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Original Research

The Role of Clinical Pharmacist in Monitoring Drug Therapy in the Cardiovascular and Coronary Care Units in Libya

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Abstract

Background: In hospitals, medication errors are common and potentially harmful resulting in unintentional discrepancies. The study's central goal is to assess the clinical pharmacy services' role in cardiovascular disease inpatients. **Methods:** The current study was a prospective study conducted on one hundred patients admitted to the CVU and CCU in Libya. The patients were classified - into two main groups (I - and II), where the guidelines of clinical pharmacy - were applied only in Group II. Each group is subdivided - into three subgroups with equal numbers of patients. As follows: (Gp a: ten outpatients, Gp b: twenty-five inpatients, Gp c: fifteen patients admitted to CCU. **Results:** By using clinical pharmacy guidelines, the patients in group I were 28 (56%) had angina pectoris, 28 (56%) responded to treatment, 20 (40%) had complications, and 8 (16%) died; while the patients in group II were 15 (30%) had angina pectoris, 43 (86%) respond to treatment, 7 (14%) had complications and 1 (2%) died. So, the results reported a dramatic decrease in the morbidity rates in all groups that undergo guidelines of clinical pharmacy. **Conclusion:** The application of clinical aspects of clinical pharmacy is outstanding in CVU and CCU in Libya.

Keywords: monitoring drugs; cardiovascular diseases; coronary care units; ccu patients; role of clinical pharmacist

INTRODUCTION

Cardiovascular diseases (CVDs) are one of the causes of global death due to the rising prevalence and consequence of mortality, thus are the most serious health problems in the world.[1] Particularly, coronary artery disease (CAD) is known as the leading cause of death worldwide in both genders.[2] Like in many other countries, cardiovascular diseases in Libya are the major cause of death, which is 47%, and 26.30% of total death are caused by coronary artery disease, and this is according to the latest World Health Organization data (2020).[3,4,5] Moreover, The death rate in Libya due to cardiovascular diseases in 2019 was 12,747 deaths, according to the annual number of deaths from cardiovascular disease in Libya, and shows a significant increase of 117% during the past decade.[6] In this context, the dangers are not in death only but must be indicated to CVDs are a big load for those living with the disease.[7] Also, cardiac emergencies pose a significant danger to the patient's life and require to be managed in a coronary care unit (CCU).[8]

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The aim of CAD treatment is managing symptoms and controlling disease progression by reducing related risks, as hyperten-sion (HTN) and dyslipidemia.[9] The risk factors such as diabetes, hy-pertension, and smoking are the major contributing factor for de-veloping CAD in Libya.[10] It is common for patients to take five or more medications in lump sum as part of lifelong treatment. Un-fortunately, multiple pharmacies increase the risk of treatment-related problems (TRPs), defined as an event or condition involv-ing drug therapy that could interfere with the desired health out-come.[11] Furthermore, TRPs occurrence can reduce the benefits of drugs and cause increased morbidity and mortality.[12,13] As hospi-talized cardiovascular patients are at risk for developing TRPs,[14] it is essential to decide the impact of clinical pharmacy on hospital cardiac patient results.[15] Over the past few decades, pharmacy services have shifted from focusing on dispensing and delivering drugs to engaging pharmacists in supplying individually specialized care as part of healthcare teams.[16]

Clinical pharmacists (CPs) are experts in safety promoting and medications rational use. Programs can improve disease man-agement, the reasonable use of pharmacology, health promotion, and disease prevention by using applied knowledge, pooled expe-rience, problematic determination, evidence-based practices, and continuing education.[17] Furthermore, a clinical pharmacist can help physicians by supplying pharmacokinetic and pharmacody-namics information about drugs.[18] The error frequencies of cardi-ac drugs are because of the number and intricacy of their choices in this treatment class.[19] Adjustment of HTN is of interest in pa-tients with cardiovascular disease. Controlling blood pressure (BP) can reduce Myocardial Infarction (MI) (20-25%) and Heart failure (HF) (more than 50%).[20] Also; the cause of elevated blood glucose levels, hyperglycemic patients with cardiovascular

disease have higher rates of death. As well as; acute MI patients should be mentioned, with those patients having arrhythmias and unstable angina. Patients with diabetes are half-patients of cardiac care units, so controlling blood glucose in people with cardiovascular disease is very important.[21] The clinical pharmacist's role is neces-sary for insulin control and decreasing hospitalization.[22] Also, clin-ical pharmacists can decrease the death rate of CCU patients by decreasing their blood cholesterol levels, which reduces the CAD risk.[23] These considerable decreases in hospitalizations or emer-gency rooms, reduced drug costs, and decreased mortality; are caused by (increased life quality for cardiac patients).[24] Conse-quently, Clinical pharmacy is considered an integral component of the health care system6, especially in CVU and CCU.[25] From the analysis of the cited literature, we can say that pharmacy services are associated with reduced mortality rates.[26] As these cardiovas-cular drugs are the category with the most excessive adverse pos-sibilities, participating clinical pharmacists in cardiology units is necessary.[27] To sum it up, the contribution of clinical pharmacists to physicians' rounds in cardiac units or visits, in which their pres-ence - has proven to be very beneficial.[28]

The aim of our current study is to assess the role of clinical pharmacists in all aspects of (CVD) in hospitalized patients and the management of Coronary Artery Disease (CAD) and their risk fac-tors (ex: HTN, Diabetes Mellitus (DM), dyslipidemia) by monitoring the drugs most commonly used in Libya. To our knowledge, this is the first study to evaluate the efficacy of clinical pharmacy guide-lines in coronary care units in Libya.

MATERIALS AND METHODS

Methodology

The current study is a randomized test controlled clinical trial. Randomization was conducted through closed envel-op. The study lasted (18 months) from January 2021 to June 2022. And it depended on assessment of the influence of application of clinical pharmacy services in Cardiovascular Units (CVU) and Cardio Care Unit (CCU). We assessed one hundred twenty-three patients but excluded twenty-three patients due to hepatic and renal dys-function. One hundred patients admitted to CVU and CCU pa-tients at Tobruk Medical Center in Tobruk city, Libya, were in-cluded. The Ethics Committee in Tobruk Medical Center ap-proved the proposal of research before beginning of the study in compliance with the guidelines of the Declaration of Helsinki. Ethical approval was obtained with number Ref. No. 9/1/840/2017), also informed consent was obtained from the studied patients or their relatives. The study was registered in Clinical Trials.gov with ID: NCT05531552.

The Tobruk Medical Center is a publicly-healthcare institu-tion that serves as the primary teaching hospital affiliated with Tobruk University's College of Medicine. The healthcare facility operates an active primary care service that provides round-clock emergency coverage, rendering its services accessible to all and admitting suitable patients into the hospital's medical wards. The Medical Center is equipped with specialized facilities to cater to patients with cardiovascular ailments; a dedicated Cardiovascular Unit (CVU) for inpatients, an intensive Cardiac Care Unit (CCU) for critical cases, and a clinic that offers follow-up services to cardiac outpatients. Throughout the period of study, a cohort of individu-als with a diagnosis of Coronary Artery Disease, including those af-flicted with stable Angina visiting the clinic in addition to those presenting with the more severe manifestations of Unstable Angi-na or Myocardial Infarction, were admitted to either the Cardio-vascular Unit or the Cardiovascular Care Unit at the Tobruk medi-cal center. The diagnostic criteria employed for myocardial infarc-tion (MI) encompassed a clinical presentation characterized by rapid onset of chest pain, supported by electro-cardiogram (ECG) alterations consistent with an acute MI, in addi-tion to changes in serum cardiac enzymes such as Troponin, after hospital admittance. The inclusion criteria of the study were all adults ≥40 years of age, with a diagnosis of CAD, with (hyperten-sion, diabetes, and hyperlipidemia or one or two of them). while exclusion criteria of the study were patients with comorbidities such as liver or kidney disease; peptic ulcer, patients intake alco-hol, cardiac surgery and refusal to give informed consent. All were coronary artery patients moreover they had DM and or hyper-lipidemia as comorbidities.

The patients were recruited into Two groups. The control group (Group I), And test group (Group II), which was the test group that applied the clinical pharmacy guidelines. Each group was subcategorized into three subgroups based on the place of registration (or admission) of the patients, and the seri-ousness of the condition. The classification illustrated: In the first subgroup [Gp Ia], (ten outpatients) suffering from HTN, DM, Hyper-lipidemia, Stable Angina - were included. While in the second subgroup [Gp Ib], (twenty-five in-patients) with Unstable angina; were included. And finally, the third subgroup [Gp Ic] - included (fifteen in-patients admitted to CCU) who had unstable angina or those who had a myocardial infarction. Regarding Group II, the three subgroups IIa, IIb, and IIc included equal numbers of the same patients in the Group I subclasses. And the difference was the application of American Clinical pharmacy guidelines to Group II (ACC - American College of Cardiology/AHA - American Heart As-sociation Guideline).[29] The study design was represented by a follow chart in (Figure1).

We worked alongside the physician to ensure that the pa-tient met the study criteria. Next, the patient was asked to select a closed envelope at random, which could contain either the control group or the test group. This step was crucial in eliminating any potential bias in our study; And the goal of divid-ing the subgroups equally to ensure an unbiased and accurate comparison. The purpose of comparing three equal subgroups was to assess how the application of clinical pharmacy guidelines af-fects each different subgroup. Once patients were randomly as-signed to study groups, we commenced registering their treat-ment charts, collecting their medical history, and monitoring their response to medication. Any complaints they had were rec-orded along with any complications or deaths that occurred dur-ing the study period. The two groups have differences in their procedures, as shown in Table. 1. Our intervention in dosing, drug side effects, and drug interactions, up on the clinical pharmacy guidelines, was limited to the test group. The interven-tion points utilized to manage the test group, as shown in Table 2.

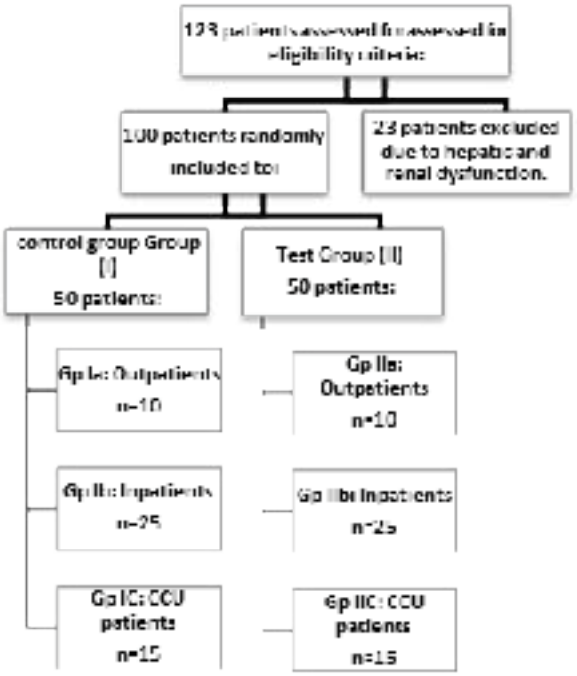

Figure 1. (follow chart of the study patients)

Table 1. The procedures performed on the two groups:		
The procedures that we performed	Group I	Group II
▪ Regist the patients history	×	×
▪ Regist the treatment chart	×	×
▪ Access to patients by phone	×	×
▪ Meeting with patients weekly	×	×
▪ Advising for diet	×	×
▪ Follow-up BP measuring	×	×
▪ Follow-up Glucose level	×	×
▪ Follow-up LDL	×	×
▪ Drug-drug interaction follow-up		×
▪ Follow-up the side effects of drugs		×
▪ Follow-up the dosing		×
▪ Regist the responsiveness of medications	×	×
▪ Regist the Complications	×	×
▪ Regist the death	×	×
The symbol (×) indicates that procedures we had taken with groups.		

All patients' histories were assumed, and demographic data including age, sex, and body mass index (BMI). marital status, edu-cation, and socioeconomic status (that may affect medication in-take) were recorded. Also, blood pressure, fasting blood glucose level, and Low-Density Lipoprotein cholesterol (LDL-C) levels were documented. Where diabetes was indicated by (fasting blood glucose levels of 126 mg/dL or higher), hypertension was indicated by (blood pressure readings of 140/90 mmHg or higher or the use of antihypertensive medication), hyperlipidemia was indicated by (total cholesterol levels of 200 mg/dL or higher or use of lipid-lowering medication). The follow-up included meas-urement of blood pressure two times per week, fasting blood glu-cose (FBG) level one time per month, and testing the (LDL-C) at the cardiologist's request. Figure 2 offers a clear explanation of the clinical data we conducted and their mechanism. The measuring of fasting blood glucose level and Low-Density Lipoprotein cholesterol were performed using a fully automated chemistry analysis instrument by Roche company (Basel, Switzerland) (Cobas Integra - 400 plus). Blood glucose levels were measured using kits (REF 04404483-190 and System ID 07-6831-6). Low-Density Lipo-protein cholesterol were analyzed using kits (REF 03039773-190 and System ID 07-6726-3). The drugs used in hypertension, diabe-tes, and dyslipidemia were monitored for efficacy and side ef-fects.

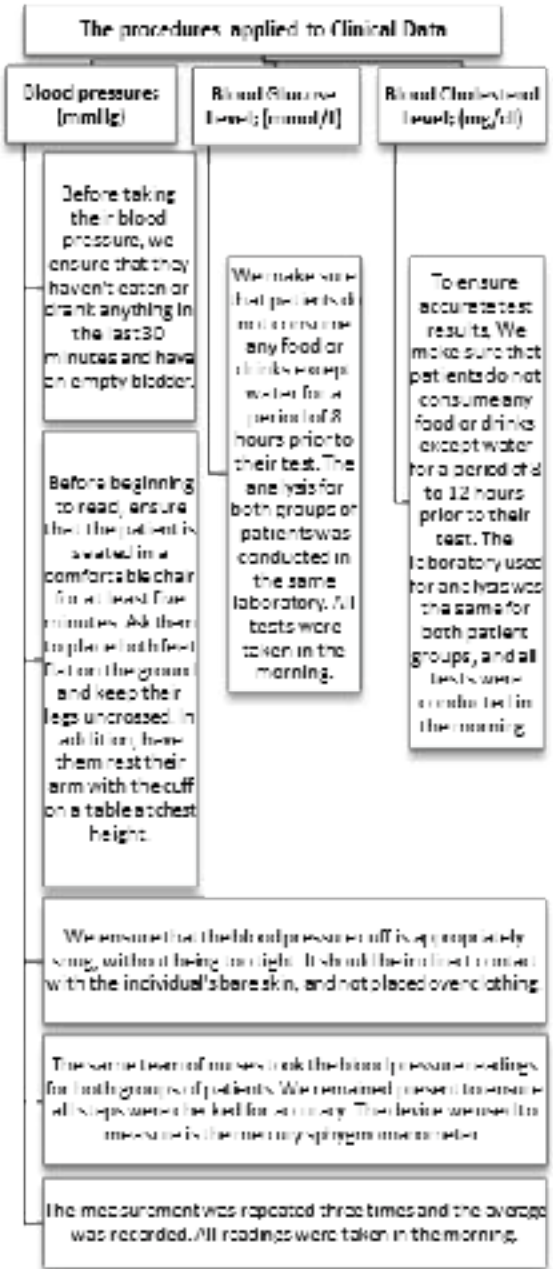

Figure 2. The procedures applied to Clinical Data

Table 2. The intervention points utilized to manage the Group (II) (test group):

Points of intervention for Group (II)
In General: ▪ We applied specialized knowledge in the scientific and clinical application of medications, taking into account medication action, dosing, adverse effects, and drug interactions, and worked collaboratively with other members of the healthcare team to provide optimal patient care. ▪ We were work to identify any untreated health issues that can be treated or resolved with proper medication therapy by using medications rationally. ▪ We were assessing the patient's response to treatment, with a focus on both safety and effectiveness.
Physicians and other health care providers: ▪ When choosing medication therapy for a patient, we consulted with their physicians and other healthcare providers to ensure that the therapy selected is the best fit for the patient's needs and contributes to the overall therapy goals.
Educate the patients: ▪ We educated patients on their health by giving them knowledge about the action of the drugs,and monitor their therapy to manage their conditions effectively and achieve better outcomes. ▪ Provide guidance to the patient regarding the optimal way to take their prescribed medications. ▪ We assisted the healthcare team in educating the patient on crucial measures that can help improve or maintain health. These measures include exercise and a healthy diet.
Drug-drug interactions: ▪ We assisted in identifying possible interactions among different medications. and considered alternative therapies. ▪ We inquired about a patient's use of over-the-counter (OTC) medications or natural products and promptly report any unexpected adverse events.
Side effect of medications: ▪ We were monitored the patient's progress to assess the impact of their medication on their overall health. ▪ We make sure that patients are informed about the potential side effects and the appropriate steps to take if they experience them.
The dosing: ▪ Collaborate with doctors, healthcare experts, and patients to guarantee that the dose of medications prescribed contributes to optimal health outcomes.
* All Interventions are done after acceptance of the physician. * ACC\AHA guidelines were followed. * Open Access Resource: (Medscape and WebMD),[30,31] (These are online and mobile resource that provides information on health and medications. It includes a Drug Interaction Checker tool that can identify any potential interactions between two or more prescriptions.). Drugs.com,[32] (Online and mobile resource that provides drug monographs, a drug identifier, has the Drug Interactions Checker for More in-depth interaction information and classifies the interaction severity as major, moderate, or minor.

Monitoring the drugs of CAD was applied by studying the pharmacodynamic properties. In addition to the therapeutic indi-cations, adverse effects, suitable doses, drug-drug interactions, and drug contraindications were reviewed by the clinical pharma-cist. During the study period, the most significant drug or drug groups utilized by the patients under investigation in the hospital were aspirin, beta-blockers, ACE inhibitors, and streptokinase. Ex-cluding the instances in which contraindications were present. Follow-up of patients included monitoring the risk factors in all phases of disease (CAD) in all groups with advising the patients to lose weight, decrease smoking, and take medication on time. By follow-up up with patients, increasing their awareness about the disease and the treatment plan, advising them to change their lifestyle, and the need for continuous communication with spe-cialists. The lifestyle of the majority of patients was either (a sed-entary lifestyle) in which they did daily activities only, or (low ac-tivity lifestyle) in which daily activities equal walking for a half hour per day. We counseled patients who had high BMI, especial-ly outpatients by a healthy diet. In light of this, It has been ad-vised to patients to restrict their intake of salt and animal-derived products; and increase their intake of vegetables, wholegrain, fruits, fish and olive oil, and nuts; We also asked the patients re-garding exercise to do regular exercise for 30 min (5 days per week); Moreover, was clarified that there exists a crucial need to curtail calorie consumption to lower Body Mass Index (BMI) to 20-25 kg/m², in conjunction with a waist circumference of less than (94 cm) in men and (80 cm) in women.

The outcome that we measured was the effect of applying clinical pharmacy guidelines on morbidity and mortality suffering coronary artery disease. Response to treatment, angina pectoris, the occurrence of complications such as (myocardial infarction, arrhythmia, Heart failure, and cardiogenic shock), and mortality rate were assessed for both groups with their causes. It is worth noting that the total number of deaths assessd was nine pa-tients. The data of all patients were collected by the system adopted at the Medical Center Hospital. Regarding the applica-tion of clinical pharmacy guidelines, a set plan with a cardiologist was conducted by the clinical pharmacist. The baseline features of the study were collected in a specialized Excel database.

Statistical Analysis

The collected data were entered, and examined using the (Statistical package for social science version 22). Descriptive sta-tistics was done for categorical variables by frequency and per-centage and for numerical variables in the form of [mean ± SD (standard deviation)]. Suitable statistical tests of significance were used, Independent Sample t-test for two unrelated samples. For categorical variables, the Chi-square ($\chi 2$) test was used, Fisher's exact test was used when more than 20% of cells have expected frequencies <5. Were considered all P-values that equal to or less than 0.05 (statistically significant). Used simple graphs to illustrate some information.

The study population of one hundred patients included two groups, namely (the control group and the test group). Was classified each group into three subgroups based on the place of registration (or admission) of the participants and severity of condition. Each cohort consisted of 50 patients: Gp Ia\Gp IIa: Patients who received in the Clinic of the Medical Center. "re-ferred to as Outpatients, were diagnosed with Stable Angina" (n=10). Gp Ib\Gp IIb: Patients in the cardiovascular unit (Inpa-tients). "were admitted with Unstable angina and received inpa-tient care" (n=25). Gp Ic\Gp IIc: Patients who were in the cardio care unit (CCU patients) "were admitted with Myocardial infarc-tion" (n=15).

RESULTS

Demographic data

The baseline characters of the examined population and the studied cases were matched - regarding age, sex, and recruitment site with no statistically significant differences between - both studied groups. The average patient's age in the group (I) was 57.74 vs. 56.74 in the group (II). Males were predominant in both groups, where 60% of studied cases in the group (I) were males, and 64% in the group (II) were males. Patient recruitment sites were distributed – between the outpatient department, inpa-tient, and CCU.

Table (3) demonstrate the baseline characters of the stud-ied population; the studied cases were matched - regarding age, sex, and recruitment site with no statistically significant differ-ences between - both studied groups. The average patient's age in the group (I) was 57.74 (SD 7.4) vs. 56.74 (SD 8.4) in the group (II). The standard deviation (SD) for patient's age in the group (I) was (7.4) vs. (8.4) in the group (II). Males were predominant in both groups, where 60% of studied cases in the group (I) were males, and 64% in the group (II) were males. Patient Recruitment Sites were distributed - between the outpatient department, inpa-tient, and CCU.

Regarding Clinical Data of the Studied Population - as demonstrated in the Table (4), there were no statistically significant differences in blood pressure measures (systolic and diastolic), blood glucose level, and blood cholesterol level;

Table 3. Baseline Characters of the Studied Population; (%):

		Studied Groups		Total	p-value
		Group (I) n= 50	Group (II) n= 50		
Sex	**Male**	**30**	32	62	0.418[a]
	%	60	64	62	-
	Female	20	18	38	-
	%	40	36	38	-
Age	**Mean (± SD)**	57.7	56.7	57.2	0.533[b]
	SD	7.4	8.4	7.9	-
	Minimum	42	41	41	-
	Maximum	75	74	75	-

[a] p-value was considered significant at ≤0.05 by Chi-Square χ^2 test.
[b] p-value was considered significant at ≤0.05 by Independent sample-t test.

Table 4. Clinical Data of the Studied Population; (%):

-		Studied Groups		Total	p-value
		Group (I) n= 50	Group (II) n= 50		
SBP; (mmHg)	**Mean**	144.9	147.6	147.6	0.553
	SD	11.9	13.9	10.9	-
	Minimum	120	115	115	-
	Maximum	165	165	165	-
DBP; (mmHg)	**Mean**	91.9	92.9	91.9	0.300
	SD	9.2	7.5	7.5	-
	Minimum	70	75	75	-
	Maximum	115	105	115	-
Blood Glucose Level; (mmol/L)	**Mean**	244.2	264.0	257.0	0.100
	SD	62.4	60.5	61.5	-
	Minimum	104	103	103	-
	Maximum	369	388	368	-
Blood Cholesterol Level; (mg/dl)	**Mean**	271.3	282.6	277.6	0.257
	SD	52.2	46.9	48.9	-
	Minimum	152	158	152	-
	Maximum	398	391	398	-

*p-value was considered significant at ≤0.05 by Independent sample-t test.

p-value >0.05. Also, the results showed the standard deviation for [SBP/DBP(mmHg)] in group (I) was (11.9/9.2) vs. (13,9/7.5) in group (II). while SD for their [Blood Glucose Level; (mmol/L)] in the group (I) was (62.4) vs. (60.5) in the group (II). And SD of [Blood Cholesterol Level; (mg/dl)] in the group (I) was (52.2) vs. (46,9) in group (II).

Parameters

Angina

Angina pectoris was more-predominant in patients from the group (I), where 56% of cases had angina pectoris in the group (I) vs. 30% in the group (II), with a statistically significant difference (p-value= 0.007).

Table (5) demonstrate the distribution of the studied cases according to the incidence of angina. Angina was more prevalent among the group (I) that underwent treatment in the (Medical Center Hospital) without applying guidelines (28 cases vs. 15, p=0.007).

Table 5. The incidence of Angina in studied groups; (%):

-		Studied Groups		Total (N= 100)	p-value*
		Group (I) n= 50	Group (II) n= 50		
Angina	**No**	**22**	35	57	**0.007***
	%	44	70	57	-
	Yes	28	15	43	-
	%	56	30	43	-

*p-value was considered significant at ≤0.05 by Chi-Square χ^2 test.

Responsiveness to medications

Responsiveness to medications was significantly higher among patients from the group (II), where 86% of cases had posi-tive responsiveness to drugs in the group (II) vs. 56% in the group (I), with a statistically significant difference (44% vs. 14%, p=0.003), as shown in Table (6).

Table 6. Distribution of Studied Population by Responsiveness to medications; (%):

-		Studied groups		Total	p-value*
		Group(I) n= 50	Group (II) n= 50		
Responsiveness to medications	No	**22**	7	29	**0.003***
	%	44	14	29	-
	Yes	28	43	71	-
	%	56	86	71	-
Total		50	50	100	-
%		100	100	100	-

p-value was considered significant at ≤0.05 by Chi-Square χ2 test.

Patients recruited from the outpatient departments showed no statistically significant difference - regarding respon-siveness to medications between both studied groups; p-value >0.05. However, patients recruited from the inpatient depart-ment and CCU who was in the group (II) applied to the clinical pharmacy guidelines - and showed higher positive responsiveness to medications compared with patients in group (I), as shown in Table (7).

Complications

Incidence of Complications

As demonstrated in the Table (8) and Figure (3) - the occur-rence of complications was significantly higher among patients in group (I) as compared with group (II). Incidence of complications was significantly higher among the group (I) as compared with group (II) (40% vs. 14%, p=0.006).

Table (8) demonstrates the distribution of the studied cases according to the incidence of complications. Complications were more-prevalent among the group (I), which underwent treatment in the (Medical Center Hospital) without applying guidelines.

Studied cases from both (inpatient and CCU departments) showed a higher incidence of complications among the CCU de-partment (40%) in the control group compared with (6.7%) among the clinical pharmacy guidelines group. While inpatient department (40%) among the control group, compared with (16%) among the clinical pharmacy guidelines group. On the other hand, studied cases from the outpatient department showed no statistically significant difference in the occurrence of complications between group (I) and group (II).

Table (9) demonstrate the distribution of the studied cases according to the incidence of complications. Complications showed a non-statistically significant difference between the pa-tients according to the site of recruitment outpatient, inpatient, and CCU, with and without guidelines of clinical pharmacy.

Type of Complications

Table (10) demonstrate comparisons between (the studied groups) according to the type of complications. There was a non-statistically significant difference between both studied groups regarding the types of (complications) except for Myocardial In-farction which was significantly more prevalent among the group (I).

Table (11) demonstrate comparisons of complication types between (the studied patients) according to their groups and site of recruitment. There was a non-statistically significant difference between (both studied groups) - regarding the types of (complica-tions), except Myocardial Infarction, which was significantly more-prevalent among the group (I), patients recruited from CCU (6 pa-tients). And the too cardiogenic shock was significantly more-prevalent among the group (I) patients recruited from CCU (2 pa-tients).

Death

Mortality rate

Table (12) and Figure (4) demonstrate that the mortality rate was significantly higher among the group (I) (8 patients vs. one patient, p=0.015).

Table 7. Distribution of Studied Population (according to their site of recruitment) by Responsiveness to medications; (%):

-		Studied Groups						Total	p-value
		Out_Gp (I)	Out_ Gp(II)	In_ Gp (I)	In_ Gp (II)	CCU_Gp (I)	CCU_Gp (II)		
Responsiveness to medications	No	**4**	2	12	4	6	1	29	**0.036***
	%	40	20	48	16	40	6.7	29	-
	Yes	6	8	13	21	9	14	71	-
	%	60	80	52	84	60	93.3	71	-
	Total	10	10	25	25	15	15	100	-
	%	100	100	100	100	100	100	100	-

*p-value was considered significant at ≤0.05 by Fissure Exact test.
Out_Gp (I): Outpatients Group I, Out_Gp (II): Outpatients Group II, In_Gp (I): Inpatients Group I, In_Gp (II): Inpatients Group II, CCU_Gp (I): CCU patients Group I, CCU_Gp (II): CCU patients Group II.

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Table 8. Distribution of Studied Population by Occurrence of Complications; (%):

-		Studied Groups		Total	p-value*
		Gp (I) n= 50	Gp (II) n= 50		
Complications	**No**	30	43	73	**0.006***
	%	60	86	73	-
	Yes	20	7	27	-
	%	40	14	27	-
Total		50	50	100	-
%		100	100	100	-

p-value was considered significant at ≤0.05 by Chi-Square χ2 test.

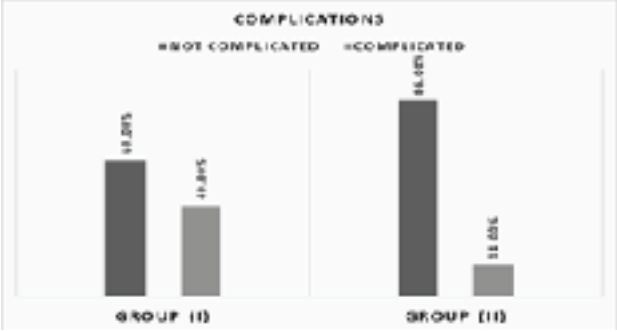

Figure 3. Distribution of Studied Population by Occurrence of Complications

Table 9. Distribution of Studied Population (according to their site of recruitment) by incidence of Complications; (%):

-		Studied Groups						Total	p-value
		Out_ Gp (I)	Out_ Gp(II)	In_ Gp (I)	In_ Gp (II)	CCU_ Gp (I)	CCU_ Gp (II)		
Complications	**No**	6	8	15	21	9	14	73	0.078
	%	60	80	60	84	60	93.3	73	-
	Yes	4	2	10	4	6	1	27	-
	%	40	20	40	16	40	6.7	27	-
	Total	10	10	25	25	15	15	100	-
	%	100	100	100	100	100	100	100	-

*p-value was considered significant at ≤0.05 by Fissure Exact test.
Out_Gp (I): Outpatients Group I, Out_Gp (II): Outpatients Group II, In_Gp (I): Inpatients Group I, In_Gp (II): Inpatients Group II, CCU_Gp (I): CCU patients Group I, CCU_Gp (II): CCU patients Group II.

Table 10. Distribution of Studied Population by type of Complications; (%):

	Groups		Total	p-value*
	Group (I) n= 50	**Group (II) n= 50**		
Arrhythmia	10	5	15	0.131
%	20	10	15	-
Myocardial Infarction	15	4	19	**0.005***
%	30	8	19	-
Heart Failure	8	4	12	0.178
%	16	8	12	-
Diabetic Ketoacidosis	3	1	4	0.309
%	6	2	4	-
HTN Crisis	4	1	5	0.181
%	8	2	5	-
Cardiogenic Shock	2	0	2	0.247
%	4	0	2	-

*p-value was considered significant at ≤0.05 by Fissure Exact test.
The same patients may had more than one complication.

Table 11. Distribution of Studied Population (according to their site of recruitment) by type of Complications; (%):

Type of complications	Groups						Total	p-value*
	Out_ Gp (I)	**Out_ Gp (II)**	**In_ Gp (I)**	**In_ Gp (II)**	**CCU_ Gp (I)**	**CCU_ Gp (II)**		
Arrhythmia	**3**	1	3	3	4	1	15	0.524
%	27.3	11.1	12	12	26.7	6.7	15	-
Myocardial Infarction	1	1	8	2	6	1	19	**0.041***
%	9.1	11.1	32	8	40	6.7	19	-
Heart Failure	1	1	4	2	3	1	12	0.826
%	9.1	11.1	16	8	20	6.7	12	-
Diabetic Ketoacidosis	0	0	2	1	1	0	4	0.734
%	0	0	8	4	6.7	0	4	-
HTN Crisis	0	0	2	1	2	0	5	0.472
%	0	0	8	4	13.3	0	5	-
Cardiogenic Shock	0	0	0	0	2	0	2	**0.041***
%	0	0	0	0	13.3	0	2	-

*p-value was considered significant at ≤0.05 by Fissure Exact test.
Out_Gp (I): Outpatients Group I, Out_Gp (II): Outpatients Group II, In_Gp (I): Inpatients Group I, In_Gp (II): Inpatients Group II, CCU_Gp (I): CCU patients Group I, CCU_Gp (II): CCU patients Group II.

Table 12. Mortality rate in the two main study groups according to guidelines of clinical pharmacy; (%):

-	Studied Groups		Total	p-value*
Mortality rate	**Group (I)**	**Group (II)**		
Survived	**42**	49	91	**0.015***
%	84	98	91	-
Died	8	1	9	-
%	16	2	9	-
Total	50	50	100	-
%	100	100	100	-

*p-value was considered significant at ≤0.05 by Fissure Exact test.

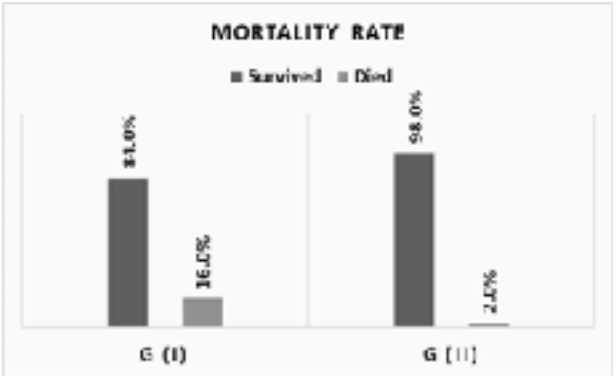

Figure 4. Mortality rate in the two main study groups according to guidelines of clinical pharmacy

As demonstrated in the Table (12), mortality was signifi-cantly higher among patients in group (I) as compared with the group (II). Table (13) demonstrate that mortality was significantly highest among CCU_Gp (I) patients (without guidelines of clinical pharmacy). Studied cases from (the CCU department) showed higher Mortality (40%) in the control group compared with the other group where the clinical pharmacy guidelines were ap-plied (6.7%). However, studied cases from outpatient and inpa-tient departments showed no statistically significant difference in Mortality between group (I) and group (II).

Cause of Death

Table (14) demonstrates a comparison between the stud-ied groups according to the cause of death.

Table (15) demonstrates a comparison of causes of death between the studied patients according to (their groups and site of recruitment). The cardiogenic shock occurred in two patients; all were CCU_Gp (I) patients without guidelines of clinical phar-macy.

Table 13. Mortality rate among Studied Population (according to their site of recruitment); (%):

-	Studied Groups						Total	p-value*
	Out_ Gp (I)	**Out_ Gp (II)**	**In_ Gp (I)**	**In_ Gp (II)**	**CCU_ Gp (I)**	**CCU_ Gp (II)**		
Survived	**10**	10	23	25	9	14	91	**<0.001***
%	100	100	92	100	60	93.3	91	-
Died	0	0	2	0	6	1	9	-
%	0	0	8	0	40	6.7	9	-
Total	10	10	25	25	15	15	100	-
%	100	100	100	100	100	100	100	-

*p-value was considered significant at ≤0.05 by Fissure Exact test.

Out_Gp (I): Outpatients Group I, Out_Gp (II): Outpatients Group II, In_Gp (I): Inpatients Group I, In_Gp (II): Inpatients Group II, CCU_Gp (I): CCU patients Group I, CCU_Gp (II): CCU patients Group II.

DISCUSSION

Making an effective healthcare team and competently em-ploying medication needs clinical pharmacists as an essential part. Their cooperation with physicians can minimize therapy-related problems (TRPs).[33,34] The frequent medication errors are severe and predictable in critical care. The progress of the medication process is the safest and most efficient means of improving pa-tient safety in cardiovascular care. Patient safety is an essential health care issue[35], and Chen B et al.[36] reported - that patient safety by designing therapeutic regimens, preventing medication errors, and decreasing the incidence of adverse drug reactions are the essential role that clinical pharmacists play. Active coopera-tion of clinical pharmacists with physicians to control cardiovascu-lar disease patients is crucial, and satisfactory management of car-diovascular (CV) risks and lower health costs need them.[28] To our knowledge, this is the first study that was conducted in Libya to analyze, understand, and evaluate the potential efficacy of clinical pharmacy services for CVD patients.

The current study reveals that there was no statistically sig-nificant differences in systolic blood pressure measures or diastol-ic blood pressure, blood glucose levels or cholesterol levels be-tween the 2 groups;(P-value=0.553, P-value=0.300,

Table 14. Causes of death in the two main study groups according to guidelines of clinical pharmacy; (N= 9).

Cause of death	Studied Groups		Total	p-value*
	Gp (I) n= 50	**Gp (II) n= 50**		
Acute Myocardial Infarction	**4**	0	4	**0.050***
%	8	0	4	-
Cardiogenic Shock	2	0	2	0.247
%	4	0	2	-
Ventricular Tachycardia	2	1	3	0.500
%	4	2	3	-

*p-value was considered significant at ≤0.05 by Fissure Exact test.

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Table 15. Causes of death among Studied Population (according to their site of recruitment); (n= 9)

Cause of death	Groups						Total	p-value
	Out_ Gp (I)	Out_ Gp (II)	In_ Gp (I)	In_ Gp (II)	CCU_ Gp (I)	CCU_ Gp (II)		
Myocardial Infarction	**0**	0	2	0	2	0	4	0.225
%	0	0	8	0	13.3	0	4	-
Cardiogenic Shock	0	0	0	0	2	0	2	**0.041***
%	0	0	0	0	13.3	0	2	-
Ventricular Tachycardia	0	0	0	0	2	1	3	0.137
%	0	0	0	0	13.3	6.7	3	-

*p-value was considered significant at ≤0.05 by Fissure Exact test.
Out_Gp (I): Outpatients Group I, Out_Gp (II): Outpatients Group II, In_Gp (I): Inpatients Group I, In_Gp (II): Inpatients Group II, CCU_Gp (I): CCU patients Group I, CCU_Gp (II): CCU patients Group II.

P-value=0.100, P-value=0.257) as indicated in Table (4). As shown in Table (5), angina pectoris was more predominant in patients from the group (I); where 56% of cases had angina pectoris in the group (I) vs. 30% in the group (II), with a statistically significant differ-ence (p-value = 0.007). In accordance with our results, O.Dell and Kucukarslan[37] reported that re-admission (in the subset of pa-tients with unstable angina) showed a notable reduction due to the role of clinical pharmacists.

Also, the results showed a statistically significant difference between the inpatients in the groups (I & II) concerning the re-sponsiveness to medication (p-value = 0.003), As shown in Tables (6,7). Similarly, Chen B, Huang, Chen HF, and Xu BM[36] reported that clinical pharmacists add helpful addition through improved pharmacotherapy and a significant reduction in adverse drug events. Notably, team-based care, including the intervention of clinical pharmacists, increases quality by improving the use of medicines, as reported by Al-Somai et al.[38] Also, pharmaceutical reconciliation and patient counseling has a vital role. Clinical pharmacists' time with patients enhanced drug use, as revealed by reducing drug-drug interaction problems, which augmented drug effectiveness. The clinical pharmacist guidance achieved more useful therapeutic outcomes with positive impacts on pa-tient teaching and adherence to advice.[39]

Moreover, Tables (8,9) and figure (3) revealed the occur-rence of higher complications for the studied cases from both in-patient and CCU departments subgroups in group I (control group) compared with the group II (intervention group), which applied the clinical pharmacy guidelines to them. On the same hand, Shareef, Sandeep B, Shastry CS[40] and O'Dell, Kucukarslan[37] reported that the documented role of clinical pharmacists is to improve the overall quality of life by lowering the incidences of TRPs and im-proving patient functional capacity and compliance with treat-ment. Also, a study by Leape et al[41] revealed the influence of clin-ical pharmacists on avoidance of adverse drug events or lowering them. In accordance with results of the current study, Talasaz[42] revealed the capability of reducing TRPs and associated adverse outcomes by actualizing the service of clinical pharmacists. Also, Altowaijri, and Phillips[43] explained that non-compliance and the added discomfort from therapy issues resulted in avoidable re-admission to the hospital and higher costs. These results support the concept of noting a positive effect of clinical pharmacists on decreasing drug problems and achieving treatment goals.[44] Also, Carey et al[45] reported that clinical pharmacist experience and training are necessary to provide medication education and reso-lution of TRPs leading to decreasing of adverse events, hospital re-admissions, and the emergency room stays.

As shown in Table (10), myocardial infarction occurred in 15 patients in group I, compared to 4 patients in group II. While, the incidence of cardiogenic shock was 2 patients in group I, com-pared to no patients in group II .Also, there was statistically signif-icant differences (P-value=0.041*), (P-value=0.041*), between all studied subgroups regarding the incidence of myocardial infarc-tion and cardiogenic shock respectively, as shown in shown in Ta-ble (11). However, there was no statistically significant difference between the two studied groups regarding the incidence of ar-rhythmia, heart failure, diabetic ketoacidosis or HTN crisis. On the other hand, it has been revealed that clinical pharmacist has a role in controlling Heart Failure medications.[46] Also, Koshman et al and Yu DS, Thompson, and Lee[47,48] reported that the collabora-tion between cardiac team and clinical pharmacists resulted in reducing hospitalization risks for heart failure patients. Moreover, this professional cooperation in healthcare team is also associated with managing any progression in ACS patients and decreasing HF rates, MI, and death.[49] In contrast to our results regarding the HT crisis, Pei-Xi et al[50] reported that pharmacist interventions effec-tively improve antihypertensive medication adherence and re-duce systolic and diastolic blood pressure. Antihypertensive drugs significantly improve through the intervention of clinical pharma-cists through various measures, such as education, supervision, follow-up, and other things. In addition, Schnipper, Kirwin, and Cotungo[51] attributed the decrease in adverse drug effects a month during homecare to the pharmacist's role in reviewing medicines, cases counseling, and follow-up them by phone. For diabetic ketoacidosis, although the statistical difference was non-significant, the incidence of diabetic ketoacidosis in group II was less than in group I. Also, a decrease in error rates of drug use has been reported in group II .In contrast, Warrigton et al. and Pres-laski, Lat, MacLaren R, and Poston.[52,53] reported that

monitoring of diabetic ketoacidosis by clinical pharmacy was conducted through appropriate insulin doses and monitoring blood glucose and fluid quantities, particularly with HF patients. An improved safety in the ICU setting and increased care quality in DM treat-ment and decreased associated complications were attributed to the role of clinical pharmacist. These discrepancies in results are attributed to the small sample size on the current study.

As demonstrated in the Table (12) and Figure (4) - Mortality rate was significantly more elevated among patients of group (I) as compared with group (II) (P-value=0.015). The studied cases from the CCU department showed a higher mortality rate (40%) in group I versus (6.7%) in group II, where clinical pharmacy guide-lines were applied. More interestingly, there was a highly statisti-cally significant difference between the studied subgroups in the two groups regarding the mortality rate in accordance with the site of their recruitment (P-value<0.001*) as indicated in Table 13.However, studied cases from outpatient and inpatient de-partments showed no statistically significant difference in mortali-ty rates between group (I) and group (II). Similarly, Richard et al.[33] documented that changes between the presence and absence of clinical pharmacists in the critical care unit did not reach statisti-cal significance On the other side, a retrospective analysis by Peterson et al.[54] revealed that hospitals with the most significant adherence to the guidelines had mortalities of 4.32% (P=0.001) compared to 7.68% in the hospitals that displayed the slightest commitment to the clinical pharmacy guidelines. Also, Chung , Lee KK, Tomlinson B, and Lee VW.[34] reported that the clinical pharmacy guidelines applications minimized the morbidity and mortality rates. The discrepancy in the results may be attributed to the lack of the possibility of distinguishing the attribution of the increased volume of interventions , to the introduction of a clinical pharmacist with increased time devoted to the CCU, or to the increased critical care knowledge of specialists and experi-ence of the individual.

Concerning acute myocardial infarction as cause of death, there was a statistically significant difference between groups I & II (P-value=0.05) as shown in Table 14. This result is attributed to the fact that clinical pharmacist has a significant role in terms of drug control and patient awareness to improve their habits, clari-fying the role of percutaneous coronary intervention (PCI) and the importance of rapid intervention to save their lives, controlling risk factors to prevent recurrent MI. Similarly, Nicole, Gasbarro, and Kristin[55] reported that the benefits of clinical pharmacists for acute myocardial infarction patients have a positive effect on medication review, counseling, follow-up, and a reduction in the thirty-day AMI re-admission rate. Also, they demonstrate that pa-tients who experience an acute myocardial infarction need signif-icant patient education regarding new medications, lifestyle mod-ifications, and health progress. Similarly, Xiao-Bo et al[56] demon-strated that clinical pharmacists' services are considerably associ-ated with decreased mortality in both [(STEMI) and (NSTEMI) pa-tients.

Regarding the cardiogenic shock as cause of death, the results revealed the presence of statistical significant differences between groups I & II (P-value=0.041*) as indicated in Table 15. Our explanation for these statistically significant differences is that application guidelines of the clinical pharmacy led to improved care for the patients and lower their mortality rate. Simi-larly, it has been reported that clinical pharmacy services are as-sociated with decreased hospital mortality rates.[57]

Study Limitations

The limitations of the current study include the smaller sample size and smaller duration of follow up. Also, monitoring was conducted for drugs only covered by the medical insurance. Future work: The current study should be conducted in future on larger scale and as multicenter study in different countries.

CONCLUSION

The clinical pharmacist's role positively affects the quality of healthcare of patients in cardiovascular unit and coronary care unit in Libya through decreasing the mortality rate. Thus, the clinical pharmacist approach is an essential part of health care in CVU and CCU and the application of clinical pharmacy services should be implemented to enhance the healthcare.

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