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ORIGINAL ARTICLE

Evaluation of Predictors of Recovery after Idiopathic Facial Palsy

Rania Y. Helal[1], Amany M. AbdAllah[2], Bothina M. Ramadan[1*], Sabah E. Fathy[1]

1. Department of Neurology, Faculty of Medicine, Zagazig University, Zagazig, Egypt
2. Department of family medicine, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Corresponding author:
Bothina M. Ramadan[1]

Address: Department of Neurology, Faculty of Medicine, Zagazig University, Zagazig, Egypt
.
E-mail:
drbothinaramadan@gmail.com

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ABSTRACT

Background: Despite Bell's palsy is not a life-threatening condition, it has a lot of psychological impact, up to now the exact underlying pathophysiology of bell's palsy is not fully understood, so we are trying to recognize the factors that affect its recovery.

Methods: This prospective cohort study was executed on 60 patients with Bell's palsy who underwent complete blood count including calculation of neutrophil lymphocyte ratio, evaluation of severity using B-H scale and neurophysiological testing of the facial nerve with evaluation of motor amplitude and degeneration index of the nerve, then follow up was done after three months. **Results:** 18.3% of our patients had severe bell's palsy, the mean NLR in mild cases was 3.1 ± 0.17 versus 3.71 ± 0.36 for severe cases, high NLR and comorbid diabetes were found to be associated with increased severity of bell's palsy, old age and high NLR were associated with poor recovery after three months**.**

Conclusion: Neutrophil lymphocyte ratio, old age, initial B-H scale, degeneration index and diabetes were found to possess a potent statistical value in predicting short term outcome of bell's palsy.

Keywords: Bell's palsy; prognosis; severity; NLR; degeneration index.

INTRODUCTION

Bell's palsy (BP) accounts for approximately 60-75% of unilateral facial palsy cases representing the most prevalent cause of this condition **[1].** However, BP does not affect the life expectancy and mostly associated with a favourable outcome with or without treatment, it produce a lot of psychological stress due the long treatment course and expectation of incomplete recovery **[2].** Up till now, the exact pathophysiologic process underlying BP is still uncertain, thus different theories had been proposed including inflammatory, infectious, and ischemic insult **[3].** Several previous studies had assessed different clinical prognostic factors in Bell's palsy including patient age, initial severity, time from symptoms onset to the start of steroid therapy, presence of comorbid chronic diseases including type 2diabetes mellitus, high cholesterol level and hypertension and obesity **[4,5,6,7].**

H-B grading system is the commonest scale used to evaluate the severity of facial palsy and also validated for assessing the degree of recovery **[8]** and higher grades were associated with incomplete recovery **[9].**

Although electrophysiological tests are powerful predictors of BP outcome in its subacute stage **[8],** their non-availability might interfere with this role, so several studies were trying to find other simple available biomarkers **[10].** Leukocytes play an important role in the development and progression of inflammatory disorders. Neutrophil – lymphocyte ratio (NLR) is an easily calculated marker from complete blood count profile reflecting the grade of inflammation **[11]** and found to record high ratios among patients with severe BP **[12].**

This study aimed at assessing complete blood count parameters in association with clinical assessment, disease severity, neurophysiological studies and outcome of Bell's palsy to improve prognosis.

METHODS

This prospective cohort study was carried out in Neurology department,Zagazig university, during the period from December 2022 to May 2023 on 60 patients (43 females and 17 males) with

definite diagnosis of Bell'spalsy. The included subjects had a mean age of 39.05± 11.79 years; they were presented within the first 48 hours of onset before starting treatment. We excluded upper motor neuron facial palsy, history of otologic surgery, otitis media, cerebellopontine angle pathology or cochlear malformation, trauma or neurological disorders causing facial paralysis or uncontrolled diabetes.

All patients were subjected to a detailed history taking, general and neurological examinations with a detailed clinical assessment of the facial nerve function using House-Brackmann (H-B) scale which is a validated tool to evaluate the degree of facial paralysis In this scale, grade I indicating normal function, and grade VI denotes complete paralysis. Intermediate grades (II-V) vary according to function at rest and with effort **[13].**

Laboratory investigations: complete blood count was done for all patients with evaluation of its different parameters including Hematocrit; WBCs count, platelets count and manual calculation of neutrophil –lymphocyte ratio (NLR) was done.

Nerve conduction study was performed at neurology department using Nihon Kohden machine for both facial nerves during the period of three to seven days from disease onset, comparing affected by healthy side regarding distal latency (DL) and compound motor action potential amplitude (CMAP) with calculation of the degeneration index according to the formula ([100 − (ENoG amplitude affected/ unaffected side) × 100] **[14].** This procedure was delayed after 3 days because it is the duration needed for the Wallerian degeneration to spread from the injured intratemporal part to the distal part at the stylomastoid foramen where electrical stimulation is done **[15].**

Outcome measurement was done after three months, the recovery was assessed by House Brackman scale and registered as unfavorable recovery with House Brackman is III or more and favorable recovery (improvement without sequale) with House Brackman is I or II **[16].**

The Institutional Review Board, Faculty of Medicine Zagazig University approved this study (ZU-IRB #10121/19-12-2022). The study was done according to the code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

STATISTICAL ANALYSIS

SPSS (Statistical Package for the Social Sciences) version 26 software was used for data analysis. Categorical variables were defined using their absolute frequencies and were compared using chi square test, fisher exact and Monte Carlo tests when applicable. Chi square was used for comparing the ordinal data between two groups, Shapiro-Wilk test was used to verify assumptions for use in parametric tests. Means, standard deviations or median and interquartile ranges were used for quantitative data description. To compare quantitative data between two groups, independents sample t test (for normally distributed data) and Mann Whitney test (for not normally distributed data) were used. Binary logistic regression was used to identify independent risk factors associated with certain health problem. All significant factors in univariate analysis were introduced in binary backward Wald regression analysis. ROC curve was used to define the best cutoff of certain quantitative parameters. The level statistical significance was set at $P < 0.05$. A highly significant difference was present if $P \leq 0.001$.

RESULTS

The baseline demographics and clinical characteristics of the studied patients were illustrated in table (1) including the findings of NCS as the median CMAPamplitude was 0.966 and median degenerative index was 23%. Thirty percent of patients were categorized as having severe to total palsy. There is a statistically significant relation between severity of Bell's palsy and sex of patients (male gender associated with severe disease), diabetes, WBCS, NLR, and degenerative index (all are associated with severe Bell's). There is statistically non-significant relation between severity of Bell's palsy and age, hypertension, ESR, CRP or CMAP amplitudeas was shown in table (2). In table (3), high NLR and comorbid diabetes significantly increase risk of having severe to total bell's palsy by 670.494 and 30.372 folds respectively. There is a statistically significant relation between recovery of Bell's palsy and all of age, sex of patients (male gender associated with poor recovery), HB scale, diabetes, WBCS, NLR, CRP and degenerative index (all are associated with no recovery). There is a statistically non-significant relation between severity of Bell's palsy and either hypertension, ESR, CRP or CMAP amplitude (table 4). While in table (5), a binary regression analysis of factors associated with no recovery among studied patients showed that older ages and elevated NLR independently increased risk of no recovery by 1.162 and 3652.39 folds respectively. ROC curve

revealed that the best cutoff of NLR in prediction of incomplete recovery is ≥3.65 with sensitivity 90.9%, specificity 93.9%, positive predictive value 76.9%, negative predictive value 97.9% and overall accuracy 93.3% ,while the best cutoff of degenerative index in prediction of poor recovery is ≥ 27.5% with sensitivity 90.9% and specificity 85.7.

Table (1): Baseline demographics and clinical characteristics of the involved patients

	Mean ± SD	Range
Age (years)	39.05 ± 11.79	20 – 65
Sex (male)	17	28.3%
Diabetes mellitus:	8	13.3%
Hypertension:	9	15%
WBCs	6.06 ± 1.1	4.5 – 8.5
NLR	3.28 ± 0.37	2.9 – 4.1
ESR (mm/hr)	12.07 ± 3.05	6 – 18
CRP (mg/L)	7.82 ± 1.46	3 – 10
NCS amplitude	0.966 ± 0.38	0.1 – 1.8
Degenerative index (%)	23(16.5 – 28%)	10 – 90%
HB scale: Mild – moderate Severe - total	 42 18	 70% 30%

WBCs white blood cells, NLR neutrophil lymphocyte ratio , ESR erythrocyte sedimentation rate , CRP C reactive protein , CMAP amplitude compound motor action potential, H-B scale House-Brackmann scale

Table (2): Association between severity of Bell's palsy and the studied patients: characteristics

	Mild to moderate N=49 (%)	Severe to total N=11 (%)	Test	P
Age (years) [Mean ±SD]	36.83 ± 9.8	44.22 ± 14.52	-1.975¥	0.06
Sex: Male Female	 7 (16.7%) 35 (83.3%)	 10 (55.6%) 8 (44.4%)	**9.384**∞	**0.002***
Diabetes mellitus:	1 (2.4%)	7 (38.9%)	**Fisher**∞	**<0.001****
Hypertension:	7 (16.7%)	2 (11.1%)	Fisher∞	0.71
WBCs [Mean ±SD]	5.83 ± 0.87	6.59 ± 1.39	**-2.158**¥	**0.042***
NLR [Mean ±SD]	3.1 ± 0.17	3.71 ± 0.36	**-6.854**¥	**<0.001****
ESR [Mean ±SD]	11.83 ± 2.81	12.61 ± 3.57	-0.905¥	0.369
CRP [Mean ±SD]	8.0 ± 1.31	7.39 ± 1.72	1.506¥	0.137
amp affected [Mean ±SD]	1.05 ± 0.5	0.93 ± 0.32	0.759¥	0.451
Degenerative index[Median, IQR]	21 (15 – 26)	28.5(22.75 – 66.25)	**Z(-3.118)**	**0.002***

§ Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant *p<0.05 is statistically significant ¥Independent sample t test ∞Chi square test Z Mann Whitney test
WBCs white blood cells , NLR neutrophil lymphocyte ratio , ESR erythrocyte sedimentation rate , CRP C reactive protein , CMAP amplitude compound motor action potential

Table (3) Binary regression analysis of factors associated with severity

	β	P	AOR	95% C.I.	
				Lower	Upper
NLR	6.508	<0.001**	670.494	18.123	24806.606
Diabetes	3.414	0.035*	30.372	1.267	727.957

AOR adjusted odds ratio **p≤0.001 is statistically highly significant *p<0.05 is statistically significant CI Confidence interval NLR neutrophil lymphocyte ratio

Table (4): Association between outcome and characteristics of the studied patients:

	Recovery N=49 (%)	No recovery N=11 (%)	Test	P
Age (years) [Mean ±SD]	36.0 ± 9.96	52.64 ± 9.77	**-5.021**¥	**<0.001****
Sex: Male Female	 9 (18.4%) 40 (81.6%)	 8 (72.7%) 3 (27.3%)	Fisher	**<0.001****
Diabetes mellitus:	4 (8.2%)	4 (36.4%)	Fisher	**0.031***
Hypertension:	6 (12.2%)	3 (27.3%)	Fisher	0.345
HB scale Mild to moderate Severe to total	 41 (83.7%) 8 (16.3%)	 1 (9.1%) 10 (90.9%)	Fisher	**<0.001****
WBCs [Mean ±SD]	5.76 ± 0.87	7.38 ± 1.05	-5.387¥	**<0.001****
NLR [Mean ±SD]	3.15 ± 0.24	3.89 ± 0.16	-2.054¥	**0.044***
ESR [Mean ±SD]	11.69 ± 2.84	13.73 ± 3.52	2.917¥	**0.005***
CRP [Mean ±SD]	8.06 ± 3.52	6.73 ± 1.79	1.506¥	0.137
amp affected [Mean ±SD]	1.04 ± 0.56	0.95 ± 0.33	0.511¥	0.611
Degenerative index [Median(IQR)]	21.0 (15 – 25)	42(29 – 78)	Z(-4.802)	**0.001****

§ Mann Whitney test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant ¥Independent sample t test ∞Chi square test Z Mann Whitney test WBCs white blood cells , NLR neutrophil lymphocyte ratio , ESR erythrocyte sedimentation rate , CRP C reactive protein , CMAP amplitude compound motor action potential, H-B scale House-Brackmann scale

Table (5) Binary regression analysis of factors associated with no recovery

	β	P	AOR	95% C.I.	
				Lower	Upper
Age	0.150	0.066	1.162	0.990	1.364
NLR	8.203	0.005*	3652.390	11.868	1124013.366

AOR adjusted odds ratio **p≤0.001 is statistically highly significant *p<0.05 is statistically significant CI Confidence interval NLR neutrophil lymphocyte ratio

Table (6) Performance of degenerative index and NLR in prediction of no recovery

	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy	p
NLR	0.97	≥3.65	90.9%	93.9%	76.9%	97.9%	93.3%	<0.001**
Degenerative index	0.966	≥27.5%	90.9%	85.7%	58.8%	97.7%	71.7%	<0.001**

**p≤0.001 is statistically highly significant AUC area under curve PPV positive predictive value NPV negative predictive value NLR neutrophil lymphocyte ratio

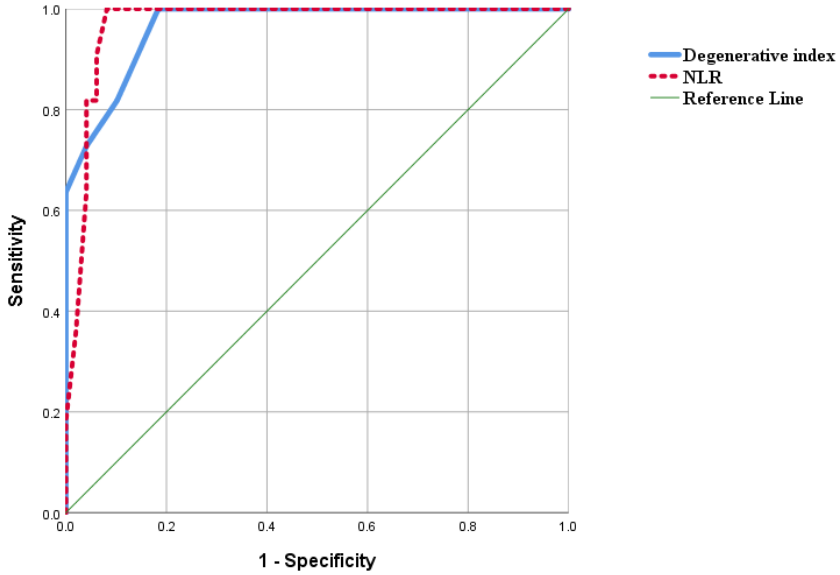

Figure (1) ROC curve showing performance of degenerative index and NLR in prediction of no recovery among studied patients

DISCUSSION

Bell's palsy is considered the commonest cause of unilateral lower motor facial nerve palsy and still the exact cause of Bell's palsy is not well recognized. Several theories have been proposed including autoimmune, vascular and inflammatory disorders **[17].** Despite it is not a life threatening condition, it has severe passive impact on the patient social life thus most of the recent studies are targeting to understand the underlying pathophysiology and predictors of outcome of Bell's palsy.

A significant increase in lymphocytes and NLR in patients with Bell's palsy when compared with age and sex matched controls was found in the current study. Also, higher ratios were found among patients with severe Bell's palsy and patients with poor recovery. These results were in the same line of other several studies **Baklacı et al. [17] and Bucak et al. [18].** These findings are supporting the theory that Bell's palsy is caused by an autoimmune process following viral infection and mediated through cell-mediated inflammatory process **[19].** The neutrophil to lymphocyte ratio is an easily calculated marker for inflammation and the more increased the ratio, the severer the inflammation so it can predict the disease severity and recovery **[20].**

The initial severity of facial palsy measured by BH scale was found to be a significant predictor for recovery and outcome. Several studies had reported that H-B grade of II or lower can indicate favorable outcomes and normal function in daily life **[21, 22, and 23]. Yoo et al. [24]** stated that initial lower H–B grade was the most important factor influencing complete recovery in pediatric age group. Also, **Mantsopoulos et al. [25]** found that the initial severity of facial palsy is the most statistically valuable predictor for long term outcome measured at 2-6years. In the same context, **Fujiwara et al. [26]** reported that the facial grading score assessed using the Yanagihara facial grading system at 1 week following treatment was associated with poor outcome of Bell palsy at 6 months.

In our work, we found that presence of hypertension is not associated with unfavorable outcome of Bell's palsy, this finding could be explained that our patients had controlled hypertension, these results were in agreement with the results of other studies **[27, 28].**

On the other hand, **Myung etal. [23]** reported that presence of severe hypertension was associated with poor outcome and this could be related to different factors including treatment non-compliance, hemorrhages into the facial canal are occurring with severe hypertension **[29].** Even more, **Agarwal et al. [30]** found that severe hypertension is one of the risk factors for facial palsy and blood pressure control is associated with spontaneous recovery.

Several previous studies had stated that diabetes mellitus is associated with poor outcome following Bell's palsy and several explanations were thought to cause incomplete recovery of facial nerve as **Kariya et al. [31]** supposed that the presence of microangiopathy in diabetics and thicker vasa nervosa of facial nerves in diabetic patient making them more exposed to ischemia producing more severe lesions , in addition, hyperglycemia can cause direct facial nerve injury by several mechanisms including increased

oxidative stress, accumulation of advanced glycation end products. On the other hand, some other studies had demonstrated that there is no correlation between DM and final recovery of facial nerve **[26, 32, 33].**

Regarding the Electrophysiological studies which were originally introduced by **Fisch [34],** they can be used as a marker of severity of facial nerve lesion .these studies including CMAP amplitudes and degeneration index .

We concluded that CMAP amplitudes were severely reduced among patients with severe facial palsy as the generated CMAP generated in affected facial muscle reflects summation of the working facial nerve fibers and this reduction was associated with poor recovery while increased degeneration index could be used as a potent predictor for both severity and outcome following Bell's palsy. These findings were going in hand with **P P and Muthukrishnan [35]** who hypothesized that presence of degeneration 90% or more is associated with poor outcome with high possibility of secondary synkinesis development because of unfavorable regeneration **[36].** While **Takemoto et al. [37]** suggested that drop of CMAP amplitudes by less than 80% is associated with complete recovery.

Old age was found to be a important prognostic marker for poor recovery of Bell's palsy and this was previously noted by **Kafle and Thakur [38]** who reported that slowness of healing process with regeneration and central adaptation with advancing age occurs. Also**, Yoo et al. [2]** found that complete recovery of Bell's palsy is noted in ages less than 40. On the other hand **Takemotoet al. [37]** stated that age doesn't affect the outcome of facial palsy.

We determined the cut-off values of NLR and degeneration index of facial nerve for predicting poor recovery of BP was ≥ 3.65 and ≥ 27.5% respectively, to our knowledge, no previous studies had covered this point of interest.

Conclusion: Many factors were found to be associated with greater muscle weakness in Bell's palsy including male gender, diabetes, elevated WBCS, increased NLR, and higher degenerative index. Also a variety of factors were found to be associated with prediction of poor functional outcome including older ages and elevated NLR.

Conflict of interest

The authors declare that they have no conflict of interest.

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