

Association of 5-HTTLPR, BDNF, and SAT1 Polymorphisms with Suicidal Tendency and Fatality: A Cross-Sectional Study in Self-Poisoning Patients

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Abstract

Background: Suicide attempts and deliberate self-poisoning represent a major public health and forensic concern worldwide. Emerging evidence suggests a significant genetic predisposition influencing suicidal behavior through altered neurotransmission and neuroplasticity. To date, there are scarce studies on the association of gene polymorphism and suicidal poisoning. **This study aimed to** investigate the distribution of genetic variants in 5-HTTLPR, BDNF rs6265, BDNF rs10835210, and SAT1 in suicide attempters and non-suicide poisoning cases in order to evaluate their potential as diagnostic markers and predictors of lethality. **Methods:** This observational cross-sectional study was performed on 460 adult patients diagnosed with acute poisoning at Benha Poisoning Treatment and Toxicology Research Unit (BPTTRU), Benha University Hospital, from August 2024 to July 2025. The patients were divided into two groups: the suicidal group and the non-suicidal group. Evaluation included medical history, vital signs, conscious state, general and systemic examination, necessary investigations, clinical outcome, and genotyping that was performed using the PCR-RFLP method. **Results:** Genotypes and alleles of studied genes showed significant differences ($P = 0.001$) between suicidal and non-suicidal groups, except BDNF rs6265 allele frequencies didn't show significant ($P = 0.447$) differences between the two groups. The 5-HTTLPR SS genotype ($OR = 4.94$) and the BDNF rs6265 AG genotype ($OR = 1.85$) were all significantly associated with an increased tendency for suicide. Conversely, the SAT1 "I" genotype served as a significant protective factor associated with lower odds of suicide. As regards the fatality of suicidal poisoning attempts, survival and death cases showed a highly statistically significant difference regarding the HTTLPR, BDNFrs6265, BDNFrs10835210, and SSAT genotypes ($P < 0.001$) and the 5-HTTLPR SS genotype, BDNF rs6265 AG, and rs10835210. AC variants showed massive increases in the odds of fatal outcomes. **Conclusion:** Specific alleles and genotypes of 5-HTTLPR, BDNF, and SAT1 are significantly associated with suicidal poisoning and fatal outcomes, indicating that these genetic markers may be combined with clinical risk factors, including psychiatric history, type of poisoning, and severity grading, as diagnostic instruments for suicidal death.

Keywords: Suicidal poisoning, Genetic polymorphisms, 5-HTTLPR, BDNF, SAT1.

Introduction

Suicide attempt (SA) refers to engaging in potentially self-injurious behavior with at least some intent to die or with a non-fatal outcome (**Kaggwa et al., 2023**). It is a major public health problem globally, with more than 700,000 deaths each year, and it is one of the leading causes of death worldwide for adolescents. (**Barry et al., 2022; World Health Organization, 2023**).

Complex and heterogeneous risk factors for suicide attempts include environmental exposures, comorbid clinical conditions, and genetic variation (**Li et al., 2023**). Psychiatric disorders may interact with serotonin gene polymorphism, while results of previous studies investigated gene-by-stress interactions have been contradictory and inconsistent (**Harika et al., 2022**).

Serotonin is highly implicated in the regulation of emotional state and the execution of cognitive tasks, so the serotonin transporter gene (5-HTT) has become the perfect candidate when studying the effects of gene polymorphism on suicidal behavior (**López-Echeverri et al., 2023**). Two of the most commonly studied 5-HTT polymorphisms are an insertion/deletion polymorphism located 1.2 kb upstream of the transcription initiation site of the 5-HTT-linked polymorphic region (5-HTTLPR) and a variable number of tandem repeat polymorphisms located in the second intron of the gene (**Pungercic et al., 2006**). The short (S) allelic variant of 5-HTTLPR has repeatedly been associated with more violent and lethal suicide methods and lethality of suicide attempts (**Wannemueller et al., 2020**).

Brain-derived neurotrophic factor (BDNF) is a widely distributed neurotrophic factor in vivo that plays a very important role in brain functions and neuroprotection (**Misztak et al., 2020 & Icick et al., 2021**).

The BDNF is synthesized as a pre-proBDNF precursor. ProBDNF is proteolytically cleaved into the propeptide and the mature BDNF following the signal peptide's removal. (**Lu et al., 2005 & Popova and Naumenko, 2019**). BDNF and proBDNF have opposite functions, and their roles are mediated by tropomyosin-associated kinase B (Trk-b) receptors and nonspecific p75 receptor 2, respectively. Trk-b has been found to be involved in the neurobiology of suicide (**Erbay et al., 2021**).

One of the molecular systems that have been investigated for their roles in suicide and other mental disorders was the polyamine system, including agmatine, putrescine, spermidine, and spermine (**Fiori and Turecki, 2008**). The polyamines influence the properties of several neurotransmitter pathways, including the catecholamines, gamma amino-butyric acid, nitric oxide, and glutamate. Alterations in the levels of the polyamines and their metabolic enzymes have been observed in several psychiatric conditions, including suicide (**Fiori and Turecki, 2008**). The polyamine-related gene is spermidine/spermine N1-acetyltransferase (SAT1) that has been most strongly implicated in suicidal behavior. Low brain expression of the SAT1 gene, the rate-limiting enzyme involved in catabolism of polyamines that mediate the polyamine stress response (PSR), has been reported in depressed suicides. However, it is unknown whether this effect is associated with depression or with suicide and whether all or only specific isoforms are expressed by SAT1 (**Pantazatos et al., 2015**).

However, previous studies investigated the association of 5-HTTLPR, BDNF, and SAT1 polymorphisms with suicidal behavior; scarce studies investigated the role of these polymorphisms in diagnosis of self-poisoning and prediction of fatality among suicide cases. This study aimed to

investigate the distribution of genetic variants in 5-HTTLPR, BDNF rs6265, BDNF rs10835210, and SAT1 in the suicide attempters and the non-suicide poisoning cases to evaluate their potential as suicide diagnostic markers and predictors of lethality.

Patients and Methods

Study design, timing, and setting:

This observation analytical cross-sectional design with comparative approach was conducted at Benha Poisoning Treatment and Toxicology Research Unit (BPTTRU), Benha University Hospital, from August 2024 to July 2025.

Patients:

Acute poisoning adult cases admitted to BPTTRU during study period were enrolled as the suicidal group that included 220 patients, while non suicide patients also admitted to emergency department were enrolled as the non-suicidal group that included 240 patients.

A. Suicidal Group:

Diagnosis of suicide attempt was based on:

- History of suicide attempt alleged by the patient or accompanying relatives.
- Clinical presentation consistent with the allegation.
- Toxicological investigations confirming exposure to a potentially harmful substance.

B. Non suicidal Group:

Diagnosis of non suicide attempt was based on:

- Evidence of accidental poisoning obtained from the patient or accompanying relatives.
- Clinical presentation consistent with unintentional self-harm.
- Toxicological investigations confirming exposure to a potentially harmful substance.
- No history of suicidal behavior,
- No known psychiatric disorders.

Patients are selected based on certain inclusion criteria. Ages were above 18 years of both sexes. Positive toxicological signs to insure true poisoning. Acceptance to participate in the study and provision of informed consent.

Exclusion criteria for patients in this study were as follows: 1) Cases with uncertain manner of toxicity. 2) Incomplete clinical or laboratory data. 3) Refusal to participate.

Ethical considerations

All eligible participants received verbal and written explanations regarding the study objectives and procedures, and written informed consent was obtained prior to enrollment. Approval for the study was obtained from the Research Ethics Committee (REC), Faculty of Medicine, Benha University (MD 3-8-2024). All procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki.

Confidentiality of participants' personal and medical data was strictly maintained, and all collected data were used solely for scientific research purposes.

Methods:

A standardized data sheet used to record case information (age, sex, and other circumstances surrounding toxicity) obtained from the toxicology databases at the recommended for Egyptian populations.

Data collection

Information about the cases (age and sex), Circumstances of poisoning (type, route and time passed between drug intake and hospital arrival). Past history to any suicide attempts, Suicide attempts in family, history of psychiatric disorders and regular drug intake.

Clinical examination

General condition of the patient: vital signs, conscious state and general and systemic examination (pupil size, neurological, cardiovascular and respiratory examination) and psychiatric evaluation conducted by a qualified psychiatrist according to Diagnostic and Statistical Manual of Mental Disorders, Fourth edition (DSM-4) criteria.

Investigations

Renal function tests, liver function tests, arterial blood gases (ABG), electrolytes and specific laboratory investigations (pseudo-cholinesterase and Toxicological drug screening in urine) were recorded for all cases. Computed Tomography of the Brain (CT Brain), Chest X-ray (CXR), Electrocardiogram (ECG) and Echocardiography (Echo) were done only in needed cases

Hospitalization and outcome data recorded:

Data included need for admission (ICU admission or no ICU admission), and outcome (complete recovery, death, referral to other hospital or discharge).

Blood sampling and DNA extraction

Venous blood samples were collected from all participants under complete aseptic conditions in EDTA tube and centrifuged at 3000 rpm for 20 min at 4°C. DNA was extracted from leukocytes using a commercial DNA extraction kit according to manufacturer's instructions. DNA purity and concentration were assessed spectrophotometrically and stored at -20°C until PCR amplification.

PCR amplification

Genotyping of 5-HTTLPR, BDNF rs6265, BDNF rs10835210 and SAT1 polymorphisms was carried out using polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP) (Wu et al., 1999).

The primer sequences used in this study are presented shown in **Table (1)**.

Table (1): Primer sequences used for PCR amplification

Gene/Polymorphism	Primer	Sequence (5'→3')	Bases
HTTLPR	F	GGC GTT GCC GCT CTG AAT GC	20
	R	GAG GGA CTG AGC TGG ACA ACC AC	23
BDNF rs6265	F	CAA ACA TCC GAG GAC AAG GT	20
	R	AGA AGA GGA GGC TCC AAA GG	20
BDNF rs10835210	F	CCT GAC CAA GCA TGA GAG AT	20
	R	GAG GCT CCA AAG GCA CTT G	19
SAT1	F	CTT GAG CCC AGG AGT TCG AG	20
	R	TGG TGA CTA AAA GAA TAT GTG CTT GTG	207

5-HTTLPR: serotonin-transporter-linked promoter region), **BDNF**: Brain-derived neurotrophic factor; **SAT1**: Spermidine/Spermine N1-Acetyltransferase 1, *F*: Forward primer; *R*: Reverse primer; *A*: Adenine, *T*: Thymine, *C*: Cytosine, and *G*: Guanine.

PCR amplification was carried out using COSMO PCR RED Master Mix in a final reaction volume of 50 µL with 25 µL master mix, primers, template DNA, and nuclease-free water.

PCR cycling conditions included an initial denaturation at 95°C for 2 min, followed by 25–35 cycles of denaturation at 95°C for 15 s, annealing at primer-specific temperatures, and extension at 72°C for 10 s, with a final extension step at 72°C for 1 min.

Restriction fragment length polymorphism analysis

PCR products were digested using Fast-Digest Eco72I restriction enzyme (Thermo Fisher Scientific, USA) according to the manufacturer's instructions. Digestion reactions were incubated at 37°C followed by enzyme inactivation at 80°C for 10 min.

Digested products were separated by agarose gel electrophoresis and visualized under ultraviolet illumination.

Statistical analysis

Statistical analysis was performed using IBM SPSS statistics for Windows, version 28 (IBM Corp., Chicago, IL, USA, 2021). Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Genotype and allele frequencies were compared using the Pearson's chi-square test or Fisher's exact test when expected cell counts were less than 5. Odds ratios (ORs) and 95% confidence intervals (CIs) were

calculated. Associations between genotypes and suicide attempt status were evaluated using logistic regression, adjusted for potential confounding factors including psychiatric disorders, age, and sex. A p-value ≤ 0.05 was considered statistically significant.

Results

The studied non-suicidal and suicidal groups showed highly significant difference ($P=0.001$) regarding demographic, exposure and medical history recorded data. Age was highly significant ($P=0.001$), with the 18–30 group being most prevalent in the suicidal group (67.3%). Sex showed no significant difference ($P=0.062$). Therapeutic drugs and pesticides via oral route were the most common methods used among suicidal patients. 64.5% of patients arrived hospital with delay less than 2 hours compared to 44.6% of the non-suicidal group. The findings reflecting poisoning severity were significantly higher among suicidal cases. Abnormalities in vital signs, conscious state, and cardiovascular signs were significantly higher in the suicidal group ($P<0.001$). The suicidal group had significantly higher poisoning severity score ($P=0.001$), with 21.8% classified as "fatal poisoning" compared to 1.7% in the non-suicidal group. The tool and laboratory investigations showed highly significant differences ($P<0.001$) regarding the frequency of abnormal findings of ABG, liver and renal function tests, and ECG between two studied groups. No significant differences were reported regarding chest X-ray, serum potassium levels, plasma pseudo-choline esterase level, and random blood sugar ($P>0.05$) between two studied groups. As regards needing for ICU admission and poisoning outcome, there was no significant variation in ICU admission rates between the two groups ($P=0.329$). A highly significant difference in outcomes was observed ($P<0.001$), with a 21.8% mortality rate in the suicidal group versus 1.7% in the non-suicidal group as showed in **tables (2, 3)**.

Table (2): Patient's age, sex, type and route of poisoning and time of delay.

Variables	Non-Suicidal group (n=240)		Suicidal group (n=220)		Test of Significance $\chi^2 =$	P- value
	N	%	N	%		
Age (years)						
18-30	80	33.3	148	67.3	72.65	0.001**
30-40	94	39.2	34	15.9		
40-50	16	6.7	25	11.4		
50-60	41	17.1	8	3.6		
>60	9	3.8	4	1.8		
Sex						
Female	121	50.4	130	59.1	3.48	0.062
Male	119	49.6	90	40.9		
Type of poison						
Alcohol	11	4.5	0	0	51.32	0.001**
Gases	34	14.3	0	0		

Corrosive	44	18.3	7	3.2		
Hydrocarbon(kerosine)	21	8.7	3	1.4		
Pesticide	122	50.8	103	46.8		
Therapeutic	8	3.4	107	48.6		
Route						
Inhalation	22	9.2	2	0.9	16.94	0.001**
Injection	1	0.4	8	3.6		
intravenous	4	1.7	5	2.3		
Oral	213	88.8	205	93.2		
Time of delay (hours)						
<2	107	44.6	142	64.5	20.38	0.001**
2-4	63	26.3	45	20.5		
>4	70	29.2	33	15.0		

- Results are expressed in number (n) and percentage (%).
- X²: Chi Square used to compare between two groups
- *: significant at p<0.05, **: Highly significant at p<0.001 difference.

Table (3): Findings reflecting poisoning severity include clinical and investigation abnormalities, poisoning severity score, need for ICU admission and poor outcome.

Variables	Non-Suicidal group (n=240)		Suicidal group (n=220)		Test of Significance X ² =	P- value
	N	%	N	%		
Vital signs						
Normal	208	86.7	93	42.3	8.59	0.003**
Abnormal	32	13.3	127	57.7		
Conscious state						
Normal	196	81.7	154	70	100.02	< 0.001**
Abnormal	44	18.3	66	30		
Pupil size						
Normal	205	85.4	199	90.5	2.72	0.099
Abnormal	35	14.6	21	9.5		
Neurological examination						
Normal	240	100	197	89.5	26.4	< 0.001
Abnormal	0	0	23	10.5		
Cardiovascular examination						
Normal	240	100	175	79.5	54.41	< 0.001**
Abnormal	0	0	45	20.5		
Respiratory examination						
Normal	191	79.6	193	87.7	5.52	0.019
Abnormal	49	20.4	27	12.3		

Poisoning severity score						
None	29	12.1	2	0.9		
Minor	131	54.6	61	27.7	92.73	0.001**
Moderate	65	27.1	86	39.1		
Severe	11	4.6	23	10.5		
Fatal	4	1.7	48	21.8		
ABG						
Normal	226	94.2	157	71.4	42.82	< 0.001**
Abnormal	14	5.8	63	28.6		
Liver Function Tests						
Normal	237	98.8	181	82.3	37.56	<0.001**
Abnormal	3	1.3	39	17.7		
Renal Function Tests						
Normal	240	100	201	91.4	21.62	< 0.001**
Abnormal	0	0	19	8.6		
ECG						
Normal	219	91.3	160	72.7	27.14	< 0.001**
Abnormal	21	8.8	60	27.3		
Brain CT (n=25)						
Normal	16	64	0	0	----	----
Abnormal	9	36	0	0		
Chest x-ray (n=55)						
Normal	40	87	6	66.7	2.26	FEX _p =0.154
Abnormal	6	13	3	33.3		
Echo (n=35)						
Normal	0	0	12	34.3	-----	-----
Abnormal	0	0	23	65.7		
K (n=18)						
Normal	1	14.3	0	0	1.66	FEX _p =0.389
Abnormal	6	85.7	11	100		
Pseudo-choline esterase (n=60)						
Normal	4	10.5	3	13.6	0.13	FEX _p =0.700
Low	34	89.5	19	86.4		
RBS (n=7)						
Normal	1	33.3	0	0	1.56	FEX _p =0.429
High	2	66.7	4	100		
ICU admission						
No	132	55	111	50.5	0.95	0.329
Yes	108	45	109	49.5		
Outcome						
Complete Recovery	227	94.6	161	73.2	53.44	< 0.001**
Death	4	1.7	48	21.8		
Referral	2	0.8	2	0.9		
Discharge	7	2.9	9	4.1		

- **ABG:** arterial blood gases analysis, **ECG:** Electrocardiogram, **CT:** computed tomography, **RBS:** random blood sugar, **ICU:** intensive care unit.

- *Results are expressed in number (n) and percentage (%).*
- *X²: Chi Square used to compare between two groups*
- **: significant at $p < 0.05$, **: Highly significant at $p < 0.001$ difference.*
- *FEXp: p value of fisher exact correction.*

Comparing history of psychological disease, previous suicide attempts, and family history of suicide between the two groups showed highly significant differences ($P=0.001$), being exclusively or predominantly found in the suicidal group. As regard psychological evaluation by the qualified psychiatrist, 68.2% of the suicidal group had abnormal psychological evaluations, with major depressive disorder (36.7%) and bipolar disorder (28.0%) being the most common diagnoses as showed in **table (4)**.

Table (4): Evaluation of suicidal tendency among patients

Variables	Non-Suicidal group (n=240)		Suicidal group (n=220)		Test of Significance $X^2 =$	P- value
	N	%	N	%		
Previous attempt of suicide						
Yes	0	0	20	9.1	22.810	0.001**
No	240	100	200	90.9		
History of psychological disease						
Yes	0	0	98	44.5	135.851	0.001**
No	240	100	122	55.5		
Family history of suicide attempts						
Yes	0	0	20	9.1	22.810	0.001**
No	240	100	200	90.9		
Psychological evaluation						
Normal	240	100	70	31.8	242.815	<0.001**
Abnormal	0	0	150	68.2		
Psychological diseases (n=150)						
Major depression disorder			55	36.7		
Bipolar disorder			42	28.0		
Schizophrenia			20	13.3		
Borderline Personality			33	22.0		

- *Results are expressed in number (n) and percentage (%).*
- *X²: Chi Square used to compare between two groups*
- **: significant at $p < 0.05$, **: Highly significant at $p < 0.001$ difference.*

As regards genotyping results, genotypes and alleles of HTTLPR ($P=0.001$), BDNFr6265 ($P=0.005$), BDNFr10835210 ($P=0.001$), and SAT1 ($P=0.001$) showed significant differences between suicidal and non-suicidal groups. BDNFr6265 alleles frequencies are the only studied alleles that not showed significant ($p=0.447$) difference between groups. SS genotype (50%) and S alleles (65%) of HTTLPR gene, AG genotype (65%) of BDNFr6265 gene, AC genotype (60%) and C

alleles (55%) of BDNFr10835210 gene, D genotype (80%) and D alleles (82.5 %) of SAT1 gene are the most frequent in suicidal cases, as shown in **Table (5)**.

Table (5): The distribution of genotypes and alleles frequencies of 5-HTTLPR, BDNFr6262, BDNFr10835210, and SAT1 genes between the studied groups:

Variables	Non-Suicidal group (n=240)		Suicidal group (n=220)		Test of Significance X ² =	P- value
5-HTTLPR genotypes	N	%	N	%	48.421	0.001**
LL	96	40	44	20		
SL	96	40	66	30		
SS	48	20	110	50		
5-HTTLPR alleles					57.479	<0.001**
L allele	288	60	154	35		
S allele	192	40	286	65		
BDNFr6265 genotypes					10.698	0.005*
AA	72	30	44	20		
AG	120	50	143	65		
GG	48	20	33	15		
BDNFr6265 alleles					0.577	0.447
A allele	264	55	231	52.5		
G allele	216	45	209	47.5		
BDNFr10835210 genotypes					14.691	0.001**
AA	72	30	33	15		
AC	120	50	132	60		
CC	48	20	55	25		
BDNFr10835210 alleles					9.183	0.002*
A allele	264	55	198	45		
C allele	216	45	242	55		
SAT1 genotypes					198.403	0.001**
D	47	19.6	176	80		
DI	0	0	11	5		
I	193	80.4	33	15		
SAT1 alleles					363.51	<0.001**
D allele	94	19.58	363	82.5		
I allele	386	80.42	77	17.5		

- **5-HTTLPR:** serotonin-transporter-linked promoter region), **BDNF:** Brain-derived neurotrophic factor, **SAT1:** Spermidine/Spermine N1-Acetyltransferase 1.
- Results are expressed in number (n) and percentage (%).
- X²: Chi Square used to compare between two groups
- *: significant at p<0.05, **: Highly significant at p<0.001 difference.

The comparison between survivals and death cases after suicidal attempts showed highly statistically significant difference was reported regarding the HTTLPR, BDNFr6265, BDNFr10835210 and SSAT genotypes (P < 0.001**), as shown in **Table (6)**.

Table (6): Comparing the distribution of genotypes' frequencies between survivals and deaths after suicidal attempts:

Variables	Suicide survivals (n=172)		Suicide deaths (n=48)		Test of Significance X ² =	P- value
5-HTTLPR	N	%	N	%	47.326	<0.001**
LL	44	25.6	0	0		
SL	63	36.6	3	6.3		
SS	65	37.8	45	93.8		
BDNFr6265					29.342	<0.001**
AA	44	25.6	0	0		
AG	96	55.8	47	97.9		
GG	32	18.6	1	2.1		
BDNFr10835210					29.499	<0.001**
AA	33	19.2	0	0		
AC	87	50.6	45	93.8		
CC	52	30.2	3	6.3		
SAT1					9.797	0.007**
D	130	75.6	46	95.8		
DI	11	6.4	0	0		
I	31	18	2	4.2		

- **5-HTTLPR:** serotonin-transporter-linked promoter region), **BDNF:** Brain-derived neurotrophic factor, **SAT1:** Spermidine/Spermine N1-Acetyltransferase 1.
- Results are expressed in number (n) and percentage (%).
- X²: Chi Square used to compare between two groups
 - *: significant at $p < 0.05$, **: Highly significant at $p < 0.001$ difference.

Prediction of suicidal tendency among presented poisoning patients using regression analysis:

Firth's Method: The use of Firth's Penalized Likelihood was necessary to provide stable estimates due to the perfect separation (high mortality) in specific severity groups. As regards firth univariate logistic regression analysis of suicide tendency, history of psychological disease (OR = 386.76), suicide in the family (OR = 173.16), and abnormal psychological examinations (OR = 1026.88) show the strongest associations with suicide tendency. The HTTLPR SS genotype (OR = 4.94) and BDNFr6265 AG genotype (OR = 1.85) are significantly associated with increased odds of suicide. Regular drug intake (OR = 0.20) and the SAT1 "I" genotype (OR = 0.047) are associated with significantly lower odds of suicide in this model, as showed in **Table (7)**.

As regards multivariate firth logistic regression analysis of suicide tendency, history of psychological disease, family history of suicide and psychological abnormalities remain the most powerful independent predictors, maintaining extremely high odds ratios after adjustment. Younger age groups (30–40 and 50–60) are identified as independent risk factors, while a time of delay longer than 4 hours is associated with lower odds of being in the suicide group. 5-HTTLPR and BDNF markers remain highly significant; however, the SAT1 (I) genotype emerges as a strong independent protector of suicidal behavior, as showed in **table (8)**.

Table (7): Prediction of suicidal tendency among presented poisoned patients using univariate logistic regression analysis of patient characteristics and studied genotypes:

Variable		Odds Ratio (OR)	95% C.I. (Lower - Upper)	p-value
Age	18-30 (Ref)	1.00	-	-
	30-40	0.30	(0.19 – 0.46)	< 0.001*
	40-50	1.77	(0.92 – 3.42)	0.086
	50-60	0.19	(0.09 – 0.42)	< 0.001*
	>60	0.51	(0.16 – 1.65)	0.258
Sex	Female (Ref)	1.00	-	-
	Male	0.71	(0.49 – 1.02)	0.064
History of psychological disease	Yes	386.76	(23.48 – 6369.8)	< 0.001*
History Previous Attempts	Yes	49.18	(2.76 – 876.85)	0.008*
History Suicide in Family	Yes	173.16	(10.38 – 2889.5)	< 0.001*
Regular drug intake	Yes	0.20	(0.13 – 0.31)	< 0.001*
Psychological evaluation	Abnormal	1026.880	(62.545 -16859.601)	< 0.001*
5-HTTLPR	LL (Ref)	1.00	-	-
	SL	1.494	0.930 – 2.402	0.0971
	SS	4.941	3.022 – 8.078	< 0.001*
BDNFr6265	AA (Ref)	1.00	-	-
	AG	1.85	(1.27 – 2.69)	0.001*
	GG	0.71	(0.44 – 1.15)	0.166
BDNFr10835210	AA (Ref)	1.00	-	-
	AC	1.50	(1.03 – 2.17)	0.032*
	CC	1.33	(0.86 – 2.07)	0.202
SAT1	D (Ref)	1.00	-	-
	DI	6.190	0.316 - 121.226	0.2297
	I	0.047	0.029 - 0.076	< 0.001*

- *5-HTTLPR*: serotonin-transporter-linked promoter region), *BDNF*: Brain-derived neurotrophic factor, *SAT1*: Spermidine/Spermine N1-Acetyltransferase 1.
- OR: Odds Ratio, 95% C.I.: 95% Confidence Interval,
- *: significant at $p < 0.05$.

Table (8): prediction of suicidal tendency among presented poisoned patients using multivariate logistic regression analysis of patient characteristics and gene markers:

Variable		Odds Ratio (OR)	95% C.I. (Lower - Upper)	p-value
Age	18-30 (Ref)	1.00	-	-
	30-40	0.31	(0.11 – 0.92)	0.034*
	40-50	1.60	(0.38 – 6.67)	0.519
	50-60	0.12	(0.02 – 0.76)	0.025*
	>60	0.63	(0.05 – 7.49)	0.717
History of psychological disease	Yes	532122.0	451.153 – 6.27e8	0.0003*
History previous attempts	Yes	0.008	(0.000 – 1.02)	0.051

History Suicide in family	Yes	6296.4	(125.4 – 3.16e+05)	< 0.001*
Regular drug intake	Yes	0.65	(0.20 – 2.11)	0.474
Psychological evaluation	Abnormal	1026.880	(62.545 -16859.601)	< 0.001*
5-HTTLPR	LL (Ref)	1.00	-	-
	SL	0.014	0.001 – 0.207	0.0019*
	SS	< 0.001	0.000 – 0.002	0.0001*
BDNFrs6265	AA (Ref)	1.00	-	-
	AG	0.001	(6.7e-05 – 0.018)	< 0.001*
	GG	14.73	(0.77 – 282.54)	0.074
BDNFrs10835210	AA (Ref)	1.00	-	-
	AC	40.529	2.469 – 665.297	0.0095*
	CC	4.271	0.343 – 53.228	0.2593
SAT1	D (Ref)	1.00	-	-
	DI	99.77	(1.07 – 9326.9)	0.047*
	I	0.002	(1.5e-04 – 0.025)	< 0.001*

- **5-HTTLPR**: serotonin-transporter-linked promoter region), **BDNF**: Brain-derived neurotrophic factor, **SAT1**: Spermidine/Spermine N1-Acetyltransferase 1.
- **OR**: Odds Ratio, **95% C.I.**: 95% Confidence Interval,
- *****: significant at $p < 0.05$.

Prediction of fatality among presented poisoning patients using regression analysis

As regards fifth univariate logistic regression analysis of poor outcome (fatality). A "Fatal" grade of poisoning severity score (OR = 6615.00) and the 5-HTTLPR SS genotype (OR = 110.575) are the most dramatic univariate predictors of a poor outcome. BDNFrs6265 AG (OR = 78.530) and BDNFrs10835210 AC (OR = 63.087) show massive increases in the odds of death, as showed in **Table (9)**. The multivariate fifth logistic regression analysis of outcome (fatality), after adjusting for all factors, showed the poisoning severity score (severe OR = 235.0, Fatal OR = 485.0), psychological disorders (OR = 3.373) become the only statistically significant independent predictors of fatality. Psychiatric history and genetic markers, while significant individually, lose significance in this model, suggesting their influence on mortality is mediated through the clinical severity at presentation, as shown in **Table (10)**.

Table (9): prediction of poor outcome (fatality) among presented poisoned patients using univariate logistic regression analysis of basic parameters and gene markers:

Variable		Odds Ratio (OR)	95% C.I. (Lower - Upper)	p-value
Route	Inhalation (Ref)	1.00	-	-
	Injection	0.442	(0.068-2.859)	0.392
	IV	0.308	(0.057-1.655)	0.169
	Oral	0.741	(0.463-1.184)	0.210
Age	18-30 (Ref)	1.00	-	-
	30-40	1.901	0.840 - 4.306	0.1234
	40-50	1.350	0.501 - 3.639	0.5527
	50-60	1.558	0.315 - 7.710	0.5868

	>60	0.450	0.017 - 12.101	0.6345
History of psychological disease	Yes	4.535	2.247 - 9.149	< 0.001*
History Previous Attempts	Yes	4.221	1.641 - 10.855	0.0028*
History Suicide in Family	Yes	1.214	0.599 - 2.460	0.5913
Regular drug intake	Yes	0.615	0.230 - 1.646	0.3331
Psychological evaluation	Abnormal	4.819	1.873 - 12.397	0.0011*
Poisoning severity score	None (Ref)	1.000		
	Minor	0.16	(0.00 – 8.71)	0.372
	Moderate	0.21	(0.00 – 11.09)	0.439
	Severe	0.91	(0.02 – 50.36)	0.965
	Fatal	6615.00	(121.73 – 3.5e5)	<0.001*
5-HTTLPR	LL (Ref)	1.00	-	-
	SL	16.540	0.914 – 299.381	0.0576
	SS	110.575	6.436 – 1899.854	0.0012*
BDNFrs6265	AA (Ref)	1.00	-	-
	AG	78.530	4.598 – 1341.374	0.0026*
	GG	13.576	0.680 – 270.867	0.0877
BDNFrs10835210	AA (Ref)	1.00	-	-
	AC	63.087	3.631 – 1096.041	0.0044*
	CC	10.361	0.548 – 195.743	0.1189
SAT1	D (Ref)	1.00	-	-
	DI	0.226	0.037 – 1.386	0.1081
	I	0.126	0.033 – 0.481	0.0025*

- *5-HTTLPR: serotonin-transporter-linked promoter region), BDNF: Brain-derived neurotrophic factor, SAT1: Spermidine/Spermine N1-Acetyltransferase 1.*
- *OR: Odds Ratio, 95% C.I.: 95% Confidence Interval,*
- **: significant at $p < 0.05$.*

Table (10): prediction of poor outcome (fatality) among presented poisoned patients using multivariate logistic regression analysis of basic parameters and gene markers:

Variable		Odds Ratio (OR)	95% C.I. (Lower - Upper)	p-value
Time of Delay	<2 (Ref)	1.00	-	-
	2-4	1.363	0.132 – 14.019	0.7948
	>4	2.376	0.095 – 59.250	0.5980
Hist. Psych. Disease	Yes	3.503	0.833 – 14.739	0.0872
Hist. Prev. Attempts	Yes	0.613	0.020 – 18.738	0.7792
Psychological Examination	Abnormal	3.373	1.074 – 10.591	0.0372*
Severity score	None (Ref)	1.000		
	Minor	0.955	(0.0167 – 32.23)	0.767
	Moderate	0.974	(0.0134 – 50.32)	0.822
	Severe	235.000	2.154 – 25639.125	0.0226*
	Fatal	485.000	4.572 – 51444.247	0.0094*
5-HTTLPR	LL (Ref)	1.00	-	-
	SL	0.647	0.021 – 19.547	0.8021
	SS	10.890	0.384 – 309.003	0.1618

BDNFRs6265	AA (Ref)	1.00	-	-
	AG	7.018	0.064 – 770.458	0.4163
	GG	1.929	0.030 – 122.255	0.7562
BDNFRs10835210	AA (Ref)	1.00	-	-
	AC	1.597	0.018 – 145.075	0.8387
	CC	2.245	0.036 – 140.806	0.7017
SAT1	D (Ref)	1.00	-	-
	DI	0.953	0.033 – 27.593	0.9776
	I	0.704	0.141 – 3.511	0.6685

- *5-HTTLPR: serotonin-transporter-linked promoter region), BDNF: Brain-derived neurotrophic factor, SAT1: Spermidine/Spermine N1-Acetyltransferase 1.*
- OR: Odds Ratio, 95% C.I.: 95% Confidence Interval,
- *: significant at $p < 0.05$.

Discussion

The differentiation between suicidal poisoning cases and non-suicidal poisoning cases is essential due to important medical (psychological), and legal considerations (Sawad et al., 2022). Furthermore, in fatal poisoning cases, determining whether the death resulted from suicide or from other circumstances represents a significant medico-legal challenge (Collados-Ros et al., 2022).

Suicide and deliberate self-poisoning represent critical public health emergencies driven by a complex interplay of demographic, psychiatric, and biological vulnerabilities (Turecki et al., 2019 & Abou Chahla et al., 2023). The primary objective of this study was to investigate the distribution of specific genetic variants in 5-HTTLPR, BDNF, and SAT1 among suicide attempters compared to non-suicidal cases to evaluating their potential as diagnostic markers and predictors of fatality.

This observation analytical cross-sectional design with comparative approach was conducted at Benha Poisoning Treatment and Toxicology Research Unit (BPTTRU), Benha University Hospital, from August 2024 to July 2025. Suicide attempters admitted to the emergency department were enrolled as suicidal group, while non suicide patients also admitted to emergency department were enrolled as non-suicidal group. Genotyping of 5-HTTLPR, BDNF rs6265, BDNF rs10835210, and SAT1 polymorphisms was performed using PCR followed by RFLP analysis.

Studying the patients' demographic, exposure data indicates that suicidal poisoning is strongly associated with younger age. There was a highly significant difference in age distribution between the two studied groups as suicide attempters were predominantly younger (18–30 years) who represented 67.3% of suicidal patients. No significant sex difference observed suggesting that gender doesn't play a major role in suspicion of suicide. Although suicidal cases were mainly associated with therapeutic drugs (48.6%) and pesticides (46.8%), mainly via the oral route.

Alhassan et al. (2025) highlighted that suicidal ideation and attempts are particularly prevalent among young people in the Middle East, North Africa, Afghanistan, and Pakistan (MENAT) region. This is mainly attributed to higher impulsivity, psychosocial stress, and incomplete neurocognitive development, particularly in brain regions responsible for decision-making and

emotional regulation (**Nock et al., 2008 & Turecki and Brent, 2016**). Gender differences are less pronounced in suicidal attempts and self-poisoning, as both males and females are similarly exposed to psychosocial stressors and have comparable access to common toxic agents in many settings (**WHO, 2021**).

Sweilum and Kandeel (2016) study found that pesticides accounted for the highest proportion of suicidal poisoning cases in Menoufia Poison Control Center, highlighting their widespread availability and accessibility, particularly in rural areas. Similarly, **Eisa et al. (2024)** reported that pesticides were the most commonly used toxic agents in suicidal cases admitted to Assiut University Hospitals, with aluminum phosphide identified as the leading cause of fatal outcomes. In addition, **Elsayed et al. (2025)** demonstrated that therapeutic (prescription) drugs represent a major category involved in acute poisoning cases, alongside pesticides, indicating that both pharmaceutical agents and agricultural chemicals constitute the predominant means of self-poisoning in Egypt. This agreement may be largely attributed to their high availability, ease of access, and high toxicity, particularly in rural settings where pesticides are widely stored and pharmaceuticals are readily accessible, making them common agents in impulsive self-poisoning behaviors (**Zaher et al., 2021 & Kasemy et al., 2022 & Eisa et al., 2024**).

The abnormal clinical findings reported by our study were markedly more frequent among suicidal group, as vital signs, conscious state, neurological, and cardiovascular signs. The poisoning severity score was significantly higher among suicidal cases, with a greater proportion classified as severe or fatal, emphasizing the strong association between severity of poisoning and suicidal poisoning proofing true suicidal attempt. Additionally, abnormal ABG, liver function tests, and renal function tests results were significantly more frequent among suicidal cases. Cardiac and neurological assessments, including ECG, echocardiography, and brain CT, also showed significantly higher abnormalities in the suicidal group. These findings reflect greater systemic, metabolic, and organ dysfunction among suicide attempters compared with non-suicidal cases indicating more serious toxicity predisposing poor outcome. It may be explained by the fact that suicidal poisoning cases are usually associated with intentional ingestion of higher doses or more toxic substances, leading to more severe clinical outcomes compared to accidental exposures (**Geith et al., 2022**). The present findings support previous evidence reported by **Lombardo et al. (2025)**, in their analysis of acute intoxication of self-poisoning cases reported that patients following intentional overdose often present with altered mental status, abnormal heart rate, and other deviations in vital signs that are indicative of clinical instability and correlate with the severity of poisoning and need for medical intervention and ICU admission. The **KAmble et al. (2021)** study on biochemical abnormalities in suicide attempters has documented that acid base disturbances (such as abnormal pH on blood gas analysis) and significant derangements in serum electrolytes and biochemical markers (including albumin and other proteins) are common, which supports the notion of more pronounced systemic and metabolic dysfunction in those who attempt suicide.

About 50% of suicidal cases needed ICU admission. In addition, mortality rate was substantially greater in the suicidal group (21.8%) compared to only (1.7%) in the non-suicidal group. These findings indicate a poorer clinical prognosis among suicide attempters compared with non-suicidal group. It may be explained by the greater severity of intoxication and the intentional nature of exposure, which often involves larger toxic doses, delayed presentation to healthcare facilities,

multi-organ dysfunction, and serious cardiovascular or neurological complications (**Sobeeh et al., 2024**).

Evaluation of suicidal tendency in the presenting cases showed highly significant difference between two studied group. History of psychological disease was presented in 44.5% of suicidal patients. However, previous attempt of suicide and a family history of suicide were only found in 9.1% of them, this indicates that patient with psychological disease are at risk even if presented with no previous suicidal history. The psychological evaluation of cases revealed that 68.2% of the suicidal group had abnormal psychological findings as major depressive disorder (36.7%) and bipolar disorder (28.0%) being the most common diagnoses. Our findings are in agreement with previous literature demonstrating that major depressive disorder and bipolar disorder represent the most common psychiatric conditions associated with suicide attempts (**Vadukapuram et al., 2022**). In addition, **Arnone et al. (2024)** highlighted that mood disorders, particularly major depressive disorder and bipolar disorder, are major predictors of suicidal behavior.

Our study investigated the difference in frequencies of genotypes and alleles of 5-HTTLPR, BDNF rs6265, BDNF rs10835210, and SAT1 genes between the two studied groups. As regards 5-HTTLPR genotyping, the SS genotypes (50%) and the S allele (65%) were markedly more prevalent in suicidal cases suggesting a strong association between S variant and suicidal behavior. These findings are supported by previous results reported by **Sarmiento-Hernández et al. (2019)** that showed a significantly higher frequency of the SS genotype and the S allele in depressed adolescents who had attempted suicide compared with healthy controls, indicating that the SS genotype confers increased vulnerability to suicidal behavior. This association suggests that reduced serotonin transporter function thought to result from the SS genotype may underlie increased impulsivity and emotional dysregulation in individuals who attempt suicide. Additionally, **Boscutti et al. (2022)** reported that polymorphisms in the 5-HTTLPR gene with the short (S) allele often associated with greater negative emotionality and stress sensitivity in clinical and population samples. Although that, this finding is inconsistent with **Culverhouse et al. (2018)**, which reported no association between 5-HTTLPR polymorphism and suicidal behavior across different populations, suggesting that genetic risk is likely multifactorial.

Growing evidence supports the role of BDNF polymorphisms in suicidal attempts. **Sarchiapone et al. (2008)** and **Kang et al. (2020)** found that carriers of the rs6265 polymorphism were significantly more likely to report a history of suicide attempts in a depressed patient cohort, suggesting that functional variation in BDNF contributes to suicide risk. BDNF plays a key role in neural plasticity and stress response, and Met allele carriers have been associated with altered neurotrophic signaling that may predispose individuals to suicidal behavior under stress.

In our study, BDNF rs6265 (Val66Met) polymorphism showed statistically significant variation between the two groups with AG genotype being the most frequent (65%) in suicidal cases. However, the same gene AG was found in 50% in non-suicidal cases and no significant difference was found in A, G alleles frequency between two groups indicating that while genotype patterns differ, overall allele distribution doesn't significantly differ between groups. These results matched with **González-Castro et al. (2017)** that suggested no association between the BDNF gene rs6265 and suicidal behavior in the overall population. The study suggested that Val66Met polymorphism might increase suicidal behavior in certain ethnic subgroups. Similar findings were reported by

El-Kattan et al. (2018) that showed the BDNF polymorphism Val66Met was not correlated with higher rate of suicide although the increased plasma levels of BDNF detected in the samples taken from suicide attempters. The study explained it by compensatory mechanisms to overcome stress related to life and economic styles.

As regards to the BDNF rs10835210 polymorphism, the present study found AC genotype (60%) were significantly higher in suicidal cases compared to non-suicidal group indicating potential suicidal tendency linked to this polymorphism. While the frequency of C allele (55%) was higher in suicidal group. These findings are supported by **Icick et al. (2021)** which reported that BDNF rs10835210 clustered with serious suicide attempts and remained significantly associated with life time suicide attempts. However, **Guillot et al. (2023)** reported that the effects of BDNF rs10835210 were more pronounced among AA genotype carriers rather than AC carriers in stress, mood symptoms and self-harm/suicidal features.

The SAT1 genotyping in our study exhibited the widest difference between two studied groups. The D genotype was obviously predominant in suicidal patients (80%) compared to (19.6%) in non-suicidal group indicating a promising diagnostic tool in detection of suicidal commission. **Fiori and Turecki, (2010)** study indicated that polymorphisms in the SAT1 gene, such as promoter variants including rs6526342 and the SAT1 in/del locus, are associated with suicide risk and related psychiatric phenotypes in multiple populations. Emerging evidence also supports a role for the polyamine metabolic pathway, particularly SAT1 gene variation, in psychiatric phenotypes and severe outcomes. SAT1 is central to polyamine catabolism and has been repeatedly reported to show altered expression in the brains of individuals who have died by suicide, suggesting a link between dysregulated polyamine metabolism and suicidal behavior across psychiatric diagnoses (**Sarchiapone et al., 2008**).

Univariate logistic regression identified a profound association between psychiatric vulnerability and suicide attempts. The strongest clinical predictors were a history of psychiatric illness (OR = 386.76, $p < 0.001$), family history of suicide (OR = 173.16, $p < 0.001$), previous suicide attempts (OR = 49.18, $p = 0.008$) and diagnosed psychological disorders (OR= 1026.880, $p < 0.001$). As regards to studied polymorphisms, several genotypes were associated with increased risk, including the SS genotype of 5-HTTLPR gene (OR = 4.941, $p < 0.001$), AG genotype of BDNF rs6265 gene (OR = 1.85, $p = 0.001$), AC genotype of BDNF rs10835210 gene (OR = 1.50, $p = 0.032$), and DI genotype of SAT1 gene (OR = 6.190, $p = 0.2297$). Conversely, the I genotype of SAT1 exhibited a robust protective effect (OR = 0.04, $p < 0.001$). In the multivariate analysis, psychiatric, family history and psychological disorders remained the most potent independent predictors. Even after adjusting for clinical variables, the genetic contributions of 5-HTTLPR (SL and SS), BDNF (rs6265 AG and rs10835210 AC), and SAT1 (DI and I) remained significant ($p \leq 0.047$), confirming that genetic predisposition persists as an independent risk factor alongside clinical determinant. **Lizardi et al. (2009)** reviewed multiple family and clinical studies and concluded that family history of suicidal behavior significantly increases the risk of suicide attempts in relatives, likely through both genetic and psychosocial mechanisms that transcend individual diagnoses and environmental exposures. Genetic association studies also substantiate the idea that variants in neurobiologically relevant genes contribute independently to suicide attempt risk alongside clinical determinants. For example, in a large meta-analysis focused on the brain-derived neurotrophic factor (BDNF) Val66Met (rs6265) polymorphism, **Zai et al. (2012)**

reported that carriers of the Met allele and Met-carrying genotypes exhibited a modestly increased likelihood of suicide attempts across diverse populations, suggesting a genetic influence on suicidality that complements clinical stressors.

This study investigated the association between the frequency of each genotype and poisoning fatality among suicidal cases and revealed highly significant differences between suicidal survival and suicidal death. The SS genotype of 5-HTTLPR (93.8%), AG genotype of BDNF rs6265 (97.9%), AC genotype of BDNF rs10835210 (93.8%), and SAT1 deletion genotype (95.8%) were strongly associated with suicidal deaths, whereas alternative genotypes were more common in suicidal survival. This is in line with genome-wide association studies indicating that suicidal behavior is a polygenic trait influenced by multiple biological pathways related to stress response, impulsivity, and neuroplasticity (**Mullins et al., 2019**). In addition, previous evidence has suggested that variations in serotonin transporter and BDNF genes may be associated with more severe suicidal phenotypes and higher lethality of attempts (**Zai et al., 2012**). Similarly, alterations in SAT1 gene activity have been implicated in neurobiological stress regulation, which may further contribute to vulnerability to severe suicidal outcomes. However, large-scale studies have also highlighted that no single genetic variant is sufficient to predict suicidal death, and that the genetic contribution is modest and highly influenced by environmental and psychiatric factors, supporting a multifactorial model of suicidal behavior (**Turecki and Brent, 2016**).

Univariate logistic regression showed that the strongest predictors of poor outcome were psychiatric history (OR = 4.535), previous attempts (OR = 4.221), and psychological disorders (OR = 4.819, $p = 0.0011$). Fatal poisoning severity was the most extreme predictor of mortality (OR = 6615, $p < 0.001$). Genetic markers, including SS genotype of 5-HTTLPR gene, AG genotype of BDNF rs6265 gene, and AC genotype of BDNF rs10835210 gene, were similarly linked to worse outcomes, while SAT1 I served as a protective variant (OR = 0.126).

However, the multivariate logistic regression revealed a crucial finding: nearly all clinical, psychiatric, and genetic variables lost statistical significance after adjustment. The only independent predictor of poor outcome was fatal (OR = 485.0, $p = 0.0094$) and severe (OR = 235.0, $P = 0.0226$) PSS scores, and psychological disorders (OR = 3.373, $p = 0.0372$). This suggests that while genetic polymorphisms and psychiatric backgrounds are essential in driving the occurrence and initial severity of a suicide attempt, the final mortality outcome is primarily determined by the physiological severity at the time of presentation. These results indicate that other risk factors likely act indirectly, contributing to the "lethality" of the attempt, which then becomes the primary driver of clinical failure or success.

Geith et al. (2022) found that higher PSS categories were associated with worse clinical outcomes, including longer inpatient treatment and greater need for artificial ventilation, while lower Glasgow Coma Scale scores (an indicator of impaired consciousness) correlated with more fatal poisonings. Additionally, **Sharif et al. (2023)** developed prognostic models in acute xenobiotic poisonings identifying ICU admission and higher PSS as key predictors of poor prognosis and mortality, which aligns with our multivariate results showing ICU admission (OR=3.97) and abnormal imaging findings as independent severity determinants. Although time-to-presentation effects vary by population, adolescent poisoning research by **Spagnuolo Brunello et al. (2025b)** has also shown that delayed presentation can paradoxically associate with higher severity

outcomes in some contexts, indicating the complex interplay of exposure timing and clinical progression. **Kang et al. (2020)** demonstrated that carriers of the Val allele of the BDNF rs6265 polymorphism exhibited significantly higher suicide lethality scores than Met/Met homozygotes, suggesting that this genetic variant may play a role in determining how lethal an attempt is at the clinical level, even if it does not independently predict death when physiological severity is taken into account.

Also, extensive clinical research highlights that the physiological severity of the attempt itself, often operationalized through method lethality or poisoning severity, outweighs traditional psychiatric and genetic risk factors in predicting mortality. Research on methods and outcomes consistently shows that method choice and resultant severity are core determinants of whether an attempt results in fatality, with more lethal approaches (such as poisoning with highly toxic agents) linked to much higher risk of death than less lethal methods. Although most work in this area focuses on epidemiological risk stratification rather than molecular genetics, logistic models predicting fatal outcomes overwhelmingly demonstrate that acute severity markers such as intensive poisoning scores, degree of physiological compromise, or injury severity dominate predictive power once comorbid factors are statistically controlled (**Arunpongpaisal et al., 2024**).

Conclusion

The alleles and genotypes of 5-HTTLPR, BDNF rs6265, BDNF rs10835210, and SAT1 gene are associated with suicidal poisoning while SS genotype of 5-HTTLPR gene and D genotype of SAT1 gene were significantly associated with completed suicide (suicide death case) that suggest these genetic markers as diagnostic tool to suicidal death in association with other risk factors as history of psychiatric disorders, type of poisoning and grading of poisoning severity.

Limitations

This study was conducted at a single center, which may limit the generalizability of the findings to other populations and healthcare settings. The sample size, particularly within genotype subgroups, may have reduced the statistical power for detecting modest genetic effects. Only selected polymorphisms in 5-HTTLPR, BDNF rs6265, BDNF rs10835210, and SAT1 were examined, while other potentially relevant genetic and epigenetic factors were not assessed. Environmental, psychosocial, and treatment-related variables that may influence outcomes were not fully explored. In addition, the case–control design precludes causal inference, and the reliance on hospital-based recruitment may introduce selection bias by excluding individuals who did not present for medical care.

Recommendations

- Future research should include multicenter, larger-scale studies to improve generalizability and enhance statistical power for genetic associations.
- Expanding the genetic panel to include genome-wide and epigenetic markers may provide a more comprehensive understanding of suicide vulnerability and lethality.

- Prospective cohort designs are recommended to better clarify causal relationships between psychiatric history, genetic predisposition, and clinical outcomes.
- Integrating psychosocial, environmental, and treatment-related variables could further refine risk prediction models.
- Clinically, early risk stratification using poisoning severity scores alongside psychiatric assessment should be emphasized to guide rapid intervention and improve survival outcomes.

Sources of funding

No specific grant from public, private, or nonprofit funding organizations was received for this study.

Author contribution

Authors precipitated equally in the study.

Conflicts of interest

No conflicts of interest.

Acknowledgment

The authors are grateful for the support from the team of technicians and colleagues.

References

- Kaggwa, M. M.; Najjuka, S. M.; Favina, A.; Griffiths, M. D. and Mamun, M. A. (2023):** Suicidal behaviors and associated factors among medical students in Africa: a systematic review and meta-analysis. *J Affect Dis Report.* 11(3):100456.
- Barry, R.; Rehm, J.; de Oliveira, C.; Gozdyra, P.; Chen, S. and Kurdyak, P. (2022):** Rurality as a risk factor for attempted suicide and death by suicide in Ontario, Canada. *Can J Psychiatr.* 67(9):679–89.
- World Health Organization (2021):** Suicide worldwide in 2019: Global health estimates. Geneva: WHO. ISBN 9789240026643.
- World Health Organization (2023):** Suicide Worldwide in 2023: Global Health Estimates. Geneva: WHO.
- López-Echeverri, Y. P.; Cardona-Londoño, K. J.; Garcia-Aguirre, J. F. and Orrego-Cardozo, M. (2023):** Effects of serotonin transporter and receptor polymorphisms on depression. *Rev Colomb Psiquiatr (Engl Ed).* 52(2):130–138.
- Li, Q. S.; Shabalin, A. A.; DiBlasi, E.; Gopal, S.; Canuso, C. M.; FinnGen, et al. (2023):** Genome-wide association study meta-analysis of suicide death and suicidal behavior. *Mol Psychiatry.* 28(2):891–900.

Harika-Germaneau, G.; Lafay-Chebassier, C.; Langbour, N.; Thirioux, B.; Wassouf, I.; Noël, X.; et al. (2022): Preliminary evidence that the short allele of 5-HTTLPR moderates the association of psychiatric symptom severity on suicide attempt: the example in obsessive-compulsive disorder. *Front Psychiatry*. 13:770414.

Pungercic, G.; Videtic, A.; Pestotnik, A. Pajnic, I. Z.; Zupanc, T.; Balazic, J.; et al. (2006): Serotonin transporter gene promoter (5-HTTLPR) and intron 2 (VNTR) polymorphisms: A study on Slovenian population of suicide victims. *Psychiatr Genet*. 16(5):187–191.

Asberg, M. & Forslund, K. (2000): Neurobiological aspects of suicidal behaviour. *Int Rev Psychiatr*. 12(1):62–74.

Wannemueller, A., Forkmann, T., Glaesmer, H., et al. (2020): The role of the 5-HTTLPR polymorphism in acquired capability for suicide. *Suicide Life Threat Behav*, 50, 1121-1126.

Spreux-Varoquaux, O., Alvarez, J. C., Berlin, I., et al. (2001): Differential abnormalities in plasma 5-HIAA and platelet serotonin concentrations in violent suicide attempters relationships with impulsivity and depression. *Life Sci*. 69(6):647–57.

Seiler, N. & Raul, F. (2005): Polyamines and apoptosis. *J Cell Mol Med*. 9:623–642.

Misztak, P., Panczyszyn-Trzewik, P., Nowak, G., et al. (2020): Epigenetic marks and their relationship with BDNF in the brain of suicide victims. *PLoS ONE*. 15:e0239335.

Icick, R., Bloch, V., Prince, N., et al. (2021): Clustering suicidal phenotypes and genetic associations with brain-derived neurotrophic factor in patients with substance use disorders. *Transl Psychiatry*, 11, 72.

Lu, B., Pang, P. T., and Woo, N. H. (2005): The yin and yang of neurotrophin action. *Nat Rev Neurosci*. 6:603–614.

Popova, N. K. & Naumenko, V. S. (2019): Neuronal and behavioral plasticity: the role of serotonin and BDNF systems tandem. *Expert Opin Ther Targets*. 23:227–239.

Erbay, L. G., Karlidag, R., Oruc, M., et al. (2021): Association of BDNF / TrkB and NGF / TrkA Levels in Postmortem Brain with Major Depression and Suicide. *Psychiatr Danub*. 33:491–498.

Fiori, L. M. & Turecki, G. (2008): Implication of the polyamine system in mental disorders. *J Psychiatry Neurosci*. 33:102–110.

Gilad, G. M. & Gilad, V. H. (2003): Overview of the brain polyamine-stress-response: Regulation, development, and modulation by lithium and role in cell survival. *Cell Mol Neurobiol*. 23:637–649.

Tabor, C. W. & Tabor, H. (1984): Polyamines. *Annu Rev Biochem*. 53:749–790.

Fiori, L. M. & Turecki, G. (2010): Association of the SAT1 in/del polymorphism with suicide completion. *Am J Med Genet B Neuropsychiatr Genet*, 153b, 825-9.

Pantazatos, S. P., Kang, H. J. and Turecki, G. (2015): Targets of polyamine dysregulation in major depression and suicide. *Mol. Psychiatry*. 20(10):1169–1176.

Wu, Z., Nagano, I., Pozio, E., et al. (1999): Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) for the identification of *Trichinella* isolates. *Parasitology*. 118(2):211–218.

Thermo Fisher Scientific (2019): FastDigest Eco72I restriction enzyme product information. Thermo Fisher Scientific, USA.

Sawad, S., Mostafa, H., and Salem, H. (2022): Medicolegal aspects of suicidal attempts by drugs in cases admitted to Poison Control Center of Ain Shams University Hospitals (2019–2020). *Ain Shams Journal of Forensic Medicine and Clinical Toxicology*, 39(2), 12–20.

Abou Chahla, M. N., Khalil, M. I., Comai, S., et al. (2023): Biological factors underpinning suicidal behaviour: An update. *Brain Sciences*, 13(3), 505.

Collados-Ros, A., Torres-Sánchez, C., Pérez-Cárceles, M. D., et al. (2022): Suicidal behavior and its relationship with postmortem forensic toxicological findings. *Toxics*, 10(6), 319.

Turecki, G., Brent, D. A., Gunnell, D., et al. (2019): Suicide and suicide risk. *Nat Rev Dis Primer*. 5:1–22.

Eddleston, M., Buckley, N. A., Eyer, P., et al. (2008): Management of acute organophosphorus pesticide poisoning. *Lancet (London, England)*, 371(9612), 597–607.

Edition, F. (2013). Diagnostic and statistical manual of mental disorders. *Am Psychiatric Assoc*, 21(21), 591-643.

Geith, S., Lumpe, M., Schurr, J., et al. (2022): Characteristics and predictive factors of severe or fatal suicide outcome in patients hospitalized due to deliberate self-poisoning. *PLOS ONE*, 17(11), e0276000.

Sobeeh, F. G., Eldayem, Y. B. A., and Khalifa, H. K. (2024): Validity of different scoring systems in prediction of intensive care unit admission and mortality in acute organophosphate poisoning. *Toxicology research*, 13(4), tfae107.

Alhassan, M. A., Alarabi, M. A., Albalawi, W. M., et al. (2025): Prevalence and risk factors of suicidal ideation and suicide attempts among young people in the MENAT region: a systematic review and meta-analysis. *BMC Psychiatry*, 25, 1149.

Eisa, G., Ebrahim, N. E., Abdel-Hady, R. H., et al. (2024): Evaluation of suicidal poisoning cases admitted to emergency units of Assiut University Hospitals, Egypt. *Zagazig Journal of Forensic Medicine and Toxicology*, 22(1), 127–146.

Elsayed, M. A., Osman, H., and Ahmed, M. G. (2025): Features, Pattern and Outcome of Acute Intoxicated Patients Presented to Zagazig Poison Control Unit, Egypt during 2022. *Ain Shams Journal of Forensic Medicine and Clinical Toxicology*, 44(1), 12-21.

Nock, M. K., Borges, G., Bromet, E. J., et al. (2008): Suicide and suicidal behavior. *Epidemiologic reviews*, 30(1), 133–154.

Sweilum, O., & Kandeel, F. (2016): Pattern of suicidal poisoning cases admitted to Menoufia Poison Control Center (MPCC) over two years (2013–2014). *Ain Shams Journal of Forensic Medicine and Clinical Toxicology*, 26(1), 53–60.

Turecki, G. & Brent, D. A. (2016): Suicide and suicidal behavior. *Lancet*. 387(10024):1227–1239.

Zaher, J., Hafez, M., Sarhan, M., et al. (2021): Impact of type of organophosphate insecticide compounds on outcome of acute poisoning. *Minia Journal of Medical Research*, 32(2), 99-103.

Kasemy, Z. A., Sharif, A. F., Amin, S. A., et al. (2022): Trend and epidemiology of suicide attempts by self-poisoning among Egyptians. *PLoS One*, 17, e0270026.

Lombardo, M., Garberi, R., Rezoagli, E., et al. (2025): Acute Intoxications Admitted to the Intensive Care Unit: A Retrospective Cohort Study. *Journal of toxicology*, 2025, 8823675-8823690.

KAmBle, A., VAtte, V. R., RAo, B. R., et al. (2021): Screening of Biochemical Abnormalities in Suicide Attempters Irrespective of Psychiatric Diagnosis: A Cross-sectional Study. *Journal of Clinical & Diagnostic Research*, 15.

Suominen, K., Isometsä, E., Ostamo, A. et al. (2004): Level of suicidal intent predicts overall mortality and suicide after attempted suicide: a 12-year follow-up study. *BMC Psychiatry*, 4, 11.

Reisinger, A.C., Schneider, N., Schreiber, N., et al. (2024): Critical care management of acute intoxications, dynamics and changes over time: a cohort study. *Intern Emerg Med* 19, 2015–2024.

Hu, K., Nguyen, T.-D., Borges, K., et al. (2025): Risk factors, impact, and healthcare use related to initial suicide attempts: comprehensive analysis of Swedish population. *BMJ Medicine*, 4, e001129.

Arnone, D., Karmegam, S. R., Östlundh, L., et al.. (2024): Risk of suicidal behavior in patients with major depression and bipolar disorder - A systematic review and meta-analysis of registry-based studies. *Neuroscience and biobehavioral reviews*, 159, 105594.

Favril, L., Yu, R., Hawton, K., et al. (2020): Risk factors for self-harm in prison: a systematic review and meta-analysis. *The lancet. Psychiatry*, 7(8), 682–691.

Sarmiento-Hernández, E. I., Ulloa-Flores, R. E., Camarena-Medellín, B., et al. (2019): Association between 5-HTTLPR polymorphism, suicide attempt and comorbidity in Mexican adolescents with major depressive disorder. *Actas Espanolas de Psiquiatria*. 47(1):1–6.

Vadukapuram, R., Trivedi, C., Mansuri, Z., et al. (2022): Common Methods of Suicide and Self-Inflicted Poisoning/Injury by Individuals With Major Depressive Disorder and Bipolar Disorder: A Nationwide Inpatient Sample Analysis. The primary care companion for CNS disorders, 24(4), 21m03159.

Sarchiapone, M., Carli, V., Roy, A., et al. (2008): Association of polymorphism (Val66Met) of brain-derived neurotrophic factor with suicide attempts in depressed patients. Neuropsychobiology, 57, 139-45.

Kang, S. G., Lee, J. H., Lee, K., et al. (2020): The rs6265 Polymorphism of the BDNF Gene Is Related to Higher-Lethality Suicide Attempts in the Korean Population. Psychiatry Investig, 17 (5), 417-423.

Culverhouse, R. C., Saccone, N. L., Horton, A. C., et al. (2018): Collaborative meta-analysis finds no evidence of a strong interaction between stress and 5-HTTLPR genotype contributing to the development of depression. Molecular psychiatry, 23(1), 133–142.

Boscutti, A., Pigoni, A., Delvecchio, G., et al. (2022): The Influence of 5-HTTLPR, BDNF Rs6265 and COMT Rs4680 Polymorphisms on Impulsivity in Bipolar Disorder: The Role of Gender. Genes (Basel), 13.

Eisen, R. B., Perera, S., Banfield, L., et al. (2015): Association between BDNF levels and suicidal behaviour: A systematic review and meta-analysis. Systematic Reviews, 4, 187.

El-Kattan, M. A., Helaly, A. M. N. Z., Lotfy, Z., et al. (2018): Plasma brain-derived neurotrophic factor level and its gene polymorphism in toxic suicidal behavior. Mansoura Journal of Forensic Medicine and Clinical Toxicology, 26(1), 53–63.

González-Castro, T. B., Salas-Magaña, M., Juárez-Rojop, I. E., et al. (2017): Exploring the association between BDNF Val66Met polymorphism and suicidal behavior: Meta-analysis and systematic review. Journal of psychiatric research, 94, 208–217.

Guillot, C. R., Kelly, M. E., Phillips, N. B., et al. (2023): BDNF and stress/mood-related interactions on emotional disorder symptoms, executive functioning, and deliberate self-harm. Journal of Psychiatric Research, 163, 195–201.

Sarchiapone, M., Carli, V., Roy, A., et al. (2008): Association of polymorphism (Val66Met) of brain-derived neurotrophic factor with suicide attempts in depressed patients. Neuropsychobiology, 57, 139-45.

Zai, C. C., Manchia, M., De Luca, V., et al. (2012): The brain-derived neurotrophic factor gene in suicidal behaviour: a meta-analysis. International Journal of Neuropsychopharmacology, 15, 1037-1042.

Mullins, N., Bigdeli, T. B., Webber, C., et al. (2019): Genome-wide association study of suicide attempts in psychiatric disorders. American Journal of Psychiatry, 176(8), 609–617.

Lizardi, D., Sher, L., Sullivan, G. M., et al. (2009): Association between familial suicidal behavior and frequency of attempts among depressed suicide attempters. *Acta Psychiatr Scand*, 119, 406-10.

Nakagawa, M., Kawanishi, C., Yamada, T., et al. (2009): Characteristics of suicide attempters with family history of suicide attempt: a retrospective chart review. *BMC Psychiatry*, 9, 32.

Geith, S., Lumpe, M., Schurr, J., et al. (2022): Characteristics and predictive factors of severe or fatal suicide outcome in patients hospitalized due to deliberate self-poisoning. *PLOS ONE*, 17(11), e0276000.

Sharif, A. F., Kasemy, Z. A., Alshabibi, R. A., et al. (2023): Prognostic factors in acute poisoning with central nervous system xenobiotics: development of a nomogram predicting risk of intensive care unit admission. *Toxicol Res (Camb)*, 12, 62-75.

Spagnuolo Brunello, G. C., Frizon Alfieri, D., Molino Guidoni, C. et al. (2025b): Factors Associated With the Severity of Suicide Attempts by Poisoning in Adolescents. *Rev Colomb Psiquiatr (Engl Ed)*, 54, 446-453.

Kang, S. G., Lee, J. H., Lee, K., et al. (2020): The rs6265 Polymorphism of the BDNF Gene Is Related to Higher-Lethality Suicide Attempts in the Korean Population. *Psychiatry Investig*, 17 (5), 417-423.

Arunpongpaisal, S., Assanangkornchai, S. and Chongsuvivatwong, V. (2024): Developing a risk prediction model for death at first suicide attempt—Identifying risk factors from Thailand's national suicide surveillance system data. *PLOS ONE*, 19, e0297904.

