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Incidence of New Onset Diabetes Mellitus in Acute Coronary Syndrome Patients

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Introduction
Diabetes Mellitus

Diabetes mellitus is a group of diseases characterized by insufficient production of insulin or by the failure to respond appropriately to insulin, resulting in hyperglycemia. The mounting incidence and prevalence of type 2 diabetes, driven by increasing population age, obesity, and physical inactivity, compound this high global burden as does the increasing longevity of patients with diabetes.

Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases. In 2013, according to International Diabetes Federation, an estimated 381 million people had diabetes. Its prevalence is increasing rapidly, and by 2030, this number is estimated to almost double.

India has more diabetics than any other country in the world, according to the International Diabetes Foundation. According to the Indian Heart Association, India is the diabetes capital of the world with a projected 109 million individuals with diabetes by 2035. The disease currently affects more than 62 million Indians, which is more than 7.1% of India's adult Population. An estimate shows that nearly 1 million Indians die due to Diabetes every year. The average age on onset is 42.5 years. [1]

There is limited information on the incidence of diabetes in India. One such data source is the New Delhi Birth Cohort study, which reported an annual incidence of 1.0% for males and 0.5 % for females, even though this population was in the 4th decade of life. In a longitudinal cohort from Chennai, the incidence of diabetes was calculated as 20.2 per 1000 person years among subjects with prior normal glucose tolerance, and 64.8 per 1000 person years in those with prediabetes.[2] Kerala is the diabetes capital of India with a prevalence of diabetes as high as 20% ─ double the national average of 8%. In a large multicenter study involving nearly 20,000 subjects, the prevalence of diabetes in Thiruvananthapuram was 17% compared to 15% in Hyderabad and New Delhi, 4% in Nagpur and 3% in Dibrugarh. In a recent study Kerala, has reported an incidence rate of 138.2 per 1,000 person years among those in the prediabetic stage. Incidence of diabetes among people with normal glucose tolerance at baseline was 30.7 per 1,000 person years, while the incidence of prediabetes among people with normal glucose tolerance was 165.2 per 1,000 person years. The high incidence is attributed to a combination of genetic susceptibility plus

adoption of a high-calorie, low-activity lifestyle by India's growing middle class.[3] Additionally, a study by the American Diabetes Association reports that India will see the greatest increase in people diagnosed with diabetes by 2030. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India.

Coronary Artery disease

Cardiovascular diseases (CVD), comprising coronary heart (CHD) and Cerebro-vascular diseases, are currently the leading cause of death globally, accounting for 21.9 per cent of total deaths, and are projected to increase to 26.3 per cent by 2030. It may affect individuals at any age but becomes dramatically more common at progressively older ages, with approximately a tripling with each decade of life. Males are affected more often than females.

It is estimated that 60% of the world's cardiovascular disease burden will occur in the South Asian subcontinent despite only accounting for 20% of the world's population. This may be secondary to a combination of genetic predisposition and environmental factors.

CAD & Diabetes Mellitus

Of the risk factors, diabetes, and its predominant form, type 2 diabetes mellitus (T2DM), has a distinctive association with CHD. Those with diabetes have two- to four-fold higher risk of developing coronary disease than people without diabetes, and CVD accounts for an overwhelming 65-75 per cent of deaths in people with diabetes. [4]

The risk of New Onset Diabetes (NOD) is associated with many factors like diet, physical activity, medical conditions like hypothyroidism, CKD, family history, smoking, dyslipidemia, hypertension and with a wide variety of drugs including statins, thiazide diuretics, beta-blockers, glucocorticoids, niacin etc. [5]

Among patients with multivessel CAD and preserved left ventricular ejection fraction, whatever the treatment regimen is, rates of overall and cardiac-related deaths is high among diabetic compared with non-diabetic patients. [6]

Though much of data is available in patients already diagnosed with diabetes but data regarding the new onset diabetes in the subset of post PCI patients is very limited. The present study is the opportunity to look at the magnitude of NOD in this population subset aimed at detecting the incidence of NOD.

The outcomes from this study are expected to enhance our knowledge about the NOD in ACS patients and various measures that can be taken to improve it.

Background Study

A study conducted by *Kyeong-Hyeon Chun etal a*mong 6,777 patients who underwent DES implantation between January 2006 and December 2011, were analyzed. Out of them 6,048 patients were studied after exclusion of 729 pre-diabetic patients. After the PCI, statins were prescribed at discharge in 5,831 patients (96.4%), and 423 of them (7.3%) were treated with high dose statins. [5]

Materials and Methods

This is a Cohort study. 200 consecutive ACS patients in department of cardiology, Government Medical College, Trivandrum are taken up for study after having proper written and informed consent. A brief history including chief complaints; history of presenting & past illness; personal & family history; drug & addiction history was taken. The patients were also studied on several lab & biochemical parameters i.e. FBS; PPBS; Lipid profile; Hba1c which were studied at the time of admission, after discharge at 2 weeks, 6 weeks, 3,6 & 12 months post ACS.

Study Design: Cohort study.

Sample Size: With an estimated risk of 7.3% from available previous data and confidence level of 99% calculated sample size for present study is 178.

Study Period: April 2016 to March 2017 along with the CATH REGISTRY data of Department of Cardiology, Government Medical College Trivandurm.

Study Population: Any ACS patient admitted in the Department of Cardiology, Government Medical College, Trivandrum.

Study Centre: Department of Cardiology, Government Medical College, Trivandrum.

Sample Size Calculation

Population size(for finite population correction factor or fpc)(*N*):	1000000
Hypothesized % frequency of outcome factor in the population (*p*):	7.3%+/-1
Confidence limits as % of 100(absolute +/- %)(*d*):	1%
Design effect (for cluster surveys-*DEFF*):	1

Sample Size(*n*) for Various Confidence Levels	
Confidence Level(%)	Sample Size
95%	103
80%	44
90%	73
97%	126
99%	178
99.9%	290
99.99%	405
Equation	
Sample size $n = [DEFF*Np(1-p)]/ [(d^2/Z^2_{1-\alpha/2}*(N-1)+p*(1-p)]$	

Inclusion Criteria

- Any ACS Patient.

Exclusion Criteria

- Patients diagnosed to have diabetes mellitus at time of admission (As per standard definition: Hba1c > 6.5, FBS>126 mg/dl, 2 hour PPBS>200 mg/dl or RBS>200 mg/dl with symptoms consistent with diabetes mellitus)
- Patients who are already diagnosed or on treatment for diabetes mellitus.
- Patients who do not give consent for participation in the study.

Results and Discussion

The baseline characteristics of study population were comparable to prevalent characteristics of ACS patients quoted in several studies of the region. (Table 1)

There is limited information on the incidence of diabetes in India. One such data source is the New Delhi Birth Cohort study, which reported an annual incidence of 1.0% for males and 0.5 % for females, even though this population was in the 4th decade of life [117]. In a longitudinal cohort from Chennai, the incidence of diabetes was calculated as 20.2 per 1000 person years among subjects with prior normal glucose tolerance, and 64.8 per 1000 person years in those with prediabetes [7,8]

K. R. Thankappan et al studied incidence of diabetes in 326 industrial workers in kerala. At two years follow up, 13.3 % of the 241 workers who were either normal or had pre-diabetes at baseline developed diabetes providing an incidence rate of 6.65 % per year. Among the 134 workers with normal FPG at baseline 28.4 % progressed to pre-diabetes, 5.2 % developed diabetes, and among the 107 pre-diabetics, 23.4 % developed diabetes at year two. The odds of progressing to diabetes from pre-diabetes were five times higher compared to those from normal FPG (OR 5.53; CI 2.28–13.37). [9]

In our study New onset diabetes was detected in 20% (n=40) , Impaired Fasting Glucose in 2.5% (n=5) , Impaired glucose tolerance in 6% (n=12) and both Impaired fasting glucose and Impired Glucose tolerance in 1.5% (n=3) over a follow up period of 1 year out of total study population of 200. (Table 2)

The calculated incidence rate in our study is 0.2 per person per year, this is very high in comparison to available data on incidence of diabetes. This can be explained on the fact that the study population was selected from Acute coronary syndrome patients which itself is an absolute marker of presence of atherosclerotic vascular disease. Multiple comorbidities like dyslipidemia, obesity, Hypertension, smoking and genetic predisposition puts these patients at higher risk of coronary events as well as make them prone to develop new onset diabetes. Not only the comorbidities the presence of statins and beta blockers along with thiazide diuretics also adds

fuel to fire in new onset diabetes in these group of patients.

Kyeong-Hyeon Chun etal studied around 6,777 patients who underwent DES implantation between January 2006 and December 2011. At a median follow-up of 3.9 years, new onset diabetes occurred in 436 (7.2%) patients. This was a comparative and background study for our study but the incidence of new onset diabetes is far below than our study re-iterating the fact our countrymen are more predisposed to this illness. [5]

Another important data we got from our study While analyzing the time trends of Blood sugar & Hba1c levels of patients (Fig. 1,2 & 3), that most of the patients (n=37; 92.5%) who developed new onset diabetes in the first 6 months duration after the acute coronary event. Thus implicating that the latent diabetes gets clinically revealed very rapidly after occurrence of ACS. The time trends of FBS, PPBS and Hba1c clearly shows the gap between New onset diabetes patient and Control group starts diverging from 2 weeks onwards and gets maximally separated at 6 months then almost plateaus suggesting that derangement in glucose homeostasis occurs severely in first 6 month which then persist stationary. Atleast checking of blood sugars should be done atleast for first 6 months at every follow up after the acute coronary event so as to pick up any revealing latent new onset diabetes thus preventing morbidity and mortality arising out of it or its consequences.

In a study conducted to find NOD after renal transplant in 2014 founded that the need for more aggressive DM treatment (suggesting a worsening of DM status) was most usually seen between discharge and 3 months; 50% of patients with preexisting DM required more aggressive DM treatment post-transplantation ($X3(2) = 13.25$; P = .001) [10,11,12]. This study supports our finding relative rapid onset of Diabetes in predisposed individual.

**Table 1** Baseline characteristics of study population

Baseline Characteristics	N (200)	%
Mean Age	56.2 years	
Males	170	85
Dyslipidemia	84	42
Smoking	42	21
POAD	15	7.5
CKD	17	8.5
Hypothyroidism	71	35.5
F/H of ACS	73	36.5
F/H of DM	120	60
Drugs i.e steroids	0	0
Physically active	23	11.5
ACS -TYPE		
STEMI	119	59.5
NSTEMI	37	18.5
UA	44	22

Table 2 Number of Patients developed deranged Blood sugars and Hba1c in study population over one year

Impaired Blood Sugar Category	No.	%
NOD	40	20%
IFG	5	2.50%
IGT	12	6%
IFG+IGT	3	1.50%

Table 3: Incidence of NOD per person per year

No.	Person-time incident rate
40	0.2 person year

FIG. 1 TREND OF FBS IN STUDY POPULATION vs. NOD

FIG. 2 TREND OF PPBS IN STUDY POPULATION VS NOD

FIG.3 TREND OF Hba1c IN STUDY POPULATION VS NOD
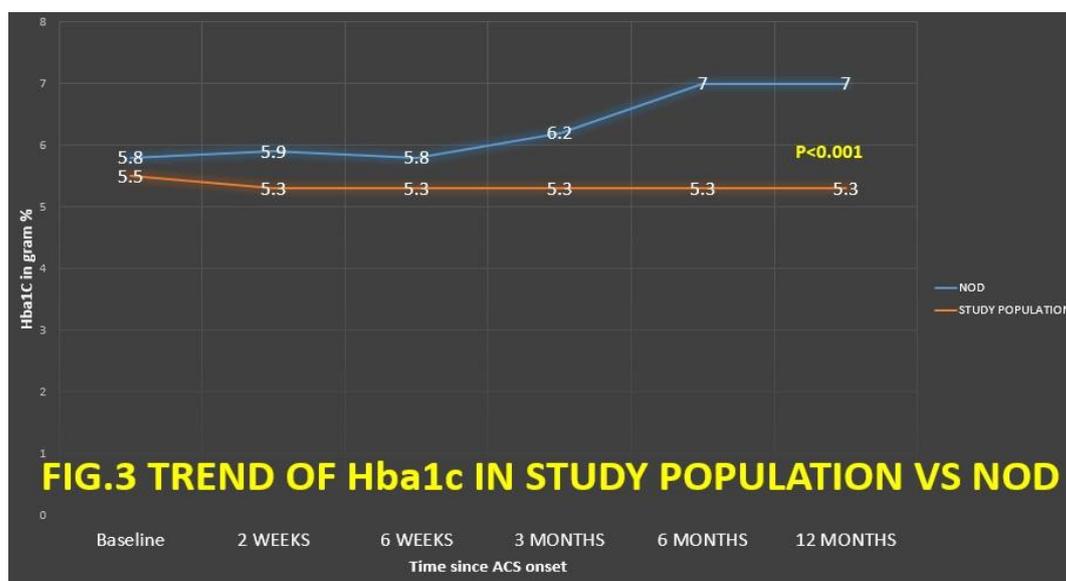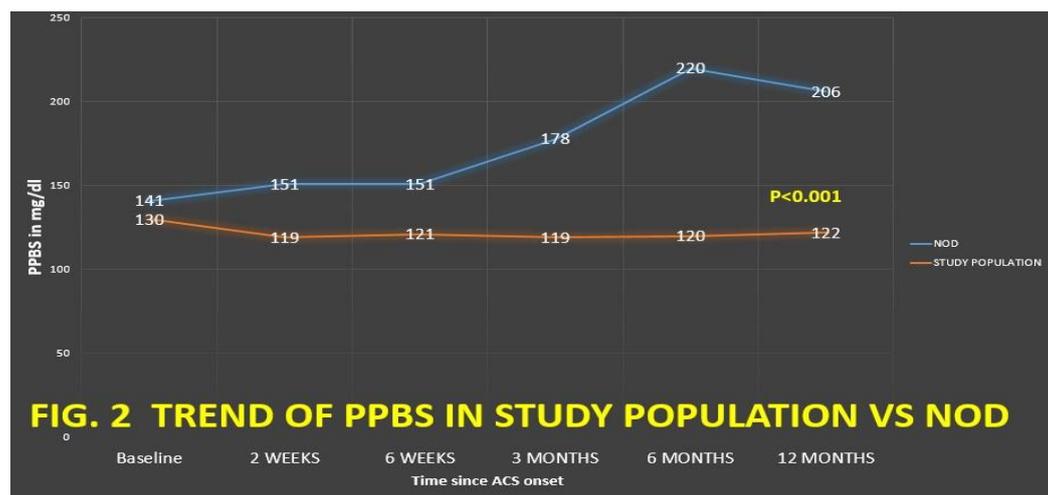
Conclusion

It is well known that diabetes itself is hallmark of complex atherosclerotic process with varying manifestations, causing morbidity and mortality. Coronary artery disease which is an end result of atherosclerotic vascular process has a bad impact

on patient health. Presence of diabetes worsens the outcomes in a Coronary artery disease patient by many times. This has been proved time and again in multiple studies. However, the occurrence of new onset diabetes in a coronary artery disease patient has not been studied well till date. With only miniscule data available on this subject, this study is a modest attempt to quantify the new onset diabetes in coronary artery disease patients after acute coronary syndrome.

This study highlights two important things, first incidence of new onset diabetes in acute coronary syndrome patients is High nearly three times more than the general population, Second the onset of diabetes is very rapid especially in the first six months after acute coronary syndrome.

Thus early and regular screening of blood glucose of Coronary artery patients should be done to prevent, detect and treat diabetes mellitus so as morbidity and mortality can be decreased.

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