



Assessment of Prognostic Markers of Heart Failure Following Acute Myocardial Infarction in Patients Treated With Primary Percutaneous Coronary Intervention

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Abstract

Background / Aim: The concentration of N-terminal brain natrium peptides (NT-proBNP) is an important marker within the diagnostic and prognostic analysis of patients with chronic heart failure. In patients with ST-segment elevation myocardial infarction, natriuretic peptides are dominant predictors of death, heart failure and additional myocardial infarctions. The aim of this study was to correlate prognostic markers of heart failure following acute myocardial infarction.

Methods: 193 patients with myocardial infarction were divided into two groups: 69 patients with NT-proBNP \leq 1000 pg/mL and 124 patients with NT-proBNP $>$ 1000 pg/mL. During the hospitalisation, laboratory data, clinical data and information on previous medications were collected. Echocardiography was used to identify left ventricular ejection fraction (LVEF). All statistical analysis were done in SPSS, version 23.

Results: The group with elevated NT-proBNP ($>$ 1000 pg/mL) was older ($p < 0.001$) and suffered more often of arterial hypertension ($p = 0.04$) and atrial fibrillation ($p = 0.003$). Heart rate was higher and LVEF was lower in patients with elevated NT-proBNP values ($p < 0.001$). Mean LVEF in the 193 patients was 46.86 %. In both linear and binary logistic regression analysis multiple predictors of elevated NT-proBNP have been identified.

Conclusion: Increased ranges of NT-proBNP in patients following acute myocardial infarction are in correlation with decreased LVEF, elevated high-sensitive troponin I, lactate dehydrogenase, urea, creatinine, C-reactive peptides. This may guide clinicians to assess and treat early stages of heart failure.

Key words: NT-proBNP; Acute myocardial infarction; Heart failure.

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Introduction

Defining the concentration of circulating natriuretic peptides is a crucial in the diagnostic and prognostic assessment of patients with persistent coronary heart disease.^{1,2} In patients who suffered from ST-segment elevation myocardial infarction, natriuretic peptides can be dominant predictors of left ventricular dysfunction and death.^{1,3}

The aim of this study was to correlate N-terminal brain natrium peptides (NT-proBNP) ranges with indicators of myocardial necrosis, left ventricular ejection fraction (LVEF), heart rhythm and other measures such as creatinine, cholesterol, sodium, potassium, C-reactive peptides (CRP) as well as with smoking habits and on-going medications ie, antiplatelet therapy, beta-blockers, ACE-inhibitors.

Methods

Study population and data collection

In this study, 193 adult consecutive patients who were treated with primary percutaneous coronary intervention (PCI) between January 2021 and October 2021 at the University Clinical Centre of Republic of Srpska were included. All patients with measured NT-proBNP levels were included.

Clinical data

During the hospitalisation, clinical documentations on previous medications were collected. Study included data on hypertension, diabetes mellitus, family history of coronary artery disease, smoking status and previous interventions (PCI, coronary artery bypass grafting). Heart rhythm was analysed by electrocardiography for detecting normal sinus rhythm and abnormalities (atrial fibrillation, atrial flutter and patients with implanted pacemaker).

Laboratory data

Blood samples were collected in first 24 hours after admission. Parameters were NT-pro BNP levels, markers of myocardial necrosis (creatinine kinase (CK), CK-MB, lactate dehydrogenase (LDH), troponin), total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, urea, creatinine, sodium, potassium, magnesium, calcium, CRP, D-dimer, prothrombotic time, activated partial thromboplastin time (aPTT), prothrombin time - international normalised ratio (INR).

Echocardiography

Echocardiography was used to determine LVEF.

Statistical analysis

Continuous variables were presented as mean with standard deviation or median and interquartile range, based on data distribution. For normal distribution was used a T-test and in cases with abnormal distribution Mann Whitney test was used. Categorical variables were presented as number with percentage and compared using a Chi-square test. In order to assess correlation between different parameters, linear regression analysis and Person's coefficient were used. All variables were implemented into a univariate ie, multivariate binary logistic regression model. Independent predictors of elevated NT-proBNP were identified. All analysis was done in SPSS, version 23.

Results

Clinical data

Patients were divided into two groups according to the NT-proBNP levels. First group, 69 patients (NT-proBNP ≤ 1000 pg/mL) and second group 124 patients (NT-proBNP > 1000 pg/mL). The mean age of the 193 patients was 74.6 years. There was a predominance of male patients, 120 patients ie, 62.18 %. The vast majority had hypertension (65.8 %). There were 27.46 % smokers (53 patients) and 57 out of 193 had positive family history for cardiovascular diseases. Patients had mainly sinus rhythm (83.42 %), whereas in 29 patients (15.06 %) there was atrial fibrillation. Atrial flutter was found at 1 patient (0.52 %) and there were 2 patients with pacemaker (1.04 %). Mean LVEF in the 193 patients was 46.86 % (Table 1).

Table 1: Baseline characteristics in patients with heart failure following acute myocardial infarction related to NT-proBNP values

	Total n = 193	NT-proBNP (pg/mL)		p
		≤ 1000 (n = 69)	> 1000 (n = 124)	
Age		61 (IQR 19)	72 (IQR 19)	
Male	120	43 (62.3 %)	77 (62.1 %)	< 0.001
Hypertension	127	40 (57.9 %)	87 (70.2 %)	0.97
Diabetes mellitus	47	12 (17.4 %)	35 (29.0 %)	0.04
Smoking	53	23 (33.3 %)	30 (24.2 %)	0.28
Family history	54	27 (39.1 %)	27 (21.8 %)	0.37
Previous PCI	39	13 (18.8 %)	26 (20.9 %)	0.07
Previous CABG	7	2 (2.9 %)	5 (4.0 %)	0.72
ACE inhibitor	101	36 (52.2 %)	65 (52.4 %)	0.69
Beta blocker	138	43 (62.3 %)	95 (76.6 %)	0.97
Acetylsalicylic acid	104	34 (49.3 %)	70 (56.5 %)	0.04
Clopidogrel	73	23 (33.3 %)	50 (40.3 %)	0.34
Rhythm				0.34
Sinus rhythm	161	65 (94.1 %)	96 (77.4 %)	0.003
Atrial fibrillation	29	2 (2.9 %)	27 (21.8 %)	
Atrial flutter	1	1 (1.5 %)	0 (0 %)	
Pacemaker	2	1 (1.5 %)	1 (0.8 %)	
Heart rate		81.22 \pm 19.127	94.69 \pm 23.266	< 0.001
LVEF (%)		55 (IQR 15)	38 (IQR 15)	< 0.001

PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; ACE: angiotensin-converting enzyme; LVEF: left ventricular ejection fraction; NT-pro-BNP: N-terminal proBrain natriuretic peptide;

The group with elevated NT-proBNP (> 1000 pg/mL) were older ($p < 0.001$) and suffered more often of arterial hypertension ($p = 0.04$) and atrial fibrillation ($p = 0.003$). As expected (Table 1), heart rate was higher and LVEF was lower in patients with elevated NT-proBNP values ($p < 0.001$).

Table 2: Laboratory findings in patients with heart failure following acute myocardial infarction related to NT-proBNP values

	NT-proBNP (pg/mL)		p
	≤ 1000 (n = 69)	> 1000 (n = 124)	
Hs troponin I (µg/L)	62.6 ± 4355.2	1345 ± 14057.2	0.001
LDH (U/L)	229 ± 237	298 ± 352.8	0.005
CK (U/L)	164 ± 400	121 ± 358.5	0.378
CK-MB (U/L)	24 ± 30	23.5 ± 59.8	0.334
Total cholesterol (mmol/L)	5.04 (IQR 1.46)	4.79 (IQR 1.46)	0.441
HDL (mmol/L)	1.1 (IQR 0.4)	1 (IQR 0.4)	0.318
LDL (mmol/L)	3.44 (IQR 1.29)	3.29 (IQR 1.17)	0.563
Triglycerides (mmol/L)	1.74 ± 0.98	1.656 ± 0.87	0.675
Urea (mmol/L)	5.9 ± 2.3	7.25 ± 6.7	0.002
Creatinin (µmol/L)	78 (IQR 31.8)	94 (IQR 47)	0.002
Sodium (mmol/L)	140 (IQR 3)	139 (IQR 6)	0.195
Potassium (mmol/L)	4.26 ± 0.42	4.34 ± 0.64	0.406
Magnesium (mmol/L)	0.83 ± 0.09	0.78 ± 0.09	0.018
Calcium (mmol/L)	2.27 ± 0.3	2.2 ± 0.2	0.034
CRP (mg/L)	2.8 ± 16.2	13.5 ± 59.3	< 0.001
D dimer (µg/L)	5.97 ± 11.4	2.42 ± 10.3	0.788
Prothrombotic time	1.62 ± 2.1	2.29 ± 3.4	0.765
aPTT	58.29 ± 32.5	57.18 ± 29.48	0.909

PCI: percutaneous coronary intervention; ACE: angiotensin-converting enzyme; LVEF: left ventricular ejection fraction; NT-pro-BNP: N-terminal proBrain natriuretic peptide; CK: creatine kinase; LDH: lactate dehydrogenase; CRP: C-reactive protein;

Regression analysis

Regression analysis data are given in Table 2. Patients in whom NT-proBNP was higher of 1000 pg/mL had values of high-sensitive troponin I, LDH, urea, creatinine and CRP. In the linear regression analysis, serum NT-proBNP levels correlated well with LVEF, serum creatinine (µmol/L) and CRP (Figure 1). When univariate binary logistic regression analysis were applied, multiple predictors of elevated NT-proBNP (> 1000 pg/mL) were identified (Table 3).

Discussion

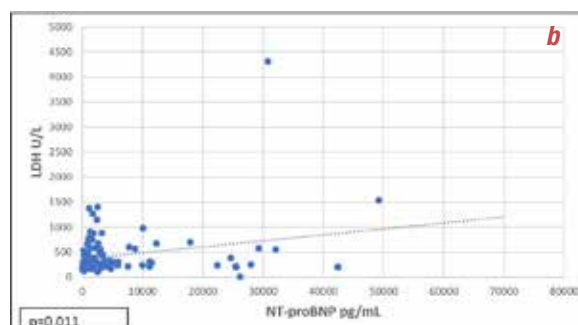
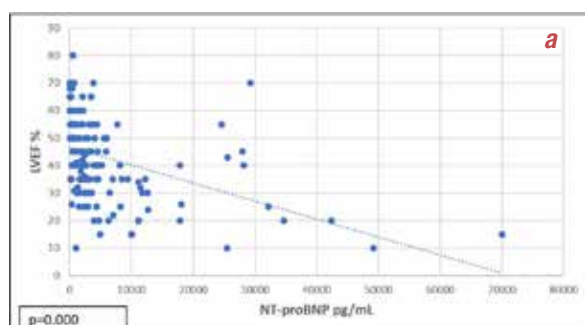
This study was focused on patients with acute myocardial infarction treated with primary PCI.

Table 3: Univariate binary logistic regression analysis in patients with heart failure following acute myocardial infarction related to NT-proBNP values

Variable	Univariate logistic regression		p
	OR	95 % CI	
Age	0.984	0.97-1.01	0.100
Male	1.009	0.55-1.85	0.976
Hypertension	1.705	0.92-3.15	0.088
Diabetes	1.868	0.90-3.90	0.096
Smoking	0.638	0.33-1.22	0.174
Prior PCI	1.143	0.54-2.40	0.724
Atrial fibrillation	2.747	1.12-6.73	0.027
LVEF (%)	0.914	0.89-0.94	< 0.001
ACEi	1.010	0.56-1.82	0.974
Beta-blockers	1.981	1.04-3.76	0.036
Acetylsalicylic acid	1.334	0.74-2.41	0.338
CK (U/L)	1.000	0.99-1.01	0.285
LDH (U/L)	1.003	1.00-1.05	0.028
CK-MB (U/L)	1.001	0.98-1.04	0.484
hsTroponin (µg/L)	1.005	1.00-1.10	0.078
Cholesterol (mmol/L)	1.002	0.99-1.01	0.715
LDL (mmol/L)	0.997	0.97-1.03	0.840
Triglycerides (mmol/L)	1.010	0.96-1.06	0.672
Urea (mmol/L)	1.013	1.01-1.02	0.003
Creatinine (µmol/L)	1.019	1.01-1.03	0.002
Sodium (mmol/L)	0.927	0.84-1.02	0.133
Potassium (mmol/L)	0.983	0.96-1.01	0.203
Magnesium (mmol/L)	0.994	0.98-1.01	0.563
CRP (mg/L)	1.001	1.00-1.01	0.077
D-Dimer (µg/L)	1.00	0.99-1.01	0.614

PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; ACE: angiotensin-converting enzyme; LVEF: left ventricular ejection fraction; NT-pro-BNP: N-terminal proBrain natriuretic peptide; OR: odds ratio; CI: confidence interval;

The major result of this study was the positive correlation between NT-proBNP levels with LVEF and other indicators (troponin I, LDH, urea, creatinine and CRP). LVEF was lower in patients with elevated NT-proBNP values ($p < 0.001$). Troponin I ($p = 0.078$) and LDH ($p = 0.028$) levels were considerably related with NT-proBNP levels. Previous study showed that kidney failure and aging are significant factors for elevated plasma NT-proBNP levels.⁴ When serum creatinine levels are higher than 2.0 mg/dL, NT-proBNP levels elevate remarkably.⁵⁻⁷ This study showed posi-



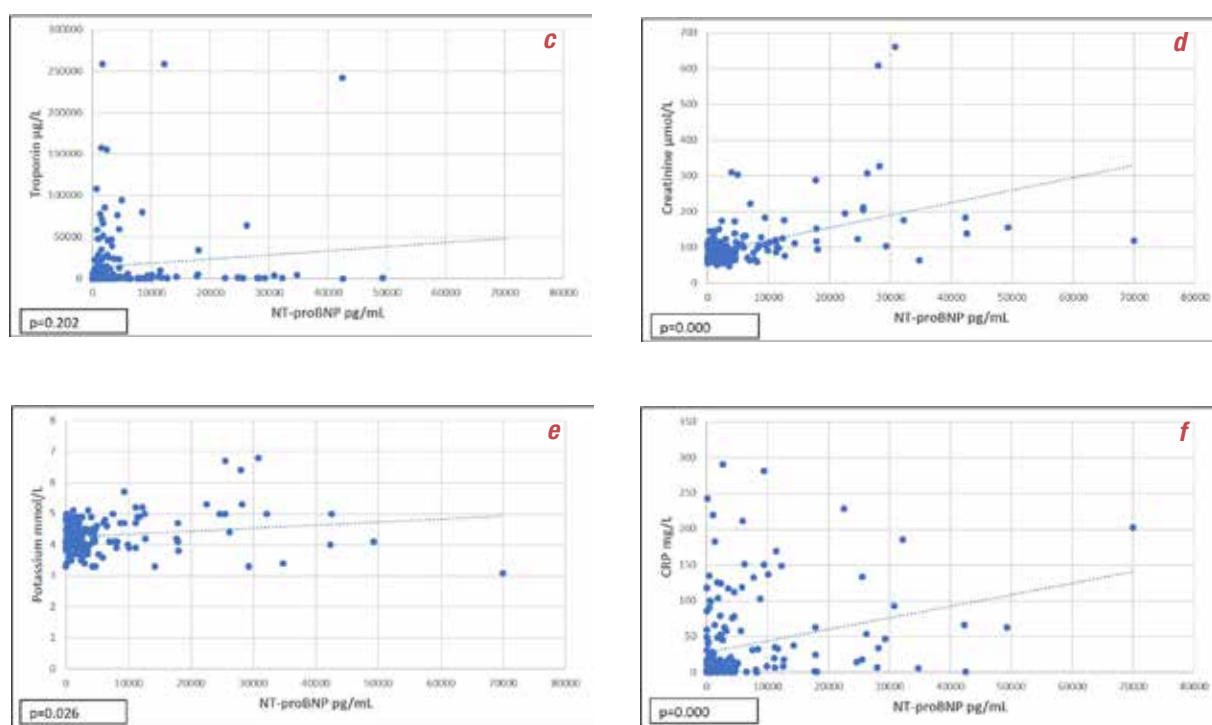


Figure 1 a-f: Linear regression analysis of parameters in patients with heart failure following acute myocardial infarction

tive correlation with urea ($p = 0.003$) and creatinine ($p = 0.002$) levels. The group with elevated NT-proBNP (> 1000 pg/mL) had higher CRP levels ($p = 0.077$) and suffered more often of arterial hypertension ($p = 0.04$) and atrial fibrillation ($p = 0.003$).

Study showed negative correlation with CK-MB ($p = 0.484$) and atherosclerosis markers (cholesterol and triglycerides). Cholesterol ($p = 0.715$) and triglycerides ($p = 0.672$) were not associated with higher NT-proBNP levels.

High NT-proBNP levels are in some measure related to the degree of ischaemic myocardial infarction, which may have prognostic value.⁸ In previous study, older patients formed an enlarged amount of individuals with acute myocardial infarction and age was a powerful predictor of significant complications and death after acute myocardial infarction.⁸ However, this study did not find significantly association with age and high NT-proBNP levels ($p = 0.100$).

Findings from this study indicate that high NT-proBNP levels can bring relevant information because of their possibility to outline the quantity of injured myocardium.

Limitations

The study has some limitations, which needs to be acknowledged. Retrospective nature of the study cannot exclude potential selection bias as well as confounding variables. Relatively small number of patients. Data on total ischaemic time were not available.

Conclusion

There are many important predictors for worse patient condition and poor outcomes. NT-proBNP levels correlated with LVEF, but also with troponin I, LDH, urea, creatinine and CRP levels. There was a relation of high NT-proBNP levels with hypertension and atrial fibrillation. This may guide clinicians to assess and treat early stages of heart failure.

Acknowledgements

None.

Conflict of interest

None.

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Prescribing Patterns in Type 2 Diabetes Mellitus Outpatients at a Tertiary Care Centre in Jaipur, India

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Abstract

Background: Over the last few years, an unexpected increase in the prevalence of diabetes in India have been witnessed. The present study was planned to analyse prescribing patterns of anti-hyperglycaemic drugs and assess the influence of Chief Minister's Free Drug Scheme in Rajasthan, India. It aimed to evaluate, monitor and if possible, suggest modifications in prescribing practices to make medical care rational and also to assist minimising adverse drug reactions (ADRs).

Methods: This was a cross-sectional, observational study carried out for a 12-month period. A total 400 known patients of type 2 diabetes mellitus (T2DM) from endocrinology outdoor of SMS Medical College Hospital (a tertiary care hospital in Jaipur, Rajasthan, India) were recruited and their prescriptions were analysed using the World Health Organization (WHO) prescribing indicators.

Results: Most commonly observed age group was of 40-50 years (mean age 53.76 ± 8.84), with a male preponderance (57.5 %). Among them, 67.5 % of patients were found to be obese (mean BMI 29.79 ± 3.26). All anti-hyperglycaemic were prescribed in their generic names only. Metformin was the most frequently prescribed anti-hyperglycaemic agent. Among the fixed dose combinations, the most common was that of glimepiride and metformin (40.75 %), while most prescribed add on anti-hyperglycaemic was teneligliptin (51.5 %), followed by pioglitazone (30.5 %). A total of 53.25 % of these patients received insulin along with oral anti-hyperglycaemic agents.

Conclusion: The anti-hyperglycaemic agent prescribing among endocrinology outpatients at tertiary care hospital in Jaipur was found to be satisfactory.

Key words: Glimepiride; Metformin; Teneligliptin; WHO prescribing indicators.

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Introduction

According to the World Health Organization (WHO), "Diabetes is a chronic, metabolic disease characterised by elevated levels of blood glucose (or blood sugar), which over time leads to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The most common type is type 2 diabetes mellitus (T2DM), which affect mainly adults. This occurs when the body becomes resistant to insulin or doesn't make enough insulin."¹

Glucose regulation is mainly done by two hormones insulin and glucagon secreted by pancreas and this regulation gets interrupted in diabetes mellitus.² According to global report of WHO, in October 2018, 72.9 (8.8 %) million people in India were living with diabetes in 2017.³ And this has increased to 77 million in 2019 according to International Diabetes Federation report, 2019.⁴

The initial treatment strategies are mainly based on the severity and type of diabetes. The subsequent addition of anti-hyperglycaemic and other agents would depend on the co-morbid conditions of the patient. For the management of T2DM, both the pharmacological approach, in form of anti-hyperglycaemic agents and non-pharmacological approach, in the form of lifestyle modifications (diet, exercise, reduced alcohol and smoking cessation) are applied.⁵

Rational use of medications in such chronic conditions can prevent the complications and suffering.⁶ It is a complex issue with a goal that is difficult to achieve, it is defined as: "Patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time and at the lowest cost to them and their community".⁷

Multiple reasons have been observed behind the persistence of disease and suffering which include improperly prescribed, dispensed and sold medications, failure of patients to take the medications as advised and failure of access to the essential drug list (EDL). Thus, it is necessary to identify irrational prescribing patterns.⁸ The WHO defines drug utilisation as "The marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences." The WHO has also formulated a set of "core prescribing indicators" for improvement in the rational drug use. It includes the prescribing indicators, the patient care indicators and the facility indicators.^{9, 10}

Therefore, this study was planned to analyse the prescribing patterns of anti-hyperglycaemic agents among the outpatients of endocrinology department of SMS Medical College Hospital, Jaipur. This study was aimed to evaluate, monitor and if possible, suggest modifications in prescribing practices to make medical care rational and also to assist in minimising adverse drug reactions (ADRs).

Methods

Study design and sample size determination

It was a cross-sectional, observational study which was carried out in the outpatients of endo-

crinology department of SMS Medical College Hospital (a tertiary care hospital in Jaipur) after taking permission from the research review board of the institute (protocol No 36600 dated 10/07/2018). The sample size for the study was calculated at 95 % Confidence Level expecting 50 % adherence (maximum variance) to the treatment of type 2 diabetes mellitus (T2DM) in endocrinology department. At the precision (relative allowable error) of 10 %, a minimum of 400 patients of T2DM were recruited as sample size.

Data collection and statistical analysis

A total 400 known cases of diabetes in age group of 40 to 70 years, irrespective of their co-morbid status were recruited and the data in the form of socio-demographic profile, personal history and WHO core indicators were collected in a pre-designed study forms. Data collected was tabulated and analysed using descriptive statistical tools (mean \pm standard deviation and percentage). Chi-square test was used for categorical data. The data were analysed using SPSS for Windows (version 16.0 Chicago, SPSS Inc.) with the statistical significance evaluated using two-sided P value at a 5 % level of significance.

WHO Core Indicators

The drug data obtained was assessed for "Prescribing Indicators" by the WHO.¹⁰

- i. Average number of drugs per encounter = $\frac{\text{Total number of drugs prescribed}}{\text{Number of medication charts}}$.
- ii. Percentage of drugs prescribed by generic name = $\frac{\text{Number of generic drugs prescribed}}{\text{Total number of drugs}} \times 100$.
- iii. Percentage of patient medications charts with antibiotics prescribed = $\frac{\text{Total number of charts with antibiotics prescribed}}{\text{Total number of charts}}$.
- iv. Percentage of patient medications charts with injections prescribed = $\frac{\text{Total number of charts with injections}}{\text{Total number of charts}}$.

Percentage of drugs prescribed from Essential Drug List of Rajasthan¹¹ = $\frac{\text{Total number of drugs from EDL}}{\text{Total number of all drugs prescribed}} \times 100$.

Results

Out of the 400 patients, 57.5 % were men and 42.5 % were women. The recruited patients in this study were between 40-70 years of age. Mean age was found to be 53.76 ± 8.84 years.

A total 39.56 %, out of the 230 men gave history of current alcohol intake while 17.3 % stated that they have quit alcohol. Rest denied any history of alcohol intake. Similarly, 35.21 % of men were currently smokers, while 28.69 % men said that they have quit smoking. Rest said they have never smoked. All the women denied any intake of alcohol and/or smoking, although, tobacco chewing history was present in 33.5 % of the women and 52 % of men. Smokers were asked about their number of cigarettes smoked per day, it was more than 5 cigarettes a day in 76.5 % of smokers and less in the rest. Out of the total patients, 67.5 % were found to be obese (BMI ≥ 30), 24.5 % patients were overweight and only 8 % had normal weight (Table 1).

Table 1: Distribution of patients with diabetes mellitus type 2 according to body mass index

BMI (in kg/m ²)	Men	Women	p value*
18.5 - 24.9	24	8	0.085
25 - 29.9	58	40	
≥ 30	148	122	
Total	230	170	
Mean \pm SD	29.79 \pm 3.26		

* p value calculated using Chi square test

WHO core indicators were assessed after seeing their prescriptions and they gave results as below (Table 2).

Table 2: Estimated WHO Core Prescribing Indicators

Number of prescription analysed	400
Average number of drugs per encounter (Mean \pm SD)	4.58 \pm 1.8
Percentage of encounter with antibiotics prescribed (%)	4
Percentage of encounter with an injection prescribed (%)	53.25
Percentage of drugs prescribed by generic name (%)	100
Percentage of drugs prescribed from Rajasthan Essential Drug List 2019 (%)	94

Individual drug distribution

Most commonly prescribed anti-hyperglycaemic agent was metformin, prescribed in 154 patients. Metformin was also prescribed in fixed dose combinations with glimepiride, gliclazide and teneligliptin in 163, 59 and 24 patients respectively (Figure 1).

In patients with poor glycaemic control other add-on anti-hyperglycaemic drugs were also prescribed. Teneligliptin was prescribed in a total of

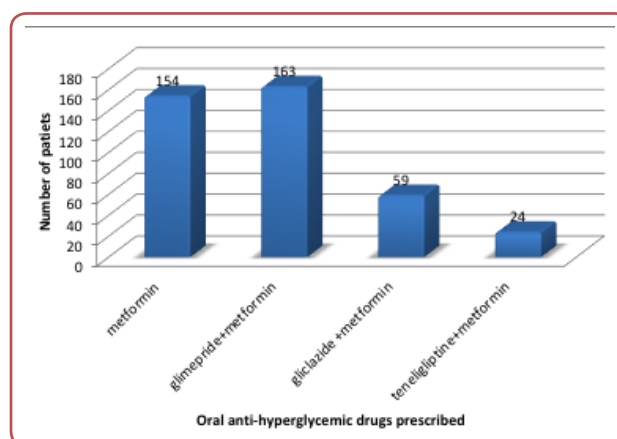


Figure 1: Distribution of patients according to oral anti-hyperglycaemic drug prescribed

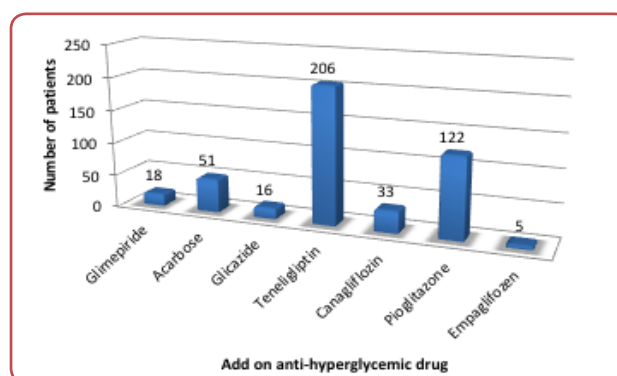


Figure 2: Distribution of patients according to add on anti-hyperglycaemic drugs prescribed

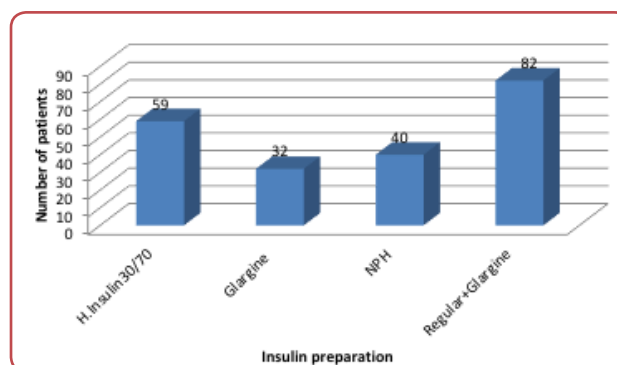


Figure 3: Distribution of patients according to insulin preparations prescribed

NPH: Neutral protamine Hagedorn insulin;

206 patients as an add-on drug with either fixed dose combination or with metformin. Second most common as an add-on was pioglitazone in 122 patients. Acarbose, glimepiride, gliclazide, canagliflozin and empagliflozin were prescribed in 51, 18, 13, 33, 5 patients respectively (Figure 2).

Along with oral anti-hyperglycaemic agents human insulin was prescribed in 59 patients (Figure 3).

Conclusion

The anti-hyperglycaemic agent prescribing among endocrinology outpatients at tertiary care hospital in Jaipur was found to be satisfactory. The average number of drugs per prescription was found to be 4.58. This seems to be justified as a chronic disease like diabetes mellitus is associated with comorbidities and deteriorates over time might require multiple drugs for its management. The most common add on drug was teneligliptin. Antibiotics were prescribed to only 4 % patients, which seemed judicious. Patients were also taught about the importance of lifestyle modifications and diet. This is also in accordance with the American Diabetes Association (ADA) recommendations. Adherence to lifestyle and dietary modifications will not only improve glycaemic control but will also help in reducing the long term complications of diabetes mellitus.

Limitations

The sample was not random and could have been a potential source of bias. The inherent limitations of a cross-sectional study cannot be ignored. Indeed, only prospective studies can demonstrate a causal association between the determinants and uncontrolled T2DM. Besides, the self-reporting of participants could not rule out the possibility of bias in the participant's responses. Glycosylated HbA1c was not recorded but recommended in the study.

Future perspectives

In future, similar studies can be planned in private tertiary care hospital settings. Studies for evaluating defined daily doses (DDD) for anti-hyperglycaemic agents can also be envisaged.

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Conflict of interest

None.

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