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A study on the level of serum neopterin a new novel biomarker in acute myocardial infarction

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***Abstract*---Introduction:** Acute myocardial infarction (AMI) is one of the most common diseases, and it is one of the important medical emergencies admitted in the hospitals. It is characterized by the presence of clinical features like sudden onset of severe chest pain with dysponea, palpitation and profuse sweating leading to cardiac arrythmias, cardiogenic shock, cardiac failure and death if not treated early(2). Among the biomarkers for diagnosis and prognosis in AMI, the Neopterin, a pteridine derivative is considered to be one of the new novel bio-markers which is found to be elevated in patients with AMI. Neopterin was first isolated from larvae of bee in 1963(3). Eventually Neopterin was identified as the fluorescent component that was elevated in the urine of mice with Ehrlich ascites tumor (4). Estimation of Serum levels of Neopterin is a new novel biomarker in AMI and seems to be a prognostic marker for MACE in AMI. **Aim:** To elucidate the role of Neopterin levels and its short term prognostic significance in AMI. **Methods**: Neopterin is an activation marker for monocytes / macrophages and its circulating levels in the Serum is considered to be one of the prognostic markers in the treatment of AMI. **Results:** From the data illustrated in the Table No. 1 age matched statistical analysis

between the study group and the control group of age less than 45 years is analysed. The following results are obtained as the statistical outcome. The parameters are analysed between the study and the control group. Among the parameters, there is a significant difference in the levels ofCKMB (P Value < 0.05) which is statistically significant. **Conclusion:** To conclude Neopterin concentrations are usually increased in AMI. Highly elevated Neopterin concentrations are among the best predictors of adverse outcome in patients with AMI risk. This study postulates that Neopterin can be considered as a new novel Biomarker for the disease activity in AMI and also as a prognostic marker for risk stratification in AMI to prevent mortality and MACE.

***Keywords*---**Neoprotien, AMI, MACE.

Introduction

Acute myocardial infarction (AMI) is one of the most common diseases in hospitalized patients in industrialized countries. The early (30-day) mortality rate from AMI is ~30%, with more than half of these deaths occurring before the stricken individual reaches the hospital. Although the mortality rate after admission for AMI declined by ~30% over the past two decades, approximately 1 of every 25 patients who survives the initial hospitalization dies in the first year after AMI. Mortality is approximately four fold higher in elderly patients (over age 75) compared with younger patients [(1)]. AMI is one of the important medical emergencies admitted in the hospitals. It is characterized by the presence of clinical features like sudden onset of severe chest pain with dysponea, palpitation and profuse sweating leading to cardiac arrythmias, cardiogenic shock, cardiac failure and death if not treated early[(2)]. Among the biomarkers for diagnosis and prognosis in AMI, the Neopterin, a pteridine derivative is considered to be one of the new novel bio-markers which is found to be elevated in patients with AMI. Neopterin was first isolated from larvae of bee in 1963[(3)]. Eventually Neopterin was identified as the fluorescent component that was elevated in the urine of mice with Ehrlich ascites tumour[(4)]. Now it is proved that this is the exclusive product of monocytes / macrophages that have been stimulated by interferon gamma, a cytokine that is produced by activated T-lymphocytes and nature killer cells[(5)]. Biochemically Neopterin belongs to pteridines group. It is a catabolic product of guonosine-tri-phosphate [GTP]. Its molecular formula is $C_9H_{11}N_5O_4$. Its molecular mass is 253.215. Neopterin is synthesised from GTP via GTP cyclohydrolase (GTP-CH). The activity of GTP-CH can be greatly enhanced by interferon gamma [(6)]. 7,8 dihydroneopterintriphosphate (NH_2TP) is on the biosynthetic pathway of 5,6,7,8 tetrahydrobiopterin (BH_4). BH_4 represents the electron donor in the amino acid metabolic pathways. Human monocytes / macrophages lack the enzyme 6-pyruvoyl-tetra-hydro biopterin synthasewhich converts NH_2TP to 6-pyruvoyl-tetra-hydro biopterin. Thus, in these cells NH_2TP accumulates and after hydrolysis by phosphatases is excreted as dihydroneopterin or Neopterin [(7)]. Neopterin reflects the of monocytes / macrophages activity stimulated by interferon gamma, a cytokine that is produced by the activated T-lymphocytes

the nature killer cells[8]. Estimation of Serum levels of Neopterin is a new novel biomarker in AMI and seems to be a prognostic marker for MACE in AMI.

Aim & Objectives

To elucidate the role of Neopterin levels and its short termprognostic significance in AMI, the following objectives are formulated.

1. Estimation of levels of Serum Neopterin in AMI.
2. Significance of levels of Serum Neopterin during the treatment in the ICCU.
3. Correlation of levels of Serum Neopterin with the other cardiac risk factors.
4. The role of Neopterin for the prognostic stratification in AMI.

Materials And Methods

Neopterin is an activation marker for monocytes / macrophages and its circulating levels in the Serum is considered to be one of the prognostic markers in the treatment of AMI.

Inclusion Criteria: Patients admitted in the ICCU with the AMI and with the increased cardiac enzyme levels,ECG findings, ECHO findings and associated findings like Hypertension, Diabetes Mellitus and Hypercholesterolemia etc**.**
(2) The group of patients in the age group between 45 – 65 years were selected irrespective of the gender difference.

Exclusion Criteria:
1. Patients with features with Koch's lesion, atypical chest pain, renal transplant recently, malignant diseases and autoimmune diseases.
2. Patients who had recent blood transfusion.
   The patients who had fulfilled the above criteria were selected for the study. The present study is the estimation of the Serum Neopterin in patients with AMI and its short term prognostic significance during hospitalization. For this study 40 patients were selected as study group and 40 patients were selected as control group, based on the inclusion / exclusion criteria. The study groups were collected from the ICCU Department of Cardiology, JIMSH, Kolkata. After perfect centrifugation the blood samples were properly stored in the deep freezer. The control group were collected from the normal persons. Samples were centrifuged again before assay, to remove any particulate material. The Quantitative estimation of Serum Neopterin was done using Neopterin ELISA, Enzyme linked Immuno sorbent Assay for the In vitro Diagnostic Quantitative Determination of Serum Neopterin, obtained from IBLInternational.

(I) QUANTITATIVE DETERMINATION OF SERUM NEOPTERIN
(II) ESTIMATION OF CKMB: CKMB (Immuno inhibition / Modified IFCC Method)

(III) ESTIMATION OF GLUCOSE**:** GLUCOSE OXIDASE PEROXIDASE (GOD/POD) METHOD– MANUAL ANDAUTOANALYSER METHOD
(IV) ESTIMATION OF TOTAL CHOLESTEROL**:** The test is performed in the reagent kit by Enzymatic cholesterolesterase method.
(V) ACCUCARE TRIGLYCERIDES-SLR:METHOD: Enzymatic colorimetric test
(VI) ESTIMATION OF HDL - CHOLESTEROL**:**PHOSPHOTUNGSTATE METHOD.

Results & Discussion

Table No. 1. T-Test
Age Matched Statistical Analysis between the study group and thecontrol group age less than 45 years

Sl.No	Group	Mean	Std. Deviation	Statistical inference
1	**BP1**			T = .352
	Test (n=3)	136.67	30.551	P > 0.05
	Control (n=4)	130.00	20.000	Not Significant
2	**BP2**			T = .849
	Test (n=3)	90.67	4.163	P > 0.05
	Control (n=4)	85.50	9.713	Not Significant
3	**FBG**			T = 1.081
	Test (n=3)	119.33	37.541	P > 0.05
	Control (n=4)	99.50	4.726	Not Significant
4	**CK_MB**			T = 5.300
	Test (n=3)	45.33	10.066	P < 0.05
	Control (n=4)	16.50	4.123	**Significant**
5	**N**			T = 2.319
	Test (n=3)	22.57	13.568	P > 0.05
	Control (n=4)	7.21	1.635	Not Significant
6	**PH**			T = 2.390
	Test (n=3)	3.67	.577	P > 0.05
	Control (n=4)	3.00	.000	Not Significant
7	**MACE**			T = 2.390
	Test (n=3)	3.67	.577	P > 0.05
	Control (n=4)	3.00	.000	Not Significant
8	**D**			T = 2.390
	Test (n=3)	3.67	.577	P > 0.05
	Control (n=4)	3.00	.000	Not Significant
9	**SR.CHOLE**			T = 3.353
	Test (n=3)	193.33	17.898	P > 0.05
	Control (n=4)	153.50	13.772	Not Significant
10	**TGL**			T = -.374
	Test (n=3)	125.00	6.557	P > 0.05
	Control (n=4)	128.00	12.463	Not Significant
11	**HDL**			T = -1.036
	Test (n=3)	36.00	12.490	P > 0.05
	Control (n=4)	46.00	12.728	Not Significant
12	**LDL**			T = 3.166

Sl.No	Group	Mean	Std. Deviation	Statistical inference
	Test (n=3)	132.33	16.773	P > 0.05
	Control (n=4)	76.25	26.625	Not Significant
13	**VLDL**			T = -.319
	Test (n=3)	25.00	1.000	P > 0.05
	Control (n=4)	25.50	2.517	Not Significant

Df = 5

From the data illustrated in the Table No. 1 age matched statistical analysis between the study group and the control group of age less than45 years is analysed. The following results are obtained as the statistical outcome. The parameters are analysed between the study and the control group. Among the parameters, there is a significant difference in the levels of CKMB (P Value < 0.05) which is statistically significant. The other para meters between the study and the control group are notshowing statistically significant difference.

Table No. 2. (T-Test)
Age Matched Statistical Analysis between the study group and thecontrol group age between 45 to 55 years

Sl.No	Group	Mean	S.D	Statistical inference
1	**BP1**			T = .822
	Test (n=13)	130.31	17.997	P > 0.05
	Control (n=18)	125.44	14.901	Not Significant
2	**BP2**			T = .952
	Test (n=13)	85.85	9.881	P > 0.05
	Control (n=18)	83.11	6.106	Not Significant
3	**FBG**			T = .451
	Test (n=13)	113.38	27.488	P > 0.05
	Control (n=18)	109.11	24.916	Not Significant
4	**CK_MB**			T = 5.445
	Test (n=13)	47.15	21.575	P < 0.05
	Control (n=18)	18.67	4.887	**Significant**
5	**N**			T = 4.726
	Test (n=13)	37.55	28.227	P < 0.05
	Control (n=18)	6.28	1.160	**Significant**
6	**PH**			T = 5.191
	Test (n=13)	3.62	.506	P < 0.05
	Control (n=18)	3.00	.000	**Significant**
7	**MACE**			T = 6.155
	Test (n=13)	3.69	.480	P < 0.05
	Control (n=18)	3.00	.000	**Significant**
8	**D**			T = 3.799
	Test (n=13)	3.46	.519	P < 0.05
	Control (n=18)	3.00	.000	**Significant**
9	**Sr.chole**			T = 5.028
	Test (n=13)	213.08	32.607	P < 0.05
	Control (n=18)	166.83	18.402	**Significant**

Sl.No	Group	Mean	S.D	Statistical inference
10	**TGL**			T = -1.087
	Test (n=13)	121.00	12.281	P > 0.05
	Control (n=18)	128.22	21.493	Not Significant
11	**HDL**			T = -4.881
	Test (n=13)	34.31	7.005	P < 0.05
	Control (n=18)	47.89	8.065	**Significant**
12	**LDL**			T = 6.073
	Test (n=13)	154.46	34.452	P < 0.05
	Control (n=18)	93.50	21.443	**Significant**
13	**VLDL**			T = -.927
	Test (n=13)	24.15	2.609	P > 0.05
	Control (n=18)	25.44	4.488	Not Significant

Df = 29

From the Table No. 2. the data illustrated is the statistical analysis between the study group and the control group. In the age group of between 45 to 55 years. It is clear that the Serum levels of CKMB, Neopterin, Cholesterol, HDL, LDL are having statistically significant difference between the 2 groups at the P level P<0.05 significant.

The parameters like systolic Blood Pressure, diastolic blood pressure, FBG are not having significant difference between the two groups. P Value more than 0.05 not significant. The parameters like History of previous hospitalization, MACE and death are having significant difference between the two groups. P Value less than 0.05 significant.

Table No. 3. - T-Test Age Matched Statistical Analysis between the study group and thecontrol group age more than 55 years

Sl. No	**Group**	**Mean**	**S.D**	**Statistical inference**
1	**BP1**			T = .211
	Test (n=24)	127.00	22.341	P > 0.05
	Control (n=18)	125.78	11.680	Not Significant
2	**BP2**			T = .000
	Test (n=24)	83.67	9.898	P > 0.05
	Control (n=18)	83.67	7.236	Not Significant
3	**FBG**			T = .116
	Test (n=24)	106.42	19.675	P > 0.05
	Control (n=18)	105.61	25.435	Not Significant
4	**CK_MB**			T = 2.405
	Test (n=24)	41.33	21.902	P > 0.05
	Control (n=18)	26.28	17.306	Not Significant
5	**N**			T = 5.846
	Test (n=24)	25.68	13.413	P < 0.05
	Control (n=18)	7.05	1.551	**Significant**
6	**PH**			T = 2.124
	Test (n=24)	3.21	.415	P > 0.05

Sl. No	Group	Mean	S.D	Statistical inference
	Control (n=18)	3.00	.000	Not Significant
7	**MACE**			T = 4.140
	Test (n=24)	3.50	.511	P < 0.05
	Control (n=18)	3.00	.000	**Significant**
8	**D**			T = 2.124
	Test (n=24)	3.21	.415	P > 0.05
	Control (n=18)	3.00	.000	Not Significant
9	**SR.CHOLE**			T = 4.891
	Test (n=24)	213.63	40.858	P < 0.05
	Control (n=18)	163.39	17.161	**Significant**
10	**TGL**			T = .659
	Test (n=24)	135.08	18.606	P > 0.05
	Control (n=18)	130.28	28.617	Not Significant
11	**HDL**			T = -3.026
	Test (n=24)	34.83	9.361	P < 0.05
	Control (n=18)	43.33	8.506	**Significant**
12	**LDL**			T = 6.198
	Test (n=24)	151.71	36.901	P < 0.05
	Control (n=18)	92.22	19.681	**Significant**
13	**VLDL**			T = .745
	Test (n=24)	27.08	3.647	P > 0.05
	Control (n=18)	26.00	5.760	Not Significant

Df=40

From the Table 3. the data obtained is the age matched Statistical Analysis between the study group and the control group of age more than 55 years. From the table is clear that there is statistically significant difference between the study and the control groups for the following parameters like Serum Neopterin, MACE, Serum cholesterol, HDL. LDL. The P value Less than 0.05 significant. The statistical difference with the other parameters like systolic blood pressure, diastolic blood pressure, FBG, CKMB, pH, Death, TGL and VLDL isnot significant.
P value more than 0.05.

Table No. 4 (T – Test)
Sex Matched Statistical Analysis between the study group and thecontrol group
Females

Sl. No	Group	Mean	S.D	Statistical inference
1	**BP1**			T = -.071
	Test (n=12)	120.33	20.535	P > 0.05
	Control (n=13)	120.77	7.981	Not Significant
2	**BP2**			T = -.034
	Test (n=12)	80.67	10.491	P > 0.05
	Control (n=13)	80.77	3.113	Not Significant
3	**FBG**			T = -.387
	Test (n=12)	105.67	20.214	P > 0.05

Sl. No	Group	Mean	S.D	Statistical inference
	Control (n=13)	109.54	28.637	Not Significant
4	**CK_MB**			T = 5.429
	Test (n=12)	52.75	21.730	P < 0.05
	Control (n=13)	19.08	5.220	**Significant**
5	**N**			T = 5.268
	Test (n=12)	21.57	10.015	P < 0.05
	Control (n=13)	6.80	1.427	**Significant**
6	**PH**			T = 1.547
	Test (n=12)	3.17	.389	P > 0.05
	Control (n=13)	3.00	.000	Not Significant
7	**MACE**			T = 2.445
	Test (n=12)	3.33	.492	P > 0.05
	Control (n=13)	3.00	.000	Not Significant
8	**D**			T = 1.547
	Test (n=12)	3.17	.389	P > 0.05
	Control (n=13)	3.00	.000	Not Significant
9	**SR.CHOLE**			T = 4.497
	Test (n=12)	222.83	44.315	P < 0.05
	Control (n=13)	164.00	15.722	**Significant**
10	**TGL**			T = 1.022
	Test (n=12)	136.42	21.177	P > 0.05
	Control (n=13)	125.62	30.426	Not Significant
11	**HDL**			T = -3.595
	Test (n=12)	33.08	10.689	P < 0.05
	Control (n=13)	46.23	7.429	**Significant**
12	**LDL**			T = 5.743
	Test (n=12)	162.33	40.708	P < 0.05
	Control (n=13)	89.38	20.271	**Significant**
13	**VLDL**			T = 1.011
	Test (n=12)	27.33	4.141	P > 0.05
	Control (n=13)	25.23	6.002	Not Significant

Df = 23

Sex Matched Statistical Analysis between the study group and the control group Females

From the Table No. 4 Sex Matched Statistical Analysis between the study group and the control group in the Females is obtained. It is clear from the data that the parameters like CKMB level, Serum Neopterin level, Serum Cholesterol, HDL and LDL are having statistically significant difference between the control and the study groups. P Value Less than 0.05 significant. The other parameters like systolic blood pressure, diastolic blood pressure, FBG, history of previous hospitalisation, Death, TGL and VLDL are not showing statistically significant difference. P Value more than 0.05 not significant.

Table No. 5. (T- Test)
Sex Matched Statistical Analysis between the study group and the control group (Males) Control group (Males)

Sl. No.	Group	Mean	S.D	Statistical inference
1	**BP1**			T = .778
	Test (n=28)	132.43	20.780	P > 0.05
	Control (n=27)	128.59	15.270	Not Significant
2	**BP2**			T = .783
	Test (n=28)	86.71	8.798	P > 0.05
	Control (n=27)	84.96	7.733	Not Significant
3	**FBG**			T = .990
	Test (n=28)	111.36	24.897	P > 0.05
	Control (n=27)	105.15	21.431	Not Significant
4	**CK_MB**			T = 3.469
	Test (n=28)	39.57	19.687	P < 0.05
	Control (n=27)	23.22	14.833	**Significant**
5	**N**			T = 6.065
	Test (n=28)	32.62	22.172	P < 0.05
	Control (n=27)	6.68	1.436	**Significant**
6	**PH**			T = 4.749
	Test (n=28)	3.46	.508	P < 0.05
	Control (n=27)	3.00	.000	**Significant**
7	**MACE**			T = 7.411
	Test (n=28)	3.68	.476	P < 0.05
	Control (n=27)	3.00	.000	**Significant**
8	**D**			T = 4.103
	Test (n=28)	3.39	.497	P < 0.05
	Control (n=27)	3.00	.000	**Significant**
9	**SR.CHOLE**			T = 5.980
	Test (n=28)	207.25	32.929	P < 0.05
	Control (n=27)	163.93	18.562	**Significant**
10	**TGL**			T = -.816
	Test (n=28)	126.89	14.793	P > 0.05
	Control (n=27)	130.81	20.511	Not Significant
11	**HDL**			T = -4.249
	Test (n=28)	35.46	7.743	P < 0.05
	Control (n=27)	45.37	9.487	**Significant**
12	**LDL**			T = 7.371
	Test (n=28)	146.36	31.602	P < 0.05
	Control (n=27)	92.07	21.963	**Significant**
13	**VLDL**			T = -.530
	Test (n=28)	25.39	3.010	P > 0.05
	Control (n=27)	25.93	4.349	Not Significant

Df = 53

Males

From the Table No. 5 the data obtained is Sex Matched Statistical Analysis between the study group and the control group in males. From the data it is clear that the parameters like CKMB, Serum Neopterin, MACE, history of previous Hospitalization, Death, Serum Cholesterol, HDL and LDL are having statistically significant difference between the control and test groups. P Value less than 0.05 significant (P < 0.05). The other parameters like systolic blood pressure, diastolic blood pressure, FBG, TGL, VLDL are not showing statistically significant difference between control and the test group. P Value more than 0.05 not significant. (P < 0.05)

Table No- 6
Independent Samples Test For Serum Neoprotein Level between the control and the test group

Group Statistics					
	Group	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
N	Test	40	29.30	19.873	3.142
	Control	40	6.72	1.416	.224

Independent Samples Test										
		Levene's Test for Equality of Variances		**t-test for Equality of Means**						
		F	**Sig.**	**t**	**df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
									Lower	**Upper**
N	Equal variances assumed	23.181	.000	7.170	78	.000	22.59	3.150	16.315	28.858
	Equal variances not assumed			7.170	39.396	.000	22.59	3.150	16.216	28.956

From the table No. 6 the results obtained is the independent sample test between the study and the control group with respect to the levels of Serum Neopterin. The results obtained show that there is statistically highly significant difference between the study and the control group with respect to the Serum Neopterin levels. 0.000 Less than 0.05 less than P sig. 2 tailed. Highly Significant. (P < 0.000 < 0.05)

Table No. 7. T-Test One Sample statistical analysis in the study group between SerumCKMB and Serum Neopterin Level

One-Sample Statistics				
	N	**Mean**	**Std. Deviation**	**Std. Error Mean**

Neopterin	40	1.95	.221	.035
CK_MB	40	1.78	.423	.067

One-Sample Test						
	Test Value = 25					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Neopterin	- 660.475	39	.000	-23.05	-23.12	-22.98
CK_MB	- 347.333	39	.000	-23.23	-23.36	-23.09

From the Table No. 7. One Sample statistical analysis in the study group between Serum CKMB and Serum Neopterin Level. The results obtained show that there is significant statistical difference is found in the study group between Serum Neopterin levels and the Serum CKMB levels. 0.000 less than 0.05 less than P Value Highly Significant (P < 0.000 < 0.05) CKMB – Highly Significant in the study group with respect to Serum Neopterin Level.

Table No. 8.Crosstabs
Chi-Square Test
Neopterin more than 25 *MACE Cross tabulationStudy Group

Case Processing Summary						
	Cases					
	Valid		Missing		Total	
	N	%	N	%	N	%
N25 * MACE	40	100.0%	0	.0%	40	1%

N25 * MACE Cross tabulation					
			MACE		
			Negative	Positive	Total
N25	Less 25	Count	17	1	18
		% within N25	94.4%	5.6%	100.0%
	More 25	Count		22	22
		% within N25		100.0%	100.0%
Total		Count	17	23	40
		% within N25	42.5%	57.5%	100.0%

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	36.135(b)	1	.000		
Continuity Correction(a)	32.374	1	.000		
Likelihood Ratio	46.824	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	35.232	1	.000		
N of Valid Cases	40				
a Computed only for a 2x2 table					

b 0 cells (.0%) have expected count less than 5. The minimum expected count is 7.65.

From the Table No. 8. the data obtained is Chi-Square Test analysis between the Serum Neopterin levels more than 25 nmol/lit. and its association with MACE in the study group. The statistical inference obtained in the study group proves that there is statistically highly significant association between the Serum Neopterin levels more than 25 nmol/lit and the occurrence of the MACE. 0.000 Less than 0.05 Less than P Value. Highly Significant association between Serum Neopterin and MACE inthe study group. ($P < 0.000 < 0.05$).

Table No. 9.Crosstabs Chi-Square Test
Neopterin morethan 25 *Death Cross tabulationStudy Group

Case Processing Summary						
	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
N25 * D	40	100.0%	0	.0%	40	100.0%

N25 * D Crosstabulation					
			D		Total
			Negative	Positive	
N25	Less 25	Count	18		18
		% within N25	100.0%		100.0%
	More 25	Count	9	13	22
		% within N25	40.9%	59.1%	100.0%
Total		Count	27	13	40
		% within N25	67.5%	32.5%	100.0%

Chi-Square Tests					
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	15.758(b)	1	.000		
Continuity Correction(a)	13.179	1	.000		
Likelihood Ratio	20.679	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	15.364	1	.000		
N of Valid Cases	40				
a Computed only for a 2x2 table					
b 0 cells (.0%) have expected count less than 5. The minimum expected count is 5.85.					

From the Table No. 9 the result obtained is the Chi-Square Test analysis in the study group with respect to Serum Levels of Neopterin more than 25 nmol/lit and the occurrence of death in the study group. The statistical

inference is there is highly significant association between the Serum levels more than 25nmol/lit and the occurrence of death in the study group. 0.000 less than 0.05 less P value Highly significant association between the high levels of Serum Neopterin andthe occurrence of the Death. (P < 0.000 < 0.05)

Table No. 10. Chi-Square Test
N10 *Blood Pressure Cross tabulation

N1 * BP1G systolic

Sl. No	**Nepterin**	**BP1G**		**Statistical inference**
		Below 120 (n=23)	**above 120 (n=17)**	
1	Below10	1 (50%)	1 (50%)	X^2=.048Df =1 P < 0.05 Significant
2	more than 10	22 (57.9%)	16 (42.1%)	

Diastolic

Sl. No	**Nepterin**	**BP2G**		**Statistical inference**
		Below 80 (n=19)	**above 80 (n=21)**	
1	Below10	1 (50%)	1 (50%	X^2=.005Df =1 P < 0.05 Significant.
2	more than 10	18 (47.4%)	20 (52.6%)	

From Table No. 10 the data obtained is the Chi-square test analysis between the systolic blood pressure more than 120 mm of Hg. and its association with Serum Neopterin Levels more than 10nmol/lit. The results show that there is significant association between the systolic blood pressure and the Serum Neopertin levels more than 10nmol / lit. P Less than 0.05 significant.

From the same table the association between the diastolic bloodpressure more than 80mm of Hg. and the Serum Neopertin levels more than 10nmol/lit is obtained and it is found that the association between the two is significant. P Less than 0.05 significant. There is significant association between the Serum Neopertin and theHypertension. P < 0.000 < 0.05)

Table no 1. Spearman's correlations

	AGE	SEX	N	BP1	BP2	FBG	CK_MB	PH	MACE	D	SR. CHOLE	TGL	HDL	LDL	VLDL
AGE	1	.344(*)	-.178	-.165	-.234	-.058	-.146	-.406(**)	-.253	-.311	.217	.322(*)	.109	.185	.334(*)
SEX	.344(*)	1	-.279	-.325(*)	-.347(*)	-.092	.317(*)	-.282	-.320(*)	-.221	.158	.218	-.152	.248	.211
N	-.178	-.279	1	.315(*)	.363(*)	.224	-.312	.707(**)	.857(**)	.735(**)	-.270	-.132	-.081	-.286	-.117
BP1	-.165	-.325(*)	.315(*)	1	.878(**)	.079	-.254	.194	.230	.299	-.283	-.117	.036	-.359(*)	-.125
BP2	-.234	-.347(*)	.363(*)	.878(**)	1	.129	-.259	.324(*)	.234	.356(*)	-.351(*)	-.113	-.035	-.399(*)	-.116
FBG	-.058	-.092	.224	.079	.129	1	-.102	.166	.242	.332(*)	-.195	-.237	.058	-.162	-.235
CK_MB	-.146	.317(*)	-.312	-.254	-.259	-.102	1	-.056	-.127	-.222	.030	.038	.075	.012	.031
PH	-.406(**)	-.282	.707(**)	.194	.324(*)	.166	-.056	1	.666(**)	.565(**)	-.271	-.103	-.056	-.313(*)	-.109
MACE	-.253	-.320(*)	.857(**)	.230	.234	.242	-.127	.666(**)	1	.597(**)	-.287	-.138	-.031	-.313(*)	-.138
D	-.311	-.221	.735(**)	.299	.356(*)	.332(*)	-.222	.565(**)	.597(**)	1	-.433(**)	-.303	-.028	-.423(**)	-.279
SR. CHOLE	.217	.158	-.270	-.283	-.351(*)	-.195	.030	-.271	-.287	-.433(**)	1	.154	.254	.956(**)	.210
TGL	.322(*)	.218	-.132	-.117	-.113	-.237	.038	-.103	-.138	-.303	.154	1	-.331(*)	.106	.982(**)
HDL	.109	-.152	-.081	.036	-.035	.058	.075	-.056	-.031	-.028	.254	-.331(*)	1	.065	-.287
LDL	.185	.248	-.286	-.359(*)	-.399(*)	-.162	.012	-.313(*)	-.313(*)	-.423(**)	.956(**)	.106	.065	1	.158
VLDL	.334(*)	.211	-.117	-.125	-.116	-.235	.031	-.109	-.138	-.279	.210	.982(**)	-.287	.158	1
n	40	40	40	40	40	40	40	40	40	40	40	40	40	40	40

* Correlation is significant at the .05 level (2-tailed).
** Correlation is significant at the .01 level (2-tailed).

Spearman's Correlations

From Table No. 11 the Spearman's Correlations are statistically analysed between the Serum Neopterin levels more than 10nmol/lit and the various parameters taken for the study. The Serum Neopterin level more than 10 nmol/lit is having statistically highly significant relationship with the parameters like MACE, Death and thehistory of previous hospitalisation at the level 0.01 level (2 tailed) Highly Significant. The Serum Neopterin level more than 10nmol/lit is having statistically significant relationship with blood pressure (both systolic and diastolic) at 0.05level significant.

Frequency Table For Age Group And Sex

- 60% of patients are in the age group of more than 56 years.
- 32.5% of Patients are in the age group of 46 – 55 years.
- 7.5% of Patients are in the age group of below 45 years.

From the above data around 60% (ie) large group of AMI Patients arein the age group of more than 56 years. This data justifies that AMIoccurrence is directly proportional to the increase in age group.

AMI INCREASE AGE

This proves that as age advances the frequency of AMI occurrence is higher

- From the above data 70% of Patients are found to be males.
- 30% of Patients are found to be female.

From the data it is evident that Males are having high risk and more prone for AMI then females. It is justified that the occurrence of AMI is more common in males than the females.

Occurrence of AMI in Male > Occurrence of AMI in Female

Frequency For Systolic Blood Pressure

- From the above data 57.5% (23 patients) are having systolic Blood pressure below 120mm of Hg.
- 42.5% (17 Patients) are having systolic Blood Pressure more than 120.

According to the data the systolic blood pressure does not have any significant influence over AMI occurrence. According to the previous studies there is no significant correlation between a systolic blood pressure and the occurrence of AMI. The data justifies that there is no influence of the systolic blood pressure on the occurrence of AMI.

Frequency For Diastolic Blood Pressure

- From the above ta ble it is evident 52.5% (21 patients) are having diastolic Blood Pressure above 80mm of Hg.
- 47.5% (19 Patients) are having diastolic Blood Pressure less than 80mm of Hg.

From Table it is evident that there is significant correlation between the diastolic Blood Pressure and the occurrence of AMI. More than 50% of patients are having diastolic Blood Pressure above normal. From the data it is justified that the diastolic blood pressure is having influence on the occurrence of AMI.

Frequency Table For Fbg

From the data it is noted 72.5% (29 patients) are having fasting blood sugar below 120 and 27.5% (11 patients) are having fasting blood glucose more than 120. From the dat it is evident that the FBG does not influence the occurrence of AMI. According to the data around more than 70% of patients who had AMI are showing FBG within normal limits and around 27% of patients with AMI are having abnormal FBG.

Frequency Table For CKMB

From the data 77.5% (31 patients) are having CKMB levels more than 25, 22.5% (9 Patients) are having CKMB levels less than 25. From the above data it is clear that the levels of CKMB are increased in around 77.5% of patients with AMI and around 22.5% of patients with AMI are having CKMB levels within normal limits. This data justifies there is proportionate increase in the Serum level of CKMB in patients with AMI. Serum levels of CKMB is having influence on the occurrence of AMI.

Frequency Table For Neopterin

- From the above data 95% of patients (38 patients) are having Serum Neopterin level more than 10.
- 5% of patients (2 patients) are having Serum Neopterin level less than 10.

From the above data it is evident that Serum Neopterin level are more than normal in around 95% of patients with AMI and only 5% of patients is within normal limits. This justifies that there is highly significant correlation between SerumNeopterin and the occurrence of AMI.

Serum Neopterin AMI.

Frequency For Previous Hospitalisation

- From the above data it is noted 62.5% (25 patients) are presented with previous history of hospitalisation.
- 37.5daa (15 patients) are not presented with previous history of hospitalisation.

From the above table it is evident that there is no proportionate correlation between the occurrence of AMI and the previous history ofhospitalisation.

Frequency For Mace

- the above illustration 57.5% (23 patients) are having 'B' response(+)
- 42.5% (17 patients) are in the A response (–)

From the above data it is clear that the occurrences of MACE is associated in more than 50% of patients with AMI and around less than 50%of patients are not associated with MACE with AMI. From this data it is justified that the occurrence of the MACE has significantcorrelation in patients with AMI.

MACE AMI

Frequency Table For Death

- From the above data it is found 67.5% (27 Patients) are in the A response 32.5% (13 patients) are in the B response.

From the above data the mortality rate in patient with AMI is less than 50% that is around 32.5% of patients and the remaining 67.5% of patients are discharged without mortality. The mortality rate can further be reduced by early detection and intervention of MACE during hospitalisation.

Frequency For Serum Cholesterol

From the table it is evident that more than 50% of patients with AMI arehaving Serum Cholesterol level more than 200 mg/dl. Therefore the high Serum cholesterol levels are having influence over the occurrence of AMI.

Increased Serum Cholesterol occurrence of AMI

Frequency For Serum Hdl

From the table it is evident that around 75% of patients with AMI are having Serum HDL levels less than 40 mg/dl and remaining 25% of patients with AMI are having HDL levels more than 40mg/dl.

Serum HDL 1/ occurrence of AMI.

Therefore from the table it is evident that low level of HDL is having influence over the occurrence of AMI. The high levels of Serum HDL will prevent the occurrence of AMI.

The present study was undertaken in patients who were admitted with clinical features of AMI in ICCU Thanjavur Medical College, Thanjavur. The study was started during November 2009 and was concluded during June 2010. The patients were in the age group of between 45 – 65 years including both genders with or without associated risk factors like Hypertension, Diabetes Mellitus, Hypercholesterolemia, etc. The levels of Serum Neopterin were estimated both in the study group and the control group and the levels were statistically correlated with other biochemical factors and clinical features.
Serum Neopterin levels were more than normal in the entire study group which signifies that Serum Neopterin levels were increased in AMI. The statistical correlation between the high levels of Neopterin and AMI was found to be highly significant [P(0.000) at 0.01 level 2 tailed]. In contrast Serum Neopterin level were found to be within normal limits in the control group which signifies that there is no disease activity in this group.

The high Serum Neopterin levels were associated with Massive Adverse Cardiac Events (MACE) like Cardiac Arrythmias, Cardiac Blocks, Cardiogenic Shock, Cardiac Failure, etc. The correlation between the higher levels of Serum Neopterin more than 25 nmol/lit and the occurrence of MACE in the patients was statistically significant [P (0.000) at 0.01 level 2 tailed].

Hence, Neopterin can be considered not only as a biomarker for disease activity but also a prognostic marker to identify the high risk patients during treatment and to implement emergency and essential medical intervention to prevent mortality. The study group with high Serum Neopterin levels were followed up critically during their hospitalisation and it is evident from the study that the occurrence of MACE and mortality is highly significant [P(0.000) at 0.01 level 2 tailed]. According to the above study it is proved that Serum levels of Neopterin can be considered as an independent biomarker for the disease activity and for the prognostic activity in AMI.

There is correlation between Serum Neopterin more than 25 nmol/lit and with previous history of hospitalisation and there is statistically significant correlation [P(0.000) at 0.01 level 2 tailed]. There is significant correlation with high levels of Serum Neopterin more than 25 and the occurrence of Death in patients with AMI. The statistical analysis shows that highly significant correlation [P(0.000) at 0.01 level 2 tailed] is found.

Apart from the above the Serum Neopterin levels were correlated with other biochemical markers like fasting blood glucose, lipid profile, CKMB levels and hypertension. A significant correlation was found between the levels of Serum Neopterin and CKMB levels in the study group. And this correlation was found to be statistically significant [P(0.000) at 0.01 level 2 tailed].

Serum Neopterin levels were compared with fasting blood glucose, lipid profile and the correlation was found to be not significant statistically. The Serum Neopterin levels were correlated in the study group who had hypertension and there is significant correlation.

From these studies the major finding is that Neopterin, a biomarker for monocyte / macrophage activation and it is a prognostic marker to predict adverse cardiac events in patients suffering from AMI. When the levels of CKMB were added the disease activity was proved even stronger due to the statistically significant correlation that exists between higher Serum Neopterin levels and higher CKMB levels.

The studies reviewed, have demonstrated that Neopterin level is an important predictor of future cardiac as well as vascular adverse event. In particular, Neopterin levels predict future major cardiac and vascular adverse events in patients presenting with chronic coronary artery disease with acute coronary syndromes. In those with many of the above cited studies underline the strong association between high Neopterin levels and complex atherosclerotic lesions but not with disease extension giving account for the prognostic properties of Neopterin. This renders this molecule a useful marker of atherosclerotic plaque activity, permitting the identification of the subjects at highest risk for MACE.

Taken together, observations from all the studies reviewed propose the existence of a strong link between high Neopterin levels and cardiovascular risk profile, suggesting a potential clinical use of Neopterin as a marker for disease activity in subjects with cardiovascular disease. This could help in identifying patients who are at a higher risk of developing cardiovascular adverse events who might benefit from urgent preventive strategies exploitation or extensive diagnostic work-up, as well as actual therapy, depending from their co-morbidities.

Conclusion

In this study it is proved that monocyte / macrophage activation in AMI is reflected by the levels of Neopterin and a strong correlation was found between high levels of Neopterin and MACE. To conclude Neopterin concentrations are usually increased in AMI. Highly elevated Neopterin concentrations are among the best predictors of adverse outcome in patients with AMI risk. Braunwald had initially proposed risk stratification based on the History, Physical examination and Electrocardiogram. The American college of Cardiology / American Heart Association guide lines Committee later refined and incorporated cardiac markers for risk stratification. This study postulates that Neopterin can be considered as a new novel Biomarker for the disease activity in AMI and also as a prognostic marker for risk stratification in AMI to prevent mortality and MACE.

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