

(2012 / 2 / 27                      2011 / 12 / 7                      )

(30.27 U/ml)

(15-77year)

(14-83 year)

(19.17 U/ml)

## **Clinical Study of Myeloperoxidase and some Biochemical Parameters in Diabetes Mellitus Patients**

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### **ABSTRACT**

The research included a clinical studying of Myeloperoxidase enzyme and some biochemical parameters in serum. The normal value of Myeloperoxidase activity in control group was (30.27 U/ml) for both sexes in age group (15-77 year). The results showed that Myeloperoxidase activity in the serum of control group was not affected by sex and marital status, while it was affected by age, smoke and body mass index.

The study also showed a significant decrease in serum Myeloperoxidase activity of Diabetes Mellitus patients group (19.17 U/ml) for both sexes at in age group (31-80 year) comparison with control, and the enzyme activity in serum of patients group was not affected by sex, marital status and type of disease, while it was affected by age, smoke and body mass index.

The results indicated a significant decrease in serum Myeloperoxidase activity in type I, type II Diabetes Mellitus male in comparison with control male, and enzyme activity in type I, type II Diabetes Mellitus female in comparison with control female. Also the results showed a significant decrease in enzyme activity in age groups of type I, type II patients in comparison with age groups of control, so that in comparison the body mass index for type I patients with control. The results also predicted a significant decrease in serum Myeloperoxidase activity in type I, type II Diabetes Mellitus smokers in comparison control smokers, and nonsmokers in comparison control nonsmokers.

The study also showed a significant increase in the level of Glucose, Total Cholesterol and Low Density lipoprotein, while a significant decrease in the level of Total protein, Albumin, Globulin and High Density lipoprotein in serum of type I Diabetes Mellitus patients in comparison control. Also noticed a significant increase in the level of Glucose, Triglyceride, Total Cholesterol, Low Density lipoprotein, Very Low Density lipoprotein, while a significant decrease in the level of Total protein, Albumin, Globulin and High Density lipoprotein in serum of type II Diabetes Mellitus patients in comparison control.

**Keywords:** Myeloperoxidase, Diabetes Mellitus, lipoprotein, Biochemical parameters.

## Diabetes Mellitus

Tiwari and Rao, 2002 ; Holt *et al.*, )

.(2010

Nagar and Nau, )

.(2005

(Kant *et al.*, 2002)

.(Rafecuddin *et al.*, 2009)

(Arora *et al.*, 2009)

Insulin dependent diabetes mellitus (Type I) (IDDM)

.(Harrison *et al.*, 1998) %0.3

Non-Insulin Dependent Diabetes Mellitus (TypeII ) (NIDDM)

(Insulin Resistance)

(Vander *et al.*, 1998)

Robert )

%90-80

.(and Henry, 1996; Frost *et al.*, 2003

Gestational Diabetes Mellitus

.(Frost *et al.*, 2003)

( *Myeloperoxidase*) MPO

(E.C. 1.11.1.7)

(Homodimer)

.(Arnhold, 2004)

(73 KDa)

Michael *et al.*, ) (106 Aminoacid; 14.5 KDa)

(467Aminoacid.,58.5 KDa)

Polymorph Nuclear Leukocyte

.(2008

%5

Neutrophil

Tissue Macrophage

Monocyte

.(Lau and Baldus, 2006)

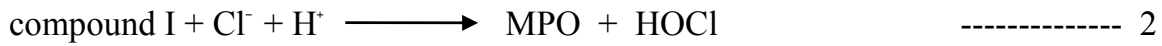
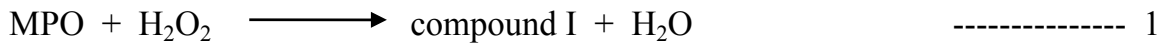
MPO

MPO

.(Lau and Baldus, 2006)

(Klebanoff, 1999) :

HOCl

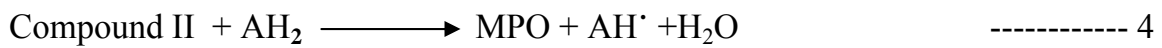
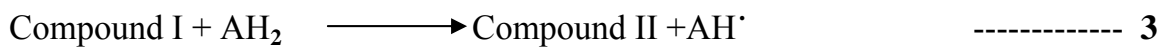


MPO

II I

(AH<sub>2</sub>)

(Vandalen, 1997 ; Valdacic, 2005)



Sulphydryls

:AH<sub>2</sub>

.(Arnhold, 2004)

(30)

(47)

(77)

(106) .(15-77 year)

(55)

(51)

(14-83 Year)

.(Bacchus *et al.*, 1980)

:

Biolabo

.....

(Kit)

(Kaplan, 1984)

(Gornall *et al.*, 1949) Biuret Method

Bromocresol Gree

( + = )

.(Doumas *et al.*, 1971)

.(Richterich, 1969)

(Fossati and Prencipe, 1982)

(Allain *et al.*, 1974)

: Friede Wald

$$\text{LDL Conc. (mg/100ml)} = \text{Cholesterol Conc.} - \text{HDL Conc.} - \frac{\text{TG}_{\text{conc.}}}{5}$$

(Burtis and Ashwood, 1982)

$$\text{VLDL Conc. (mg/100 ml)} = \frac{\text{TG}_{\text{conc.}}}{5} \quad (\text{Fischbach, 2000})$$

(Kumar *et al.*, 2002)

o-dianisidin  
.(450 nm)

:

(T-test) (Anova)

(Correlation coefficient "r")

MPO

(15-77 year)

(2010 Gururajan *et al.*, 2009)

(30.27 U/ml)

(Schindhelm *et al.*, 2009) .(28.87 U/ml)

:

: .1

(1)

( $P \leq 0.001$ )

( $26.56 \pm 0.6 \text{ U/ml}$ ) ( $\leq 25 \text{ year}$ )

( $34.7 \pm 0.96 \text{ U/ml}$ ) ( $55 \leq \text{ year}$ )

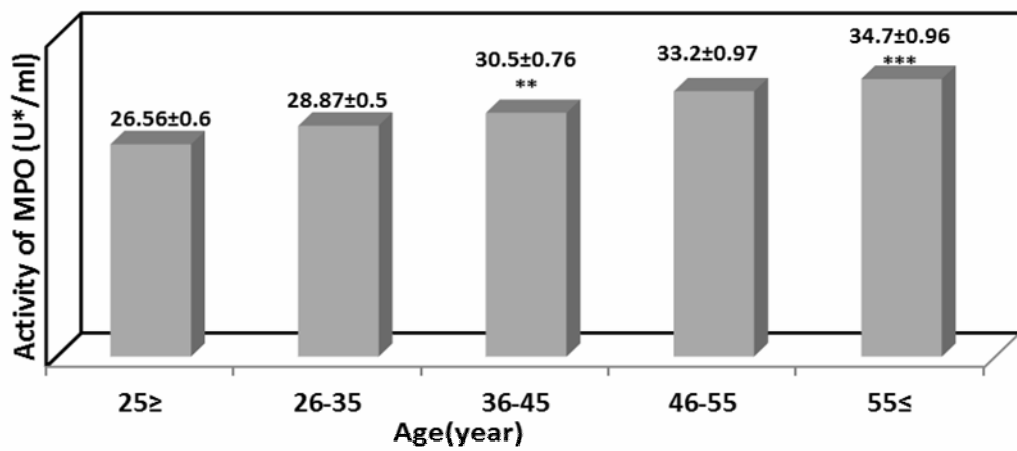
36-) ( $28.87 \pm 0.5 \text{ U/ml}$ ) ( $26-35 \text{ year}$ )

( $P \leq 0.01$ )

MPO

( $30.5 \pm 0.76 \text{ U/ml}$ ) ( $40 \text{ year}$ )

.(Hoy *et al.*, 2001; 2010 )



:(U) \*

.( $p \leq 0.01$ )

\*\* ( $p \leq 0.001$ )

\*\*\*

:1

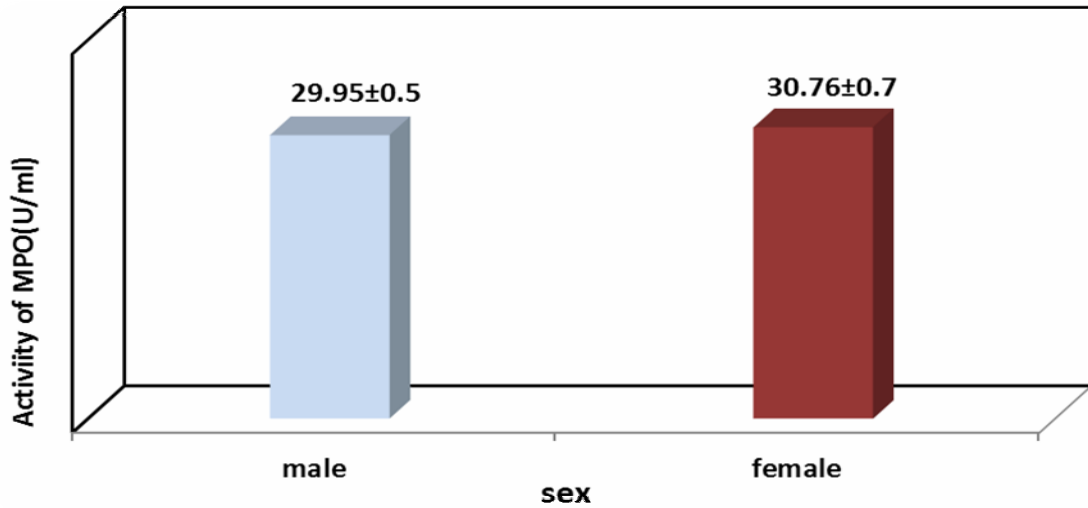
: .2

(2)

( $29.95 \pm 0.5 \text{ U/ml}$ )

.(2010 )

( $30.76 \pm 0.7 \text{ U/ml}$ )



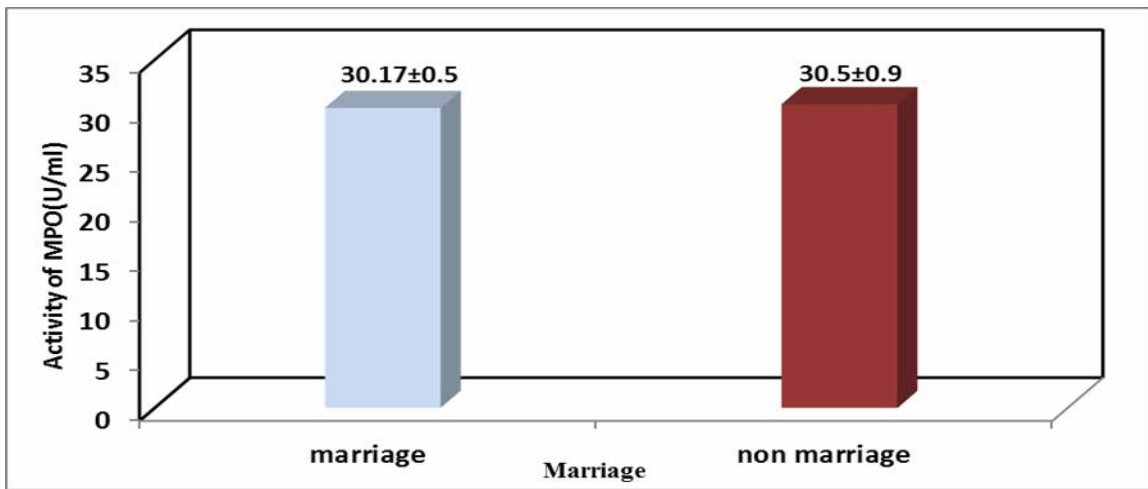
:2

: .3

(3)

(30.5±0.9 U/ml)

(30.17±0.5 U/ml)



:3

: .4

(p≤0.01)

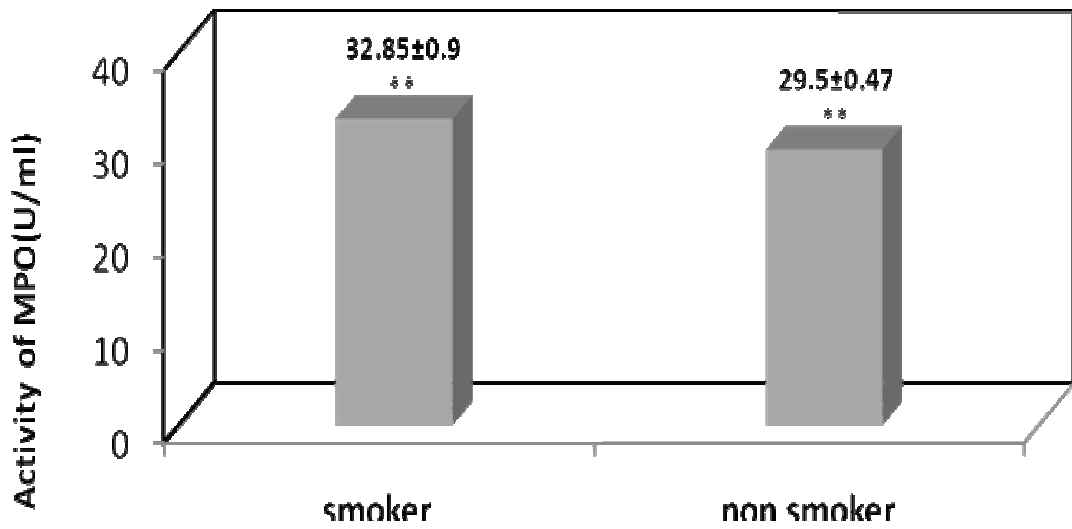
(4)

(29.5±0.47 U/ml)

(32.85±0.88 U/ml)

MPO

(lavi et al., 2007 ; Rudolph et al., 2008)



(p≤0.01)

\*\*

:4

.5

(5)

(28.15±0.4 U/ml)(20-24.9)

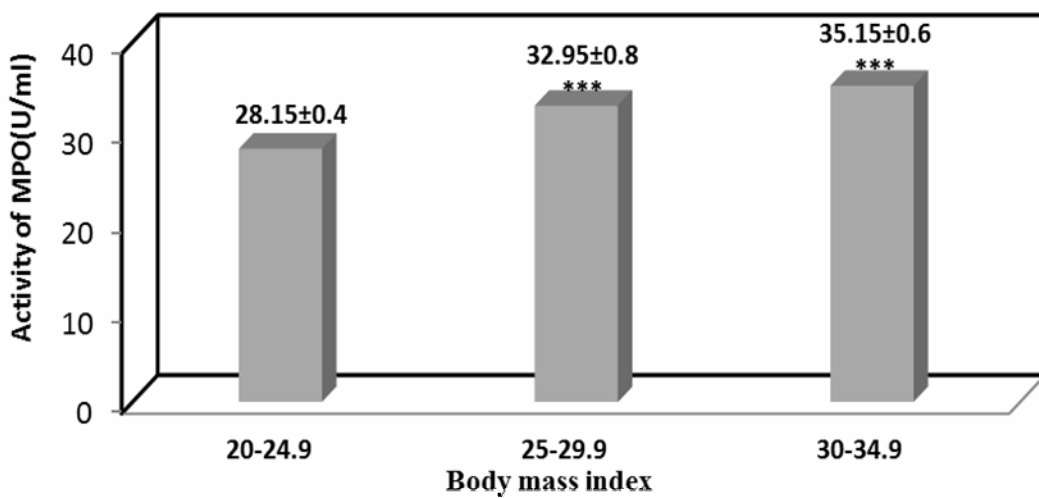
(p≤0.001)

(30-34.9)

(32.95±0.8 U/ml)(25-29.9)

( Zur *et al.*, 2011)

.(35.15±0.6 U/ml)



(p≤ 0.001)

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:5



.....

(83- 14 Year)

.(19.17 U/ml)

: .1

(6)

( $p \leq 0.01$ )

(17.34±0.95 U/ml) (25≤)

(21.57±1.0 U/ml ) (26-35)

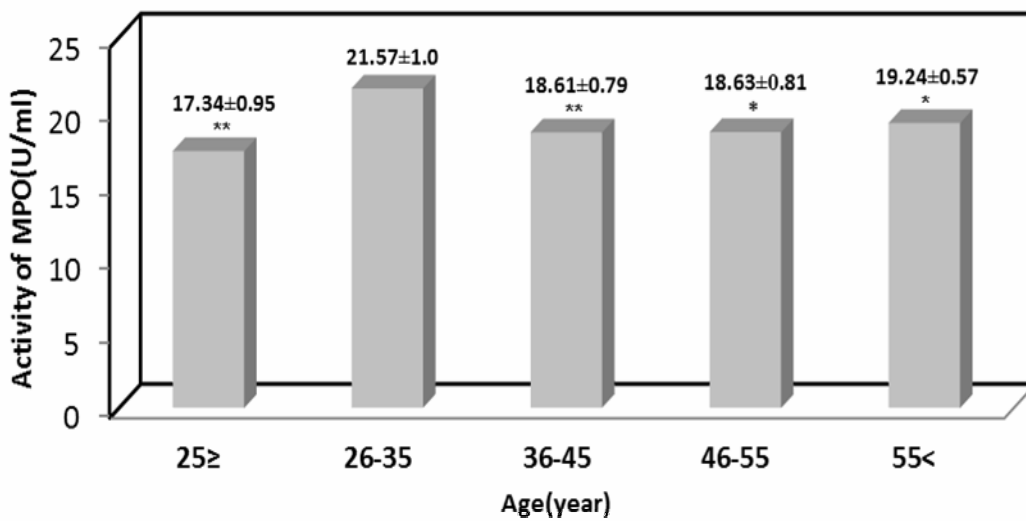
( $P \leq 0.05$ )

(18.61±0.79 U/ml) (36-45)

.(19.24±0.57 U/ml) (55<)

(18.63±0.81U/ml) (46-55)

. (Hoy *et al.*, 2001)



.( $p \leq 0.01$ )

\*\*

.( $p \leq 0.05$ )

\*

:6

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.2

(21.78±1.32U/ml)

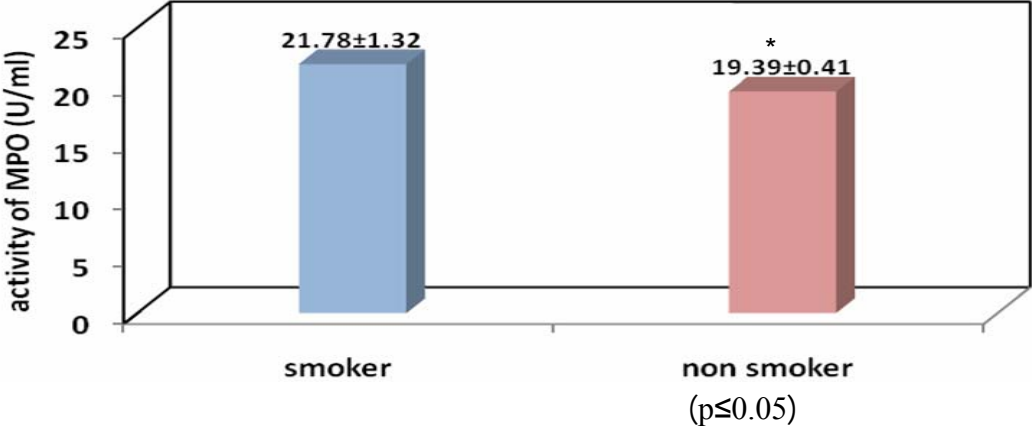
( $p \leq 0.05$ )

lavi *et al.*, 2007 ; )

(7)

(19.39±0.41U/ml)

(Rudolph *et al.*, 2008)



:7

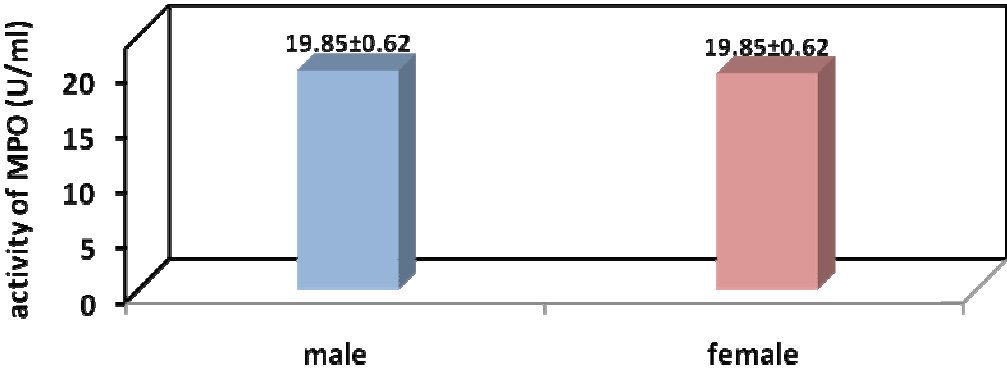
\*

(p≤0.05)

: .3

(8)

(Wiersma *et al.*, 2008) (19.85±0.62 U/ml) (19.85±0.62 U/ml)



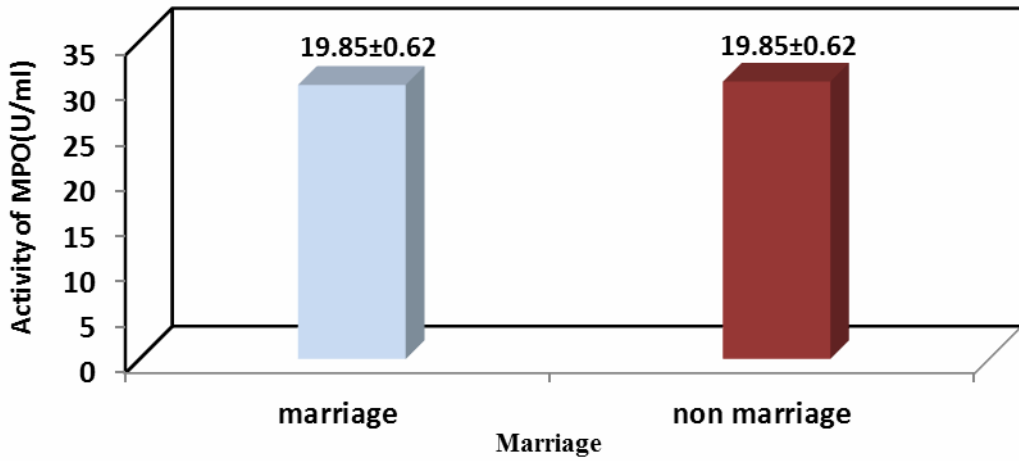
:8

: .4

(9)

(19.41±0.39 U/ml)

(17.13±0.93 U/ml)



:9

(p≤0.05)

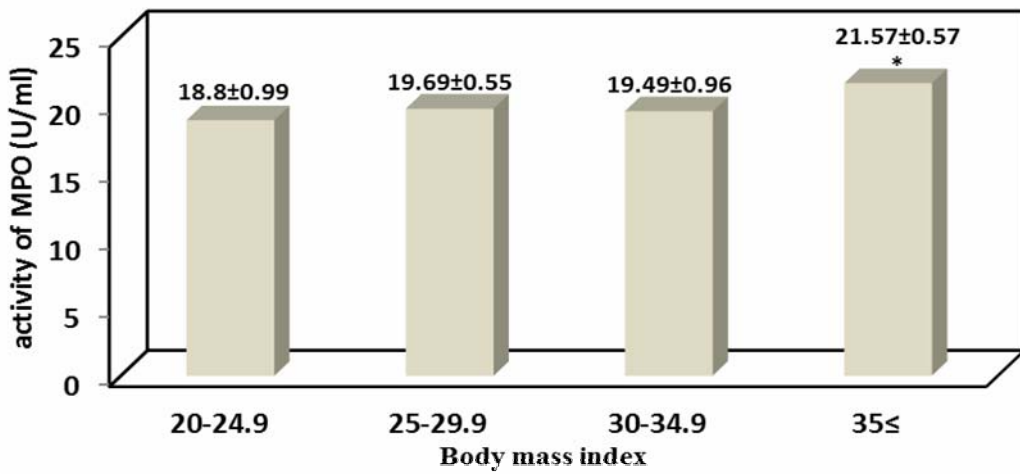
(10)

(18.82±0.99U/ml) (20-24.9)

(Zur *et al.*, 2011 ; Zwan *et al.*, 2010)

(21.57±0.57U/m) (35≤)

.5



.(p≤0.05)

\*

:10

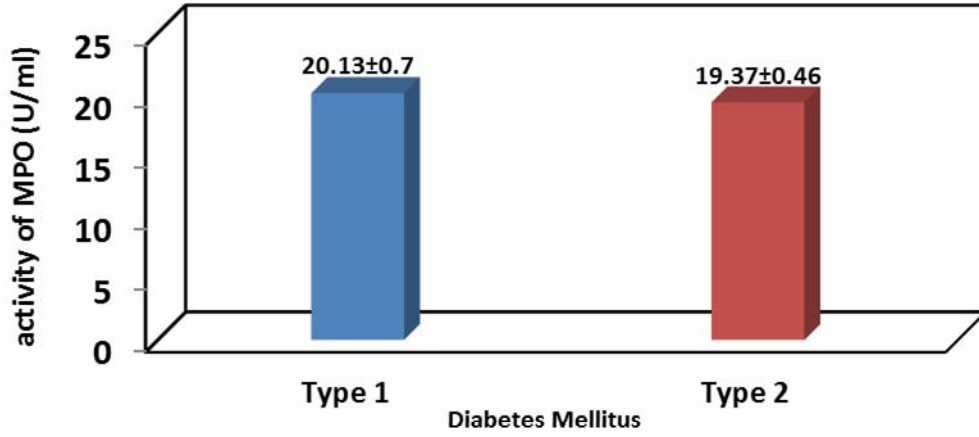
.6

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(11)

(20.13±0.7 U/ml)

.(19.37±0.46 U/ml)



:11

.1

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(1)

(p≤0.001)

.(Uchimura *et al.*, 1999)

(1)

(p≤0.001)

(1)

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( $p \leq 0.05$ )

(Iavi *et al.*, 2007 ; Rudolph *et al.*, 2008)

(1)

(20-24.9)

( $p \leq 0.001$ )

(25-29.9)

(30-34.9)

(Sato *et al.*, 1992)

:1

	U/ml				
	(Mean±S.E)	(Mean±S.E)	(Mean±S.E)		
$p \leq 0.001$	-----	(17.33±0.95)***	(26.56±0.62)	25≥	
$p \leq 0.001$	-----	(21.56±1.0)***	(28.87±0.49)	26-35	
$p \leq 0.001$	(18.5±0.66)***	(20.59±1.57)***	(30.48±0.76)	36-45	
$p \leq 0.001$	(19.8±0.9)***	-----	(33.2±0.97)	46-55	
$p \leq 0.001$	(20.15±0.7)***	-----	(34.7±0.96)	55<	
$p \leq 0.001$	(19.23±0.7)***	(20.72±1.1)***	(29.95±0.56)		
$p \leq 0.001$	(19.51±0.59)***	(19.64±0.9)***	(30.76±0.73)		
$p \leq 0.001$	(20.37±1.8)***	(24.3±1.34)***	(32.85±0.88)		
$p \leq 0.001$	(19.2±0.4)***	(19.63±0.73)***	(29.54±0.47)		
$p \leq 0.001$	(16.78±0.66)***	(19.14±1.1)***	(28.15±0.37)	(20-24.9)	
$p \leq 0.001$	(18.98±0.48)***	(20.63±1.06)***	(32.95±0.8)	(25-29.9)	
$p \leq 0.001$	(18.67±1.16)***	(21.23±1.63)***	(35.15±0.62)	(30-34.9)	
$p \leq 0.001$	(19.37 ±0.46)***	(20.13±0.7)***	(30.27±0.44)		

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(Uchimura *et al.*, 1999 ; Sato *et al.*, 1992)

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.2

(2)

(p<0.001)

.(Heilman *et al.*, 2009)

VLDL-C

LDL-C

(2)

.(Guy and Ogden, 2009)

(p<0.001)

.(Mohammadi *et al.*, 2009) lipoprotein lipase

(p<0.001)

HDL-C

(Mohammadi *et al.*, 2009)

.(Suryawanshi *et al.*, 2006)

(2)

.(Kalogerakis *et al.*, 2005 )

(P<0.001)

.(Wiirner *et al.*, 1992)

.(p<0.001)

:2

	Mean±S.E1	Mean±S.E	
p≤0.001	(259.52± 7.3)***	(181.11± 2.34)	Total Cholesterol (mg/dl)
p>0.05	(151.47± 6.9)	(139.5± 5.19)	Triglyceride (mg/dl)
p≤0.001	(36.45± 1.6)***	(53.15± 1.2)	HDL-Cholesterol (mg/dl)
p≤0.001	(192.7± 7.56)***	(100.05± 2.68)	LDL-Cholesterol (mg/dl)
p>0.05	(30.29± 1.38)	(27.9±1.04)	VLDL-Cholesterol (mg/dl)
p≤0.001	(6.5±0.09)***	(7.8± 0.12)	Total Protein (g/dl)
p≤0.001	(4.1±0.05)***	(4.79±0.07)	Albumin (g/dl)
p≤0.001	(2.4± 0.08)***	(3.0±0.11)	Globulin (g/dl)
p≤0.001	(209.0± 6.35)***	(95.5± 1.4)	Glucose (mg/dl)

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:

.3

(3)

(p<0.001)

.(Pasaoglu *et al.*, 2004)

(p<0.001)

VLDL-C

(3)

.(Smith and Lall, 2008)

(p<0.001)

(Suryawanshi *et al.*, 2006)

(p<0.001)

LDL-C

(3)

.(Erkelens, 2001)

:3

	<b>2</b>		
	<b>Mean±S.E</b>	<b>Mean±S.E</b>	
p≤0.001	( 267.7 ± 5.75) ***	(181.11 ± 2.34)	<b>Total Cholesterol (mg/dl)</b>
p≤0.001	( 178.0 ± 7.3) ***	(139.5 ± 2.19)	<b>Triglyceride (mg/dl)</b>
p≤0.001	( 37.68 ± 1.3) ***	(53.15 ± 1.2)	<b>HDL-Cholesterol (mg/dl)</b>
p≤0.001	( 194.4 ± 5.69) ***	(100.05 ± 2.68)	<b>LDL- Cholesterol (mg/dl)</b>
p≤0.001	( 35.6 ± 1.46) ***	(27.9 ± 0.43)	<b>VLDL- Cholesterol (mg/dl)</b>
p≤0.001	( 6.85 ± 0.08) ***	(7.8± 0.12)	<b>Total Protein (g/dl)</b>
p≤0.001	( 4.28 ± 0.05) ***	(4.8 ± 0.07)	<b>Albumin (g/dl)</b>
p≤0.001	( 2.57 ± 0.08) ***	(3.0 ± 0.11)	<b>Globulin (g/dl)</b>
p≤0.001	( 200.0 ± 4.42) ***	(95.5 ± 1.4)	<b>Glucose (g/dl)</b>

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(3)

(p<0.001)

.(Ayman *et al.*, 2011)

.(2011)

- Allain, C. C.; Poon, L. S.; Chan, C. S. G.; Richmond, W. ; Fu, P.C. (1974). Enzymatic determination of total serum cholesterol. *Clin. Chem.*, **20**(4), 420-475.
- Arnhold, J. (2004). Free Radicals–Friends Of Foes ? Properties, Functions, And Secretion of Human Myeloperoxidase. *Biochem. (MOSCOW)*, **69**(1), 4-9. Translated from *Biokhimiya*,( 2004), **69**(1), 8-15.
- Arora, S. ; Ojha, K. ; Vohora, D. (2009). Characterization of streptozotocin induced diabetes mellitus swiss AlbinoMice. *J. Pharmacol.*, **3**(2), 81-84.
- Ayman, S. I. ; Faisal, K. H., (2011). "Liver Function Tests I n Type 2 Sudanese Diabetic Patients" Department of Biochemistry, Faculty of Science and Technology, Al-Neelain University, Khartoum, Sudan.
- Bacchus, R.; Kilshaw, B.H.; Madkour, M.; Al-Bassam, M.S. ; Al-Farhan, C.B. (1980). Preliminary students in a reference rang for Saudi Arabian males : (1) serum uric acid . *Saudi Med. J.* **1**(3), 160-162.
- Burtis, C. A. ; Ashwood, E. R. (1982). "Tietz Fundamental of Clinical Chemistry". 2nd edn. W.B. Saunders company, U.S.A., pp. 302, 337, 539, 901.
- Doumas, B.T.; Watson, W.A. ; Briggs, H.G. (1971). Albumin standards and the measurement of serum albumin with brom o cresol green. *Clin. Clim. Acta.*, **31**, 87-96.
- Erkelens, D. W. (2001). Insulin resistance syndrome and type (2) diabetes mellitus. *Am. J. Cardiol.* **88** (7B), 38J-42J.
- Fischbach, F. (2000). "A Manual of Laboratory and Diagnostic Tests". 6th edn. Lippincott Williams and wilkins, U.S.A., 472 p .
- Fossati, P. ; Prencipe, L. (1982). Serum triglycerides determined colorimetrically with an enzyme that produces hydrogen peroxide. *Clin. Chem.* **28**(10), 2077.
- Frost, G.; Dornhorst, A.; Moses, R. (2003). "An Introduction to Type 2 Diabetes". Imperial school medical , London, UK. LTD. ISBN,0-471-49751.
- Gornall, A. G.; Bardawill, C. J.; David, M. M. (1949). Determination of serum proteins by means of the biuret reaction. *J. Biol. Chem.*, **177**(2), 751–766.
- Gururajan, P.; Gurumurthy, P.; Nayar, P.; Babu, S.; Sarasabharati, A.; Victor, D.; Cherian, K. M. (2009). Serum myeloperoxidase: a novel biomarker for evaluation of patients with acute coronary syndrome. *Heart Asia* . **10**, 1-6. doi:10.1136/ha.2009.000778.
- Guy, J. M. ; Ogden, L.P. (2009). Lipid and lipoprotein profiles in youth with and without type 1 diabetes. *J. Diabetes care*, **32**(3).
- Harrison, C. L.; Collier, D. W.; Kvamer, R. D. ; Takahashi, K. (1998). Aerosol insulin induces regulatory CP8Y  $\alpha$ -cells that perevent murine insulin-dependent diabetes. *J. EXP. Med.*, **84**, 2167-2174.



- Heilman, K.; Zilmer, M.; Zilmer, K., (2009). Arterial stiffness, carotid artery intima-media thickness and plasma myeloperoxidase level in children with type 1 diabetes. *Diabetes Research and Clinical Practice*, Diab – 4444, 6.
- Holt, R. I.; Cockram, C. S.; Flyrbjerg, A.; Goldstein, B. J. (2010). "Text Book of Diabetes". 4th edn. Wiley-Blackwell. 25p.
- Hoy, A.; Tre'gouet, D.; Leininger-Muller, B.; Poirier, O.; Maurice, M.; Sass, C. (2001). Serum myeloperoxidase concentration in a healthy population: biological variations, familial resemblance and new genetic polymorphisms . *Eur. J. Hum. Genet.* **9**, 780–786.
- Kalogerakis, G.; Baker, A. M. ; Christov, S. (2005). Oxidative stress and high-density lipoprotein function in Type I diabetes and end- stage renal disease. *Clin. Sci.*, **108**, 497–506
- Kant, S.; Sahu, M.; Sharma, S. ; Kulkarni, S. K. (2002). Effect of diabecon (D-400), an ayurvedic herbomineral formulation on diabetic retinopathy. *Ind. J. Clin. Prac.*, **12**(9), 49-56.
- Kaplan, L. A., (1984). Glucose. *Clin. Chem.* the C.V. Mosby Co. St Louis. Toronto. Princeton; 1032-1036
- Klebanoff, S. J. (1999). Myeloperoxidase. *Proc. Assoc. Am. Physi.* **111**, 383-389.
- Kumar, P.; Pai, K.; Pandey, H. P. ; Sundar, S. (2002). NADH–oxidase, and myeloperoxidase activity of visceral leishmaniasis patients. *J. Med. Microb.*, **51** (22), 832-836.
- Lau, D. ; Baldus, S. (2006). Myeloperoxidase and its contributory role in inflammatory vascular disease . *pharmacology and therapeutics*, **111**, 16-26.
- Lavi, S.; Prasad, A.; Yang, E. H.; Mathew, V.; Simari, R. D.; Rihal, C. S.; Lerman, L. O. ; Lerman, A. (2007). Smoking is associated with epicardial coronary endothelial dysfunction and elevated white blood cell count in patients with chest pain and early coronary artery disease . *Circulation*, **115**, 2621–2627
- Michael, J. D. ; Clare, L. H., (2008). Mammalian peroxidases: from molecular mechanisms to health implications . *Antioxidants and Redox Signaling*, **10**(7).
- Mohammadi, H.; El Malki, A.; Hassar, M.; Bouchrif, B. (2009). Glycaemic control, hba1c, and lipid profile in children with type 1 diabetes mellitus. *European J. Sci. Research.* **29**(2), 289-294.
- Nagar, A. ; Nadu, T. (2005). Antihyperlipidemic and ntiperoxidative rats. *BMC complementary and Alternative Medicine*, **5**(14), 1-8
- Pasaoglu, H.; Snacak, B.; Bukan, N. (2004). Lipid peroxidation and resistance to oxidation in patients with type 2 diabetes mellitus. *Tohoku J. Exp. Med.*, **203**, 211-218
- Rafecuddin, N.; Venkatro, S. M.; Shanta, K. ; Bheemachari, J. (2009). Comparative efficacy of four Ayurvedic Antidiabetic formulation in alloxan-induced diabetic rabbits. *Act. pharm. Sci.*,(Ind), **51**, 33-38.
- Richterich, R. (1969). "Clinical Chemistry Theory and Practice". S. Karger A.G, Basel, Switzerland, pp. 245-249.
- Robert, R. ; Henry, M. (1996). Glucose control and insulin resistance in noninsulin dependent diabetes mellitus. *Ann. Int. Med.*, **124**(1 pt 2), 97-103.
- Rudolph, T. K.; Rudolph, V. ; Baldus, S.(2008). Contribution of Myeloperoxidase to smoking dependent Vasculsr inflammation. *Proc Am Thorac-Soc*, **5**, 820-823.

- Sato, N.; Shimizu, H.; Suwa, K.; Shimomura, Y.; Kobayashi, I.; Mori, M. (1992). Mpo Activity and Generation of Active O<sub>2</sub> Species in Leukocytes from Poorly Controlled Diabetic Patients. *Diabetes Care*, **15**, 1050-1052
- Schindhelm, R.K.; VanderZwan, L.P.; Teerlink, T. ; Scheffer, P.G. (2009). Myeloperoxidase: A useful biomarker for cardiovascular disease Risk stratification. *Clinical chemistry*. **55**( 8), 1462-1470.
- Smith, S.; Lall, A. M. (2008). A Study on Lipid Profile Levels of Diabetics and Non Diabetics Among Naini Region of Allahabad, India . *Turk J. Biochem* , **33** (4), 138–141.
- Suryawanshi, N. P.; Bhutey, A. K. ; Nagdeote, A. N. (2006). Study of lipid peroxide and lipid profile in diabetes mellitus. *Ind. J. Clini. Biochem.*, **21**(1), 126-130
- Tiwari, K. A. ; Rao, M. J. (2002). Diabetes mellitus and multiple therapeutic approaches of phytochemicals : present status and future prospects . *Current. Sci.*, **83**(1), 734-73 .
- Uchimura, K.; Nagasaka, A.; Hayashi, R.; Makino, M.; Nagata, M. ; Kakizawa, H.; Kobayashi, T.; Fujiwara, K.; Kato, T.; Iwase, K.; Shinohara, R.; Kato, K. ; Itoh, M. (1999). Changes in Superoxide Dismutase Activities and Concentrations and Myeloperoxidase Activities in Leukocytes from Patients with Diabetes Mellitus. *J. Diabetes and Its Complications* , **13**, 264–270
- Vander, A.; Sherman, J. and Luciano, D. (1998). "Human physiology The mechanisms of body function". 7th edn. The McGraw. Hin. New York. USA.
- Vandalen, C. J.; Whitehouse, M. W.; Winterbourn, C. C. ; Kettle, A. J. (1997). Thiocyanate and chloride as competing substrates for myeloperoxidase. *Biochem. J.*, **327**, 487-492.
- Wiersma, J. J.; Meuwese, M. C.; Kastelein, A. ; piek, J. J.; Trip, M. D. (2008). Diabetes mellitus type 2 is associated with higher levels of myeloperoxidase. chapter 4. *Medical Scie. Monitor*; **14**(8), CR406-410
- Wiirner, W.; Preissner, A. ; Rietbrock, N. (1992). Drug-protein binding kinetics in patients with Type I diabetes . *Eur. J. Clin. Pharmacol* . **43**, 97-100
- Zur, B.; Look, M.; Holdenrieder, S.; Stoffel, B. (2011). Elevated plasma myeloperoxidase concentration in adults with obesity . *Elsevier J. CCA*. 06-010. doi: 10.1016
- Zwan, V. L.; Scheffer, P.G.; Dekker, J. M.; Heine, R.J. (2010). Hyperglycemia and Oxidative Stress Strengthen the Association Between Myeloperoxidase Blood Pressure. *Hypertension J. American Heart Association*. **55**, 1366-1372