

## THE RATIONAL USE OF DRUG AND ANTIBIOTICS

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### ABSTRACT

Recently, the rational use of drug has been taken part in literature as a contemporary issue that is evaluated from the perspective of public education in terms of creating a social awareness by especially politicians and government. Drug expenses which have an important part of health expenses including developed countries is also a significant issue with regard to the more effectively uses of limited sources. Even though patients get the suitable remedy that is directed by a physician during the treatment, controlling of the process cannot be conducted easily since they are the final decision makers on the use of drugs. The problems starting as individually on the irrational use of drug can negatively affect public welfare in the long term. The most common drugs that are used irrationally are antibiotics; and it causes an interruption for the sustainability of health gains in terms of both cost and productivity. The aim of this study is to form a general framework on the issue of the rational use of drug both in Turkey and in the world, and is to reveal the current position of antibiotics, which is the most popular one for the irrational use of drug, with the help of statistical data and studies in the related literature.

**Key Words:** Rational Use, Drug, Antibiotics

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## AKILCI İLAÇ VE ANTİBİYOTİK KULLANIMI

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### ÖZ

*Akılci ilaç kullanımı son zamanlarda toplumsal farkındalıđın oluşturulması açısından özellikle politikacılar ve hükümet tarafından halk eğitimi perspektifinde deđerlendirilen güncel bir konu olarak literatürde yerini almaktadır. Refah düzeyi gelişmiş ülkeler de dahil olmak üzere sağlık harcamalarının önemli bir kısmını oluşturan ilaç harcamaları kıt kaynakların daha verimli bir şekilde kullanılması açısından da önem arz eden bir konudur. Hastalar tedavi sürecinde hekimin uygun gördüğü tedaviyi alsalar bile, ilaç kullanımı konusunda son karar vericiler kendileri olduğu için bu konuda denetim kolaylıkla gerçekleştirilememektedir. Akılci olmayan ilaç kullanımı ile ilgili birey düzeyinde başlayan problemler daha uzun vadede toplumun refah düzeyini de olumsuz etkilemektedir. Akılci kullanılmayan ilaçların başında ise antibiyotikler yer almakta, hem maliyet hem de verimlilik açısından sağlık kazancının sürdürülebilirliğinin sekteye uğramasına neden olmaktadır. Bu çalışmanın amacı dünyada ve Türkiye’de akılci ilaç kullanımı konusunda genel çerçeveyi çizmek ve akılci kullanılmayan ilaç kategorilerinin başında gelen antibiyotik kullanımı ile ilgili mevcut durumu literatürde yer alan istatistiki verilerle ve çalışmalarla ortaya koymaktır.*

**Anahtar Kelimeler:** Akılci Kullanım, İlaç, Antibiyotik

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## **I. INTRODUCTION**

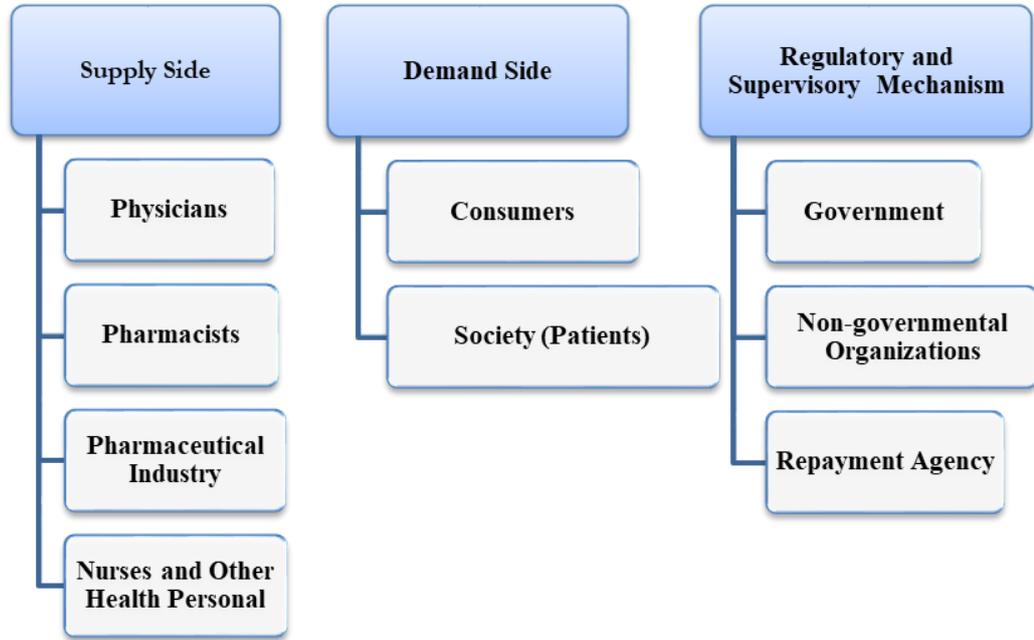
World Health Organization (WHO) states the concept of drug as “a product that is used or the use of it is foreseen to change or examine physical or pathologic cases of patients for their benefits” (WHO 1985). The process of drug usage is a case that should be sensitively controlled and examined, because the use of wrong drug or wrong dosage leads up to prognosis that may causes death of patients.

In WHO’s Conference in Nairobi-1985, the term Rational Use of Drug is defined as the whole demands that “the appropriate drug be prescribed, that it be available at the right time at a price people can afford, that it be dispensed correctly and that it be taken in the right dose at the right intervals and for the right length of time” (Peköz 2018). In other words, the rational use of drugs is using appropriate drug in correct dose, right time and correct price for the aim of preventing a disease, controlling it and finally treating the disease (Akkurt 2016; Akıcı et al. 2004). The rational use of drug consists of a process in which patients consult a physician, the physician prescribes an appropriate medicine in terms of the clinic features and characteristics of patients and gives necessary information about the medicine, then patients get the medicine and they use it in correct dose and right length of time (Akıcı 2015).

The process of the rational use of drug requires a systematic process which involves in defining the problem for patients after getting a correct diagnosis, determining the aim of treatment and selecting a safety treatment, then beginning the treatment after prescribing the appropriate medicine and presenting the treatment obviously to patients, following the results of the treatment and finally evaluating the treatment (Oktay, Akıcı 2001).

In Figure 1, the stakeholders having responsibilities for the rational use of drug is indicated. The stakeholders are “the physician who gets the diagnosis and determining the medicine, the pharmacist who supplies the medicine, the nurse who applies the medicine, the patient, the patients’ relative, other health personal, the producers in health sector, the students, government, media and educational institutions” (Akkurt 2016). Since diagnosis and prescribing is physician’s responsibility, the most responsible person on the rational use of drug is also physician. Drugs are presented in different pharmacologic-therapeutic categorizations in terms of indications in pharmacies. This presentation is organized based on two kinds of drug categorizations as the approval of health authorities. These are categorized as drugs that can be sold with a prescription and sold without a prescription. Both the presentation of these drugs and giving information the drugs are pharmacists’ responsibility. Thanks to this responsibility, pharmacists have a crucial role on the rational use of drugs. Accordingly, the use of drugs in hospitals, firstly physicians, and then pharmacist, nurses and other health personals have significant roles in the rational use of drugs (Oktay 2006). The most important role in the step of demand for the rational use of drugs is stated to patients.

As in the whole world, the irrational use of drug is a significant problem in Turkey. All of the mistakes that are related to the use of drugs can be named as the irrational use of drug. The irrational use of drugs such as buying drugs without consulted a physician, using drugs that are available at home, using drugs with the references of others, using drugs in wrong doses, finishing the treatment before the suggested date, asking for injectable form of the drugs and requesting physicians to prescribe unnecessary drugs is seen commonly (Sürmelioglu et al. 2015; Pinar 2012).

**Figure 1. The Responsible Stakeholders for the Rational Use of Drugs**

**Source:** Sürmelioglu et al. 2015.

The irrational use of drugs may cause unsuccessful treatments, the increasing effects of drugs, resistance for antibiotics, repeated diseases or long-period health problems, unsuitable patient demands that are the results of overused drugs, problems on supplying drugs because of the decreases in drug stocks, drug dependency and the increases in the prices of treatments (Tuncer et al. 2016; Aksoy et al. 2015). According to the estimations of WHO, over 50% of drugs are prescribed, supplied or sold wrongly. Half of the all patients, also, do not use drugs rationally (Aksoy et al. 2015). The irrational use of drug may be originated because of both the effects of health personals and the factors that are related to patients. Some of these main factors can be stated as instructions of physicians for irrational use of drugs, patients' use of drugs that are not prescribed and their disorganized use of drugs. For whatever reason, irrational use of drug causes disorder for human health and economic losses (WHO 1985). As in this scope, the main aim of this study is to create a general framework on the issue based on the rational use of drug both in Turkey and in the world; accordingly, it is aimed to reveal the current position of antibiotics with the help of statistical data and studies in the related literature.

## II. THE RATIONAL USE OF DRUGS IN THE WORLD

Until the use of drugs for the treatments of patients, the problems on this concept such as unnecessary drug prescriptions, the wrong or aimless use of drugs and preferences of high afforded drugs have begun to increase in the world. With the help of studies on the solutions of those problems, it has come into effect and the policy of the rational use of drug has become a step of this solution process (WHO 1985).

WHO designed the Essential Drugs List in 1977; it developed Essential Drugs List Action Plan in 1979, and in 1985, it gave a chance to get a number of decisions on the rational use of drugs in the conference organized in Nairobi. In 1986, national policies on the rational use of drugs were designed and performing of them was advised. In 1987, Rudolf Bucheim who was Estonian supplied institutionalism of pharmacologic treatment as

constituted the first pharmacology institution at his home and he put his stamp on history as the first researcher who stated the idea of the rational use of drug. Although there have been some approaches on the field of pharmacology, it was the first systematic application of sorting out the philosophy of the rational use of drug (Tez 2001).

When countries are examined, Australia designed guidebooks for evaluating pharmacologic products in terms of economic afford in 1992 and it was a country which wanted pharmacology companies to prove cost efficiency of products in order to go in for their national formulas (Neumann 2004; Hjelmgren et al. 2001). In some other countries such as Belgium, France, Italy and Sweden, it has also begun to be wanted the analyses of cost-efficiency related to drugs while appealing production of new drugs (Gafni, Birch 2003). As in the same way, in Japan, the price of all drugs and medical products has been begun to be determined by Ministry of Labor and Social Policy and Ministry of Health until 1994, and it has also been wanted to be analyzed as pharma-economically by drug companies while appealing the production of new drugs (Doherty, Sato 2003).

However, in spite of the positive results of those developments, the rate of the use of unnecessary, wrong and highly-affordable drugs has increased all over the world. For instance, in USA, there has been an increase at the rate of 4% to 6% on admission to hospital that has been based on the adverse effects of drugs. Accordingly, it was seen that approximately the irrational use of drugs caused 30-130 million dollars of costs on mortality and morbidity. In 2006, WHO determined that the costs of all drugs were 859 billion dollars in all over the world. In the context of Gross National Product (GNP), it is stated that the rate of drug costs is 1,52%; the total rate of all drug costs is also determined as 24,9% in the World (WHO 2006). Besides, according to WHO, nearly half of the all drugs in the world have been irrationally prescribed and used. Half of the all patients have not also used drugs in the correct doses or methods (The Rational Drug Use National Action Plan 2014-2017).

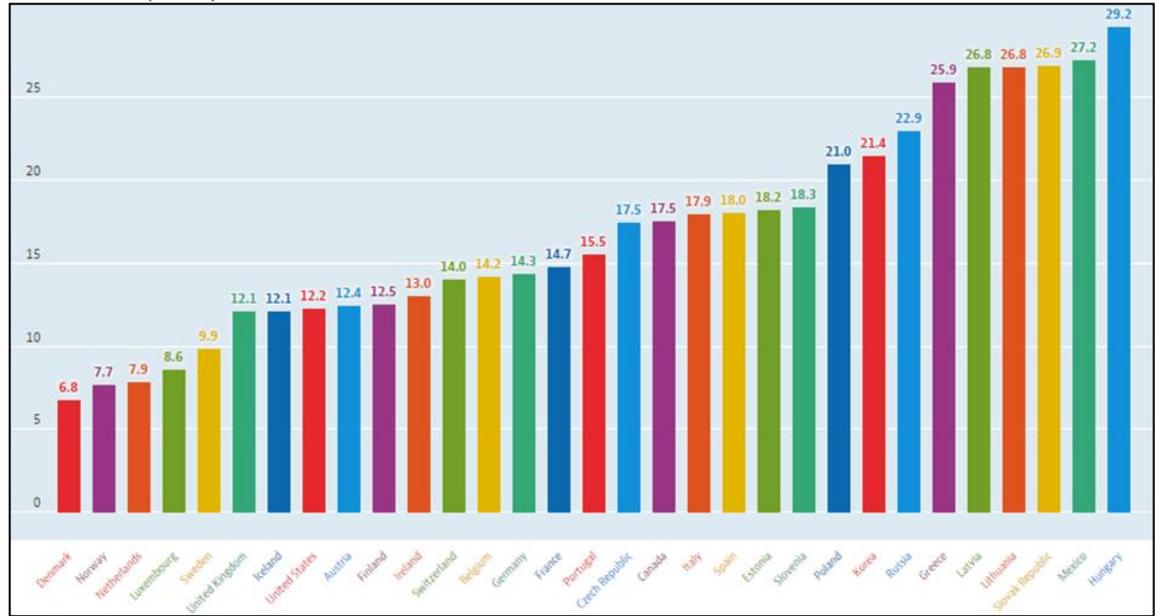
With those developments, WHO states that the developments on the rational use of drug will increase via supplying all of the drugs equally and using them effectively and correctly. It also predicates that developments in this concept can come true with the use of suitable and well-afford drugs by the policies that would be applied for this aim, the presenters of health services and patients (WHO 1995).

In many researches on this field that have been conducted in the world, it is stated that there have been positive developments thanks to educating physicians on pharmacology (patients' drug treatment) within the other precautions on the irrational use of drug. For instance, as a result of a study conducted on the pharmacotherapy education for physicians on the rational use of drug, it was confirmed that after the education, the physicians in Holland, Sweden, Norwegian, Germany and Slovakia behaved more sensitively and selectively while having prescribed drugs (Lagerlov et al. 2000). Accordingly, in a study that aimed to reveal the behavioral changes of the physicians who have short-term education on pharmacotherapy, it was stated that 219 physicians who have been working in faculties of Medicine in Holland, Nigeria, Australia, USA, Japan and India were more successful after the education (De Vries et al. 1995). In the light of those studies, WHO published a handbook on the rational use of drug for the students who have been in faculty of medicine in order to lead the students on this field, WHO also developed Prescription Guidebook in 2003 and it has been translated into 18 different languages until 2006. As in this way, that guidebook was a model for the students on the rational use of drugs (Akkurt 2016).

In Figure 2, for the year of 2015, the total rates of the drug payments in the all health expenses in OECD countries were showed as percentages. Total drug payment means "clear" expense in many countries; that is, it is arranged for probable discounts that will be paid by

producers, wholesalers or pharmacists. As the figure is taken into consideration, it is seen that the lowest rate of the drug payments in all health expenses is in Denmark (6,8%); the highest payment is seen in Hungary (29,2%). In the study conducted by Ersöz, it was stated that the reason of high payment rate in Hungary was the direction of pecuniary resources to health sector because of the common chronic diseases and high rates of mortality and morbidity (Ersöz 2008).

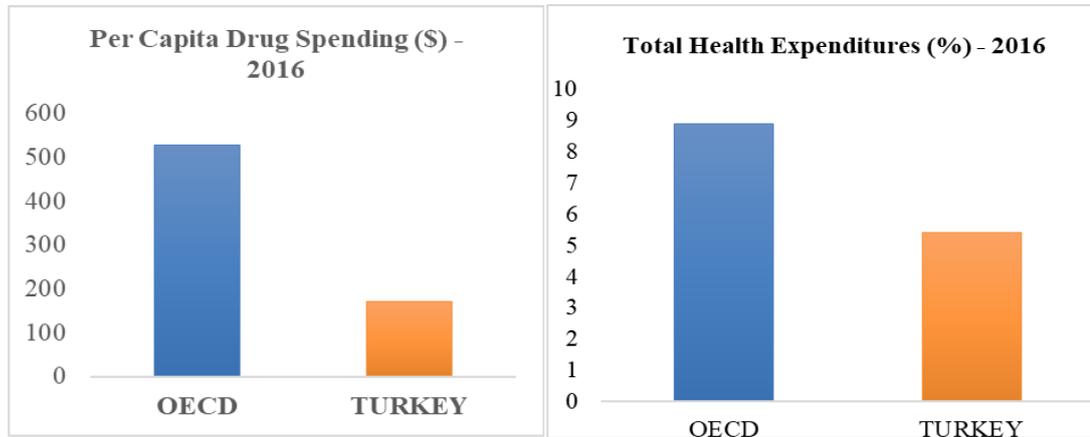
**Figure 2. The Rate of Drug payments in all Health Expenses in OECD Countries (%) (2015)**



**Source:** <https://data.oecd.org/healthres/pharmaceutical-spending.htm#indicator-chart>.

In Figure 3, for 2016, the drug payments per capita in Turkey and in OECD and the total health expenses in Gross Domestic Product (GDP) are showed. As Figure 3 is examined, it is seen that the total health expenses and the rate of drug payment per capita in Turkey is lower than the average of OECD. When the rate of total health expenses in GDP in 2016 is taken into consideration, it is seen that this rate is 8, 9% OECD countries, however it is 5,4% in Turkey (Sayılı et al. 2017). According to 2016 Budget presentation of Ministry of Health, while the payments of drug per capita were 170 dollars in Turkey, the average in OECD countries was 527 dollars per capita. As seen in those rates, payments of drug and health expenses in Turkey is less than the OECD countries. (as cited in <https://www.turuncuhat.com/ilac-harcamalari-infografik-c231>, Access Date: 18.04.2018).

**Figure 3. The Rate of Drug Payments per capita and Total Health Expenses in Turkey and in OECD Countries (2016)**



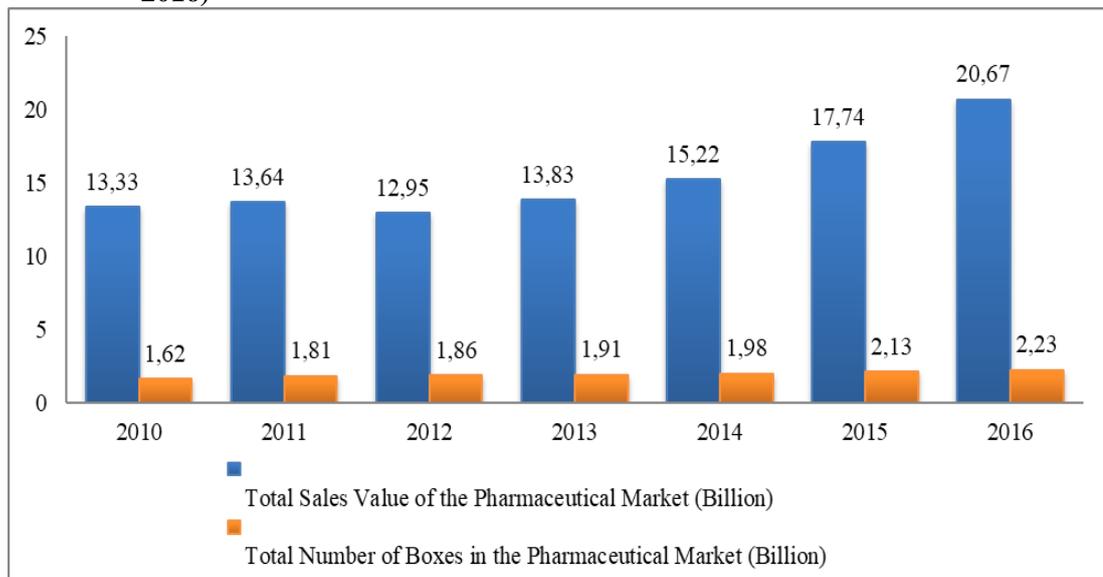
Source: <https://www.turuncuhat.com/ilac-harcamalari-infografik-c231>.

### III. THE RATIONAL USE OF DRUG IN TURKEY

In Turkey, the market share of drug industry has reached a high capacity as increasing in per year. It is thought that there can be some inferences on the rational use of drug in Turkey that is based on some factors such as increases of reference drugs, the market share of them, the numbers and variations of import and export drugs, the usage drugs in terms of treatment groups, and it is also believed that these factors are important while determining policies on this field.

In Figure 4, the market share of drugs and costs of producers in Turkey is shown. It is seen in the figure that in 2010, the total sales value of the market share in drugs was 13,33 billion Turkish liras in Turkey and it was 1,62 billion Turkish liras per each box. It is also observed that, the number was 20,67 billion Turkish liras in 2016 and it was 2,23 billion Turkish liras per each box.

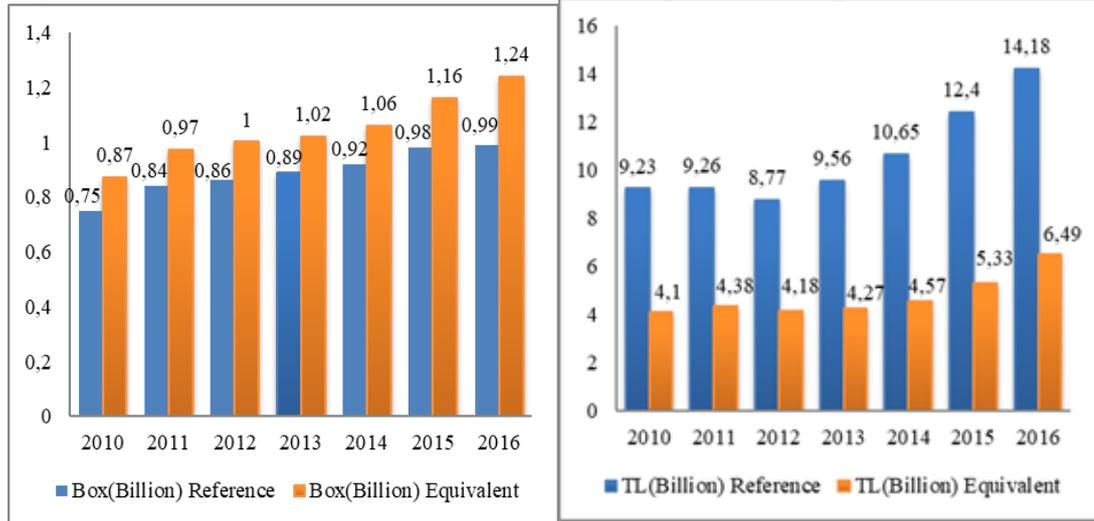
**Figure 4. The Position of Market Share on Producers' Drug Costs in Turkey (2010-2016)**



Source: IMS and İEİS, 2016 Report.

In Figure 5, the current position of reference and equivalent drugs are shown. When Figure 5 is examined, it is seen that the reference drug marketing was 14, 18 billion Turkish liras in 2016 and it is 0,99 billion Turkish liras per each box. Accordingly, it is seen that the sales of equivalent drugs were 6,49 billion Turkish liras and it was 1,24 billion Turkish liras in boxplot, and it is also observed that those rates tended to be higher than the previous years.

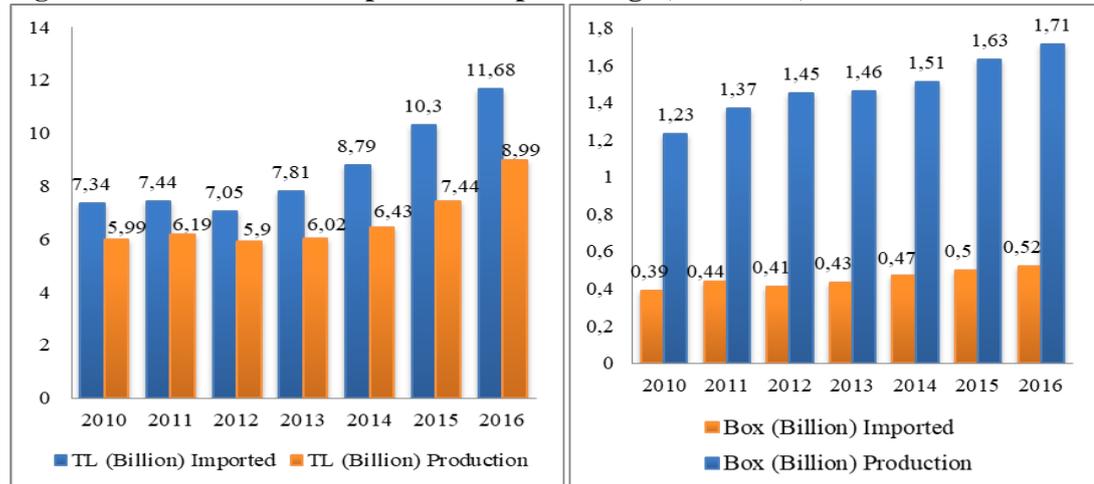
**Figure 5. The Current Positions of Reference and Equivalent Drugs (2010-2016)**



Source: IMS and IEIS, 2016 Report

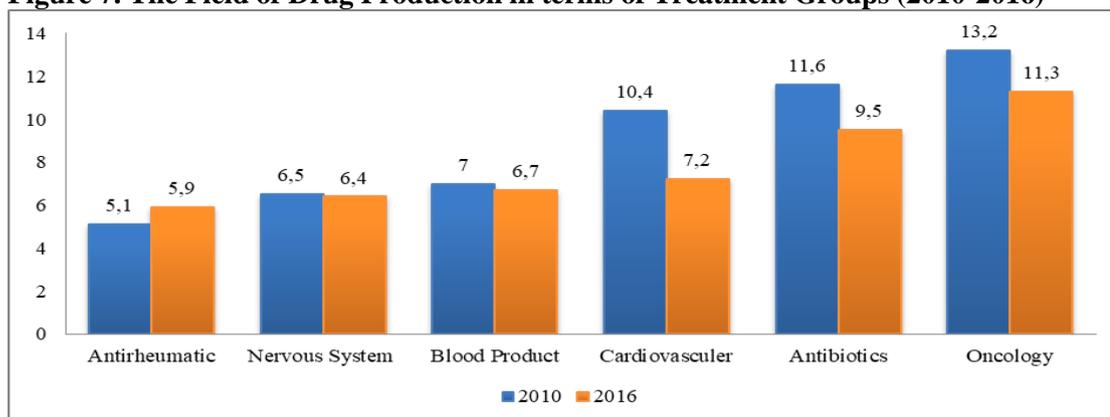
In Figure 6, the number of import and export drugs is shown. As it is seen in the figure given above, it is seen that the value of import drugs was 11,68 billion Turkish liras in 2016 and it was 0,52 billion Turkish liras per each box; the value of produced drugs was 8,99 billion Turkish liras and it was 1,71 billion Turkish liras per each box.

**Figure 6. The Number of Import and Export Drugs (2010-2016)**



Source: IMS and IEIS, 2016 Report

In Figure 7, the fields of drug use is shown in terms of treatment groups. When the figure is examined, it is observed that the level of drug usage in the field of oncology, cardiovascular systems, nervous systems and antirheumatic was decreased, whilst the level of drug usage in the field of antibiotics and blood products was increased between 2010 and 2016.

**Figure 7. The Field of Drug Production in terms of Treatment Groups (2010-2016)**

Source: IMS and IEIS, 2016 Report

As in the countries in which the use of antibiotics have been increased, in Turkey, antibiotics use causes a significant problem on the rational use of drugs. The main reason of this problem can be physicians' prescriptions of antibiotics for antiviral diseases even if it is not necessary or it can be patients' persisting for prescribing antibiotics by physicians since they think they can be come around easily thanks to antibiotics. In this sense, it is thought that the rational use of antibiotics should be mentioned.

#### IV. THE RATIONAL USE OF ANTIBIOTICS

Antibiotics that have been used for nearly 50-60 years heavily contribute to human health for treating infection diseases which would be mortal. With the help of rational use of antibiotics, becoming chronic diseases has been inhibited for a number of current infection diseases and the resistance or severity of diseases has been limited. However, it is seen that the irrational use of antibiotics has been increased day by day rather than those goals. In other words, the abuse of these kinds of drugs has been convenient. Even in USA which uses a well systematic mechanism on the field of rational use of drugs, the rate of irrational use of antibiotics has been nearly 50%. As a result of the unnecessary and misusing of antibiotics, there is a resistance against antimicrobial factors and it causes financially loses beside negative effects for human health. With the resistance against antibiotics, there is prolonged hospital stay for patients and the length of mortality has increased (Öztürk 2008).

Antibiotics are a group of drugs which are used for bacteria based infection treatments. Especially the treatment of viral based diseases like Acute Upper Respiratory Tract Infection (acute u.r.t.i), it is not suitable. When the literature is taken into consideration, it is seen that antibiotics have been generally prescribed for this kind of viral infection based diseases. The resistance develops because of preferring antibiotics apart from bacteria based diseases or the use of antibiotics in wrong doses, wrong durations and wrong ways (Meer, Gyssens 2001; Özgüneş 2005; Durmaz 2006). As a result of this resistance, especially in the cases of infection caused by multiplex microorganisms, patients cannot response to treatment or the length of treatment can be longer (Özgüneş 2005). In a microorganism that is resistant against any antimicrobial factor, there can also be a resistance against other antimicrobial which has similar structures or effects of this substance and it is called as cross resistance (Öztürk 2002).

The resistance against antibiotics may cause damages for patients and society besides increasing costs in terms of pharmaco-economic aspects. As it is examined in terms of patients, the length of treatment can be longer and so, either patients may be lately getting

well or they may die because of late treatments. In addition to this, prolonged hospital stay can be seen and the risk of having hospital based infection increases because of prolonged treatments for patients. As it is examined in terms of society, the diseases that are not treated can cause a genetic resistance as spreading to all society and it may cause a mortal threat. As it is examined in terms of pharmaco-economic factors, costs of treatments increase due to the long duration of treatments and it may not be handled because of different microorganism diseases' existence (Çöplü 2012).

In order to apply rational use of antibiotics in a wide range, it is necessary to conduct some researches which aim to reveal the relationship between resistance and active ingredient of antibiotics (Berild et al. 2001; MacDougall, Polk 2005). Thank to systematic researches on the rational use of antibiotics, it is thought that the speed of mortality and morbidity will decrease, the length of staying at hospital will be shorter, the life standards will be better and low-cost health services will be realized economically (Paladino 2005). The elements of the rational use of antibiotics can be summarized as given below (Mannino 2003) :

- Determining the aims on this field and collecting suitable data,
- Designing advisor guidebooks and updating them regularly,
- Coordinating the results of microbiologic laboratory and guidebooks,
- Creating an awareness for all stakeholders via face to face education on the use of antibiotics,
- Limiting the use of antibiotics.

Managing antibiotics means the mechanism of determining policies on prescribing correct antibiotic for correct patients in a suitable treatment duration and correct way, applying these policies and inspecting them. The aim in this process is decreasing resistance against antibiotics and saving the real effects of antibiotics and realizing the expected effects. As in this way, the costs can be controlled (Sipahi 2009).

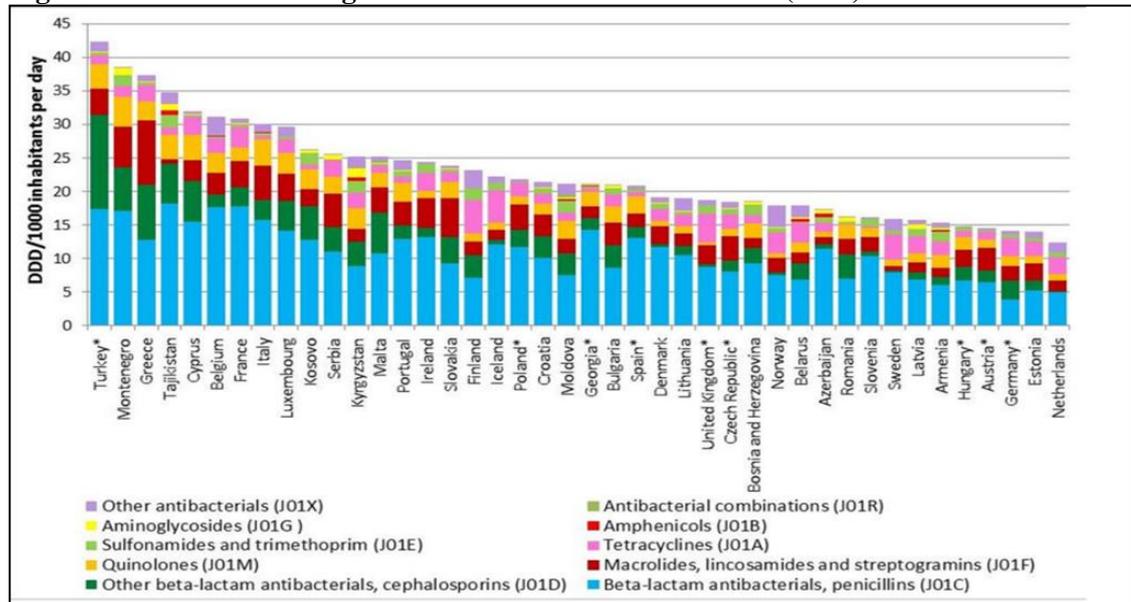
The rational use of antibiotics is firstly physicians' responsibility and then it is patients', organizations' and policy makers' responsibility. However, for solving current problems, the prescription performances of physicians who have a significant role on patients' treatments should be controlled closely (Sürmelioglu et al. 2015).

For the rational use of antibiotics, some factors such as physicians' conscious behaviors while prescribing antibiotics, getting patients' detailed anamnesis, understanding the reasons of infection correctly, decision on using antibiotics whether it is necessary or not, the correct doses of antibiotics, duration of usage, supporting treatment process with culture analysis and following the possibility of resistance for antibiotics are seen as significant applications (Öztürk 2008).

Turkey is one of the countries in which antibiotic is mostly used. According to the recent statistical data, one out of every three patients has used antibiotics. Normally, this rate should be one out of every six patients (Versporten 2014). In Figure 8, the rate of using antibiotics in countries for 2014 is shown. According to this figure, it is seen that the mostly preferred group of antibiotics is penicillin for all over the world. This rate is high in Georgia and Azerbaijan; it is low in Tajikistan and Armenia. However, the rate of using of cephalosporin group of antibiotics is high in Turkey and it is low in Serbia, Montenegro, Kirghizia and Georgia. When it is compared with other countries, Turkey is determined as the country which is mostly used antibiotics and with the activities developed by The Rational Use of

Drug National Action Plan (2013-2017), studies have begun for the aim of decrease this rate in Turkey (Versporten 2014).

**Figure 8. The Rate of Using Antibiotics in terms of Countries (2014)**



Source: Versporten et al. 2014

In 2016, Health Minister of Turkey declared in a conference about “The Rational Use of Antibiotics” that the rate of using antibiotics has been very high in Turkey and precautions for this field should be developed. The Health Minister who stated there were two significant ways for solving this problem figured out that patients needed to consult to their physicians while using antibiotics and they should not use antibiotics individually. Additionally, the Health Minister who thought that patients should not force to physicians for prescribing antibiotics referred to the significance of this field as saying “Our citizens should force to physicians for prescribing antibiotics. Antibiotics are not antifebriles or painkiller. Since cold and flu are diseases that are caused by viruses, antibiotics are not useful for these diseases (<http://www.milliyet.com.tr/saglik-bakanligi-gereksiz-antibiyotik-ankarayerelhaber1796002/>).

In that period, buying antibiotics in pharmacies without prescription was forbidden in order to prevent the irrational use of antibiotics. For physicians, the application determining the necessity of antibiotics that is namely “Rapid Antigen Test” which gives result in five minutes was begun to be realized. With the help of Rapid Antigen Test (Beta Test), the need of antibiotics can be determined in a short time via a specimen getting from throat and kits. Accordingly, in the context of repayment schedule as a dissuasive policy, the lowest costly antibiotics would be afforded by the government and it was decided to get contribution margin for the highly-cost antibiotics (<https://www.yenisafak.com/amphtml/hayat/antibiyotik-testi-uygulanmaya-basladi2603039>).

## V. DISCUSSION AND CONCLUSION

In all over the world, there have been some problems because of the use of unnecessary, ineffective and highly-cost drugs. The necessity of the rational use of drugs has come to exist because of some problems such as prescribing drugs which are not suitable for current guidebooks or essential drug lists, prescribing drugs which are not suitable for special groups of patients, unnecessary prescribing of expensive drugs. Also, it has come true because of the

antibiotics and injection preparates and using of them, not giving information to patients on their treatments by physicians, not paying attention for the information about drugs in prescriptions, pharmacists' recovery of prescriptions, not being sensitive for giving information to patients about drugs and health personals' medication errors.

The irrational use of drugs causes decrease in balance for patients' treatments, interaction between drugs, resistance for some drugs, repetition of diseases or longer duration for treatments, sequence of adverse actions and increase in treatment cost. One of the most important sample of the irrational use of drug is unnecessary use of antibiotics. It is common that antibiotics are used for the treatments of infection diseases. However, infection diseases may be formed because of many microbes (viruses, fungi etc.) without bacteria for which antibiotics are not effective. The unnecessary use of antibiotics is useless for infections which are caused by other reasons and also they may cause a resistance towards antibiotics. Due to resistance towards antibiotics, there can be some problems in transplantation, prosthesis surgery, intensive care treatments, chemotherapy treatments, premature baby services. Treatments with more expensive drugs are come up and because of this reason, economic responsibility of government increases. The duration of staying hospital is longer and the frequency of mortality based on the disease increases during infection.

As it is stated by WHO, the most important step while preventing resistance towards bacteria that is one of the biggest problems in this era is developing an awareness on the field of "the rational use of antibiotics". With this idea, it is a necessity that health professionals should inform to society on the rational use of antibiotics in order to prevent the resistance towards antibiotics and spreading out of this resistance as globally. Only physicians should decide to use of antibiotics and without physicians' decisions, people should not use antibiotics with others' advices. It is necessary that patients should use antibiotics in correct duration that is advised by physicians, in correct doses and length; even patients feel good, they should not give up antibiotics. The drugs should be prepared as advised by pharmacists, they should be kept in terms of suitable conditions and it should not be forgotten that if drugs are not kept in suitable conditions, their stabilizations can be disorder and there can be some negative effects because of it.

The responsible stakeholders for creating an awareness on the rational use of drugs and increasing public consciousness are qualified as physician, pharmacist, nurse, other health personal, patient relative, the sector, the regulatory authority, professional society and other groups (media, academy etc.). In addition to the policies for decreasing negative effects, responsible stakeholders have a key role in this field. However, it is known that patients use unnecessary drugs and they force physicians because of unawareness on the rational use of drugs and antibiotics. Although there is an increase in both national and international awareness of the rational use of drugs and antibiotics and development in policies based on the health services related to pharmaco-economic and pharmacovigilance studies, it is thought that desired progress on the rational use of drugs and antibiotics has not been seen yet. For the general aims of preventing society health, supporting the rational use of drugs and decreasing the resistance towards antibiotics, it is thought that the use of antibiotics should be limited for both humans and animals, unprescribed sales should be controlled, the studies on the rational use of drugs and antibiotics should be conducted via international collaboration, the studies for awareness and sensitiveness for society should be designed and the process of resistance should be regularly pursued.

All of the stakeholders should not forget that not every drug but correct drug and not too many drugs but correctly-dosed drug rescues life.

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