www.ThePharmaJournal.com

The Pharma Innovation

Dr. Cyril Tom
Associate Professor, Department Of Pharmacy Pharmacy Practice, Shree Devi College of Pharmacy, Kejar Airport Road, Dakshina Kannada, Mangalore, Karnataka, India

Fathimath Noushana
5th Pharm, D, Department of Pharmacy Practice, Shree Devi College of Pharmacy, Kenjar Airport Road, Dakshina Kannada, Mangalore, Karnataka, India

Aishwarya
5th Pharm, D, Department of Pharmacy Practice, Shree Devi College of Pharmacy, Kenjar Airport Road, Dakshina Kannada, Mangalore, Karnataka, India

Sruthy Sunil
5th Pharm, D, Department of Pharmacy Practice, Shree Devi College of Pharmacy, Kenjar Airport Road, Dakshina Kannada, Mangalore, Karnataka, India

Febin Varghees
5th Pharm, D, Department of Pharmacy Practice, Shree Devi College of Pharmacy, Kenjar Airport Road, Dakshina Kannada, Mangalore, Karnataka, India

Corresponding Author:
Dr. Cyril Tom
Associate Professor, Department Of Pharmacy Pharmacy Practice, Shree Devi College of Pharmacy, Kejar Airport Road, Dakshina Kannada, Mangalore, Karnataka, India

A prospective observational study on drug utilization evaluation of anxiolytic and antidepressants in cardiovascular disease patients

Dr. Cyril Tom, Fathimath Noushana, Aishwarya, Sruthy Sunil and Febin Varghees

Abstract
Background: The main aim of this study is to conduct an assessment of the drug utilization evaluation of anxiolytics and antidepressants in CVD patients. And to estimate the quality of life of the patients using the WHO-QOL BREF questionnaire.
Results: The distribution of drugs was studied among the 97 patients, and it was found that antiplatelet agents were the most commonly prescribed drugs among CVD patients. The most commonly prescribed anxiolytics and antidepressants among the CVD patients were found to be benzodiazepines. Using the WHO-QOL BREF questionnaire to assess patient quality of life, this study discovered that DOM1, or physical health, graded the highest among the other four categories.
Conclusion: The study showed that advancing age was the predominating risk factor for causing anxiety and depression among CVD patients. In CVD patients, benzodiazepines were the most commonly prescribed anxiolytics. The WHOQOL-BREF was used to assess the quality of life and found that the physical domain remains the highest among the other domains. This indicated healthy daily activities, a reduced dependence on medications and medical devices, adequate energy and mobility, a lower level of pain and discomfort, adequate sleep and rest, and good working capacity.

Keywords: Cardiovascular disease, anxiolytics, antidepressants, WHOQOL-BREF questionnaire, co-morbidities, diagnosis

Introduction
Cardiovascular disease are a group of disorders of heart and blood vessels. They include coronary heart disease, cerebrovascular disease, peripheral artery disease, rheumatic heart disease, congestive heart disease and deep vein thrombosis etc. [1].

Depression and cardiovascular diseases (CVDs) are two of the major factors contributing to the burden of disease worldwide. Mental illnesses, especially depression and anxiety, are very common in people with CVD. 15–30% of CVD patients experience depressive disorders. Two to three times as many people experience depression as the general population. Additionally, it has been discovered that depression and anxiety in patients with coronary artery disease (CAD), myocardial infarction (MI), heart failure (HF), unstable angina, and coronary artery bypass grafting (CABG) decrease prognosis and quality of life [2].

Anxiety is defined as an unpleasant emotional state that is linked to a state of alarm and fear that develops in the absence of a significant threat but that is excessive in response to any triggering stimulus [3].

Gender differences, low education, single (individuals who are unmarried, divorced, or widowed), High hospitalization cost, smoking or intake of alcohol, history of hypertension/diabetes/myocardial.

Infraction, or longer duration of cardiovascular diseases are all potential risk factors for anxiety after coronary heart disease. Anxiety symptoms in patients with CHD include autonomic arousal, hyper vigilance, tremor or shaking, avoidance behavior and physiological reactivity.

Depression is a mental condition that is characterized by a depressed mood and reluctance to action. Depressive symptoms in patient with CVD include Persistent low mood or loss of interest in most activities for at least 2 weeks, including some of the following, totaling at least five symptoms:

- Lack of energy
- Weight change
- Increase or decrease in appetite
- Poor concentration
- Altered sleep pattern
- Reduced self-esteem
- Suicidal intention [4].

The main goals of treating depressive and anxiety symptoms in cardiovascular disease patients are

- To reduce the intensity of depressive symptoms
- To reduce the level of dysfunction
- To reduce the risk of suicidal thoughts or behavior.

Non-pharmacological treatment
CBT is a psycho-social intervention that focuses symptomatic relief in a variety of psychological illnesses, primarily depression and anxiety disorders. The goal of cognitive-behavioral therapy (CBT) is to systematically modify unwanted, dysfunctional thoughts and feelings. Exercise may reduce depressed symptomatology through a number of physiological and psychological processes. First, engaging in physical activity may alter endorphin and monoamine levels physiologically, potentially lowering depression symptoms. Second, by giving participants the chance to talk to other cardiovascular patients about their experiences, group training sessions may provide social support. A more realistic understanding of cardiovascular disease and its effects, as well as greater self-esteem, may come via group psychosocial education sessions and/or individual psychotherapy [5].

Pharmacological treatment
Patients with formal anxiety disorders, such as generalized anxiety disorder, panic disorder, or post-traumatic stress disorder, may also be treated with antidepressants. In patients with heart disease, the older tricyclic antidepressants like amitriptyline and nortriptyline should be avoided. First, due to their anticholinergic actions, these drugs cause negative cardiovascular side effects in this population, such as tachycardia and orthostatic hypotension. Additionally, these substances can prolong cardiac intervals (eg, QRS and QTc). In cardiac populations, SSRIs seem to be both safe and effective. In cardiac patients, these medications can be used to treat formal anxiety disorders such generalized anxiety disorder and panic disorder as well as depression. Although some patients may experience milder side effects including increased anxiety, sleeplessness, or restlessness during the first few days of treatment with SSRIs, these effects are typically present. They are well tolerated in this population and rarely result in orthostasis, tachycardia, or other negative cardiovascular consequences. Small studies on the safety and effectiveness of SSRIs and other antidepressants in individuals with ischemic heart disease have revealed that these medications are effective in reducing depressive symptom [6].
The quality of life is defined as the individual's perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. The WHOQOL-BREF is a 26-item questionnaire that measures QOL and general health as well as four domains: physical health (7 items), psychological health (6 items), social relationships (3 items), and environmental health (8 items). Each individual question on the WHOQOL-BREF is graded on a response scale, which

is defined as a five-point ordinal scale, with scores ranging from 1 to 5. The results are then linearly translated to a scale of 0 to 100. The mobility, everyday activities, functional ability, energy, pain, and sleep topics are all part of the physical health domain. Self-image, unfavorable ideas, favorable attitudes, self-esteem, mentality, learning capacity, memory focus, religion, and mental state are all measured within the psychological area. Personal relationships, social support, and sexual life are all included in the social relationships domain of the test. The living physical environment, opportunities to learn new skills and knowledge, recreation, the general environment (noise, air pollution, etc.), and transportation are all covered under the environmental health domain [7].
Drug Utilization Evaluation is an ongoing, authorized and systematic quality improvement process, which is designed to:

- Review drug use or prescribing patterns
- Provide feedback of results to clinicians and other relevant groups,
- Develop criteria and standards which describe optimal use of drug
- Promote appropriate drug use through education and other interventions.

To enhance drug use and health outcomes, the discipline of DUE attempts to comprehend how and why drugs are used the way they are. DUE has a significant impact on the healthcare system's ability to prescribe, administer, and use pharmaceuticals in a better way. DUE data may help hospitals and healthcare organizations create teaching initiatives that could enhance medication prescribing and usage. Some DUE programmes might give doctors feedback on how their performance and prescription habits relate to standards or treatment guidelines. DUE might also enable doctors to evaluate how they manage particular diseases in comparison to their peers. The peer pressure created by these comparisons may be helpful in encouraging doctors to alter their prescribing practices in an effort to enhance treatment [8].

Materials and Methods
The study was carried out for a period of 6 months among 97 inpatients in the cardiology department of Indiana hospital and medical institute, Mangalore. Patients of both sex, of above 18years with or without co morbidities were included. Out patients, pregnant and lactating females were excluded from the study.
A suitably designed data collection form was prepared to collect the data. The data collection includes demographics of the patients, diagnosis, medications prescribed, dose, frequency and total duration of treatment. WHOQOL-BREF questionnaire was used to collect information regarding the quality of life of patient. For statistical analysis, Microsoft excel version 12 and SPSS [statistical package for social science] version 22 were used.

Results
A Prospective observational study was conducted for 6 months in Indiana Hospital & Heart Institute. A total of 97 patients with cardiovascular diseases having depression or anxiety were included in the study.

**Patient distributed with respected to their age groups**
Out of 97 patients, majority of them i.e,55(56.7%) patient

were found in the age group of ≥60 years followed by 28(28.8%) patients in the age group of 50-59years, followed by 9(9.3%) patients in the age group of 40-49years, 3(3.1%) patients in the age group of 30-39years, 2(2.1%) patients in the age group of 18-29 years which is represented in table1.1 and figure 1.1 Table 1: Frequency and percentage distribution of samples according to demographic variables.

Table 1: Age wise distribution of study participants N= 97

Sl. No	Demographic variables	Frequency	Percentage
1	Age in years		
	18-29	2	2.1
	30-39	3	3.1
	40-49	9	9.3
	50-59	28	28.8
	≥ 60	55	56.7
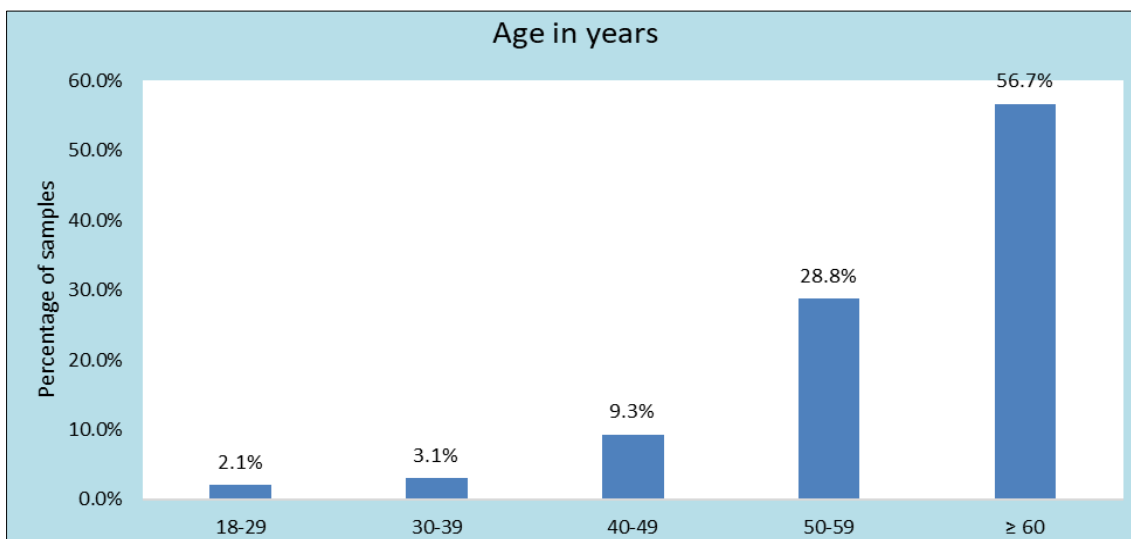
Majority of patients were in the age group of ≥60years.

Fig 1: Bar graph representing age wise distribution of study participants.

Gender wise distribution of subjects

Out of 97 subjects 65(67.0%) patients were male and 32(33.0%) were female which is represented in table1.2 and figure1.2

Table 2: Gender wise distribution of study participants

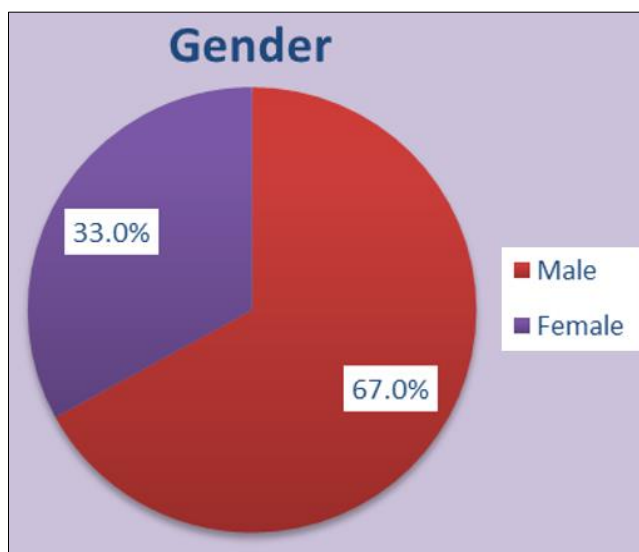| 2	Gender	Frequency	Percentage
	Male	65	67.0
	Female	32	33.0

Fig 2: Pie chart representing gender wise distribution of study participants

Patient distribution based on risk factors:

In this study, sleep, social status and education were found to be the risk factors of anxiety and depression in CVD patients. Table 2: Frequency and percentage distribution of samples according to risk factors.

Out of 97 patients, 18 (18.55%) were neither satisfied nor dissatisfied, and 79 (81.44%) were dissatisfied with sleep which is represented in table 2.1 and figure 2.1

Table 3: Frequency and percentage distribution of samples according to risk factors (Sleep) N= 97

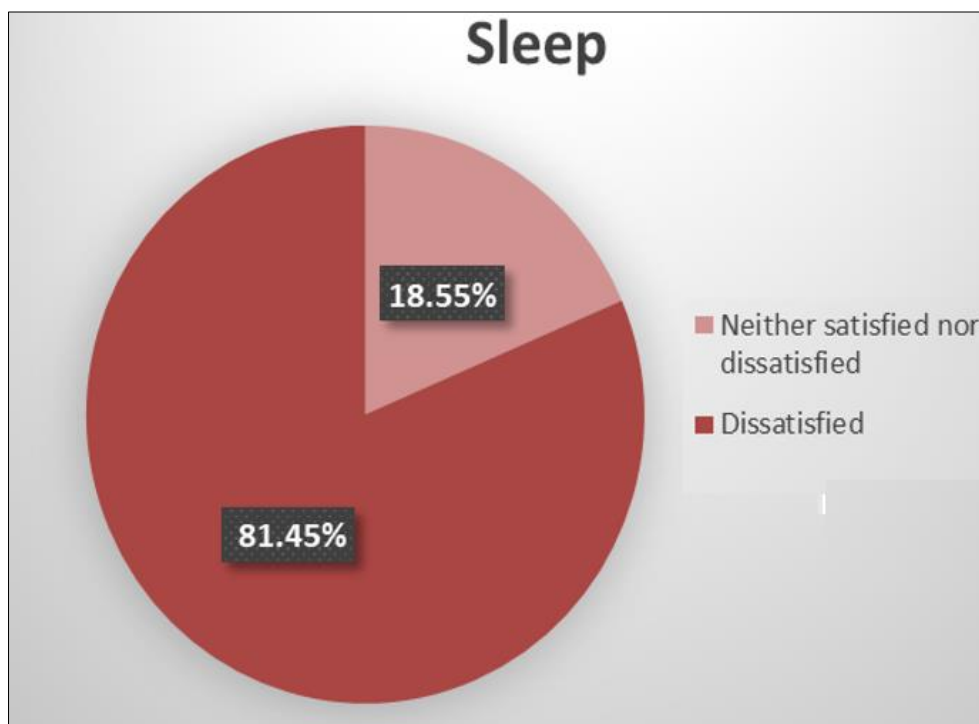| Sl. No	Risk factors	Frequency	Percentage
1	Sleep		
	Neither satisfied nor dissatisfied	18	18.55
	Dissatisfied	79	81.44

Fig 3: Pie chart representing percentage distribution of risk factor(sleep)

Out of 97 patients, 26 (26.80%) were smoker, 14 (14.43%) were alcoholic, 17 (17.53%) were smoker and alcoholic, 40 (41.24%) were none which represented in table 2.2 and figure 2.2.

Table 4: Frequency and distribution of samples according to risk factors (Social status)

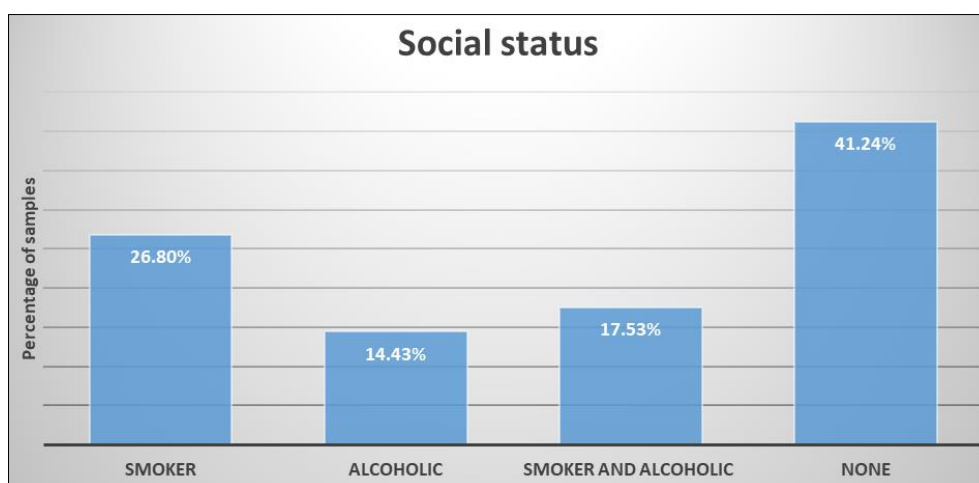| 1	Social status	Frequency	Percentage
	Smoker	26	26.80
	Alcoholic	14	14.43
	Smoker and alcoholic	17	17.53
	None	40	41.24

Fig 4: Bar graph representing percentage distribution of risk factors (Social status)

Out of 97 patients 18(18.55%) were elementary school, 23(23.71%) were high school, 17(17.52) were college, 17(17.52%) were graduate professional degree, 22(22.68) were illiterate which is represented in table 2.3 and figure2.3

Table 5: Frequency and percentage distribution of samples according to risk factors (Education)

1	Education	Frequency	Percentage
	Elementary school	18	18.55
	High school	23	23.71
	College	17	17.52
	Graduate/professional degree	17	17.52
	None at all	22	22.68

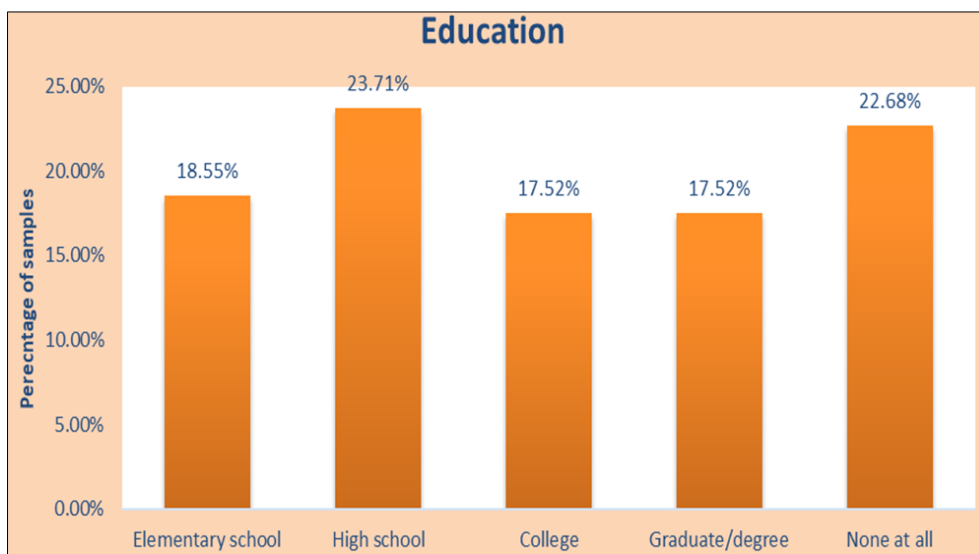**Fig 6:** Bar graph representing percentage distribution of risk factors (Education)

Patient distribution based on diagnosis of the disease
Out of 97 patients, majority of the patients i.e, 80(82.5%) were diagnosed with coronary artery disease followed by 54(55.7%) with hypertension, 31(32.0%) with acute coronary syndrome, 31(32.0%) with myocardial infarction, 16(16.5%) with unstable angina, 7(7.2%) with aortic valve replacement, 5(5.2%) with congestive heart failure, 5(5.2%) with congenital heart disease, 4(4.1%) with pericardial effusion which is represented in table3 and figure3.

Table 3: Frequency and percentage distribution of samples according to diagnosis N= 97

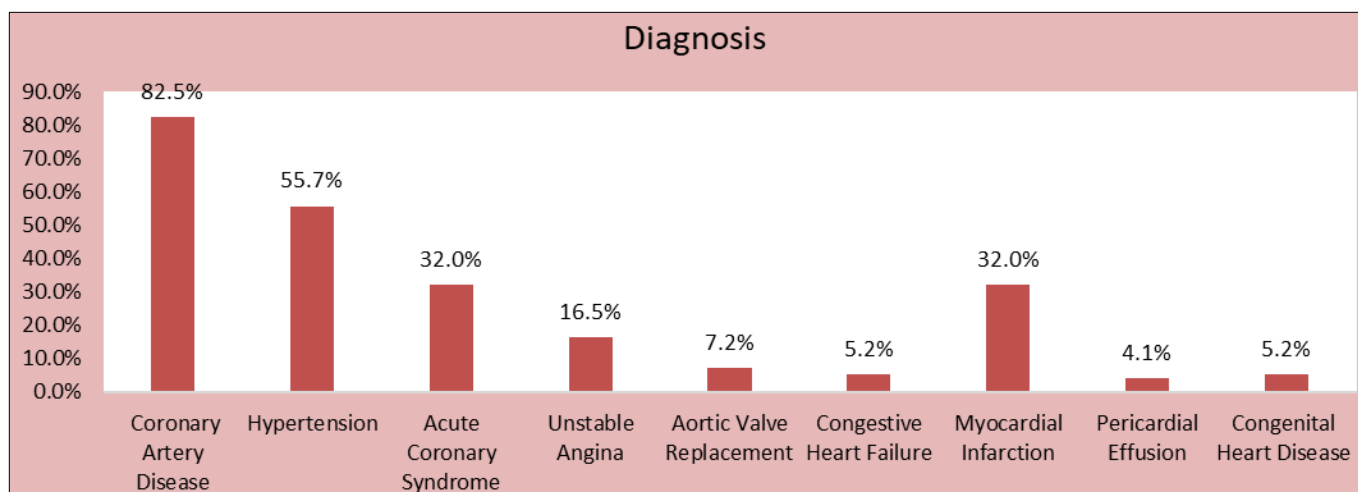| Sl. No	Diagnosis	Frequency	Percentage
1	Coronary Artery Disease	80	82.5
2	Hypertension	54	55.7
3	Acute Coronary Syndrome	31	32.0
4	Unstable Angina	16	16.5
5	Aortic Valve Replacement	7	7.2
6	Congestive Heart Failure	5	5.2
7	Myocardial Infarction	31	32.0
8	Pericardial Effusion	4	4.1
9	Congenital Heart Disease	5	5.2

Fig 7: Bar graph representing percentage distribution of samples according to diagnosis

Patient distribution based on co-morbidities

Out of 97 patients, majority of the patient i.e, 65 (67.0%) had diabetes mellites followed by 29 (29.9%) patients with CKD. Some of the patients had other comorbid condition which is represented in the table4.1 and figure 4.1.

Table 4: Frequency and percentage distribution of samples according to comorbidities N= 97

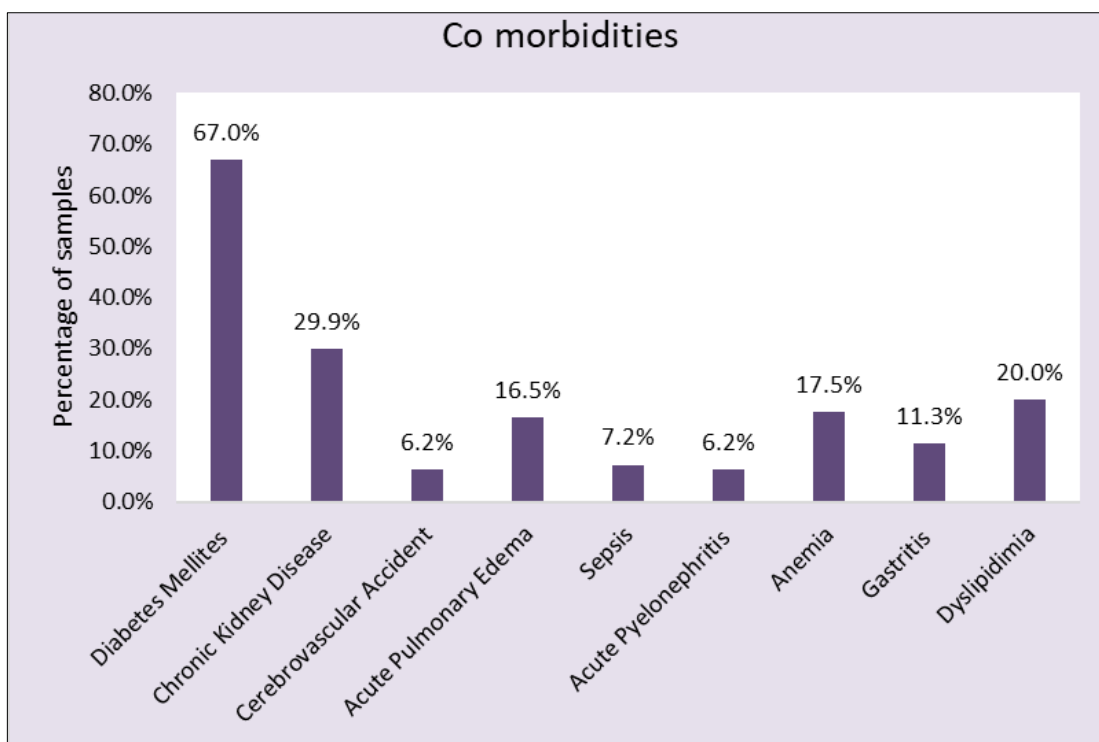| Sl. No	Comorbidities	Frequency	Percentage
1	Diabetes Mellites	65	67.0
2	Chronic Kidney Disease	29	29.9
3	Cerebrovascular Accident	6	6.2
4	Acute Pulmonary Edema	16	16.5
5	Sepsis	7	7.2
6	Acute Pyelonephritis	6	6.2
7	Anaemia	17	17.5
8	Gastritis	11	11.3
9	Dyslipidaemia	20	20.6

Fig 8: Bar graph representing percentage distribution of samples according to co-morbidities

Patient distribution based on drugs prescribed

Out of 97 patients, the most commonly prescribed cardiovascular drugs was found to be statins 79 (81.44%) followed by beta blocker 73 (75.25%) which is followed by diuretics 70 (72.16%) and followed by other cardiovascular drugs as represented in table

Table 5: Frequency and percentage distribution of prescribed Cardiovascular drugs N= 97

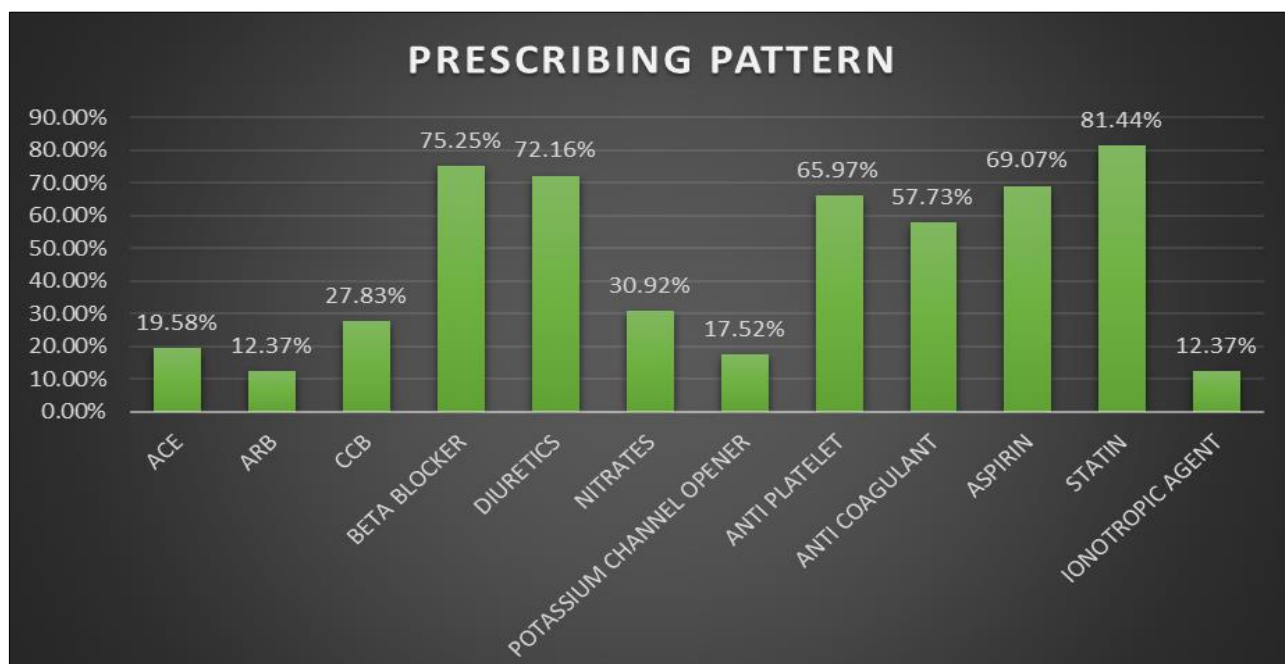| SL. No	Prescribed drugs	Frequency	Percentage
1	ACE inhibitors	19	19.58
2	ARB inhibitors	12	12.37
3	Calcium channel blocker	27	27.83
4	Beta blockers	73	75.25
5	Diuretics	70	72.16
6	Nitrates	30	30.92
7	Potassium channel opener	17	17.52
8	Anti-platelet agents	64	65.97
9	Anti-coagulant	56	57.73
10	Aspirin	67	69.07
11	Statins	79	81.44
12	Inotropic agents	12	12.37

Fig 9: Bar graph representing percentage distribution of prescribed cardiovascular drugs

Frequency and percentage distribution of anxiolytics and antidepressants in CVD patients.

Out of 97 patients, the most commonly prescribed anxiolytics and antidepressants in CVD patient was found to be Qutan 33(34.02%) followed by Anxit 28(28.86%) and other drugs were represented in table 5.1 and figure 5.1.

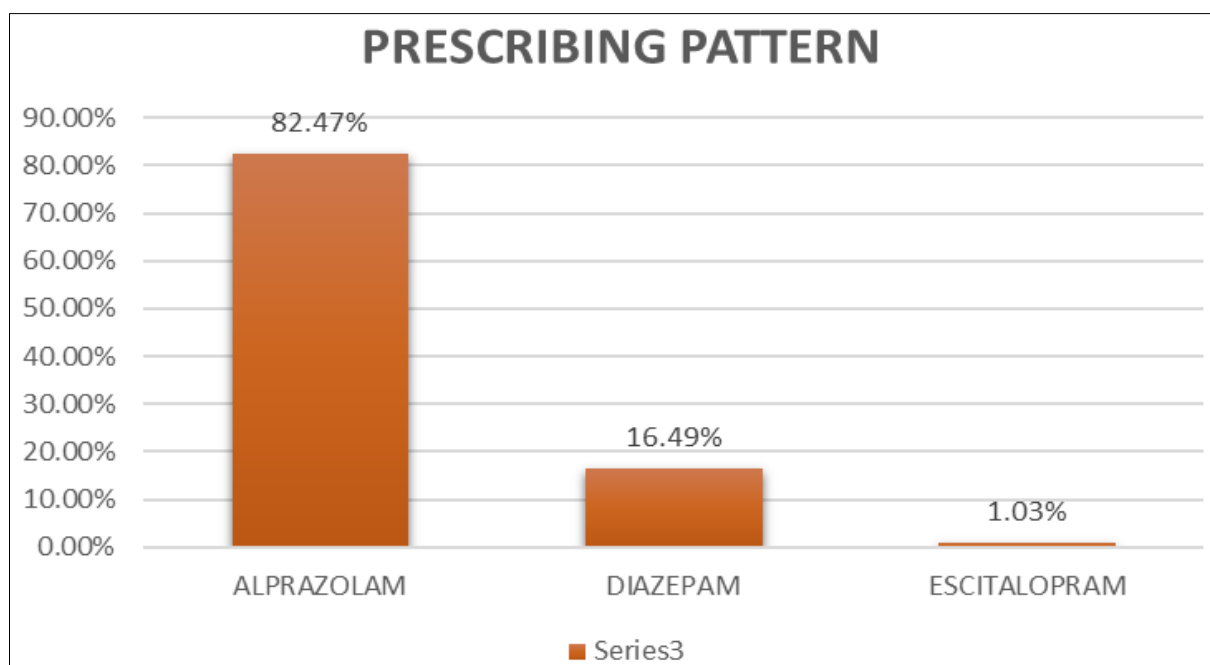| SL No	Drugs prescribed	Frequency	Percentage
1	Alprazolam	80	82.47
2	Diazepam	16	16.49
3	Escitalopram	1	1.03

Fig 10: Bar graph representing percentage distribution of prescribed anxiolytics and antidepressant

Frequency and distribution of sample according to Whoqol-Bre questionnaire

In this study, among the 4 domains of WHOQOL-BREF, the highest quality of life was found for DOM4 (environmental health, mean =59.81) implying very good financial resources, opportunities for acquiring new information, skills and leisure activity. The least mean score was found for DOM1 (physical health, mean=38.57) indicating not very good activities of daily living, insufficient sleep and rest and more pain and discomfort.

Table 6: Range, mean, standard deviation, median and mean percentage of different domains of quality of life among cardiovascular disease patients N=97

Domain	Range	Mean	Standard deviation	Median
Physical	0-69	38.57	15.27	38.0
Psychological	0-61	44.33	16.02	44.0
Social	0-81	52.67	21.10	52.61
Environmental	31-94	59.81	11.83	59.81

Table 6: Paired t test for the four domains of WHOQOL BREF N=97

Domain	Mean	SD	95% CI of the difference		t value	df	p-value
			Lower	Upper			
Physical Vs Psychological	5.76	11.42	-8.07	-3.46	4.969	96	<0.001***
Physical Vs social	14.10	20.53	-18.24	-9.97	6.767	96	<0.001***
Physical Vs environmental	21.25	15.34	-24.34	-18.16	13.640	96	<0.001***
Psychological Vs social	8.34	20.56	-12.48	-4.20	3.995	96	<0.001***
Psychological Vs environmental	15.48	14.38	-18.38	12.58	10.609	96	<0.001***
Social Vs environmental	7.14	19.19	-11.01	-3.28	3.667	96	<0.001***

t (96)= 1.985
***Significant at 0.001 level
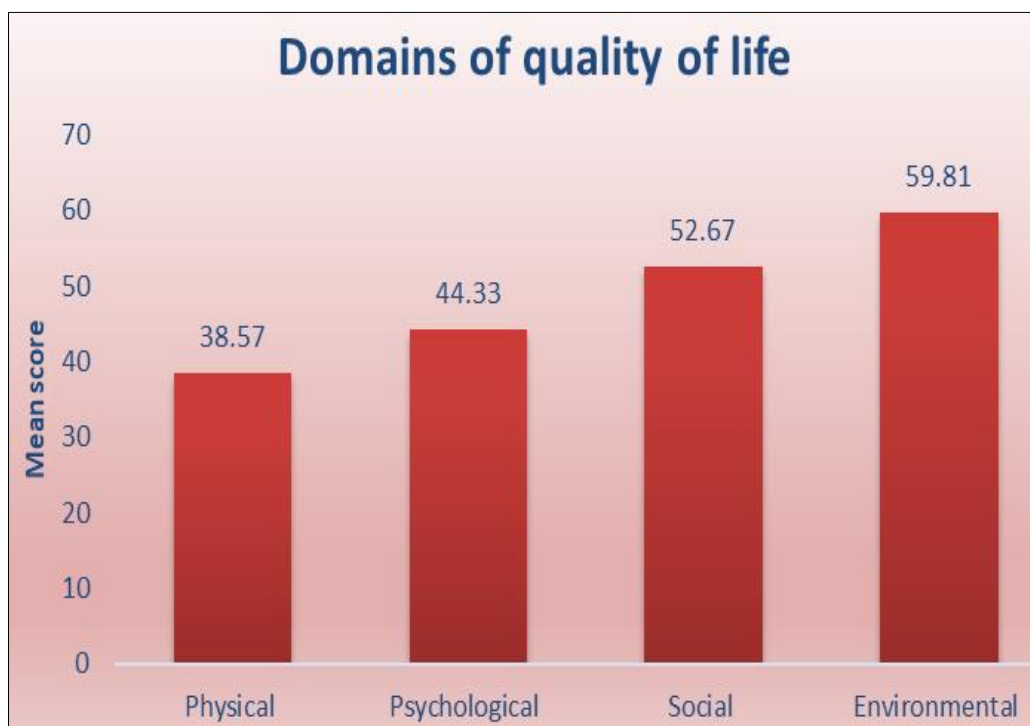
Discussion

- In our study, the male subjects (67%) predominated than female subjects (33%) which is supported by the article conducted by Bunevicius A *et al*. [9].

- The patients were classified into different age groups that is 18-29,30-39,40-49,50-58 and above 60 years and the number of patients in each group 2(2.1%),3(3.1%),9(9.3%),28(28.8%),55(56.7%) respectively. The majority of the patients were in the age group of above 60 years which is supported by the study conducted by Ho Siew Eng *et al*. [16].

- In this study, the risk factors are sleep and social habits. The majority of the population were dissatisfied with their sleep and the remaining population were neither satisfied nor dissatisfied with their sleep. This is in accordance with the study conducted by Christine Norra *et al*. [11].

- Out of 97 patients, it was found that 26(26.80%) were smokers, 14(14.43%) were alcoholics, 17(17.53%) was both smoker and alcoholic and 40(41.24%) were non-

smoker and non-alcoholics. The majority of the patients were non-smokers and non-alcoholics 40(41.24%) which was supported by the study conducted by Ashish Kumar Saha *et al*. [12].

- According to our study, the most commonly prescribed drug among CVD patients was found to be Antiplatelets agents 84(86.59%) which is supported by the study conducted by Thomas BR *et al*. [13].

- Distribution of anxiolytic and antidepressant drugs among CVD patients were studied and it was found that benzodiazepines 44(45.36%) were the most commonly used anxiolytic. Careful literature review suggests that the addition of benzodiazepine with the cardiovascular medications could bring beneficial effect by providing sufficient sleep which in turn reduces anxiety, stress hormone response, and stress induced low grade inflammation. This was supported by the article conducted by Uddin MM *et al*. [14].

- WHOQOL-BREF questionnaire was used to assess the quality of life of CVD patients and found that physical

domain (mean-59.81) was the highest domain among the others. This is supported by the study conducted by Snarska K *et al.* [15].

Conclusion
Our study found that anxiety and depression are more common in people over the age of 60, and that the majority of men with CVD who experience these symptoms are also male. The main risk factors for the disease were sleep, social status. Most of the patients were dissatisfied with their sleep, whereas majority of them were non-smokers and non-alcoholics.

This prospective study concluded that nearly half of the patients were diagnosed with coronary artery disease, some had hypertension, and a few had acute coronary syndromes and myocardial infraction, respectively. The most common co-morbidity associated with the disease was diabetes mellitus, which was followed by CKD and dyslipidemia.

Antiplatelet agents were the most often prescribed medication among the study population, according to our evaluation of the prescription patterns for CVD medications.

Anxit were the most frequently prescribed anxiolytics and antidepressants in our study of the prescription patterns for CVD patients.

Using the WHO-QOL BREF questionnaire to assess patient quality of life, this study discovered that DOM1, or physical health, graded highest among the other four categories. This indicates healthy daily activities, a reduced dependence on medications and medical devices, adequate energy and mobility, a lower level of pain and discomfort, adequate sleep and rest, and good working capacity.

References
1. World Health Organization. Definition of Cardiovascular disease. Available from https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) [Assessed on 11 June 2021].
2. Ahmad A, Rahman I, Agarwal M. Factors influencing mental health during COVID-19 outbreak: an exploratory survey among indian population. MedRxiv. 2020 Jan 1.
3. Perrotta G. Anxiety disorders: definitions, contexts, neural correlates and strategic therapy. J Neur Neurosci. 2019;6(1):042.
4. Davies SJ, Jackson PR, Potokar J, Nutt DJ. Treatment of anxiety and depressive disorders in patients with cardiovascular disease. Bmj. 2004 Apr 15;328(7445):939-943.
5. Dobbels F, De Geest S, Vanhees L, Schepens K, Fagard R, Vanhaecke J. Depression and the heart: a systematic overview of definition, measurement, consequences and treatment of depression in cardiovascular disease. European Journal of Cardiovascular Nursing. 2002 Feb 1;1(1):45-55.
6. Huffman JC, Celano CM, Januzzi JL. The relationship between depression, anxiety, and cardiovascular outcomes in patients with acute coronary syndromes. Neuropsychiatric Disease and treatment. 2010;6:123.
7. Snarska K, Chorąży M, Szczepański M, Wojewódzka-Żelezniakowicz M, Ładny JR. Quality of life of patients with arterial hypertension. Medicina. 2020 Sep 9;56(9):459.
8. Parthasarathi G, Nyfort HK, Nahata Milap C. A textbook of clinical pharmacy practice. Essential concept and skills. Second edition. Universities press private limited; c2012. p. 720.
9. Bunevicius A, Staniute M, Brozaitiene J, Pop VJ, Neverauskas J, Bunevicius R. Screening for anxiety disorders in patients with coronary artery disease. Health and quality of life outcomes. 2013 Dec;11(1):1-9.
10. Suryawanshi VS. Greener and efficient synthesis of Benzodiazepines using mixed Ferrite under solvent free condition. Int. J Adv. Chem. Res. 2020;2(2):32-35. DOI: 10.33545/26646781.2020.v2.i2a.25
11. Norra C, Kummer J, Boecker M, Skobel E, Schauerte P, Wirtz M, *et al*. Poor sleep quality is associated with depressive symptoms in patients with heart disease. International Journal of Behavioral Medicine. 2012 Dec;19(4):526-534.
12. PR AV, Singh AV, Saha AK, Srikar K. Assessment and prevalence of depression among cardiovascular disease patients in Nilgiris District observational cross-sectional study.
13. Uddin MM, Kabir MS, Al-Amin MM, Hasan M, Emran TB, Islam MT, *et al*. Evaluation of prescription pattern of psycholeptic medications at hospital discharge for patients with cardiovascular diseases in national cardiovascular disease hospital of Bangladesh. Journal of Applied Pharmaceutical Science. 2017 Mar 30;7(3):017-023.
14. Thomas BR, Catherin TJ, Sabu N, Lekshmi ES, Baby N, Menaka K, *et al*. Prescribing Pattern of Cardiovascular Drugs-A Prospective Observational Study. Indian Journal of Pharmacy Practice. 2017;10(4).
15. Snarska K, Chorąży M, Szczepański M, Wojewódzka-Żelezniakowicz M, Ładny JR. Quality of life of patients with arterial hypertension. Medicina. 2020 Sep 9;56(9):459.
16. Eng HS, Yean LC, Das S, Letchmi S, Yee KS, Bakar RA, *et al*. Anxiety and depression in patients with coronary heart disease: a study in a tertiary hospital. Iranian journal of medical sciences. 2011 Sep;36(3):201.