CHILD MALTREATMENT: ADOLESCENTS' PSYCHIATRIC SEQUELS IN THE LIGHT OF OXYTOCIN RECEPTOR GENE SNP RS2254298 AND GLOBAL DNA METHYLATION: A CASE CONTROL STUDY

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ABSTRACT

Background: For decades, the negative impact of childhood adversity and maltreatment has been limited to the immediate harm and injuries. Recently, several studies connected child maltreatment with further long-term consequences in childhood, adolescents and adulthood among them psychiatric symptoms and disorders. **Objectives:** We aimed at determining the association between psychiatric consequences and different types of child maltreatment among adolescents between 12-18 years, exploring the role of Oxytocin Receptor Gene Polymorphism (rs2254298) in moderating the relation between different types of child maltreatment and psychiatric consequences and to examine the relation between childhood abuse and global DNA methylation. **Methodology:** A case-control study was carried out on 90 children aged between 12- 18 years divided equally into two groups; cases suffering from psychiatric illness and attending child and adolescent psychiatric outpatient clinics at Al-Hadara University Hospital in Alexandria, Egypt and controls recruited from different outpatient clinics at Alexandria university hospitals. **Results:** A significant difference was detected between cases and controls regarding four types of child maltreatment; physical abuse, sexual abuse and emotional abuse and neglect. Moreover, a significant positive correlation was detected between these four maltreatment types and depressive symptoms detected by children depression inventory (CDI) and total scale of child behavior checklist (CBCL). However, no significant interaction between OXTR gene SNP rs2254298 and child maltreatment in the prediction of depressive symptoms and total scale of CDI and CBCL, respectively. On the other hand, a significant negative correlation was detected between the means of global DNA methylation and three types of child maltreatment: physical abuse and emotional abuse and neglect.

Key words: child abuse, maltreatment, psychiatric, epigenetic, (OXTR), DNA methylation.

INTRODUCTION

Child maltreatment, abuse, neglect, and victimization are interchangeable terms that refer to a serious global violation of human rights of children. In addition to immediate medical and psychological trauma, several chronic long-term consequences of experiencing child maltreatment may also occur. Among these dire consequences are psychiatric disorders as poor academic performance, low self-esteem, cognitive deficits, depression, anxiety, anger, psychological distress, anti-social behavior, relationship problems, drug and alcohol abuse and violence **(Giardino, 2010; Seltzer et al.,**

2014; Abdellah and Ali, 2018; Elkholy et al., 2018).

Although some children experience long-term sequelae of maltreatment and neglect, others exhibit remarkable resilience and appear relatively unscarred. The individuality role is even evident upon children, given similar conditions as siblings and identical twins, but they acquire different consequences **(Masten, 2001; Zaghloul et al., 2017)**.

Accumulating evidence suggest resilience as dynamic process without a single factor behind it however it is a multi-domain resilience. Among the theories of its explanation is the three-hit model. It considers the interaction of personal and genetic factors with environmental factors as early life experiences resulting in altered endocrine regulations and different changes during brain development **(Daskalakis et al., 2013)**.

At the same time, several genetic polymorphisms have been identified to affect vulnerability to the development of psychopathology after early exposure to child maltreatment. Among them different components of the hypothalamic pituitary adrenal (HPA) axis as human corticotropin-releasing hormone receptor gene (CRHR), the serotonin system as polymorphism in the serotonin-transporter-linked promoter region (5HTTLPR) as well as the brain-derived neurotrophic factor gene (BDNF) and the oxytocin receptor gene (OXTR) **(Gillespie et al., 2009; Montag et al., 2011; Lucas-Thompson and Holman, 2013; Webb et al., 2016)**.

Beside its known role in parturition and milk production, oxytocin (OXT) is also involved in shaping of individual responses to different stresses. Its action is mediated by a receptor that is encoded by the oxytocin receptor gene (OXTR) **(Hostinar et al., 2014)**. There are about 30 SNPs in the OXTR region; one of them is re2254298 which is in the intron number three of OXTR gene. Information from different populations suggests an interaction between the SNP rs2254298 and the quality of experiences during early childhood. This may result in variable possibility to develop psychiatric problems such as anxiety or depression with big alterations depending on racial background **(Brüne, 2012)**.

Beside gene polymorphisms, other types of gene–environment interactions in the form of different epigenetic mechanisms are also involved and may be attributed to a change in gene expression by silencing or activating genes. This alteration in phenotype without a change in genotype may affect body ability to adapt itself to the environment and adversely affect health **(Gershon and High, 2015)**.

Epigenetic changes may be initiated and sustained through DNA methylation, histone modification and regulation by small or large non-coding RNA (ncRNA). In DNA methylation, adding a group of methyl to the chromatin structure around a gene often modifies its function. Methylation of cytosine bases occurs in gene promoters and at CpG sites, where cytosine nucleotide is followed by a guanine nucleotide in the linear arrangement of bases alongside its 5' → 3' direction. This methylation usually results in gene silencing, whereas loss of methylation is associated with activation of that gene **(Suderman et al., 2014; Gershon and High, 2015)**. The correct regulation of gene activity is disturbed through abnormal DNA methylation, so even genes that don't carry any polymorphisms that may lead to disease, will be turned risky as they are not expressed at the proper level in the right type of cell at the correct time of the cell cycle **(Feinberg, 2010)**.

Although epigenetic change is regular and naturally occurring, it can also be influenced by several factors including age, environmental factors, and diseases. It is believed that child abuse can leave marks, not only physically and emotionally, but also epigenetic marks that

influence the gene **(Gershon and High, 2015)**. However, results of the gene-environmental interaction studies demonstrate pleiotropy in the genetics of stress-related psychiatric disorders. It is interesting to study this area of research among the Egyptian population. The determination of the mediating role of genetic and epigenetic influences on the negative health consequences of child maltreatment may give an opportunity to establish new prevention and intervention policies reducing the load linked to this universal problem.

So, the present study aimed to determine the association concerning psychiatric consequences and different types of child maltreatment among adolescents between 12-18 years, to explore the role of Oxytocin Receptor Gene Polymorphism (rs2254298) in moderating the relation between different types of child maltreatment and psychiatric consequences and to examine the relation between childhood abuse and global DNA methylation.

METHODS

Ethical statement

Written informed consent was obtained from caregivers or legal authority of the study participants after explaining the nature and objectives of the procedure. At the same time, oral assent was obtained from the adolescents themselves for their own participation. All children in the present study participated on a voluntarily basis and were not paid for their participation. At the same time, they were provided with researcher contact information. Confidentiality of collected data was preserved. Approval for this study procedure was given by the Ethics Committee of Alexandria University. (IRB NO: 00007555, FWA NO: 00018699).

Study participants

A case-control study was performed on 90 children aged between 12- 18 years divided into two groups. Cases included forty-five children (31 males, 14 females), suffering from psychiatric illness and attending child and adolescent psychiatric outpatient clinics at Al-Hadara University Hospital in Alexandria, Egypt. Controls which included another 45 children (24 males, 21 females). Children in control group were enrolled from different outpatient clinics at Alexandria university hospitals.

Children having developmental abnormalities or severe physical conditions such as malignancies or neurological disease were excluded from the present work. Among the case group, children with psychiatric illnesses that result in severe cognitive damage as moderate, severe and profound intellectual disorders and psychotic disorders were also excluded.

The following items were fulfilled to all research subjects in the study:

1. Demographic data:

Self-reported information on demographics including age, sex, biosocial data, education level and school performance were obtained.

2. History taking:

- Guardians were interviewed and asked about:

- History of present illness: symptoms, onset, and time lapse since starting treatment.
- Psychological insult during childhood: as death of one or both parents or separation of parents.
- Medical history: for any previous diseases, injuries and operative procedures with special emphasis on repeated injuries, its causes and mechanism.
- Parental consanguinity.

- History of psychiatric illness and psychiatric evaluation was done by the psychiatric residents who assessed the children according to Kiddie-SADS-Present and lifetime for diagnosis of psychiatric disorders. It is a semi-structured questionnaire that combines dimensional and categorical assessment approaches to diagnose existing and previous occurrences of psychiatric problems in children and adolescents following diagnostic and

statistical manual of mental disorders, fourth edition, text revision (DSM-IV-TR) **(Kaufman et al., 1997)**.

3. Maltreatment history:

- Evaluation of the severity of five categories of childhood trauma including; physical, emotional, and sexual abuse, and emotional and physical neglect, were performed by using the Arabic version of the short form of Childhood Trauma Questionnaire (CTQ-SF) **(Bernstein et al., 2003)**.

- The CTQ cut-off scores were used to express the severity of child maltreatment and were categorized into; none, low to moderate, moderate to severe and severe to extreme.

- As regard cut-off scores for low to moderate severity were **(Webb et al., 2016)** for physical abuse and physical neglect **(Montag et al., 2011)**, for sexual abuse **(Hostinar et al., 2014)**, for emotional abuse and **(Brüne, 2012)** for emotional neglect. However, moderate to severe cut-off scores were **(Feinberg, 2010)**; for emotional abuse,**(Brüne, 2012)** for physical abuse and physical neglect **(Webb et al., 2016)**, for sexual abuse and **(Bernstein et al., 2003)** for emotional neglect **(Mansour et al., 2010)**.

- Supplementary information was taken to determine age of onset, duration and frequency of maltreatment.

4. Psychometric assessment:

- All subjects were requested to complete the Arabic version of Kovac's Children's Depression Inventory (ACDI) **(Kovacs, 1985)**.

- This is a self-reported questionnaire and one of the best extensively used screening tool for evaluating the existence and severity of depressive symptoms during childhood and adolescence. Its Arabic version has proven worthy reliability and validity and can be finished by children and adolescents in about five to ten minutes **(Ghareeb and Beshai, 1989; El-Defrawi, 1997)**.

- ACDI contains 27 points measuring symptoms like depressed mood. Each point contains three statements ordered in increasing severity from 0 to 2. Scores were summited to give a total depression score that ranges from 0 to 54. A greater CDI score means a greater depressive condition.

- In the present study the cutoff score was set at 13 as recommended by Kovacs.

- At the same time, the parents were given the Arabic version of Child Behavior Checklist (CBCL) to fill or administered by an interviewer for those who cannot read **(Khater et al., 2005; Seedhouse et al., 2009)**.

- CBCL is designed to obtain standardized parent's or other primary caregiver's report of children's problems and competencies.

- In the current study, an Arabic version which demonstrated good reliability and validity was used with Egyptian parents. It includes 113 items through which several subareas can be measured by a three-point likert- type scale.

- In addition, the CBCL had three broad-band scores: internalizing, externalizing and total Problems. The internalizing scale consisted of items from the withdrawn, somatic complaints and anxious / depressed scales. The externalizing scale consisted of items from the delinquent behavior and aggressive behavior domains. The total problems scale included all the items, except for two items (allergies and asthma).

Genotyping:

In the present work, two milliliters (2 ml) of whole blood was collected in EDTA tubes from all research participants who completed the previous assessment and gave informed consent. Upon collection, blood samples were immediately kept in refrigerator 4-8 °C for less than two weeks before DNA extraction.

DNA extraction from whole blood was done using QIAamp blood DNA isolation kit **(QIAGEN, 2016)**. DNA was kept at −20 °C prior to further analysis.

The oxytocin Receptor Gene Polymorphism (rs2254298) was genotyped

for individual alleles using a Taq Man SNP rs2254298 assay **(ThermoFisher scientific)** from Applied Biosystems with TaqMan universal Master Mix II **(ThermoFisher scientific, 2009)** and the analysis of the data was done depending on real time PCR instrument.

Epigenetics- DNA methylation analysis:

Global DNA methylation in blood samples of study contributors was assessed by quantifying 5-methylcytosine (5-mC) using MethylFlash methylated DNA quantification colorimetric kit **(Epigentek, 2016)**.

In this assay, DNA is bound to strip wells that are specially treated to have a high affinity to DNA. The methylated portion of DNA is discovered using capture and detection antibodies (anti-5-mC monoclonal antibodies) that are sensitive and specific for 5-mC. The 5mC amount was measured colorimetrically by evaluating the absorbance in a microplate spectrophotometer. The amount of methylated DNA is comparative to the optic density intensity measured.

Statistical analysis

Data of the present work were collected and fed to a personal computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results was judged at the 5% level. The used tests were Chi-square test for categorical variables, to compare between different groups, Monte Carlo correction for chi-square when more than 20% of the cells have expected count less than 5, Student t-test for normally distributed variables, to compare the two studied groups, Mann Whitney test for abnormally distributed quantitative variables, to compare between two studied groups, F-test (ANOVA) for quantitative normally distributed variables, to compare between more than two groups, and Post Hoc test (LSD) for pair wise comparisons, Pearson coefficient to correlate between two normally distributed quantitative variables and Regression to identify the most independent/ affecting element for children depression inventory and CBCL total scale. **(Kotz et al., 2006; Kirkpatrick and Feeney, 2013)**

RESULTS

I. Demographic data:

- **Age:**

More than half (51.1%) of the cases existed in the age group (12 -14 years). This is followed in a descending manner by the age group of 16-18 years (28.9%), then nine cases in the age group of 14-16 years (20%). As regard the controls; (44.4%) of children were in the age group between (12-14 years) followed by (31.1%) in the age group (16-18 years) and eleven children (24.4%) in the age group (14-16 years). The mean age for the cases was (14.24 ± 2.01 years) and for the controls (14.98 ± 2.16 years) with a non-significant difference between both groups where p = 0.099. (Table 1)

- **Sex:**

In the present study, more than two thirds of the cases (68.9%) were males while (31.1%) were females. On the other hand, 24 children (53.3%) of the controls were males and 21 (46.7%) were females. Table (1) shows a non-significant difference between the two groups concerning sex where p = 0.130.

- **Residence:**

As regard residence, (84.4%) of the cases were from Alexandria, (13.3%) came from Albehira and only one child (2.2%) was living in Sohag. On the other hand, in the control group, the highest percentages (64.4%) were from Alexandria, (26.7%) were from Albehira and four children (8.9%) were from Marsa-Matrouh. (Table 1)

- **Level of education**:

The highest percentages of cases (44.4%) were in primary school, while

(13.3%) of cases didn't continue their primary school. On the other hand, (51.1%) of the controls were in secondary school and only (4.4%) of them didn't continue their primary school education. The difference between the level of education of the two groups was statistically significant where $^{MC}p= <0.001$. (Table 1)

- **School performance:**

A statistical significant difference was perceived between the two groups regarding school performance, where (44.4%) and (28.9%) of the cases successively failed and had weak school performance respectively. However, (44.4%) of the controls achieved good grades ($p <0.001$). (Table 1)

- **Habits:**

Table (1) shows that more than two thirds of the cases (68.9%) had no special habits, (28.9%) of the cases were smokers and only (2.2%) reported chalk dust inhalation. On the other hand, the majority of the controls (88.9%) had no special habits and only (11.1%) of them were smokers. The difference between habits of the two groups was found to be statistically significant where $^{MC}p=0.040$.

II. Biosocial data:

- **Data of the family:**

In the present study, a non-significant difference was noted between cases and controls regarding consanguinity, number of family members of the participated child where p was 0.533 and 0.896 respectively. Regarding the birth order, although the first child was the commonest in the cases group (53.3%), a non-significant difference was present between cases and controls where p= 0.580.

However, a significant difference was observed between both groups regarding death of one or both parents and state of relationship of parents where $^{MC}p = 0.012$ and 0.014 respectively. 44 children, in the cases group, had living parents. While only one child was adopted. On the contrary, (84.4%) of the controls had living parents and (15.6%) of them had either dead fathers or mothers.

On the other hand, less than two thirds of children in the cases group (64.4%) had married parents compared to (86.7%) in the control group.

- **Data of the father:**

In the present work, the highest percentage of fathers (65.9%) and (73.3%) of the cases and controls respectively were in the age group 35-<50 years.

As regard fathers' education, less than one quarter (22.7%) of the fathers, of the cases were university-educated whereas (20.5%) did not continue their primary school education. On the other hand, fathers who completed their university education represented (39%) in the control group and only (7.3%) did not continue their primary school education. A significant difference was observed between both groups where $^{MC}p=0.008$.

On analysis of the data of research participants, (40.9%) of fathers belonging to the cases were workers. However, (46.3%) of children in the control group belonged to employed fathers. The difference between both groups regarding father's occupation was found to be statistically significant where $^{MC}p= 0.014$.

Moreover, it was found that (70.3%) and (61%) of the cases and controls respectively belonged to smoker fathers, while (6.8%) of the cases belonged to drug abusing fathers. However, only one father of a child in the control group (2.4%) was drug abuser. The difference between both groups regarding father's habits was found to be non-significant where $^{MC}p= 0.268$.

- **Data of the mother:**

In the current work, mothers of children in the cases group (mean age = 38.93 ± 7.44 years) were significantly younger than mothers of children in the control group (mean age =45.90 ± 4.67 tears) where p was <0.001.

As regard education of the mother, more than one quarter (27.3%) of the cases belonged to mothers who finished preparatory school. On the other hand,

(38.1%) of mothers of the controls finished their secondary school and (23.8%) were university educated. A significant difference was noted between both studied groups, regarding mother's education, where p=0.037.

However, a non-significant difference was detected between both groups regarding mother's occupation where (72.7%) and (81%) of mothers of cases and controls respectively were unemployed.

Also there was no significant difference between both groups concerning habits of mothers as all mothers of cases and controls were non-smokers and non-drug abusers.

III. Medical history:

In the current study, medical history of previous diseases, injuries and operative procedures were taken from all participants and the most notable point was the presence of previous non accidental injuries in (13.3%) of the cases. A significant difference between the cases and control groups was found regarding the previous injuries where $^{MC}p= 0.026$.

IV. History of psychiatric illness:

In the present study, psychiatric evaluation was done to all participated children by psychiatric residents of AL-Hadara University Hospital. They assessed participated children according to Kiddie-SADS- present and lifetime for diagnosis of psychiatric disorders.

Regarding the cases, less than one quarter (22.2%) were diagnosed as having attention deficit hyperactivity disorder "ADHD". This is followed in a descending manner by depressive disorders (20%), post-traumatic stress disorder "PTSD" (17.8%) then nocturnal enuresis (11.1%) and encopresis (4.4%). Conduct disorder, avoidant disorder and oppositional affiant disorders were recorded in equal percentages (6.7%) among the studied cases. Also, tic disorders and obsessive compulsive disorders (OCD) were recorded in equal percentages (2.2%) of the studied cases.

On the other hand, none of the children of the controls was diagnosed to have a psychiatric disorder.

V. Maltreatment history:

In the present study, evaluation of the severity of different forms of child maltreatment was done using the Arabic version of childhood trauma questionnaire (CTQ-SF).

- **Emotional abuse:**

More than one third of the cases (35.6%) gave history of exposure to emotional abuse with low to moderate severity. On the other hand, (86.7%) of children in the control group gave no history of exposure to emotional abuse. A statistically significant difference was observed between both groups where $^{MC}p <0.001$. (Table 2)

- **Physical abuse:**

The current study demonstrated that the highest percentage of the cases (62.2%) complained of severe to extreme physical abuse while (17.8%) of them denied exposure to physical abuse. On the other hand, more than half (51.1%) of children in the control group recorded non exposure to physical abuse, (46.7%) of them experienced low to moderate severity of physical abuse and only (2.2%) were exposed to moderate to severe forms of physical abuse. A statistically significant difference was detected between cases and controls regarding exposure to physical abuse where $^{MC}p <0.001$. (Table 2)

- **Sexual abuse:**

In the current study, a statistically significant difference between cases and controls was observed where $^{MC}p= 0.012$. Six children in the cases group (13.3%) were exposed to severe to extreme forms of sexual abuse (sodomy with variant durations ranging from only one time in one child to frequent times for more than two years in another one). However, only 2 girls (4.4%) of the control group were exposed to low to moderate forms of sexual abuse in the form of harassment. (Table 2)

- **Emotional neglect:**

Out of 45 participated children with psychiatric illness, only 15 cases (33.3%) did not experience emotional neglect. The remaining children in the cases group exposed to emotional neglect with variable degrees of severity; low to moderate in (37.8%), moderate to severe in (22.2%) and severe to extreme in (6.7%). On the other hand, all the controls reported non exposure to emotional neglect. The difference between the case and control groups was statistically significant where ^{MC}p <0.001. (Table 2)

- **Physical neglect:**

A non-significant difference was noticed between the case and control groups with ^{MC}p= 1.000, where the majority of cases (97.8%) of the cases were not exposed to physical neglect. On the other hand, all controls were not exposed to physical neglect. (Table 2)

- **Age of onset of child maltreatment:**

The highest percentage of cases (77.5%) started exposure to child maltreatment between 6-10 years, (15%) of the cases reported onset of child maltreatment at 5 years or less and (7.5%) of them began exposure above 10 years.

On the other hand, (80.8%) of the controls, with maltreatment history, started exposure at the age of (6-10 years). A statistically significant difference was detected between the cases and controls regarding the age of onset of child maltreatment where p <0.001.

- **Duration of child maltreatment:** In the current study, it was found that the mean duration of exposure to child maltreatment in the children of the cases was (4.85 ± 2.07 years), while that in the control group was (2.15 ± 0.97 years). A statistically significant difference was observed between the two studied groups where p <0.001.

- **Frequency of exposure to child maltreatment:** In the current study, (45%) of children in the cases group could not remember the actual number of traumatic experiences that started very early during their childhood. However (40%) of them reported exposure to more than ten traumatic experiences. In the control group, (32%) of children reported exposure to maltreatment 3-5 times, while (28%) of them could not remember the number of traumatic experiences. Only one child reported more than ten traumatic experiences. A significant difference was noted between both groups where ^{MC}p <0.001.

- **Witnessing of domestic violence:** In the current study, it was found that (60%) of the cases witnessed domestic violence between their parents compared to (8.9%) of the controls. A significant difference was noted between both groups where p <0.001.

- **Exposure to force to leave school and start work:** In the present work, (6.7%) of the cases were forced by their parents to leave school and start work while only one child (2.2%) in the control group was forced to leave school and start work after death of his father. However, a non-significant difference was noted between both groups where ^{FE}p= 0.616.

VI. Psychometric assessment:

- **Psychometric assessment by children depression inventory (ACDI):** All subjects in the current study were requested to complete the Arabic version of Kovac's children's depression inventory (ACDI). The mean score for depression symptoms of the cases was (22.13 ± 8.28) which was significantly greater than that of the controls (8.24 ± 2.70) where p<0.001.

Moreover, a significant positive correlation was detected between the depression score assessed by CDI for the whole study sample (cases and controls) and four types of child maltreatment: emotional abuse, physical abuse, sexual abuse and emotional neglect where (r = 0.666, 0.710, 0.230 and 0.673) and (p= <0.001, <0.001, 0.029, <0.001) respectively. On the other hand, no significant correlation was detected between the depression score assessed by CDI and physical neglect where (r = 0.090 and p= 0.401). (Fig.1)

- **Psychometric assessment by child behavior checklist (CBCL):**

Furthermore, guardians were asked to fill in the Arabic version of Child Behavior Checklist (CBCL) to measure other psychometric problems. A statistically significant difference was noticed between the cases and controls regarding the total scale, externalizing symptoms, and internalizing symptoms scales where p <0.001.

Also, a significant positive correlation was detected between the total scale of Child Behavior Checklist (CBCL) for the whole study sample (cases and controls) and four types of child maltreatment: emotional abuse, physical abuse, sexual abuse and emotional neglect where (r = 0.530, 0.522, 0.247 and 0.620) and (p= <0.001, <0.001, 0.019, <0.001) respectively. On the other hand, no significant correlation was detected between the CBCL total scale and physical neglect where (r = 0.082 and p= 0.445). (Fig. 2)

VII. Oxytocin Receptor Gene (rs2254298) polymorphism:

In the current study, the observed genotype frequencies were consistent with Hardy-Weinberg with a non-significant difference between both groups where p = 0.073. GG genotype represented the most frequent genotype among both cases and control groups (73.3% and 57.8% respectively). As regard AG genotype, it was detected in (30%) of the cases and (28.9%) of the controls. However, AA genotype represented the least frequent genotype. It occurred in (6.7%) of the cases and (13.3%) of the controls.

- **Relation between OXTR polymorphism and psychometric assessment of children using children depression inventory (ACDI):**

In the current work, the mean score of depression symptoms in children in the cases group was higher in AA genotype (37.67± 9.07) followed in a descending manner by GG genotype (22.09± 7.51) and lastly AG genotype (17.11± 3.52). A statistically significant difference was present between AA and AG genotypes and between AA and GG genotypes regarding depressive symptoms where p_1<0.001 and p_2=0.001 respectively. However, a non-significant difference between AG and GG genotypes' relation to depressive symptoms in the cases group where p_3=0.066.

In the control group the presence of allele A in AA and AG genotypes was associated with lower scores of depressive symptoms than the homozygous GG genotype. However, this difference was not statistically significant where p =0.108. (Table 3)

- **Relation between OXTR Genotyping and psychometric assessment performed by children behavior checklist (CBCL):**

Moreover, cases with AA genotype achieved the highest scores of CBCL (total and externalizing scales) while the controls with genotype AA had the lowest scores of CBCL (total, externalizing and internalizing). A non-significant statistical relation was observed between different genotypes and CBCL total scale, externalizing scale and internalizing scale among both cases and control group where p > 0.05.

Multivariate Linear regression was done in the present study to examine the effect of OXTR gene SNP rs2254298 and its interaction with different forms of child maltreatment on the depressive symptoms assessed by (ACDI) and total scale of (CBCL). However, no significant interaction between this SNP and child maltreatment was found in the prediction of both depressive symptoms (ACDI) and (CBCL) total scale in our study. (Table 4, 5)

VIII. Epigenetics changes (global DNA methylation):

In the current study, the mean level of global DNA methylation in the cases (0.20 ± 0.03) was lower than it in the control group (0.30 ± 0.03) with a statistically significant difference between where p

<0.001. A significant negative correlation was detected between the global DNA methylation and three types of child maltreatment: emotional abuse, physical abuse and emotional neglect where (r = -0.429, -0.527 and -0.456) respectively and (p= <0.001). On the other hand, no significant correlation was detected between the global DNA methylation and sexual abuse and physical neglect where (r = -0.190, -0.060) and (p= 0.072 and 0.573) respectively. (Fig. 3)

Table (1): Difference between the two studied groups according to demographic data

	Cases (n= 45)		**Control (n= 45)**		**Test of Sig.**	**p**
	No.	**%**	**No.**	**%**		
Age (years)						
12 –< 14	23	51.1	20	44.4	χ^2= 0.446	0.800
14 – <16	9	20.0	11	24.4		
16 – 18	13	28.9	14	31.1		
Min. – Max.	12.0 – 18.0		12.0 – 18.00			
Mean ± SD.	14.24 ± 2.01		14.98 ± 2.16		t=1.667	0.099
Median	14.0		16.0			
Sex						
Male	31	68.9	24	53.3	χ^2= 2.291	0.130
Female	14	31.1	21	46.7%		
Residence						
Alexandria	38	84.4	29	64.4	χ^2= 7.792*	^{MC}p= 0.026*
Albehira	6	13.3	12	26.7		
Marsa matrouh	0	0.0	4	8.9		
Sohag	1	2.2	0	0.0		
Level of education						
Primary school	20	44.4	4	8.9	χ^2= 36.903*	^{MC}p= <0.001*
Preparatory school	16	35.6	14	31.1		
Secondary school	1	2.2	23	51.1		
Did not continue primary school	6	13.3	2	4.4		
Didn't continue preparatory school	1	2.2	1	2.2		
Didn't continue secondary school	1	2.2	1	2.2		
School performance						
Excellent	3	6.7	7	15.6	χ^2= 33.097*	<0.001*
Very good	1	2.2	10	22.2		
Good	8	17.8	20	44.4		
Weak	13	28.9	7	15.6		
Failure	20	44.4	1	2.2		
Habits						
None	31	68.9	40	88.9	χ^2= 5.564*	^{MC}p= 0.040*
Smokers	13	28.9	5	11.1		
Drug addiction	0	0.0	0	0.0		
Others	1	2.2	0	0.0		

χ^2, p: χ^2 and p values for **Chi square test** for comparing between the two groups.
^{MC}p: p value for **Monte Carlo** for Chi square test for comparing between the two groups.
t, p: t and p values for **Student t-test** for comparing between the two groups.
*: Statistically significant at $p \leq 0.05$

Table (2): Difference between the cases and control groups according to history of child maltreatment assessed by childhood trauma questionnaire (CTQ-SF)

	Cases (n= 45)		**Control (n= 45)**		□□	**^{MC}p**
	No.	**%**	**No.**	**%**		
Emotional abuse					35.111*	<0.001*
None	13	28.9	39	86.7		
Low to moderate	16	35.6	6	13.3		
Moderate to severe	5	11.1	0	0.0		
Severe to extreme	11	24.4	0	0.0		
Physical abuse						
None	8	17.8	23	51.1	49.830*	<0.001*
Low to moderate	7	15.6	21	46.7		
Moderate to severe	2	4.4	1	2.2		
Severe to extreme	28	62.2	0	0.0		
Sexual abuse						
None	39	86.7	43	95.6	7.896*	0.012*
Low to moderate	0	0.0	2	4.4		
Moderate to severe	0	0.0	0	0.0		
Severe to extreme	6	13.3	0	0.0		
Emotional neglect						
None	15	33.3	45	100.0	49.416*	<0.001*
Low to moderate	17	37.8	0	0.0		
Moderate to severe	10	22.2	0	0.0		
Severe to extreme	3	6.7	0	0.0		
Physical neglect						
None	44	97.8	45	100.0	1.011	1.000
Low to moderate	1	2.2	0	0.0		
Moderate to severe	0	0.0	0	0.0		
Severe to extreme	0	0.0	0	0.0		

χ^2, p: χ^2 and p values for **Chi square test** for comparing between the two groups.
^{MC}p: p value for **Monte Carlo** for Chi square test for comparing between the two groups.
*: Statistically significant at $p \leq 0.05$

Table (3): Relation between OXTR Genotypes and psychometric assessment performed by children depression inventory (ACDI) in the two studied groups.

		OXTR Genotypes						Test of sig.	p
		AA		AG		GG			
		No.	%	No.	%	No.	%		
Cases	Children depression inventory	(n = 3)		(n = 9)		(n = 33)			
	More than 13	3	100.0	8	88.9	29	87.9	χ^2= 0.367	^{MC}p= 1.000
	Less than 13	0	0.0	1	11.1	4	12.1		
	Min. – Max.	31.0 – 48.0		12.0 – 23.0		1.0 – 33.0		**F**= 9.655*	<0.001*
	Mean ± SD.	37.67± 9.07		17.11± 3.52		22.09± 7.51			
	Median	34.0		16.0		23.0			
	Sig. bet. types	p_1<0.001*, p_2=0.001*, p_3=0.066							
Control	Children depression inventory	(n = 6)		(n = 13)		(n = 26)			
	More than 13	0	0.0	0	0.0	2	7.7	χ^2= 1.062	0.666
	Less than 13	6	100.0	13	100.0	24	92.3		
	Min. – Max.	4.0 – 11.0		5.0 – 9.0		3.0 – 16.0		**F**= 2.344	0.108
	Mean ± SD.	7.50± 2.59		7.15± 1.28		8.96± 3.07			
	Median	7.50		7.0		9.0			

χ^2, p: χ^2 and p values for **Chi square test** for comparing between the two groups.
^{MC}p: p value for **Monte Carlo** for Chi square test for comparing between the two groups.
F,p: F and p values for ANOVA test, Sig. bet. grps was done using Post Hoc Test (LSD)
p_1: p value for comparing between AA and AG
p_2: p value for comparing between AA and GG
p_3: p value for comparing between AG and GG
*: Statistically significant at $p \leq 0.05$

Table (4): Multivariate Linear regression for children depression inventory in total sample (n= 90)

	B	SE	Beta	t	p
Emotional abuse	0.524	0.162	0.272	3.233	0.002*
Physical abuse	0.424	0.127	0.306	3.340	0.001*
Sexual abuse	0.331	0.115	0.179	2.871	0.005*
Emotional neglect	1.004	0.215	0.364	4.660	<0.001*
Physical neglect	-0.411	2.776	-0.009	-0.148	0.883
Genotyping	0.393	0.864	0.028	0.455	0.650
R^2 = 0.686, , SE = 5.39, F = 30.192*, p <0.001*					

R: coefficient of regression
B: Unstandardized Coefficients
SE: Estimates Standard error
Beta: Standardized Coefficients
t: t-test of significance
F, p: F and p values for ANOVA test
*: Statistically significant at $p \leq 0.05$

Table (5): Multivariate Linear regression for CBCL total scale in total sample (n= 90)

	B	SE	Beta	t	p
Emotional abuse	1.521	0.660	0.240	2.304	0.024*
Physical abuse	0.392	0.516	0.086	0.760	0.449
Sexual abuse	1.284	0.468	0.210	2.741	0.007*
Emotional neglect	4.375	0.892	0.481	4.904	<0.001*
Physical neglect	-2.342	11.317	-0.016	0.207	0.837
Genotyping	5.364	4.204	0.100	1.276	0.205
R^2 = 0.718, , SE = 22.03, F = 14.748*, p <0.001*					

R: coefficient of regression
B: Unstandardized Coefficients
SE: Estimates Standard error
Beta: Standardized Coefficients
t: t-test of significance
F, p: F and p values for ANOVA test
*: Statistically significant at $p \leq 0.05$

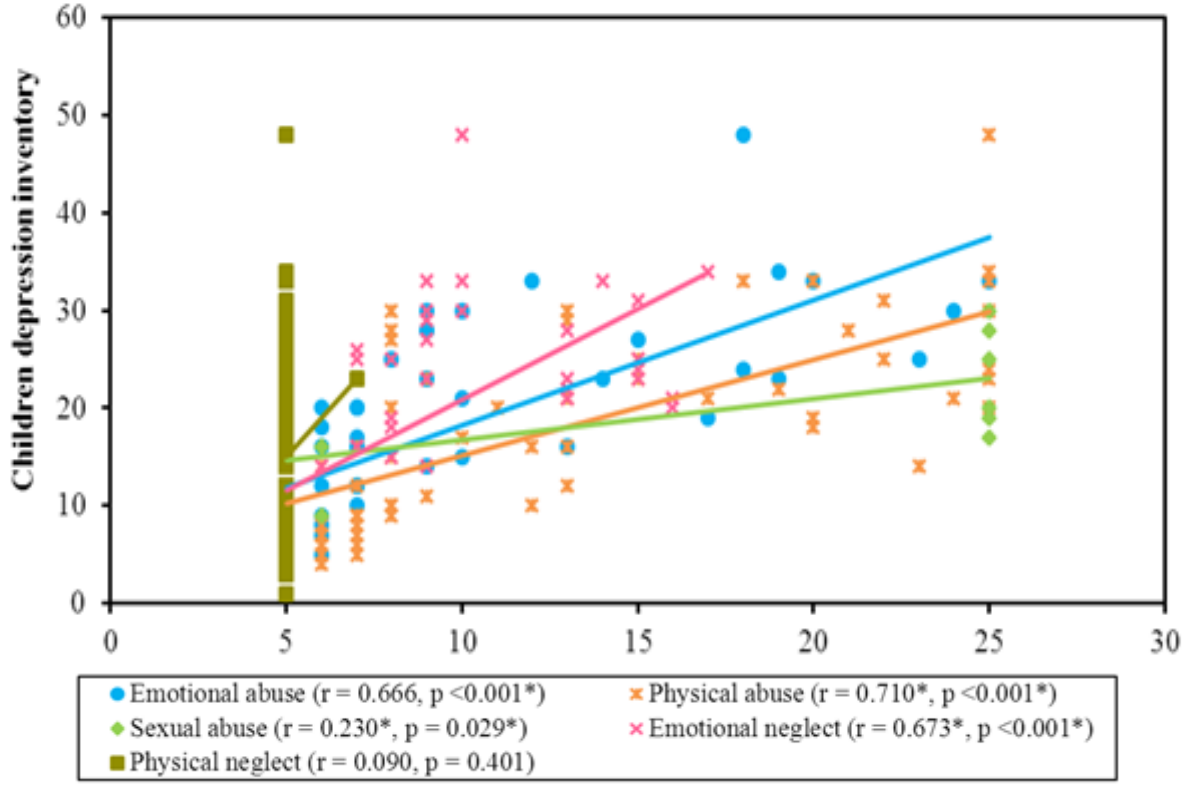

Figure (1): Correlation between different types of child maltreatment and depression scores assessed by CDI in total sample (n= 90).

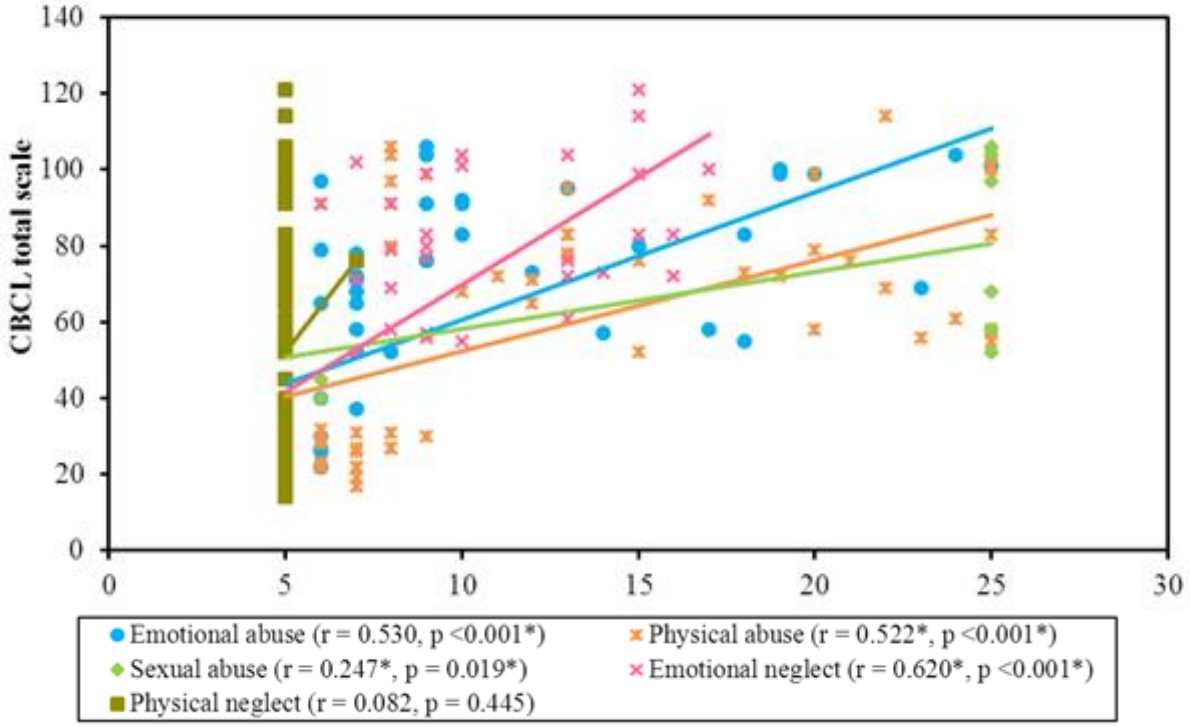

Figure (2): Correlation between different types of child maltreatment and CBCL total scale in total sample (n= 90).

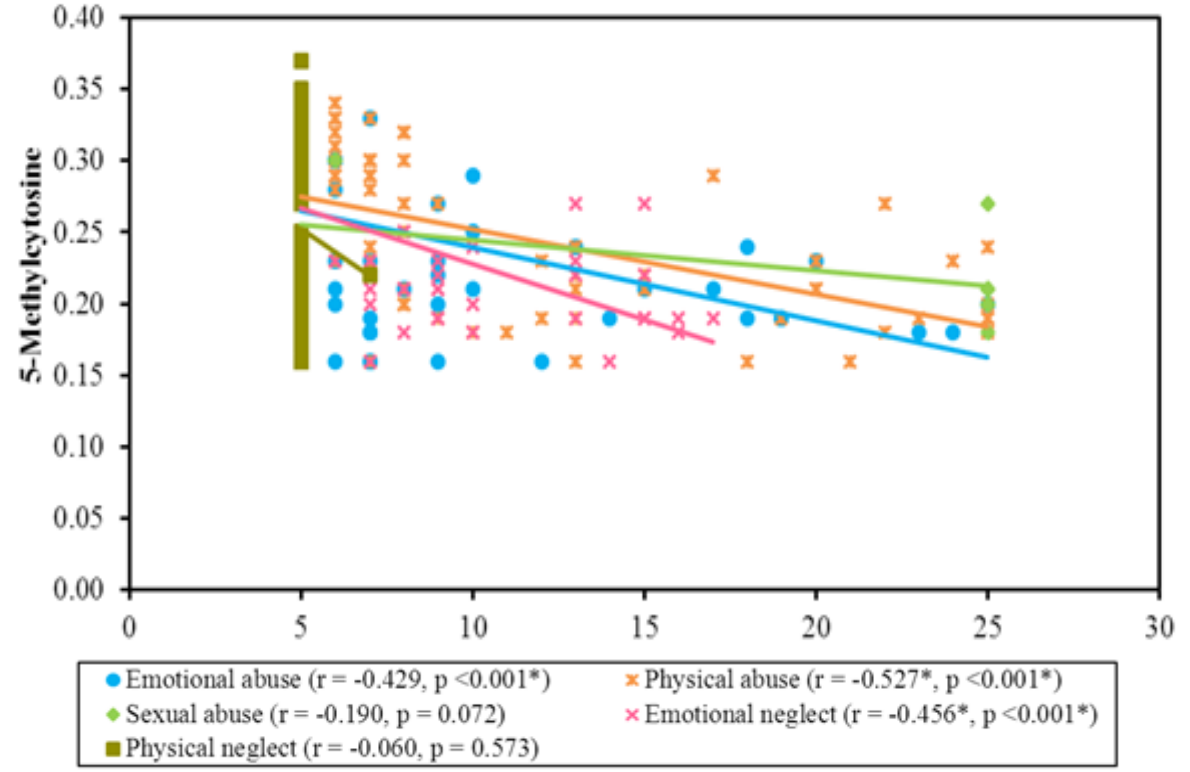

Figure (3): Correlation between different types of child maltreatment and global DNA methylation in total sample (n= 90).

DISCUSSION

The diagnosis of the non-accidental nature of child maltreatment injuries represents both ethical and legal challenges which may help in preventing many long-term consequences. However, not all individuals that have experienced childhood maltreatment develop such disorders in later life, indicating the presence of resilience **(Rutter, 2006; Koc et al., 2014)**.

There have been several studies that have tried to uncover aspects behind resilience and alterations in individual vulnerability to the adverse consequences linked to child abuse and neglect **(Hornor, 2017)**.

In the present study, we are concerned with psychiatric consequences seen in adolescence between 12-18 years and its association with child maltreatment and the explanation of resilience in the light of three hit model; the interaction between early life stress (child maltreatment) and genetic factors (both genotyping and epigenetic changes) and different psychiatric consequences **(Daskalakis et al., 2013)**. Moreover, we examined the role of (OXTR) rs2254298 polymorphism and global DNA methylation in the relation between child maltreatment and psychiatric consequences. This SNP seems to play differential roles under high and low distress conditions among different populations so it is interesting to study its effect among a sample of the Egyptian maltreated children **(Brüne, 2012)**.

This work included ninety children, aged between 12-18 years. They were distributed equally into two groups; case group suffering from psychiatric illness and control group with no psychiatric illness attending outpatient clinics in Alexandria main university hospital.

In the current work, no statistical significant difference was observed between the cases and controls regarding age and sex. Adolescent's age, as selected in the present work, is considered a time of intense variations in body and behavior. It is also a phase of growing occurrence of different types of psychiatric illnesses, including anxiety and mood disorders, psychosis, eating disorders, personality disorders and substance abuse. At the same time, in the adolescent's age group it would be easier to remember and recall events from the early childhood and to detect their exposure to maltreatment **(Paus et al., 2008)**.

In the present study a statistically significant difference between cases and controls was noted regarding level of education and school performance that were significantly lower in cases of psychiatric illness. It may be attributed to diminished functional ability among psychiatric patients.

This result coincides with **McLeod et al. (2012)** who concluded that different psychiatric disorders such as substance abuse, delinquency and attention problems were significantly associated with diminished school achievement.

Regarding study participants' habits, more than one quarter of the studied cases were smokers which was significantly higher than the controls. This was in agreement with **Degenhardt and Hall (2001)** and **Minichino et al. (2013)** who found that smokers are more likely than non-smokers to meet diagnostic criteria for mental health conditions, such as mood disorders. It can be explained by the usage of smoking habit as a relieving method to regulate the symptoms associated with their psychiatric disorders. Also it may be a sign of lack of care that those children suffered from.

In the current work, there is a non-significant difference between cases and controls regarding consanguinity. However, more than half of the controls living with parents having positive consanguinity. It may reflect the role of blood relationship; which is a socio-cultural tradition in the Arab world. Those parents may find support from their extended family and advices about effective parenting skills which may reduce their stress and decrease any conflicts.

Also a non-significant difference between cases and controls was observed regarding the number of family members where the majority of cases living in families consisting of five members. It is similar to the results of the study done by **Solari and Mare (2012)** who concluded that living in a crowded home is negatively associated with external behavior problems.

Regarding the birth order of the participated child, a non-significant difference was also noted between cases and controls. However, the first child was the commonest (53.3%) to be affected in the cases group. This coincides with **Ghanem et al. (2018)**. It may be clarified by the fact that new parents lack experience in handling stressful conditions and have low knowledge about proper parenting.

However, the present study shows a significant difference between both groups regarding death of one or both parents and state of relationship of parents. Regarding cases, (44 children) had living parents; (35.6%) of them were divorced and only one child was adopted. On the contrary, (15.6%) and (13.3%) of the controls had dead fathers or mothers and divorced parents respectively. These results demonstrate that parental separation is more linked to psychiatric illness in children than parental death. These results are in accordance to **Veijola et al. (2004)** and **Tyrka et al. (2008)**.

On the contrary, other studies **(Furukawa et al., 1998; Furukawa et al., 1999)** have found no association of childhood parental death or separation with psychopathology. These discrepancies may be attributed to differences in parental behavior after separation or divorce and the age of the children at time of parental loss.

In the current work data of the parents were collected; a significant difference was detected between both groups in parent's education and father's occupations where (20.5%) and (27.3%) of the cases belonged to fathers who did not continue their primary school education and mothers who finished preparatory school respectively. It is coincide with a study conducted by **Charak and Koot (2014)** aimed at determining the association of abuse and neglect in Indian adolescents with the level of parental education and they found that children of less educated mothers reported higher abuse and neglect than those of educated mothers.

Moreover, it coincides with **Costello et al. (2003)**, **Jansen et al. (2009)**, **Flouri et al. (2010)** and **Bøe et al. (2012)** who concluded that the behavior and the risk of psychopathology of children could be affected by parental conditions, comprising socioeconomic status.

Regarding father' habits, in the current work, (70.3%) and (6.8%) of the cases belonged to smoker fathers and drug abusing fathers respectively and it was not significantly different than that of the control group. However, **Clark et al. (2004)** demonstrated that parental drug addiction and smoking habits may result in financial stress, parental conflict and social isolation that can negatively affect parenting and parent-child interactions increasing the risk of developing psychopathology in their children.

Regarding child maltreatment, in the present study, a statistically significant difference was present between the cases and controls as regard exposure to different types of child maltreatment; emotional abuse, physical abuse, sexual abuse and emotional neglect. However, a non-significant difference was detected between both groups regarding physical neglect. In addition to that a significant difference was detected between both groups regarding exposure to previous injuries including non-accidental one.

Moreover, a significant difference between the cases and controls, in the current work, was noted regarding; the age of onset of child maltreatment, duration and frequency of exposure to child

maltreatment and witnessing domestic violence.

These findings may demonstrate that different environmental factors may moderate the long term sequels of child maltreatment. Among them are the types of child maltreatment, its frequency, duration and severity. In addition to the environmental factors, personal factors are also important comprising the age of the child and developmental stage when the abuse or neglect happened.

These results are in agreement with **Gil et al. (2009)**, **Alvarez et al. (2011)**, **Larsson et al. (2013)** and **Sala et al. (2014)**. They concluded that in addition to be a risk element for developing psychiatric problems during adulthood, child maltreatment aggravates the prognosis of a wide variety of illnesses, with the poorest psychopathological consequence in patients who were at earlier age of onset and with greater number of experiences of abuse.

In the present work, three children (6.7%) of the cases group were forced by their parents to leave school at an age less than 13 years and start work for financial gain before finishing their primary school education in two children and after finishing primary school education in the last child. On the other hand, only one child (2.2%) in the control group was forced to leave school and start work after death of his father.

Actually it is against the Egyptian law which allows the work of children above 14 years old after putting serious restrictions to protect child health and safety. Firstly, it determined certain industries where children are not allowed to be employed, as all types of welding and glass manufacturing. Secondly, children at the age of fourteen or more shouldn't work for more than six hours daily with the presence of at least an hour to rest. Thirdly, it is prohibited for a child to work after 7 pm **(**2003 ,قانون العمل**)**.

All subjects in the current study were requested to complete the Arabic version of Kovac's children's depression inventory (ACDI). It was found that the mean score for depression symptoms of the cases was significantly higher than that of the controls. This can be attributed to many reasons; their psychiatric disorder, their experience of difficulties during early life time as higher levels of child maltreatment, witnessing domestic violence, parental loss due to death or separation or even their low socio-economic background. These results are in accordance to **Tollenaar et al. (2017)**.

In the current work, correlation between different types of child maltreatment and depression scores for all study participants was done and revealed a significant positive correlation between the depression scores assessed by ACDI and four types of child maltreatment; emotional abuse, physical abuse, sexual abuse and emotional neglect. this coincides with **Rehan et al. (2017)** who found that severe forms of physical abuse, emotional neglect were connected to greater scores of depression and anxiety that reaches to the clinical levels in severe sexual abuse. This indicates that increasing severity of childhood maltreatment increases the clinical levels of psychopathology and depressive symptoms later in life.

On the other hand, in the current work, no significant correlation was detected between the depression score and physical neglect. It is contrary to **Rehan et al. (2017)** who found that severe physical neglect were also associated with clinical levels of depression and anxiety. This may be attributed to the fact that only one child in our study participants reported exposure to low to moderate physical neglect.

Furthermore, to measure other psychometric problems of research participants in the current study, guardians were asked to fill in the Arabic version of Child Behavior Checklist (CBCL). A significant difference was noticed between the cases and controls regarding the total scale, externalizing symptoms and internalizing symptoms scales. This is in

agreement with **Krueger et al. (2001)**. However **Cosgrove et al. (2011)** explained internalizing and externalizing symptoms not only in the light of psychiatric disorders, but also according to different genetic and environmental influences.

Moreover, a significant positive correlation was detected in the current work between CBCL total scale and four types of child maltreatment; emotional abuse, physical abuse, sexual abuse and emotional neglect. On the other hand, no significant correlation was noticed between the CBCL total scale and physical neglect.

These results are in accordance to **Ackerman et al. (1998)**, **Evans et al. (2008)**, **Moylan et al. (2010)** and **Norman et al. (2012)** who found that exposure to maltreatment during childhood period could result in greater risk for internalizing behavioral problems (e.g., depression, anxiety) and externalizing behavioral problems (e.g., aggressive behavior, delinquency).

In the current study, the observed genotype frequencies were consistent with Hardy-Weinberg with a non-significant difference between both groups. GG genotype represented the most frequent genotype among both cases and control groups followed by AG genotype. However, AA genotype represented the least frequent genotype in both groups. These findings coincide with comparative genetics studies which concluded that G is the wild allele, while the allele A has happened at some time during human evolution by a mutation replacing guanine (G) by adenine (A) **(Chelala et al., 2009; Brüne, 2012)**.

In the present work, the mean score of depression symptoms (ACDI), total and externalizing scales (CBCL), in the cases group, was higher in AA genotype. A statistically significant difference was detected between AA and AG genotypes and between AA and GG genotypes regarding depressive symptoms. This is in accordance to **Kawamura et al. (2010)** who found that a haplotype block of seven SNPs containing rs2254298 G was accompanied by lesser scores of depressive affect in Japanese individuals than those carrying A allele.

It was concluded that genetic alteration at OXTR is probably connected to differential vulnerability, as carriers of the AA genotype of the rs2254298 SNP was found to be more susceptible to get a psychiatric disease, including depressive conditions with intense variations depending on racial background **(Costa et al., 2009; Lucht et al., 2009)**.

However these above mentioned researches did not discuss the interaction between genes and environment. So, it is hard to examine the extent of early life maltreatment exposure that may result in psychiatric symptoms later in life.

Furthermore to judge gene-environmental interaction in the current study, Multivariate Linear regression was performed to study the effect of OXTR gene SNP rs2254298 and its relation to various types of child maltreatment on the depressive symptoms (ACDI) and total scale (CBCL). However, no significant interaction between this SNP and child maltreatment was found in the prediction of both depression sensitivity (ACDI) and (CBCL) total scale in our study. This was in agreement with **Tollenaar et al. (2017)** who found that OXTR SNPs (rs2254298, rs53576, rs2268498) not uniquely moderate the relation between specific forms of maltreatment and depressive symptoms nor had main effects on psychiatric outcomes.

On the other hand, it was against some other studies **(McQuaid et al., 2013; Myers et al., 2014; Thompson et al., 2014)** which reported interactions between OXTR SNPs and stressful early life experiences on symptom levels of depression. One of these studies was that done by **Thompson et al. (2011)**; who highlighted the potential importance of this OXTR gene polymorphism and its interaction with adverse environment in the etiology of depression disorder. These

differences in the results between different studies may be attributed to the difference in allele frequency when comparing studies in different populations.

Regarding epigenetic mechanisms, the most comprehensively defined one in the setting of psychiatry is DNA methylation. Explanation of how epigenetic modifications may partly be responsible for trauma-associated changes and its role in psychological and biological consequences of child maltreatment is very interesting **(McCoy et al., 2017)**.

In the current study, Global DNA methylation in study contributors was assessed by measuring 5-methylcytosine (5-mC) using MethylFlash methylated DNA quantification colorimetric kit. It was found that the mean level of global DNA methylation in the cases of psychiatric illness was significantly lower than it in the control group. Also a significant negative correlation was noted between the mean level of global DNA methylation and three forms of child maltreatment; emotional abuse, physical abuse and emotional neglect. On the other hand, no significant correlation was observed between the global DNA methylation and sexual abuse and physical neglect.

To our knowledge no other literature used the same method of measuring global DNA methylation on human being with psychiatric illness. However, one study conducted by **McCoy et al. (2017)** on adult rat amygdale shown that decreasing DNA methylation would exacerbate high levels of depression-like behavior.

On the other hand, **Meaney and Ferguson-Smith (2010)** studied the DNA methylation of single genes to see its association with early life adversity and poor late consequences. They concluded that child maltreatment was linked to extensive differences in methylation across the whole genome. This points epigenetics as a probable mechanism by which adverse early environments may lead to long-term biological alterations that can increase the risk for poor long term outcomes.

CONCLUSIONS

From the results obtained in the present study it was concluded that:

Risk for psychopathology is related to a complex interaction of multiple factors; personal and environmental. Among the environmental factors; child maltreatment which is an avoidable risk linked to a range of psychiatric disorders. Moreover, a positive correlation was detected between the depression scores and four types of child maltreatment; physical, emotional, sexual abuse and emotional neglect. However, we found no significant interaction between OXTR gene SNP rs2254298 and the various types of child maltreatment in the prediction of depression score by ACDI and CBCL total scale.

Regarding epigenetics, the cases group showed significant DNA hypomethylation. In addition to that, a significant negative correlation was noticed between the global DNA methylation and three types of child maltreatment; physical, emotional abuse, and emotional neglect which may explain one of mechanisms of psychiatric illness among maltreated children.

RECOMMENDATIONS

Depending on the conclusions of the current study, the following recommendations are proposed:

- Future larger-scale studies are needed to validate our findings regarding the moderating role of (OXTR) gene polymorphism on the relation between early life adversity and psychiatric consequences.
- Further studies are also needed to confirm our DNA methylation findings and to examine further confounds as genetic polymorphisms that may moderate methylation effects.
- National guidelines and strategies are needed to be established for preventing child abuse and neglect which may be the only hope for preventing and reducing the burden of any further consequences.

- Improve the knowledge and awareness of parents about child labour and the laws which protect the rights of children.
- A specific parent-training programme regarding good parenting skills and coping with stress are needed.

LIMITATIONS

Several limitations are present in this study. First, research participants were selected from a single institution in Alexandria and thus may be unrepresentative of the general population in Egypt.

Secondly, the small sample size which makes it difficult to generalize findings on the whole Egyptian population.

Thirdly, the current study provides just support about involvement of epigenetic mechanisms/ global DNA methylation as a cause of risk for health problems later in life among persons having a history of child maltreatment, but we didn't obtain gene expression data.

CONFLICTS OF INTEREST

All authors of the current research declared no conflict of interest.

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سوء معاملة الأطفال: العواقب النفسية لدى المراهقين في ضوء جين مستقبل ونموذج الحمض النووي العالمي: دراسة SNP RS2254298أوكسيتوسين الحالات والشواهد

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نبذة عن الموضوع: على مدى عقود، اقتصر التأثير السلبي لمحنة سوء معاملة الأطفال على الأذى والإصابات الفورية. في الآونة الأخيرة، ربطت العديد من الدراسات سوء معاملة الأطفال مع المزيد من العواقب على المدى الطويل في مرحلة الطفولة والمراهقة والبلوغ من بينها أعراض واضطرابات نفسية. **الأهداف:** هدفنا إلى تحديد الارتباط بين العواقب النفسية والأنواع المختلفة من سوء معاملة الأطفال بين المراهقين بين 12-18 سنة، واستكشاف دور تعدد أشكال مستقبلات الأوكسيتوسين (rs2254298) في العلاقة بين أنواع سوء معاملة الأطفال المختلفة والعواقب النفسية لذلك ولدراسة العلاقة بين إساءة معاملة الأطفال ومثيله الحمض النووي العالمي. **المنهجية:** أجريت دراسة الحالات والشواهد على 90 طفلاً تراوحت أعمارهم بين 12 و18 سنة مقسمة بالتساوي إلى مجموعتين؛ "مجموعة الحالات" والتي تعاني من أمراض نفسية وتم جمعهم أثناء حضورهم للعيادات الخارجية للأمراض النفسية للأطفال والمراهقين بمستشفى الحضرة الجامعي بالإسكندرية، مصر و"مجموعة الشواهد" و قد تم جمعهم أثناء حضورهم لمختلف العيادات الخارجية في مستشفيات جامعة الإسكندرية. **النتائج:** أظهر البحث وجود إختلاف ذو دلالة إحصائية بين مجموعة الحالات والشواهد فيما يتعلق بأربعة أنواع من سوء معاملة الأطفال وهم الاعتداء الجسدي والاعتداء الجنسي والإعتداء العاطفي والإهمال. علاوة على ذلك، تم الكشف عن وجود ارتباط إيجابي ذو دلالة إحصائية بين هذه الأنواع الأربعة من سوء المعاملة والأعراض الإكتئابية التي تم الكشف عنها بواسطة مقياس الإكتئاب لدى الأطفال والقياس الكلي لقائمة سلوك الطفل (CBCL). ومع ذلك، كشفت الدراسة عن عدم وجود تفاعل ذو دلالة إحصائية بين جين OXTR SNP rs2254298 وسوء معاملة الأطفال في التنبؤ بالأعراض الإكتئابية والمقياس الكلي لـ CDI وCBCL على التوالي. من ناحية أخرى، تم الكشف عن ارتباط سلبي ذو دلالة إحصائية بين قيمة متوسط مثيلة الحمض النووي وثلاثة أنواع من سوء معاملة الأطفال؛ الإعتداء الجسدي والاعتداء العاطفي والإهمال.