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Plasma Malondialdehyde Level is a Good Predictor of Portal Hypertension in Egyptian Cirrhotic Patients

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Keywords: Malondialdehyde (MDA); Oxidative stress; Portal hypertension (PH).

Abbreviations: MDA: Malondialdehyde; PH: Portal Hypertension; PV: Portal Vein; ROC: The Receiver Operating Characteristic Curve.

Abstract

Background and aim: Malondialdehyde (MDA) results from lipid peroxidation of polyunsaturated fatty acids and it is a marker for oxidative stress. Its level is higher in cirrhotic patients with viral etiology than in matched healthy controls. So, it may strongly correlate with Portal Hypertension (PH) in cirrhotic patients. This work aims at evaluation of the relevance between plasma MDA level and portal hypertension in cirrhotic patients.

Methods: 30 patients with cirrhotic portal hypertension and esophageal varices, and 30 healthy control participants were included in a case control study. These patients were admitted to Tropical Medicine Department, Ain Shams University Hospital.

Results: MDA level was found with a high significance in the studied patients with cirrhotic portal hypertension than in the healthy control group with p-value < 0.001. Also, a significant positive correlation between MDA level and PV diameter in the Child-Pugh score of the studied patients was found. Conclusion: there was a strong correlation between the increased plasma MDA level and hemodynamic disorder and portal hypertension in cirrhotic patients. As a result, MDA acts as a new non-invasive diagnostic marker of portal hypertension in patients with liver cirrhosis.

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Introduction

malondialdehyde (MDA) concentration: Using Enzyme-Linked Immunosorbent Assay (ELISA) test. Serum MDA was measured by Enzyme Linked Immunosorbent Assay (ELISA), using Human MDA ELISA KIT by Glory Science Co., Ltd 2400 Veterans Blvd. Suite 16 - 101, Del Rio, TX 78840, USA.

Abdominal ultrasonography with doppler: Abdominal ultrasound with measurement of Portal Vein (PV) caliber and PV duplex. In addition to detection of Abdominal portosystemic collaterals in the form of recanalized paraumbilical vein, splenorenal collaterals, dilated left and short gastric veins.

Equipment used: Hitachi, EUB-5500, 2-5 MHz convex probe, (China, Mainland); the patients were examined in supine position with emphasis on liver by an experienced sonographist, who was blind to all biochemical characteristics of the participants.

- Upper gastrointestinal endoscopy.

Statistical analysis

Descriptive statistics:

- Mean, Standard deviation (± SD) and range for numerical data.
- Frequency and percentage of non-numerical data.

Analytical statistics:

- Student T Test was used to assess the statistical significance of the difference between two study group means.
- Correlation analysis (using Pearson's method): To assess the strength of association between two quantitative variables. The correlation coefficient denoted symbolically "r" defines the strength (magnitude) and direction (positive or negative) of the linear relationship between two variables.
- The ROC Curve (Receiver Operating Characteristic) provides a useful way to evaluate the Sensitivity and specificity for quantitative Diagnostic measures that categorize cases into one of two groups.

Results

The studied patients are divided into 21 males (70%) and 9 females (30%) with mean age (57.13 ± 6.90) as described in table 1. Also, all the 30 patients (100%) had HCV and only one patient (3.3%) had combined HCV and HBV (Table 1).

The laboratory investigations of the studied patients revealed Hb (gm/dl) with mean (9.69 ± 1.64), WBCS (X103/dl) with mean (5.80 ± 3.19) and Plts (X103/dl) with mean (77.07 ± 31.91), the results of Liver profile showed Albumin (gm/dl) with mean (3.08 ± 0.28), T.Bilirubin (mg/dl) with mean (1.55 ± 0.55) and INR with mean (1.40 ± 0.20) (Table 2).

The clinical findings of the studied patients showed that 10 (33.3%) patients had hepatomegaly, 30 (100.0%) patients had splenomegaly and 9 (30%) patients had ascites (Table 3). As regard the esophageal varices, 8 (26.6%) of the studied patients had small OV, 6 (20.0%) had medium OV, 7 (23.3%) had large OV and 2 (6.66%) had eradicated OV (Table 4). Twenty-three (76.6%) of the studied patients had mild PHG and 5 (16.6%) had severe PHG (Table 5).

The mean of MDA level among the studied patients was (228.50 ± 136.20) nM which was higher and statistically significant than the mean of MDA level among the group of healthy controls which was (30.37 ± 18.73) nM with p-value < 0.001 as seen in Figure 1 and Table 6.

Correlation between MDA and laboratory parameters in studied patients showed that there was no statistically significant correlation (Table 7). No statistically significant correlation found between the level of MDA and degree of O.V (Table 8).

A significant positive correlation was illustrated between MDA level and PV diameter of the studied patients as described in Table 9 and Figure 2. A statistically significant difference was observed between MDA plasma level and abdominal collaterals being 290.25 ± 124.97 nM in the studied patients with abdominal collaterals and 49.02 ± 40.63 nM in the studied patients without abdominal collaterals as seen in Table 10 and Figure 3.

The Receiver Operating Characteristic Curve (ROC) in Figure 4 shows that the best cut-off point for MDA in prediction of cirrhotic patients together with PH is found at > 45 nM with sensitivity of 100% and specificity of 90%.

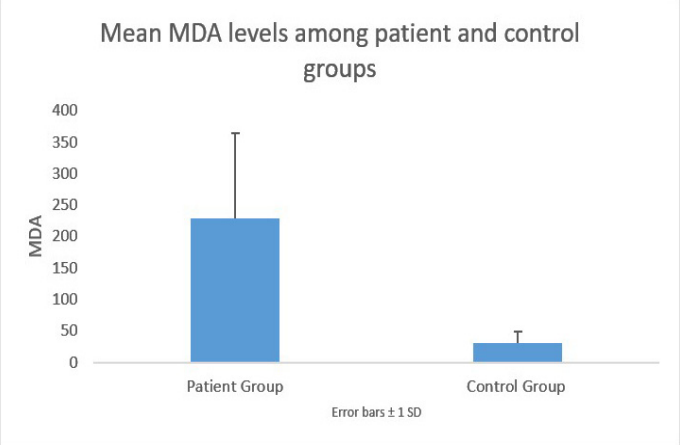

Figure 1: The mean level of MDA among the studied patients was (228.50 ± 136.20) and the mean level of MDA among the control group was (30.37 ± 18.73).

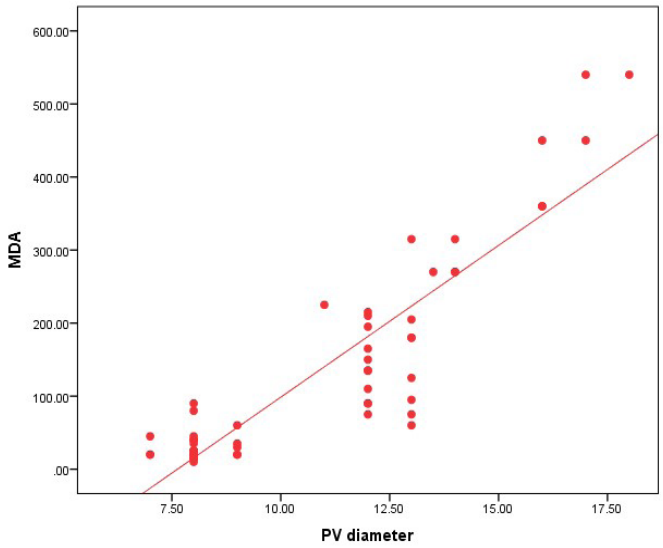

Figure 2: Showed increase in the level of MDA with increase in PV diameter.

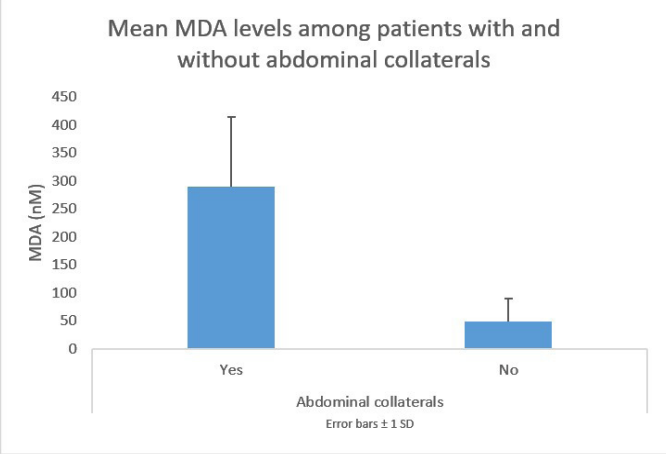

Figure 3: Showed statistically significant positive correlation found between the level of MDA (nM) and abdominal collaterals.

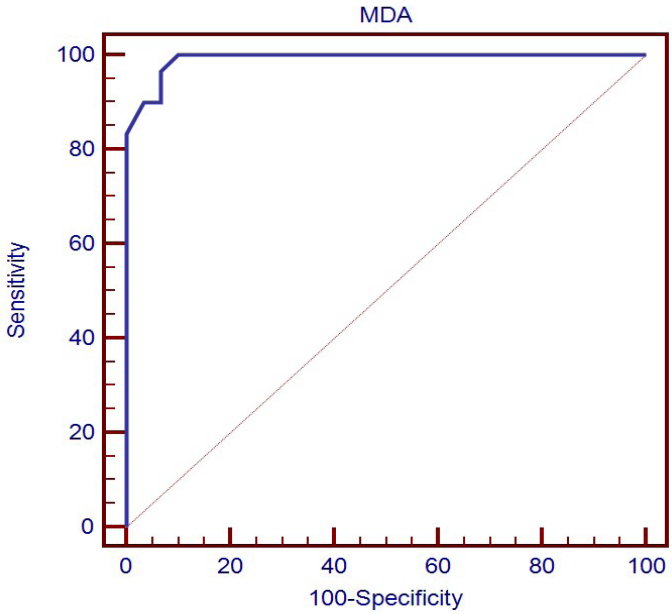

Figure 4: Showed statistically significant positive correlation found between the level of MDA (nM) and abdominal collaterals.

Table 1: Demographic data of the studied patients as regard age, gender and etiology of liver disease.

		No. = 30
Gender	Male	21 (70.0%)
	Female	9 (30.0%)
Age(Years)	Mean ± SD	57.13 ± 6.90
	Range	46 -70
HBV	Yes	1 (3.3%)
	No	29 (96.7%)
HCV	Yes	30 (100.0%)
	No	0 (0.0%)

Table 2: Laboratory investigations among the studied patients.

			No. = 30
CBC	Hb(gm/dl)	Mean ± SD	9.69 ± 1.64
		Range	7.5 - 15.4
	WBCS($X10^3$/dl)	Mean ± SD	5.80 ± 3.19
		Range	2.6 - 16.8
	Plts($X10^3$/dl)	Mean ± SD	77.07 ± 31.91
		Range	33 - 189
Liver profile	Albumin(gm/dl)	Mean ± SD	3.08 ± 0.28
		Range	2.7 - 4
	T.Bilirubin(mg/dl)	Mean ± SD	1.55 ± 0.55
		Range	0.9 - 2.8
	D. Bilirubin(mg/dl)	Mean ± SD	0.72 ± 0.31
		Range	0.2 - 1.3
INR		Mean ± SD	1.40 ± 0.20
		Range	1 - 1.65

*SD: Standard Deviation.

Table 3: The relevant clinical findings on local examination of the studied patients.

		No. = 30
Hepatomegaly	Yes	10 (33.3%)
	No	20 (66.7%)
Splenomegaly	Yes	30 (100.0%)
	No	0 (0.0%)
Ascites	No	21 (70%)
	Yes	9 (30%)

Table 4: Oesophageal varices among patients group.

Oesophageal varices (OV)	No. = 30	
	No.	%
No	7	23.30%
Small	8	26.60%
Medium	6	20.00%
Large	7	23.30%
Eradicated	2	6.66%

Table 5: Portal hypertensive gastropathy in patients group.

PHG	No. = 30	
	No.	%
No	2	6.66%
Mild	23	76.60%
Severe	5	16.60%

Table 6: Comparison between control group and patients group regarding MDA level.

MDA	Control group	Patient group	Independent t-test		Significance
	No. = 30	No. = 30	t	P-value	
Mean ± SD	30.37 ± 18.73	228.50 ± 136.20	7.894	0.000	Highly significant
Range	10 - 90	60 - 540			

*SD: Standard Deviation.

Table 7: Correlation of MDA level with the laboratory investigations of the studied patients.

		MDA		Significance
		r	p-value	
CBC	Hb	-0.304	0.102	Non-significant
	WBCs	0.235	0.211	
	Plts	-0.107	0.572	
Liver profile	Albumin	0.095	0.616	Non-significant
	Bilirubin	0.277	0.138	
	D. Bilirubin	0.243	0.195	
INR		-0.013	0.945	Non-significant

*P > 0.05: Non-significant; P < 0.05: Significant; P < 0.01: Highly significant.

Table 8: Correlation of MDA level with degree of oesophageal varices (O.V).

		MDA		Independent t-test		Significance
		Mean ± SD	Range	T	P-value	
OV	No	204.29 ± 119.07	60 - 360	0.533	0.712	Non-significant
	Small	195.63 ± 111.53	95 - 450			
	Medium	277.50 ± 115.31	135 - 450			
	Large	223.57 ± 161.13	75 - 540			
	Eradicated	315.00 ± 318.20	90 - 540			

*P > 0.05: Non-significant; P < 0.05: Significant; P < 0.01: Highly significant.

Table 9: Correlation of MDA level with portal vein (PV) diameter of the studied patients.

	MDA		Significance
	R	p-value	
PV diameter	0.857**	0	significant

*P > 0.05: Non-significant; P < 0.05: Significant; P < 0.01: Highly significant.

Table 10: Correlation of MDA level with ultrasound findings regarding abdominal collaterals of studied patients.

		MDA		Independent t-test	
		Mean ± SD	Range	T	P-value
Abdominal collaterals	Yes	290.25 ± 124.97 nM	135 - 540	11.163	0.000
	No	49.02 ± 40.63 nM	10 - 180		

*P > 0.05: Non-significant; P < 0.05: Significant; P < 0.01: Highly significant.

Discussion

Malondialdehyde (MDA), a typical aldehydic product, results from polyunsaturated fatty acids peroxidation [3]. The lipid peroxidation degree can be estimated by the MDA amount in tissues, which considers an oxidative stress marker. MDA has been found to be up-expression significantly in patients with liver cirrhosis [6]. Plasma MDA concentrations are higher in patients with liver cirrhosis due to viral etiology than in matched healthy controls [7].

Regarding the clinical data of the studied patients in this study, all our patients had splenomegaly and 9 patients (30%) had ascites. These results agreed with results of Sherlock and Dooley, 2002 [9] who reported that splenomegaly and ascites were the commonest portal hypertensive signs in patients with liver cirrhosis. Also Berzigotti et al., 2013[10] confirmed that and agreed with the conclusion of Sharma et al. [11] that splenomegaly was present as an independent predictor for esophageal varices presence, while ascites was explained by cirrhosis, portal hypertension and splanchnic vasodilation resulting mainly from increased production of nitric oxide which represented the main pathophysiological mechanism of ascites [12].

In our study, the mean haemoglobin level was low at 9.69 gm/dl ± 1.64 in patients with cirrhotic portal hypertension. Further, the mean platelet level was also low in patients with liver cirrhosis at 77.07 ×103/dl ± 31.91. These results were similar to results of Ohta et al. [13] who found that the mean haemoglobin level was 11.2 gm/dl ± 1.7 in cirrhotic patients with portal hypertension. Additionally, investigators in other studies reported that the mean platelet levels were lower at 104-109 × 103/dl and 93-109 × 103/dl, respectively, in cirrhotic patients with portal hypertension [14,15]. These findings could be attributed to the severity of portal hypertension causing hypersplenism [16].

In the present study, MDA level was found with a high significance in the studied patients than in the healthy control group with p-value < 0.001. Similarly, in another study, where 60 liver cirrhotic patients and 30 healthy controls were enrolled, it was found that the MDA plasma level was significantly higher in cirrhotic patients than the controls (P < 0.001); and it increased significantly according to the severity of liver fibrosis and portal hypertension (P < 0.01) [17].

Similarly, investigators in other studies reported that the virus-related cirrhotic patients had a higher oxidant level of MDA, and suggested that more oxidants stress and weaker antioxidants protection existed in the cirrhotic patients than in the control cohort [1,18].

In our study, we found a statistically significant positive correlation between MDA level and PV diameter in the studied patients. Similarly, another study found that MDA level of patients with liver cirrhosis was significantly associated with the width of the portal vein [17], which could be contributed to the fact that the vessel diameter width of the venous system was positively linked to the portal vein pressure in portal hypertension caused by cirrhosis [19].

Finally, this Receiver Operating Characteristic Curve (ROC) shows that the best cut-off point for MDA in prediction of cirrhotic patients with portal hypertension was found at > 45 nM with sensitivity of 100% and specificity of 90%, while Sheng-Lan et al. [17] showed that the cut-off value of plasma MDA to differentiate between cirrhotic patients and the control was 426.5 nM, with sensitivity and specificity at 78.2% and 86.2%, respectively.

Conclusions

The portal hypertension is defined by the pathological increase in the pressure of the portal venous system, and cirrhosis is the commonest cause of the portal hypertension. The outcome results showed that the MDA level was significantly higher in the cirrhotic patients with portal hypertension than in the healthy ones and directly correlated with the PVD, esophageal varices, PHG, Child Pugh score. So, MDA acts as an important non-invasive diagnostic marker of portal hypertension in Egyptian patients with liver cirrhosis.

Declarations

Ethics approval and consent to participate: Written consent was taken from each patient who agreed to participate in the research process. The agreement for participation of the subjects was taken after the aim of the study has been simply explained to them prior to data collection. They were assured that anonymity and confidentiality would be guaranteed and about their right to withdraw from the study at any time without giving any reason. Values, culture, and beliefs were respected. This was done according to the regulations of the research ethical committee, Faculty of Medicine, Ain Shams University. The number of the ethical approval is 137/2017 (2/4/2017).

Consent for publication: Informed consent to publish patients' data was signed by all participants prior to the beginning of the research.

Availability of data and material: The data used to support the findings of the study will be shared on reasonable request to the corresponding author.

Competing Interests: The authors declare that there is no conflict of interest.

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Authors' Contributions: Ahmed A. EL-khattib, Enas H. Allam and Kareem A. Abd El-hafeez designed the research; Nourhan B. Thabet performed the research; Ahmed A. EL-khattib, Enas H. Allam and Kareem A. Abd El-hafeez contributed analytic tools; Ahmed A. EL-khattib, Enas H. Allam, Kareem A. Abd El-hafeez analyzed the data; Safaa R. Askar wrote the paper.

References

1. Parola M, Robino G. Oxidative stress-related molecules and liver fibrosis. J Hepatol. 2001; 35: 297-306.

2. Negre-Salvayre A, Coatrieux C, Ingueneau C, Salvayre R. Advanced lipid peroxidation end products in oxidative damage to proteins. Potential role in diseases and therapeutic prospects for the inhibitors. Br J Pharmacol. 2008; 153: 6-20.

3. Davey MW, Stals E, Panis B, Keulemans J, Swennen RL. "High-throughput determination of malondialdehyde in plant tissues". Analytical Biochemistry. 2005; 347: 201-207.

4. Palmieri B, Sblendorio V. Oxidative stress tests: overview on reliability and use. Part I. Eur Rev Med Pharmacol Sci. 2007; 11: 309-342.

5. Palmieri B, Sblendorio V. Oxidative stress tests: overview on reliability and use. Part II. Eur Rev Med Pharmacol Sci. 2007; 11: 383-399.

6. Uchida k. Role of reactive aldehyde in cardiovascular diseases. Free Radic Biol Med. 2000; 28: 1685-1696.

7. Loguercio C, Federico A. Oxidative stress in viral and alcoholic hepatitis. Free Radic Biol Med. 2003; 34: 1-10.

8. Molina E, Reddy K. Noncirrhotic portal hyp- ertension. Clin Liver Dis. 2001; 5: 769-787.

9. Sherlock S, Dooley J. Diseases of the liver and biliary system eleventh edition. 2002.

10. Berzigotti A, Seijo S, Reverter E, Bosch J. Assessing portal hypertension in liver diseases. Expert Rev Gastroenterol Hepatol. 2013; 7: 141.

11. Sharma S, Aggarwal R. Prediction of large esophageal varices in patients with cirrhosis of the liver using clinical, laboratory and imaging parameters. J. Gastroenterol. Hepatol. 2007; 22: 1909-1915.

12. Wiest R, Groszmann RJ. The paradox of nitric oxide in cirrhosis and portal hypertension: too much, not enough. Hepatology. 2002; 35: 478-491.

13. Ohta M, Hashizume M, Higashi H. Portal and gastric mucosal hemodynamics in cirrhotic patients with portal-hypertensive gastropathy. Hepatology. 1994; 20: 1432-1436.

14. Bang CS, Kim HS, Suk KT, Kim SE, Park JW, et al. Portal hypertensive gastropathy as a prognostic index in patients with liver cirrhosis. BMC Gastroenterol. 2016; 16: 93.

15. Merli M, Nicolini G, Angeloni S, Gentili F, Attili AF, et al. The natural history of portal hypertensive gastropathy in patients with liver cirrhosis and mild portal hypertension. American journal of Gastroenterol. 2004; 99: 1959-1965.

16. Zaman A. Portal hypertension-related bleeding: management of difficult cases. Clin Liver Dis. 2006; 10: 353.

17. Sheng-Lan Wang, Xin-Yan Zhu, Dong-Wei Zhang, Zhao-Jie Zhang, Heng-Jun Gao, et al. Relevance of plasma malondialdehyde level and severity of portal hypertension in cirrhotic patients. Int J Clin Exp Med. 2015; 8: 11007-11013.

18. Trevisani F, Caraceni P, Simoncini M, Micati M, Domenicali M, et al. Evidence of oxidative imbalance in long-term liver transplant patients. Dig Liver Dis. 2002; 34: 279-284.

19. Rodríguez-Martínez MA, Martínez-Orgado J, Salaices M, Marín J. Impairment of acetylcholine relaxations by malondialdehyde, a marker of lipid peroxidation. J Vasc Res.1996; 33: 463-470.