Drug Related Problems and Contributing Factors Among Adult Ambulatory Patients with Cardiovascular Diseases at Gebretsadik Shawo General Hospital, Bonga, South west Ethiopia

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Abstract
The identification of drug related problems is the focus of the assessment and the last decision made in that step of the patient care process. Although drug therapy problem identification is technically part of the assessment process, it represents the truly unique contribution made by pharmaceutical care practitioners. It is also a common scenario in chronic non communicable diseases, like cardiovascular diseases. The objective of the research was to determine the prevalence of drug therapy problems among adult ambulatory patients with cardiovascular diseases in Gebretsadik Shawo General Hospital (GSGH). Hospital based prospective cross sectional study design was employed. 130 adult patients with cardiovascular disease who fulfilled the inclusion criteria were included. The principal investigator was involved in collecting the data. The data was analyzed manually using scientific calculator. A total of 163 DRPs were identified with the mean number of 1.5 ± 0.8. While the DRP per patient was 1.08 ± 0.75. Most of the patients (108, 72%) had drug related problem, of which drug indication related problems constituted the highest part 64(39.26%). Followed by non compliance to drugs 46(28.22 %), drug safety (32, 19.63%) and drug effectiveness (21, 12.89%) related issues.
Key words: Drug related problems, ambulatory, cardiovascular diseases, Ethiopia

Acronyms and abbreviations
ADR-----------------------Adverse Drug Reaction
CCB-----------------------Calcium Channel Blockers
DRP-----------------------Drug Related Problems
FHRH----------------------Felege Hiwot Referral Hospital
FMHACA-----------------Food Medicine and Health care Administration and Control Authority
GSGH----------------------Gebretsadik Shawo General Hospital
JUSH-----------------------Jimma University Specialized Hospital
MOH----------------------Ministry Of Health
NSAIDs---------------------Non Steroidal Anti-Inflammatory Drugs

Introduction
The increasing number of available drugs and drug users as well as more complex drug regimens led to more side effects and adverse drug reactions and complicates follow-up. The availability of large number of medicines and the constant efflux of new information make them practically impossible for any health care professional to be updated in all aspects.

Helper and strand define pharmaceutical care as, 'the responsible provision of drug therapy for the purpose of achieving definite outcomes which improve the patient's quality of life' (Hepler C. et al, 1990). Hepler used the terms like drug-related problem, drug treatment failure, and pharmacotherapeutic problem in one article to describe DRPs

According to Pharmaceutical Care Network Europe (PCNE) classification volume 6.2, a drug related problem is 'an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes (Zuidlaren , 2010).

According to Robert J. Cipolle text book of pharmaceutical care practice (3rd edition), DRPs are classified into seven classes, including: Need additional drug therapy, unnecessary drug therapy, ineffective drug, too low or too high dosage, adverse drug reactions, and noncompliance (Cipolle R. 2nd ed.).

Drug related problems are relatively common in hospitalized patients and can result in patient morbidity and mortality, and increased costs besides their alarming rise among patients who are on chronic care follow up (Gaziano T., 2009).

Cardiovascular diseases are a group of disorders of the heart and blood vessels. Most of patients with cardiovascular disease can be treated and managed by proper follow and check up in an outpatient department, though these CVDs accounts for 7-10% of all adult medical admissions in African hospitals (Van den bemt P. et

al ,2000).

Numbers of patients who are on follow up have a diverse drug related needs and problems which require intervention to reduce development of complications at home and thereby improve quality of life of patients with CVD. (Braun L. et al, 2012).

Drug related problems are of a major concern in health care because of increased cost, morbidity and mortality. The cost of drug related morbidity and mortality exceeded $177.4 billion in 2000 of total costs, followed by long-term-care admissions, which accounted for 18% ($32.8 billion) (Andreaza R. et al, 2011).

DRP is associated with prolonged length of stay, increased economic burden, and an almost 2-fold increased risk of death. Drug related problems are major reasons for admission ranging from the emergency ward up to the intensive care unit, despite their preventability. (Stafford A. et al, 2009).

The study tried to find out drug related problems among patients with cardiovascular diseases. Furthermore there are no studies conducted in the area. Therefore, the study findings will help in devising strategies to optimize proper drug use.

Moreover the finding of this study will be important source of information which might support the decision makers of the institution as well as other stake holders to design appropriate programs to deal with the problem. It will also lay background to researchers to conduct further research on the issue.

Objectives
General objective:
❖ To determine drug therapy problems among adult patients with cardiovascular diseases attending a chronic care unit at GSGH.

Specific objectives
❖ To determine the prevalence of DRPs
❖ To identify the common types of DRPs encountered
❖ To identify drugs involved in DRPs

Methods and materials
Study area and period
The study was carried out among adult ambulatory patients with CVD in GSGH. GSGH is one of the general Hospitals in southern Ethiopia. It is found in Bonga town which is located 444km south west of Addis Ababa, the capital city of Ethiopia. The hospital has various units including the inpatient ward with a total of 120 beds. It has 52 technical and 103 administrative staffs. The hospital serves the people of Bonga town, the administrative town of Kafa zone, and 10 woredas under its administration as a general hospital. The study was conducted from March 28 to April 12 2015 GC.

Study design
A hospital based prospective cross sectional study design was employed.

Source population
All ambulatory patients with CVD in the chronic care unit.

Study population
All adult patients with CVD on follow up in chronic care unit

Inclusion criteria
✓ Patients following chronic care unit for cardiovascular diseases.

Exclusion criteria
✓ Those not willing to participate

Sample Size and Sampling Technique
Based on a study conducted in Felege Hiwot referral hospital regarding the prevalence of DTP in 2014, the prevalence rate of DTP among CVD patients was found to be 90%.so we can take the 90% as a previous prevalence rate.

$$n= \frac{Z^2 pq}{d^2}$$

n= the minimum sample size
Z=reliability coefficient for desired interval (CI) for 95% = 1.96
p = proportion of self-medication = 90% (0.9)
q= 1-p = 0.1
d= desired interval (degree of precision) = 5% (0.05)

Then n= $\dfrac{(1.96)^2 0.9(1-0.9)}{(0.05)^2}$ = 138

Since the study population is less than 10,000 correction formula was used to get the final sample size (n*f*).

N*f*=n/*1*+n/*N =138/1+138/900=120*

Where

n*f*= final sample size, N=total study population

10% non response was added, so sample size will be 132. Therefore sample size of 132 was considered.

Convenience sampling was employed to interview the patients.

Data collection tools and procedure

Data collection was undertaken during the study period. The data was collected through medical record reviews of patients using a prepared standard checklist and structured questionnaire. DTPs were identified by evaluating patient card by the use of checklist and the appropriateness of prescriptions in terms of indication, dosage, safety and efficacy.

Issues related with adherence were assessed by the questionnaire. The existence of DRP was identified using Ethiopian treatment guideline (2014 version) and guideline of American heart association (AHA)(2013 version).

Variables

Independent variables

- Sociodemographic characteristics
- Social drug use
- Traditional medicine use
- Type of CVD
- Presence of co morbidities
- Number of drugs

Dependent variable

- Presence of DTP

Ethical consideration

Formal letter was obtained from the department of Pharmacy and the letter was given to the Hospital (GSGH). Written consent was taken in the form of signature so that patients were willing to give their medical information. Patients were assured that lack of willingness to involve in the study would not affect the service they get from the hospital. Confidentiality of patient data was ensured, thus name and address of the patient was not recorded in the data collection material.

Operational definition

- ➤ **A drug therapy problem**: is when there is an occurrence of one of the problems related to indication, effectiveness, safety and compliance.
- ➤ **Adverse drug reaction**: is any potential, harmful and unintended effect associated with the drug during the medication use process.
- ➤ **Co-morbid condition**: a disease condition other than CVD
- ➤ **Cardiovascular disease:** are disease of the heart and blood vessels
- ➤ **Adherence**: is drug taking behavior of a patient and when a patient says no at least for one of the question, he/she is non-compliant.

Results

Socio-demographic characteristics of patients in GSGH.

Total of 130 patients with CVD were included making a response rate of 98.5%. The study consisted of 68(52.30%) females. The mean age of the patients was 50±15.8 years with the minimum age of 18 and the maximum of 85 years. Around 98(75.3%) patients were Kafa nationals.

Majority of the patients were followers of orthodox Christianity and live in urban areas and have an average monthly income each constituting 78(60%) of the study participants.

Around 101(77.70%) the patients used at least one of the social drugs (coffee, tea, chat, alcohol or cigarette) where coffee was the most consumed social drug (76, 75.25%) (Table-1)

Table 1-sociodemographic characteristics of adult ambulatory patients with CVDs attending the chronic care unit of GSGH, 28th march-12th April, 2015 (n=130)

Variables	Response	Frequency	Percent
1.sex	Male	62	47.7%
	Female	68	52.3%
2.Age in years	18-24	6	4.64%
	25-34	24	18.45%
	35-44	14	10.74%
	45-54	22	16.93%
	55-64	32	24.62%
	≥65	32	24.62%
3.Marital status	Single	24	18.45%
	Married	87	66.91%
	Divorced	6	4.64%
	Widowed	13	10.0%
4.Religion	Orthodox	78	60%
	Muslim	38	29.23%
	Protestant	14	10.77%
5.Residence	Urban	78	60%
	Rural	52	40%
6.Ethnicity	Kaffa	98	75.38%
	Amhara	16	12.30%
	Oromo	10	7.68%
	Others	6	4.64%
7.Education	Illiterate	52	40%
	Elementary	36	27.69%
	High school	24	18.46%
	College and above	18	13.85%
8.Occupation	Farmers	56	43.08%
	Governmental	44	33.85%
	Private	16	12.30%
	Student	9	6.92%
	Others	5	3.85%
9.Monthly income	446-1200	12	9.23%
	1201-2500	28	21.54%
	2501-3500	78	60%
	>3501	12	9.23%
10.Social drug use (n=101)	Coffee	76	75.25%
	Tea	10	9.9%
	Alcohol	8	7.92%
	Chat	5	4.95%
	Cigarette	2	1.98%

Specific types of CVDs and common co-morbid conditions

The most common cardiovascular diseases encountered during the data collection period were hypertension (84, 64.6%) and congestive heart failure (40, 30.77%).Out of 130 patients around 86(66.15%) experienced at least one co morbid conditions during the study period.

The most commonly encountered co-morbid conditions were community acquired pneumonia(32,37.20%),acute febrile illness(21,24.45%),dyspepsia(18,20.95%) and upper respiratory tract infection(15,17.40%) A maximum of two number of co morbidities were observed, while the mean number of co morbidity was 1.4±0.6.

Commonly prescribed medications among patients with CVD in GSGH

A total of 282 numbers of cardiovascular drugs were used to manage these cardiovascular problems among 144 patients. The mean number of drug was 1.9 ±1.08 per patient. A maximum of five numbers of drugs were prescribed. ACEI inhibitors (66, 44%) and Calcium channel blockers (66, 44%) were the most commonly used drugs. Besides around 6(4%) of CHF patients were not given any medication

The most commonly prescribed groups of drugs for management of co-morbid condition were antibiotics(90,48.93%),Gastrointestinal drugs(36,19.35),Non steroidal anti inflammatory

drugs(NSAIDs)(33,17.74%) and Vitamins and Minerals(26,13.98%) .

**Prevalence of DRPs among patients with CVD in GSGH**

A total of 108 patients had one or more DTPs. The prevalence of DTPs in the current study is 72%. There was a total of 163 DTPs identified. The mean number of DTP was 1.5±0.8 per patient. The maximum number of DTPs was three. Most of the patients (56, 51.85%) had two DTPs. (fig 1)

"Fig-1" prevalence of DRPs among adult ambulatory patients with CVDs attending the chronic care unit of GSGH, 28th march-12th April,2015
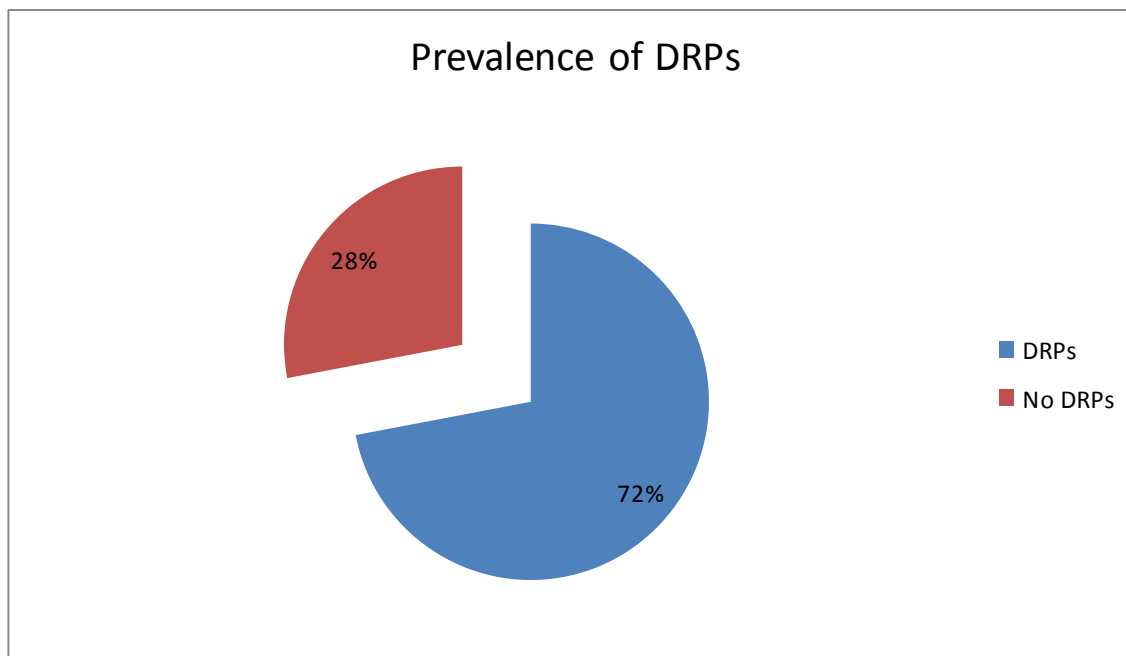
Common types of DRPs among patients with CVD in GSGH

There were 64 (39.26%), 46 (28.22%), 32 (19.63%) and 21 (12.89%) number of DTPs obtained representing indication, compliance, safety and effectiveness related problems respectively. (fig 2)
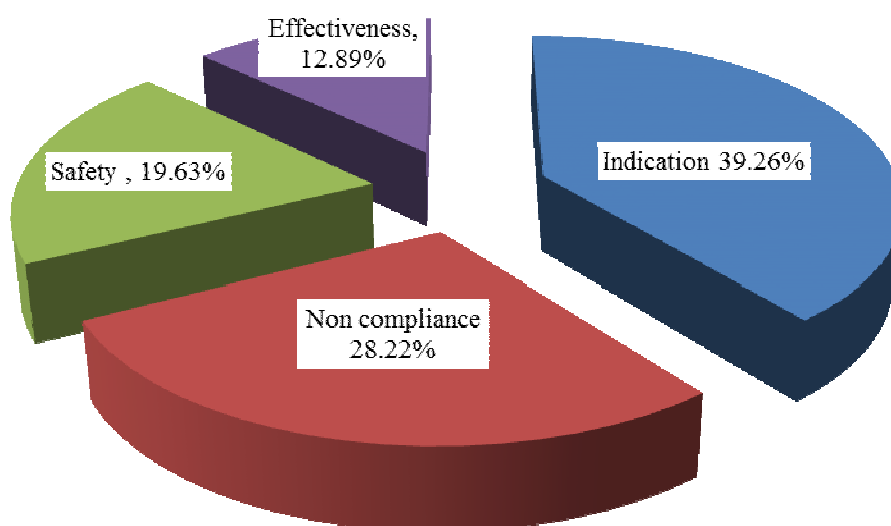
"Fig-2" percentages of DTPs among adult ambulatory patients with CVDs attending the chronic care unit of GSGH,28th march-12th April,2015

Most of the indication problem was need additional drug therapy (54,33.12%). There were 21 (12.89%) numbers of DTPs among effectiveness related problems; where effective drug available (17, 10.42%) and inappropriate frequency (4, 2.45%) were the common DTPs respectively. Around 32 (19.63%) number of DTPs

were obtained regarding safety, where 21 (12.88%) and 8(4.90%) number of patients had contraindications and inappropriate frequency respectively. In an effort to assess the compliance issue, majority (29,17.80%) of patients forgot taking medication at least once in their treatment course.

Majority of the indication problem was need additional drug therapy. Ineffective drug therapy was common among effectiveness related issues followed by contraindication under safety issue and forgetting to take the medication was prominent in compliance related problems(table-2)

Table-2 Specific DTPs identified among adult ambulatory patients with CVDs attending the chronic care unit of GSGH,28th March-12th April,2015(n=108)

DRP involved	Type of DRP	Reasons	Freq/%	Total
Indication	1.Unnecessary drug therapy	a)Multiple drug therapy used	3(1.85)	10(6.14%)
		b)Non drug therapy is more appropriate	7(4.30)	
	2.Needs additional drug therapy	a)Medical condition needs initiation of drug therapy	11(6.74)	54(33.12%)
		b)Preventive therapy required	34(20.85)	
		c)Drug needed for synergistic effect	9(5.52)	
Effectiveness	3.Ineffective drug therapy	a)More effective drug available	17(10.42)	17(10.43%)
	4.Dosage too low	b)Frequency inappropriate	4(2.45)	4(2.45%)
Safety	5.Adverse drug reaction	a)Contraindications exist	21(12.88)	21(12.88%)
	6.Dosage too high	a)Too short dosing frequency	8(4.90)	11(6.75%)
		b)Drug interaction	3(1.84)	
Compliance	7.Non compliance	a)Do not understand instructions	8(4.90)	46(28.23%)
		b)Forget to take the medication	29(17.80)	
		c)Drug product is too expensive	9(5.52)	

Drugs responsible for DRP among CV patients in GSGH

Generally the groups of drugs used among CV patients in GSGH were ACEIs,CCBs,Diuretics, BBs and digoxin. Accordingly the drugs responsible for DTP were among these groups and the common drugs responsible for DTP are listed below. (Table-3)

Table-3 Most commonly encountered drugs with DTPs among adult ambulatory patients with CVDs attending the chronic care unit of GSGH,28th March-12th April,2015

Drug/drug class	Need additional therapy No/%	Unnecessary drug therapy No/%	Ineffective drug No/%	Low dosage No/%	ADR No/%	High dose No/%	Non compliance No/%
CCBs	3(1.84)	8(4.9)	-	2(1.22)	1(0.61)	3(1.84)	11(6.75)
Digoxin	6(3.68)	-	-	-	2(1.22)	-	2(1.22)
NSAIDs	-	-	-	-	21(12.88)	-	-
Diuretics	2(1.22)	2(1.22)	11(6.75)	2(1.22)	1(0.61)	5(3.06)	-
ACEIs	5(3.06)	8(4.9)	5(3.06)	-	1(0.61)	-	1(0.61)
Aspirin/Statin	34(20.85)	-	-	-	-	-	-
Beta blockers	5(3.06)	-	3(1.84)	-	-	-	4(2.45)

Discussion

The most common cardiovascular disease encountered during the data collection period were hypertension (78,52%) and congestive heart failure (50,33.4%),where the study in Felege Hiwot referral hospital(FHRH)showed hypertensive heart disease (32%), rheumatic heart diseases (31.6%) and functional heart failure (18.4%) as a major diagnosis(Gobezie T. et al,2014). The variation might be due to the high number of hypertensives in the study groups.

CAP (29.5%), AFI (19%) and dyspepsia (16.9%) were the most commonly observed co morbidities while in Venezuela, Urinary tract infection (13.75%)anemia (12.5%) and pneumonia (11.25%) were the common co morbidities(Carlos H. et al.2013). The relative similarity among these two studies can be explained by the higher prevalence of infection in developing countries.

A total of 282 numbers of drugs were used to manage these cardiovascular problems among 144 patients. The mean number of drug was 1.9 ± 1.08 per patient which is smaller than the study in Adama, which had a mean of 3 ± 1.4 number of drugs per patient(Likisa L.,2013) because the number of patients in combination therapy were more numerous in Adama hospital than GSGH.

ACEI inhibitors (44%) and Calcium channel blockers (44%) were the commonly used drugs among

cardiovascular patients while in Belo Horizonte, the most commonly used drugs were Diuretics (76.3%), ACE inhibitors (52.6%) and antibiotics (27.6%)(Yone D., 2009). This could be due to higher number of hypertensive patients in this study.

Most of the patients (102,72%) had DTP, which is similar to the study by Mekonnen AB (22). A total of 163 numbers of DTPs were identified. The study in FHRH showed that there were 105 DTPs(Gobezie T. et al,2014). On the other hand a study in JUSH internal medicine ward showed, 149 DTPs(Bereket M. et al,2011) this variation can be due to the absence of clinical pharmacy service in the study area.

The mean number of DTP in this study was 1.28±0.8 per patient but studies in FHRH and JUSH showed 1.38±0.8(Gobezie T. et al,2014) and 3.014(Bereket M. et al,2011) DTPs per patient. This is because the number of medications used in this study are relatively lower than the two studies.

The major DTP type was indication (39.26%), from which need additional drug therapy was the common, which is similar to a study in Los angeles (Elaine L. et al ,2009) while in China efficacy and safety DTP types were the common(Xiao Li, 2009); such difference can be explained with higher number of drug use in China and can be due to absence of specific and comprehensive national CVD treatment guide line in Ethiopia.

Need additional drug therapy (84.37%) is one of the most common DTPs. It was also common problem in the FHRH(90.69%)(Gobezie T. et al,2014) and in JUSH internal medicine ward (83%)(Bereket M. et al,2011) and Adama(76%). This can be due to the absence of specific and comprehensive disease management guideline in Ethiopia.

The common untreated indications were anemia(9) and thrombocytopenia(2) respectively. While in Nigeria anemia (13), hypertension (5) and urinary tract infection (3)(Lotte S. et al,2010).Anemia is common in both studies mainly because of the poor nutritional status of the community in Ethiopia.

There were21(12.89%)patients with effectiveness related DTP,which is lesser than the study by FHRH (31) and Mekonnen AB (22) this might be due to the types of effectiveness related problems, where this study obtained only 2 types of effectiveness related problems .

Relatively lower number of safety related problems(19.63%)were found in this study than in JUSH (45.83%) (Bereket M. et al,2011) and by Mekonnen AB (31.39%)(Mekonnen A. et al,2013). This can be due to less types of safety related issues covered with this study including dosage too high and contraindications.

Unlike Belo Horizonte(Lotte S. et al,2010) and European studies(Ena I. et al,2013) the highest percentages of safety related issues encountered were contraindication(12.88%) and inappropriate frequency(4.90%).In Belo Horizonte the common safety issue was adverse drug events while in European studies it was dosage too high(27.5% and 13.75%) respectively. This primarily depends on patient and drug related factors.

Around 46(28.22%) number of patients were non compliant. Forget taking the medication was the major non-compliance issue; this can be due to patient factor. Even though different measurement of adherence was used, 27% of patients in Nigeria and 29% of patients in JUSH research were non compliant.

Unlike this, studies in USA (8%), Brazil (11%) and Venezuela (13%) showed relatively lower rates of non compliance. This is primarily due to the awareness of population towards rational medication use and presence of intact drug information provision system.

The most common drugs/groups of drugs responsible for the existence of DTP in this study were diuretics,CCBs and ACEIs but a study in JUSH showed antimicrobials,vitamins and minerals and antacids.This might be due to the existence of diverse co morbid conditions in JUSH study.

Conclusions

In the present study the most common CVDs encountered were hypertension and congestive heart failure. The prevalence of DTP among the studied population was high.The major DTP type was indication followed by non compliance, safety and effectiveness related problems.The most commonly encountered drugs with DTPs were Calcium channel blockers,Angiotensin converting enzyme inhibitors and Diuretics.

Recommendations

Drug therapy problem was relatively high in GSGH, so following recommendation were forwarded.
(A) Physicians:-To prescribe medications based on the current and evidence based recommendations provided by the guidelines.
(B)Pharmacist:- To deliver pharmaceutical care services for CV patients.
(C) Hospital:- To strengthen and support pharmaceutical care services.
(D) MOH and FMHACA:- To establish nationwide specific and comprehensive cardiovascular disease management guideline.
(E) MOH and FMHACA:- To support and facilitate the implementation of pharmaceutical care services in Hospitals.

Acknowledgements

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