A PROSPECTIVE STUDY ON QUALITY EVALUATION OF DIABETES MELLITUS MANAGEMENT IN PATIENTS WITH ACUTE CORONARY SYNDROME AND/OR HEART FAILURE

Dr. Gurumayum Ramcharan Sharma, Resident, Dept. of Cardiology, JMMC&RI
Dr. Manoj Ravi, Associate Professor, Dept. of Cardiology JMMC&RI, Thrissur
Dr. Govindan Unni T, Professor & Head, Dept. of Cardiology, JMMC&RI, Thrissur
Dr Prasannakumar, Professor, Dept. of Cardiology, JMMC&RI, Thrissur
Dr Bino Benjamin, Associate Professor, Dept. of Cardiology JMMC&RI, Thrissur

Abstract

Objectives:
Primary objective of the study was to measure and inquire glycemic control, blood pressure control, blood cholesterol control, BMI and smoking habits in diabetic mellitus patients presenting with acute coronary syndrome and/or heart failure. Similar parameters were measured in 6month follow up and compared as secondary objective

Methodology: The study was a prospective cross sectional observational study which recruited a total of 77 consecutive diabetic patients with first episode of ACS and/or symptomatic heart failure admitted at a tertiary care hospital. Data focusing on HbA1c, [bloo2d] pressure, lipid profile esp. LDL, statin consumption, BMI and smoking status were collected at enrolment and at 6month follow up.

Results: At enrolment, mean age was 56.35yrs ± 9.687yrs (σ). Mean HbA1c was 9.544%±1.8917% (σ) and 92.2% of the patients having HbA1c $\geq$7%. Out of 77 patients, 40.3% of the patients did not have their blood pressure controlled. Mean LDL was 127mg/dl± 33.9mg/dl (σ) and 77.9% of the patients have LDL $\geq$100mg/dl. In this study 79.2% of the patients were not on statin and those on statin was not on recommended intensity of statin therapy (except for 1.4% of the patient). Mean SCORE II Diabetes score was 27% and median ASCVD score was 16.1%. In this study, 64.9% of the patients had their BMI $\geq$ 23Kg/m2 . At enrolment, 10.4% of the patient were currently smoking.
At 6 month follow up, median HbA1c was reduced to 6.95% with IQR 6.700% to 8.675 (compared with paired enrolment, Wilcoxon signed ranks test had p<0.001. Half of the patient (50.0%) had controlled HbA1c p=0.019. All the patients (100%) were on statin. Median LDL improved to 57.5mg/dl with IQR 50mg/dl to 80.75mg/dl (cf paired enrolment LDL Wilcoxon signed ranks test p<0.001). Half of the patients (50.0%) had their LDL at target level < 55mg/dl(McNemer test p<0.001). Only 1.4% of the patient continue to smoke in follow up (McNemar test p=0.016). BMI changes remained statistically insignificant.

Conclusion: The study demonstrates that primary prevention in DM is far below the guideline directed levels with respect to HbA1C, Blood Pressure control, LDL cholesterol, statin treatment and BMI values.

Key words: Quality of Diabetic care, Diabetes Mellitus, Acute Coronary Syndrome, Heart Failure

1. BACKGROUND:

Type 2 diabetes Mellitus (T2DM) is a chronic complex metabolic disease. The management requires holistic approach with behavioural and pharmacological treatments to maintain quality of life and prevent or delay complications. European Society of Cardiology 2019 guideline has listed the major targets listed for cardiovascular disease prevention in diabetic patient[1]. These include management of glycemic control, blood pressure (BP) control, blood cholesterol control, body mass indexed (BMI) and smoking habits, among others which will help in mitigation of micro and macro vascular complications.

2. AIM:

2.1 Primary Objective

To measure and inquire quality of T2DM care in patients presenting with first episode of acute coronary syndrome (ACS) and/ or symptomatic Heart Failure (HF) in terms of guideline directed goals of glycemic control, BP control, blood cholesterol control, BMI and smoking habits[1,2].

2.2 Secondary Objective

To study whether these patients achieve the treatment target after 6 months follow up in terms of glycemic control, BP control, blood cholesterol control, BMI and smoking habits.

3. METHODOLOGY:

3.1 Study design, setting and sample size:

The study was a prospective cross sectional observational study at a tertiary care hospital Jubilee Mission Medical College, Thrissur, Kerala where enrolment of patients were done from January 2023 to December 2023 and followed up for 6month with each patient receiving routine standard treatment.

Institutional Ethics Committee approval were obtained. Informed written consents were obtained from each participant. Based on distribution of HbA1c & BMI observed in an earlier publication "An implementation of the St. Vincent Declaration for Quality Improvement in

Diabetes Care" by Gudbj ̈ornsdottir et al with 95% confidence interval and 5% relative allowable error, sample size was calculated to 77[3].

$$n= (Z1-\propto/2)^2.(SD)^2/d^2$$

3.2. Eligibility criteria

Adult Patient ≥ 18 years of age with T2DM presenting with first known episode of either ACS and/or symptomatic HF were included in the study. Patients refusing consent, pregnancy or cancer patients were excluded.

3.3 Definitions

The definition of diabetes was as per Diagnosis and Classification of Diabetes Mellitus, American Diabetes Association[2].The definition of STEMI was as per *Fourth Universal Definition of Myocardial Infarction (2018)[4]. The definition of "NSTEMI" & "Unstable Angina" was as per"* 2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes" & *"2000 AHA/ACC Guideline for the management of patients with unstable angina and Non-ST-Segment Myocardial Infarction"*[5,6]. The definition of HF was as per *Universal Definition of Heart Failure*[7]. The staging of HF was as per ACC/AHA stages of HF and patient should be at stage C /D of the HF on enrolment wherever applicable[8]. BP targets were defined as either SBP<130 mmHg and DBP <80 mmHg for patients on anti-hypertensive medication or SBP <140mmHg and DBP<90 mmHg for those not on antihypertensives[1]. SCORE II Diabetes cardiovascular risk chart for very high risk region has been used for risk stratification wherever applicable[1,9]. ESC CVD risk calculation app has been used.(9) Online ASCVD risk calculator has been used[10]. The lipid targets was as per 2019 ESC/EAS Guidelines for the management of dyslipidaemias[1]. Estimated Glomerular Filtration rate (eGFR) was calculated as per 2021CKD EPI equation[11,12]. BMI Target for Indians has been taken as 18-22.9kg/m^2 as against 20-24.9kg/m^2 in the Caucasian populations as per WHO recommendations and adopted in Indian Council of Medical Research (ICMR) & the National Health Policy, Government of India[13,14]. Currently smoker, former smoker and never smoked were as per CDC and ministry of health New Zealand[15,16]. In the current study, ECS/ESA 2019 recommendations on treatment targets and goals for cardiovascular disease prevention will be used with some modifications. BMI target has been taken as 18-22.9 kg/m^2 instead of 20-24.9kg/m^2 as per WHO and National Health Policy recommendations

3.4 Study Procedures

Consecutive patients with T2DM who presented with ACS and/or symptomatic HF satisfying the inclusion and exclusion criteria has been assessed regarding quality assessment of diabetes care. Those found eligible has been included after an informed written consent. However, the participation in this study was non-mandatory for patient's treatment at the centre. Clinical characteristics which had been included were glycemic control, BP control, blood cholesterol control, BMI and smoking habits. The patients HbA1c, BP, Low Density Lipoprotein Cholesterol (LDL-C) , Body Mass Index (BMI) and smoking habit was collected

and compared against the targets. Binary response of yes or no/ achieved or not achieved for all the five parameters has also been recorded. The actual values of these targets measured or inquired has also been recorded. Recent pre-event blood pressure if recorded was preferred. Patients were enrolled during the period of January 2023 to December 2023. Further, they follow up to 6 months to reassessed and compared for glycemic control, BP control, blood cholesterol control, BMI and smoking habits.

5. RESULT & DISCUSSION

In this study, it was attempted to estimate the quality of diabetic care in patients presenting with ACS and/or symptomatic HF in terms of glycemic control, BP control, blood cholesterol control, BMI and smoking habits at enrolment.

A total of 77 patients were enrolled and data were collected. Male constituted 88.3% and 76.6% were from rural area. The mean age was 56.35yrs $\pm$ 9.687yrs (σ) with median age of 57.0yrs (IQR 49.5yrs to 62.0yrs). Family history of either ischemic heart disease (36.4%) or diabetes mellitus (59.7%) or dyslipidemia (18.2%) in the first or second degree relatives was present in 70.1% of the enrolled patients. In a Korean national cohort study by Park et al (ACS with diabetes n=3989), mean age was 64.4yrs$\pm$9.5yrs (σ). Males formed 61.7% of the enrolment.(17) On the other hand, in a metanalysis segregating data for diabetic Asian patient with ACS (n=1252) from five randomized clinical trials by Koshizaka et al, median age was 65.0yrs (IQR 56.0yrs to 72.0yrs).The RCTs included were PARAGON B, EARLY ACS, APPRAISE-2, TRACER and PLATO. In this study, 33.2% were female[18]. Our current study has a median age with almost a decade younger compared to this Asian population. In PARAGON B trial, family history of arteriosclerosis was present in 40% of the enrolment. In a multicentric case-control observational Indian study of ACS by Rao et al (MERIFACS), mean age was 56.11yrs $\pm$ 11.63yrs (σ) which is comparable to our current study. In this Indian study, 76.5% were male and 53.1% of the enrolled cases were from rural area[19]. In a case-control observational INTERHEART STUDY by Yusuf et al (AMI n=12461 of which 18.45% were diabetic and South Asian geographic region n=1732), median age among South Asian region cases with AMI was 53yrs (IQR 46yrs-64yrs). Male constituted 85.5%[20].

At enrolment, diabetes mellitus was poorly controlled with mean HbA1c of 9.5%$\pm$ 1.8917% (σ). 92.2% of patients had their HbA1c $\geq$7%. Only 7.8% of patients had controlled HbA1c of <7%. In the 6month follow up of 72 patients, median HbA1c was 6.950 % with IQR of 6.700% to 8.675%. HbA1c was controlled with level <7% in 50.0% of the patients. There was significant improvement in the HbA1c level comparing at enrolment and 6month follow up of 72 patients with Wilcoxon signed Ranks test (W) of -6.805 with p value of <0.001. In the Korean study, Park et al has observed median FBS of 106.0mg/dl (IQR 92.0mg/dl-131.0mg/dl)[17]. In MERIFACS study, mean HbA1c (including both diabetic and non-diabetic patients) was 7.02%$\pm$ 1.91% (σ). Blood sugar was uncontrolled with HbA1c $\geq$7% in 37.8% of the patients[19].

Table 1 Patient characteristics

	Variables	Enrolled patients n=77	Percentage (%)
Gender	Males	68	88.3
	Females	9	11.7
Rural vs Urban	Rural	59	76.6
	Urban	18	23.4
Presentation	ACS without HF	69	89.6
	ACS with HF	6	7.8
	HF without ACS	2	2.6

Table 2 Major determinants of quality of T2DM care

	Mean	Std. Dev.	Median	Range	IQR
HbA1c (%)	9.544	1.8917	9.200	5.9 to 13.8	8.050 to 11.050
Total Cholesterol (mg/dl)	204.55	47.964	201.00	111 - 343	170.50 - 240.00
LDL (mg/dl)	127.01	33.855	123.00	60 - 203	105.00 - 153.50
SCORE II Diabetes risk score (%)	27.018	11.6549	25.500	9.1 to 59.7	16.800 to 34.000
ASCVD risk score (%)	19.636	13.9048	16.100	2.9 to 56.9	8.500 to 27.300
BMI (kg/m^2)	24.1277	3.71116	24.2000	17.5 to 35.2	21.4 to 26.3

Table 3 Comparison of major determinants of T2DM care against the target

Blood Pressure Control Status				
Blood Pressure in Target	Hypertensive			
	Yes	No	Total	
Yes	11	35	46 (59.7%)	X^2=23.943
No	25	6	31 (40.3%)	(p<.001)
Total	36 (46.8%)	41 (53.2%)	77 (100%)	
LDL level and statin status pre-event				
	LDL			
	<100mg/dl	≥ 100mg/dl		
On statin	7	9	16 (20.8%)	χ^2= 5.514
Not on statin	10	51	61 (79.2%)	(p=0.019)
Total	17 (22.1%)	60 (77.9%)	77 (100%)	

Table 4 Comparison of major determinants of T2DM care at enrolment and 6month follow up

HbA1c at Target level (<7%)				
At Enrolment	Follow up		Total	McNemar Test
	<7%	≥7%		
<7%	6	0	6 (8.3%)	p <0.001
≥7%	30	36	66 (91.7%)	
Total	36 (50.0%)	36 (50.0%)	72 (100%)	
Blood pressure control				
At Enrolment	Follow up		Total	McNemar Test
	Yes	No		
Yes	41	4	45 (62.55%)	p= 0.019

No	15	12	27 (37.5%)	
Total	56 (77.8%)	16 (22.2)	72 (100%)	
LDL level				
At enrolment	**At Follow up**		**Total**	**McNemar**
	<55mg/dl	**≥55mg/dl**		**Test**
<100mg/dl	13	2	15 (20.8%)	**p<0.001**
≥100mg/dl	23	34	57 (79.2%)	
Total	36 (50.0%)	36 (50.0%)	72 (100%)	
Currently Smoking				
At Enrolment	**Follow up**		**Total**	**McNemar**
	Yes	**No**		**Test**
Yes	1	7	8 (11.1%)	**p= 0.016**
No	0	64	64 (88.9%)	
Total	1 (1.4%)	71 (98.6%)	72	
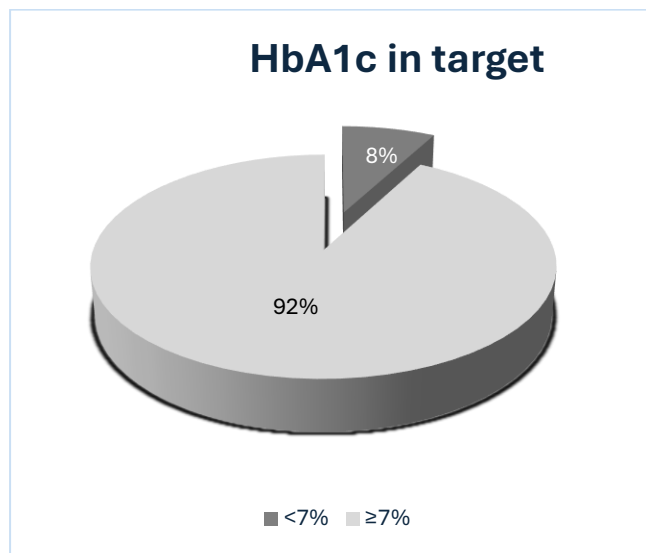
Figure 1: HbA1c against target level at enrolment
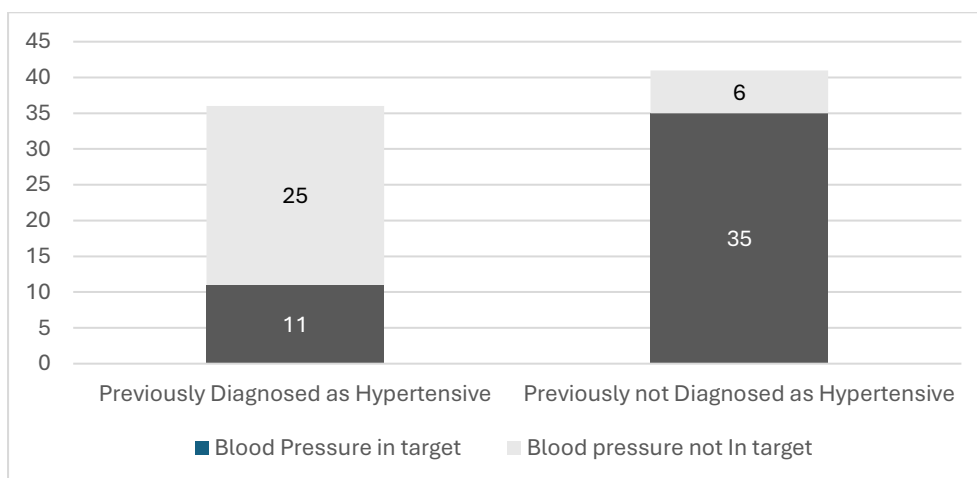
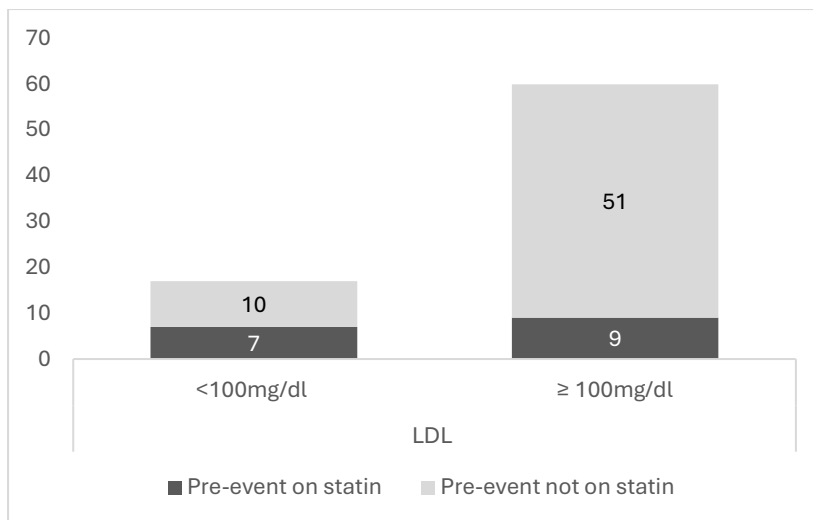**Figure 2:** Blood Pressure control at enrolment
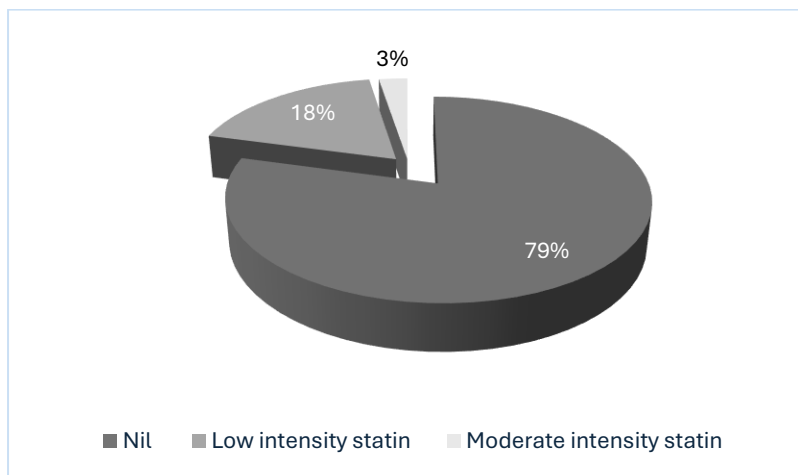
Figure 3: LDL level and statin status pre-event

Figure 4: Intensity of statin therapy pre-event

In our study, 46.8% of the enrolled patients were "previously diagnosed as hypertensive" and 53.2% of the patients were not hypertensive. Blood pressures were controlled for 59.7% of the patients at enrolment, with 40.3% of patients having their blood pressure uncontrolled. At the 6 month follow up, significant proportion (77.8%) of patients had their blood pressure at controlled level with chi square test value $\chi=23.943$ and p <0.001. However, 22.2% of the patient had their blood pressure above the target level. In the Korean study by Park et al, mean SBP was 131.7mg/dl±17.9mg/dl. Mean DBP was 80.4mmHg±11.3mmHg[17]. In the study by Koshizaka et al, Asian diabetic with ACS group has median SBP of 130mmHg (IQR 115mmHg to 145mmHg) and median DBP of 73mmHg (IQR 65mmHg to 82mmHg). 77.6% of the patients had history of hypertension[18]. In MERIFACS study(case=2153 ACS patients), 39.4% of the patients were hypertensive[19]. In INTERHERT study, 39.02% were hypertensive[20].

In our study, at enrolment, mean LDL level was 127mg/dl ± 33.855mg/dl (σ). Pre-event LDL level was controlled at <100mg/dl which is the recommended LDL level, for 22.1% of patients. Of these 22.1% of patients, 41.2% of patients were on statin. Remaining 77.9% of

enrolled patients had their LDL ≥100mg/dl which is above the recommended level. ESC SCORE II Diabetes and AHA/ACC ASCVD risk score were calculated on enrolment. SCORE II Diabetes was eligible for 67 patients. Most of the patients were in high risk (34.3%) and very high risk (64.2%). Similarly, ASCVD risk scores were calculated with mean of 19.6% ± 13.9% (σ). As per the ASCVD risk scoring, majority of the patients (97.1%) should have been on at least moderate intensity statin therapy with 2.9% of the patients should have been on recommendation of high intensity statin therapy. In the enrolled patients, only one patient was on the recommended intensity of statin therapy. Majority of the patients (79.2%) were not on any statin. If on statin, most of the patients (87.5%) were on low intensity statin. 43.8% of those who were on statin, regardless of the intensity of statin therapy, had their LDL level at the recommended level of <100mg/dl. In the 6month follow up post-enrolment, all the patients (72 patients compliant with the follow up) were on high intensity statin therapy. Median LDL in follow up was 57.50mg/dl with IQR 59.00mg/dl to 80.75mg/dl compared to median of 121.50mg/dl with IQR of 105.25mg/dl to 152.25mg/dl for the same set of 72patients. 50.0% of the patients had their LDL level at the recommended level of <55mg/dl. There was statistically significant drop in LDL level in the follow up with Wilcoxon signed Ranks test (z) of -7.352 with p value of <0.001. In comparison, study by Park et al observed total cholesterol of 201.5mg/dl±44.6mg/dl in ACS with diabetes. In the Korean study, 84.8% of the patients were on statin[17]. Koshizaka et al noted 74.8% of Asian diabetic patient presented with ACS to be on statin or any other lipid lowering drugs. Previously diagnosed history of hypercholesterolemia was present in 59.0% of patient[18]. In the MERIFACS study, mean LDL-C was 120mg/dl±36.6mg/dl and 70.2% of the patients has LDL-C≥100mg/dl[19]. Our current study only 20.8% of patients were on statin at enrolment.

In the current study, on enrolment, 10.4% of the patients were current smoker and 18.2% of patients were former smoker. In the 6 month follow up, 7 out of 8 patients quit smoking with 1 patient continued to smoke. In a 2012 study in Philippines by Merlin et al, 60% of the ACS patients were smoker which is much higher proportion probably due to cultural difference[21]. In the Korean study by Park et al,, current smoking comprised 22.5% and former smoker 15.8%[17]. Koshizaka et al reported 25.3% of the Asian patient to be current smoker.(18) In MERIFACS study, 28.3% were smoker[19]. In INTERHEART study, among AMI cases, 45.17% were current smoker and 20.02% were former smoker[20]. Thus significant proportion of the study population were current or former smoker. The difference in the proportion with our study population having lower smokers may have reflected the difference in the culture and time scale of the study.

Mean BMI of the enrolled patients was 24.1kg/m^2 ± 3.7 kg/m^2(σ). Only 28.6% of the patients were on ideal BMI of 18.5 kg/m^2 to 22.9 kg/m^2. In our study, 6.5% of the patients were underweight and vast majority 64.9% of the patients had their BMI ≥ 23 kg/m^2. In the 6month, follow up there was no significant change in the BMI with 68% of 72 patients in the follow up having BMI ≥ 23 kg/m^2. This observation may reflect the need for more persistent and longer period of monitoring. Park et al has observed BMI of 24.6 kg/m^2 ±3.1kg/m^2(σ)[17]. In the metanalysis by Koshizaka et al, mean BMI was 24.7kg/m^2.[18] In MERIFACS study, mean BMI

was 25.21kg/m^2 ± 4.1kg/m^2(σ) with 54.1% of the patients having BMI≥25kg/m^2 compared with 35.1% in our current study[19].Mean BMI were comparable with our current study.

The current study gave the overall poor quality of diabetic care in the patients presenting with ACS and/or heart failure and the need to improve the quality of care which may help in reducing the complications of diabetes.

6. Strength and limitations:

It was a single centre study. The sample size was relatively small. "Previously diagnosed dyslipidemia" was as per their previously consulted physician and there may be un-uniformity in the diagnostic criteria used. However, the findings in terms of glycemic control, blood pressure control, blood pressure control, target BMI were highly significant. It may have direct implication in our day today management of diabetic patients.

7. Conclusion

This study showed poor quality of diabetes mellitus care in patients presenting with ACS and/or HF in terms of glycemic control, blood pressure control, blood cholesterol control, BMI and smoking habits, and the need for further improvement in meeting the targets. Glycemic control was poor with mean HbA1c of 9.5% and 92.2% of the patients having HbA1c above 7%. Blood pressure were not controlled for 40.3% of patients. In our study, 79.2% of the patients were not on statin and those on statin were not on recommended intensity of statin therapy (except for 1.4% of the patient). SCORE II Diabetes or ASCVD score can further help in understanding risk stratification. In this study, mean SCORE II Diabetes score was 27% and median ASCVD score was 16.1%. 64.9% of the patients had their BMI ≥ 23Kg/m^2. 10% of this cohort of patient continued to smoke at admission despite heightened cardiovascular risk noted. Glycemic control, BP control and blood cholesterol control have improved in the 6month follow up. There was further improvement in the smoking cessation. However, BMI control may need a longer term and consistent approach. The need to educate both the patients and treating primary physicians for primary prevention by further emphasizing the needs to meet the targets of diabetic care cannot be overemphasized.

The study demonstrates that primary prevention in DM is far below the guideline directed levels with respect to HbA1C, Blood Pressure control, LDL cholesterol, statin treatment and BMI values.

REFERENCES

1. 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. - Abstract - Europe PMC [Internet]. [cited 2022 Dec 11]. Available from: https://europepmc.org/article/med/31591002
2. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care. 2010 Jan 1;33(Supplement_1):S62–9.
3. Gudbjörnsdottir S, Cederholm J, Nilsson PM, Eliasson B, for the Steering Committee of the Swedish National Diabetes Register. The National Diabetes Register in Sweden. Diabetes Care. 2003 Apr 1;26(4):1270–6.

4. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth Universal Definition of Myocardial Infarction (2018). Circulation [Internet]. 2018 Nov 13 [cited 2022 Jul21];138(20).Available from:https://www.ahajournals.org/doi/10.1161 /CIR.0000000000000617

5. 2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes. :83.

6. ACC/AHA Guidelines for the Management of Patients With Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction: Executive Summary and Recommendations. :17.

7. Bozkurt B, Coats AJ, Tsutsui H, Abdelhamid M, Adamopoulos S, Albert N, et al. Universal Definition and Classification of Heart Failure. J Card Fail. 2021 Apr;27(4):387–413.

8. www.heart.org [Internet]. [cited 2025 Jan 25]. Classes and Stages of Heart Failure. Available from: https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure

9. ESC CVD Risk Calculation App [Internet]. [cited 2024 Aug 16]. Available from: https://www.escardio.org/Education/ESC-Prevention-of-CVD-Programme/Risk-assessment/esc-cvd-risk-calculation-app, https://www.escardio.org/Education/ESC-Prevention-of-CVD-Programme/Risk-assessment/esc-cvd-risk-calculation-app

10. ascvd-risk-estimator-plus [Internet]. [cited 2024 Aug 16]. Available from: https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/

11. CKD-EPI Creatinine Equation (2021) | National Kidney Foundation [Internet]. [cited 2024 Aug 26]. Available from: https://www.kidney.org/ckd-epi-creatinine-equation-2021-0

12. MDCalc [Internet]. [cited 2024 Aug 26]. CKD-EPI Equations for Glomerular Filtration Rate (GFR). Available from: https://www.mdcalc.com/calc/3939/ckd-epi-equations-glomerular-filtration-rate-gfr

13. Obesity | National Health Portal Of India [Internet]. [cited 2022 Dec 10]. Available from: https://www.nhp.gov.in/disease/non_communicable_disease/obesity

14. ResearchGate [Internet]. [cited 2022 Dec 10]. Table 1 : WHO Asian-BMI classification. Available from: https://www.researchgate.net/figure/WHO-Asian-BMI-classification_tbl1_296026141

15. NHIS - Adult Tobacco Use - Glossary [Internet]. 2019 [cited 2022 Dec 10]. Available from: https://www.cdc.gov/nchs/nhis/tobacco/tobacco_glossary.htm

16. Ministry of Health NZ [Internet]. [cited 2022 Dec 10]. Definitions of smoking status. Available from: https://www.health.govt.nz/our-work/preventative-health-wellness/tobacco-control/tobacco-control-information-practitioners/definitions-smoking-status

17. Park SJ, Ha KH, Kim DJ. Body mass index and cardiovascular outcomes in patients with acute coronary syndrome by diabetes status: the obesity paradox in a Korean national cohort study. Cardiovasc Diabetol. 2020 Nov 10;19(1):191.

18. Koshizaka M, Lopes RD, Newby LK, Clare RM, Schulte PJ, Tricoci P, et al. Obesity, Diabetes, and Acute Coronary Syndrome: Differences Between Asians and Whites. Am J Med. 2017 Oct 1;130(10):1170–6.

19. Hygriv Rao B, Rama Raju NS, Srinivasa Raju CS, Patel P, Korabathina R, Raj JP, et al. Metabolic risk factors in first acute coronary syndrome (MERIFACS) Study. Indian Heart J. 2022 Jul 1;74(4):275–81.

20. Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. The Lancet. 2004 Sep 11;364(9438):937–52.

21. Merin E, Limpin ME, Ayuyao F, Guia T de. Burden of Smoking in Acute Coronary Syndrome. CHEST. 2012 Oct 1;142(4):1083A.