DIAGNOSTIC ACCURACY OF GLIAL FIBRILLARY ACIDIC PROTEIN (GFAP) AND UBIQUITIN C-TERMINAL HYDROLASE 1 (UCHL-1) FOR DISCRIMINATION BETWEEN ACUTE AND CHRONIC DRUG ABUSE CASES PRESENTED TO BENHA GOVERNMENTAL HOSPITALS

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Abstract

Background: The overuse of drugs that affects the brain functions (behaviours, and the production of memories) is referred to as drug or substance abuse disorder (SAD).

Aim: This work aimed to study validity of two of brain biomarkers (GFAP and UCHL-1) for discrimination between acute and chronic drug abuse cases presented to benha governmental hospitals (Benha Poisoning Treatment and research unit [BPTRU] and Benha mental health hospital).

Methods: This study carried out on 200 cases of substance abuse disorder from September 2022 till March 2023. Patients were selected and divided into two equal groups both with confirmed diagnosis of substance abuse disorder: Acute cases and Chronic cases. All cases were subjected to laboratory investigations.

Results: GFAP was conducted for discrimination between acute and chronic cases. GFAP showed a high accuracy. UCHL-1 showed high accuracy AUC (AUC=0.906). GFAP demonstrated a significant +ve correlation with UCHL and substance measurement. UCHL-1 demonstrated a significant +ve correlation with GFAP, and substance measurement.

Conclusions: Acute cases 0f SAD demonstrated higher GFAP and UCHL-1 levels.

Keywords: Acute, chronic, Drug abuse cases, GFAP, UCHL-1

Introduction:

The overuse of drugs that affects the brain functions (behaviours, and production of memories) is referred to as drug or substance abuse disorder (SAD) **(Huckle et al., 2018)**. Substance-induced disorders appear to be due to changes in the brain biomarkers resulting in impaired emotional and cognitive performance and an increase in the vulnerability for other illicit drugs **(Realini et al., 2009).**

Protein biomarkers are biological molecules present in the brain that diffuse into the cerebrospinal fluid (CSF) or serum after injury to the brain cells **(Laterza et al., 2008).** Examples are the glial protein S-100 beta (S100β), glial fibrillary acidic protein (GFAP), tau protein, and ubiquitin carboxy-termina1 hydro1ase (UCH-L1) (**Roberts et al. 2015).**

The main component of the astroglia cytoskeleton is GFAP which is a monomeric intermediate filament protein presents in cells of glia, it is CNS highly specific marker **(Yang et al., 2015)**. GFAP's main function is to maintain the glial cells' cytoskeletal structure and their mechanical strength; also to support the blood–brain barrier and the neighbouring neurons **(Abdelhak et al., 2022)**.

UCH-L1 has high abundance and specific expression in neurons **(Wang et al., 2021)**. UCH-L1 is associated with neuronal injury, (NfL) is an axonal injury marker, and (GFAP) is related to astrogliosis and glial injury **(Ashton et al., 2021).**

Substance abuse disorder (SAD) rises progressively among world population, its prevalence increases among Egyptian adolescents, which indicating growing rates of substance use among young adults **(Bassiony et al., 2022)**.

Social & economic changes have been associated with a large increase in the problem, since the last 12 months in Egypt prevalence reveals higher incidence of substance abuse (about l2% for alcoho1 and 2–3% for il1icit drugs) and those of other menta1 disorders as well as chronic physical disorders with major public health impact **(McHugh et al., 2018, Komro et al., 2022).** Acute care has traditionally been used as treatment for all cases of substance abuse. There is a great progress in dealing with treatment of chronic substance abuse (addiction), it is treated as a chronic illness. Aftercare has been developed to extend the benefits of the initial treatment , and recovery monitoring has been developed to assess patients' status and return them to treatment as needed **(Lawn et al., 2016).**

This work aimed to study validity of (GFAP) and (UCHL-1) application for discrimination between acute and chronic drug abuse cases presented to benha governmental hospitals (Benha Poisoning Treatment and research unit [BPTRU] and Benha mental health hospital) Understanding the difference between acute and chronic drug abuse is critical for both prevention and treatment. Acute abuse can often lead to long-term issues, making early intervention important to prevent the development of chronic addiction, while chronic cases need an addiction management, like chronic disease not only the episodic care used as usual for acute cases.

Patients and Methods:

This study carried out at Benha University Hospita1s (BPTRU) and Benha Mental Health hospital. 200 cases of substance abuse disorder (144 males & 56 females and their mean age ± SD is 31.67 ±7.26 years with a range 18-47 years) were selected. Our study performed during the period from 1st September 2022 till 31st March 2023. Sample size was calculated using EP1 info statistica1 package.

The patients of this cross-sectiona1study gave informed written consent. Every patient received an exp1anation of the aim of the study and had a secret code number. The study was done after being approved by the Research Committee of Ethics, Facu1ty of Medicine, Benha University (MS 27-8-2022).

Inclusion criteria were SAD cases came to BPTRU and Benha Mental Health Hospital (Patients who fulfil the criteria for diagnosis of drug abuse disorder according to DSM-V criteria) **(First et al., 2022).**

Exclusion criteria were.

Patients did not fulfil the criteria for diagnosis of drug abuse disorder according to DSM-V criteria, and Patients with the history of the following **(Clergue, 2022):**

a) Head trauma, neurodegenerative disorders, seizures, stroke and/or brain neoplasia.

b) Cardiac, pulmonary, renal, hepatic, autoimmune and gastric diseases.

Grouping:

A total of 200 patients with confirmed diagnosis of SAD were included and classified into two equal groups.

Acute cases: 100 selected individuals (70 males & 30 females and their mean age ± SD is 29.12±6.88 years with a range of 18-42 years) who manifested with acute symptoms of SAD due to accidental intake, overdose of drug abuse, or suicidal poisoning.

Acute Drug Abuse refers to the immediate effects of drug use that occur during or shortly after taking a drug. It typically involves short-term or one-time use of a substance, leading to a range of physical, psychological, and emotional reactions **(Hasin et al., 2013)**.

Chronic cases: 100 selected individuals (74 males & 26 females and their mean age ± SD is 34.22 ±6.74 years with a range of 18-47 years) had a known history of SAD.

Chronic drug abuse represents long-term, repeated use (months or years), that can lead to profound complications. Chronic use often results in dependence **(Hasin et al., 2013)**.

All cases were subjected to the following investigations:

Samples were obtained from all patients at the onset of admission and before giving any treatment.

1- **Multi drug screening test:** Each urine specimen was collected in a clean container. Specimen were kept at 15-30 0C for 8 hours, at 2-8 0C for 3 days and was left at -20 0C for longer term storage. The sample was transferred to the Lab for screening using immunoassay techniques (rapid card test and auto-analyser device). The end of the device was dipped into the specimen. The timer was started, and device was removed from specimen after 10 seconds. The cap back was replaced back onto the device. Device was set on a clean and level surface. Results were read between 4-7 minutes (**Raouf et al.,2018)**.

Confirmation was performed using high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS) for qualitative and quantitative analysis. The quantitative analysis of alcohol was achieved by headspace gas chromatography (HS-GC) with automated sampling with a flame ionization detector (FID).

2- **Blood sampling for GFAP and UCH-L1 tests**

Whole blood was put in centrifuge tube. Promptly centrifuged the blood at 2,000 to 3,000 for 15 minutes. Transferred and stored serum samples in separate tubes.

Samples were used freshly and stored at –20°C to -70°C for later use. Avoid freeze/thaw cycles.

GFAP and UCH-L1 tests were performed by using the sandwich enzyme-linked immunosorbent assay (ELISA) kit from (Glory Science Co., Ltd. Del Rio, USA) with detection of the resulting enzyme signal electrochemically. Approximately 15 min was the test time for each assay.

Human GFAP Antibody Monoclonal Mouse IgG1 Clone # 273807, Catalog Number: MAB2594.

Human UCH-L1Antibody Monoclonal Mouse IgG2A Clone # 671108, Catalog Number: MAB6007.

A standard curve is constructed by plotting absorbance values against concentrations of standards, and concentrations of GFAP, or UCHL-1 in unknown samples are determined using this standard curve.

Standard Curve Range for GFAP: 1.5 to 100 ng/mL. Sensitivity for GFAP: 0.02 ng/mL.

Standard Curve Range for UCH-L1: 0.156-10 ng/mL. Sensitivity for UCH-L1:0.02 ng/mL.

Reagents and chemicals were purchased from Sigma (St.Louis, USA). All biochemical measurements were performed in the Biochemistry lab. And toxi. Lab. in Faculty of Medicine, Benha University.

Statistical analysis:

The collected data was revised, coded, and tabulated using the Statistica1 package for Socia1 Science (1BM Corp. Released 20l7. 1BM SPSS Statistics for Windows, Version 25.0. Armonk, NY: 1BM Corp.). Data were presented and suitable analysis was done according to the type of data obtained for each parameter. Shapiro-Wi1k test was done to test the normality of data distribution. Mean, Standard deviation (± SD) or Median, interquartile rang (IQR) for numerica1 data. Frequency and percentage of non-numerica1 data. Wilkoxon signed rank test was used to assess the statistica1 significance of the difference between two measurements nonparametric variables. Also, Z= Mann-Whitney, and t student test were used. The re1ationship between two qua1itative variables examined by Chi-Square test. Spearman correlation (rs). Corre1ation ana1ysis: To demonstrate the strength of association between two quantitative variables. The ROC Curve (receiver operating characteristic) provides a useful way to evaluate the sensitivity and specificity for quantitative diagnostic measures that

categorize cases into one of two groups. The optimum cut off point was defined as that which maximized the AUC value. AUC is that a test with an area greater than 0.9 has high accuracy, while 0.7–0.9 indicates moderate accuracy, 0.5–0.7, low accuracy and 0.5 a chance result.
A p value is significant if <0.05 at confidence interval 95%.

Results:

There was non-significant difference in frequency of substance abuse between acute & chronic cases except a significant higher distribution of tramadol in chronic cases. On the other hand, a significant higher frequency of benzodiazepine in acute cases **(Table 1)**.

Table 1: Frequency of substance abuse in acute and chronic cases

		Acute cases N=100	Chronic cases N=100	Test	P
Frequency of substance abuse	Amphetamine	10(9.9%)	13(13%)	X2=0.442	0.506
	Benzodiazepine	13(12.9%)	5(5%)	X2=3.907	0.048*
	Cannabis	63(62.4%)	57(57%)	X2=0.75	0.386
	Heroin	-	1(1%)	--	-
	Methamphetamine	-	4(4%)	-	-
	Methanol	1(1%)	-	-	-
	Morphine	1(1%)	2(2%)	X2=0.338	0.561
	Opioid	-	1(1%)	-	-
	Stroks	3(3%)	6(6%)	X2=1.047	0.306
	Tramadol	1(1%)	11(11%)	X2=11.64	0.0006*
	Vodoo	9(8.9%)	-	-	-

X^2 = Chi-Square test, *: significant p value.

According to measurements of different substance abused, there was non-significant difference between 2 groups (acute & chronic cases) (**Table 2)**

Table 2: measurements of substance abuse in acute versus chronic cases

	Acute group n=100	Chronic group n=100	Test	p
Substance	Measurement (ng/mL)	Measurement (ng/mL)		
Amphetamine	59.6±6	72.11±10.01	0.035	0.616
Benzodiazepine	520.60±302.18	506.25±209.84	1.080	0.326
Cannabis	330.47±326.42	227.50±14.97	0.055	0.416
Methanol	75±10	_	-	-
Heroin	_	38.5±6	-	-
Methamphetamine	_	95±3.5	-	-
Morphine	86.25 ±72.25	56.92±20.67	1.075	0.316
Opioid	_	240.5±2	-	-
Stroks	112±20	150±42	0.04	0.515
Tramadol	161.5±10	141.5±66.95	0.085	0.386
Voodoo	500±50	_	-	-

Mean (M), Standard deviation (± SD), Z= Mann-Whitney, t student test.

GFAP level showed significant difference between acute and chronic subjects (p<0.001*). Mean level in acute group was 2.51 ng/ml and 0.87 ng/ml in chronic group. UCHL-1 level showed significant difference between acute and chronic subjects.

Table 3: GFAP and UCHL-1 level in acute versus chronic cases

	Acute group n=100	Chronic group n=100	Test	p
GFAP	2.51±0.38	0.87±0.27	11.567	<0.001*
UCHL-1	**3.41±0.67**	**0.92±0.4:**	**11.442**	**<0.001***

n: number, GFAP: Glia1 fibrillary acidic protein, UCHL-1: Ubiquitin C-termina1 hydrolase, Z test= Man-Whitney, t student test, *= p< 0.05 (significant)

According to abused substances, acute cases demonstrated significantly more GFAP and UCHL-1 levels in comparison to chronic cases in all studied substances (p<0.05) **Table 4**

According to (GFAP) among acute cases of the present study for type of substances, there was non-significant difference and the substance that stood out with the highest mean GFAP level was morphine at 3.09 ng/ml.

UCHL-1 among acute cases for type of substances, there was non-significant difference and the substance that stood out with the highest mean UCHL-1 level was tramadol, 3.63 ng/ml.

The statistical test showed no significant difference among chronic cases regarding to GFAP and UCHL-1 level according to substance used. with the highest mean GFAP level belong to heroin **Table 4**.

Table 4: Serum level GFAP and UCHL-1 in acute versus chronic cases according to different substance abused

	Acute n=100	**Chronic** n=100	**Test**	**P Value**
GFAP level				
	M±SD	**M±SD**		
Amphetamine	2.61 ± 0.27	0.91 ± 0.19	3.907	<0.001*
Benzodiazepine	2.53 ± 0.35	0.88 ± 0.27	3.205	<0.001*
Cannabis	2.57 ± 0.31	0.87 ± 0.25	9.442	<0.001*
Heroin	-	1.15 ±0.45	-	-
Methamphetamine	-	0.92 ± 0.36	-	-
Methanol	2.27 ± 0.87	-	-	-
Morphine	3.09 ± 0.9	0.76 ± 0.22	2.225	0.043*
Opioid	-	0.60 ±0.71	-	-
Stroks	2.64 ± 0.45	1.03 ± 0.32	2.324	0.024*
Tramadol	2.23± 0.51	0.93 ± 0.22	2.593	0.015*
Vodoo	2.86 ± 0.21	-	-	-
Statistical test	K= 12.288 P=0.091	K= 6.646 P=0.575		
UCHL-1				
Amphetamine	3.07 ± 0.29	1.12 ± 0.37	3.912	<0.001*
Benzodiazepine	3.38 ± 0.46	1.29 ± 0.33	3.214	0.002*
Cannabis	3.45 ± 0.56	1.06 ± 0.37	9.442	<0.001*
Heroin	-	0.79 ± 0.00	-	-
Methamphetamine	-	0.98 ± 0.44	-	-
Methanol	3.41 ± 0.00	-	-	-
Morphine	3.39 ± 0.00	1.17 ± 0.83	2.223	0.046*
Opioid	-	0.85 ± 0.00	-	-
Stroks	3.50 ± 0.14	0.86 ± 0.35	2.325	0.027*
Tramadol	3.63 ± 0.00	0.87 ± 0.28	2.594	0.048*
Vodoo	3.49 ± 0.60	-	-	-
Statistical test	K=6.523 P=0.520	K=7.732 P=0.460		

GFAP: Glia1 fibrillary acidic protein, UCHL-1: Ubiquitin C-termina1 hydrolase, Z: Mann Whitney test, t student test, K: Kruskal-Walli's test, * for significant p.

ROC curves of GFAP and **UCHL-1** for discrimination between acute and chronic cases showed high accuracy AUC (0.927) and (0.906) respectively **Table 5, figure 1& 2**.

Table 5: Validity of GFAP and UCHL-1 for discrimination between acute and chronic cases

GFAP (ng/mL)								
AUC	95% C1	p	Cut 0ff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
o.927	o.882-o.959	< o.oo1*	>1.35	93.00	95.00	93.13	93.89	93.5

UCHL-1 (ng/mL)								
AUC	**95% C1**	**p**	**Cut off**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Accuracy (%)**
o.906	o.856-o.942	<o.oo1*	>1.83	90.00	92.00	90.35	91.7	91

GFAP: Glia1 fibrillary acidic protein, UCHL-1: Ubiquitin C-termina1 hydrolase, AUC: area under ROC curve; C1: confidence interva1; PPV: positive predictive va1ue; NPV: negative predictive va1ue, *: significant p.

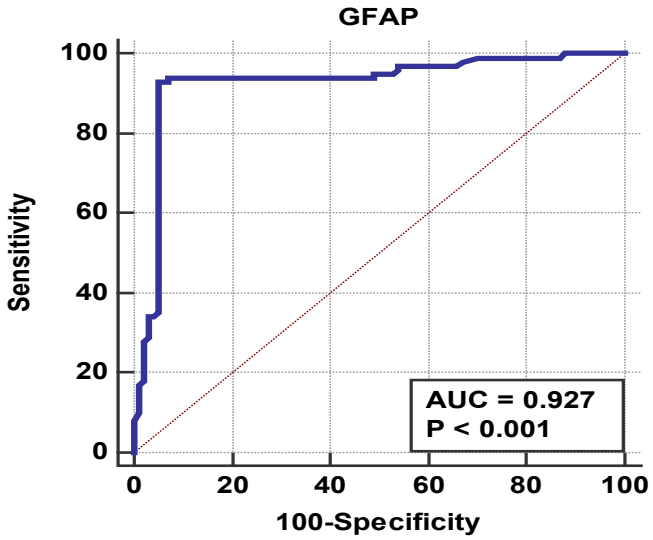

Fig. 1: R0C curve analysis 0f GFAP f0r discrimination between cases (acute & chronic)

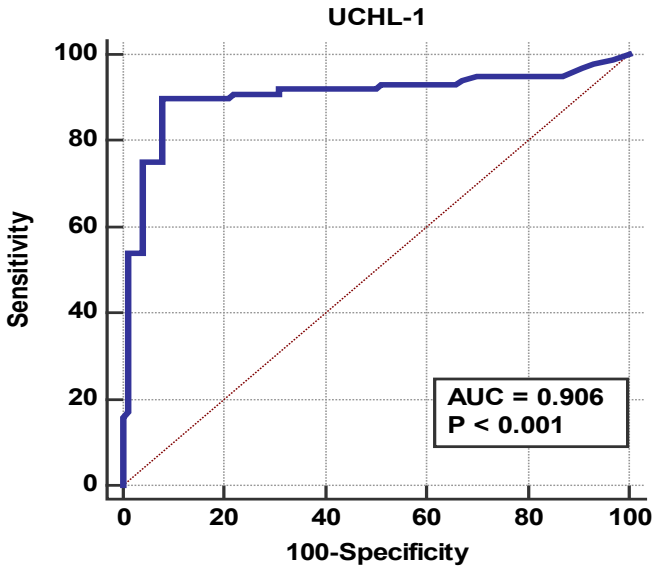

Fig. 2: R0C curve ana1ysis of UCHL-1 for discrimination between cases (acute & chronic).

GFAP showed a significant positive correlation with each of UCHL & substance measurement. **Table 6,** Figure 3 & Figure 4

Table 6: Correlation between GFAP, and each of UCHL-1 and Substance measurement in the studied subjects

		rs	p
UCHL ng/ml	**GFAP**	0.654	<0.001*
Substance measurement	**GFAP**	0.338	<0.001*

GFAP: Glia1 fibrillary acidic protein, UCHL-1: Ubiquitin C-termina1 hydrolase, rs: spearman corre1ation, *: significantp.

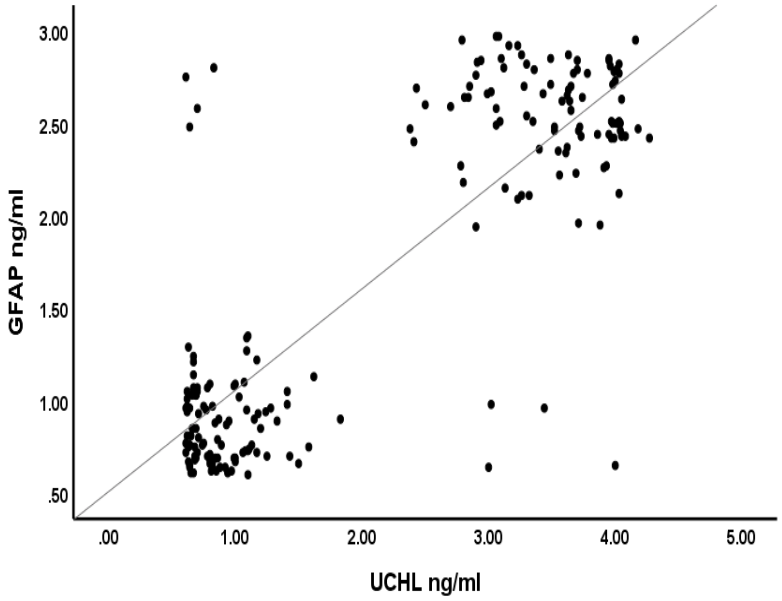

Fig. 3: Correlation between GFAP and UCHL-1

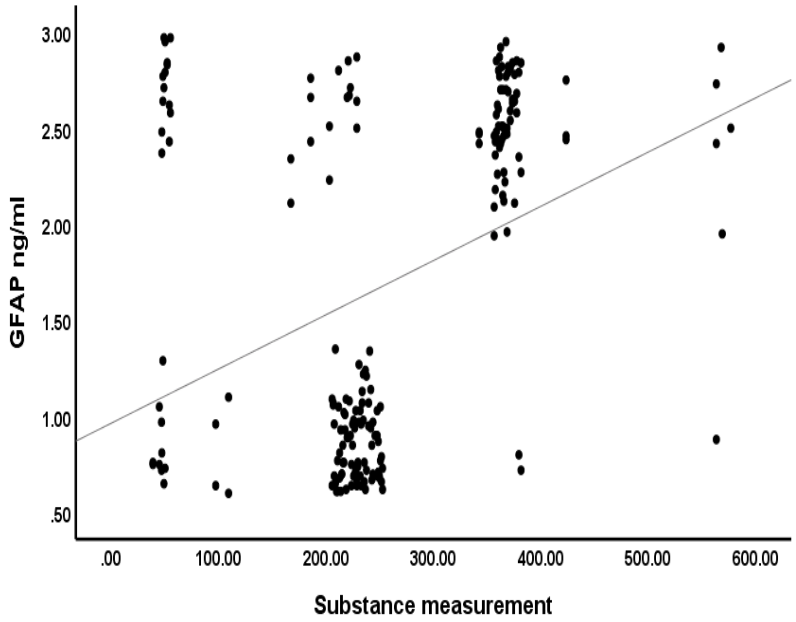

Fig. 4: Correlation between GFAP and substance level

UCHL-1 showed a significant positive correlation with each of GFAP & substance level. **Table 7& figure 5**

Table 7: Correlation between UCHL-1, and each of GFAP and Substance measurement in the studied cases.

		rs	p
GFAP ng/ml	**UCHL-1**	.654	<0.001*
Substance measurement	**UCHL-1**	.384	<0.001*

GFAP: Glia1 fibrillary acidic protein, UCHL-1: Ubiquitin C-termina1 hydrolase rs, spearman corre1tion, *: significantp.

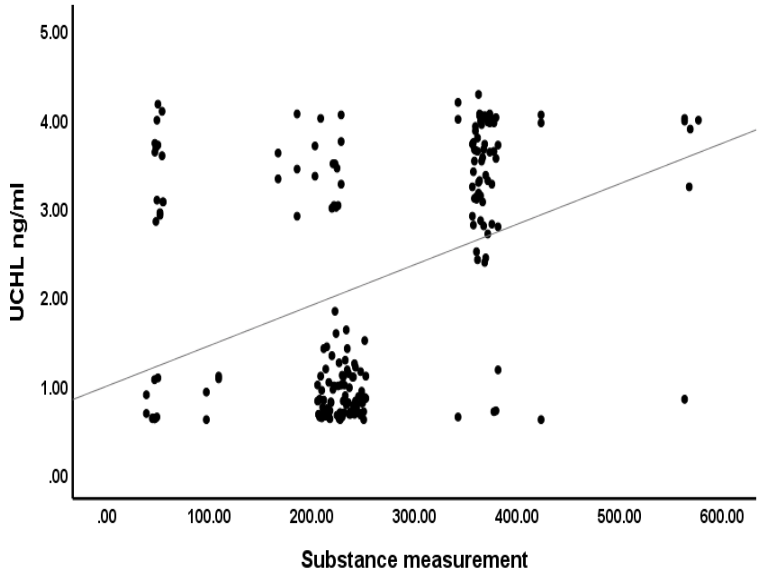

Fig. 5: Correlation between UCHL-1 and substance level

Discussion

Substance abuse is use of a drug where the user consumes the substance in amounts or with approaches that are hazardous to themselves, the National Institute of Drug Abuse (NIDA) Studies revealed that incidence of substance abuse was 8% for alcohol and 3% for illicit substance use. Cannabis is the most common abused drug 2.2%, followed by opioid o.29%, amphetamine o.10%; cocaine o.06%) **(Whitehead & Wells, 2022).**

Our results according to incidence of substance abuse, revea1ed that there was non - significant difference between acute & chronic cases except a significant higher frequency of tramadol in chronic cases and, a significant higher distribution of benzodiazepines in acute cases. Furthermore, there was non-significant difference between 2 groups (acute & chronic cases) according to measurements of different substance abused,

Tramadol is an analgesic which commonly used worldwide for the treatment acute or chronic pain, but unfortunately it is a common drug of abuse with significantly higher distribution in chronic cases according to results of **Randa1l & Crane (20l4); E1-Hadidy & Helaly (20l5)** who explained that Availability of tramadol, cheaper prices and its perception as being a safe drug due to its medica1 use are major factors 1eading to its chronic abuse (**Lord et a1., 20ll). El-Sawy et al., (2010)** found that acute toxicity of cannabis and benzodiazepines was higher than other drugs.

Substance abuse is a growing crisis globally, it is a serious problem in Egypt and all over the world that threats both the society and government. Drug abuse related brain damage is a major complication that cause most of social, psychological and physical consequences **(Abdel-Moniem, 2020),**

Understanding the difference between acute and chronic drug abuse is critical for both prevention and treatment. Acute abuse can often lead to long-term issues, making early intervention important to prevent the development of chronic addiction, while chronic cases need an addiction management, like chronic disease not only the episodic care used as usual for acute cases **(Chan Yiu-Cheung, 2012)**.

Non-significant difference found in our results between 2 studied groups (acute and chronic cases) according to type and measurements of different substance abused, directed us to note that there is a need to identify biomarkers which could indicate the occurrence of brain injury in drug abuse and can be used for discrimination between acute and chronic drug abuse cases

This work aimed to study validity of two of brain biomarkers (GFAP and UCHL-1) for discrimination between acute and chronic drug abuse cases presented to benha governmental hospitals (Benha Poisoning Treatment and research unit [BPTRU] and Benha mental health hospital).

Regarding GFAP and UCHL-1 level in our study, we found that there was a higher significant value in acute cases as compared with chronic cases ($p<0.001$*).

According to (GFAP) levels among acute cases of the present study for type of substances, there was non-significant difference and the substance that stood out with the highest mean GFAP level was morphine, at 3.09 ng/ml.

The statistical test showed no significant difference between GFAP level among chronic cases according to substance used, with the highest mean GFAP level belong to heroin.

According to type of abused substances, GFAP 1evels were significantly more in acute cases in comparison to chronic cases in all studied substances.

Clergue-Duval et al., (2022) conducted a study that reported that the individuals with opioid use disorder (OUD) had significantly higher serum GFAP levels compared to healthy controls. The increase of GFAP were associated with markers of neuroinflammation & cognitive impairment, suggesting that acute and chronic opioid use may lead to persistent changes in glial cell activity and brain health.

Sveinsson et a1., (2017) who studied heroin effect on GFAP and revealed that CSF showed extremely elevated level of nerve injury markers like GFAP, reflecting a toxic effect on astrocytes.

Miguel-Hidalgo et al., (2009) showed in his study that cocaine, amphetamines and most psychostimulants cause activation of astrocytes. This activation is defined by rise in (GFAP), GFAP is known to be upregu1ated in response to brain damage and neurotoxicity, a1though GFAP 1evel changes are not 1imited to overt brain injury and many 0ther plastic changes in the neuropil also result in raised GFAP.

As regards our results, according to the data on (UCHL-1) level among acute cases for type of substances abused, there was non-significant difference. Tramadol exhibited the highest mean UCHL-1 level, recorded at 3.63 ng/ml.

No significant differences in chronic cases' UCHL-1 levels across the different substances.

UCHL-1 levels according to abused substances, were significantly higher in acute cases compared to chronic cases in all studied substances

Clergue-Duval et al., (2022) indicated in their study that patients with 0pioid use disorder had significant1y raised serum UCH-L1 leve1s compared to healthy controls. The elevation in UCH-L1 was associated with neuroinflammatory processes and cognitive impairment, suggesting that acute opioid use can lead to increased neuronal damage and glial activation.

Diaz-Arrastia et al., (2014) emphasized in his study that UCH-L1 is a sensitive pointer that there is acute neuronal damage and is often raised in conditions of neuroinflammation, which can be triggered by acute substance abuse, including alcohol and opioids. This suggests that monitoring UCH-L1 levels could provide valuable insights into the extent of neuronal damage in individuals with substance use disorders.

Additionally, **Mondello et a1., (2012)** demonstrated that UCH-L1 leve1s were significantly raised in both cerebrospinal fluid (CSF) and plasma within 48 hours after a seizure. This increase was indicative of neuronal damage and could be relevant for assessing brain damage in patients with a history of substance abuse, as fits can be a consequence of acute intoxication or withdrawal.

The Current work studied Validity, sensitivity, and specificity of GFAP and UCHL-1 for differentiation between acute & chronic abuse cases, we found that ROC curves of GFAP and UCHL-1 for differentiation between acute & chronic cases showed high significant accuracy AUC (0.927) and (0.906) respectively and each biomarker had good sensitivity, while GFAP was more sensitive and specific.

Correlation between GFAP & UCHL1 and between each of them & substance measurement showed a significant positive correlation (rs=0.654).

Abdel-Salam et al., (2019) who aimed to investigate UCH-L1 and GFAP as putative markers for neuronal injury due to cannabis, tramadol, or their combined use. They found that either cannabis or tramadol increased UCH-L1 and GFAP in the brain, serum UCH-L1 and GFAP increased by the highest dose of cannabis or tramadol. They suggested that changes in UCH-L1 and GFAP are likely to reflect neurotoxicity and serum levels could be used to detect neuronal damage in drug users. They showed that a dose of 5 mg/kg of cannabis was not enough to produce histopathological changes in the striatum and cortex. Yet, such dose significantly increased UCH-L1 in the brain tissue, while a significantly increased serum UCH-L1 was recorded only after the highest dose of cannabis (20 mg/kg).

Another study of chronic tramadol effects on the zebrafish brain showed that proteins modified by chronic administration of 0ne or more 0ther substances of abuse, such as nicotine, alcohol, cocaine, heroin, and morphine. UCHL-1 was depressed in almost a11 substances of abuse (**Zhuo et a1**., **2012**).

Luger et al., (2020) reported that GFAP may differentiate ICH from ischemic stroke and stroke mimics. Blood samp1es were analyzed for GFAP and UCH-L1 using EL1SA. Area-under-the-

curve values were 0.866 (95% CI 0.809-0.924, p < 0.001) for GFAP, and 0.590 (0.511-0.670, p = 0.033) for UCH-L1. Regarding overall diagnostic accuracy, UCH-L1 did not add significantly to the performance of GFAP. A point-0f-care test to distinguish between ischemic and hemorrhagic strokes might facilitate triage to different treatment pathways.

Hindawy et al., (2024), studied using an alternative method such brain biomarkers as S100B and NSE serum levels to demonstrate the presence of an intracranial patho1ogy and thus lowering the number of patients exposed to unnecessary imaging radiation. They found that validity of S100, and NSE predicting outcome in their results showed that sensitivity and specificity of S-100B are 94.4%, 95.1% respectively and those of NSE are 77.8%, 42.7%

Conclusions and Recommendations:

Acute cases demonstrated significantly more GFAP and UCHL-1 levels in comparison to chronic cases. Non-significant differences in GFAP & UCHL-1 levels were observed among acute cases based on the substance used. GFAP & UCHL-1 levels were positively correlated with each other and with substance measurement. GFAP and UCHL-1 showed high accuracy in discriminating between acute and chronic cases. Further larger randomized clinical trials are required to validate our findings and establishing standardized protocols for measuring GFAP and UCH-L1, including age-stratified reference ranges, would improve the reliability of biomarker assessments and their clinical implications.

Future studies should consider including a control group of individuals. This would help to differentiate the specific effects of substance abuse from other potential factors.

- More studies discriminating between acute and chronic drug abusers for establishing suitable accuret plan of ttt.
- Investigating additional biomarkers associated with substance abuse disorders could further elucidate their underlying mechanisms and improve diagnostic accuracy. This could include exploring markers related to neuroinflammation, neurotransmitter systems, or genetic factors.

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الملخص العربي

صلاحية البروتين الحمضي الليفي الدبقي و هيدرولاز يوبكتين الكربوكسي الطرفي 1 في التمييز بين الحالات الحادة والمزمنة فى حالات تعاطِي المَخدرات بمستشفيات بنها الحكومية

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المقدمة:

يعتبر إدمان المخدرات، والذي يسمى أيضًا اضطراب تعاطي المخدرات، مرض يؤثر على دماغ الشخص وسلوكه تنتشر اضطرابات تعاطي المخدرات بشكل كبير في جميع أنحاء العالم وتعتبر سببًا رئيسيًا للمراضة والوفيات على مستوى العالم،

إن تزايد انتشار اضطراب تعاطي المخدرات في المجتمع المصري يستدعي المزيد من الاهتمام من جانب المؤسسات الأسرية والتعليمية والصحية.

الهدف من الدراسة:

هدفت هذه الدراسة إلى دراسة صلاحية البروتين الحمضي الليفي الدبقي و هيدرولاز يوبكتين الكربوكسي الطرفي 1 في التمييز بين الحالات الحادة والمزمنة فى حالات تعاطِي المَخدرات بمستشفيات بنها الحكومية(المقدم إلى وحدة علاج التسمم والأبحاث في مستشفى بنها الجامعى و مستشفى الصحه النفسية بنها) لتنفيذ الخدمات الوقائية الموجهة للشباب لمكافحة هذه الظاهرة

المرضى وطرق البحث:

شملت هذه الدراسة حوالي 200 مريض تم عرضهم على وحدة علاج وأبحاث التسمم ببنها بمستشفيات جامعة بنها ومستشفى بنها للصحة النفسية خلال فترة الدراسة.

النتائج:

- أظهر البروتين الحمضي الليفي الدبقي وجود علاقة إيجابية مهمة احصائياً مع هيدرولاز يوبكتين الكربوكسي الطرفي وقياس المادة.
- أظهر هيدرولاز يوبكتين الكربوكسي الطرفي 1 ارتباطًا إيجابيًا مهم احصائياً مع البروتين الحمضي الليفي الدبقي، وقياس المادة.

الاستنتاج:

كانت مستويات البروتين الحمضي الليفي الدبقي أعلى في الحالات الحادة، حيث أظهر المورفين والهيروين أعلى المستويات المتوسطة. لم يلاحظ أي فروق مهمة احصائياً في مستويات البروتين الحمضي الليفي الدبقي بناءً على المادة المستخدمة. كانت مستويات هيدرولاز يوبكتين الكربوكسي الطرفي 1 أعلى في الحالات الحادة، مع وجود أعلى مستويات متوسطة للترامادول والبنزوديازيبين. ارتبطت مستويات البروتين الحمضي الليفي الدبقي وهيدرولاز يوبكتين الكربوكسي الطرفي 1 بشكل إيجابي مع بعضها البعض ومع قياس المادة، أظهر البروتين الحمضي الليفي الدبقي دقة عالية في التمييز بين الحالات الحادة والمزمنة (المنطقة تحت المنحنى = 0.927).