and imposes a high financial burden on health systems and patients. Therefore, based on WTO's agreements, most countries try to reduce tariffs on imported pharmaceutical raw materials and finished products [(10–19)]. As Table 4 shows, many countries try to keep the value-added taxes on medicines less than general taxes [(20,21)].

3.5. Production and trade

Medicines are produced in Iran at various levels, including the production of raw pharmaceutical materials, the formulation of finished products, and the primary and secondary packaging of finished products. Shedding light on this matter, up to 95% of the medicines used in the Iranian pharmaceutical market and almost half of the raw pharmaceutical materials are domestically produced. Although Iran has not yet joined the World Trade Organization and is not a signatory to the Agreement on Trade-Related Aspects of Intellectual Property Rights (*TRIPS*), national regulations exist to support intellectual property rights regarding internally registered inventions. So, patent protection affairs in the pharmaceutical industry would be handled by the "Country Registration of Deeds and Properties Organization."

In half of low-income, most middle-income, and all high-income countries, patent protection is applied in pharmaceutical industries [(9)]. Regardless of countries' income levels, many WTO members enjoy TRIPs waivers in pharmaceuticals. Given there are over 100 pharmaceutical factories in Iran, it has a remarkable capacity for producing pharmaceutical products. As Table 5 demonstrates, except for the production of new pharmaceutical molecules, Iran can make medicines at other levels [(10–19)].

Table 4. Standard value added tax (%) versus medicines value added tax (%)

	FI	AT	AR	NL	CH	PT	JO	IQ	OM	SA	IR
Standard VAT	24	20	21	21	7.7	23	16	NA	0	5	9
Medicines VAT	10	10	10.5	9	2.5	8	8	0	0	0	0

FI: Finland, AT: Austria, AR: Argentina, NL: The Netherlands, CH: Switzerland, PT: Portugal, JO: Jordan, IQ: Iraq, OM: Oman, SA: Saudi Arabia, IR: Iran

Table 5. The country situation of Pharmaceutical production capabilities

	FI	AT	AR	NL	CH	PT	JO	IQ	OM	SA	IR
The number of Pharmaceutical manufacturers	65	220	402	202	468	51	16	23	4	19	184
Research and Development for discovering new molecules	✓	✓	✓	✓	✓	✓	✓	✗	✗	✗	✗
Production of APIs	✓	✓	✓	✓	✓	✓	✓	✗	✓	✗	✓
Formulation of finished products	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Repackaging of finished dosage forms	✗	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓

FI: Finland, AT: Austria, AR: Argentina, NL: The Netherlands, CH: Switzerland, PT: Portugal, JO: Jordan, IQ: Iraq, OM: Oman, SA: Saudi Arabia, IR: Iran

3.6. Rational use of drugs

Iran EML is being drawn up, so it has not yet been notified nationally. Standard clinical guidelines have been developed at a national level for the severe diseases of children and adults by the MoH. However, the compliance of prescription activities with these guidelines is not being monitored. Similarly, a national formulary corresponding to the IDL was developed and updated regularly; however, some physicians do not follow it. Iranian physicians, dentists, and pharmacists are subject to mandatory continuing education on medical treatments, pharmacotherapy guidelines, and RUD development. In addition, a national information center has been established using the public budget to provide physicians, pharmacists, and people with classified pharmaceutical information. The services of this round-the-clock center, known as "The *National* Information Center of Medicines and Poisons," are provided on the phone, being free of charge. In the same vein, some universities of medical sciences have recently started providing such services at a provincial level. Likewise, the IRFDA, in collaboration with the media, plans some education to improve RUD through radio programs, newspapers, public notifications, and public seminars. The National Drug and Therapeutic Committee (DTC) is in charge of monitoring and promoting RUD in Iran. Moreover, most reference (level 3), public (level 2), and regional (level 1) hospitals, as well as universities of medical sciences, have RUD committees.

The MoH has published a written national strategy titled "antibiotic stewardship," implemented with government support for national supervision of antibiotics. Moreover, there is a national reference laboratory to monitor antimicrobial resistance. A government-funded task force tries to promote the rational use of antibiotics and prevent developing microbial resistance. However, despite all these measures and legal prohibitions, some injectable medicines and antibiotics are still sold illegally at pharmacies without prescriptions.

Although the EML has been prepared in most low and middle-income countries, this list has not been drawn up in about 30% of high-income countries [(9)]. As already mentioned, this list is currently being compiled in Iran.

The number of medicines on this list increases(9) with an increase in a country's income [(8)]. This list is quite prevalent in the insurance systems in high-income countries. In addition, the presence of a formulary at medical centers is welcomed by high-income countries [(9)]. This indicates that high-income countries are willing to provide clinical guides at hospitals and health centers. However, low-income countries are eager to provide such guides at a national level [(9)]. Among 27 countries of the European Union, in the nine countries of Austria, Belgium, Germany, Hungary, Romania, Slovakia, Italy, Spain, and Cyprus, prescriptions are made up based on clinical guides [(22)].Standard Clinical Guides (STG) presence in Finland, Austria, Argentina, The Netherlands, Portugal, Jordan, Oman, Saudi Arabia, and Iran [(10–19)].

Similar to 70% of high-income countries and 50% of other countries, continuous training courses are run for physicians in Iran. The "National information centers of medicines" are available for health professionals and people in three-quarters of high-income countries and one-third of low-income countries. In almost half of the nations, there are campaigns to promote RUD. High-income countries have a more significant number of such movements and programs [(9)].

In most countries, such as Iran, pharmacists are allowed to substitute brand medicines with generic ones. This type of substitution is done more prevalently in the public sector than in the private sector [(9)]. In European countries, private and public sectors are equally allowed to follow this rule [(22)]. Moreover, more incentives are applied in high-income countries than in low-income countries to facilitate substitution. In two-thirds of low-income countries and about 20% of high-income countries, the prescription of generic medicines is mandatory at public health centers [(9)]. This is the case in the public sector of Iraq, Oman, and Jordan [(12,13,15)]. In addition, the prescription of generic medicines is mandatory in both the private and public sectors of Portugal, Romania, Lithuania, and Estonia [(22)]. This obligation complies with the private-sector pharmacies of 20% of low and middle-income countries. However, it is not common in high-income countries [(9)]. In countries where such substitution is optional, the lawmaker has provided some financial incentives to promote the usage of generic medicines. For instance, if pharmacists in France substitute brand medicines with generic ones, they will be paid the same amount of profits as considered for brand medicines by insurance companies [(22)].

There are special committees for RUD in Iran. Such committees are more prevalent in countries with higher incomes [(9)]. The national policy of countering antimicrobial resistance in most high-income countries is followed in Iran and one-fourth of low-income countries [(9)]. Despite all measures adopted and legal prohibitions, some injectable medicines and antibiotics are still sold at pharmacies without prescriptions. The sales of injectable medicines and antibiotics without prescriptions are limited in high-income countries, yet it is widespread in low-income countries [(9)]. Finally, the monitoring of prescription patterns is conducted by both regulatory authorities and insurance companies in Iran, yet it is conducted by third parties in most EU countries [(22)].

Conclusion and Managerial Implications

The pivotal processes and structures' indicators of the Iran pharmaceutical system were evaluated in this study. In other words, this research was an attempt to inform the pharmaceutical policy-makers about the status of Iran NDP, the capacities of the medicines regulatory system, defects of the medicine supply system, the framework of medicine financing as well as the requirements for implementing a more efficient financial management system, the capabilities of medicine production and trade, and the status of RUD in Iran. The information provided by the present study and similar studies can be highly useful in reforming regulations, policies, and the country's NDP. Such studies can determine the progress of activities by strategic goals of pharmaceutical sectors. Furthermore, this study can facilitate the participation of various stakeholders in achieving these strategic goals. Thus, considering our findings, the following items are suggested to improve the structural status of the pharmaceutical system.

The IRFDA is recommended to evaluate the organizational structures of the pharmaceutical system at regular intervals and monitor the progression or regression of the system's performance. It can lead to the modification of policymaking structures in the long term. Then, it is recommended to formulate an action plan compatible with the country's NDP and regulate all activities, responsibilities, financial resources, and timetables based on this action plan. This improvement plan should be consistent with the macro policies of the health system. Similarly, the lack of EML is a significant challenge facing the efficient management of financial resources. Given the absence of such a list, the government is required to do its best to supply a wide range of medicines. It is necessary that such a list to be drawn up and its items to be classified based on the country's financial resources. In addition, it is essential that the authority, power, and duties of the IRFDA to be defined accurately and in detail. Moreover, the transparency and accountability of the commission's decisions should be promoted so that the stakeholders will be informed about the reasons for the commission's findings. The following recommendation is group purchasing plans with other countries to maximize financial resource savings.

Moreover, it is highly recommended to determine some incentives to substitute brand medicines with locally produced generic ones in pharmacies. Finally, it is required that the inefficiency of current controls on dispensing antibiotics and injectable medicines without prescriptions be investigated. Moreover, it is

recommended to prohibit such a trend by offering more incentives and taking punitive steps to align various stakeholders in promoting RUD.

Ethical Statement

This is an original work, and all authors have contributed to this article. This research has not partly or as a whole been submitted to any other journals for publication.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

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