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Study of insight in patients with obsessive compulsive disorder and its relation to executive functions and serum brain-derived neurotrophic factor

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Abstract

Background Obsessive–compulsive disorder (OCD) is usually associated with insight's heterogeneity, and those with poor insight showed lower BDNF and cognitive deficiencies. The aim was to detect the relation between insight to executive dysfunction and BDNF.

Materials and methods Forty patients diagnosed with OCD and forty matched healthy controls. Also, both poor and good insight groups (assessed by The Brown Assessment of Belief Scale) were compared as regard Trail Making Test and serum level of BDNF).

Results OCD patients group gave a significant worse performance in TMT and lower BDNF serum level than healthy control. Also, OCD patients with poor insight had lower BDNF level than patients with good to fair insight. ROC curve analysis confirmed that BDNF is a valuable diagnostic biomarker of insight in patients with OCD with 100% sensitivity and 72.41% specificity, p value < 0.001. Insight of OCD patients was not significantly associated with executive dysfunction detected by Trail Making Test.

Conclusions OCD patients with poor insight had longer duration of illness, severe OCD symptoms, lower serum BDNF level, and longer time on TMTA-B than good insight patients. BDNF is a valuable diagnostic biomarker of insight in patients with OCD.

Keywords OCD, BDNF, Executive functions, Insight

Background

Obsessive–compulsive disorder (OCD) is defined as recurring, intrusive beliefs, urges, visions, or mental activities or behaviors that cause substantial suffering and psychosocial damage [5].

The approximate life expectancy incidence of OCD is about 2.3% [38]. 15–30% of cases with OCD are suggested to be correlated with inadequate understanding of one's symptoms' nature and severity [4, 8, 12]. This is associated with the insight's heterogeneity in the disorder [8, 12].

Insight was known as a possible reason for the poor success of intervention in OCD, with 20–25% as an inefficacy rate. In addition, emphasis has been brought to the various elements impacting insight, including the brain-derived neurotrophic factor (BDNF) [23, 24]. Cognitive

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deficiencies and neuropsychological issues may also contribute to poor insight [2].

Individuals with OCD perform worse in a number of executive function domains, such as processing speed, working memory, and sustained attention, as well as verbal memory/fluency and visuospatial abilities recall [1].

In contrast to OCD cases with excellent understanding and healthy control subjects, [23, 24] discovered that cases with OCD who had poor understanding could have worse executive performance in the Wisconsin Card Sorting Test (WCST) and Trail Making Test (TMT).

Many neuropsychiatric illnesses, particularly OCD, have been connected to the pathophysiology of BDNF. Much interest has revealed regarding BDNF in the pathophysiology of OCD due to its role in brain development, its documented role in the serotonergic neurons' development and growth, and the proven influence of SRIs on levels of peripheral BDNF [26, 33].

This study aimed to assess executive functions and BDNF in patients with OCD and control group and to find the relation between both of them and insight in patients with OCD.

Materials and methods

This study is an observational, case–control study.

Procedure

The study passed through the following phases:

1- Preparation phase

After a through literature review, the study question was formulated and the study protocol was prepared. The methods used in the current study were chosen based on the availability in Arabic Language, feasibility of application, and validity of the tools.

The research protocol was then granted the approval of the scientific and ethical committee of the Faculty of Medicine, Fayoum University (No. (M 587) in its session 93 on 10/4/2022).

2- Data collection

The patients were enrolled from the Psychiatry Outpatient Clinic, Fayoum University that is conducted 3 days weekly through the period from first April 2022 till first of September 2022 by consecutive sampling.

The patients fulfilling the inclusion criteria were interviewed using the semi-structured interview derived from the psychiatric sheet of Fayoum Psychiatry Department, Relevant data involve (age at illness beginning, socio demographic data, duration of illness, family

history), Clinical Interview dependent on DSM-5 to diagnose OCD, Yale-Brown Obsessive Compulsive Scale to evaluate severity of OCD, The Brown Assessment of Belief Scale (BABS) to detect insight among OCD cases. Then both of cases group and Control group were evaluated for cognition utilizing trail making test, and determining serum brain-derived neurotrophic factor level in both groups.

3- Data analysis

Data was gathered, encoded, and secured in a personal computer with only the primary investigator having access. The suitable statistical tests were then selected after the data had been analyzed utilizing SPSS (Statistical Package for Social Sciences).

Each group's minimum sample size was 40 individuals, based on the findings of prior study (Experimental Psychology Department, University of Heinrich Heine in Düsseldorf, Germany, used G power software version 3.1,7 to verify the sample size). Type 1 mistake with two tails, a power of 95%, and two sides. 1.2 impact size.

4- Data interpretation

Discussion of the results was carried out to detect the significant findings and find out whether they support or refuse the study hypothesis. Conclusions, limitations, and recommendations were then addressed.

Subjects

Group A (patients group)

Inclusion criteria

Forty patients diagnosed with OCD (both genders, 18–50 years old, and drug naïve according to DSM 5 and severity was detected using the Yale-Brown Obsessive Compulsive Scale and was divided into two groups according to insight into patients with good insight and inadequate insight according to The Brown Assessment of Belief Scale.

Exclusion criteria

Other psychiatric comorbidities, substance use disorders, and inflammatory illness were excluded as they can affect executive functions and BDNF levels.

Group B (control group)

Forty healthy volunteers with absence of any psychopathology were selected among medical and paramedical health workers from Fayoum University Hospital and matched with the patients group in age, gender, education, socio-demographic, and economic status.

1 Psychometric assessment

- Semi-structured clinical interview depending on DSM-5: it is used to diagnose OCD and to rule out other comorbidities.
- Yale-Brown Obsessive Compulsive Scale [14]: Arabic Version by [31] To evaluate OCD severity: it contains five items on obsessions and five items on compulsions (score 0–4 for each item). The highest total score is 40. Patients who have both compulsions and obsessions fall into the following severity score ranges: score of sub-clinical = 0–7, mild = 8–15, moderate = 16–23, severe = 24–31, while extreme cases have 32–40. The threshold value for clinically significant symptoms is higher than 16.
- The Brown Assessment of Belief Scale (BABS): [10] to estimate insight: this was translated and back translated by colleagues in Psychiatry Department, Kasr El Eini Hospital, the Arabic version was prepared for publication but not submitted.
The total BABS number is calculated by adding the first six items out of the seven items. The final score does not take into account an extra item (ideas of reference). Each object has a rating from 0 to 4 (from least to most severe). The final response chosen for each item relies on the interviewer's clinical judgment; however, the items are generally rated depending on the patient's statement.
- Trail Making Test (quoted by [35] (Arabic Version) by [39]: to detect executive function: the task is divided into two parts, and the subject must associate a group of 25 dots instantaneously and precisely. The exam can reveal details about executive functioning as well as scanning, processing speed, visual search speed, and mental flexibility.

- 2 Biochemical measures to assess BDNF: The Department of Clinical Pathology, Fayoum University conducted the study of the clinical chemistry parameter. A nurse used aseptic venipuncture to gather venous samples from each participant. The blood sample was then put in serum separator vacutainer tubes, and then an experienced laboratory technician centrifuged the specimens at a speed of 3000 rpm, within 30 min. The separated serum was kept and frozen in an Eppendorf tube until analysis at -20°C . BDNF was quantified using a widely available enzyme-linked immunosorbent assay (ELISA) kit.

Statistical analysis

Statistical analysis was done by SPSS version 28 (IBM Co., Armonk, NY, USA). The normality for each variable was tested by Wilk-Shapiro test and for every non-parametric variable, the median was used. Numerical variables such as median and interquartile range (IQR) were studied by Mann–Whitney test. Categorical variables were showed as frequency and percentage (%) and tested using the chi-square test.

Spearman's rank correlation coefficient was used to estimate the correlation between two non-parametric quantitative variables. The overall diagnostic performance of BDNF was evaluated by ROC curve analysis. A two-tailed P value <0.05 was considered statistically significant.

Results

The two studied groups show no statistically significant difference regarding socio-demographics represented by (age, gender, marital status, occupation, residence, educational level, and socio-economic level) (Table 1).

Out of the forty OCD patients, 27.5% had family history of OCD. The onset of OCD occurred at a median age of 22.5 years with IQR from 20–31.5 years. The median duration of illness was 4 years with IQR from 3–6 years. Symptoms' severity was assessed by Y-BOCS which gave a median score of 22 with IQR from 16 to 28 as demonstrated in Table 2.

Executive functions were evaluated via tests as TMT. OCD patients had a problem adapting to the rules change, therefore gave a worse performance in TMT with significantly longer time as compared to healthy participants (P values <0.001) (Table 3). BDNF serum level is lower in OCD patients (0.51) than healthy control (0.75) with p value 0.013 (Table 3).

The forty OCD patients were divided and further analyzed according to The Brown Assessment of Belief Scale that evaluates insight into good insight group which included 29 patients and poor insight group that included 11 patients.

No statistically significant association between insight and sociodemographic data was found in OCD patients as shown in Table 4.

There was no significant relation between insight and family history and age at onset of OCD. Duration of illness showed statistically significant difference as, OCD patients who with poor insight had OCD with higher median 6 years and IQR from 4 to 8 years than patients with good to fair insight with median 4 years and IQR from 2 to 5 years, p value = 0.003. Also, insight of OCD patients was not significantly associated with executive function detected by Trail Making Test (Table 5).

Table 1 Sociodemographic characteristics of the studied groups

	Group A (n = 40)	Group B (n = 40)	P value
Age (years)			
Median	28	30.5	0.35
IQR	22–36.75	25–35.75	
Gender			
Male	17 (42.5%)	20 (50%)	0.501
Female	23 (57.5%)	20 (50%)	
Marital status			
Single	21 (52.5%)	17 (42.5%)	0.370
Married	19 (47.5%)	23 (57.5%)	
Occupation			
Housewife	13 (32.5%)	8 (20%)	0.094
Non skillful	6 (15%)	4 (10%)	
Skillful	5 (12.5%)	10 (25%)	
Employee	6 (15%)	13 (32.5%)	
Student	10 (25%)	4 (10%)	
Not working	0 (0%)	1 (2.5%)	
Residence			
Rural	20 (50%)	22 (55%)	0.654
Urban	20 (50%)	18 (45%)	
Educational level			
Illiterate	4 (10%)	4 (10%)	0.971
Read and write	6 (15%)	7 (17.5%)	
Primary school	5 (12.5%)	4 (10%)	
Preparatory school	2 (5%)	3 (7.5%)	
Technical	9 (22.5%)	11 (27.5%)	
University	14 (35%)	11 (27.5%)	
Socioeconomic level			
High	10 (25%)	9 (22.5%)	0.698
Middle	14 (35%)	19 (47.5%)	
Low	10 (25%)	7 (17.5%)	
Very low	6 (15%)	5 (12.5%)	

Data are presented as frequency (%) unless otherwise mentioned, Statistical significance at $P < 0.05$

The correlation between BDNF and both executive function and severity of symptoms in OCD patients was demonstrated in Table 6, showing a significant negative correlation between BDNF and Y-BOCS severity ($r = -0.430$, $P = 0.006$) in all OCD patients (Table 6).

ROC curve analysis confirmed that BDNF is a valuable diagnostic biomarker of insight in patients with OCD with 100% sensitivity and 72.41% specificity, p value < 0.001 as shown in Fig. 1.

Discussion

Serum brain-derived neurotrophic factor levels

As regard the median serum brain-derived neurotrophic factor there was statistically significant difference in

Table 2 Family history and symptoms severity assessment in OCD patients

OCD patients (n = 40)	
Family history of OCD	
Yes	11 (27.5%)
No	29 (72.5%)
Age at onset (years)	
Median	22.5
IQR	20–31.5
Duration illness (years)	
Median	4
IQR	3–6
Y-BOCS severity	
Median	22
IQR	16–28

Data are presented as frequency (%) unless otherwise mentioned, OCD obsessive compulsive disorder, IQR interquartile range

Table 3 Executive function tests and BDNF of the studied groups

	Group A (n = 40)	Group B (n = 40)	P value
Trail Making Test (second)			
Part A	60	50	< 0.001
	52.25–80	35–60	
Part B	120	90	< 0.001
	108–172.75	80–100	
BDNF (ng/ml)	0.51	0.75	0.013
	0.38–0.79	0.60–0.96	

Data are presented as median and IQR

Statistical significance at $P < 0.05$, BDNF brain-derived neurotrophic factor

which case group was lower than control group (Table 3). This result was in accordance with those obtained by [15, 42] who found OCD sufferers have lower plasma amounts of BDNF than healthy controls. Additionally, patients had significantly lower blood levels of BDNF contrasted to healthy controls, according to a random-effects meta-analysis (Hedges' $g = -0.722$, 95% confidence interval [CI] = -1.152 to -0.292 , $P = 0.001$). These outcomes indicate that BDNF may be a prospective biomarker for OCD [17].

However, these findings were inconsistent with [3] as serum BDNF concentrations in the OCD patients group were greater than in the control group. The present study was different with [3] study whose OCD patients were under SRIs medications, had demonstrated that SRIs elevate peripheral BDNF levels in humans while cases in the present study were drug naïve.

Table 4 Association between insight and socio-demographics in OCD patients

	Insight		P value
	Poor (n = 11)	Good to fair (n = 29)	
Age (years)			
Median	28	28	0.280
IQR	23.5–38	20–34	
Gender			
Male	3 (27.3%)	14 (48.3%)	0.297
Female	8 (72.7%)	15 (51.7%)	
Marital status			
Single	6 (54.5%)	15 (51.7%)	0.873
Married	5 (45.5%)	14 (48.3%)	
Occupation			
Housewife	2 (18.2%)	11 (37.9%)	0.768
Non skillful	2 (18.2%)	4 (13.8%)	
Skillful	1 (9.1%)	4 (13.8%)	
With occupation	2 (18.2%)	4 (13.8%)	
Student	4 (36.4%)	6 (20.7%)	
Residence			
Rural	6 (54.5%)	14 (48.3%)	0.723
Urban	5 (45.5%)	15 (51.7%)	
Educational level			
Illiterate	0 (0%)	4 (13.8%)	0.475
Read and write	2 (18.2%)	4 (13.8%)	
Primary school	0 (0%)	5 (17.2%)	
Preparatory school	1 (9.1%)	1 (3.4%)	
Technical	3 (27.3%)	6 (20.7%)	
University	5 (45.5%)	9 (31.0%)	
Socioeconomic level			
High	2 (18.2%)	8 (27.6%)	0.359
Middle	6 (54.5%)	8 (27.6%)	
Low	1 (9.1%)	9 (31.0%)	
Very low	2 (18.2%)	4 (13.8%)	

Data are presented as frequency (%) unless otherwise mentioned

Statistical significance at $P < 0.05$

Executive functions deficit in OCD

In the present study, as regard the median scores of TMT-A and TMT-B, they were significantly greater in OCD patients than in controls (Table 3). These results agreed with [19] who stated that both TMT A and B were greater in cases with OCD (with significant p value = 0.01, and p value = 0.0005, consecutively).

The length of time it takes for OCD cases and controls, to respond to TMT-A was observed to be significantly different between them [37] in which the OCD cases responded more slowly than the controls did. Also, Spalletta et al. 2014 found selective impairments in executive functioning measures of cognitive flexibility (TMT

Table 5 Association between insight and clinical and laboratory variables in OCD patients

	Insight		P value
	Poor (n = 11)	Good to fair (n = 29)	
Family history of OCD			
Yes	3 (27.3%)	8 (27.6%)	> 0.999
No	8 (72.7%)	21 (72.4%)	
Age at onset (years)			
Median	21	25	0.060
IQR	14–30	20–32.5	
Duration of illness (years)			
Median	6	4	0.003
IQR	4–8	2–5	
Y-BOCS Severity	32	20	< 0.001
	28–35	16–23	
Trail Making Test (second)			
Part A	66	60	0.207
	60–84	50–80	
Part B	150	120	0.157
	105–180	108–155	
BDNF (ng/ml)	0.3	0.64	< 0.001
	0.29–0.39	0.47–0.90	

Y-BOCS Yale-Brown Obsessive Compulsive Scale, BDNF brain-derived neurotrophic factor

Data are presented as frequency (%), median and IQR unless otherwise mentioned, statistical significance at $P < 0.05$

part B) with OCD patients (171.40 s) and control group (110.95 s) with (p value = 0.007) [16]; discovered that OCD samples performed inadequately on set-shifting tasks like the TMT-B.

The present study was in line with [7] who exhibit that OCD cases had a great dysfunctions across all cognitive domains (flexibility, decision-making, inhibition, attention, memory, verbal fluency, and planning). [34] had been recommended that deficits in cognitive flexibility might express a cognitive endophenotype for OCD.

The insight's belief has been the controversy's object so the forty OCD patients were divided and further analyzed according to The Brown Assessment of Belief Scale that evaluates insight into good insight group which included 29 patients and poor insight group that included 11 patients.

Insight and sociodemographic factor

There was no statistically significant correlation between insight and sociodemographic in OCD represented by age, gender, marital status, occupation, residence, educational level, and socioeconomic level (Table 4).

Table 6 Correlation between BDNF and both executive function and severity of symptoms in OCD patients

	BDNF in all OCD patients (n = 40)		BDNF in good to fair insight patients (n = 29)		BDNF in poor insight patients (n = 11)	
	r_s	P	r_s	P	r_s	P
Y-BOCS Severity	−0.430	0.006	0.114	0.555	−0.291	0.385
Trail Making Test (second)						
Part A	−0.005	0.974	0.133	0.492	0.171	0.616
Part B	−0.113	0.489	0.041	0.832	0.009	0.978

Y-BOCS Yale-Brown Obsessive Compulsive Scale, BDNF brain-derived neurotrophic factor

r_s Spearman's rank correlation coefficient, statistical significance at $P < 0.05$

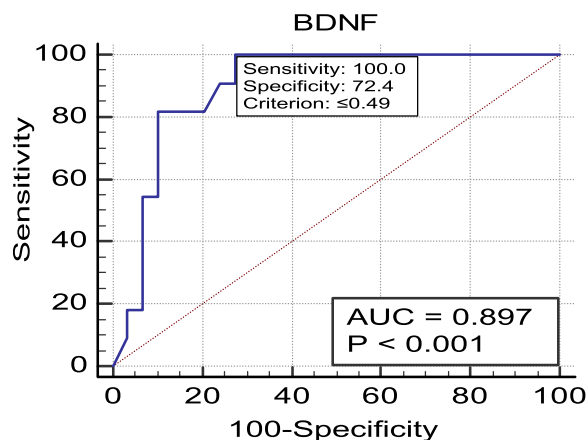


Fig. 1 ROC curve of BDNF in predicting poor insight in OCD patients (n = 40). AUC: area under the curve, BDNF: brain-derived neurotrophic factor

These results were consistent with [22, 40], and [21] who observed that no significant group differences (good, poor, and controls) in different socio-demographic aspects of age, gender, and education levels, background (urban/rural), and marital status.

Insight and family history in OCD patient

Regarding the present study, there was no significant correlation between insight, family history of OCD and age of onset (Table 5).

These findings contradicted those of [8, 21], in which poor insight had been correlated with an early-age of beginning. Poor insight cases with obsessive-compulsive disorder (OCD) were linked to worse OCD symptoms, a younger age of onset, comorbid depression, and poor medication outcomes, according to [18]. The difference between the present study and their studies as regard age of onset may be owing to small sample size (poor insight patients = 11).

Regarding family history, these results were in line with [21] who observed that family history did not

differ significantly with (p value = 0.76) between cases with poor insight and patients with good insight).

Regarding duration of illness, our results showed statistically significant difference as OCD cases who with poor insight had OCD with higher median 6 years than patients with good to fair insight with median 4 years (p value = 0.003) (Table 5) this finding was in line with that observed in [6, 21, 27, 32].

Also, [8] stated that poor insight had been linked to longer period of illness.

Insight and severity of OCD symptoms

Our findings stated a potent correlation between poor insight and OCD severity according to Y-BOCS (Table 5).

These results were consistent with [32] study in which the severity was the greatest indicator of poor insight, making poor insight the severest obsessive-compulsive continuum. Also [8], discovered that OCD cases with poor insight demonstrated an obsessive-compulsive's extreme severity. As regards [41]'s study, poor insight was linked to severe prevalence of OCD and a greater medication resistance.

Insight and serum BDNF

In this study, regarding median serum BDNF level there was statistically significant difference between poor and good patients insight (Table 5).

This outcome was consistent with that of Manarte et al. [23, 24] who discovered that the BDNF levels in the poor-insight group were lower than in the control groups and good-insight.

Marinova et. al [25] showed that glutamate-modulating drugs in OCD (memantine) demonstrated a positive impact as an augmentation treatment in intense cases of OCD which may have poor insight. [36] demonstrated elevated BDNF protein levels in the prefrontal cortex which shed light for the relation between BDNF and OCD.

Insight and executive function deficit in OCD patient

Regarding (TMT), TMT A and B scores were higher in poor insight cases but not statistically significant than good insight patients.

Manarte et al. [23, 24] found clear differences between good and poor insight group with p value for TMT-A and TMT-B = 0.003, 0.002 respectively. The difference may be due to small sample size (poor insight patient (11) for good insight (29)).

Additionally, Kashyap et al. [20] discovered that on the Trail Making test (TMT), the OCD patients whom had poor insight was worst in the test than patients with good insight.

Correlative results

In the present study, as regards association between BDNF and symptoms' intensity in OCD patients there is a significant negative relationship between BDNF and YBOCS severity (p value = 0.006) (Table 6). There is a negative correlation between BDNF in poor insight patient and OCD severity which indicate low BDNF serum level associated with poor insight patient and severe OCD symptom. These findings were similar to [9], in validating the association between intensity of OCD and serum BDNF levels, particularly in sexual/religious symptom's dimension. However [42], found that there was no significant relation between illness severity and plasma levels of BDNF (Y-BOCS score).

Regarding Trail Making Test (A-B) there was a negative correlation between BDNF in all OCD patient and trail making test (A-B) but not statistically significant (Table 6) which indicate patient took longer time to perform TMT associated with low BDNF serum level.

This result was in accordance with those obtained by [13] and [29, 30], their study found that BDNF Val66Met genotype has been linked with changes in variety cognitive functions as EF. Additionally, Mohapatra et al. 2020 revealed that patients with OCD whose serum BDNF level is significantly lowered (p value = 0.002) have significantly lower levels of visuospatial capability, attention, and concentration.

Diagnostic performance of BDNF in predicting poor insight in OCD

Different levels of understanding of the biological causes of diseases result in significantly different conditions for successful treatment [43].

The present study confirmed that BDNF is a valuable diagnostic biomarker of insight in patients with OCD with 100% sensitivity and 72, 41% specificity (Fig. 1). Our

results support findings from [23, 24] shown that the poor-insight group's BDNF values were lower than good-insight group. This is a likely path for future research for medication of poor insight OCD cases. This is also, supported by genetic studies as [11] found that the genotypic frequency of Val66Met of the BDNF gene differed between people with OCD and healthy participants and MJ et al. [28] observed that protective impact of the 'Met' allele in OCD especially at the Val66Met locus.

Limitation of the study

The whole sample size in our study and those with poor insight were relatively small, which may affect the meaningful associations. This study enrolled only clinically based participants and they may have sufficient ability to detect their insight and to acknowledge symptom severity which may lead to skewed insight scores. This may affect the power to detect significant associations among the predictor variables.

Conclusion

OCD patients with poor insight had longer duration of illness, severe OCD symptoms, lower serum BDNF level, longer time on TMTA-B than good insight patients. BDNF is a valuable diagnostic biomarker of insight in patients with OCD with 100% sensitivity and 72.41% specificity (p value < 0.001).

Abbreviations

BABS	Brown Assessment of Beliefs Scale
BDNF	Brain-derived neurotrophic factor
CI	Confidence interval
DSM-5	Diagnostic and Statistical Manual of Mental Disorders-5
OCD	Obsessive compulsive disorder
P-value	Probability value
SCID-5-RV	Structure clinical interview 5
SRI	Serotonin reuptake inhibitors
TMT	Trail Making Test
Y-BOCS	Yale-Brown Obsessive Compulsive Scale

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Authors' contributions

MS prepared the main idea and contributed in writing the manuscript. MD and LM 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. MA 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

The Fayoum University Faculty of Medicine's Ethical Committee gave their stamp of approval to the study proposal (No. (M 587) in its session 93 on 10/4/2022). All participants were required to provide written informed permission. The primary investigator was in charge of going over consent forms that had been signed and examining the subject's files and data. Patient's data was coded and secured in a personal computer with no access not including for principal and co-investigator.

Consent for publication

All authors approved the manuscript and give their consent for submission and publication.

Competing interests

The authors declare that they have no competing interests.

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