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# Oxytocin level among patients with opioid use disorder and its correlation with personality traits and perceived childhood trauma

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## Abstract

**Background** Personality traits and perceived childhood maltreatment are of the predictors of substance use disorder development. Many studies have discussed oxytocin effect on personality traits and its relation with childhood trauma and how both affect the addictive process. The main aim was to compare oxytocin level between patients with opioid use disorder and controls and the potential association of oxytocin level with the basic dimensions of personality traits and perceived childhood adverse experiences in patients group. Forty male patients with opioid use disorder and 40 healthy controls matched in age and gender were assessed and compared regarding serum oxytocin level by ELISA, personality traits using Temperament and character inventory - revised (TCI-R) scale, and childhood adverse events using childhood trauma questionnaire.

**Results** A significant difference between the patient group and the control group regarding the serum oxytocin level was found. Negative correlation with  $p$ -value  $<0.05$  between oxytocin level and each of novelty seeking, and harm avoidance, in addition to a positive correlation between oxytocin level and each of reward dependence, self-directedness, and cooperativeness items of (TCR-R), among cases were found. Cases did not show statistically significant difference in oxytocin level between different Childhood Trauma Questionnaire (CTQ) items.

**Conclusions** The interaction between serum oxytocin levels, personality traits, and childhood trauma has to be considered in management with heroin-dependent patients as it plays a crucial role.

**Keywords** Oxytocin, Personality traits, Childhood trauma, Heroin

## Background

Heroin is a highly addictive substance, which is an agonist of the mu opioid receptors (MORs), delta (DOP), kappa ( $\kappa$  (KOP)), and the nociception receptor (NOP) [38]. Heroin metabolism to morphine is then followed by

combination to MORs, leading to its neuro-pharmacological effects [42].

Based on the fact that oxytocin (OXT) peptides as a hypothalamic neuropeptide interact with opiate addiction [36], the application of using OXT, in addition of opioid substance, psychostimulant, and alcohol, was emerged [31].

The early-life adverse events like insecure attachment and abuse during childhood lead to affection of the oxytocin network responsible for psychiatric and substance use disorders and resilience affection [6, 25].

An Egyptian study by Mobasher et al. [24] considered the importance of interrelation between oxytocin, craving, and personality traits in opioid use disorder patients.

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The hypothesis of this study was that there are significant differences in oxytocin levels and personality traits between patients with opioid use disorder and controls which can constitute a possible marker of general vulnerability for substance use disorders. Also, the derangement of OXT secretion was associated with early-life adverse experiences, e.g., childhood abuse.

This case-control study aimed at evaluating in OXT levels' difference between patients with opioid use disorder and healthy controls, the potential association of OXT levels with the basic dimensions of personality traits, and perceived childhood adverse experiences in patient group.

## Methods

The study design was a case-control that was held for 1 year at the inpatient Addiction Unit and Outpatient Psychiatric clinic – Fayoum University Hospital from the period of first January 2020 till first of January 2021.

The sample was sized according to the statistical formula of Epi Info 2000, based on the disease's prevalence with 95% confidence interval and precision of 2%. Ten percent was increased to overcome non-responses and missing data problems.

Forty male patients from the inpatient Addiction Unit and outpatient Psychiatric clinic at Fayoum University Hospital were included. All patients were fulfilling the inclusion criteria: male patients only, age ranged between 18 and 60 years, patients were fulfilling the criteria for diagnosis of substance use according to DSM5, patients were using heroin in past 12 months. Exclusion criteria include the following: medical comorbid conditions like (e.g., hepatic, renal, or any heart diseases), patients with history of comorbid psychiatric disorders—as it can affect oxytocin level [40]—and history of endocrinal disorder or hormonal replacement therapy.

Also, forty healthy participants from the paramedical staff were volunteers used as the control group. They were matched in age and gender to the case group with no evidence of substance abuse. Written informed consent for enrolling in the study was taken from all volunteers.

### Patients group was subjected to

General data as well as the drug habits of the patient (type of drug, route of administration, dose, etc.) were gathered using a semi-structured interview for addiction.

Clinical Structured Interview for DSM 5 (SCID 5-RV) (Research Version) [13] was used in this study to diagnose substance use disorders and to exclude other comorbid psychiatric disorders.

The Egyptian Brief Addiction Severity Index (ASI) [17, 22] (EBASI) was used in this study to assess the

eight areas and domains of functioning similar to the ASI. It is administered to examine sociodemographics, history of substance use, and history of treatment.

The temperament character inventory/revised (TCI-R) [7], a self-reported, 240-item questionnaire, was used to assess the seven basic dimensions and temperaments of personality, novelty seeking (NS), harm avoidance (HA), reward dependence (RD), and persistence and the self-concepts of character, namely, cooperativeness, self-directedness, and self-transcendence (ST).

The Childhood Trauma Questionnaire (CTQ) [5] Arabic language [11] was used to assess the level of maltreatment during childhood. The construction of the questionnaire was based on childhood maltreatment literature. This questionnaire has five subscales, in which three of them are assessing abuse (physical, emotional, and sexual) and two are assessing neglect (physical and emotional). The structure of each subscale contains five items and another three items, and minimization/denial subscale is found to check for response bias, like minimization of childhood maltreatment experiences. These three items are divided (1 = very often true, while all other responses = 0); if a total sum of them equals one or greater, a false negative result is suggested.

It is worth noting that all illiterate participants were helped by the author to fulfil the self-assessment tools.

A urine drug screening for common substances (opiates, barbiturates, cocaine, cannabis, benzodiazepines, and amphetamines) was performed on admission of patient. The urine screening is performed at the laboratory of Fayoum University Hospital.

Biochemical measures to assess oxytocin are as follows: The biochemical analysis of oxytocin was performed at the department of Clinical Pathology. Nurses collected venous samples using aseptic venepuncture which then added to serum separator vacutainer tubes. Samples were centrifuged at a rate of 3000 rpm by a trained laboratory technician maximum of 30 min after collection and harvested in an Eppendorf tube and frozen till assay is at  $-20^{\circ}\text{C}$ . The measurement of oxytocin was done using commercially available enzyme linked immune sorbent assay (ELISA) kit.

### Ethical consideration

This work gained approval by the Faculty of Medicine, Fayoum University, Egypt Research Ethical Committee. Written informed consent containing the whole information about the study was obtained from all the participants.

### Statistical analysis

Data analysis was performed using the (SPSS) software version 22 in windows 7 (SPSS, Inc., IL, Chicago, USA). Simple descriptive analysis is in the form of numbers and percentages of qualitative data, and arithmetic means as central tendency measurement and standard deviations as a measure of dispersion of quantitative parametric data. Independent sample test and one-way ANOVA test were used to compare quantitative measures between two independent groups and between more than two independent groups respectively

Regarding qualitative results, chi-square test was used to compare between two of more than two qualitative groups. A bivariate Pearson correlation test was used to test the association between variables.

### Results

Table 1 illustrates different socioeconomic status, family history, and age of onset. However, results regarding education level, occupation, socioeconomic, marital status, and family history of psychiatric disorders showed significant differences between case and control, yet after regression analysis of those factors, this discrepancy had no effect on our results (showed in Table 2)

Figure 1 illustrates that drug use status and its problematic severity in the patient group according to drug severity index

Table 3 illustrates that there was a statistically significant higher percentage of moderate and severe degree of emotional, physical, and sexual abuse, in addition to physical and emotional neglect with  $p$ -value  $<0.05$  among cases.

Figure 2 illustrates that there were a statistically significant higher mean of NS, HA, and ST, and with lower mean of RD, self-directedness, and cooperativeness with  $p$ -value  $<0.05$  among cases, while no statistically significant difference with  $p$ -value  $>0.05$  as regards persistence was found.

Figure 3 illustrates that there was a statistically significant lower mean of oxytocin level with  $p$ -value  $<0.001$  among cases.

Table 4 illustrates that there was a statistically significant negative correlation ( $p$ -value  $<0.05$ ) between oxytocin level and each NS and HA, in addition to a positive correlation between oxytocin level and each of RD, self-directedness, and cooperativeness items of TCR-R, among cases. On the other hand, there was no statistically significant correlation ( $p$ -value  $>0.05$ ) between oxytocin level and persistence, and self-transcendence.

Table 5 illustrates that there was no statistically significant difference in oxytocin level ( $p$ -value  $>0.05$ ) between

different Childhood Trauma Questionnaire (CTQ) items among cases.

Table 6 illustrates that dose of heroin showed a statistically significant positive correlation ( $p$ -value  $<0.05$ ) with persistence and a negative correlation with cooperativeness, with no significant correlation with oxytocin level and other TCI-R items. On the other hand, there was a statistical significant negative correlation ( $p$ -value  $<0.05$ ) between age of onset and both self-directedness, and ST, with no significant correlation with oxytocin level and other TCI-R items.

### Discussion

In the present study, the range of age of onset of substance use was 18–30 years old (mean:  $21.9 \pm 3.1$ ). This is in agreement with the results of [2], an Egyptian study of motive in Tramadol and Heroin users, in which the age of onset was over age 18; however, in heroin patients, it was at 18 or younger.

Regarding socioeconomic status (SES), 35% of cases had low socioeconomic status and 27% had middle socioeconomic status. This is in agreement with a study done by [3], about duration of opioid use and association with socioeconomic status. Australia showed that the higher the doses of opioid use and the lower the socioeconomic status, the more the risk of long-term dispensing of opioid prescriptions. This can be explained by the negative social and economic effects of substance use [24] and explained also by the catchment area of this study at El Fayoum University Hospital which had low treatment services' costs.

A higher percentage of divorce was present among cases (22.2%) in comparison to only (2.5%) among healthy control.

This is consistent with a study by Day and Rosenthal [9] based on data from National Survey on Drug Use and Health (NSDUH) for years 2015 to 2017 [23] who had found that those who are not married showed three times increased odds of associated benzodiazepine and opioid misuse.

Rajkumar [28] results were not in line with us as he found that divorce was a positive correlate to opioid use; however, it does not reach the level of significance.

In the present study, there was a statistically significance between the two groups regarding the family history of substance abuse and psychiatric disorders, whereas it was 60 and 50%, respectively, in cases while it was 25 and 15%, respectively, in controls.

These results agreed with Ramsewak et al. [29] who found that 73% of Mauritian male patients had positive family history for substance use disorder, and the most prevalent psychiatric disorder recorded was psychotic disorder (17.1%).

**Table 1** Comparisons of demographic characters in different study groups

Variables	Cases (N=40)		Control (N=40)		p-value	Sig.
Age						
26–35 years	12	30%	18	45%	0.37	NS
36–50 years	26	65%	20	50%		
51–60 years	2	5%	2	5%		
Educational level						
Illiterate	6	15%	0	0%	<0.001	HS
Read and write	2	5%	0	0%		
Primary	4	10%	0	0%		
Secondary	14	35%	0	0%		
Technical	4	10%	1	2.5%		
University	10	25%	21	52.5%		
Post grade	0	0%	18	45%		
Occupation						
Employed	26	65%	40	100%	<0.001	HS
Unemployed	14	35%	0	0%		
Socioeconomic status						
High	13	32.5%	6	15%	<0.001	HS
Middle	11	27.5%	32	80%		
Low	14	35%	2	5%		
Very low	2	5%	0	0%		
Marital status						
Single	6	15%	7	17.5%	0.001	HS
Engaged	0	0%	10	25%		
Married	24	60%	19	47.5%		
Separated	1	2.5%	3	7.5%		
Divorced	9	22.5%	1	2.5%		
Medical comorbidities						
No	17	42.5%	28	70%	0.02	S
Yes	23	57.5%	12	30%		
Family history of substance abuse						
Negative	16	40%	30	75%	0.002	HS
Positive	24	60%	10	25%		
Family history of psychiatric disorders						
Negative	20	50%	34	85%	0.002	HS
Positive	20	50%	6	15%		
Variables (n=40)	Mean ±SD		Range		Median / IQR	
Age of onset	21.9±3.1		18–30		22.5 / 5	

The table illustrates different socioeconomic status, family history, and age of onset

These findings can be explained by the genetic attribution to substance use disorders [24].

As regards considerable problems resulting from substance abuse according to Addiction Severity Index Scale, the drug use status was a considerable problem in forty subjects (100%) of cases.

As regards the psychological status, it was considered a problem in 80% of cases. These results are in agreement with Shahin et al. [32] who found that most of patients

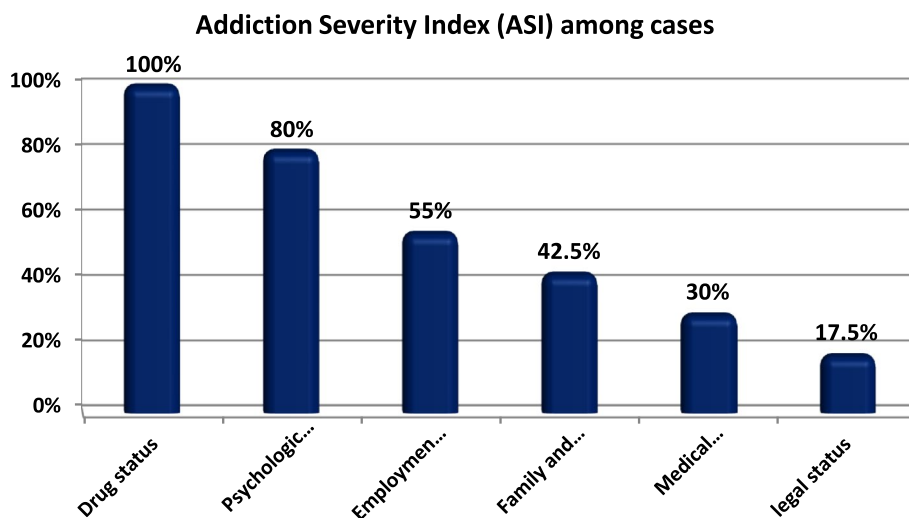
with substance use disorders suffered from depressive disorders and many of them had a higher risk of self-harm and suicide. As regards the employment and support status, they were considered a problem in twenty two subjects (55%) of cases. Most of the patients reported problems varying from warning of termination to problems with absenteeism. These results demonstrated that the impact of drug use can affect both employment probability and quality [21].

**Table 2** Coefficients<sup>a</sup> and oxytocin

Model		Unstandardized coefficients		Standardized coefficients Beta	t	Sig.
		B	Std. error			
1	(Constant)	124.690	46.935		2.657	.012
	• Age	9.752	9.537	.200	1.023	.314
	• Education	-1.423	3.402	-.090	-.418	.679
	• occupation	-18.683	10.291	-.341	-1.815	.079
	• Socioeconomic	-2.159	5.836	-.077	-.370	.714
	• Marital	-.979	4.633	-.046	-.211	.834
	• Family History of psychiatric disorders	-4.359	9.205	-.083	-.474	.639
	• Medical comorbidity	5.719	10.573	.108	.541	.592

The table illustrates regression analysis of different coefficients and oxytocin as a dependent variable

<sup>a</sup> Dependent variable: oxytocin



**Fig. 1** Severity of addiction according to Addiction Severity Index scale among cases

As regards the family and social relationship subscales, they were considered a problem in 42.5% of cases. The social stigma related to addiction affects the patients' families as well. Egyptian culture foster a strong family-based social life, which make addiction-related problems, like drug-seeking behaviors, occupational and marital problems, affect families of afflicted individuals to a great extent [16].

As regards the medical status subscale, it was considered a problem in 30% of cases. The medical problems in both groups ranged from intoxication, convulsions, and overdose up to chronic diseases such as hepatitis B and C as well as HIV from needles. A recent Russian study found a higher prevalence of hepatitis markers in people who had a history of injecting illicit drugs [4]

As regards legal status subscale, it was considered a problem in 17.5%. Most of legal problems reported were associated with aggressive behavior toward other people including family members or neighbors and stealing in order to afford money for buying the substance.

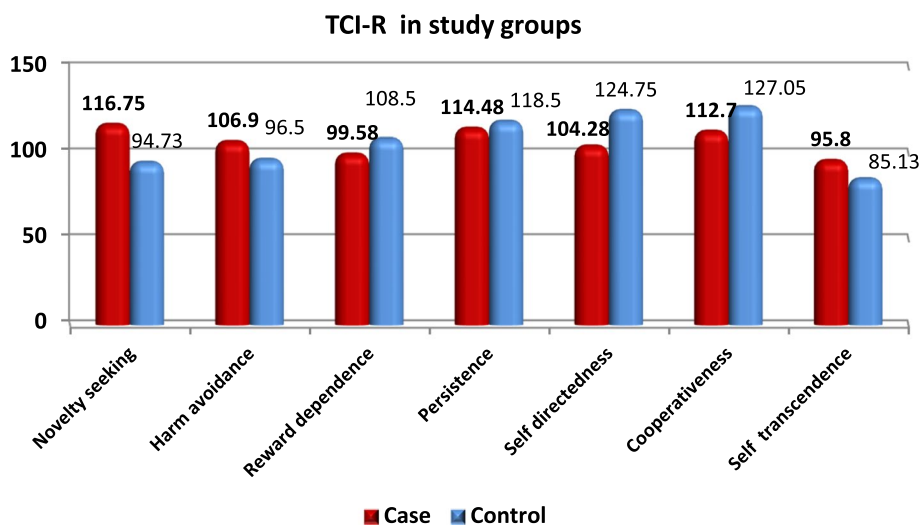
Our results are consistent with the results of Moses et al. who found that 10% of cases underwent arrest or legal problems [26].

As regards temperament and character inventory-revised (TCI-R) items, our results showed that there were a statistically significant higher means of NS, HA, and ST, and lower means of RD, self-directedness, and cooperativeness (*p*-value <0.05) among cases.

In a recent Egyptian study by Okasha et al. [27], cases with substance use disorder had significantly higher

**Table 3** Comparisons of Childhood Trauma Questionnaire (CTQ) in different study groups

Variables (N=40)		Cases (N=40)		Control (N=40)		p-value	Sig.
		NO.	%	NO.	%		
Emotional abuse	None	7	17.5%	13	32.5%	<0.001	HS
	Low	15	37.5%	26	65%		
	Moderate	14	35%	1	2.5%		
	Sever	4	10%	0	0%		
Physical abuse	None	5	12.5%	18	45%	<0.001	HS
	Low	13	32.5%	21	52.5%		
	Moderate	10	25%	1	2.5%		
	Sever	12	30%	0	0%		
Sexual abuse	None	34	85%	33	82.5%	0.005	HS
	Low	0	0%	7	17.5%		
	Moderate	3	7.5%	0	0%		
	Sever	3	7.5%	0	0%		
Emotional neglect	None	9	22.5%	13	32.5%	<0.001	HS
	Low	16	40%	26	65%		
	Moderate	15	37.5%	1	2.5%		
Physical neglect	None	6	15%	17	42.5%	<0.001	HS
	Low	19	47.5%	22	55%		
	Moderate	13	32.5%	1	2.5%		
	Sever	2	5%	0	0%		



**Fig. 2** Temperament and character inventory revised scale in the studied groups

scores in NS, and they had significantly lower HA and persistence using the same scale.

Another study in Iran by Shahini et al. [33] showed that the scores of RD, persistence, cooperativeness, self-directedness, and ST were significantly lower in the case group compared to healthy individuals. In

contrast, the score of NS was significantly higher in the case group with SUD. On the other hand, HA was not significantly different between the two groups.

Also a study by Hashemi et al. [18] showed that the drug users obtained high scores in the dimensions of NS and HA versus low scores in RD, persistence, and self-directedness.

Oxytocin level in different study groups

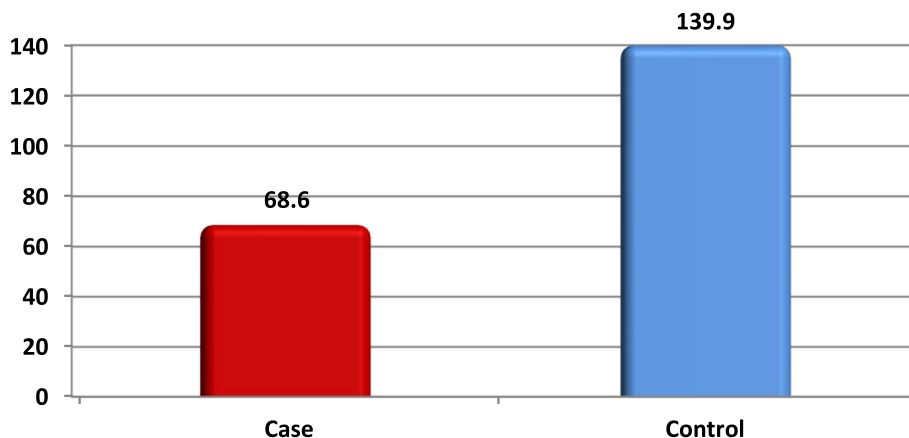


Fig. 3 Oxytocin level in different study groups

Table 4 Correlation between oxytocin level and temperament and character inventory - revised (TCI-R)

Variables	Oxytocin		
	R	p-value	Sig.
Novelty seeking	-0.32	0.004*	HS
Harm avoidance	-0.25	0.02*	S
Reward dependence	0.25	0.02*	S
Persistence	0.12	0.3	NS
Self-directedness	0.32	0.004*	HS
Cooperativeness	0.29	0.008*	HS
Self-transcendence	-0.20	0.07	NS

\*p-value < 0.05

Abbate-Daga et al. [1] found that men with opiate dependency showed higher HA and lower self-directedness and cooperativeness scores than the participants of the control group. One Taiwanese study revealed opiate-dependent patients had higher NS and HA scores [39] and NS scores were also higher in men with opiate dependency from Hungary than controls [10]. The possible mechanisms, as shown in animal studies, may be related to dopaminergic and serotonergic system [37], but more studies in human are required [34].

Our results revealed that there was a significant difference between the two groups regarding the serum oxytocin level (OXT) with p-value <0.001.

Our results are consistent with a study done by Mobasher et al. [24] who revealed that there was a statistically significant difference between the patient with opioid use disorder and the control groups in serum OXT levels (P<0.05). Also, there is evidence that endogenous and exogenous opioids can affect oxytocin. Endogenous

Table 5 Comparisons of oxytocin level in different Childhood Trauma Questionnaire items (CTQ) among cases

Variables (N=40)		Oxytocin level		p-value	Sig.			
		Mean	SD					
Emotional abuse	None	70.9	25.6	0.9	NS			
	Low	67.2	24.3					
	Moderate	68.4	32.9					
	Sever	69.8	18.1					
Physical abuse	None	73.8	30.8	0.8	NS			
	Low	72.7	26.9					
	Moderate	65.3	23.4					
	Sever	64.5	23.09					
Sexual abuse	None	69.3	24.8	0.8	NS			
	Moderate	58.6	44.1					
	Sever	70.5	37.4					
	None	63.8	34					
Emotional neglect	Low	69.8	26.9	0.8	NS			
	Moderate	70	22.3					
	Physical neglect	None	64.5			29.8	0.8	NS
	Low	71.6	28.3					
Moderate	68	25.4						
Sever	54.9	8.2						

This table illustrates that there was no statistically significant difference in oxytocin level with p-value >0.05 between different Childhood Trauma Questionnaire (CTQ) items among cases

opioids tend to naturally inhibit oxytocin levels [30]. Exogenous opioid use will inhibit oxytocin release, and chronic opioid use has been shown to decrease levels of oxytocin [41].

Our results were in disagreement with the results of Gerra et al. [15] who revealed that oxytocin levels in

**Table 6** Correlation between dose of heroin and age of onset with other variables among cases

Variables	Dose of heroin			Age of onset		
	R	p-value	Sig.	r	p-value	Sig.
Oxytocin level	-0.12	0.4	NS	-0.11	0.5	NS
TCI-R						
Novelty seeking	-0.06	0.7	NS	0.004	0.9	NS
Harm avoidance	0.28	0.09	NS	0.12	0.4	NS
Reward dependence	0.27	0.08	NS	-0.29	0.07	NS
Persistence	0.54	0.001*	HS	0.03	0.8	NS
Self-directedness	-0.007	0.9	NS	-0.37	0.01*	S
Cooperativeness	-0.41	0.008*	HS	-0.13	0.4	NS
Self-transcendence	0.14	0.4	NS	-0.37	0.01*	S

\**p*-value < 0.05

serum samples were significantly higher among patients with drug use disorders than healthy controls. This inconsistency may be explained the character of our sample being larger and studied OXT among users in contrary to a small sample by the latter author and studying OXT in abstinent patients.

There was a significant higher percentage of moderate and severe degree of emotional, physical, sexual abuse, in addition to physical and emotional neglect with *p*-value <0.05 among cases in comparison to healthy controls.

These results are in agreement with Levis et al. [19] who stated that adverse childhood events and experiences are also greatly associated with later-life substance use disorder. Another study showed that moderators (emotional abuse, neglect, and physical neglect) caused interaction between post-traumatic stress disorder (PTSD) and opioid use disorder [35].

In accordance with El-Shinnawy et al. [12] who found that cases with the diagnosis of comorbid substance dependence and other mental disorder had significant history of child abuse than cases with the diagnosis of substance dependence only (*p*-value 0.024).

There was a significant negative correlation (*p*-value <0.05) between oxytocin level and each NS and HA, in addition to a positive correlation between oxytocin level and each of RD, self-directedness, and cooperativeness among cases.

This is in agreement with the results of Lin et al. [20] who stated the negative correlation between blood level of plasma oxytocin and NS among those on methadone as maintenance treatment ( $r = -0.34$ ,  $p = 0.003$ ).

There was no statistical significant difference in oxytocin level with *p*-value >0.05 between different Childhood Trauma Questionnaire (CTQ) items among cases.

In a study about daily oxytocin in relation to childhood trauma and psychopathy in residential youth done by

Fragkaki et al. [14], results showed that significant interplay between callous-unemotional (CU) traits and emotional neglect on mean daily oxytocin was detected.

Another study done by Dator [8], about oxytocin, risk-taking, and childhood maltreatment at East Carolina University resulted in lower salivary OXT which is related to higher overall levels of childhood maltreatment.

Our results revealed that dose of heroin showed a positive significant correlation (*p*-value <0.05) with persistence and a negative correlation with cooperativeness, which indicated that increase dose of heroin associated with decrease in cooperativeness and increase in persistence with no significant correlation with oxytocin level and other TCI-R items. Meanwhile, there was a statistical significant negative correlation (*p*-value <0.05) between age of onset and both self-directedness and self-transcendence, which indicated that increase age of onset was associated with decrease in self-directedness and self-transcendence, with no significant correlation with oxytocin level and other TCI-R items.

In line with our results, in a study done by Shahini et al. [33] about temperament and character in substance use disorder in Iran, only self-transcendence was significantly positively correlated with age.

### Limitations of the study

A larger sample size would help in giving more information and data especially regarding the correlation. The area in which the study has been carried on is limited to a specific socioeconomic class and therefore results cannot be generalized to the whole population. The sample in this study is limited to only a specific type of substance, and as a result, the relation of oxytocin to addiction or substance dependence in general cannot be concluded. Females were not included in this study as the oxytocin



level in females is affected by many other factors which would have been difficult to control.

## Conclusions

Oxytocin level is affected by opioid use disorder and has a lower level than healthy controls. Patients with opioid use disorder obtained higher scores of NS, HA, and ST and lower mean of RD, self-directedness, and cooperativeness than controls. Patients with opioid use disorder showed a higher percentage of moderate and severe degrees of emotional, physical, and sexual abuse, in addition to physical and emotional neglect. Regarding correlation between oxytocin level and temperament, patients with opioid use disorder showed high significant correlation between oxytocin level and NS.

## Recommendation

Future research is recommended in the same area with a larger sample of patients of different age groups and more matched sociodemographic data to optimize the statistical power of considering oxytocin as a biological marker for heroin use disorder.

## Abbreviations

CTQ	Childhood Trauma Questionnaire
EBASI	Egyptian Brief Addiction Severity Index
HA	Harm avoidance
NS	Novelty seeking
OXT	Oxytocin
PTSD	Post-traumatic stress disorder
RD	Reward dependence
ST	Self-transcendence
TCI-R	Temperament and character inventory - revised

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## Authors' contributions

MS prepared the main idea and contributed in writing the manuscript. MD and AM prepared the questionnaires, analyzed and interpreted the patient data regarding the clinical data and psychometric tools, and was a major contributor in writing the manuscript. HD was the major contributor in revising the manuscript. HA was the main supervisor of clinical chemistry work. All authors read and approved the final manuscript.

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## Availability of data and materials

Not applicable.

## Declarations

### Ethics approval and consent to participate

This study was approved by the Research Ethics Committee, Faculty of Medicine, Fayoum University. Contents of consent were clarified and written and completed by all participants.

### Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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