Logistic Regression Analysis

Clinical and Electroencephalographic Profiles of Patients with Metabolic Encephalopathies

Methodology:

Data Processing:

Binary coding (1 = present, 0 = absent) was used for all categorical variables. Dummy coding was employed for categorical variables with more than two categories.

Descriptive Statistics:

Frequency distributions were used to summarize descriptive variables, historical clinical features, and malignant classification.

Test of Association:

To establish association between classification and clinical outcome, test of association using Fisher Exact Test will be used. Fisher Exact Test is chosen over Chi-Squared Test of Independence to account for the small sample size that the study is working on. Having a low p-value in these test means that classification and clinical outcome shows significant association between them. If such significant association exist, Cramer's V will be used to quantify and interpret the strength of the association. (Interpretation of Cramer's V value can be found in this link.)

Logistic Regression:

To examine associations, binary logistic regression was used to compute odds ratios and their confidence intervals.

All descriptive variables were used to model classification and clinical outcome and identify which variables are associated.

Separate logistic regression models were built for each classification (Benign, Malignant, and Highly Malignant), using etiology and mortality as predictors. Adjusted models were used after identifying significant variables. Significant predictors for malignance were used on a separate logistic model to associate poor/death clinical outcomes to these factors.

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Distribution of Classification

Table 1. Distribution of classification among patients

Classification	n	%
Benign	47	65
Malignant	20	28
Highly Malignant	5	7

Descriptive Statistics

Table 2. Demographics and historical clinical features of patients

Demographics	**N = 72**	
	n	**%**
Gender		
Female	39	54
Male	33	46
Age (years)		
Mean ± SD	69 ± 18	
Admission		
ICU	32	44
Room	40	56
Seizure		
Focal Motor	8	11
Generalized	7	10
Myoclonic Jerks	3	4
None	54	75
Comorbidities		
Cancer	10	14
Kidney Disease	13	18
Diabetes	22	31
Hypertension	42	58
Liver Disease	10	14
Previous Stroke	17	24
Risk Factors		
Alcohol Intake	10	14
Smoking	31	43
Drugs	1	1
Neuroimage Findings		
Cerebral Edema	2	3
Cerebrocerebellar Atrophy	42	58
Chronic Infarct	30	42
White Matter Changes	37	51
Unremarkable	9	13

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Type of Encephalopathy		
Anorexic-Ischemic	9	13
Drug-Induced	2	3
Electrolyte Disturbance	13	18
Endocrine	4	6
Hepatic	8	11
Hypercapnic	1	1
Septic	43	60
Uremic	7	10
Withdrawal Syndrome	2	3
MRS Scores		
Good Outcome	27	38
Poor Outcome	22	31
Death	23	32

Table 3. Demographics and historical clinical features of patients with classification

Demographics (OR)	**Benign (n = 47)**		**Malignant (n = 20)**		**Highly Malignant (n = 5)**		**p-value***
	n	**%**	**n**	**%**	**n**	**%**	
Gender							
Female (0.02)	30	64	7	35	2	40	**0.0006**
Male	17	36	13	65	3	60	
Age in years							
Mean ± SD (1.11)	69 ± 18		67 ± 20		73 ± 12		**0.0011**
Admission							
ICU (9.49)	17	36	12	60	3	60	**0.0012**
Room	30	64	8	40	2	40	
Seizure							
Focal Motor (1.03)	2	4	5	25	1	20	**0.0324**
Generalized	6	13	0	0	1	20	0.1953
Myoclonic Jerks	2	4	0	0	1	20	0.9242
None	37	79	15	75	2	40	
Comorbidities							
Cancer	7	15	2	10	1	20	0.8314
Kidney Disease	11	23	1	5	1	20	0.6845
Diabetes	15	32	6	30	1	20	0.7633
Hypertension	27	57	12	30	3	60	0.2144
Liver Disease	6	13	3	15	1	20	0.1073
Previous Stroke	10	21	6	30	1	20	0.1450
Risk Factors							
Alcohol Intake (3.07)	5	11	4	20	1	20	**0.0314**
Smoking	19	40	7	35	5	100	0.9959

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Drugs	1	2	0	0	0	0	0.3989
Neuroimage Findings							
Cerebral Edema	0	0	2	10	0	0	0.9943
Cerebrocerebellar	28	60	12	60	2	40	**0.0490**
Atrophy (0.05)							
Chronic Infarct	17	36	12	60	1	20	0.8638
White Matter Changes	24	51	12	60	1	20	0.0587
Unremarkable (3.52)	6	13	3	15	0	0	**0.0422**
Etiology							
Anorexic-Ischemic	5	11	3	15	1	20	0.5389
Drug-Induced** (7.45)	1	2	1	5	0	0	**0.0002**
Electrolyte Disturbance	8	17	4	20	1	20	0.2048
Endocrine	2	4	2	10	0	0	0.8909
Hepatic (9.78)	3	6	4	20	1	20	**0.0046**
Hypercapnic	1	2	0	0	0	0	0.9975
Septic	28	60	12	60	3	60	0.3070
Uremic	6	13	0	0	1	20	0.5791
Withdrawal	2	4	0	0	0	0	0.9970

*Bold p-values are significant at α = 5%
**Low frequency variable

Table 3 indicates that among all demographic and clinical factors examined, being female, increasing age, being admitted in the ICU, presence of focal motor seizure, history of alcohol intake, presence of cerebrocerebellar atrophy, unremarkable neuroimage findings, and having drug-induced or hepatic etiology are significantly associated with malignant classification.

Being female and having cerebrocerebellar atrophy, having ORs of less than 1, is associated to less odds of being in the malignant association. All other significant variables are positive predictive of malignance.

Test of Association

Table 4. Frequency distribution and test of association results between classification and clinical outcome.

Clinical Outcome	Good	Poor	Death	Total	p-value*
Benign	20 (14%)	15 (10%)	12 (8%)	47 (65%)	
Malignant	7 (5%)	5 (3%)	8 (6%)	20 (28%)	**0.0233**
Highly malignant	0 (0%)	2 (1%)	3 (2%)	5 (7%)	

*Bold p-values are significant at α = 5%

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The test of association using Fisher Exact Test shows that the classification and clinical outcome have significant association between them $(\chi^2 = 9.54)$. The corresponding Cramer's V value is 0.182 which indicates a strong association between the two. The frequency distribution also directs that across clinical outcome from good to death, the number of benign classification decreases. Moreover, malignant and highly malignant classification have more poor and death outcomes rather than good.

Logistic Regression

Table 5. Association between factors and poor/death clinical outcomes.

Variables	Risk Estimate		
	OR	95% CI	p-value
Gender: Female	0.43	0.18 – 1.03	0.0586
Age	1.10	1.05 – 1.14	**<0.001**
Admission: ICU	12.16	3.86 – 38.33	**<0.001**
Seizure: Focal Motor	5.03	0.90 – 28.2	0.0662
Risk Factor: Alcohol	0.23	0.05 – 0.97	**0.0454**
NF: Cerebrocerebellar Atrophy	0.40	0.14 – 1.12	0.0835
NF: Unremarkable	1.47	0.31 – 6.92	0.6281
Etiology: Drug Induced	5.21	0.10 - 280	0.4174
Etiology: Hepatic	5.76	1.29 – 25.90	**0.0228**

*Bold p-values are significant at α = 5%

Table 5 indicates that among all significant predictors of malignance, increasing age, being admitted in the ICU, history of alcohol intake, and having hepatic etiology are significantly associated with poor and death clinical outcomes.

Among all of the significant predictors of poor/death clinical outcomes, only alcohol intake has inverse relationship with it (OR less than 1). This means that alcohol intake might be related to malignance, but it is not necessarily a predictive factor for poor/death clinical outcomes. Age, admission in the ICU, and having hepatic etiology have ORs greater than 1 indicating that these factors are significantly associated with poor/death clinical outcomes.

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Logistic Regression Models

Table 6. Distribution of etiologies of metabolic encephalopathy across classification

Etiology	Benign	Malignant	Highly Malignant	Total
Anorexic-Ischemic	5	3	1	9
Drug-Induced	1	1	0	2
Electrolyte Disturbance	8	4	1	13
Endocrine	2	2	0	4
Hepatic	3	4	1	8
Hypercapnic	1	0	0	1
Septic	28	12	3	43
Uremic	6	0	1	7
Withdrawal Syndrome	2	0	0	2

Table 7. Association between etiologies of metabolic encephalopathies and classification.

Etiology/EEG Patterns	Crude			Adjusted		
	OR	95% CI	p-value	OR	95% CI	p-value
Anorexic-Ischemic						
Benign	0.40	0.09-1.83	0.2380			
Malignant	1.48	0.30-7.25	0.6276			
Highly Malignant	-	-	-			
Drug-Induced						
Benign	0.16	0.01-3.20	0.2332			
Malignant	4.74	0.26-86.0	0.2924			
Highly Malignant	-	-	-			
Electrolyte Disturbance						
Benign	0.17	0.06-0.49	**0.0012**	0.15	0.05-0.43	**0.0004**
Malignant	3.64	1.18-11.2	**0.0244**	2.54	1.01-6.63	**0.0465**
Highly Malignant	7.60	0.82-70.2	0.0739			
Endocrine						
Benign	0.16	0.03-0.93	**0.0412**	0.14	0.03-0.80	**0.0269**
Malignant	4.64	0.82-26.2	0.0820			
Highly Malignant	-	-	-			
Hepatic						
Benign	0.11	0.02-0.46	**0.00026**	0.10	0.03-0.39	**0.0009**
Malignant	7.05	1.56-32.0	**0.0113**	5.18	1.49-18.0	**0.0095**
Highly Malignant	28.5	1.40-58.2	**0.0295**	12.5	1.02-70.4	**0.0481**
Septic						
Benign	0.52	0.18-1.50	0.2235			
Malignant	1.61	0.55-4.72	0.3850			
Highly Malignant	3.55	0.50-25.2	0.2053			
Uremic						
Benign	2.05	0.48-8.83	0.3331			
Malignant	-	-	-			
Highly Malignant	80.0	2.71-235	**0.0111**	25.0	1.72-364	**0.0185**

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Tables 6 and 7 present the association between etiologies of metabolic encephalopathy and classification. Table 5 identifies the etiologies that significantly differentiate classification, while Table 4 provides the distribution of each etiology across classification. These data suggest that the low frequencies observed in certain classification may be influenced by the specific etiologies involved, leading to unusual odds ratio estimates.

Although both significant, electrolyte disturbance is more related to malignant classification over benign, where presence of electrolyte disturbance multiplicatively increases the odds of malignance by 2.54 (154%). Endocrine etiology is inversely related to being benign, where the odds of being benign decrease by 0.14 (86%) on its presence. On the other hand, the odds of being highly malignant increases by 25 times when the etiology is uremic. Hepatic etiology is significant on all classification, but hepatic etiology is highly associated on high malignance.

No tests were made for Hypercapnic and Withdrawal Syndrome etiologies because of insufficient data as they only exist on benign patients.

Table 8. Distribution of MRS identification across classification.

MRS Identification	Benign	Malignant	Highly Malignant	Total
Good Outcome	20	7	0	27
Poor Outcome	15	5	2	22
Death	12	8	3	23

Table 9. Association between classification with MRS scores

Discharge Destination	Crude			Adjusted		
	OR	95% CI	p-value	OR	95% CI	p-value
MRS – Poor Outcome						
Benign	0.74	0.27-2.03	0.5598			
Malignant	0.83	0.3002.26	0.7090			
Highly Malignant	-	-	-			
MRS – Death						
Benign	0.32	0.12-0.90	**0.0298**	0.41	0.17-0.97	**0.0433**
Malignant	1.23	0.40-3.76	0.7165			
Highly Malignant	-	-	-			

*Bold p-values are significant at α = 5%

Tables 8 and 9 present the association between MRS outcome and classification. Table 8 identifies the MRS outcome that significantly differentiate classification, while Table 7 provides the distribution of each MRS outcome across classification.

Only MRS score pertaining to mortality have significant inverse relation with being benign. Having an MRS score of 6 multiplicatively decreases the odds of being benign by 0.41 (59%). No tests were made for high malignance because of absence of good outcome on highly malignant patients which is expected.