TURKISH REPUBLIC OF NORTH CYPRUS
NEAR EAST UNIVERSITY
HEALTH SCIENCES INSTITUTE

DRUG RELATED PROBLEMS IN INTENSIVE CARE PATIENTS AT UNIVERSITY HOSPITAL IN NORTHERN CYPRUS

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MASTERS

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Dedication

I dedicate this work to Almighty Allah for giving me the knowledge, wisdom, and strength.

Also, to my dad, mom for giving me all supports I need.

Approval

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SUMMARY

Introduction: Drug-related problems (DRPs) are one of the leading causes of morbidity and mortality, especially in ICU Patients. The critically ill patients in ICU are more vulnerable to DRPs than others. Moreover, the administration of multiple drugs is a common event in the ICU, which can lead to an increased incidence of DRPs. Pharmacists play a major role in providing patients care with their knowledge base of drugs and identifying and resolving DRPs and adverse events.

Aim: The aim of this study is to assess the prevalence and distribution of DRPs in Near East University Hospital (NEUH) in-patients, who were admitted to the Intensive Care Unit.

Method: A retrospective observational study was carried out on patients (aged 18 years and more) admitted to the Intensive Care Unit (ICU) of Near East University Hospital (NEUH) in Northern Cyprus. A total of 53 patients were included in the study. DRPs were documented and classified using Pharmaceutical Care Network Europe (PCNE) DRP classification system V 8.02. DRPs were reviewed by a clinical pharmacist and specialist physician and documented by the researcher.

Result: Out of 53 patients, 35 cases (66%) have DRPs; 21 (60%) of these patients were men and 14 (40%) of them were women, with an average age of 71.7 (SD ±13.9). The most frequently reported DRPs were unnecessary drug treatment in 38.6% of cases, followed by untreated symptoms or indication (22.9%). Drug selection (C1) was the most identified error to cause a drug-related problem 87.1%. Patients had cardiovascular disease counted for the highest frequency of DRPs 46%.

Conclusion: DRPs may occur in many hospitalization patients especially in ICU. Identifying DRPs and reducing them will increase health status and patient safety. And we need prospective studies with interventions to evaluate the outcomes in the patients, the clinical pharmacist in the health care system will help to reduce the incidence of the DRP events.

Key Words: Drug Related Problem - Clinical Pharmacist - PCNE DRP classification –Intensive Care Unit – Northern Cyprus

CONTENTS

Figures

Tables

ABBREVIATIONS

ABBREVIATION	EXPLANATION
DRPs	Drug-Related Problems
ADE	Adverse Drug Events
ME	Medication Error
MAEs	Medication Administration Errors
ADR	Adverse Drug Reaction
DDIs	Drug-Drug Interactions
PEG	Percutaneous endoscopic gastrostomy
COPD	Chronic Obstructive Pulmonary Disease
CPOE	Computerized Physician Order Entry systems
DM	Diabetes Mellitus
CKD	Chronic Renal Failure
HF	Heart Failure
AF	Arterial Fibrillation
AHD	Atherosclerotic heart disease
CVD	Cardiovascular Disease
VTE	Venous Thromboembolism
HVD	Heart Valve Disease
NSAID	Non-Steroidal Anti-Inflammatory Drug
CAD	Coronary Artery Disease
IHD	Ischemic Heart Disease
HIV	Human Immunodeficiency Virus

ACEI	Angiotensin Converting Enzyme Inhibitor
B-blocker	Beta-blocker
B2-agonist	Beta 2-agonist
ADME	Absorption, Distribution, Metabolism, and Excretion
pH	Power of Hydrogen
SPSS	Statistical Package for the Social Sciences
NEU Hospital	Near East University Hospital
ICU	Intensive Care Unit
GI	Gastrointestinal
PT	Prothrombin Time
INR	International Normalized Ratio
AKI	Acute Kidney Injury

1. INTRODUCTION AND BACKGROUND

1.1 Drug related problem

1.1.1 Definitions:

A Drug Related Problem (DRP) is "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes". (PCNE E. , 2010). The identification and resolution of drug-related problems associated with prescriptions errors are the core activities of pharmaceutical care. There is a strong evidence linking the negative outcomes of DRPs and major health issues and the cost of mortality and morbidity associated with DRPs are very high, they account for 76.6$ billion in hospital costs, 17 million emergency department visits, and 7.7 million hospital admissions annually in the united states as shown in the probability used in that study. (johnson JA, 1995)

A DRP exists when the patient experience or is likely to experience either a disease or a symptom having a present or suspected relationship with the medicine. Eight different categories of DRPs are described each category presented. This categorization serves a number of functions, such as (1) to clarify how adverse drug reactions form but one category of extant DRPs, (2) to make noticeable the pharmacist's role for the future, (3) to serve as a focus for developing a systematic process whereby the pharmacist engage significantly to the overall positive result of patients, (4) to make pharmacy practice vocabulary understood by healthcare professionals, and (5) to assess in the development of standards of practice for pharmacist.. (DJCP, 1990)

Adverse drug event (ADE): Any damage identified with the use of a medication (noxious and unintended), occurs at doses used for prophylaxis, diagnosis, treatment, or modification of physiological functions. (WHOannex, 2009)

Adverse drug reaction (ADR): Any undesirable response associated with used a drug that caused compromise therapeutic efficacy, enhances toxicity or both. (WHOannex, 2009)

Medication error (ME): Any preventable event that may cause inappropriate medication use (prescribing, dispensing, administering drugs) or jeopardize patient safety.. (WHOannex, 2009)

Drug-related problems (DRPs): is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. (PCNE, 2017)

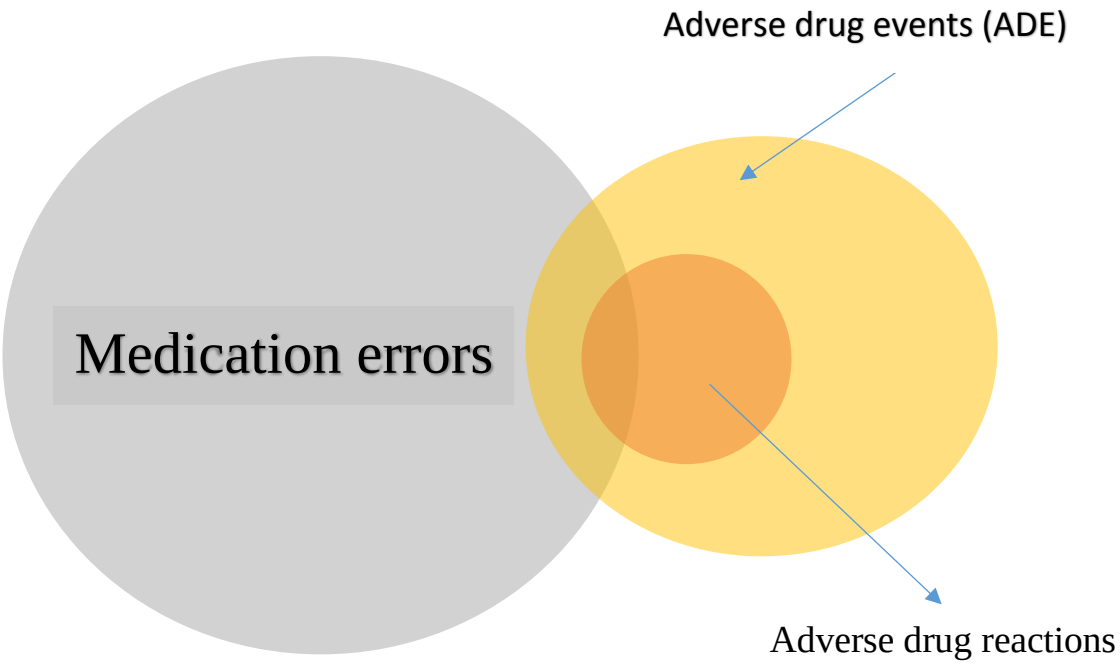


Fig.1*: Relationship between medication error (ME), adverse drug event (ADE), and adverse drug reaction (ADR).* (Krähenbühl-Melcher, 2007)

1.1.2 DRPs classification systems

The DRPs classification system is an essential tool for clinical practice to contribute in identifying, to resolve, and to prevent such problem. (Ginny D. Crisp, Development and testing of a tool for assessing and resolving medication-related problems in older adults in an ambulatory care setting: the individualized medication assessment and planning (iMAP) tool, 2011)

The validity of any classification system depends on its meeting to requirements such as being:

- Suitable for both scientific studies and clinician practice.

- Easy to use in daily routine.
- Suitable for the documentation.
- At least consist of three parts: problem, intervention, and the cause.
- Structured and detailed.
- Designed with a coding system.
- Each drug-related problem must be defined clearly and lead to a specific code.

Various classifications systems of DRPs were published in literature and studies. Those publications divided the drug-related problems into various categories. (Basger BJ1, 2014)

Most of the classification systems do only have *Problem* and *Intervention* parts, only a few of them include and focus on the *Causes* part separately.

The differences in the methodologies focus and definitions of DRPs caused the lack of the optimal classification system that could be universal and could meet all the criteria. (ADUSUMILLI PK, 2014)

The PCNE's v (8.02) DRPs classification system was chosen in this study to identify the DRPs.

The outcomes are:

1. Cure of a patient's disease.
2. Elimination or reduce a patient's symptomatology.
3. Prevent or slowing of a disease process.
4. Prevention of a disease or symptomatology (LM, 1990)

1.1.3 Categories of Drug-Related Problems

DRPs are identified and characterized by the following distinction:

a) Untreated indication

The patient has a medical condition that requires drug therapy, but the patient is not receiving a drug to treat it.

b) Improper drug selection

The patient has a medical condition and the wrong drug is being taken.

c) Sub therapeutic dosage

The patient has a medical Condition for which too little of the correct drug is being taken.

d) Over dosage

The patient has a medical condition for which too much of the correct drug is being taken.

e) Adverse drug reactions

The patient has a medical condition resulting from an adverse drug reaction.

f) Drug interactions

The patient has a medical condition resulting from a drug-drug, drug-food, and drug-laboratory interaction.

g) Medication use without indication

The patient is taking a medication for no medically valid indication.

h) Indication without medication

The patient has a medical condition that is the result of not receiving the prescribed drug. (Strand L. M., 1992)

1.1.4 Factors affecting DRPs

a) Polypharmacy: The term "polypharmacy" express the use of multiple medications by one patient. Polypharmacy has variously defined depending on the number of medications used. However, there is no exact number of drugs used by a patient could be related to the increases in the incidence of drug-related problems. (Emily R. Hajja, 2007). Type 2 diabetes Mellitus with dyslipidemia patients clearly represent this fact especially when those patients have liver or kidney impairments (which alter the pharmacokinetics of antidiabetic and anti-hyperlipidemia agents). An average of 4 DRPs per patient with those two comorbidities have appeared in a study. (Hasniza Zaman, 2013).

b) Age: Age is a critical factor in the occurrence of DRPs because the elderly and pediatric ages have variable and less predictable pharmacodynamics and pharmacokinetic characteristics.

Elderly patients are at high risk to face DRPs due to several reasons. They are most likely to have multiple diseases and health problems that often associated with flowing more than one prescription. The amount of the water inside the body decreases with age while the fat tissue relatively increases, thus the water-soluble drugs will reach higher concentration while the lipid-soluble drugs tend to accumulate inside the body. Also, as people are getting older, their liver functions to metabolize the drugs decrease, as well as their kidney sufficiency to excrete the drugs and its metabolite (Budnitz DS, 2007). Neonates are likely to develop drug-related problems due to low body weight and fat, immature renal tubular function, blood-brain barrier, baroreceptors, immunity system and physiological hypoalbuminemia. (Clavenna A, 2009)

c) Gender: The biological and physiological variance between females and males including body weight, liver metabolism, and renal function will affect the incidence rate of DRPs. For example, hepatic enzyme CYP3A4 (which affect the metabolism rate of the drugs) is more active in females**.** (Makkar RR1, 1993)

d) Disease-Related Factors: Health status of the patient is an essential factor that might increase the incidence of DRPs. For example, Congestive Heart Failure patients might be at high risk to have drug-disease interaction if they have other diseases like Chronic Obstructive Pulmonary Disease (COPD) when they use beta-blocker. (Dipak Chandy, 2013) In summary, many factors such as alcohol intake, smoking, body weight, and allergies also play a significant role in the frequency of the incidence of DRPs.

1.1.5 Drug Related Problems in Hospitals

Many problems and diseases associated with pharmacotherapy (in particular, medication errors and adverse drug events) are frequent and are associated with increased costs for treatment. However, inappropriately used medicine may be harmful and could cause new symptoms. A 15-year study by LaPointe NMI in 2003 showed that the medication errors and/or adverse events in hospitalized patients, focusing on the frequency of, risk factors for and avoidance of such problems associated with pharmacotherapy, specified that medication errors occurred in a mean of 5.7% of all event of drug administration, but with a high variability among the 35 studies retrieved. This variability was explained by the methods by which medication errors were

detected and by the way drugs were administered (IV administered drugs are associated with the highest error frequencies). Important risk factors included insufficient pharmacological knowledge of health professionals, errors in the patient charts or documentation by nurses and inadequate pharmacy services. (LaPointe NM1, 2003)

Adverse events, on the other hand, affects 6.1 patients per 100 hospitalized and also showed a high variability among the 46 studies retrieved. This variability could also be explained by drugs with a narrow therapeutic range, use of anticoagulants or diuretics, polypharmacy, elderly patients, renal elimination of drugs and duration of the stay in the hospital. (uhl-Melcher, 2007)

A study has been done in Gondar University Hospital, Ethiopia it was a cross-sectional study, structured systematic data review was designed focusing on patients with CVDs (both out and inpatients) older than 18 years old, from April to June 2015. A total of 227 patients with CVDs were reviewed with a mean age of 52.0 ± 1.7 years. Patients who're diagnosed with heart failure (71, 31.3%). Diuretics (199, 29.5%) were the most commonly prescribed drugs. A total of 265 DRPs were identified, 63.4% of patients have at least one DRP (1.17 ± 1.1). The most common DRPs were found to be an inappropriate selection of drug (36.1%) and dose (24.8%). The most identified risk factors causing DRPs were: Need of additional drug therapy and lack of therapeutic monitoring. (Ousman Abubeker Abdela, 2016)

Also, prospective interventional study estimated in university hospital in Northern Cyprus, CPSs were provided for inpatients by independent clinical pharmacists and documented over 4 months. The study includes all patients who were admitted to the hospital in cardiology or cardiovascular surgery departments, a total of 133 patients were admitted to the wards during the 4-month study period. Clinical pharmacists reviewed all the patients, and 81 patients (60.9%) had at least one DRP. A total of 217 DRPs were identified (mean DRP per patient1.6 ± 1.7), 95%. (Al-Baghdadi, Introducing clinical pharmacy services to cardiovascular clinics at a university hospital in Northern Cyprus, 2017)

A prospective interventional study was conducted from November 2017 to March 2018 in university hospital in Northern Cyprus, A total of 102 patients were included in the study, who were treated with at least two cycles of any cancer type and stage. A

total of 55 (53.9%) patients had 251 drug-related problems. Drug-related problems mainly involved antihypertensive (31.6%), antidiabetic (17.8%), and herbal agents (31.6%). Treatment effectiveness was the major type of drug-related problems (50.2%) followed by treatment safety (29.1%). (Ahmet S Bosnak, 2018)

1.2 Intensive Care Unit

An Intensive Care Unit (ICU) is specially staffed and prepared. It is the separate and independent territory of a clinic devoted to the administration and monitoring of patients with a serious stipulation. It gives special expertness and the facilities for the help of vital social function and uses the skills of medical, nursing and other staff experienced in the management of these problems. (Stephen A. McClave, 2009)

Intensive care, also known as critical care, refers to the level of medical treatment provided to patients with acute life-threatening illnesses or injuries (Bone R.C., 1993). These patients frequently have sustained or are at risk of suffering the failure of one or more vital systems, functions, or organs. These patients require intensive care and observing to help them while they recover from the underlying disease or damage. This care may be necessary over a period of hours, days, or weeks. It is most often provided in specialized intensive care units within a healthcare organization and hospitals. (Villar J., 2001).

The Intensive Care Unit came into existence during the half of the 20th century. During World War II, isolated rooms in hospitals (known at the time as "shock wards") were set up as a place to resuscitate and care for injured soldiers before and after surgery. (Maureen Carr, 2010) Intensive care was primarily intensive nursing care. With the development of techniques of hemodialysis and the widespread introduction of mechanical ventilation after World War II, the contemporary model of the ICU began to take shape. Ibsen in Denmark first used prolonged mechanical ventilation to support victims of the polio epidemic of 1952 and created the first intensive care unit in 1953, (L, 2011) . ICU units were established in France in 1954, (F., 2011) in Baltimore in 1957, and Toronto in the late 1950s as discrete geographic areas within the hospital that brought together developing technologies for organ support such as positive pressure ventilation, hemodialysis, and invasive cardiovascular monitoring. Within a

decade, the ICU had become an essential element of hospital-based health care, and intensive care emerged as a distinct medical sub-specialty. (Weil MH, 2011)

1.2.1 Classification of Intensive Care Units

Based on the potential of the ICU to provide expert care to the acute seriously ill patients, they are categorization by the following:

1. Availability of skilled medical personnel.

2. Availability of skilled nursing personnel.

3. Availability of other specialists – respiratory therapists, physiotherapists, pharmacists, nutritionists, etc.

4. Capacity to monitor acutely ill patients.

5. Availability of resources for the support of failing organ function.

6. Design and structure of the physical space.

7. Integration with ICU outreach services – in the emergency department and hospital ward, as well as services for follow-up of discharged patients.

8. Presence of formal educational and professional development services for staff.

9. Presence of dedicated house staff and role as a center for training expert personnel.

10. Capacity for research and quality improvement activities.

11. Role in acting as a referral service for the hospital, the community, and the country.

12. Ability to scale up services in response to a natural or human-made disaster or pandemic outbreak.

1.2.2 Tools mechanical in Intensive Care Unit

There are different machines or devices in the ICU should be connected to patients whilst in the ICU such as:

1. **Breathing Machines or Ventilators**

Many patients need help with breathing and usually to be sedated and have to insert a breathing tube into their windpipe or through the neck. Such tubes are connected to a breathing machine known as a ventilator. Ventilators use complex computers to help patients to breathe well. Sometimes, patients' respiration can be supported with tightly fitting masks if they don't need a breathing tube putting into their windpipe. ((HTM), 1994). There are two types of breathing tubes. The endotracheal (ET) tube which is a plastic tube placed through the patient's mouth or nose into the trachea. Most patients need sedation when using this tube to keep them comfortable. And the other type is the Tracheostomy which is a plastic tube placed into the patient's trachea through a small incision in the front of the patient's neck. Tracheostomy is usually used when the patient needs for breathing support for a prolonged period of time. ((HTM), 1994)

2. **Monitors**

Patients in intensive care are constantly monitored at least hourly to track their condition and alert staff to changes. This monitoring includes:

- Heart rate and heart electrical tracing (ECG).
- Oxygen levels in the blood.
- Blood pressure.
- The pressure in the veins (CVP).
- Urine output.
- Temperature.
- All the fluids, food and drugs. (HMSO, 1992)

3. **Lines**

These are plastic catheters or tubes inserted by the doctors and nurses into the patient's blood vessels, sometimes called drips or lines and these lines help to give fluids and medications for patients, to monitor blood pressure, and to take blood samples for regular investigation. Examples; Arterial line, Central line, Dialysis line or Vascath, and PICC lines. (Ferdinande., 1997)

4. **Feeding in the Intensive Care Unit**

It is essential to maintain an adequate nutrition for patients in the ICU at risk of malnutrition because of their illness to fight the infection and assist recovery after a prolonged illness. Some example for feeding in the ICU are:

a) Nasogastric tube

This tube is used to feed the patients in the intensive care who are unable to eat or drink, and is the most common type used in the critical care inserted by the doctor or nurse, which goes into the nose, down the esophagus until it reaches the stomach.

b) Intravenous feeding

The nutrition is provided through a central line into the veins if there are problems with absorption of the feed through the stomach. But as feeding through the stomach is more physiological, intravenous feeding is usually not the first choice as it has the risk of causing infection.

c) Nasojejunal tube

This method is similar to the nasogastric tube but the tip of the tube is positioned in the small intestine (jejunum) instead of the stomach. It is usually used if there are problems with the absorption of the feed using the nasogastric tube

d) PEG tube

PEG tube is inserted in the patients who need long-standing feeding, or are at a high risk of aspirated food contents into the lung. It is inserted through the skin on the abdomen leading into the stomach (Hospitals, 2018)

5. Urinary catheter

A urinary catheter is used for the patients who are unable to use the toilet normally. It is a flexible tube that is inserted into the bladder to drain urine. It is inserted by a doctor or a nurse via the urethra until it reaches the bladder. It is essential to check the amount of urine produced by the patient. (Hospitals, 2018)

6. Kidney machines

Kidney machine is used when patients' kidneys stop working due to their illness. It is a special large tube put into one of the big veins in the leg or neck, functioning as

kidneys to filter the blood and remove waste products (and doing so produce urine). (Hospitals, 2018)

1.2.3 Common disease in intensive care unit

The common cases which may require treatment and monitoring in the ICU:

- Cranial neurosurgery.
- Head injuries with airway obstruction.
- After surgery for major trauma.
- Shock.
- Trauma.
- Stroke
- Hypoxia
- Meningitis.
- Traumatic Brain Injury.
- Ruptured Brain Aneurysm.
- Post-operative Intensive Care.
- Cancer-related Intensive Care.
- Heart Failure (Unstable pulse or blood pressure, high or low).
- Respiratory (Lung) Failure (Ventilation difficulties).
- Hypothermia.
- Neonates, after any surgery.

Also, there are Risks and complications with patients in the ICU, which may occur such as Deep Vein Thrombosis (blood clot), Kidney Failure, Infections, Liver Failure Stomach Ulcers, Skin ulcers (pressure ulcers), Weakness, Confusion, Medication Side Effects, and Procedural Complications. (Hospital., 2017)

1.2.4 Common medication in Intensive Care Unit

Critically ill patients generally receive double the number of medications than non-critically ill patients, thus increasing the risk for drug-related problems such as drug

drug interactions or sensitively to drug responses due to the unstable status of these patients. (Sandra L. Kane-Gill, 2017)

There are a lot of medications used in the ICU but the most common medications used within the ICU are: Fluids Crystalloids (Dextrose 5%- Normal Saline), Fluids Colloids (Albumin 5%), and Blood Products (Packed Red Blood Cell (PRBC)- Fresh Frozen Plasma (FFP)- Cryoprecipitate), Vasoactive Agents like Vasopressors (Dopamine-Norepinephrine-Norepinephrine-Phenylephrine) and Inotropes (Dopamine-Dobutamine- Milrinone), Vasodilators (Nitroglycerin), Sedatives agent (Benzodiazepines-Morphine- Hydromorphone), Antipsychotics (Haloperidol-Olanzapine), Anticoagulants (Enoxaparin), Fibrinolytic (Alteplase- Reteplase) (ICHP/MSHP, 2011).

1.3 Clinical pharmacist

Clinical pharmacists work directly with physicians, to ensure that the medications prescribed for patients to contribute to the best possible health outcomes. Clinical pharmacists practice in health care settings where they have frequent and regular interactions with physicians and other health professionals, contributing to better coordination of care. (ACCP A. C., 2008).

Clinical pharmacists assume responsibility and accountability for achieving therapeutic goals; which of these:

1. Assess the status of the patient's health problems and determine whether the prescribed medications are optimally meeting the patient's needs and goals of care.

2. Evaluate the suitability and effectiveness of the patient's drugs.

3. Recognize untreated health problems that could be resolved with appropriate medication therapy.

4. Follow the patient's progress to determine the effects of the patient's medications on his or her health.

5. Consult with the health-care providers and other patient's physicians in selecting the drug's therapy that best meets the patient's needs and contributes effectively to the overall therapy goals.

6. Advise the patient on how to best take his or her medications.

7. Support the health care team's efforts to educate the patient on other important steps to improve and maintain health, such as exercise, diet, and preventive steps like immunization.

8. Refer the patient to the physician or other health professionals to address specific health, wellness, or social services concerns as they arise. (ACCP A. C., 2008).

Clinical pharmacist researcher generates, disseminates and applies new knowledge that contributes to improved health and quality of life. Within the system of health care, the clinical pharmacist is the expert in the therapeutic use of medication. They routinely provide drug therapy evaluation and recommendation to patient and healthcare professional. The clinical pharmacist is the primary source of scientifically valid information and advice regarding safety, rational, and cost-effective use of medication. (illustrared, 2007).

1.3.1 Clinical Pharmacist Roles within the Health Care System

Clinical pharmacists apply evidence-based medicine guidelines, evolving sciences, emerging technologies, and relevant legal, ethical, social, cultural, economic, and professional principles, to achieve required therapeutic goals.

Moreover, to manage medication therapy in direct patient care settings, whether practicing independently or in consultation or collaboration with other healthcare providers, clinical pharmacist assumes responsibility and accountability.

The clinical pharmacist is most expert in the therapeutic use of the drug, provides unique information and skills sets to the health care system, and thus, it is sufficient to assume the role of specialists in drug therapy.

Furthermore, this expertise is used proactively to ensure and advance rational drug therapy use, that way averting many of the drug's therapy misadventures that ensure following inappropriate therapeutic decisions made at the point of prescribing.

This expertise also covers non-traditional treatments outside of conventional medicine. Finally, it indicates that a clinical pharmacist provides therapeutic assessment suggestions, recommendations, and it underscores the fact there are regular consultations between the evaluation of drug treatment in daily practice with patients and healthcare professionals. (ACCP A. C., 2008)

1.3.2 The Role of Pharmacists in Discovering and Preventing DRPs

Clinical pharmacy is a health specialty that involves the roles and services of the clinical pharmacist to develop and promote the rational and appropriate drugs and devices use. (ESCP, Clinical Pharmacy - a Definition, 2006) More specifically, clinical pharmacy services are oriented to the patient care and aimed to reduce irrational prescribing (Lipton, 1994, Hanlon J. T., 1996), improve disease management (Bogden, 1998, Donovan, 2006), reduce ADEs (Schnipper, 2006), reduce length of stay, ADRs and mortality (Bond, 2006), and give economic benefit (Dooley, 2004). The core practice clinical pharmacy in DRPs involve the detection of DRPs, solving, and prevention. Also, pharmacist has a major role in documenting ADRs. (Palanisamy, 2009) In addition, the assessment of DRPs by clinical pharmacists is applicable in different settings as in hospital multidisciplinary teams, nursing homes, and primary care. (Viktil, 2008) Nevertheless, identifying and resolving clinically important DRPs by pharmacist's role is most valuable in hospital settings. Collaborative drug therapy in hospital is a service of clinical pharmacy that involves cooperation between physicians and pharmacists on the drug therapy of individual patient. The collaboration results in optimizing the patient's drug therapy and quality of life. (Gattis, 1999) This can be explained based on pharmacists' extensive knowledge of medicine; they can correlate the symptoms appeared in the patient to the possible adverse effects of the drug therapy. Furthermore, clinical pharmacists reduce the incidence of ADRs by their

ability to avoid drugs with potential side effects in susceptible patients. (Palanisamy, 2009)

In fact, pharmacist's contributions in DRPs are used to evaluate their role in optimization of drug therapy; because this evaluation includes determining the number of DRPs addressed or prevented, or by assessing the clinical outcomes for the patients. (Viktil, 2008) Hanlon et al showed that inappropriate drug prescribing and ADRs was minimized by the revision of the patients drugs by the pharmacist along with the discussions with physicians during the 12 months follow up period. (Hanlon, 1996).

One of the goals of pharmaceutical care is to prevent drug-related problems that might interfere with patient safety and the desired health-outcome. Moreover; the pharmacists play an essential role in improving the public health around and in the disaster areas such as the refugees' areas. The pharmacists have specialized knowledge of drug-body interactions to optimize their pharmacological benefits with safe, rational, and liable use of medications. Clinical pharmacist contributes significantly to improving safety and cost-effectiveness of treatment, active monitoring and evaluation of drug therapy, patient understanding and compliance to the prescribed medication. (Shah Jainam V.a, 2016) (Mohamed Azmi Hassali, 2016).

The community pharmacists are in unique position to discover and prevent the incidence of DRPs among patients outside the hospitals. The analysis of prescriptions before the dispensing process helps potentially in increasing the quality of life and reduces therapeutic cost. The interventions of the community pharmacists help in relief vast numbers of DRPs in ambulatory patients. (Buurma, 2004) (Huysmans K, 2014).

Evidence had documented the pharmacists' role and their efforts in reducing the incidence of preventable adverse events and identifying and resolving the drug-related problems significantly in the health system. According to research published in 2013 in *International Journal of Clinical Pharmacy* showed that the clinical pharmacists could combine current diagnoses, laboratory values, and medical history with the pharmacotherapy medications of a patient. Thus, the clinical pharmacist can detect and help in resolving more DRPs than any other computerized systems such as Computerized Physician Order Entry systems (CPOE). (Zaal RJ, 2013) (Hussain Al Rahbi, 2014).

However, more researchers are necessary to study the cost-effectiveness of clinical pharmacy services for the community. Establishing a continuing system of identification, intervention and preventing DRPs (that has been conducted by pharmacists) is a useful tool to improve the patient's healthcare system. (Zaal RJ, 2013).

1.3.3 The Role of a Clinical Pharmacist in Intensive Care Unit

The use of medication to support patients and optimize outcomes is a fundamental strand of care, especially for critically ill patients in an intensive care unit (ICU). The ICU is a rapidly changing, complex, and costly environment where polypharmacy is the norm and medications are frequently used in combinations involving ever-changing doses based on physiologic responses and critical illness-related organ dysfunction. This creates the 'perfect storm' scenario that is ripe for medication errors. A study over a three-week period in two ICUs in the U.S. found an adverse event rate of 80.5/1000 patient-days, with medications being responsible for 78% of the serious events. Also, other a European study conducted across 27 countries and 113 ICUs involving 1,328 patients revealed that during a brief 24-hour observation period 81% of ICUs reported at least one parenteral medication error that involved 37% of patients. (Valentin A, 2009). Fortunately, The Role of Pharmacists in Intensive Care Unit provides a key role managing medication within the complexity of various routes of administration, severe and rapidly shifting pharmacokinetic and dynamic parameters, extremes of physiology in critical illness, intercept and resolve medication errors, optimize medication therapy and undertake broader professional activities within the job role that contribute to the smooth running of ICU. These activities are associated with improved quality, reduced mortality and reduced costs. (Borthwick, 2018)

In 1999, a study reported that pharmacist attendance at (ICU) rounds reduced the rate of preventable adverse drug events by 66%. (Leape LL, 1999) Another study in a retrospective review of patients with the thrombolytic disease, clinical pharmacists were able to significantly reduce patient mortality, ICU length of stay, bleeding complications, and need for blood product transfusions. (MacLaren R, 2009)

A prospective, observational study: 86 patients out of 2389 admitted to the ICU were reported to experience DRPs. Variables studied were: reason for ICU admission; length of ICU stay; need for cardiovascular support; need for mechanical ventilation or dialysis; Glasgow Coma Scale score on presentation to hospital; Acute Physiology and Chronic Health Evaluation (APACHE) II score; predicted mortality. The number of patients admitted due to a drug overdose was 45 (52%; 16 female), which was more than the rest of the patients put together (41 (48%; 11 female). The former were older and suffered more deterioration of renal function. The need for inotropic drugs and mechanical ventilation, the APACHE II score and median LOS were significantly higher in drug overdose patients. Only four (4.6%) admissions were due to a suicide attempt, and three (3.4%) trauma patients were admitted for DRPs; all were related to drug overdose. Hypoglycemic medication was the cause of the DRPs in 19% of the patients. The total mortality rate was 4.6%; all of the deaths were unpreventable. DRPs represented a small proportion of admissions to the ICU. Drug overdose represented a large proportion of the DRPs. Hypoglycemia was the most common cause of admission for DRPs

In conclusion, while it is unsatisfactory to see that ICU clinical pharmacists are not present in all institutions that have an ICU. Ongoing support from professional organizations, such as the Faculty of Intensive Care Medicine and the Intensive Care Society. Even in developing countries such as Jordan, India, and Brazil, studies on the impact of ICU pharmacists are being published. (LeBlanc JM, 2008) (Hisham M, 2016) (Fideles GM, 2015) (Aljbouri TM, 2013)

1.4 Aims of the study:

- To assess the prevalence and distribution of DRPs in Near East University Hospital (NEUH) ICU patients.
- To classify DRPs and determine the most common causes of DRPs using the PCNE classification V8.02.
- To discuss the role of the pharmacist in identifying, reducing and preventing the DRPs incidence.

2. METHODOLOGY

A retrospective observational study was carried out on patients (aged 18 years and more) who admitted to the Intensive Care Unit (ICU) in Near East University Hospital (NEUH) in North Cyprus. There was 12 beds in ICU which serves cases referred from governmental hospital as well as cases admitted from NEUH wards. There were 6 physicians, 8 nurses and 4 porter who works in ICU for 24 hours per week as shifts.

The data was collected for a period of 6 months (01 January 2018 till 01 June 2018). Identifying the DRP cases was done by clinical pharmacist and research pharmacist, DRP were the classified using the tool Pharmaceutical Care Network Europe (PCNE). DPR classification tool version 8.02. The descriptive statistics (Mean ± SD, Percentage) represent the data.

2.1 PCNE's Drug-Related Problems Classification System

The Pharmaceutical Care Network of Europe published in January 1999 a drug-related problem (DPR) classification scheme. Over the years, the PCNE's classification system has been devolved and improved by experts. The latest version, 8.01, has been published on the 5th of November, 2017, and has been used in this study. This classification version is a hierarchical coded system and has three primary domains for problems (P-code): treatment effectiveness, treatment safety, and others, eight primary domains for causes (C code): drug selection, drug form, dose selection, treatment duration, dispensing, drug use process, patient related, and others, and five primary domains for interventions (I code): no intervention, at prescriber level, at patient/care level, at pharmacist level, and others). Moreover, on the more detailed level, there are 8 subgroups for problems, 37 subgroups for causes and 17 subgroups for interventions, and 20 subdomains for intervention acceptance.

2.2 Inclusion Criteria

- Patients admitted to the ICU of NEU Hospital.
- Being hospitalized during the study period (last 6 months) for a duration not less than one day.

2.3 Exclusion Criteria

- Patients without completely documented files.
- Pediatric and adolescent (younger than 18 years old).

2.4 Sample Size and Data Collection

The data have been collected from the medical files of all hospitalized patients during the last 6 months (01 January 2018 till 01 June 2018).

Patients' age, gender, principal diagnosis, concomitant disease states, medical history, concurrent medications, dosage, and medications taken prior to admission have been recorded. Other data collected include biochemistry and haematology results, microbiological culture and sensitivity tests, and plasma drug concentrations when these are available. Normal laboratory values for the hospital have been used to determine the presence of abnormalities. Renal function was estimated using glomerular filtration rate calculated using the creatinine clearance formula Chronic Kidney Disease Epidemiology Collaboration CKD-EPI formula expressed as:

$$GFR = 141 * \min(Scr/\kappa,1)^{\alpha} * \max(Scr/\kappa, 1)^{-1.209} * 0.993^{Age} * 1.018 \text{ [if female]} * 1.159 \text{ [if black]}$$

Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.

DRPs experienced by the patients on admission and during their inpatient stay, together with the suspected drugs have extracted from their medical records.

2.5 Statistical Analysis

Data analyses have conducted using Microsoft Excel 2016 and Statistical Package for the Social Science (SPSS) programming software version 24.0. To estimate DRP in ICU patients, the continuous data have presented as mean (± standard deviation) or median (range), Mann Whitney test was used to test for significant difference between the number of medications taken and the risk of DRPs, while absolute information will be presented as frequency and percentages (%).

2.6 Guidelines and references used to determine DRPs

- Lexi comp (Online database was used to analyze potential drug-drug interactions).
- The PCNE's drug-related problems v 8.01 was used to classify the type of DRPs, causes, interventions, and the outcomes when applicable.

2.7 Ethical Consideration

Privacy of the patient was assured during the study. The study was approved by the Near East Institutional Review Board (IRB) of Near East University Hospital that assigned this research as being just an observational study. Private patient data were not recorded. Only the patients' file numbers, age, and gender were used during the study.

3. RESULTS

3.1 Characteristics of the Patients

There were 70 patients' medical cases that had registered in NEUH archive from (01 January 2018 till 01. June 2018). Of these 17 patients were excluded because without completely documented files and who were younger than 18 years old and rest 53 patients' cases were included in this research, 33 (62.3%) of the patients were male and 20 (37.7%) patients were female, with an average age of 70.6 years (SD ±14.4). 35 patients (66%) were identified to have DRP; 21 (60%) of these patients were men and 14 (40%) of them were women, with an average age of 71.7 (SD ±13.9). There were 18 (34%) patients without DRPs.

The ICU mortality was 19%. Compared to other study reported 15% ICU mortality in Norwegian. (Johansen e. T., 2012)

The average number of medication was (7.1) per patient and the average number of diagnoses was 1.5 for each patient.

The patients who were included in this study had an average of 1.5 active medical conditions.

For each patient, one medical condition was classified to be the primary disease of the case which was associated with the drug-related problem incidence and increased its complications. 46 % of the drug-related problems cases occurred in Cardiovascular Disease patients (Figure1).

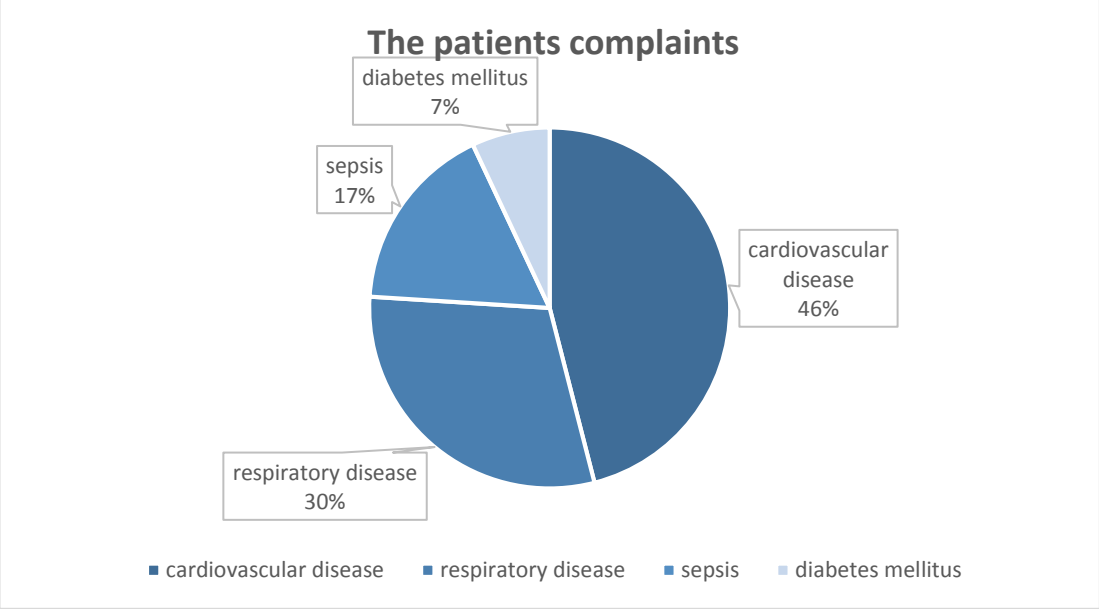
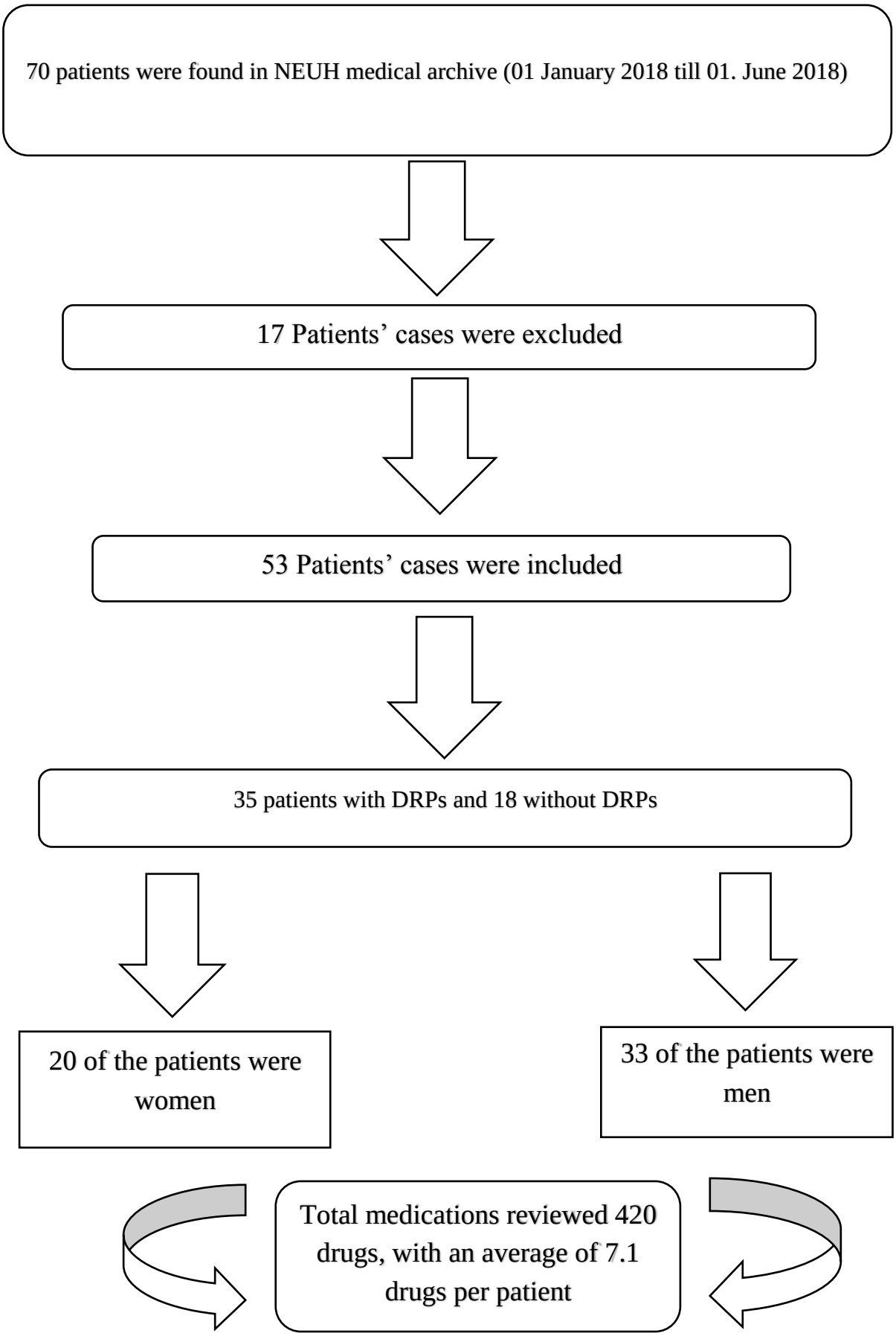


Fig.2: *The patient's complaint*


70 patients were found in NEUH medical archive (01 January 2018 till 01. June 2018)
17 Patients' cases were excluded
53 Patients' cases were included
35 patients with DRPs and 18 without DRPs
20 of the patients were women
33 of the patients were men
Total medications reviewed 420 drugs, with an average of 7.1 drugs per patient

3.2 Drug-related problems

Out of 53 total patients' cases were included, 35 cases **(66%**) of drug-related problems were identified, reviewed by one clinical pharmacist and one specialist physician and documented by the researcher.

In those 35 cases, 70 drug-related problems were found (more than one DRPs per patient. The most frequently identified DRPs were unnecessary drug treatment (38.6%). Followed by untreated symptoms or indication (22.9%), Effect of drug treatment not optimal (20%)

Adverse drug event (possible) occurring (14.3%) followed by no effect of drug treatment (4.3%)

Table 1: Distribution of Drug Related Problems

Category	Frequency	Percentage
No effect of drug treatment (P1.1)	3	4.3%
Effect of drug treatment not optimal (P1.2)	14	20%
Untreated symptoms or indication (P1.3)	16	22.9%
Adverse drug event (possible) occurring (P2.1)	10	14.3%
Unnecessary drug treatment (P3.2)	27	38.6%
Total	**70**	**100%**

3.3 Causes of the problem

The cause “medication error” section domain is vital for identifying the type of errors (might be more than one) that caused the incidence of the drug-related problem. Identifying those causes is important to highlight the way of problems happened to be easier to solve.

Only one error was identified to be the leading cause of each drug-related problem registered.

The drug selection (C1) was the most identified error to cause a drug-related problem 87.1%, followed by dose selection at 12.9%.

Table 2: Cause Frequencies

Category	Frequency	Percent
Drug selection (C1)	61	**87.1%**
Dose selection (C3)	9	**12.9%**
Total	**70**	100%

Table 3: Causes Analysis

Causes Categories	Frequency	Percent
Inappropriate drug according guidelines (C1.1)	1	1.4%
Inappropriate drug according guidelines but contra indication (C1.2)	9	12.9%
Medication without indication (C1.3)	25	35.7%
Inappropriate combination of drug or drugs and herbal (C1.4)	7	10%
Indication without medication (C1.6)	17	24.3%
Too many drugs prescribed for indication(C1.7)	2	2.9%
Drug dose too low (C3.1)	3	4.3%
Drug dose too high (C3.2)	6	8.6%
Total	**70**	**100%**

3.4 Relationship between ages, gender and number of problems

The total number of patients were 35; 29 of them were over 65 years old and 6 of them were less than 65 years old. Among the 29 patients of over 65 years old, there were 12 patients with 1 problem, 8 patients with 2 problems, 8 patients with 3 problems and 1 patient with 4 problems. While among the 6 patients of less than 65 years old, there were 3 patients with 1 problem, 2 patients with 2 problems, 1 patient with 3 problems and 0 patient with 4 problems. The total number of patients from both groups with one problem was 15 out of 35 patients.

Table 4: Relationship between ages and number of problems

Characteristics		**No. problems**				**Total**
		1	**2**	**3**	**4**	
Ages	Younger than 65	3	2	1	0	**6**
	Over than 65	12	8	8	1	**29**
Total		**15**	**10**	**9**	**1**	**35**

P < 0.05, there is statistically significant association between ages and number of DRPs in patients.

Table5: Correlation between ages and number of problems

Correlations

		NO. PROPLEMS	AGES
NO.PROPLEMS	Pearson Correlation	1	-.378-*
	Sig. (2-tailed)		.025
	N	35	35
AGES	Pearson Correlation	-.378-*	1
	Sig. (2-tailed)	.025	
	N	35	35

*. Correlation is significant at the 0.05 level (2-tailed).

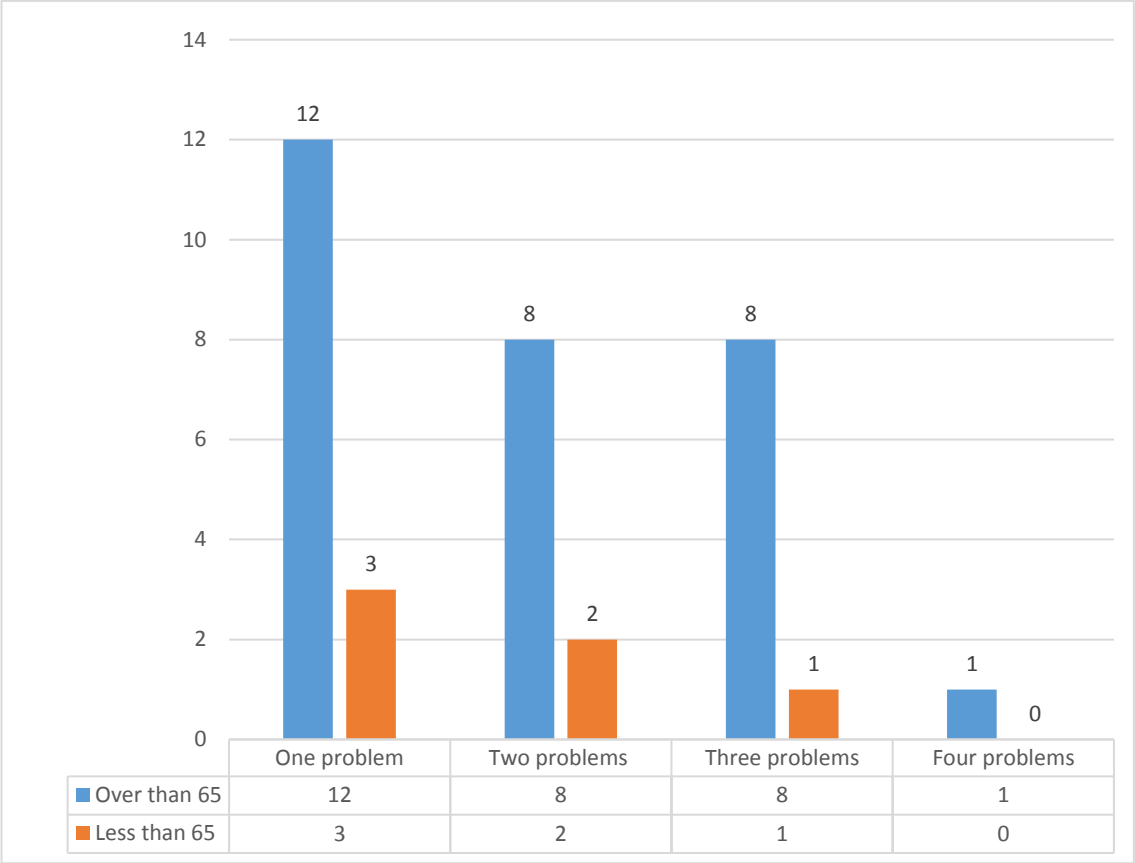


***Fig 3**: Relationship between age and number of problems*

3.5 Relationship between the numbers of medications and the number of problems

By reviewing 53 patients' cases, we classified these cases into two categories according to the number of the drugs these patients have been taking. The first category was for the patients who were taking less than five drugs (7 patients) **(13.2%),** the second one was for the patients who were taking more than five drugs (46 patients) **(86.8%).**

Among the 7 patients who were taking less than five drugs, no patient any problems. While among the 46 patients who were taking more than five drugs, 11 patients were without problems, 15 patients were with 1 problems, 13 patients were with 2 problems, 6 patients were with 3 problems, and one patient with 4 problems.

Table 6: Relationship between the number of medications and the number of problems

Characteristics		No. problems					Total
		0	**1**	**2**	**3**	**4**	
NO. medication	**Less than five drugs**	7	0	0	0	0	**7**
	More than five drugs	11	15	13	6	1	**46**
Total		**18**	**15**	**13**	**6**	**1**	**53**

(P-value<0.05), there is statistically significant between the number of medication and number of problems. (P=0.01).

Table 7: Correlation between number of medication and number of problems

Correlations

		NO. PROPLEMS	NO. MEDICATIONS
NO.PROPLEMS	Pearson Correlation	1	.428**
	Sig. (2-tailed)		.001
	N	53	53
NO.MEDICATIONS	Pearson Correlation	.428**	1
	Sig. (2-tailed)	.001	
	N	53	53

**. Correlation is significant at the 0.01 level (2-tailed).

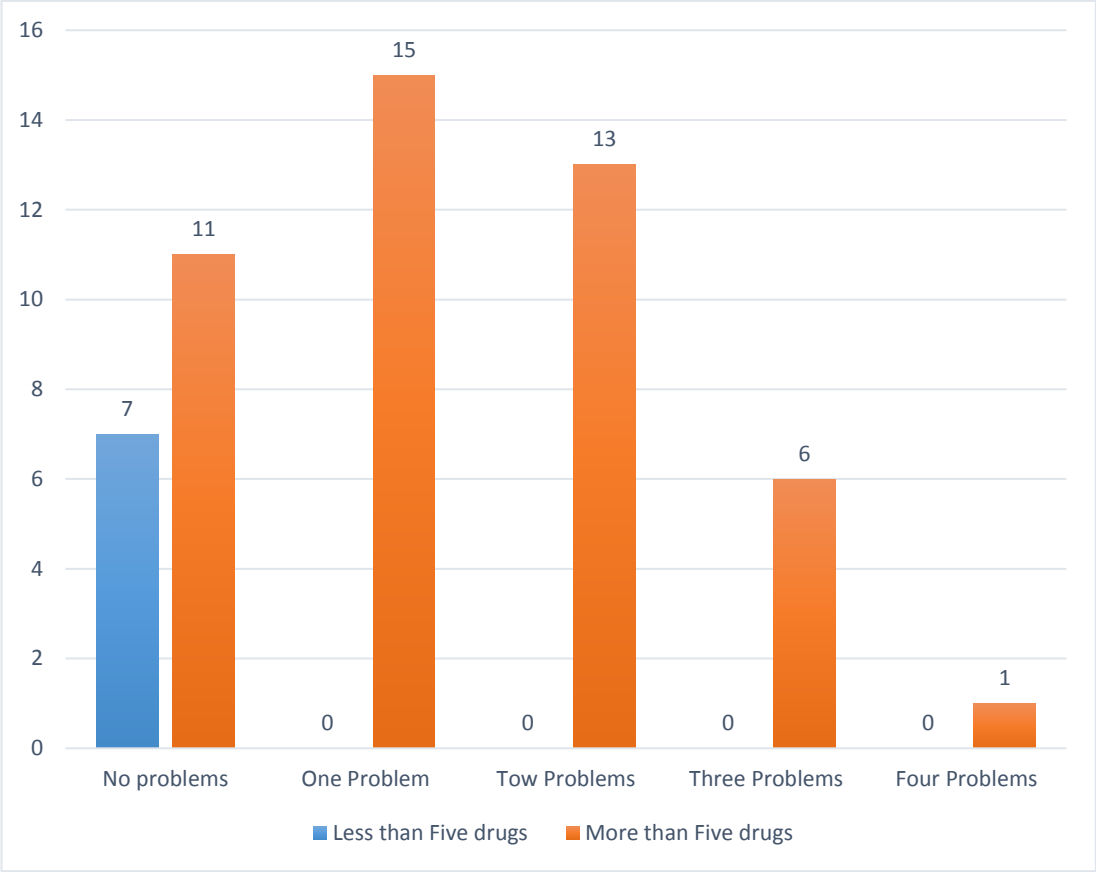


Fig 4: *Relationship between numbers of medications with number of problems (columns)*

3.6 Relationship between the periods of stay in ICU with number of problems

The average ICU stay was 4.39 (SD ±3.2) days per patient.

Among the patients who stayed 1-2 days, 8 patients were with 1 problem, 7 patients were with two problems, 3 patients were with 3 problems and no patient was with 4 problems.

While among the patients who stayed 3-7 days, 7 patients were with 1 problem, 1 patient was with 2 problems, 3 patients were with 3 problems and 1 patient was with 4 problems.

For those patients who stayed more than 7 days, 2 patients were with 1 problem, 1 patient was with 2 problems, 2 patients were with 3 problems, and 1 patient was with 4 problems.

The patients who stayed fewer days in the ICU showed higher incidence of DRPs of 51.4%.

Table 8: Relationship between the periods of stay in ICU with number of problems

Characteristics		No. problems				Total
		1	2	3	4	
Period Stay	1-2 days	8	7	3	0	18
	3-7 days	7	1	3	1	12
	More than 7 days	2	1	2	0	5
Total		17	9	8	1	35

(P-value>0.05), there is No statistically significant between the periods of stay ICU and number of problems. (P=0.75).

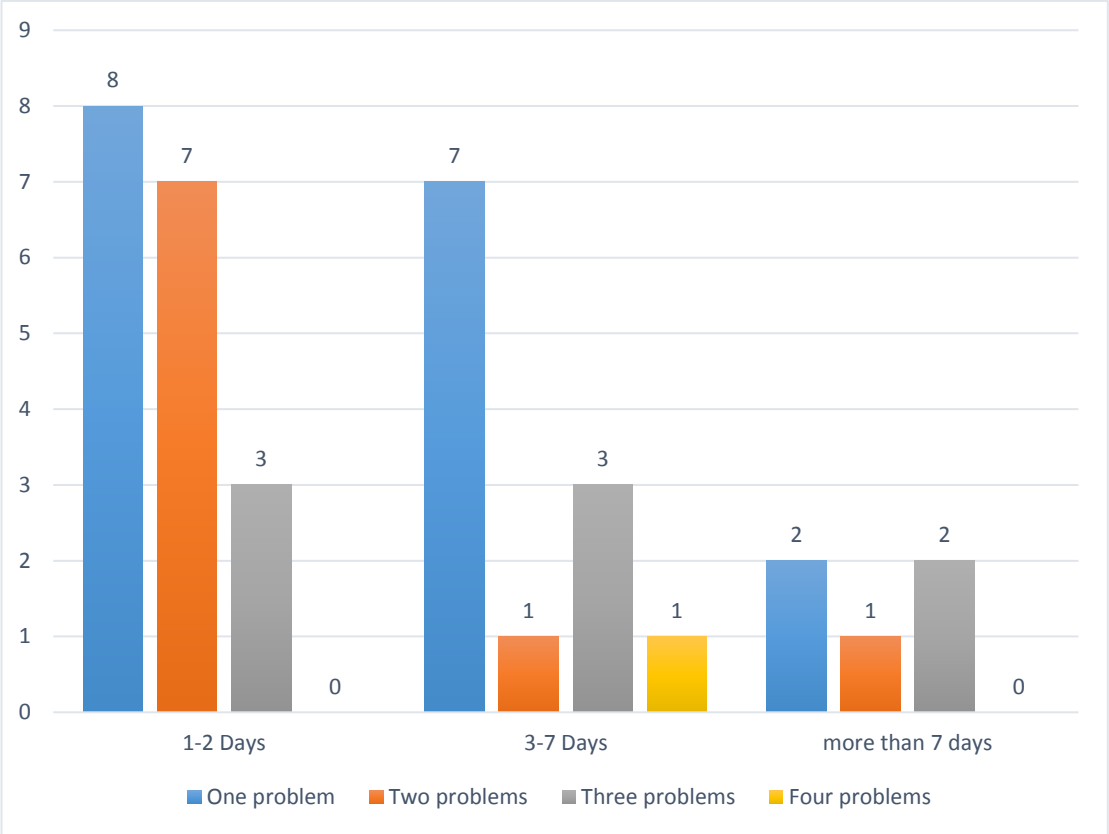


***Fig.5**: Relationship between the periods of stay in ICU with number of problems*

3.7 Medications with DRPs

By reviewing the medication for our patients, we specified causing the most DRP medications.

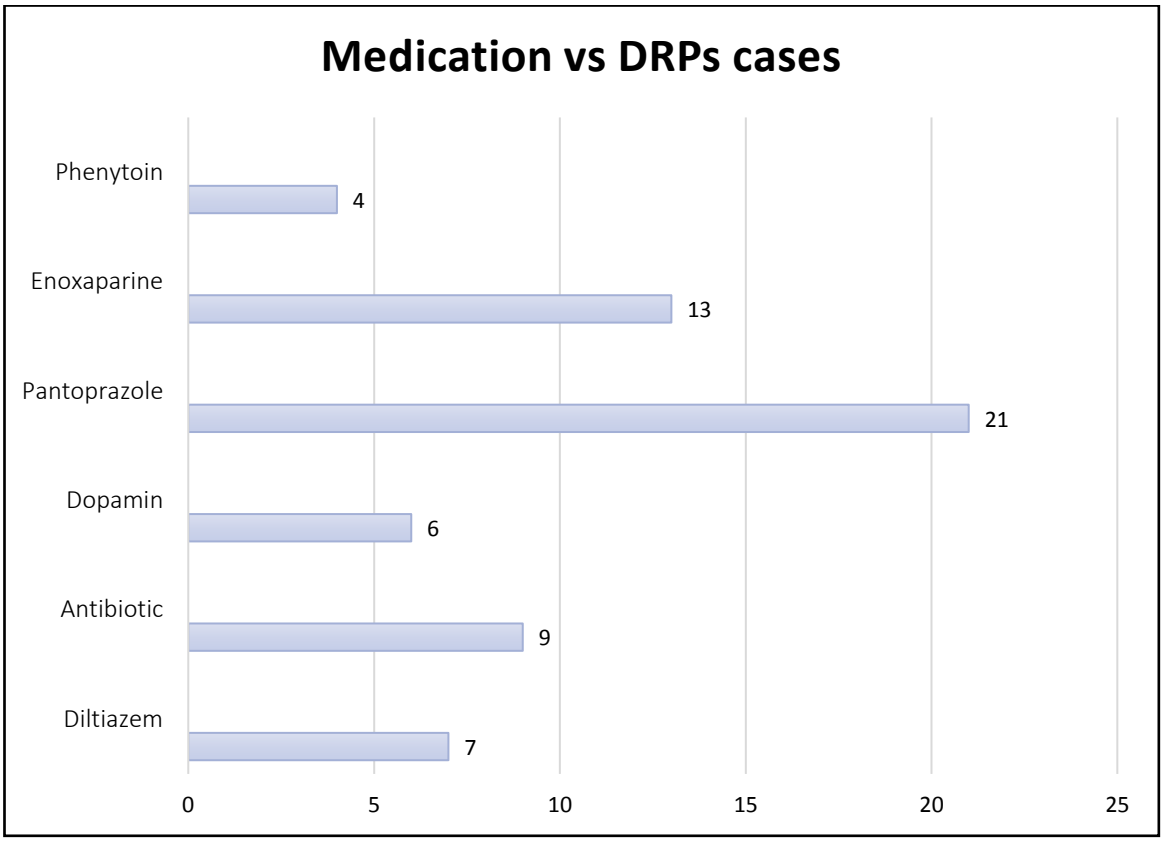


***Fig.6**: Medications with DRPs*

4. DISCUSSION

Drug therapy is considered a cornerstone of patient care for the treatment of disease and symptoms, but it can also cause DRPs resulting in increased hospitalization and mortality. (Bondesson A, 2013). Drug-related problems occur at high rates in the ICU due to many reasons including severity of disease of ICU patients and complicated regimens of multiple medications used. Also, the high-risk nature of the patient cases and medications added to the high frequency of changes in therapeutics used. (Ernst FR, 2001)

The main finding of our study was the prevalence of DRPs identified (66%) with the average of 1.3 DRP per ICU patient during 6 months of the study duration. In 2012 a 12 months study in the ICU of a tertiary Norwegian hospital, a prevalence of 53% DRPs was reported with average of 1.8 DRP per patient. (Johansen e. T., 2012) Other studies reported prevalence of 54% DRPs and an average of 1.2 DRP per patient in the ICU of a Rural Referral Hospital, Tamworth, Australia respectively. (Howle, 2018) While in 4 hospitals in Denmark, 85% prevalence of DRP was reported with 3 DRP per patient in ICU reported. (Nielsen, 2013)

60% of males had at least one DRPs while (**40**%) of females had at least one DRPs. Age and gender may not be as important as the number of drugs prescribed as predictors of experiencing a DRP in patients with polypharmacy. (Koh Y, 2005) In the present study, DRPs increased with increasing numbers of medications per patient, and also increasing number of critical illness conditions per patient, the same as reported elsewhere. (Al-Baghdadi, Introducing clinical pharmacy services to cardiovascular clinics at a university hospital in Northern Cyprus, 2017)

The average patient age was 70.6 years old (SD ±14.4) while other researchers reported 72.1 (±12.4) in Denmark, 52 (±22) in Norway. Polypharmacy was obvious as the average number of medicines prescribed per patient was (7.3) compared with 8 average number of medications in Denmark ICUs (Nielsen, 2013) while in hospital at Norway was 4 average number of medication. (Lundereng, 2013). The patients who are included in this study had an average of 1.5 active diagnoses.

In our study, cardiovascular disease was most common causes of admission for patients with DRPs (46%), followed by respiratory diseases (30%), sepsis (19%) and diabetes mellitus (7%). Other researchers reported most common cause's respiratory diseases (47%) followed by cardiovascular disease (36%), miscellaneous symptoms (10%) and Nervous system (7%) in Nielsen et al study.

In our study, we found 70 drug-related problems (more than one DRPs for one patient), unnecessary drug treatment (38.6%) was the most common problems of DRPs. Untreated symptoms or indication (22.9%) was the second, followed by effect of drug treatment not optimal (20%), adverse drug event (14.3%) and no effect drug treatment (4.3%). Compared to other study reported 'effect of drug treatment not optimal' was the most common in Nielsen et al study, while unnecessary drug treatment was most common reported by Johansen et al.

(30%) of patients had DRPs due to PPI medication with causes (medication without indication (C1.3) this causes is the most common in our study with a percentage (35.7%), followed by ((24.3%) Indication without medication (C1.6)), ((12.9%) Inappropriate drug according guidelines but contra indication (C1.2)), ((10%) Inappropriate combination of drug or drugs and herbal (C1.4)), ((8.6%) Drug dose too high (C3.2)), ((4.3%) Drug dose too low (C3.1)), ((2.9%) Too many drugs prescribed for indication (C1.7)), and ((1.4%) Inappropriate drug according guidelines (C1.1)). Other researchers found the most common problems seen was 'over\under dose' (38%) followed by 'drug selection' (22%) in Howle et al study, (Howle, 2018) while too high dose (28%) was the most common causes followed by significant drug interaction (16%) reported by Johansen et al.

The four primary medication classes associated with DRPs were PPIs (30%), anticoagulant (19%), antibiotic (6%) and antidepressants (4%). PPIs and Antidepressants were the main DRPs type unnecessary drug-treatment, the cause was medication without indication (C1.3). Anticoagulant was the leading medicine associated with adverse drug event (possibly) occurring, the cause was 'drug dose too high' (C3.1). An 'inappropriate drug' (within guidelines but otherwise contra-indicated) of antibiotic pharmacological group was the most common cause of problems classed as 'the effect of drugs not optimal'. Compared to other study reported most frequently

involved in the DRPs, were antibacterial for systemic use (22%), antiepileptic's (13%), drugs for acid-related disorders (9%), cardiac therapy (8%) and antithrombotic agents (8%). (Johansen e. T., 2012) While were anti-infective (18%), cardiovascular (13%), analgesic (10%), gastrointestinal (8%), psychotropic (8%), blood and electrolytes (7%), endocrine (7%), respiratory (7%), other (4%) and neurological (4%) reported by Howle in Australian. (Howle, 2018)

The average of staying period in ICU was 4.39 days (SD ±3.2) per patient of total patients. There were (18) patients stayed in ICU less than two days, we found three problems at least for each patient. Patients who stayed 3-7 days they found with four problems at least with total number 12 patients. The patients with less hospitalizations in (ICU) showed a higher incidence of DRPs in a percentage 51.4% for one problem at least. Our study showed that no significant difference between the length of hospital stay and DRPs. In our study (P-value>0.05), there is No statistically significant between the periods of stay ICU and number of problems. (P=0.75). Compared to other study reported length of stay in the ICU was 4.1 (5.7) days, time on a mechanical ventilator was 2.9 (5.0) days by Johansen et al.

In comparing ages with number of problems we found that the number of problems increases while the ages increase (82.9%) for patients over than 65 years old) and (17.1%) for patients ages between 18 and 65 years old), the present study showed a significant between the number of DRPs and the number of medications. We found a significant association between ages and the presence of DRPs P-value=0.025 (P-value<0.05). But, we cannot generalize this because of its need more studies and large number of patients.

Total medications reviewed 420 drugs, with mean of 7.33 drugs per patient (SD±2.44). There were (46) patients taking more than five drugs with four problems at least. Patients who take less than five drugs they found no any problems with total number seven patients. The patients who take more than 5 drugs in (ICU) showed a higher incidence of DRPs. Commonly, more than 5 medications are considered as polypharmacy. (What is polypharmacy? A systematic review of definitions, 2017) In our study (P-value<0.05), There is statistically significant between the number of medications and number of problems. (P=0.01).

- Limitations of the study

This study has the following limitations:

First, our study is retrospective, that's prevented us from applying intervention and sees the outcomes clinically in patients.

Second, the only source of our information was the patient's files that not allowed us to contact with patients and indicate other problems.

Third, our time limit and a small number of the sample we can't generalizing our study findings.

We recommend further controlled multicenter studies, where interventions are evaluated regarding both updated therapy guidelines and clinical endpoint, to further characterize DRPs incidence. Rove the quality of acute care but also to allow early and appropriate treatment.

Implementation of clinical pharmacy service in Intensive Care Units is more likely to reduce the number of DRPs detected and increase safety and quality.

5. CONCLUSIONS

The critically ill patients in ICU are more vulnerable to DRPs than others. Moreover, administration of multiple drugs is a common event in the ICU, which can lead to an increased incidence of DRPs, could be avoided by including more pharmacists whose play a major role in providing healthcare with their knowledge in drugs and their associated problems.

The identification and documentation of DRPs are an important part that will eventually lead to reduce and solve the frequently incidence drug-related problems.

The most frequently reported DRPs among this population were unnecessary drug treatment (38.6.2%).

The most apparent cause that contributed to the DRPs incidence was the Drug selection.

At least including one pharmacist in the health centers will increase the chance to avoid drug and dose selection-related problems. According to this study, the pharmacists identified 66% of DRPs cases.

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7. Appendix

Near East University Hospital

Drug Related Problem in Intensive Care Unit at University Hospital in Northern Cyprus

Advisor: Prof. Mesut Sancar Co-advisor:-Assist. Dr. Abdikarim Abdi investigator: Mhd Feras Chbib

<table>
<tr><td colspan="11"><u>Demographic information</u></td></tr>
<tr><td colspan="2">Patient no.</td><td>H.unit</td><td>Wt.kg</td><td colspan="2">Da te</td><td colspan="2">Age “YRS”</td><td colspan="3">Gender</td></tr>
<tr><td colspan="2"></td><td></td><td></td><td colspan="2">/ /</td><td colspan="2"></td><td colspan="3">M F</td></tr>
<tr><td colspan="4">Past medical history</td><td colspan="2">Current diagnosis</td><td colspan="2">Staying periods</td><td colspan="3">Sr. cr</td></tr>
<tr><td colspan="4"></td><td colspan="2" rowspan="3"></td><td colspan="2" rowspan="3"></td><td colspan="3" rowspan="3"></td></tr>
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<tr><td colspan="4"></td></tr>
<tr><td colspan="11"><u>Medical charts</u></td></tr>
<tr><td>No</td><td colspan="3">Trade name</td><td colspan="3">Generic name</td><td colspan="2">Dose & duration</td><td>Indication</td><td>Time& day</td></tr>
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<tr><td>20</td><td colspan="3"></td><td colspan="3"></td><td colspan="2"></td><td></td><td></td></tr>
<tr><td colspan="2">B P</td><td>PO 2</td><td>H R</td><td>E F</td><td colspan="6">Additional information</td></tr>
<tr><td colspan="2">/</td><td></td><td></td><td></td><td colspan="6"></td></tr>
<tr><td colspan="5">Other abnormal lab results</td><td colspan="6"></td></tr>
</table>

Patient_____

Male ☐ Female ☐

Medication and dosing regimen

A _____

B _____

A: OTC ☐ Rx ☐ (B): OTC ☐ Rx ☐

DRP potential ☐

manifest ☐

1. Type of problem
(tick one box only)

- P1 ☐ **Treatment effectiveness**
  - P1.1 ☐ No effect of drug treatment
  - P1.2 ☐ Effect of drug treatment not optimal
  - P1.3 ☐ Untreated symptoms or indication
- P2 ☐ **Treatment Safety**
  - P2.1 ☐ Adverse drug event (possibly) occurring
- P3 ☐ **Others**
  - P3.1 ☐ Problem with cost-effectiveness of the treatment
  - P3.2 ☐ Unnecessary drug-treatment
  - P3.3 ☐ Unclear problem/complaint. Further clarification necessary
  - P3.4 ☐ Compromise quality of the medicine

Notes:

2. Cause of problem
(one problem can have more than one cause)

- C1 ☐ **Drug selection**
  - C1.1 ☐ Inappropriate drug according to relevant (national or international) guidelines/formulary as applicable
  - C1.2 ☐ Inappropriate drug (within guidelines but otherwise contra-indicated)
  - C1.3 ☐ Medication without indication
  - C1.4 ☐ Inappropriate combination of drugs or drugs and herbal medication
  - C1.5 ☐ Inappropriate duplication of therapeutic group or active Ingredient
  - C1.6 ☐ Indication without medication
  - C1.7 ☐ Too many drugs prescribed for indication
- C2 ☐ **Drug form**
  - C2.1 ☐ Inappropriate drug form (for this patient)
- C3 ☐ **Dose selection**
  - C3.1 ☐ Drug dose too low
  - C3.2 ☐ Drug dose too high
  - C3.3 ☐ Dosage regimen not frequent enough
  - C3.4 ☐ Dosage regimen too frequent
  - C3.5 ☐ Dose timing instructions wrong, unclear or missing
- C4 ☐ **Treatment duration**
  - C4.1 ☐ Duration of treatment too short
  - C4.2 ☐ Duration of treatment too long
- C5 ☐ **Dispensing**
  - C5.1 ☐ Prescribed drug not available
  - C5.2 ☐ Necessary information not provided
  - C5.3 ☐ Wrong drug, strength or dosage advised (including OTC, herbal or any other medications if applicable)
  - C5.4 ☐ Wrong drug, strength or dosage dispensed
- C6 ☐ **Drug use process**
  - C6.1 ☐ Inappropriate timing of administration and/or dosing Intervals
  - C6.2 ☐ Drug dosage under-administered
  - C6.3 ☐ Drug dosage over-administered
  - C6.4 ☐ Drug not administered at all
  - C6.5 ☐ Wrong drug administered
  - C6.6 ☐ Drug administered via wrong route
- C7 ☐ **Patient related**
  - C7.1 ☐ Patient uses/takes less drug than prescribed or does not take the drug at all
  - C7.2 ☐ Patient uses/takes more drug than prescribed
  - C7.3 ☐ Patient abuses drug (unregulated overuse)
  - C7.4 ☐ Patient uses unnecessary drug
  - C7.5 ☐ Patient takes food that interacts
  - C7.6 ☐ Patient stores drug inappropriately
  - C7.7 ☐ Inappropriate timing or dosing intervals
  - C7.8 ☐ Patient administers/uses the drug in a wrong way/technique
  - C7.9 ☐ Patient unable to use drug/form as directed
- C8 ☐ **Other**
  - C8.1 ☐ No or inappropriate outcome monitoring (incl. TDM)
  - C8.2 ☐ Other cause; specify
  - C8.3 ☐ No obvious cause

3. Type of intervention
(one problem can lead to more than one intervention)

- I0 ☐ **No intervention**
  - I0.1 ☐ No intervention
- I1 ☐ **At prescriber level**
  - I1.1 ☐ Prescriber informed only
  - I1.2 ☐ Prescriber asked for information
  - I1.3 ☐ Intervention proposed, approved by prescriber
  - I1.4 ☐ Intervention discussed with prescriber
- I2 ☐ **At patient / carer level**
  - I2.1 ☐ Patient (drug) counselling
  - I2.2 ☐ Written information provided only
  - I2.3 ☐ Patient referred to prescriber
  - I2.4 ☐ Spoken to family member / caregiver
- I3 ☐ **Atpharmacistlevel**
  - I3.1 ☐ Drug changed to …
  - I3.2 ☐ Dosage changed to …
  - I3.3 ☐ Formulation changed to …
  - I3.4 ☐ Instructions for use changed to …
  - I3.5 ☐ Drug stopped
- I4 ☐ **Other**
  - I4.1 ☐ Nurse administration
  - I4.2 ☐ Side effect reported to authorities
  - I4.3 ☐ Other intervention (specify)

4. Intervention Acceptance
(tick one box only)

- A1 ☐ **Interventionaccepted**
  - A1.1 ☐ Intervention accepted and fully implemented
  - A1.2 ☐ Intervention accepted, partially implemented
  - A1.3 ☐ Intervention accepted but not implemented
  - A1.4 ☐ Intervention accepted, implementation unknown
- A2 ☐ **Intervention not accepted** (byprescriber caregiver orpatient)
  - A2.1 ☐ Intervention not accepted: not feasible
  - A2.2 ☐ Intervention not accepted: no agreement
  - A2.3 ☐ Intervention not accepted: other reason (specify)
  - A2.4 ☐ Intervention not accepted: unknown reason
- A3.1 ☐ **Intervention proposed, acceptance unknown**
- A3.2 ☐ **Intervention not proposed**

5. Outcome of Intervention
(tick one box only)

- O0 ☐ **Problem status unknown**
- O1 ☐ **Problem totally solved**
- O2 ☐ **Problem partially solved**
- O3 ☐ **Problem not solved**
  - O3.1 ☐ Lack of cooperation of patient
  - O3.2 ☐ Lack of cooperation of prescriber
  - O3.3 ☐ Lack of cooperation of pharmacist
  - O3.4 ☐ Lack of cooperation of nurse
  - O3.5 ☐ Intervention not effective
  - O3.6 ☐ No need or possibility to solve problem

Unnecessary-Drug treatment

Drugs	Frequency
Pantoprazole & lansoprazole	17
Phenytoin	4
Dopamine	2
Acetyl cysteine	1
Digoxin	2
Antibiotic (Meropenem)	1
Total	**27**

Untreated symptoms or indication

Vancomycin	2
Ciprofloxacin	2
Moxifloxacin	1
Enoxaparin	6
Allopurinol	1
Atorvastatin	1
Vitamin k	1
Pantoprazole	1
Levofloxacin	1
Total	**16**

No effect of drug treatment	
Ceftriaxone	1
Metoprolol	1
Budecort	1
Total	**3**

Effect of drug treatment not optimal	
Cefazolin	1
Warfarin	1
Adrenalin	1
Dopamine	1
Metformin	1
Diltiazem	2
Colchicine	1
Atorvastatin	1
Metoprolol	1
Meropenem	2
Ciprofloxacin	2
Total	**14**

Treatment Safety: adverse drug event (possibly) occurring					
Drug A	**Drug B**	Severity	clinical significance	Recommendation	Frequency
Dopamine	**Noradrenalin**	Moderate		Monitor for increased effects of sympathomimetic.	**2**
Diltiazem	**Metoprolol**	Major	Additive reductions in heart rate, cardiac conduction, and cardiac contractility (combination may be useful and effective in some situations)	TDM Monitoring of patient hemodynamic response	**1**
Diltiazem	**Atorvastatin**	Major	Diltiazem may increase the serum concentration of atorvastatin.	Consider using lower doses of atorvastatin, and monitor closely for signs of HMG-CoA reductase inhibitor toxicity.	**2**
Cefuroxime	**Pantoprazole**	Moderate	Reduce the oral bioavailability of Cefuroxime	Avoid combination	**2**
Doxazosin	**Tamsulosin**	Moderate	Postural hypotension, Dizziness, Headache, Syncope, Priapism, and Nasal congestion	Avoid combination	**2**
Spironolactone	**Potassium chloride**	Major	Hyperkalemia	Serum potassium and renal function should be checked regularly	**1**
Total					**10**

CURRICULUM VITAE

Name	Mhd Feras	**Surname**	Chbib
Place of Birth	Damascus/Syria	**Date of Birth**	8/3/1993
Nationality	Syrian	**Tel**	05488205642
E-mail	Firas.shbib956@gmail.com		

Educational Level

	Name of the Institution where he/she was graduated	**Graduation year**
Postgraduate/Specialization	-	-
Masters	Near East University	2019
Undergraduate	Arab International University	2016
High school	Al Sham Privacy School	2011

Job Experience

	Duty	**Institution**	**Duration (Year - Year)**
	Pharmacist	Raed pharmacy	2015-2017
	-	-	-

Foreign Languages	**Reading comprehension**	**Speaking***	**Writing***
Arabic	Very good	Very good	Very good
English	Good	Good	Good

Foreign Language Examination Grade								
YDS	ÜDS	IELTS	TOEFL IBT	TOEFL PBT	TOEFL CBT	FCE	CAE	CPE

	Math	**Equally weighted**	**Non-math**
ALES Grade			
(Other) Grade			

Computer Knowledge

Program	**Use proficiency**
ICDL	