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The Relationship between Serum Hemoglobin and Creatinine Levels and Intra-Hospital Mortality and Morbidity in Acute Myocardial Infarction

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ABSTRACT

***Background*:** Studies have shown that Glomerular Filtration Rate (GFR) and Hemoglobin (Hb) concentrations are two predictive values for ST-elevation Myocardial Infarction (MI) mortality.

***Objectives*:** This study aimed to investigate the relationship between GFR and Hb concentrations and intra-hospital mortality and electrocardiographic (ECG) and echocardiographic abnormalities in ST-elevation MI patients admitted to a highly equipped hospital in Mashhad. The results will help define some factors to manage these patients more efficiently.

***Patients and Methods*:** This descriptive study aimed to assess the relationship between Hb and GFR concentrations and mortality and morbidity among 294 randomly selected patients with ST-elevation MI. Echocardiography, ECG, and routine laboratory tests, including Hb and creatinine, were performed for all the patients. Then, the data were entered into the SPSS statistical software, version 16 and were analyzed using chi-square, t-test, and ANOVA. $P < 0.05$ was considered as statistically significant.

***Results*:** Intra-hospital mortality rate was 10.5%. Besides, the results showed higher levels of serum blood sugar ($P < 0.001$), higher levels of creatinine ($P < 0.001$), lower levels of GFR ($P < 0.001$), lower ejection fraction ($P < 0.001$), higher grades of left ventricular diastolic dysfunction ($P = 0.002$), and lower mean Hb concentration ($P = 0.022$) in the dead compared to the alive cases. Besides, the patients with mechanical complications had lower Hb levels ($P = 0.008$). The results showed no significant relationship between creatinine level and mechanical and electrical complications ($P = 0.430$ and $P = 0.095$, respectively). However, ejection fraction was significantly associated with GFR ($P = 0.016$).

***Conclusions*:** According to the results, low levels of Hb and GFR could predict mortality caused by ST-elevation MI and ECG abnormalities could notify intra-hospital death. Moreover, lower Hb levels were associated with mechanical complications and could be used as a parameter for diagnosis of high-risk patients.

►*Implication for health policy/practice/research/medical education:*
Practitioners can consider and use Hb and GFR as two important criteria for prediction of mortality and morbidity.

1. Background

Ischemic Heart Disease (IHD), including Myocardial Infarction (MI), is one of the major causes of mortality and morbidity in developed countries. IHD is responsible for 19.6% of total deaths in the world (1). Besides, 30-day mortality and disability rate caused by Acute Myocardial Infarction (AMI) is almost 30%. IHD is a condition occurred by insufficient blood flow to myocardium mainly caused by

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atherosclerosis, which narrows epicardial coronary arteries. Some of the major risk factors of atherosclerosis are high levels of Low-Density Lipoprotein (LDL), low levels of High-Density Lipoprotein (HDL), cigarette smoking, Hypertension (HTN), and diabetes mellitus. Additionally, age, Left Ventricular (LV) function, and location and severity of coronary artery narrowing are some of the most important prognostic indicators in IHD (2).

A study in the U.S. showed that low levels of Hemoglobin (Hb) and creatinine clearance, as two routine laboratory tests, significantly increased the risk of death in ST-elevation MI patients treated with fibrinolysis or primary angioplasty (3). Low levels of Hb (< 100 mg/dL in females and < 110 mg/dL in males) (4) and Hb concentrations > 17 mg/dL increased mortality due to Acute Coronary Syndrome (ACS), including ST-elevation and non-ST-elevation MI. Anemia also has the potential to worsen myocardial ischemia both by decreasing the oxygen content of the blood supplied to the jeopardized myocardium and by increasing myocardial oxygen demand (5). Although precise mechanisms of the interaction between impaired renal function and coronary artery disease and their associated mortality have not been clarified (6), impaired GFR, even a mild decrease in GFR (between 60 and 90 ml per min per 1.73 m^2), is a major risk factor for mortality and morbidity in AMI (7).

2. Objectives

The present study aims to investigate the relationship between GFR and Hb concentrations and intra-hospital mortality and morbidity, including Electrocardiographic (ECG) abnormalities and mechanical complications (echocardiographic abnormalities), in ST-elevation MI patients admitted to a highly equipped educational hospital in Mashhad (a metropolitan in Northeast of Iran). The results will help define some factors to predict occurrence of mechanical complications, electrical complications, and death and apply them to identify and manage high-risk patients.

3. Patients and Methods

This cross-sectional study was conducted on 300 cases of AMI admitted to Ghaem hospital diagnosed by ECG changes (ST-elevation more than 1 mm in anterior leads and more than 2 mm in precordial leads) and rise in blood Troponin I (TPI) level measured by Delaware Biotech kits (TPI > 1 ng/mL was considered positive). The patients with cardiogenic shock and those with history of kidney disease, peritoneal dialysis or hemodialysis, and blood transfusion were excluded from the study. The study participants were randomly selected from the archive of Ghaem Hospital using the table of random numbers. Information about age, gender, history of cigarette smoking, history of previous MI (more than 1 month ago), consumption of antihypertensive drugs (Beta blockers, diuretics, ACE inhibitors, and ARBs) and diabetes drugs (subcutaneous insulin, metformin, and gelibenclamide), and intra-hospital death was inserted in the checklists. Systolic and Diastolic Blood Pressure (SBP and DBP) were measured at patients' arrival to the hospital and BP ≥ 140/90 mmHg or history of using hypertensive drugs was determined as HTN. Levels of blood sugar, creatinine, Triglyceride (TG), and total cholesterol were measured by Pars Azmoon kits (mg/dL). Besides, Hb concentration (mg/dL) was measured using Sysmex K21 at the local laboratory of the hospital on the first day of admission. Hypercholesterolemia was defined as total cholesterol > 200 mg/dL or consumption of anti-lipidemic drugs, mainly statins. Additionally, TG > 250 mg/dL was called hypertriglyceridemia. GFR was calculated using MDRD calculator based on age, race, gender, and serum creatinine level. Classical 12-lead ECG was performed for all the patients at least once and electrical complications, including PSVT, VF, VT, PVC, AF, BBB, PAC, complete heart block, and AV block, were noted. Ejection Fraction (EF), LV diastolic dysfunction (based on diastolic filling pattern defined as Grades 1, 2, and 3) (1), pericardial effusion, tamponade, rupture of heart, LV clot, VSR, MR, and TR, known as mechanical complications, were determined by transthoracic echocardiography during the admission. After all, the data were entered into the SPSS statistical software, version 11.5 and were analyzed using chi-square test and one-way ANOVA. $P < 0.05$ was considered as statistically significant.

4. Results

This study was performed on 294 out of the 300 patients 10.5% of whom (31 cases) died in the hospital. Most of the dead cases were female ($P = 0.020$) and had higher mean age ($P = 0.010$), lower means of SBP ($P = 0.002$), higher means of serum blood sugar ($P < 0.001$), lower levels of GFR ($P < 0.001$), higher levels of creatinine ($P < 0.001$), decreased EF ($P < 0.001$), higher grades of LV diastolic dysfunction ($P = 0.002$), slightly lower Hb concentrations ($P = 0.022$), and lower DBP (Table 1). The results showed a significant association between intra-hospital mortality and consumption of ACE inhibitors or ARBs ($P = 0.018$) and aspirin ($P = 0.041$). Accordingly, 64.5% and 56% of the dead cases had not consumed aspirin and ACE inhibitors or ARBs, respectively. Also, a significant relationship was observed between intra-hospital deathand electrical complications irrespective of the type of complication ($P = 0.004$).

Furthermore, different concentrations of Hb; i.e., < 11, 11 - 13, 13 - 15, and > 15 mg/dL, were significantly associated with age ($P = 0.001$), gender ($P < 0.001$), smoking ($P < 0.042$), SBP ($P < 0.001$), and DBP ($P < 0.001$). In addition, the cases that had consumed statins and aspirin had lower Hb concentrations. Although there was no relationship between different Hb concentrations and mechanical complications ($P = 0.251$), the mean Hb concentration was lower in the patients with mechanical complications ($P = 0.008$). However, this was not the case in the patients with electrical complications (Table 2).

The patients with lower levels of GFR tended to be older ($P < 0.001$), female ($P < 0.001$), and non-smoker ($P = 0.025$) and had lower SBP ($P = 0.013$), higher levels of blood sugar ($P < 0.001$), and lower EF ($P = 0.016$). Moreover, the patients who had the history of consumption of ACE inhibitors or ARBs had lower GFR levels. The patients with lower GFR levels also had lower Hb concentrations ($P = 0.008$). However, GFR level was not associated with electrical and mechanical

Table 1. Relationship between Intra hospital and Baseline Characteristics

Baseline Characteristics		Intra Hospital Death		P value
		Yes (n = 31)	No (n = 263)	
Age [a]		70.77 ± 10.39	61.94 ± 14.16	0.001
Gender [b]	Male	15 (7.7)	181 (92.3)	0.021
	Female	16 (16.3)	82 (83.7)	
Smoking [b]		10 (8.2)	112 (91.8)	0.182
Previous MI [b]		6 (9.5)	57 (90.5)	0.488
MI location [b]	Anterior	1 (2.7)	36 (97.3)	c
	Antero septal	5 (14.7)	29(85.3)	
	Extensive anterior	11 (16.9)	54 (83.1)	
	Posterior	0	6 (100)	
	Posterior inferior	0	27 (100)	
	Isolated inferior	0	26 (100)	
	Inferior + RV	5 (15.3)	28 (84.7)	
	Inferior posterior RV	5 (23.8)	16 (76.2)	
	Others	1 (10.0)	9 (90.0)	
Statin [b]		6 (15.0)	34 (85.0)	0.248
SBP [a]		112.78 ± 32.67	129.52 ± 25.18	0.002
DBP [a]		75.71 ± 16.22	81.41 ± 15.05	0.099
BS [a]		241.36 ± 145.65	163.17 ± 90.60	< 0.001
Hb [a]		12.06 ± 2.76	13.37 ± 2.04	0.020
Cr [a]		2.21 ± 1.96	1.20 ± 0.97	< 0.001
GFR [a]		44.71 ± 29.68	67.72 ± 25.69	< 0.001
Diabetic drugs [b]		7 (16.7)	35 (83.3)	0.132
Aspirin [b]		11 (18.3)	49 (81.7)	0.041
B blockers [b]		10 (14.1)	61 (85.9)	0.156
ACEI or ARBs [b]		11 (16.4)	56 (83.6)	0.018
Cholesterol [a]		171.12 ± 77.72	174.97 ± 45.42	0.750
Triglyceride [a]		122.65 ± 41.29	116.86 ± 52.57	0.658
EF [a]		28.41 ± 16.28	41.32 ± 11.83	< 0.001
LV diastolic dysfunction [b]	Normal	24 (13.3)	157 (86.7)	0.002
	Grade 1	2 (2.3)	85 (97.7)	
	Grade 2	1 (7.1)	13 (92.9)	
	Grade 3	4 (33.3)	8 (66.7)	
	Normal	15 (10.0)	134 (90.0)	
	Pericardial effusion	1 (50.0)	(50.0)	
Mechanical complications [b]	Tamponade	0	1 (100.0)	c
	LV clot	1 (50.0)	1 (50.0)	
	MR	13 (9.4)	125 (90.6)	
	TR	1 (50.0)	1 (50.0)	
Electrical complications [b]	Normal	20 (8.2)	224 (91.8)	c
	VF	0	3 (100.0)	
	PVC	1 (33.3)	2 (66.7)	
	AF	2 (40.0)	3 (60.0)	
	BBB	5 (19.3)	21 (80.7)	
	PAC	1 (25)	3 (75)	
	Complete heart block	0	2 (100)	
	AV bloc	2 (28.6)	5 (71.4)	

Abbreviations: MI, Myocardial Infarction; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; BS, Blood Sugar; Hb, Hemoglobin; Cr, Creatinine; GFR, Glomerular Filtration Rate; EF, Ejection Fraction

[a] Mean ± SD; [b] N (%); [c] Impossible to statistical analysis because of limited number of cases

complications and LV diastolic dysfunction. The relationships between GFR and other parameters have been presented in Table 3. The results also indicated that previous MI, serum cholesterol level, serum TG level, HTN, MI location, taking diabetes drugs, and B-blockers consumption, were not related to intra-hospital death and different GFR and Hb concentrations.

5. Discussion

Similar to the previous studies (3, 6-9), the findings of the present study showed that lowers levels of GFR and higher levels of creatinine were strongly associated with intra-hospital death and could, thus, be used as a predictive parameter for intra-hospital death, but the mechanism still remains unclear. According to the study results, LVEF was

Table 2. Baseline Characteristics Stratified by Hemoglobin (mg/dL)

Baseline Characteristic	All Patients	< 10.9 mg/dL (12.6%) (Group 1)	11 - 12.9 mg/dL (29.6%) (Group 2)	13 - 14.9 mg/dL (36.5%) (Group 3)	> 15 mg/dL (21.1%) (Group 4)	Total P value Between Groups	Sig Post Hoc
Age [a]	62.8 ± 13.9	68.3 ± 13.6	65.3 ± 13.1	61.7 ± 13.6	57.8 ± 13.9	0.001	e,g
Male sex [b]	190(66.7)	14(38.9)	47(55.3)	81(77.9)	48(80.0)	< 0.001	
Smoking [b]	118(41.4)	7(19.4)	38(44.7)	46(44.2)	27(45.0)	0.048	
Previous MI [b]	63(22.1)	6(16.7)	24(28.2)	21(20.2)	12(20.0)	0.416	
SBP [a]	128.5 ± 25.9	117.2 ± 24.0	121.2 ± 23.8	133.8 ± 26.1	136.6 ± 24.9	< 0.001	d, e, f, g
DBP [a]	81.0 ± 15.2	74.8 ± 11.4	77.0 ± 14.4	84.5 ± 16.5	83.9 ± 13.6	< 0.001	d, e, f, g
BS (mg/dL) [a]	170.0 ± 100.1	195.1 ± 116.7	158.4 ± 92.0	161.0 ± 80.4	186.9 ± 125.6	0.122	
GFR (mL/min) [a]	65.6 ± 26.5	53.1 ± 26.9	62.4 ± 23.3	68.8 ± 26.4	72.1 ± 27.9	0.003	d, e
Diabetic drug [b]	40(14.0)	9(25.0)	12(14.1)	12(11.5)	7(11.7)	0.221	
Aspirin [b]	59(21.8)	7(20.6)	21(27.6)	22(21.8)	9(15.0)	0.365	
B blocker [b]	69(25.9)	8(24.2)	20(27.0)	27(27.3)	14(23.3)	0.940	
Statins [b]	38(14.1)	9(26.5)	12(16.0)	14(14.0)	3(5.0)	0.035	
ARB or ACE Inhibitors [b]	65(24.1)	13(37.1)	20(26.0)	21(21.2)	11(18.6)	0.186	
Hypertension [b]	170(60.3)	21(58.3)	51(61.4)	63(61.2)	35(58.3)	0.972	
Hyper TG [b]	8(3.2)	1(3.4)	3(4.1)	1(1.1)	3(5.4)	0.514	
Hyper Chol [b]	91(34.2)	11(34.4)	30(38.0)	29(29.6)	21(36.8)	0.659	
EF [a]	40 ± 12	39 ± 12	41 ± 13	40 ± 14	39 ± 10	0.05	
Mechanical complication [b]	141(49.5)	21(58.3)	46(54.1)	50(48.1)	24(40.0)	0.251	
Electrical complication [b]	49(17.2)	6(16.7)	17(20.0)	14(13.5)	12(20.0)	0.609	
LV diastolic dysfunction [b]	285(90.5)	35(97.2)	77(90.6)	95(91.3)	51(85.0)	0.251	
Intra hospital Death [b]	27(9.5)	8(22.2)	8(9.4)	8(8.7)	2(3.3)	0.023	

Abbreviations: MI, Myocardial Infarction; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; BS, Blood Sugar; GFR, Glomerular Filtration Rate; TG, Triglyceride; Chol, Cholesterol; EF, Ejection Fraction

[a] Mean ± SD; [b] N (%); [c] P value between group 1 and 2; [d] P value between group 1 and 3; [e] P value between group 1 and 4; [f] P value between group 2 and 3; [g] P value between group 2 and 4; [h] P value between group 3 and 4

Table 3. Baseline Characteristics Stratified by GFR (mL/min/1.73 m^2)

Basic Characteristics	All Patients	< 29.9 (Group 1)	30 - 59.9 (Group 2)	> 60 (Group 3)	Total P Value between Groups	Significant Post Hoc
Age [a]	63.1 ± 13.9	72.0 ± 10.7	67.1 ± 13.7	59.4 ± 13.2	< 0.001	d, e
Male sex [b]	186(66.7)	7(3.8)	58(31.2)	121(65.1)	< 0.001	
Smoking [b]	102(36.4)	4(3.9)	33(32.4)	65(63.7)	0.172	
Previous MI [b]	58(22.1)	4(6.9)	21(36.2)	33(56.9)	0.956	
SBP [a]	127.8 ± 26.2	113.8 ± 32.0	126.0 ± 24.7	130.9 ± 25.7	0.013	e
DBP [a]	80.9 ± 15.2	75.6 ± 15.4	79.2 ± 14.5	82.4 ± 15.5	0.092	
BS (mg/dL) [a]	171.3 ± 99.3	229.5 ± 117.4	186.8 ± 116.3	153.7 ± 79.0	< 0.001	d, e,
Hb (mg/dL) [a]	13.2 ± 2.1	11.9 ± 2.8	12.9 ± 2.1	13.6 ± 2.0	0.008	d, e
Cr (mg/dL) [a]	1.3 ± 1.1	3.8 ± 3.1	1.4 ± 0.3	0.9 ± 0.2	< 0.001	c, d, e
Diabetic drug [b]	41(14.0)	4(9.8)	20(48.8)	17(41.5)	0.105	
Aspirin [b]	58(21.8)	6(10.3)	20(34.5)	32(55.2)	0.805	
B blocker [b]	69(26.4)	7(10.1)	23(33.3)	39(56.5)	0.747	
Statins [b]	39(14.1)	5(12.8)	17(43.6)	17(43.6)	0.152	
ARB or ACE Inhibitors [b]	65(24.3)	7(10.8)	31(47.7)	27(41.5)	0.010	
Hypertension [b]	169(60.3)	13(7.7)	65(35.5)	91(53.8)	0.558	
Hyper TG [b]	8(3.2)	1(12.5)	1(12.5)	6(75.0)	0.350	
Hyper Chol [b]	91(34.2)	8(8.8)	33(36.3)	50(54.9)	0.504	
EF [a]	40 ± 12	37 ± 13	38 ± 12	42 ± 12	0.016	
Mechanical complication [b]	140(49.5)	10(7.1)	55(39.3)	75(53.6)	0.430	
Electrical complication [b]	47(17.2)	2(4.3)	23(48.9)	22(46.8)	0.095	
LV diastolic dysfunction [b]	255(90.5)	22(8.6)	90(35.3)	143(56.1)	0.295	
Intra hospital Death [b]	28(10.5)	10(35.7)	10(35.7)	8(28.6)	< 0.001	

Abbreviations: MI, Myocardial Infarction; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; BS, Blood Sugar; Hb, Hemoglobin; TG, Triglyceride; Chol, Cholesterol; EF, Ejection Fraction

[a] Mean ± SD; [b] N (%); [c] P value between group 1 and 2; [d] P value GFR between group 2 and 3; [e] P value between group 1 and 3

significantly related to GFR, which was not indicated in Mehmet's study in 2012 (6) and Nagesh's study in 2004 (9). Moreover, as expected, GFR level was associated with age, gender, and SBP, which is in agreement with most of the studies conducted on the issue (2, 3, 6-9). These three parameters were also related to intra-hospital mortality. The patients with lower GFR levels had higher levels of blood sugar. In addition, dead cases had higher levels of blood sugar, which was not shown in other studies (3, 7-10). These studies showed that the patients with history of diabetes mellitus had lower levels of GFR. On the other hand, our study demonstrated no significant relationship between diabetes drugs consumption and GFR. Thus, our findings regarding these two parameters (blood sugar and diabetes drugs consumption) were both similar to and different from those obtained in the previous studies. Lack of any relationships between GFR and complications may show that GFR can affect intra-hospital death irrespective of complications, which should be investigated in future studies. The patients with lower levels of GFR had lower levels of serum Hb, which may be attributed to the decrease in Erythropoietin (EPO) resulting from impaired renal function (11, 12).

Furthermore, the results indicated a significant relationship between GFR and consumption of ACE inhibitors or ARBs, which is similar to the results of two studies published in 2003 and 2009 (3, 9), but in contrast to those obtained by Nagesh (7). Moreover, smoking, prior MI, HTN, and consumption of aspirin and B-blockers were not related to GFR level, which was on the contrary to the results of the studies performed by Roberto in 2009 and Nagesh in 2003 (3, 9). These differences probably result from the limited number of cases, because our findings were more similar to those of a study conducted on 161 patients in Turkey (6).

As we expected, similar to the previous studies, lower Hb levels increased the risk of intra-hospital death (3, 5, 13-15). Oxygen delivery depends critically on Hb concentration and cardiac output. Because of its nature, blood flow to the heart decreases in AMI and anemia (Hb < 11) makes it worse by decreasing oxygen delivery to the infarcted tissue (5). The patients with mechanical complications determined by echocardiography had lower mean Hb concentrations that could lead to death, but we could not find any relationship between mechanical complications and intra-hospital death. Thus, a follow-up study may indicate this association. Low levels of Hb were more prevalent among older patients (10), which can be due to nutritional deficiencies or chronic diseases (16), and among females probably because of iron deficiency due to menstruation, pregnancy, and childbirth (17).

According to the current study findings, lower SBP was associated with lower Hb and GFR levels and intra-hospital death. Therefore, it can be a valuable predictive factor for ST-elevation MI mortality.

Multiple studies have noted that patients with anemia are less likely to receive aspirin, B-blockers, and statins (18-20), but our study results were completely different. We found that the patients who consumed aspirin and statins had lower Hb concentrations probably because of some interfering factors, such as comorbidities, in the patients who used these drugs.

The study results also indicated that age, LVEF, and LV diastolic dysfunction, as mentioned in a textbook (2), predicted MI outcomes. Additionally, mortality due to MI was more prevalent among females, which was consistent with the results of the studies by Valente and De Luca (21, 22). However, some studies have come to controversial results (23, 24) mainly because of women's clinical and profile risk factors.

In the present study, aspirin and ACE inhibitors or ARBs improved the surveillance in ST-elevation MI, which was similar to a meta-analysis published in 2011 (25). That meta-analysis also disclosed that B-blockers and statins had similar effects, which was not in line with our study results. This might be due to the fact that these medications improve long-term surveillance. Presence of electrical complications determined by electrocardiogram increased the mortality rate irrespective of the type of complications. Similar results were obtained about QRS duration in some researches performed in 2009 and 2011 (26, 27).

Overall, the current study findings revealed that Hb and GFR, as two laboratory parameters routinely measured in ST-elevation MI patients, could be used as predictive values for mortality and electrical complications. Some other factors, such as age, gender, blood sugar, EF, LV diastolic dysfunction, and electrical abnormalities in ECG, have to be taken into account, as well.

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Authors' Contribution

Study concept and design: Fazlinezhad, Hami, Shakeri, Saffar Soflaei; Analysis and interpretation of data: Fazlinezhad, Hami, Shakeri, Saffar Soflaei, Dadgarmoghadam, Khadem-Rezaiyan; Drafting of the manuscript: Saffar Soflaei, Dadgarmoghadam, Khadem-Rezaiyan, Khatibi-Moghaddam; Critical revision of the manuscript for important intellectual content: Fazlinezhad, Hami, Shakeri, Khatibi-Moghaddam, Dadgarmoghadam, Khadem-Rezaiyan, Saffar Soflaei; Statistical analysis: Shakeri, Dadgarmoghadam, Khadem-Rezaiyan, Saffar Soflaei | The authors would like to thank Dr. Hamid Reza Rahimi for his assistance in preparation of this manuscript.

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