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INTRODUCTION Pharmacists are becoming more tired as the workload of dispensing and therapy grows, and the demand-supply goal becomes more difficult. This encourages more pharmacists, who are often active in clinical pharmacy within the healthcare system¹. The clinical pharmacy's facilities are the primary reason for its increased demand. As a result, it has become an essential and important component of the healthcare system, which is critical in this multidisciplinary setting². Pharmacists play a critical role in patient education and encouragement, as well as advising and engaging with prescribers³.

Clinical pharmacists bridge the gap between doctors and their patients by having a thorough understanding of medications and treatment plans. As a result, clinical pharmacists and doctors will work together to build a strong pillar for society by providing high-quality patient care⁴. The presence of a clinical pharmacist in and around healthcare is critical to the pharmacy field's growth⁵. It is assumed that a professional person who can treat patients is titled a doctor, physician, clinician, medical practitioner, and others in the present scenario.

These people support the medical system and improve the healthcare departments as they have achieved a degree in medical or allied health⁶. A system like this is critical for any country's growth. These individuals are regarded as the best because they lead a healthcare system that is constantly in need of perfection and change⁷. Thus, the necessity for a clinical pharmacist also becomes crucial. They are the ones who not only share the load but often be a responsible part of the system for their advice which is needed to be a cure, treats or even save a life¹.

This review will discuss several things related to the role of clinical pharmacists in patient-oriented pharmaceutical services, including various activities undertaken, such as medication reviews, counseling, therapeutic drug monitoring, and adverse drug reactions that may occur due to negligence in pharmaceutical care, as well as the expected outcomes of patient-centered clinical services. DRUG-RELATED PROBLEMS Drug-related problems (DRPs) have often been a systemic concern that must be recognized, avoided, and handled as soon as possible. Any cure for the problem isn't new⁸.

Different terms are proposed; for instance, 'drug-treatment issue' is regularly utilized as well, and this term was presented by Cipolle et al⁹. Krska¹⁰ proposed the term 'Drug Care Issue' in 2002. This is regularly utilized in the UK. Pharmacotherapy disappointment compares to negative clinical results coming about because of the usage or the absence of meds¹¹. Various reports have come forward which enlists "drug-induced problem" since many efforts have been put forward to optimize the rational usage of the drug and

medical preparations¹².

In such cases, a variety of factors can play a crucial role, like social pressure on the physician, the law and system of healthcare services, and the marketing strategies of pharmaceuticals, plus the patient itself play an **essential role in this** system.

Polypharmacy and increased drugs use are two factors that contribute to problems that defy pharmacotherapeutic concepts. Such issues are then categorized as DRPs^{13,14}. Niriayo et al.¹⁵ describe the points included in the DRPs based on Cipolle's method as presented in Table I. Table I.

Category of DRPs DRPs _Conditions _Unnecessary drug therapy _There are no valid medical indications for drug therapy at that time _ _Several medicinal products are used for conditions sufficient with single drug therapy _ _Medical conditions are more appropriately treated with non-drug therapy _ _Drug therapy is used to treat the side effects associated with other drugs that can be avoided _ _Need for additional drug therapy _Medical conditions requiring **initiation of drug therapy** _ _Preventive drug therapy is needed **to reduce the risk of developing** new medical conditions _ _Medical conditions require additional drug therapy to achieve a **synergistic or additive effect** _ _Ineffective drug therapy _The least effective drugs are used while the most effective drugs are available _ _Drugs **are used to treat** medical problems that are resistant to most treatments.

_ _The medicinal products used are ineffective for the medical condition that is being treated _ _Dosage too high _The drug **dose is too high** _ _The frequency of drug doses was too short _ _Drug interactions that can cause toxic reactions to medicinal products. _ _The drug dose was given too quickly _ _Dosage too low _The drug dosage is insufficient to achieve the desired effect. _ _Interactions between drugs that can minimize the number of active drugs available _ _The length of drug therapy is insufficient. _ _The dose period is just too short.

_ _Adverse drug reaction _The medicine has an unfavorable side effect that is not dose-related. _ _An unfavorable reaction is caused by a drug interaction that is not dose-related. _ _The medication **causes an allergic reaction** _ _The drug is contraindicated due to risk factors _ _Too quickly changing or administering a dosage regimen _ _Non-compliance _Inability to comprehend the instructions _ _Choosing not to take the drug _ _Negligence _ _Inability to properly take the drug on its own _ _Issues related to affordability and availability _ _MEDICATION ERROR Many therapies and medications have been involved that cure, prevent, or diagnose a disease, sign, or symptom to enhance the standard of life in health. However, improper usage of those drugs can cause severe damage by creating new adverse situations, be it morbidity or

mortality¹⁶. From 1.5

to 35%, errors related to medication were reported to the patients under hospitalization, and DRPs were seen to be common. Around 6.5% of morbidity and mortality rates of these errors were considered liable for costs of hospitalized persons, and It was discovered that two-thirds of these incidents could have been avoided¹⁷. To reduce the potential risk of these errors, pharmaceutical care provided by clinical pharmacists in the hospital setting allows multiple layers of patient protection¹⁸.

Although few reports have uttered the improvement in medication error management by involving clinical pharmacists, there is insufficient knowledge in some of the developing countries¹⁹, such as Iran. A clinical drug store residency program was begun in the year 1994 in Iran, and till now, almost 100 clinical drug specialists got earned their diplomas. A large portion of them was the academic staff and was occupied with the clinical treatment group in the instructing clinics.

Drug audit by the drug specialists in the emergency clinic setting is in advancement because of the association of clinical drug specialists on the medical care group in the irresistible sicknesses ward of Imam Hospital, Tehran, Iran²⁰. Pharmacists are expected to review medical charts as part of their normal duties. They reported pharmacotherapy monitoring, and all the reports of drug problems were submitted to the head of the medical team²¹. To optimize the result in a complex situation, it must possess an emergency system, diagnostic procedure, sufficient clinical therapy, availability of antidotes, supportive services, and the best knowledge for managing the clinical cases.

A multidisciplinary team gives more results than a monodisciplinary way^{22,23}. Hospital pharmacy and pharmacists have got a synonymous role here. CLINICAL PHARMACY AT EMERGENCY DEPARTMENT For assessing the efficacy and safety of a particular medication combination of the knowledge of pharmaceuticals, pharmacokinetics, pharmacodynamics, and therapeutic drug monitoring (TDM) is required in various clinical settings²⁴. The development of modern analytical techniques has made the determination of pharmacokinetic parameters easier by measuring the concentration of drugs in the blood.

Such parameters give necessary information about a medicament by assessing it clinically²⁵. As a result, TDM is a method that aids a medical practitioner in providing a patient with a safe and successful care. Next, good monitoring from medical practitioner can confirm plasma-drug concentration above or below in the therapeutic range²⁶. Adverse drug reactions (ADRs) are life-threatening situations. This imparts a negative effect on the standard of life and strives significant expenses on the healthcare

systems^{27,28}. In the United States, the fourth cause of death rate is ADRs²⁹.

The death rates are much higher due to medication errors and ADRs than the death caused by any highway accident, cancers, or AIDS, stated by recent data³⁰. Moreover, it has been reported that around 7% of hospitalizations are the results of ADRs^{29,31,32}.

THE ROLE OF CLINICAL PHARMACISTS In the patient-oriented era, the clinical pharmacist is defined as a discipline that focuses on improving the efficacy and rationality of drugs and minimizing drug toxicity in patients based on pharmaceutical care. In general, patient-oriented clinical pharmacists' role includes medication reviews, providing counseling, therapeutic drug monitoring, and ADRs monitoring^{33,34}, as illustrated in Figure 1.

In addition, clinical pharmacists also have other roles, such as identifying drug-related problems, promoting and recommending medication fulfillment, reviewing treatment data and medical history, examining medication errors including drug prescriptions, dispensing errors and drug administration, identifying drug interactions, suggest individual dosages, provide patient consultations, and more³⁵⁻³⁹. Clinical pharmacy services are not limited to the activities mentioned above, in which clinical pharmacists can also carry out an expanded role such as conducting complete interviews with patients or their families about patient history such as medical, social, allergies, use of OTC drugs, dietary supplements, and alternative medicine^{4,40}. / Figure 1.

The role of the patient-centered clinical pharmacists **MEDICATION REVIEW** In terms of patient care and safety, medication-related errors are quite frequent and are an important factor that should be given extra attention. As a result, **it is important to pay attention to the** weak points of healthcare systems as well as the patients involved⁴¹. Pharmacist intervention is useful in promoting proper therapy compliance, interviewing patients, reconciling prescriptions, and advising patients for proper follow-up, according to findings from different studies^{42,43}.

Hence, clinical pharmacists are mandatory to participate actively as a member of the healthcare team and teach. Their fundamental responsibility is to check on drug therapy, review patient(s) medical records, attend ward rounds, and educate health care workers about disease management pharmacologically and non-pharmacologically⁴⁴. These outcomes of the drug therapy care given by clinical pharmacists are fresh to the hospitals. Infectious diseases may be spread through medication errors.

The number of errors varies depending on the patient's demographics, as well as his or her illness and drug background, both past and current⁴⁵. Another related research drew attention to drug mistakes by putting them in the context of patients' problems⁴⁶.

Drug dosing and therapy choice problems can cause most errors—reasons for medication errors in a pediatric surgical ward **may be due to** improper dose adjustment to that patient⁴⁷. The qualities of drug blunders during the organization period of the medicine use measure were contemplated.

Out of the relative multitude of preeminent basic mistakes should be oversight blunders, blunders of the wrong portion of medication, and wrong time⁴⁸. The high chance and event of drug mistake could likewise be because of paper-based requests in clinical history alongside automated enlistment of medicine, inaccessibility of the clinical record for drug specialists in the medical clinic drug store, tolerant over-burden in a showing clinic, and therefore working over-burden of doctor and attendants as well as inaccessibility or absence of therapy guidelines⁴⁹⁻⁵¹.

The reason for contrasts between frequencies of meds blunders is prescription blunders, the precision of information assortment technique, and revealing framework. Furthermore, the degree of polished methodology, individual execution, and individual social abilities of the elaborate medical services laborers may impact the term and kind of the prescription mistake⁵². Intercessions of clinical drug specialists inside the entire treatment measure, starting from apportioning to the organization to the patient, can limit the odds of medicine mistakes and be advantageous to tolerant care.

This accomplishment is simply due to the contribution of clinical drug specialists in unique prescription ward adjusts and noticing and breaking down various strides of drug care⁵³. Thus, the principal part of crisis division drug specialists is to lessen possibly hurtful medicine mistakes brought about by any factor⁵⁴. For the medicine mistakes, it has been discovered that patients more than 50 years of age, male sex, and quantities of controlled medications had no huge impacts except that non-antitoxin drug classes probably show hazard factor identified with a quiet segment or illness and treatment^{55,56}. Even though the connection between the recurrence of prescription mistakes and quantities of regulated medications has not found as a danger factor.

Medical service workers are included as therapy and patient care groups in providing instructions to emergency clinics to reduce prescription errors⁵⁷. Horribleness, death rate, and cost of patient consideration get influenced by medicine errors. Most of the prescription mistakes were distinguished, detailed, and introduced in the beginning stage of medication treatment by clinical drug specialists⁵⁸. DRUG-RELATED PROBLEMS IDENTIFICATION It is well recognized that taking an excessive number of drugs can lead to a person being admitted to the hospital, either directly or indirectly.

According to the Pharmaceutical Care Network Europe (PCNE), DRPs are characterized

as an occasion or situation, including drug treatment that really or possibly meddles with the ideal wellbeing outcomes¹⁷. Some DRPs like prescription blunders and unfriendly medication responses are truly basic on account of hospitalized patients and may cause patients some dreariness or mortality⁵⁹. There are a few characterization frameworks for DRPs; some are by Strand et al.⁶⁰, an agreement bunch in Granada, the PCNE⁶¹, and Apoteket AB (National Corporation of Pharmacies in Sweden)⁶².

Drug-related problems can be experienced throughout the entire medication process and perhaps tell you all the risk factors for **adverse drug reactions and** events. In recent years, drug-induced morbidity has often been related to adverse drug reactions; still, these occupy **a small portion of** DRPs⁶³. Clinical drug specialists are assigned specialists who can co-relate determination, research center qualities, clinical history, and solutions with the progressing treatment of an individual patient⁶⁴.

Thus, the presence of a clinical drug specialist is essential so he can distinguish and tackle a few DRPs more effectively than a fake framework can, for example, Computerized Physician Order Entry frameworks (CPOE) or Clinical Decision Support System (CDSS). Many investigations have detailed that a clinical drug specialist is crucial, which offers better assistance for persistent consideration and wellbeing^{65,66}. In one study, the contingency of DRPs was correlated with age, gender, polypharmacy, and several comorbidities. An identical study was done, in which correlation of variables like age, gender and polypharmacy was established with an increase in DRPs^{67,68}.

The research was carried out that stresses the role in identifying, assessing, and preventing DRPs in elderly patients. They also focused on polypharmacy (six or more concomitantly) leading to DRPs⁶⁹. The factors leading to DRPs were polypharmacy, comorbidities, and patient age reported by a study. As far as age-related DRPs are concerned, most patients were in the geriatric age group; a maximum number of DRPs were seen in this group. Maximum numbers of medicines were prescribed in this group, i.e., approximately an average of 10 to 15 drugs per patient.

The number of DRPs and medications prescribed is eventually increased depending on the patient's illness or disease, which was accompanied by **an increase in the** age range of patients^{70,71}. Moreover, this leads to **an increase in the** age group, which shows a rise in the number of comorbid conditions, which is the highest amongst the other population groups. Multiple comorbid conditions, polypharmacy, inadequate knowledge about the disease, and others can be the reason behind it. The correlation coefficient of age v/s DRPs was 0.13, indicating a positive correlation between the two variables⁷².

Chances of DRPs increase with the rise in age. With the increase in DRPs, age development, comorbid conditions increase, and as a result, the number of drugs prescribed increases⁷³. The leading cause of DRPs is considered to be polypharmacy. Drug-drug interaction is the main reason for a positive correlation between the numbers of drugs prescribed and DRPs⁷⁴. Maximum of major and significant drug-drug interactions was recognized in this age bunch, out of which few were intentional/beneficial. Drug-drug interactions can lead to a decrease or increase in a drug's effect, eventually causing a sub-therapeutic or supra-therapeutic dose⁷⁵.

Thus, to reduce the occurrence of drug-drug interactions, pharmacokinetics and pharmacodynamic properties of drugs should be kept in mind as DRPs are mostly dependent on chemical as well as physical properties of the drug and, as a consequence, are often more difficult to influence and prevent⁷⁶. Various methods have been proposed to prevent drug interactions and made to work. Firstly, the pharmacokinetic properties of each drug are observed. If found any discrepancy such as the half-life of the drug is not crossed, then the administration timing can be varied and changed accordingly⁷⁷. The following method is to provide an alternate therapy plan to a patient.

Such interactions are notable and are needed to be checked and monitored often. For such instances, an alternate therapy plan works well by minimizing interactions with substituting medications for their counterparts. When these plans are carried out and implemented, the medication reactions are better presented, and the patient receives the best care possible⁷⁸. THERAPEUTIC DRUG MONITORING Therapeutic drug monitoring is a branch of the clinical chemist in which data is determined by a clinician, how a patient responds to a specific therapy and the factors that influence that response.

When a therapy fails due to a patient's insufficient reaction, quantitative examination of plasma levels will show who is truly following the instructions and who is not²⁶. The approach also provides data on individual reactions to drug use habits and changes in drug usage as a result of the altered physiological condition. A critical point of TDM is to seek out the dose-response relationship, its affectivity, rationale, and others⁵¹. This TDM is much acceptable and needed for a few categories of drugs when value and quality of life are considered.

Such a category may be noted by public bodies and regulatory agencies for TDM to be carried out. The reality of TDM is that it is based on estimating drug concentrations in body fluids like saliva, plasma, serum, and others⁷⁹. Except for drugs that do not follow the dose-response relationship or facts such as individual variations, particular

variations, or ethnic variations, the TDM is also very effective in delivering a beneficial service if the medication has a dose-response relationship⁸⁰. Reporting blood concentrations can be of no use or may even make treatment more difficult. The TDM assay must be performed for both the administered drugs and their metabolite for particular drug groups where the metabolite is also active.

The use of therapeutically low concentrations of drugs in fewer patients than the normal dose has been shown to be highly successful⁸¹. In a few patients, a higher concentration than the normal range of serum concentration is needed without causing any harmful effects and yielding a satisfactory result. However, such circumstances may indicate that higher doses are toxic concentrations, causing undesirable anxiety and necessitating a dose reduction.

One must consult the physician and clinical pharmacist to urge a better conclusion by approaching a team discussion^{82,83}. Therapeutic drug monitoring is the best option required for critical conditions and requires emergency support. The reports should be made available within a short duration to make TDM very effective⁸⁴. Therapeutic drug monitoring can also be helpful for neonates and pregnant ladies. During pregnancy, physiological changes are expected, like increased renal function, increased cardiac output, increased placental blood flow, variations in the concentration of plasma proteins, hormonal changes, and others⁸⁵.

Since drugs are administered to sustain and promote good health and ill conditions throughout pregnancy, these drugs may be capable of crossing the placental barrier and causing toxic effects on the fetus, TDM is needed. This method is also crucial for neonates during their treatment, but many issues are also observed⁸⁶. Many medications, for example, must be started right away without any prior knowledge of the neonate's clinical history. Drugs are appreciated more than their adverse effects, such as jaundice, in such situations.

The issues that can cause some alteration in TDM of neonates can be the cluster of samples, correct administration of drugs, their response to drugs, the presence of drugs in the body that are received through the placenta, or the exposure of the body to drugs in the fetus. In such cases, the clinical team's combined effort will have further advantages and justification^{87,88}. The medication level assessment in body fluids must be cost-effective in terms of expenses. The expenditure of operating a specific test is directed by the summation of equipment, personnel, supply, and overall expenditure for particular time duration and dividing that amount by the number of analytical tests performed in the same duration^{89,90}.

The overall charges are then **calculated by multiplying the** desired benefit by the expense of the test. The use of clinical pharmacokinetics by therapeutic drug monitoring services was considered to reduce adverse reactions, reduce intensive care unit length of stay, and shorter overall hospital care costs²⁶. As mentioned earlier, TDM can appear to be of less benefit in certain countries, but when special therapies are taken into account, it proves to be extremely valuable in terms of delivering effective service.

When the failure of a therapy or harmful effects is considered, this method rises as a powerful tool used in the treatment. It necessitates the use of pharmaceutical, pharmacokinetic, and pharmacodynamic techniques in tandem⁹¹. The system's proper operation necessitates a simple calculation of the drug level in the blood and reference to the normal range. It also increases a drug's protection and efficacy in a specific person; additionally, it helps identify noncompliant patients' problems⁹².

The time of sample collection after dose administration, the dosage history, the patient's response, and the desired clinical goals all play a role in providing patient-centered disease management⁹³. ADVERSE DRUG REACTIONS One study found that after education and the establishment of Pharmacovigilance Committees in hospitals, there was a substantial increase in ADR reporting. It is engrossing that despite sending the documents, posters, and pamphlets of the Iranian Adverse Drug Reactions Monitoring Center (IADRMC) since 2004, the number of ADRs was deficient from 2004 until 2007.

Despite the fact that the author saw a rise in the number of ADRs after 2007, an essential aspect of the experience was that the frequency of reports was not as good as it should have been^{94,95}. The lack of awareness of the national center, the absence of serious drug reactions, and skepticism about the causality relationship between the reaction and suspected drug were all stated as major reasons in the report⁹⁶. Pharmacists and nurses were proposed for similar reasons. It was stated from the above studies that the top cause of ADRs were antibiotics approximately 45.5%.

Moreover, ceftriaxone was **the most common antibiotic** linked to ADRs, with side effects such as rash, hives, and anaphylactic shock⁹⁷. Technically, high levels of antibiotic-associated ADRs are frequently linked to high drug use, both within and outside the world. More than half of all patients who take antibiotics see a doctor, and this number rises to 59% for general practitioners⁹⁸. Adverse drug reactions are more reported in nurses as compared to physicians and pharmacists. Due to the close contact with both the physicians and the patients and management of drug administration of those patients, it is counted as the leading cause⁹⁹.

Until 2002, the nurses in England were not allowed to fill out yellow cards. The role of

nurses in the pharmacovigilance system was demonstrated by relating all previous studies and experience¹⁰⁰. At least one injectable drug is used in 45% of prescriptions. By avoiding needless injections, such ADRs can be avoided. Since injectables are not often needed for successful outcomes, and because of the higher costs and serious and immediate adverse reactions, oral drugs are likely to be preferred wherever possible to minimize the highest risk of injectable ADRs^{101,102}.

CONCLUSION Clinical pharmacists **play an important role in** the crisis center, which is continuously evolving. Other medical care laborers claim additional time from clinical pharmacists to be given to the office to offer fundamental types of assistance. Experienced clinical pharmacists can assist with calming tension on other staff and give compelling patient consideration. Nevertheless, a proper investigation of clinical practice and patient results would be needed to survey the general effect and advantages. Clinical pharmacists are recognized patient consideration advantage by **working together with doctors** or wellbeing frameworks.

This enables them to participate in dynamic treatment exercises as part of the patient's care services team, assisting in the rational use of drugs for patient safety and improving long-term consideration. The executives' findings assume liability for threat factors related to treatment and reduce medical care expenses based on their level of consideration and illness. Therefore, clinical pharmacists are a resource for the health care team and patients.

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