

Relation between Serum Prolactin and Troponin Type 2 Diabetes Mellitus Patients

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Abstract

Background: Patients with type 2 diabetes frequently present with various manifestation of atherosclerosis at the time of diagnosis. Coronary artery disease is a major vascular complication of diabetes mellitus and reveals high mortality. A high prolactin level plays a potential role in the development of ischemic cardiac disease. The study aimed to assess relation between prolactin and troponin in type 2 diabetes mellitus patients. **Methods:** This study was performed in Clinical pathology, Cardiology and Internal medicine departments zagazig university hospitals. This study was conducted on 88 male subjects (66 patients and 22 healthy subjects as a control group). The patients were selected from patients admitted in the Cardiology and the Internal Medicine Department in zagazig University Hospitals. Subjects in the study were classified into 4 groups: Group 1: Twenty two diabetic patients with recent myocardial infarction. Group 2: Twenty two Non diabetic patients with recent myocardial infarction. Group 3: Twenty two diabetic patients but not known to have acute myocardial infarction. Group 4: Twenty two healthy subjects (control group). Determination of serum level of troponin and prolactin were done. **Results:** Regarding FBS and HbA1c, there is a statistically significant increase when compare group 1 with group 2 & 4 ($P<0.001$). Also, there is a statistically significant increase when compare group 3 with group 2 ($p<0.001$), in addition to significance increase when compare group 3 with 4 ($p<0.001$). Regarding TC, TG and LDL, there is a statistically significant increase when compare group 1 with group 3 & 4 ($P<0.001$). Also, there is a statistically significant increase when compare groups 2 and 3 with group 4 ($p<0.001$). Moreover, there is significance increase when compare group 2 with 3 regarding TG and LDL ($p=0.005$, $p=0.001$, respectively). Meanwhile, there is significance increase when compare group 1 with 2 regarding TC and LDL ($p=0.001$, $p=0.048$, respectively). Regarding troponin level, there is a statistically significant increase when compare group 1 with group 3 & 4 ($P<0.001$). Also, there is a statistically significant increase when compare group 2 with group 3 and 4 ($p<0.001$). Moreover, there is increase in troponin level when compare group 1 to group 2 but without statistically significant difference ($p=0.326$). Meanwhile, there is increase in troponin level when compare group 3 to group 4 but without statistically significant difference ($p=0.187$). Regarding prolactin level, there is a statistically significant increase when compare group 1 with group 2, 3 & 4 ($P=0.016$, $P<0.001$, respectively). Also, there is a statistically significant increase when compare group 2 with group 3 and 4 ($p<0.001$), in addition to significance increase when compare group 3 with 4 ($p=0.012$). Regarding the correlation between prolactin and other variables studied among MI and DM groups, there was positive correlation between prolactin versus troponin ($r=0.78$ and $p<0.001$). Therefore, a

positive correlation between cardiac troponin and serum prolactin in this study elucidate that acute MI occurrence is due to long-term vascular complications. **Conclusion:** Roc curve of Prolactin level for discrimination of diabetic with AMI and non-diabetics with AMI at cut off value = 20.56, show specificity 92 % and sensitivity 86%. Serum prolactin level increased in acute myocardial infarction, and positively correlated with cardiac troponin level and reflects underlying cardiovascular complications.

Key words: Relation- prolactin- troponin- type 2 diabetes mellitus.

Introduction

Patients with type 2 diabetes frequently present with various manifestation of atherosclerosis at the time of diagnosis. A diabetic patient without a history of heart disease carries a risk of future cardiovascular mortality equal of non-diabetic patient with previous myocardial infarction ⁽¹⁾.

Coronary artery disease is a major vascular complication of diabetes mellitus and reveals high mortality. Up to 30% of diabetic patients with myocardial ischemia remain asymptomatic and have worse prognosis compared to non-diabetic subjects, which warrants routine screening for CAD in diabetic population ⁽²⁾.

Diagnosis and management of CAD is a vital issue. A lot of inflammatory markers play an important role in the diagnosis and management of patients with coronary artery disease. Myocardial infarction (MI) have a similar risk for coronary artery related events as non-diabetic individuals, who have had a prior MI ⁽³⁾.

Prolactin may have dual effect worsening DM, increasing the atherosclerotic process and hence occurrence of AMI, as one of the serious macrovascular complications in diabetics ⁽⁴⁾.

A high prolactin level plays a potential role in the development of ischemic cardiac disease, as hyperprolactinemia leads to dyslipidemia, augmentation of platelets aggregation and amplification of vascular thrombosis that leading to increase in the risk score of acute coronary syndrome ⁽⁵⁾.

The study aimed to assess relation between prolactin and troponin in type 2 diabetes mellitus patients.

Patients and Methods

This study was performed in Clinical pathology, Cardiology and Internal medicine departments at Zagazig university hospitals in the period between July and October 2019. Approval for study was obtained from research administration and research ethics committee, faculty of medicine Zagazig University.

Subjects

This study was conducted on 88 male subjects (66 patients and 22 healthy subjects as a control group). Subjects in the study were classified into 4 groups:

Group 1: Twenty two diabetic patients with recent myocardial infarction.

Group 2: Twenty two Non diabetic patients with recent myocardial infarction.

Group 3: Twenty two diabetic patients but not known to have acute myocardial infarction.

Group 4: Twenty two healthy subjects (control group).

Exclusion Criteria

- 1) Patients with renal, hepatic failure.
- 2) Any condition or medication that can cause alteration in the serum prolactin as phenothiazines, butyrophenones and metoclopramide.
- 3) Type I DM patients.

All subjects enrolled in the study were subjected to the following:

i. Clinical assessment include:

Detailed history taking and complete clinical examination including pulse, blood pressure, temperature, respiratory rate, chest and abdominal examination.

ii. Laboratory investigation include:

A) Routine laboratory investigation

i. Complete blood picture.

ii. liver function and kidney function test.

iii. fasting blood sugar and Lipid profile.

iv. Glycosylated hemoglobin.

B) Specific laboratory investigation include:

Determination of serum level of troponin and prolactin

Methods

Sample Collection

An overnight 5ml fasting blood sample was collected from each subject fasting from 10 to 12 hrs using a sterile plastic syringe, 2 ml of the collected blood was taken on EDTA concentration (1mg/ml blood) containing tube for CBC and measurement of glycated hemoglobin.

The rest of the blood was delivered in plain tube allowed to clot for 30 minutes then centrifuged to separate the serum which was used for the measurement of lipids, troponin and prolactin.

1 ml was collected from each subject fasting 8hrs for the measurement of fasting blood glucose.

Limitation and Interference

The assay is unaffected by icterus, hemolysis and lipemia. In patients receiving therapy with high biotin no samples should be taken until a minimum of 8 hours after the last biotin dose has passed.

Normal level of serum troponin: below 0.04 ng/ml

Normal level of serum prolactin:

Males: 4.6 - 21.4 ng/ml

Statistical Analysis:

❖ Analysis of information was performed by IBM computer using SPSS program version 11.

Results:

– **Table (1) and figures (1; 2)** show that there is high significant difference between the studied groups as regard fasting blood sugar and HbA1c. Regarding FBS and HbA1c, there is a statistically significant increase when compare group 1 with group 2 & 4. Also, there is a statistically significant increase when compare group 3 with group 2, in addition to significant increase when compare group 3 with 4.

– **Table (2) and figures (3; 4)** show that there is highly significant difference between the studied groups as regard Cholesterol level, Triglyceride and LDL. However, there is no significant difference between the studied groups as regard HDL. Regarding TC, TG and LDL, there is a statistically significant increase when compare group 1 with group 3 & 4. Also, there is a statistically significant increase when compare groups 2 and 3 with group 4. Moreover, there is significant increase when compare group 2 with 3 regarding TG and LDL. Meanwhile, there is significant increase when compare group 1 with 2 regarding TC

and LDL.

– **Table (3) and figure (5)** show that there is high significant difference between the studied groups as regard troponin level. Regarding troponin level, there is a statistically significant increase when compare group 1 with group 3 & 4. Also, there is a statistically significant increase when compare group 2 with group 3 and 4. Moreover, there is no significant difference when compare group 1 to group 2. Meanwhile, there is no significant difference when compare group 3 to group 4.

– **Table (4)** shows that there is highly significant difference between the studied groups as regard prolactin level. Regarding prolactin level, there is a statistically significant increase when compare group 1 with group 2, 3 & 4. Also, there is a statistically significant increase when compare group 2 with group 3 and 4, in addition to significance increase when compare group 3 with 4.

– **Table (5)** showsthat there is high significant positive correlation between Prolactin level and Troponin level in group 1 and 2

– **Table (6)** shows that prolactin level for discrimination of diabetic with AMI and non-diabetics with AMI at cut off show that value = 20.56, specificity 92% and sensitivity 86%.

Table (1): Comparison between the different studied groups according to blood glucose level

Sugar picture	DM with AMI Group 1 (n = 22)	AMI Group 2 (n = 22)	DM Group 3 (n = 22)	Control Group 4 (n = 22)	Test of Sig.	p	LSD
Fasting blood glucose (mg/dl)							P1=<0.001 P2=0.194 P3=<0.001 P4=<0.001 P5=0.894 P6=<0.001
Min. – Max.	150.0 – 250.0	100.0 – 115.0	150.0 – 200.0	90.0 – 110.0	F 219.93	<0.001	
Mean ± SD.	187.3 ± 24.53	106.6 ± 5.35	178.6 ± 13.20	95.5 ± 3.32			
HBA1C %							P1=<0.001 P2=0.985 P3=<0.001 P4=<0.001 P5=0.414 P6=<0.001
Min. – Max.	7.0 – 10.0	5.0 – 5.50	7.0 – 8.50	5.0 – 5.50	KW 72.522	<0.001	
Mean ± SD.	7.82 ± 0.78	5.18 ± 0.25	7.70 ± 0.43	5.05 ± 0.15			

F: ANOVA test

KW:Kruskal Wallis test

Post Hoc Test (Tukey) used to compare within the four groups (each two groups)

P: Probability (significance value) when *P*-value ≤ 0.001 indicates highly significant.

*P*₁: Group 1 vs Group 2

*P*₂: Group 1 vs Group 3

*P*₃: Group 1 vs Group 4

*P*₄: Group 2 vs Group 3

*P*₅: Group 2 vs Group 4

*P*₆: Group 3 vs Group 4

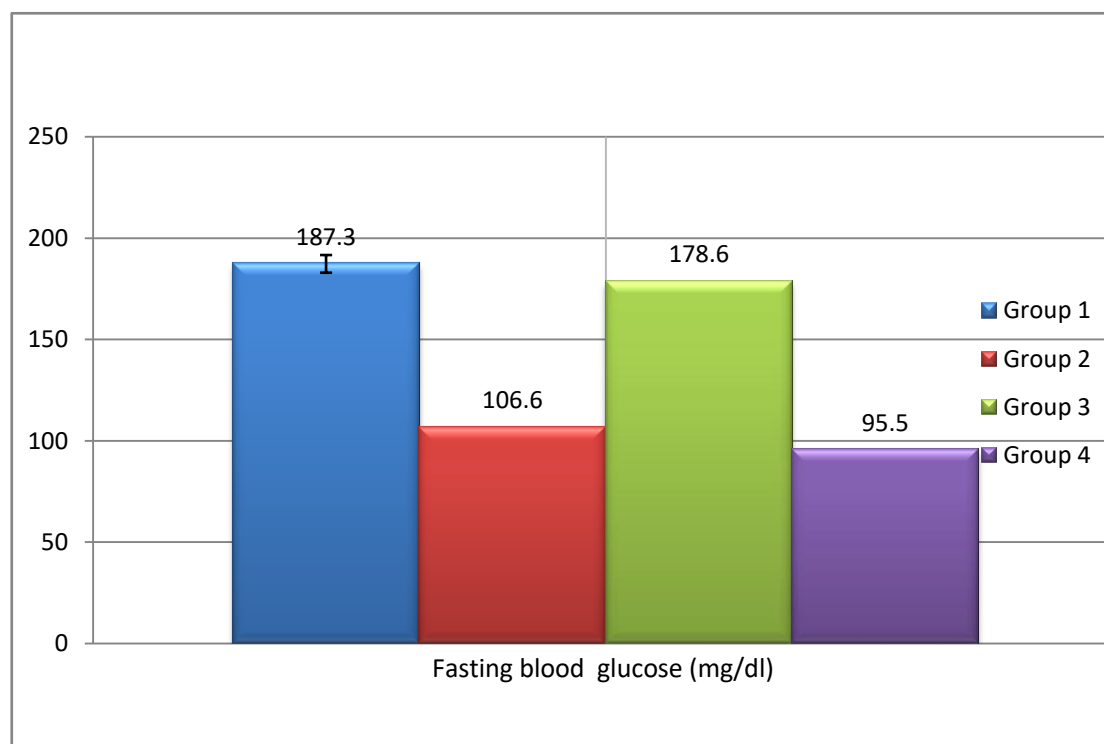


Fig.(1) Mean Fasting glucose level of the studied groups.

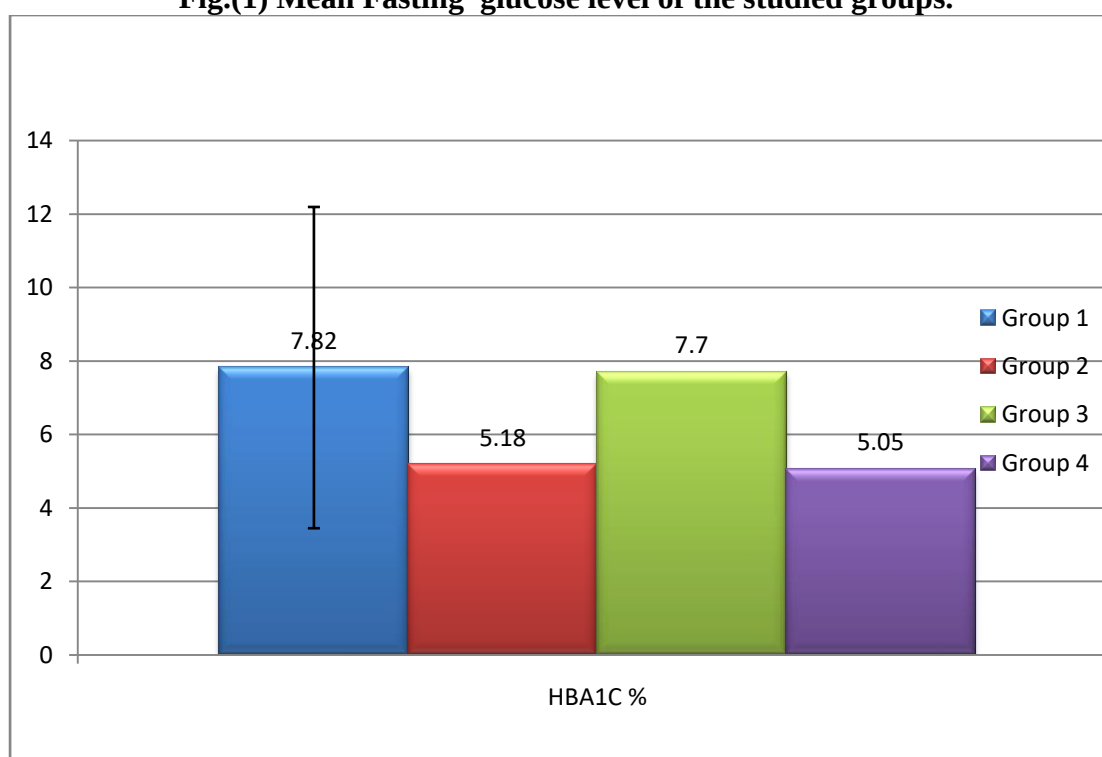


Fig.(2) Mean HBA1C level of the studied groups.

Table (2): Comparison between the different studied groups according to lipid profile

Lipid profile	DM with AMI Group 1 (n = 22)	AMI Group 2 (n = 22)	DM Group 3 (n = 22)	Control Group 4 (n = 22)	F	p	LSD
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Cholasterol (mg/dl) Min. – Max. Mean $\pm$ SD.	150.0 – 200.0 181.4 $\pm$ 15.21	150.0 – 180.0 165.4 $\pm$ 11.84	150.0 – 180.0 160.5 $\pm$ 9.99	100.0 – 150.0 117.3 $\pm$ 16.09	90.465	<0.001	P1=0.001 P2=<0.001 P3=<0.001 P4=0.611 P5=<0.001 P6=<0.001
TG (mg/dl) Min. – Max. Mean $\pm$ SD.	150.0 – 180.0 162.7 $\pm$ 13.16	130.0 – 170.0 156.4 $\pm$ 11.77	130.0 – 150.0 144.6 $\pm$ 8.0	80.0 – 130.0 101.4 $\pm$ 12.07	128.91	<0.001	P1=0.258 P2=<0.001 P3=<0.001 P4=0.005 P5=<0.001 P6=<0.001
LDL (mg/dl) Min. – Max. Mean $\pm$ SD.	130.0 – 160.0 142.3 $\pm$ 10.20	120.0 – 140.0 133.6 $\pm$ 6.58	100.0 – 130.0 120.5 $\pm$ 10.46	60.0 – 110.0 80.45 $\pm$ 14.63	139.79	<0.001	P1=0.048 P2=<0.001 P3=<0.001 P4=0.001 P5=<0.001 P6=<0.001
HDL (mg/dl) Min. – Max. Mean $\pm$ SD.	30.0 – 40.0 37.27 $\pm$ 4.56	30.0 – 45.0 35.0 $\pm$ 5.35	30.0 – 40.0 36.59 $\pm$ 4.47	30.0 – 40.0 35.91 $\pm$ 5.03	0.877	0.457	

F: ANOVA test

Post Hoc Test (Tukey) used to compare within groups (each two groups)

P: Probability (significance value) when *P*-value ≤ 0.001 indicates highly significant and *P*-value > 0.05 indicates non-significant*P*₁: Group 1 vs Group 2*P*₂: Group 1 vs Group 3*P*₃: Group 1 vs Group 4*P*₄: Group 2 vs Group 3*P*₅: Group 2 vs Group 4*P*₆: Group 3 vs Group 4

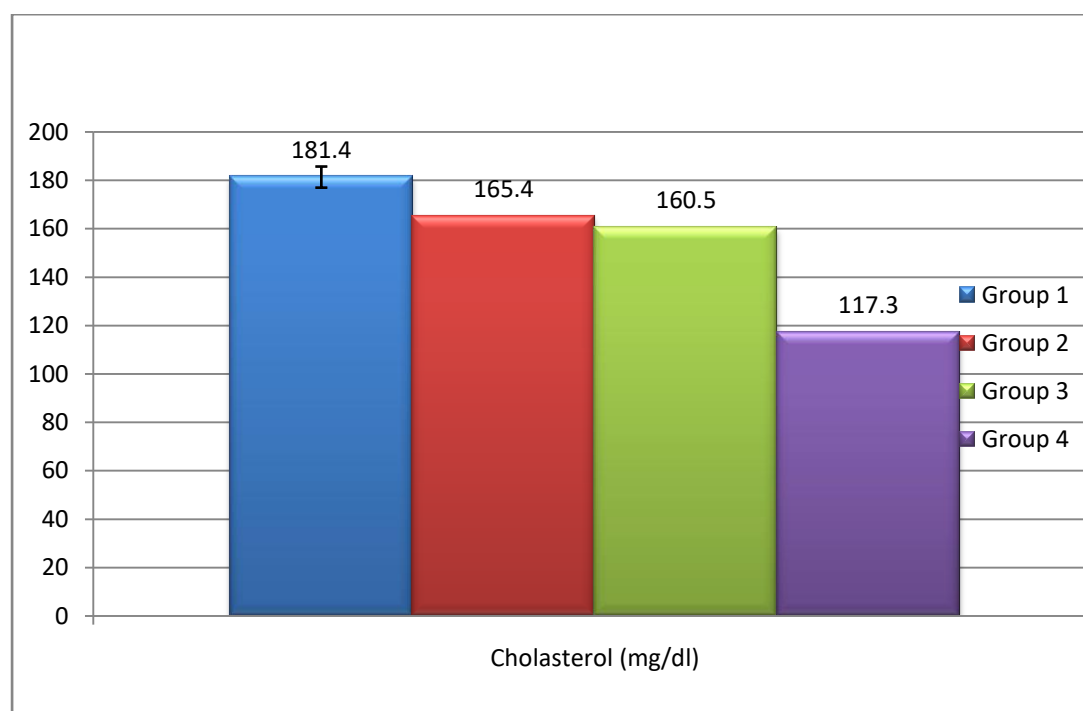


Fig.(3)Mean Cholesterol level of the studied groups.

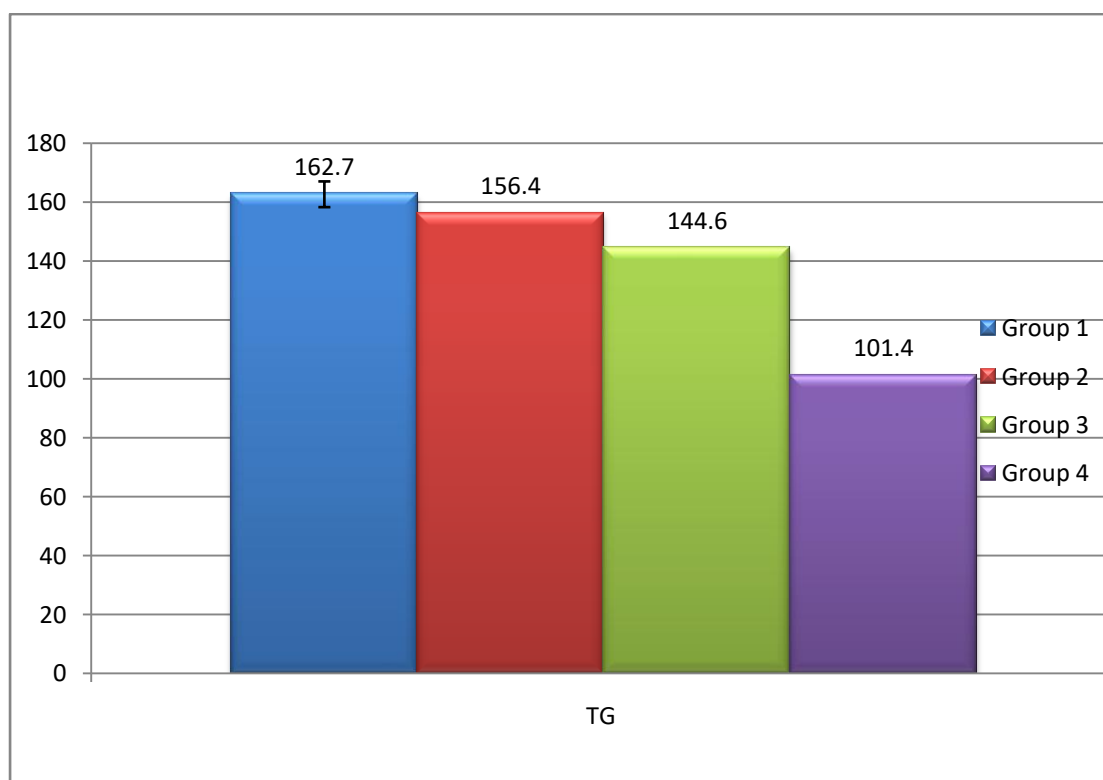


Fig.(4)Mean Triglyceride level of the studied groups.

Table (3):Comparison between the different studied groups according to troponin level

Troponin (ng/dl)	DM with AMI Group 1	AMI Group 2 (n = 22)	DM Group 3(n = 22)	Control Group 4	KW	p	LSD
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	(n = 22)			(n = 22)			
Min. –	0.18 –	0.18 –	0.01 –	0.01 –			P1=0.326
Max.	1.60	0.61	0.02	0.02			P2=<0.001
Mean ±	0.61 ±	0.38 ±	0.02 ± 0.0	0.01 ±	68.338	<0.001	P3=<0.001
SD.	0.39	0.14		0.0			P4=<0.001
							P5=<0.001
							P6= 0.187

KW:Kruskal Wallis test

Post Hoc Test (Dunn's) used to compare within groups (each two groups)

P: Probability (significance value) when $P\text{-value} \leq 0.001$ indicates highly significant and $P\text{-value} > 0.05$ indicates non-significant

P₁: Group 1 vs Group 2

P₂: Group 1 vs Group 3

P₃: Group 1 vs Group 4

P₄: Group 2 vs Group 3

P₅: Group 2 vs Group 4

P₆: Group 3 vs Group 4

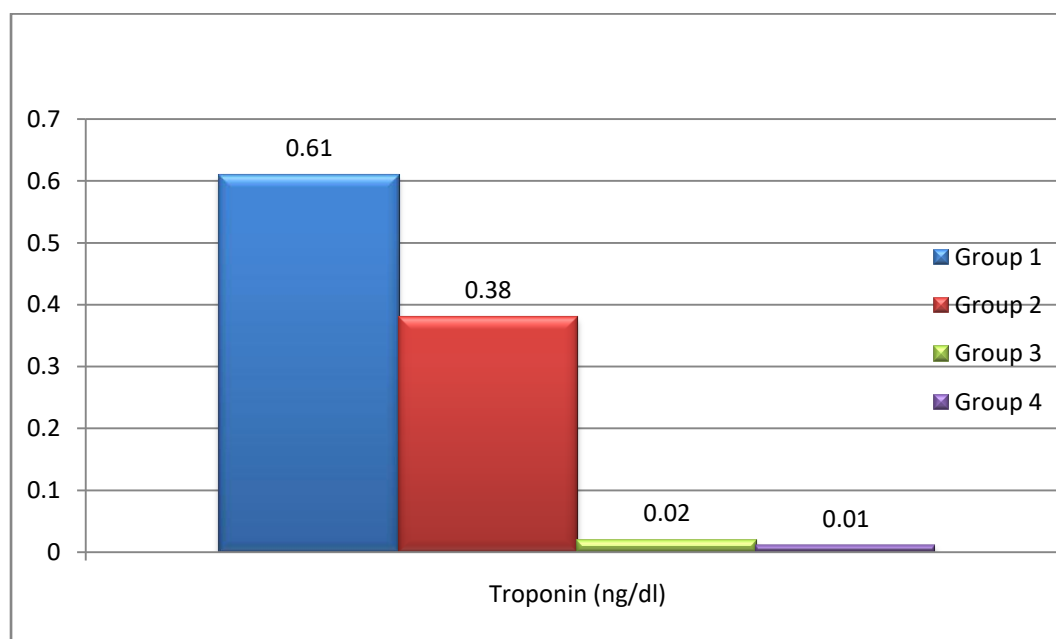


Fig.(5)Mean Troponin level of the studied groups.

Table (4):Comparison between the different studied groups according to prolactin level

Prolactin (ng/ml)	DM with AMI Group 1 (n = 22)	AMI Group 2 (n = 22)	DM Group 3 (n = 22)	Control Group 4 (n = 22)	KW	p	LSD
Min. –	17.90 –	12.30 –	6.20 –	2.60 –			P1=0.016
Max.	47.40	22.30	12.10	8.40			P2=<0.001
Mean ±	26.64 ±	16.24 ±	8.85 ±	4.97 ±	77.486	<0.001	P3=<0.001
SD.	8.09	3.37	1.97	1.61			P4=0.001
							P5=<0.001
							P6=0.012

KW:Kruskal Wallis test
Post Hoc Test (Dunn's) used to compare within groups (each two groups)
P: Probability (significance value) when $P\text{-value} \leq 0.001$ indicates highly significant and $P\text{-value} < 0.05$ indicates significant

P₁: Group 1 vs Group 2

P₂: Group 1 vs Group 3

P₃: Group 1 vs Group 4

P₄: Group 2 vs Group 3

P₅: Group 2 vs Group 4

P₆: Group 3 vs Group 4

Table (5): Correlation between prolactin and troponin in each group

Troponin (ng/dl)	Prolactin (ng/ml)	
	r_s	p
Group 1 (n = 22)	0.710	<0.001
Group 2 (n = 22)	0.756	<0.001
Group 3 (n = 22)	-0.045	0.842
Group 4 (n = 22)	0.121	0.592

r_s : Spearman coefficient

Table (6):of Prolactin level for discrimination of diabetic patients with AMI patients and non-diabetics with AMI.

Variable	Cut off	AUC	Sig.	Sensitivity	Specificity	PPV	NPV
Prolactin	20.56	0.929	0.001	86%	92%	78.2%	95.2%

Discussion

Regarding TC, TG and LDL, there is a statistically significant increase when compare DM with AMI with DM&control ($P<0.001$).

Also, there is a statistically significant increase when compare AMI and DM with control ($p<0.001$). Moreover, there is significance increase when compare group 2 with 3 regarding TG and LDL ($p=0.005$, $p=0.001$, respectively). Meanwhile, there is significance increase when compare DM with AMI with AMI regarding TC and LDL ($p=0.001$, $p=0.048$, respectively). These findings are in agreement with **Chearskulet al.**⁽⁶⁾ who reported that simultaneous measurements of serum total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, and triglycerides in 70 subjects revealed that low levels of HDL-C with high TG. Concerning LDL-Co and TC, they were significantly higher compared to control group. **Yadhav et al.**,⁽⁴⁾ found that the LDL-c and TG were significantly higher in AMI patients ($p<0.001$).

A study by **Berinder et al.**,⁽⁷⁾ on 14 patients, with hyperprolactinemia found that LDL and total cholesterol was positively correlated to PRL at diagnosis and decreased within 2 months after Medical treatment of hyperprolactinemia, thus reported that patients with hyperprolactinemia associated with hypercholesterolemia.

Regarding troponin level, there is a statistically significant increase when compare

DM with AMI with DM&control ($P<0.001$). Also, there is a statistically significant increase when compare AMI with DM & control ($p<0.001$). Moreover, there is increase in troponin level when compare DM with AMI to AMI but without statistically significant difference ($p=0.326$). Meanwhile, there is increase in troponin level when compare DM to control but without statistically significant difference ($p=0.187$).

Regarding prolactin level, there is a statistically significant increase when compare DM with AMI with AMI, DM&control ($P= 0.016$, $P<0.001$, respectively). Also, there is a statistically significant increase when compare AMI with DM and control ($p<0.001$), in addition to significance increase when compare DM with control ($p=0.012$).

In the present study, serum prolactin elevate inpatients with acute myocardial infarction neither in DM with AMI (MI&DM) (mean= $26\pm SD=8.09$) or AMI (MI) (mean= $16.24\pm SD=3.37$) which points to the possible role of hyperprolactinemia in myocardial infarction.

These findings are in agreement with **Wallaschofski et al.**,⁽⁸⁾ who reported that prolactin is a potent Cofactor for platelet activation as there's prolactin receptor on human platelets, as increased prolactin value found to be associated with enhanced P-selectin expression on platelets in patients with acute myocardial infarction.

This is in agreement with **Wallaschofski et al.**,⁽⁹⁾ who demonstrated that prolactin values are increased in stroke and myocardial infarction, and that the involvement of hormonal factors in platelets aggregation should have important clinical implication, and this also is in agreement with **Raaz et al.**,⁽¹⁰⁾ who found that patients with acute myocardial infarction showed significantly higher prolactin values compared to control group, and concluded that this data indicates an association between increased prolactin values and enhanced P-selectin expression on platelet in patients with acute myocardial infarction. These data are supported by the findings of **Elgayar et al.**,⁽¹¹⁾ who found that AMI patients with diabetes had higher prolactin levels than diabetics and control groups.

Krysiak et al.,⁽¹²⁾ measured serum prolactin in 72 diabetic males and compared it to 63 healthy males and found that the diabetic group had significantly higher serum prolactin than the control group.

They hypothesize that inflammatory environment within advanced atherosclerotic plaques could stimulate the expression of prolactin receptors, or prolactin could also stimulate the atherosclerotic process through its autocrine or paracrine action not through systemic inflammatory induction.

They concluded that elevated serum prolactin do not predict CAD in the general population. However, prolactin receptors were found in human coronary artery plaques; this observation may induce a role in prolactin within atherosclerotic plaques.

They concluded that hyperprolactinemia may be associated with increased risk of myocardial infarction. Prolactin may have dual effect worsening DM, increasing the atherosclerotic process and hence occurrence of AMI, as one of the serious macrovascular complications

in diabetics. On the other hand **Hamidi and Davidage**,⁽¹³⁾ reported that the association between hyperprolactinemia and stroke & myocardial infarction is not well investigated, and it's uncertain if prolactin levels were increased before or after the occurrence of the vascular insult, and whether prolactin is triggering platelets activation in these patients or not. As one of the most likely explanations for increased prolactin in these patients might be stress.

Hyperprolactinemia may be associated with increased risk of atherosclerotic process and hence occurrence of AMI, as one of the serious macrovascular complications in diabetics. Hyperprolactinemia detected in diabetics having AMI, supports the recent trend of using dopamine agonists, e.g., bromocriptine in treatment of type 2 DM, especially those who had a prior ischemic event. Also, hyperprolactinemia being associated with increased

troponin level in AMI patients may be considered a prognostic factor correlated with the extent of myocardial damage.

Thus, coexistences elevation of both cardiac troponin and serum prolactin in acute MI give an idea about the underlying predisposing factor of occurrences of MI, and the elevated troponin revealed myocardial necrosis due to the coronary vessel complications that appeared in association with dyslipidemia which linked to high prolactin level⁽¹⁴⁾.

Regarding the correlation between prolactin and other variables studied among MI and DM groups, there was positive correlation between prolactin versus troponin ($r=0.78$ and $p<0.001$)

Therefore, a positive correlation between cardiac troponin and serum prolactin in this study elucidate that acute MI occurrence is due to long-term vascular complications.

Conclusion:

Roc curve of Prolactin level for discrimination of diabetic with AMI and non-diabetics with AMI at cut off value = 20.56, show specificity 92 % and sensitivity 86%. Serum prolactin level increased in acute myocardial infarction, and positively correlated with cardiac troponin level and reflects underlying cardiovascular complications.

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