Original article

Role of multifocal electroretinogram in prediction of visual prognosis in patients with occult macular dystrophy.

Running title: mf-ERG in occult macular dystrophy, Abdelshafy and Abdelshafy

Received: ٢٩ February ٢٠٢٠

Revised: ١٥ June ٢٠٢٠

Accepted: ٣٠ June ٢٠٢٠

Abstract:

Background:

Occult macular dystrophy (OMD) is a rare hereditary macular dystrophy characterized by severe bilateral progressive loss of central vision with normal fundus appearance and normal fundus fluorescein angiography (FFA).

Aim:

The aim of the present study was to assess the correlation between the multifocal electroretinogram (mf-ERG) parameters and best corrected visual acuity (BCVA) in patients with OMD.

Patients and methods:

Twenty eyes of ١٠ patients with OMD and twenty eyes of ١٠ age and gender matched normal subjects were included in this study. Full ophthalmic examination, FFA, optical

coherence tomography (OCT),full field electroretinogram (ERG) and mf-ERG were performed for all participants. The average amplitude density of P١ wave, amplitude and implicit time of P١ and N١ waves were recorded in the five concentric hexagon rings. The correlation between these mf-ERG parameters and BCVA (LogMAR) were analyzed.

Results:

There were no statistically significant differences in age, gender and refraction between the studied groups (p= ٠.٥٤, ١.٠ and ٠.٨٢, respectively).Mf-ERG parameters in OMD patients showed significant central depression with less affection of peripheral rings. The average amplitude density of P١ wave, amplitude of P١ and N١ waves were significantly reduced in the central rings (ring ١,٢ and ٣),with less impairment in the paracentral areas(ring ٤ and ٥).The implicit time of P١ andN١ waves were significantly delayed across the central rings in the OMD patients. The BCVA(LogMAR) was significantly negatively correlated with the amplitude of P١ and N١ waves(p≤٠.٠٠١).The BCVA (LogMAR) was significantly positively correlated with the implicit time of P١ and N١ waves (p≤٠.٠٠١).Multiple regression analysis demonstrated that the amplitude and latency of P١ andN١waves in the central rings (١ and ٢) were the most important determinants for BCVA.

Conclusion:

Mf-ERG has a key role in detection of OMD and can be considered as a valuable objective test for detection of central/macular dysfunction. The amplitude and latency of

P١ andN١ waves in ring ١ and ٢ may be used as biomarkers for prediction of visual prognosis in these patients.

Keywords:

Multifocal electroretinogram, visual acuity, occult macular dystrophy, optical coherence tomography.

Introduction:

Occult macular dystrophy (OMD) is a rare hereditary macular dystrophy (١,٢).It is characterized by severe bilateral progressive loss of central vision with no visible abnormalities in the fundus and normal fundus fluorescein angiography(٣-٥).It was first described by Miyake in ١٩٨٩ (٦).Both scotopic (rod) and photopic (cone) components of the conventional full field electroretinogram (ERG) are essentially normal in OMD patients. However, the focal macular electroretinogram and multifocal electroretinogram(mf-ERG)show marked reduction of amplitude which indicate that the dysfunction of the retina is confined to the central macula rather than the retinal periphery (٧,٨).OMD is often misdiagnosed due to the normal appearance of both fundus and fluorescein angiography which makes the diagnosis of such patients a challenging situation (٢).

With advancement of spectral domain optical coherence tomography (SD-OCT),eyes with OMD were found to have structural changes even in absence of any macular abnormalities on fundus examination(١).SD-OCT may show disruption of the photoreceptor and/or outer nuclear layers, lost ellipsoid zone, loss of the inner segment-outer segment (IS-OS) junction and reduction of the foveal thickness. However, some cases were reported to have minimal to subtle changes in OCT in spite of macular dysfunction (٩-١١).

Multifocal ERG (mf-ERG) provides a topographic measurement of the macular function, centered on the posterior retina(٢٠°–٣٠°) on either side of fixation, by recording many local electroretinogram responses (٦١ or ١٠٣) from the cone-driven photoreceptor layer under photopic condition (١٢,١٣).

OMD has been known to be caused by mutations in the retinitis pigmentosa ١-like ١(RP١L١) gene. The most common mode of inheritance is autosomal dominant (AD). However , sporadic cases were also reported (١٤-١٦).

The aim of the present study was to highlight the crucial role of mf-ERG in diagnosis of OMD and to delineate its role in prediction of visual prognosis in these patients by studying the correlation between the mf-ERG parameters and best corrected visual acuity (BCVA).

Patients and methods:

Forty eyes of ٢٠ patients were included in this cross-sectional comparative study, which was conducted between January ٢٠١٨ and February ٢٠٢٠. All participants were recruited from the Outpatient Clinics of Benha University Hospital. After approval of the Local Ethical Committee of the Faculty of Medicine, Benha University, all participants or their legal guardians signed a written informed consent with the requirements of the Declaration of Helsinki to participate in the study and for publication of data before enrollment in the study.

Participants were divided into ٢ groups: twenty eyes of ١٠ patients diagnosed with occult macular dystrophy;٦ males and ٤ females, ranging in age from ١٤ to ٢٨ years(OMD group) and twenty eyes of ١٠ age and gender matched normal subjects; ٦ males and ٤ females, ranging in age from ١٤ to ٣٠ years (control group).OMD was diagnosed according to the following findings: presence of bilateral progressive loss of central vision, no visible abnormality on fundus examination, normal fundus fluorescein angiography, normal scotopic and photopic components of the full field ERG with marked reduction of the focal macular cone ERG. Six patients reported the presence of visual problems in other family members, while the other four patients had no positive family history. The healthy volunteers had BCVA better than ٦/٩, with no associated ocular diseases.

All participants had full ophthalmologic examination including slit-lamp examination, refraction, best corrected visual acuity (BCVA) using Snellen's chart(expressed as LogMAR), intraocular pressure (IOP) measurement by applanation tonometry, dilated fundus examination, fundus fluorescein angiography (FFA),optical coherence tomography (OCT),full field electroretinogram (ERG) and multifocal electroretinogram (mf-ERG).

Spectral-domain (SD)-OCT scans (Topcon ٣D OCT model ٢٠٠٠ FA version ٨.٣٠, Topcon Corporation Company, Tokyo, Japan) was used for analysis of macular morphology.

Full field ERG and mf-ERG were recorded after pupil dilatation, using RETI-port/scan ٢١(Roland Consult, Brandenburg, Germany) and following the International Society for Clinical Electrophysiology of Vision (ISCEV) standards (١٢).

Mf-ERG was recorded using HK Loop electrodes (Hawlina – Konec electrode , HK Med, Avantia, Ljubljana, Slovenia)which were installed into the lower fornix, with the reference skin electrodes attached on the skin near the orbital rim temporally of each eye and ground skin electrodes attached on the central part of the forehead.

The mf-ERG stimulus consisted of ٦١ hexagons, covering a visual field of ٣٠° and was presented on a monitor (at a viewing distance of ٣٣ cm from the patient). Each hexagon was alternated between light and dark. Each hexagon was stimulated with the same m-sequence (frame rate: ٧٥ Hz, hexagon luminance: ١٢٠ cd/m$^{-٢}$ in the lighted state and <١ cd/m٢ in the dark state and the contrast between white and black hexagons was ٩٣٪). Each recording session was subdivided into ٨recording cycles.

The following mf-ERG parameters were recorded in the five concentric hexagon rings: the average amplitude density of P١ wave{ Amp.P١(nV/deg٢)},amplitude of P١ wave {Amp.P١(mv)},amplitude of N١ wave{Amp.N١(mv)},implicit time of N١ wave{PeT.N١(ms)}and implicit time of P١ wave{PeT.P١(ms)}.The correlation between these mf- ERG parameters and visual acuity(BCVA, logMAR) were analyzed.

Statistical analysis:

The collected data were tabulated and analyzed using SPSS (the Statistical Package For Social Sciences software, version ١٦; SPSS Inc., Chicago, Illinois, USA). Categorical data were presented as number and percentages, and analyzed by Fisher's exact test (FET). Quantitative data were tested for normality using Shapiro-Wilks test assuming normality at p>٠.٠٥. Non parametric variables were presented as median and inter-quartile range (IQR), and were analyzed by Mann Whitney U test (Z_{MWU}) for ٢ independent groups. Spearman's correlation coefficient (rho) was used to assess non-parametric correlations. Significant factors of correlation were entered through stepwise multiple linear regression analysis to detect the significant predictors of BCVA. P≤٠.٠٥ was considered significant and p≤٠.٠٠١ was considered highly significant.

Results:

Twenty eyes of ١٠ patients diagnosed with occult macular dystrophy;٦ males (٦٠٪) and ٤ (٤٠٪) females, with a mean age of ١٩.٢±٦.٠ years (OMD group) and twenty eyes of ١٠ age and gender matched normal subjects; ٦ (٦٠٪) males and ٤ (٤٠٪) females, with a mean age of ١٩.٦±٦.١ years(control group) were included in the study. There were no statistically significant differences in age, gender and refraction between the studied groups (p=٠.٥٤, ١.٠ and ٠.٨٢, respectively,Table١ and ٢).

Table (١): Age and gender of the studied groups

Variable		OMD group (n=١٠)	Control group (n=١٠)	Test of significance	p
Age (ys)	Mean±SD Range median (IQR)	١٩.٢±٦.٠ (١٤-٢٨) ١٥.٠ (١٤.٨-٢٥)	١٩.٦±٦.١ (١٤-٣٠) ١٦.٠ (١٥.٥-٢٤)	Z_{MWU} =٠.٦١	٠.٥٤
Gender (No, %)	Male	٦ (٦٠.٠٪)	٦ (٦٠.٠٪)	FET	١.٠
	Female	٤ (٤٠.٠٪)	٤ (٤٠.٠٪)		

Z_{MWU}:Mann Whitney U test,FET:Fisher's Exact test,OMD:occult macular dystrophy

All patients with OMD had normal fundus picture and normal FFA. The OCT in OMD patients showed significant thinning of the central macular thickness (CMT) in comparison to the control group (p<٠.٠٠١, Table ٢).The OCT findings in OMD patients varied between disruption of the photoreceptor/outer nuclear layers with lost ellipsoid zone and foveal cavitation in ١٢ eyes (٦٠ %),minimal central loss of the IS-OS junction and reduction of the foveal thickness in ٦ eyes (٣٠ %),while٢eyes(١٠%) were reported to have no changes in the OCT (Fig. ١).

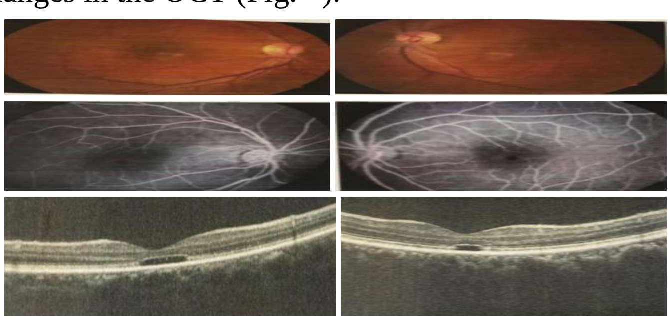

Figure (١): Fundus picture and fundus fluorescein angiography of patient with occult macular dystrophy: no visible abnormalities ,The optical coherence tomography of both eyes show lost ellipsoid zone,disruption of the photoreceptor Is/Os layer and foveal cavitation (gap in subfoveal outer segment layer not associated with diffuse retinal thinning)

Table (٢): Comparing the studied eyes regarding the studied parameters.

Variable		OMD eyes (n=٢٠)	Normal eyes (n=٢٠)	Z_{MWU}	P
		Median (IQR)	Median (IQR)		
SE		-٠.٦٣ [-٠.٧٥-(-٠.٥)]	-٠.٦٣ [-١.٢٥-(-٠.٥)]	٠.٢٣	٠.٨٢
CMT		١٥٩ (١٥٢-١٦٥)	٢٣٢ (٢٢٥-٢٤٥)	٥.٤٢	<٠.٠٠١ (HS)
BCVA(LogMAR)		٠.٨ (٠.٧-٠.٨)	٠.٠ (٠-٠.١)	٥.٥٧	<٠.٠٠١ (HS)
Amp.P١ (nV/deg ٢)	**Ring ١**	٢٢.٨ (٢١.٣-٢٦.٨)	٦٤.١ (٥٨.٢-٧٦.٠)	٥.٤١	<٠.٠٠١ (HS)
	Ring ٢	٦.٢٤ (٥.٦-٧.٧٢)	٣١.٣ (٢٩.١-٣٢.٧)	٥.٤١	<٠.٠٠١ (HS)
	Ring ٣	٨.٤١ (٦.٨-١٠.١)	١٧.٢ (١٦.٣-١٨.٢)	٥.٣	<٠.٠٠١ (HS)
	Ring ٤	٦.٢١ (٥.٤-٨.٦٧)	٩.٩٣ (٨.٩-١٠.٧)	٤.٠	<٠.٠٠١ (HS)
	Ring ٥	٥.٧٥ (٥.١-٧.٩)	٨.٤٢ (٧.١-٩.٣)	٣.٠٣	٠.٠٠٢ (S)
Amp.P١ (mv)	**Ring ١**	٠.٣٩ (٠.٣٢-٠.٤٥)	١.١١ (١.٠-١.٣)	٥.٤١	<٠.٠٠١ (HS)
	Ring ٢	٠.١٦ (٠.١٣-٠.١٩)	٠.٧٧ (٠.٧١-٠.٨٢)	٥.٤١	<٠.٠٠١ (HS)
	Ring ٣	٠.٢٨ (٠.٢١-٠.٣٦)	٠.٦١ (٠.٥٨-٠.٦٥)	٥.١٩	<٠.٠٠١ (HS)
	Ring ٤	٠.٣٤ (٠.٢٧-٠.٤٣)	٠.٥٠ (٠.٤٤-٠.٥٨)	٤.١١	<٠.٠٠١ (HS)
	Ring ٥	٠.٣٤ (٠.٣٤-٠.٥٢)	٠.٥٠ (٠.٤١-٠.٥٩٩)	٢.١٧	٠.٠٣ (S)
Amp.N١ (mv)	**Ring ١**	٠.١٨ (٠.١-٠.٢١)	٠.٤ (٠.٢٩-٠.٤٧)	٤.٧٦	<٠.٠٠١ (HS)
	Ring ٢	٠.٠٩٧ (٠.٠٥٧-٠.١)	٠.٢٣٥ (٠.٢١-٠.٢٦)	٥.٤١	<٠.٠٠١ (HS)
	Ring ٣	٠.٠٨٨ (٠.٠٨٣-٠.١١٥)	٠.١٩٣ (٠.١٤-٠.٢٧)	٤.٢٢	<٠.٠٠١ (HS)
	Ring ٤	٠.١٠٩ (٠.٠٨٧-٠.١٥٣)	٠.١٤٤ (٠.٠٧٩-٠.١٥١)	٠.٥٤	٠.٥٨٨

	Ring ٥	٠.١٥٢ (٠.١٢-٠.١٨)	٠.١٤٩ (٠.١٢-٠.١٩)	**٠.٥٩**	**٠.٥٥**
PeT.N١ (ms)	**Ring ١**	١٩.٢ (١٧.٨-٢٠.١)	١٦.٧ (١٤.٢-١٦.٩)	**٣.٥٢**	**<٠.٠٠١ (HS)**
	Ring ٢	١٦.٢ (١٥.٧-١٩.١)	١٣.٧ (١٢.١-١٥.٣)	**٣.١٨**	**=٠.٠٠١ (HS)**
	Ring ٣	١٦.١ (١٤.٧-١٧.٧)	١٤.٠ (١٢.٧-١٤.٧)	**٢.٨٣**	**٠.٠٠٥ (S)**
	Ring ٤	١٤.٧ (١٢.٥-١٧.٢)	١٣.٦ (١٢.٧-١٣.٧)	**١.٦٤**	**٠.١٠**
	Ring ٥	١٤.٧ (١٣.٧-١٦.٦)	١٤.٢ (١٢.٧-١٦.٥)	**١.٤٧**	**٠.١٥**
PeT.P١ (ms)	**Ring ١**	٤٧ (٤٥.١-٤٩.٩)	٣٧.٥ (٣٤.٥-٣٩.٢)	**٤.٢٣**	**<٠.٠٠١ (HS)**
	Ring ٢	٤٣.٨ (٣٦.٣-٤٦.٥)	٣٥.٣ (٣٥.٠-٣٧.٣)	**٣.٧٨**	**<٠.٠٠١ (HS)**
	Ring ٣	٣٧.٢ (٣٤.٥-٣٨.١)	٣٤.٣ (٣٢.٤-٣٦.٣)	**٣.٠٣**	**٠.٠٠٢ (S)**
	Ring ٤	٣٤.٦ (٣٣.٥-٣٧.١)	٣٤.٣ (٣٢.٤-٣٥.٣)	**١.٥٣**	**٠.١٢**
	Ring ٥	٣٥.٣ (٣٣.٥-٣٧.٣)	٣٤.٣ (٣٣.٣-٣٦.٣)	**١.٣١**	**٠.١٩**

SE: spherical equivalent, CMT: central macular thickness,BCVA: bestcorrected visual acuity,S: Significant, HS: highly significant,Amp.P١(nV/deg٢):the average amplitude density of P١ wave,Amp.P١(mv):amplitude of P١ wave, Amp.N١(mv):amplitude of N١ wave, PeT.N١(ms): implicit time of N١ wave, PeT.P١(ms):implicit time of P١ wave,Z_{MWU}:Mann Whitney U test, OMD: occult macular dystrophy

All patients with OMD had normal scotopic and photopic responses of the full-field ERG (Fig. ٢). Mf-ERG parameters in OMD patients showed significant central depression with less affection of the peripheral rings (Fig.٣ and ٤). The average amplitude density of P١ wave, amplitude of P١ wave and amplitude of N١ wave were significantly reduced in the central rings (ring ١,٢ and ٣),with less impairment in the paracentral areas (ring ٤ and ٥) in the OMD group in comparison to the control group (Fig.٥-٧). The implicit time of P١ and N١ waves were significantly delayed across the central rings in the OMD patients (Fig.٨ and ٩ and Table ٢).

There were significant negative correlations between the amplitude of P١ and N١ waves in the central rings (ring ١,٢ and ٣) with the BCVA(LogMAR).In OMD group, the patients with the least BCVA had the markedly reduced amplitude of P١ and N١ waves in the central rings. The implicit time of P١ and N١ waves were significantly positively correlated with BCVA (LogMAR).In the OMD group, the patients with the least BCVA had the most prolonged latency of P١ and N١ waves in the central rings (Table٣).

Table (٣):Correlation between BCVA and the mf-ERG parameters among the OMD group

mf-ERG parameters		BCVA	
		Rho	**P**
Amp.P١ (nV/deg ٢)	**Ring ١**	-٠.٩١٢	<٠.٠٠١ (HS)
	Ring ٢	-٠.٦٧٨	٠.٠٠١ (HS)
	Ring ٣	-٠.٦٤٣	٠.٠٠٣ (S)
	Ring ٤	-٠.١١٣	٠.٦٣
	Ring ٥	-٠.٠٩٣	٠.٦٩٥
Amp.P١ (mv)	**Ring ١**	-٠.٩١١	<٠.٠٠١ (HS)
	Ring ٢	-٠.٧٥٣	<٠.٠٠١ (HS)
	Ring ٣	-٠.٦٩٢	٠.٠٠١ (HS)
	Ring ٤	-٠.٠٢٤	٠.٩٢
	Ring ٥	-٠.٣١٧	٠.١٧
mp N. ١ (m	**Ring ١**	-٠.٦٩١	٠.٠٠١ (HS)
	Ring ٢	-٠.٦٢٤	٠.٠٠٣ (S)

	Ring ٣	-٠.٥٣٢	٠.٠١٦ (S)
	Ring ٤	-٠.٠٨٢	٠.٧٣
	Ring ٥	-٠.١٩٦	٠.٤١
PeT.N١ (ms)	**Ring ١**	٠.٧٠٨	<٠.٠٠١ (HS)
	Ring ٢	٠.٦٤٦	٠.٠٠٢ (S)
	Ring ٣	٠.٥٤٥	٠.٠١٣ (S)
	Ring ٤	٠.٣١٠	٠.١٨
	Ring ٥	٠.٢٥٥	٠.٢٧
PeT.P١ (ms)	**Ring ١**	٠.٧٩١	<٠.٠٠١ (HS)
	Ring ٢	٠.٧٢٠	<٠.٠٠١ (HS)
	Ring ٣	٠.٥٧٤	٠.٠٠٨ (S)
	Ring ٤	٠.٠٢٩	٠.٩٠
	Ring ٥	٠.١٥٨	٠.٥١

BCVA: bestcorrected visual acuity,S: Significant, HS: highly significant,mf-ERG: the multifocal electroretinogram, Amp.P١(nV/deg٢):the average amplitude density of P١ wave,Amp.P١(mv):amplitude of P١ wave, Amp.N١(mv):amplitude of N١ wave, PeT.N١(ms): implicit time of N١ wave, PeT.P١(ms):implicit time of P١ wave,rho:Spearman's correlation coefficient, OMD: occult macular dystrophy

The factors that were found to be significantly correlated with BCVA were entered in the stepwise multiple linear regression model to detect its significant predictors (Table٤). The model showed that the average amplitude density of P١ wave in ring ١ and ٢,amplitude of N١ wave in ring ١ and ٢ and P١ and N١ implicit times in ring ١ were the significant predictors of BCVA (p<٠.٠٥ for all).

Table (٤): Stepwise multiple linear regression analysis for the predictors of BCVA

Model summary	**R٢**	**Adjusted R٢**	**SEE**	**F**	**P**
	٠.٩٠٩	٠.٩٠٤	٠.٠٤٧	١٧٩.٤	<٠.٠٠١ (HS)
Variable	**Unstandardized Coefficients**	**Standardized Coefficients**	**٩٥٪ CIof B**	**T**	**P**

	B	Std. Error	Beta			
(Constant)	١.١٣	٠.٠٨٤	----	٠.٩٤-١.٣	١٣.٣	<٠.٠٠١ (HS)
Amp.P١ (nV/deg ٢) Ring ١	-٠.٠١٦	٠.٠٠١	-٠.٨٤٧	-٠.٠١٩- (-٠.٠١٤)	١٤.٩	<٠.٠٠١ (HS)
Amp.N١(mv) Ring ١	-١.٢٩	٠.١٠٢	-٠.٢٥٩	-١.٥- (-١.٠٧)	١٢.٧	<٠.٠٠١ (HS)
PeT.N١(ms) Ring ١	٠.٠١٤	٠.٠٠١	٠.٢٦٣	٠.٠١١- ٠.٠١٧	٩.٦٩	<٠.٠٠١ (HS)
Amp.N١(mv) Ring ٢	٠.٤٢٥	٠.٠٥٨	٠.٢٣٦	٠.٠٠٥- ٠.٠١١	٧.٣٣	<٠.٠٠١ (HS)
PeT.P١(ms) Ring ١	٠.٠٠٨	٠.٠٠١	٠.١٤٧	٠.٣-٠.٥٥	٥.٣٤	<٠.٠٠١ (HS)
Amp.P١ (nV/deg ٢) Ring ٢	-٠.٠٠٤	٠.٠٠١	-٠.٠٨١	-٠.٠٠٧- (-٠.٠٠٢)	٣.٣٣	٠.٠٠٥ (S)

BCVA: bestcorrected visual acuity,S: Significant, HS: highly significant,Amp.P١(nV/deg٢):the average amplitude density of P١ wave,Amp.P١(mv):amplitude of P١ wave, Amp.N١(mv):amplitude of N١ wave, PeT.N١(ms): implicit time of N١ wave, PeT.P١(ms):implicit time of P١ wave,R٢: Regression coefficient, SEE: standard error of estimate; F: F-ratio

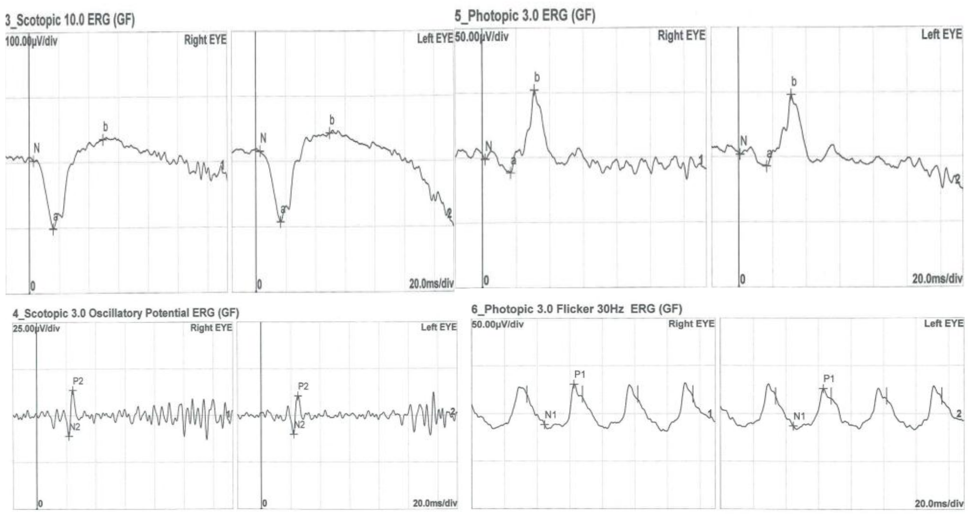

Figure (٢):Normal scotopic and photopic responses of the full-field electroretinogram in a patient with occult macular dystrophy

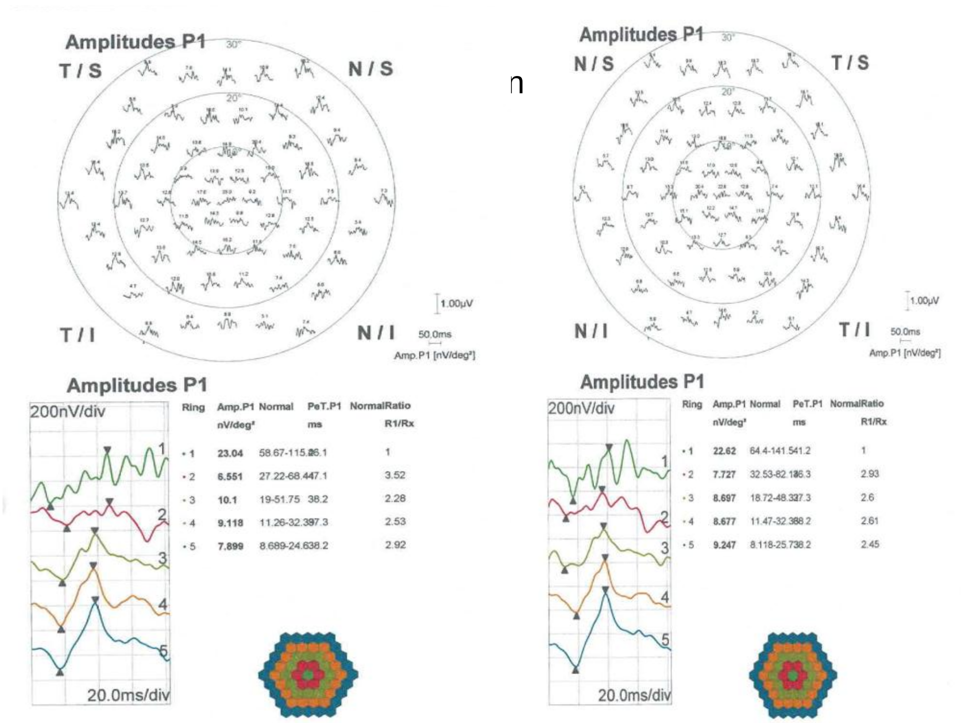

Figure (٣): The multifocal electroretinogram of a patient with occult macular dystrophy, there was reduction of the amplitude of P١ wave in the central rings (١,٢) with less affection of the peripheral rings.

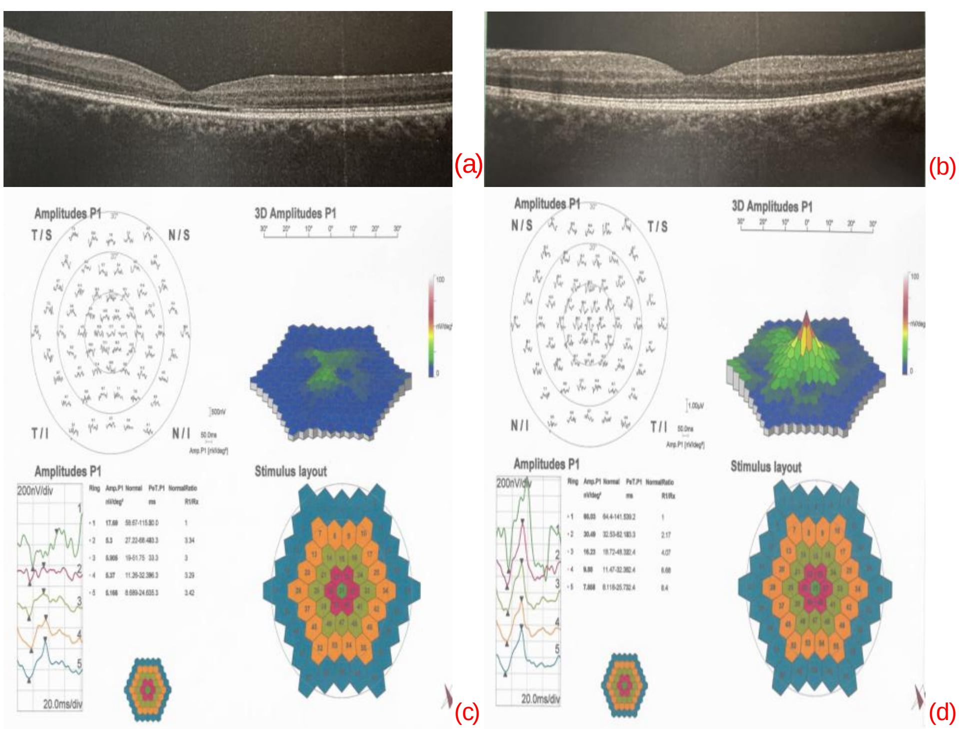

Figure (٤): a) The optical coherence tomography of a patient with occult macular dystrophy (OMD) shows disruption of IS/OS segment and decreased foveal thickness b) The optical coherence tomography of normal subject C) The multifocal electroretinogram (mf-ERG) of OMD patient with reduced amplitude of P١ wave in central ring and lost foveal peak in the ٣D layout d) mf-ERG in normal subject.

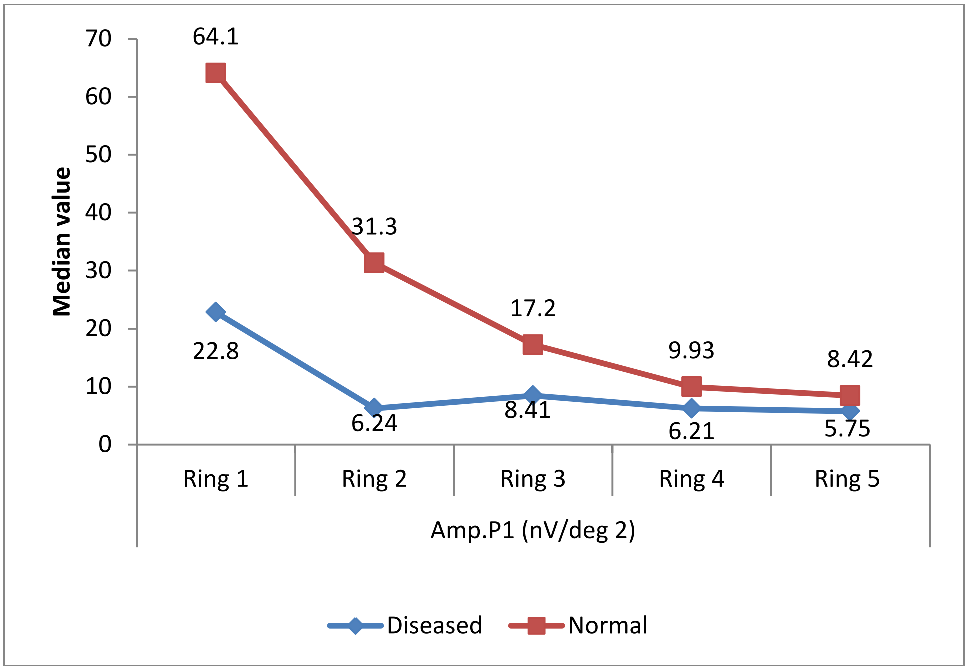

Figure (٥) :Line graph showing median average amplitude density of P١wave among the studied groups, there were marked reduction in the central rings in the occult macular dystrophy group.

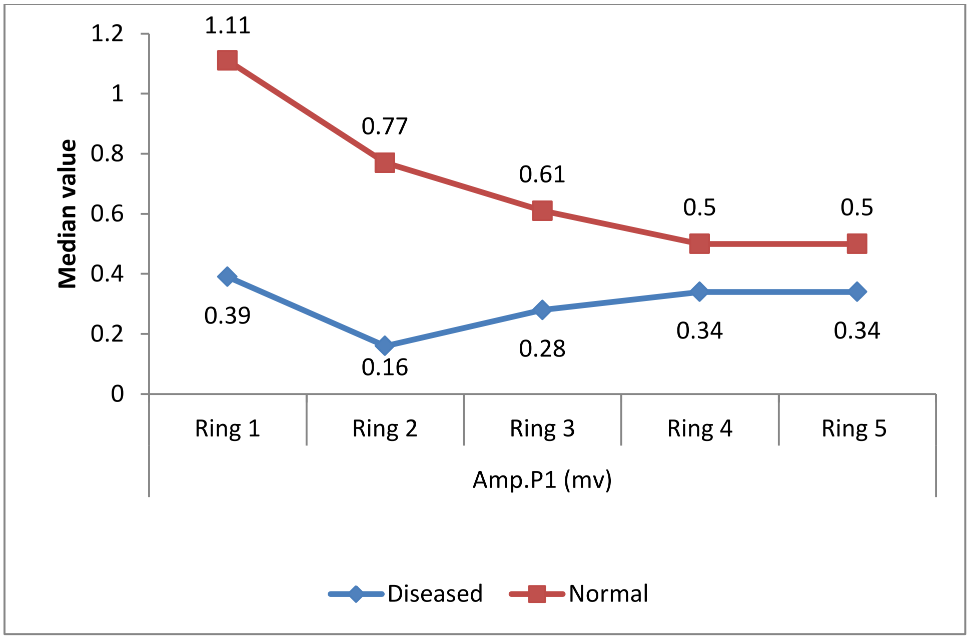

Figure (٦) :Line graph showing median amplitude of P١ wave among the studied groups

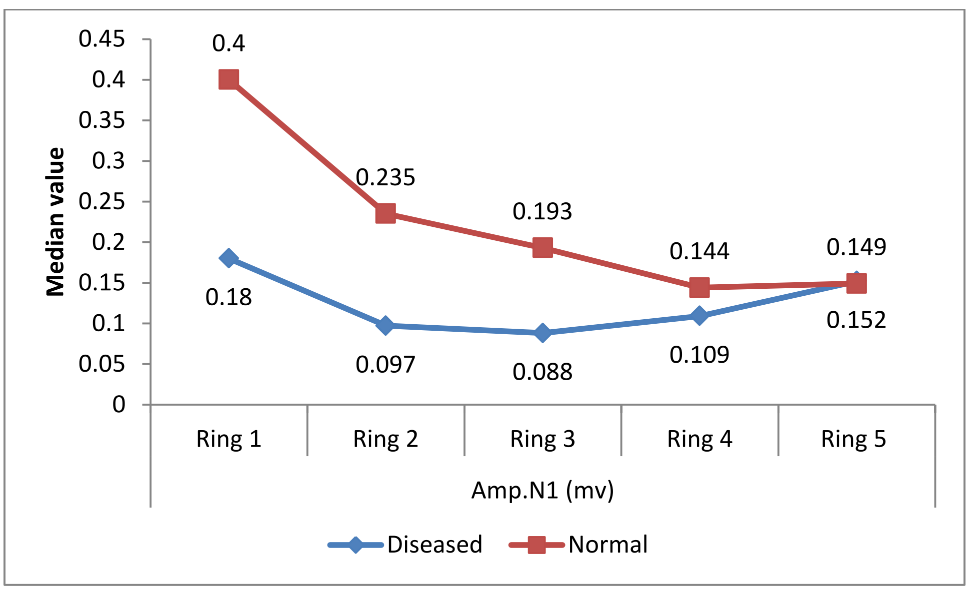

Figure (٧):Line graph showing median amplitude of N١ wave among the studied groups

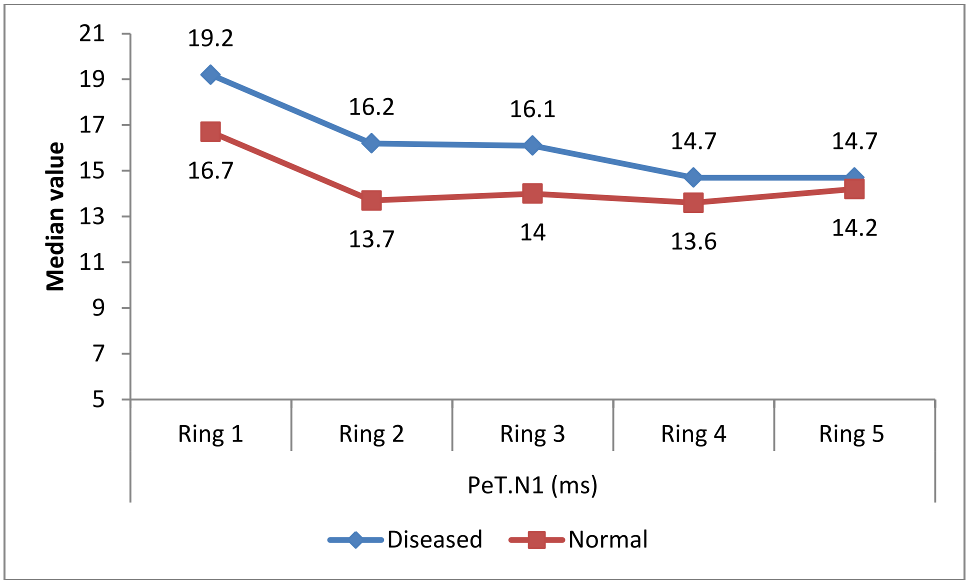

Figure (٨):Line graph showing median implicit time of N١ wave among the studied groups

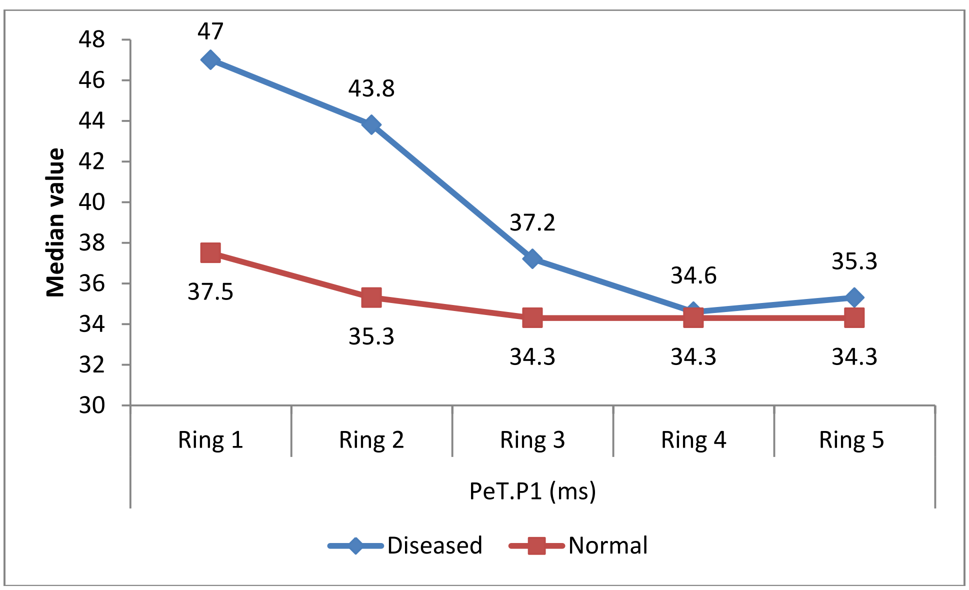

Figure (٩):Line graph showing median implicit time of P١ wave among the studied groups

Discussion:

OMD is a rare type of macular dystrophy characterized by progressive loss of central vision due to macular dysfunction (١,١٧).It is usually misdiagnosed due to associated normal fundus appearance, normal FFA and normal full-field ERG (٢-٥). The ophthalmologists should keep it in mind as a possible cause of unexplained decreased visual acuity.

We report the first ten cases with OMD in Benha University Hospital. The precise analysis of mf-ERG helped us to make the diagnosis in spite of normal fundus, FFA and flash ERG.

Mf-ERG is considered the main diagnostic tool to distinguish OMD from other causes of decreased visual acuity with no visible fundus changes such as amblyopia , non-organic visual loss or optic nerve diseases (٦,١٨).

OMD should be also differentiated from other hereditary retinal diseases with normal fundus appearance such as congenital stationary night blindness (١٩,٢٠) and cone dysfunction syndromes (٢١,٢٢).However, these diseases have abnormal full-field ERG with characteristics findings that help in their diagnosis.

Previous studies reported the presence of structural changes in the macular area of OMD patients evident by OCT (٩,١٠,٢٣-٢٥).OCT may show reduction of foveal thickness and disrupted IS/OS junction. However, these changes may be subtle in some patients even in the presence of marked reduction in mf-ERG. This indicates that the functional changes in the macular area may precede the structural changes in these patient (١,١١). Padhi et al, in their study, on two siblings with OMD reported that mf-ERG responses were markedly reduced in the central macula in spite of different OCT findings in both cases. The youngest patient had apparent mf-ERG changes with minimal OCT defect, and they concluded that the structural changes seen in the OCT might not always correspond to the degree of functional loss and that functional changes might precede the appearance of structural changes (١).

In the present study, the OMD patients showed significant depression of mf-ERG responses especially in the central rings with less affection of the peripheral rings. These results reflect that the retinal dysfunction is confined to the central macula. These findings are comparable with previous studies that also reported marked central depression in mf-ERG (١,٣,٧,٨,٢٦).

In the present study, the correlation between various mf-ERG parameters and visual acuity (V/A) were assessed. There was a significant negative correlation between the amplitude of P١ and N١ waves and the BCVA(LogMAR).In addition, there was a significant positive correlation between the implicit time of P١ and N١ waves and the BCVA(LogMAR).In the OMD group, patients with the least BCVA had the markedly reduced amplitude and prolonged latency of P١ and N١ waves. A better BCVA was associated with less extensive macular dysfunction. Multiple regression analyses demonstrated that the amplitude and latency of P١ andN١ waves in the central rings (١ and ٢) were the most important determinants for BCVA. These mf-ERG parameters may be used for early detection of subclinical cases with positive family history and can be used to detect minimal macular dysfunction at an early stage of OMD. It may also be a valuable biomarker in prediction of visual prognosis in OMD patients.

One of the limitations of the current study was the small number of included patients. Further genetic studies on a larger population sample and longitudinal follow-up are needed.

In conclusion, mf-ERG has a key role in detection of occult macular dystrophy and can be considered as a valuable objective test for detection of central/macular dysfunction , that had a profound impact on the visual acuity. The amplitude and latency of P١ and N١ waves in ring ١ and ٢ may be used as biomarkers for prediction of visual prognosis in these patients.

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