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Evaluation of Paroxonase and Interleukin-35, in Iraqi Female Patients with Multiple Sclerosis (MS) Disease

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Abstract
The present study was carried out to evaluate the effective role of PON and Il- 35 in serum female patients with multiple sclerosis (MS). In this study , 30 females were enrolled , the duration of the disease was from 3 months to 2 years (Group2 G2) were taken from Baghdad teaching hospital through the period from April-2013 to – Dec.2013. They were compared with 30 apparently healthy females with the same range of age (20 to 30) years (Group 1 G1) .Results Showed high significant decrease of PON in Group 2 compared with Group 1 , while high significant increase in IL- 35 was noted in Group 2 compared with Group 1 .Besides , high significant positive Correlation was observed between PON and IL- 35 in both of Group 1 and Group 2. It was conclude that PON and IL -35 may be used as a clinical marker In Multiple Sclerosis disease.
Keywords: Paroxonase, Multiple Sclerosis, Interleukine -35.

1.0 Introductio

Multiple Sclerosis (MS) is a chronic disorder, of the central nervous system (CNS).

Characterized by autoimmune in flammation , demyelination ,and axonal damage.[Rossalind et al., 2012] and [Manual et al., 2012]

This disease is also Known as " disseminated sclerosis "or" encephalomyelitis .disseminata which is an in flammatory disease in which the fatty myelin sheath around the axons of the brain spinal cord are damaged, leading to demyelination and scarring as well a broad of signs and symptoms. [Compston et al, 2008].

The three signs of MS now Known as Charcots , triad are nystagmus , intention tremor , and impediment speech (scanning speech). [Clanet ., 2008].

Lethal autoimmune disease can be developed in the absence of effective immune suppressive mediators.

Regulatory T cells (Treg cells) are necessary for immune homeostasis and to prevent outoimmunity , yet they are also antitumor immunity. [Vignali et al., 2008] Treg cells use a broad range of mechanisms to suppress immunity , including suppressive cytokine such as IL- 35. IL35 is distinct from other family members in that it is produced by Treg cell populations and it is suppressive. In vitro and in vivo , IL- 35 has two Known biological effects:

Supression of the proliferative of conventional T cells , and the conversion of native T cells into a strongly suppressive induced Treg cell population , called (iTr 35) cells which function in via IL -35. [Lauren et al., 2010].

On the other hand , reactive oxygen species (ROS) and subsequnt oxidative damage may contribute to the formation and persistence of multiple sclerosis (MS) lesions by acting on distinct pathological processes. Oxidative stress can be counteracted by endogenous antioxidant enzymes that confer protection against oxidative damage such as paraoxonase (PON). [Horssen et al., 2008]

PON , is an enzyme that protects low density lipoprotein from oxidative modification [Whitehead et . al, 2011].

2.0 Materials and Methods

2.1 Subjects

Thirty (30) females of age (20-30) years were enrolled in this study , who attended Baghdad Teaching Hospital and diagnosed by physicians as Multiple sclerosis patients , they were compared with (30) apparently healthy females in the same range of age.

2.2 Blood Sampling and Parameter Determination :-

Five Milliliters (5 mL) of venous blood were collected from all subjects enrolled in this study , placed in to plain tubes until coagulation was performed. Serum was separated from blood cells by centrifugation 4000 r.p.m. The quantitive sandwich enzyme immunoassay (ELISA) technique was employed for the determination of PON and IL -35.

2.3 Statistical Analysis

Student t-test was applied to compare the significance of the difference in the mean values of control and patient groups. ($p<0.001$)was considered high significance.

The correlation coefficient (r) test was used for describing the association between parameters. Standard Error of Mean (SEM) is the standard deviation of the sample mean estimate of population mean.

3.0 Results

Our results have shown that PON activity had a high significant decrease ($p<0.001$) in sera of Group 2 (784.32 ± 21.8) mL U/ml compared with Group 1(1106 . 552 ± 22.6) mLU/mL.As well, high significant increase ($p<0.001$) was found in sera of Group 2 (39.14 ± 1.4) pg /ml compared with Group 1 (29.3 ± 1.3) pg /ml.

In addition , high significant positive correlation was observed between PON and IL- 35 in both of Group 1 and Group2.

4.0 Discussion

Interlenkin – 35 (IL – 35) has been reported to show the recently discovered inhibitory cytokine that is produces by foxp 3 + regulatory T cells (Tregs)and contributes to their suppressive function in autoimmune diseases. [Mattson et al., 1995].

Interleukin – 35 (IL-35) is distinct from other Family member since that it is produced by treg cell populations and it is suppressive. In vitro and in vivo, IL -35 has three Known biological effects:

Suppression of T Cell proliferation , the conversion of naive T cells in to IL-35 , Producing induced regulatory T cells (iTr 35 Cells) , down regulation of the 17 cell development , differentiation and suppression of autoimmune inflammtion.[Vignali et al., 2012], [Collision et al., 2009] , [Collison et al., 2008] , [Kochet Kova et al., 2010] , [Bardel et al., 2008] , [Bettimi et al., 2009] , [collision et al, 2012] , [Wirtz et al, 2011] and [Xinyuan et al., 2012].

Recent studies have revealed the role of IL -35 in regulating immunologic responses through induction of inducible IL- 35 producing Treg Cells. Interlukin–35 (IL-35) suppresses T effector (T eff) functions such as Th 1 and Th 17 , on other hand activate Th 2 that change immune responses and so called immunomodulation process in body. [chung et al., 2012] and [Astry et al., 2011].

Broadly , Paraoxonase (PON) is an enzyme that protects low density lipoprotein from oxidative modification. ROS initiate lesions formation of multiple sclerosis by inducing blood – brain barrier disruption , enhance leukocyte migration and myelin phagocytosis , and contribute to lesion persistence by mediating cellular damage to essential biological macromolecules of vulnerable CNS Cells. [Whithead et al., 2011] and [Horssen et al, 2008].

A previous study have suggested a role of the oxidative stress and lipid peroxidation in the inflammatory processes and in the pathogensis of multiple sclerosis (MS) , a degenerative inflammatory disease of the central nervous system (CNS) characterized by autoimmune attack to myelin antigens, reactive Oxygen species (ROS) generated in excess primarily by macorophages, have been implicated as mediators of demyelination and axonal damage , as a result , antioxidant enzymes shch as PON is lower in plasma of MS patients with respect to healthy subjects [Ferretti et al,m 2005].

Table 1 :- Level of pataoxonase (PON) and Interleukin –35(IL-35) in the sera of studied groups .

Parameter	Mean ± SEM/ G1	Mean ± /SEM / G2	T.Test
PON	1106.552/±22.6 mL U / mL	784.32 ± 21.8 mL U / mL	H.S
IL-35	29.3± 1.3 pg / mL	39.14 ± 1.4 pg / mL	H.S

G1:- Health control Group
G2- Multiple Sclerosis patient group.
SEM: Standard error mean.
H.S :- High significant variation ($p<0.001$)

Table 2:- Corretation between PON and IL-35

Correlation		Group 1 (G1)	Group 2(G2)
PON and IL- 35	r	0.0779	0.3839
	P	P<0.001	P<0.001

r:- Correlation Coefficient test
P:- Probability (student t. test)
* There were high significant positive correlation between PON and IL- 35 ($r=0.0779$, $p<0.001$) in Group 1 (G1) and ($r= 0.3839$, $p<0.001$) in Group2 (G2) as seen in fig 1

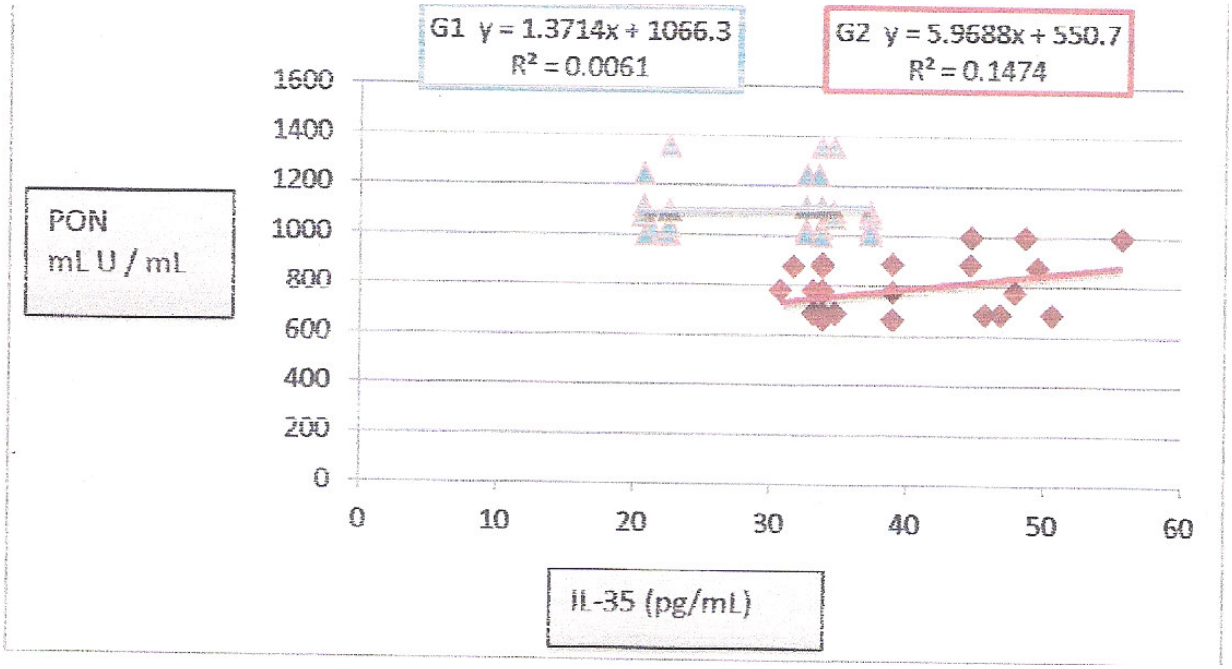

Fig 1:- Correelation between Pon and Il-35

5.0 Conclusion

It was concluded that Paroxanase and Interleukin-35, may be used as a novel clinical marker in multiple sclerosis (MS) diseases.

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