A STUDY OF MONOAMINE OXIDASE A GENE MUTATION WITH AGGRESSIVE BEHAVIOR IN CRIMINALS IN ERBIL CITY PRISON

Hemn Mamkhula Hade

MASTER THESIS

Biology Department

Supervisor: Prof. Dr. Ekrem ATALAN

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This thesis was approved unanimously by the following jury in the date of 23/01/2017

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PREFACE

First of all, my thanks are addressed to ALLAH for inspiring me with patience and strength to fulfill the study.

I would like to express the deepest appreciation and my special thanks to my supervisor Prof. Dr. Ekrem ATALAN at Bingol University for his supervision, patience and support I would like also to thank co supervisor Assist. Prof. Dr. Hazha Jamal Hidayat in Biology Department of Salahaddin University for her supervision guidance and encouragement. I would like to express my thanks to Bingol University and the head of Soil Science and Plant Nutrition department also I would like to thank Dr. Mahir and Dr. Hemn Noori and my warm thanks to Mr. Abdulmajeed Nanakali for their support through my dissertation.

Special thanks to the staff of Erbil prison for their support. Finally, I must express my very profound gratitude to my parents and to my wife for providing me with unfailing support and continuous encouragement throughout my years of study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them.

Hemn Mamkhula HADE
2017 Bingol

CONTENTS

LIST OF SYMBOLS

MAOA	: Monoamine oxidase A gene
DNA	: Deoxyribonucleic acid
XP	: Chromosome X short arm P
BP	: Base pair
VNTR	: Variable number tandem repeat
L-MAOA	: low- monoamine oxidase A gene
SLC64A	: (Neurotransmitter transporter, serotonin) solute carrier family 6
MAO	: Monoamine oxidase
5-HTRS	: Serotonin receptor
5-HTT	: Serotonin transporter
BNDF	: Brain derived neurotrophic factor
NCAM	: Neural cell adhesion molecule
DNR	: Di nucleotide repeat
KB	: Kilo base
H-Maoa	: High monoamine oxidase A gene
3R	:3Receptor
DACC	: Dorsal anterior cingulated cortex
ACC	: Anterior cingulated cortex
MDD	: Major depressive disorder
MAOA-LPR	: Monoamine oxidase A- Low promoter repeat
CSF	: Cerebrospinal fluid
PCR	: Polymerase chain reaction
COMT	: Catechol-O-methyl transfers
5-HTT	: Serotonin transporter
DRD4	: Dopamine D4 receptor
DRD2	: Dopamine D2 receptor
DAT1	: Dopamine active transporter 1 gene

NCBI	: National center for biotechnology information
G-T	: Guanine - thymine
G-C	: Guanine - cytosine
EDTA	: Ethylene diamine tetra acetic acid
GB	: Gigabyte
RPM	: Revolutions per minute
TB	: Tetris/ Borate
µl	: Microliter

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ERBIL HAPISHANESINDEKI AGRESIF SUÇLULARDA MONOAMINE OXIDIZE A GEN MUTASYONLARININ ARAŞTIRILMASI

ÖZET

Bu çalışmanın amacı Irak, Erbil hapishanesindeki suçluların monoamine oxidize Agenlerinin (MAOA) exon 8'deki mutasyonları ile davranışları arasındaki ilişki incelemektir. Bu çalışmada moleküler yaklaşım kullanılarak MAOA geninin Exon-8'in mutasyonu incelendi. DNA ekstraksiyonundan sonra polimeraz zincir reaksiyonu (PCR) ile Exon 8 bölgesi çoğaltılması, jel elektro forezde koşturulduktan sonra DNA nükleotid zinciri belirlenerek analizi yapıldı.

Bu amaç için, yaşları 21 ila 60 arasında değişen 30 mahpus ve 5 kontrol group olmak üzere toplam 35 kan numunesi alındı. Suç oranıyaşları 21 ila 30 arasında olan gençlerde yüksekiken yaş aralığı 31 ila 40 arasında olanlarda keskin bir düşüş gösterdi. Suçluların çoğunluğu eğitimde başarısız olmuş ve resmi yüksek eğitim almamışlardır. Çoğunluğu okuldan kaçmış veya ayrılmış ve 30 öğrenciden 16'sı (%53'ü) resmi ilkokul mezunu, 11'i (%36) ise orta okul mezunudur. Evlilik ile suç arasındaki ilişki incelendiğinde, 30 suçludan 25'i (%83) eviliken 5'i (%17) bekar olduğu belirlendi.

MAOA geninin Exon-8 bölgesinin DNA nükleotid analizisonucu substitüsyon ve insersiyon olmak üzere 2 mutasyon gözetlendi. Suçluların tümünde MAOA genin Exon-8 bölgesinde yaygın olarak mutasyon olduğunu sonuçlarımız gösterdi. Exon 8'in 2326 nt'deki yaygın mutasyon yüzdesi %52 olarakbulundu. SNP (G-T) arginin arginine (anlamsızmutasyon) olarakdeğişti. Aynışekildeexonon 2276 nükleotid posizyonunda G'in C'ne transversiyonulizin aspargine (yanlışanlam mutasyonu) olarak değiştiği belirlendi ve %26 oranında suçlularda görüldü. 2302 posizyonda bulunan C'in çerçeve

kayması mutasyonu oranı %4 olduğu ve tüm amino asit dizilimini değiştirdiği belirlendi.

Anahtar kelimeler: *MAOA geni, kriminal, Erbil.*

THE STUDY OF MONOAMINE OXIDASE A GENE MUTATION WITH AGGRESSIVE BEHAVIOR IN CRIMINALS IN ERBIL CITY PRISON

ABSTRACT

The aim of this study was to investigate the association between the mutation of exon 8 of monoamine oxidize A gene (MAOA) genes and aggressive behavior in criminals in the prison of Erbil city Kurdistan region- Iraq. To achieve this aim, blood sample were collected from 30 prisoners and 5 control group, their age ranged from 21 to 60 years. This work also used molecular approaches to investigate the mutation of exon 8 MAOA gene in criminals. DNA analysis performed using DNA extraction, PCR amplification, gel electrophoresis and sequence analysis.

The following result could be considered; a young offenders crime peaks between the ages of 21 to 30 and offending rates of 31 to 40 aged group decline sharply with age. Most of the cases were failed in the education system and have no formal higher school qualifications. Most of them had regularly truanted from school and 16 out of 30 cases (53%) had formal qualifications primary while 11 (36%) had formal qualifications secondary school. The correlation between marriage and crime high for 25 (83%) cases of married but only 5 out of 30 (17%) was single.

In direct DNA sequence analysis in the exon 8 in MOAO gene, we observed two mutations substitution and insertion. The result show common mutation in exon 8 type of mutation in exon 8 of MAOA gene of criminals. The percentage of common mutation in exon 8 was 52% by substitution at position 2326 nt of exon 8, that SNP (G-T) change arginine to arginine (nonsense mutation) and 26% G to C transversion at

nucleotide position 2276 change lysine to asparagine (missense mutation) and 4% insertion (C) at position 2302 change frame shift change all amino acid downstream.

Keywords: *MAOA gene, criminal state, Erbil.*

1. INTRODUCTION

Brain and the nervous system control all human behaviors, and biology's role in behavior of living organisms is obvious owing to that system. Transcription and translation of DNA into proteins makes the development of the brain Genes choreograph. Furthermore those processes in genes will affect the molecular structure of the brain at every level, which includes neurotransmitter levels and receptors, brain anatomy, and the processes that control the development of interconnections among neurons. Environment also plays a role by modifying or disrupting genetically encoded actions. Difference in the genes that control brain development may result in variation of behavior (Mark *et al*., 2000).

A conscious tendency to harm others against their will, characterized from an aggressive behavior, which illegally can be exhibited, and presented in criminal offenses and antisocial behaviors. However it is a complex behavior, but it can be regulated by multiple factors which includes environmental, genetic, neurobiological and cognitive (Teodorovic *et al*. 2015).

Aggression is one of the positive symptoms among the neuropsychiatric disorders. Genetic predispositions to antisocial personality disorder, violence, alcoholism, and other associated traits in criminal trials which belongs to a genetic basis but specific genotyping evidence has been introduced on an extremely limited basis (Lee, 2011; Butovskaya *et al*., 2013). Genes can strongly affect antisocial behavior and aggression affected. A psychosocial result in structural modifications in DNA from, that has profound influences on antisocial behavior outcome and hence neuronal functioning (Raine, 2002; Ahmed *et al*., 2014).

Rhee and Waldman (2002) recently reported a review of the majority of the twin and adoption studies on antisocial behaviors that have been carried out. The result was that a genetic background strongly influences an individual which engaged in an antisocial

behavior, while the environmental factors effect is even stronger. These results highlight the fact that even if individuals have a strong genetic predisposition, if they are not exposed to the necessary environmental factors. They may never engage in any antisocial behaviors.

Anholt and Mackay (2012) indicated a review on detailed information on the genetic determination of human aggressiveness. It is pertinent to note that the same genes as those revealed in experiments with animals are considered receptors and serotonin transporter, enzymes synthesizing and catabolizing catecholamine and catecholamine receptors.

The study of a large Dutch family reported in 1993 that the gene correct identification involved in human aggression. Mental retardation and inclination to violence showed from several men of the family, manifesting itself in impulsive violent acts, attempts at rape, arsons, and exhibitionism. Reduced activities of MAOA of these men resulted from a point mutation in exon 8 of the MAOA gene, which produced a termination codon (Kudryavtsevaa *et al*., 2015).

Human MAOA's location is at Xp11.23 (Levy *et al*., 1989) in psychiatric disorders and normal behavior several lines of evidence point to a role of MAOA (Wendlan *et al*., 2006). Brunner *et al*. (1993) identified an association between an impulsive aggression and mutation in MAOA. So that MAOA becomes the focus point of most genetic research on antisocial or criminal behavior.

Violence gene, the MAOA gene, also called the "warrior" (Widom *et al*., 2006). It is identified as a candidate susceptibility gene for aggressive behavior and schizophrenia (Cases et al., 1995). The Warrior Gene can be described as a variation of one enzyme monoamine oxidase A of a family of enzymes (monoamine oxidases). Monoamine oxidases, as a family, can break down various dietary amines and neurotransmitters such as serotonin, dopamine, and norepinephrine vital for normal mood regulation (Chen *et al*., 2004).

The 30 bp variable number tandem repeat (VNTR) shows variation in the MAOA gene which repeated 2, 3, 3.5, 4, or 5 times 1200 bp upstream of the actual MAOA sequence. Alleles with 3.5 or 4 VNTR's produce MAO 2-10 times more efficiently than those with 3 or 5 VNTR's, and those with the decreased levels of monoamine oxidase (this group of individuals with low levels of MAOA are referred to as MAOA-L) then exhibit unusually aggressive behavior when threatened or provoked (Sabol, 1998).

2. LITERATURE REVIEW

Many societies around the world consider violence as a crucial matter, especially for the systems that deals with criminal justice. By identifying genetic and neural correlates of emotional disturbances, impulsivity, personality and disorders aggressiveness, new insights into the nature of violent and criminal behavior over the last decades, have been provided from developments in cognitive behavioral genetics and neuroscience brain imaging modalities (Wahlund and Kristiansson, 2009). Such as positron emission tomography (PET) and, functional magnetic resonance (FMRI), suggested evidence that development of various forms of psychiatric diseases and overt antisocial and violent behavior are associated to the structural and functional alterations of specific brain regions (Raine,2008;Wahlund and Kristiansson, 2009).

Research in behavioral genetics provided strong evidence that the risk factors for the development of violence and other forms of psychiatric illnesses are specific genetic polymorphisms (Zuchner *et al*., 2007). For example, the low-activity alleles of the monoamine oxidase A (MAOA) gene have been associated with a significant volume reduction (i.e. 8%) in brain regions that are known to be altered in antisocial groups, such as the amygdala, the anterior cingulate cortex, and the orbit frontal cortex (Meyer-Lindenberg *et al*., 2006). MAOA was also found to be implicated in antisocial behavior in both animals (Cases *et al*., 1995) and humans (Caspi *et al*., 2002).

Dutch Kindred (1993) reported that several males showed a syndrome of borderline mental retardation and abnormal behavior, including disturbed regulation of impulsive aggression. Complete absence of activity of the enzyme monoamine oxidase A (MAOA) clearly detected among them, which breaks down many of the brain's key neurotransmitters. Moreover genetic analysis revealed that the affected men carried a mutation on the X chromosome in the gene that codes for MAOA. As intriguing as this

finding was, because of complete absence, it seems to be of limited import for a general understanding of genetic factors affecting violence, (Appelbaum, 2005).

In the socio-biological context, determined by; (1) Social environment, which can stimulates or inhibits aggression by producing motivation the main determinants of animal aggression affecting its manifestation, and (2) the biologic component of behavior, determining greater or lesser genetic predisposition of an individual to aggressive responses under provocative conditions regardless of species (Kudryavtsevaa *et al*., 2015).

Social factors and Cultural, environmental which make the shape of the manner in which it is expressed can influence violence (Eron, 1987). Nevertheless, it shows that there are specific neural substrates underlying different forms of aggressive behavior. There is a similarity between neural basis of human aggression animals neural bases such as in cat and the forms of aggression seen in humans parallel to those observed in animals. An expanding body of data is an indication of aggressive behavior appears as a component of numerous clinical disorders associated with including affective disorders, traumatic brain injury, complex partial seizures, schizophrenia, abnormal brain function, brain tumors, cerebrovascular disease, and encephalitis (Allan and Jeff, 2009).

To date, in US. Testimony depending on these research findings shows that criminal cases has been quite limited (Tiihonen *et al*., 2014). In May 2004, the faculty of Vanderbilt Forensic Psychiatry (a component of the Vanderbilt University School of Medicine Department of Psychiatry in Nashville, Tennessee) starts including genetic tests as part of their comprehensive pre-trial forensic psychiatric evaluation of defendants charged with homicide. As of February of 2006, this team has conducted MAOA and SLC64A genotyping on first-degree murders involved nine men and one woman charged. Since August 2005, this team has testified regarding MAOA and/or SLC64A genotyping of four defendants in U.S. criminal cases. In earlier unrelated cases, one criminal defendant sought MAOA testing, while several other defendants have introduced claims based on the levels of serotonin. (Farahanyn and Bernet, 2006) reported that there is

significant influencing the attitudes on court sentences in the US depending on this finding.

Recently a study using an enormous Swedish nationwide adoption database with a long follow up period found convincing evidence that both violent and nonviolent criminality among the adopted away children the criminal records can be predicted from biological parents. Two decades ago, it was observed that an impulsive and aggressive behavior was associated with rare mutation leading to a complete deficiency of monoamine oxidase A (MAOA) in Dutch kindred. So far, only two studies have reported an association between a specific gene and criminal violent offending (Tiihonen *et al*., 2014).

Waldroup brutally killed his wife's friend in 2006, and attempted to kill his wife during what the State characterized as Waldroup's intentional and premeditated actions spurred by a domestic dispute. Finally, Waldroup shot his wife's friend eight times and slit open her head, then moved on to attack his wife repeatedly with a machete. Waldroup's defense counsel requested that forensic psychiatrist William Bernet assess Waldroup, to discover that Waldroup possessed a particular variant of a very rare deficiency of mono amine oxidase A (MAOA). According to Bernet this deficiency when added to Waldroup's history of severe child abuse, resulted invulnerability that Waldroup would be a violent adult (Denno, 2011).

The impact of traumatic premature life events on the tendency to participate in violence as an adult among humans can be facilitated by Polymorphism in the MAOA gene. Particularly, adults with L-MAOA who had been abused were less likely to develop antisocial problems as children (Caspi *et al*., 2002; Caspi A. and Moffitt, 2006). Further studies shows that the threat of L-MAOA in combination with traumatic premature life events increases both psychiatric patients and healthy adult's tendencies toward physical aggression (Frazzetto, 2007).

Raine (2008) stated that the association of several candidate genes with impulsive aggression or disorders characterized by investigation. These include serotonin-related genes, catecholamine-related genes, and neuro modulator- related genes.

To date these genes are serotonin receptor (5-HTRs), serotonin transporter (5-HTT), monoamine oxidase (MAO), brain derived neurotrophic factor (BNDF), neural cell adhesion molecule (NCAM).

Monoamine oxidase A (MAOA) is an enzyme that metabolizes serotonin, dopamine and norepinephrine. MAOA became the focus of much genetic research on criminal or antisocial behavior because the study by (Brunner *et al*., 1993) identified an association between an impulsive aggression and mutation in MAOA. Although this relationship has not been confirmed outside the family examined in the original study, a number of studies on antisocial behaviors focused on MAOA. (Vanyukov *et al*., 1995) examined a dinucleotide repeat (DNR) polymorphism in the gene, but the result was no association with conduct disorder or aggressiveness. This negative result was reproduced by another study whose authors found an association between a variable numbers of tandem repeats (VNTR) polymorphism in MAOA and variation in impulsivity and aggression (Manuck *et al*., 2000). A recent study identified a relationship between MAOA and antisocial behavior (Caspi *et al*., 2002). The authors found that males with a low enzyme-activity genotype, maltreated during childhood, were more likely to develop CD and be convicted of a violent crime than maltreated males with a high-activity genotype.

2.1. The Monoamine Oxidase A (MAOA) Gene and polymorphism

Grimsby *et al*. (1991) stated that human MAOA gene was isolated from X-chromosome specific libraries spanning at least 60 kb. These genes consist of 15 exons (Figure 2.1). One of the intriguing examples of a gene associated with criminality on the basis of a study of a single family is the monoamine oxidase A (MAOA) gene on the X chromosome.

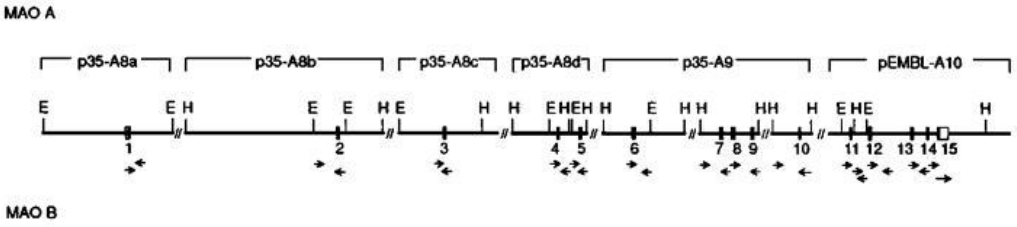


Figure 2.1. Partial structural map of the monoamine oxidase (MAO) A gene showing the location of exons. (Filled bars) coding regions; (unfilled bars) untranslated regions of the exons. Exon numbers are below the bars (horizontal arrows). The regions sequenced (vertical arrows; Grimsby *et al*., 1991)

Among several generations, male members of a Dutch family had committed various criminal acts like raping a sister, attempting to run over another man with a car and stabbing a man with a pitchfork. While there are no records of such behaviors among other males in the family line A complete absence of activity of the enzyme MAOA was found in the aggressive males, which is responsible of breaking down many of the brain's key neurotransmitters. Genetic analysis stated that the affected men carried a mutation on the X chromosome in the gene that codes for MAOA (Figure 2.2 and 2.3). The production of the enzyme in brain cells stopped by the mutation. However, a total absence of MAOA activity is so unusual that this finding seemed to be of limited import for a general understanding of genetic factors affecting violence (Kudryavtseva *et al*., 2015).

The expression of monoamine oxidase A is regulated by the MAOA gene, an enzymatic protein that breaks down important neurotransmitters in the brain, including dopamine, norepinephrine, and serotonin (Brunner *et al*., 1993).

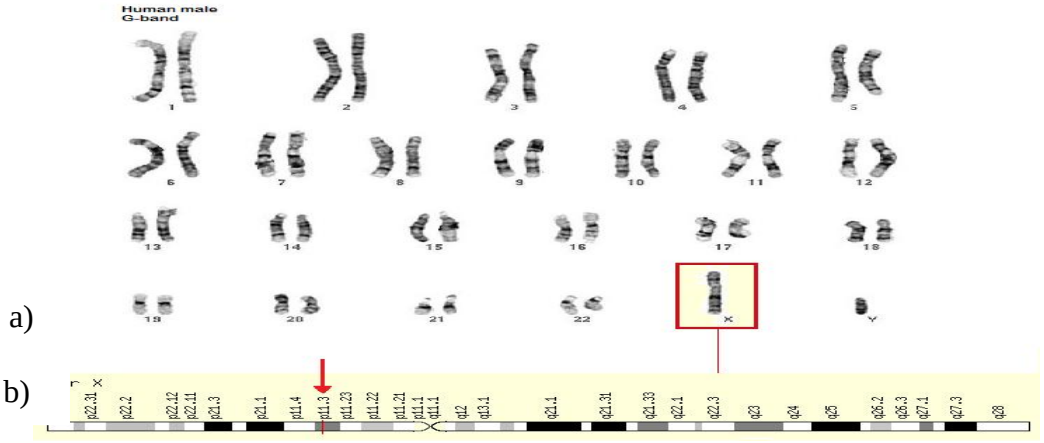


Figure 2.2. a) Karyotype of whole chromosome of human; b) X-chromosome of human (Brunner et al., 1993)

Symbol:	MAOA
Full name:	Mono amine oxidase A
Location:	Xp11.3
Organism:	Homo sapiens
Gene type:	protein coding
Gene length:	156040895 bp

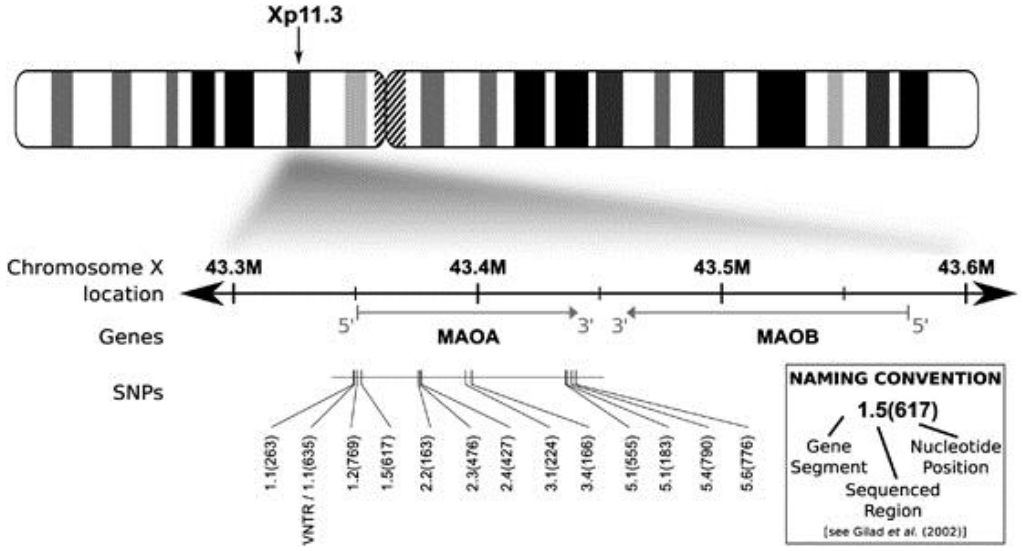


Figure 2.3. A Section of chromosome X, showing the relative positions of the MAOA and MAOB genes, and mutations typed in this study. Labels for each mutation refer to the segment, region and nucleotide position as per

DNA polymorphisms in the structural and regulatory region of MAOA gene result in influencing transcriptional activity (Pai, 2007). There are different forms of the MAOA gene in human's cells, there is a 30-base sequence that exists in 2, 3, 3.5, 4, or 5 repeats at around 1.2 kb upstream of the MAOA coding sequences, which affects transcriptional activity of the MAOA gene promoter. It was found that furthermore, alleles with 3.5 or 4 repeats (high-activity form; H-MAOA) are transcribed 2 to 10 times more efficiently compared to alleles with 3 or 5 repeats (low-activity form; L-MAOA),the study that did not include the 2 repeats variant (Sabol and Hamer, 1998).

Depression is linked to H-MAOA while aggression is associated with L-MAOA. Recent studies also showed that the 2 repeats allele is associated with an increase in the likelihood of committing serious crime or violence (Guo, 2008). In addition, suicide victims with depressive disorder show that the activity of MAOA increased, results in increasing of the hypothalamus of the brains (Sheriff, 1991). The healthy male subjects that used as healthy subjects by contrast, male carriers of the high activity alleles (3R and 5R) in the community, showed a greater responsiveness to serotonin in the central

The MAOA uVNTR polymorphism can be identified as a genetic factor that can modulate the risk for suicide, depression, or both by influencing monoaminergic activity in a sexually dimorphic manner. However, few studies show poor information about whether the MAOA uVNTR polymorphism confers suicidal behavior or vulnerability to major depressive disorder (MDD) for the Han Chinese population in Taiwan (Lung, 2011).

Moreover, the study tested the relationship between the MAOA polymorphism and individual differences in the gray matter volume of limbic regions and in the responses of these regions to emotional stimuli, specifically negative emotional faces (Meyer-Lindenberg *et al.*, 2006), compared with MAOA-H, MAOA-L individuals showed reduced gray matter volumes in limbic regions such as the dorsal anterior cingulated cortex (dACC), amygdala, and subgenual ACC and greater amygdala and subgenual ACC activity to negative emotional faces. Although this study represents an advance in understanding how the MAOA uVNT polymorphism relates to affective processing, but it did not examine self-reports or behavioral assessments of aggression. Moreover, because the affective stimuli used in this study, namely pictures of negative emotional expressions,

are not likely to elicit full blown emotions, it is difficult to know how the actual emotional responses to negative events relates to MAOA polymorphism. Moreover the study examined the MAOA polymorphism related to trait aggression as well as how it related to neural responses to a negative socio emotional experience that has been shown to elicit real negative feelings, specifically an experimental episode of social exclusion (Williams *et al*., 2000, Eisenberger *et al*., 2007)**.**

Recently it had been reported that a functional VNTR polymorphism in the MAOA promoter region (MAOA-LPR) associated with aggression. Sjoberg *et al*. (2008) carried out his study on 45 controls and 95 unrelated male criminal alcoholics indicated that the MAOA-LPR genotype and cerebrospinal fluid (CSF) testosterone interact to predict aggressive behavior and antisocial. The results reinforce the notion that the MAOA

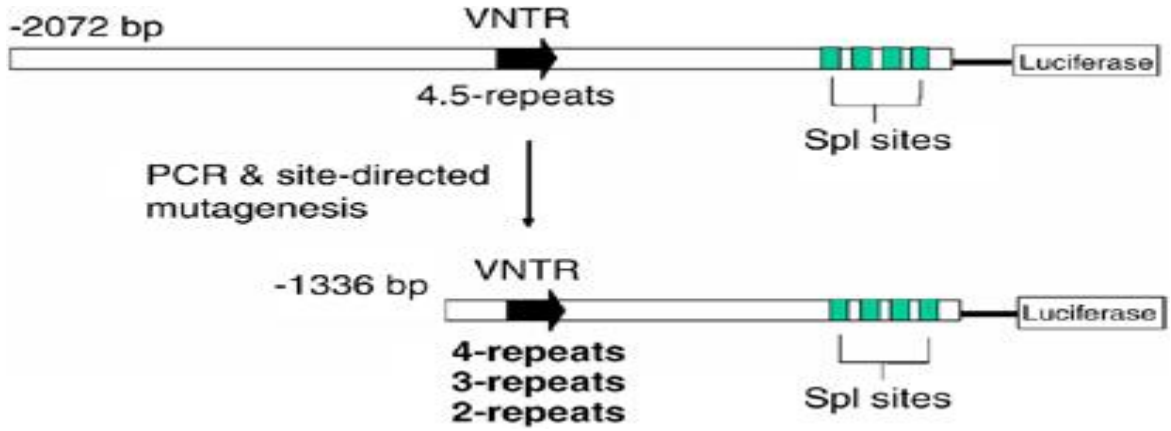


Figure 2.4. The human MAOA promoter-luciferase constructs. The MAOA 1.3 kb promoter containing 2, 3, and 4 repeats were generated by PCR and site-directed mutagenesis using MAOA 2 kb promoter luciferase reporter gene vector as a template (Guo, 2008)

The observation of Methylation pattern was used in the promoter region of the MAOA gene (Figure 2.4) (Pinsonneault *et al*., 2006), the manifestation of aggressive behavior may be enhanced by reducing transcription rate of this gene. Thus, the detection of effects of epigenetic mechanisms on the control of aggressive behavior opens up a new line of inquiry (Kudryavtsevaa *et al*., 2015).

2.2. Monoamine Oxidase (MAO)

Mood and behavior can be affected by neurotransmitters monoamines (serotonin, dopamine, adrenaline, noradrenaline, histamine), as well as violence, impulsivity and aggression is connected to awakens, memory and sexual drive and several lines of evidence suggested that serotonin deficiency (Davidson, 2000). Thus, numerous candidate genes have been researched in association with aggressive traits, including genes involved in dopamine metabolism (DRD2, DRD4, DAT1), serotonin metabolism (5-HTT, TPH), and enzymatic degradation (MAOA, COMT) (Teodorovic, 2015).

Monoamine oxidase (MAO), the enzyme responsible for metabolism of monoamine neurotransmitters, has an important role in the brain development and function, and MAO inhibitors have a range of potential therapeutic uses. In addition, the *in vitro* effects of pharmacologically different antidepressants and mood stabilizers on MAO activity were investigated (Zdenke, 2011).

The monoamine hypothesis postulates that a deficiency of monoamine neurotransmitters, norepinephrine and serotonin, 5 hydroxytryptamine at key sites in the brain caused depression. MAOA act as antidepressants by blocking of enzyme that degrades monoamine neurotransmitters; tricyclic antidepressant act as antidepressants by blocking membrane transporters ensuring reuptake of serotonin, 5 hydroxytryptamine or norepinephrine, thus causing increased extracellular neurotransmitter concentrations. But the monoamine hypothesis of depression in itself could neither explain the whole mechanism of action of antidepressants, nor could it provide an explanation for how monoamine loss occurs (Meyer *et al*., 2006).

According to advanced monoamine theory serotonin or norepinephrine levels in the brain are regulated by monoamine oxidase type A (MAO-A) activity mainly (Meyer *et al*., 2006). Also greater metabolism of monoamines in the brain resulted from MAO-A density is elevated, during a major depressive episode. However, severity of symptoms of depression is related to changes in the activity of monoamine transporters in specific brain regions So that the pathophysiology of affective disorder include both MAOA activity and density of transporters (Zdenek, 2011).

3. MATERIALS AND METHOD

3.1. Materials

3.1.1. Equipment: Equipments used in this study are given on Table 3.1.

Table 3.1. Utilized instruments, brands and manufactures

Equipment's	Brands	Origin
Laminar air flow hood	Bioquel	UK
Incubator	Binder	Germany
Water bath	Thermostatic	Taiwan
Water distillatory	GFL	Germany
Magnetic stirrer	Stuart	UK
Oven	Binder	Germany
Sensitive balance	Sartorius	Germany
Nano Drop Spectrophotometer	Thermo Scientific	USA
Micropipettes	Eppendorf	Germany
Eppendorf tube	Eppendorf	Germany
Centrifuge 13500	Gall encamp	UK
Autoclave	Binder	Germany
UV-Documentation	IVB	Germany
Gel electrophoresis instrument	GFL	Germany
PCR system (Polymerase Chain Reaction)	Eppendorf	Germany

3.1.2. Chemicals: Chemicals and compounds used in this study are given on Table 3.2.

Table 3.2. Utilized chemical material brands and manufactures

Chemicals	Brands	Origin
Genomic DNA (High Pure PCR Template Preparation Kit) (Blood/Culture cell)	Roche	Germany
Isopropanol	Merck	Germany
Agaros (Analytical Grade)	Cinna Gen	Iran
TBE Buffer 10X	Cinna Gen	Iran
Safe Stain	Cinna Gen	Iran
Primer	Macrogen	Korea
Taq 2x Master Mix Red, 1.5mM $MgCl_2$	Ampliqon	Denmark
DNA Ladder	Thermo Scientific	USA

3.1.3. Source of Blood Samples

Table 3.3. Source of blood samples

Number of blood	Prisoners age	Prisoners education level	Marital status
1B	33	Primary	Single
2B	25	Primary	Married
3B	22	Primary	Married
4B	35	None education	Married
5B	44	Primary	Married
6B	53	Secondary	Single
7B	33	Primary	Married
8B	33	Primary	Married
9B	32	Secondary	Married
10B	42	Primary	Married
11B	34	Primary	Married
12B	27	Primary	Married
13B	26	Primary	Single
14B	55	Secondary	Single
15B	37	Primary	Married
1A	37	Primary	Married
2A	39	Secondary	Married
3A	44	Secondary	Married
4A	34	Secondary	Married
5A	27	None education	Married
6A	41	Primary	Married
7A	31	Primary	Married
8A	39	Primary	Married
9A	31	Primary	Single
10A	27	Secondary	Married
11A	21	Secondary	Married
12A	44	Secondary	Married
13A	34	Secondary	Married
14A	28	Secondary	Married
15A	45	None education	Married

3.2. DNA Study

The study has been done to determine mutations in Exon 8 of MAOA gene (Brunner *et al*., 1993). Main steps of the study are shown in Figure 3.1.

3.2.1. Sample Collection

For this study, blood sample from 30 prisoners with aggressive behaviour and 5 control group were collected in sterile condition using 1-2 ml injector from blood vessel. As soon as collection of blood samples brought to the laboratory and kept in fridge at (-20˚C).

The study group included 30 males belonged to the age group of 21 to 60 years in prison in Erbil City between December 2015 to January 2016. Peripheral blood was also obtained from 5 healthy people as controls. Each cases was providing with a questionnaire from which includes information about (name, age, location, crime type, educational level, and married state).

3.2.2. Blood Sampling

Total 35 blood samples collected from 30 prisoners plus 5 control group. Three ml of blood from both case and control groups are collected from their veins using a disposable syringe and transferred into sterile EDTA tubes then transmitted to the laboratory at the same day using ice box container, then stored at -20˚C.

3.2.3. DNA Extraction

DNA extracted from 20 blood samples included 18 samples of prisoners and 2 from control group. Genomic DNA was extracted from whole blood by using a sterile disposable syringe from vein of study. Approximately 1-2 ml of blood was taken from each donor by sterile syringe and placed in to EDTA tubes that contain anticoagulant per manufactures instruction with patient number, age and date of collection written on the tube and stored at -20˚C.

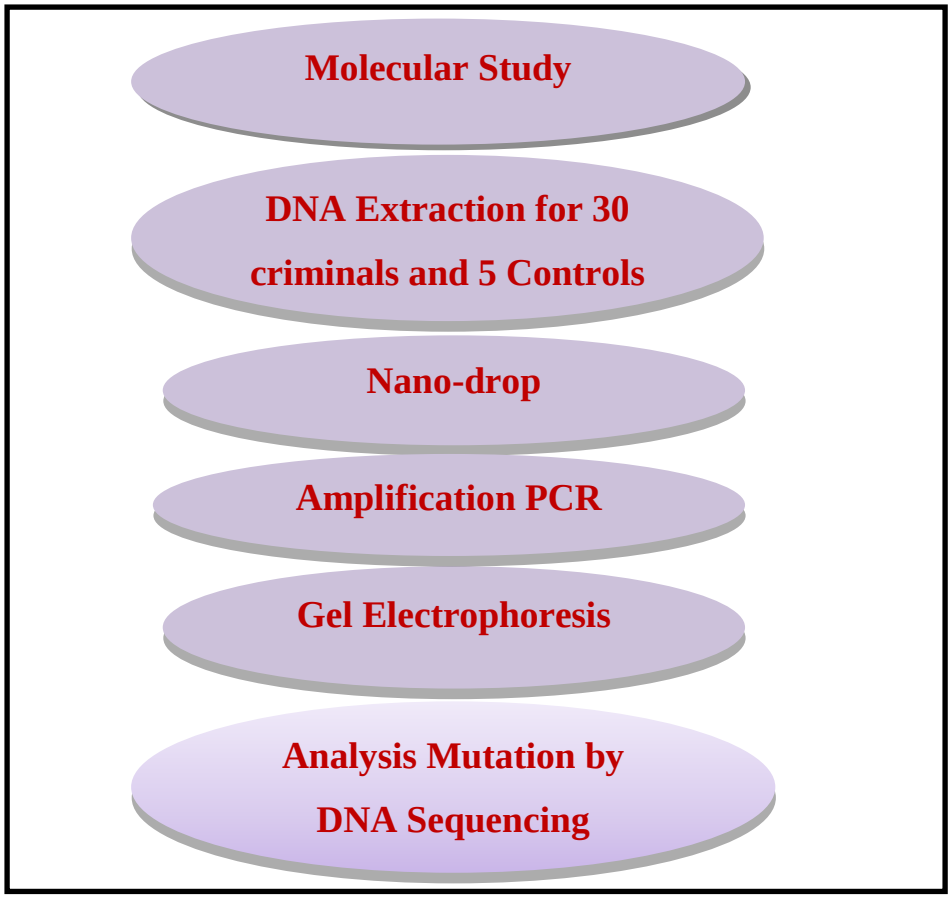


Figure 3.1. Stage of molecular study of MAOA genes (exon 8)

3.2.4. Protocol for DNA Extraction From Whole Blood Sample Using Genomic DNA Extraction Kit (Gene Aid Company)

1. 300 ul of blood transferred in to 1.5 micro centrifuge tubes.
2. 3x of the sample volume (900 ul) of RBC lysis buffer added to the blood, then vortex.
3. The mixture incubated for 10 min at room temperature.
4. Centrifuge for 5 min at (6688 rpm) then supernatant removed completely.
5. 100 ul of RBC lyses buffer added to the tube to the leukocyte pellet then proceed with lyses.
6. 200 ul of GB buffer added to the 1.5 ml centrifuge tube then shake vigorously.
7. The mixture incubated at 60˚C for at least 10 min to ensure the sample lysates clear.
8. During the incubation, the tube inverted every 3 min.

9. 200 ul of absolute ethanol added to the lysate then immediately mixed by shaking vigorously for 10 min.
10. GD column placed in a 2 ml collection tube.
11. The mixture transferred in the GD column.
12. Centrifuged at 14000 rpm for 5 min.
13. The 2 ml collection tube discarded the GD column placed in a new 2 ml collection tube.
14. 400 ul of W1 buffer added to the GD column then centrifuged at 14000 rpm for 30 to 60 second.
15. The flow-through discarded then the GD column placed back in the 2 ml collection tube.
16. 600 ul of wash buffer added to GD column.
17. Then the mixture centrifuged at 14000 rpm for 30 to 60 second, after the flow-through discarded.
18. The GD column placed back in the 2 ml collection tube.
19. The tube centrifuged again (without adding anything) for 3 min to dry the column matrix.
20. The dried GD column transferred to a clean 1.5 ml micro centrifuge tube.
21. 100 ul of pre-heated Elution buffer added the centre of the column matrix.
22. Let the mixture for at least 3 min to ensure that the Elusion buffer was completely absorbed.
23. After that centrifuged at 14000 rpm for 30 second to elute the purified DNA.
24. Finally the yield transferred to a new sterile labelled tube.

3.2.5. Quantitative Analysis of the Extracted DNA

Analysis of DNA quantity and purity was performing using a nanodrop-spectrophotometer (Nanodrop-Thermo Scientific. UK) This instrument measures the light absorbance (A) at specific frequencies, within the diluted DNA sample a wavelength 260/280 nm. Absorbance was measured at wavelengths of 260 and 280 nm. The absorbance value of 1.8< ratio (R) <2.0 was considered to be good for purified DNA (Ghatak *et al*., 2013).

According to nanodrop results the A 260/280 ratio was generally around 2.1 and 1.8 respectively (Stephenson, 2010).

3.2.6. Design of Primer

Two pair of primers of DNA sequence MAOA and Exon 8 were designed (Online primer design program http://www.nlm.nih.gov/tool/primer-blast was employed). The sequences of the forward and reverse primers were employed.

The MAOA gene (exon 8) were screened for mutation by PCR amplification and direct DNA sequencing, to screen mutation in MAOA gene Exon 8 was PCR amplified from genomic DNA using primer sets shown on Table 3.4. PCR amplified was performed in 50 µl reaction volume containing 2 µl of genomic DNA, amplification buffer containing 1 µl of each primer and 25 µl Taq 2x Master mix.

Table 3.4. Sequence of the primers used for MAOA Exon 8 amplification

Primer Name	Primer Sequence	Primer length (bp)	Tm	GC%	Product Length (bp)
MAOA Exon 8	Forward 5'TGCAAATACGTAATTAA TGCGATCC-3 Reverse: 5'TCCAGAAGGCCTCCTTG TAAT-3	25 21	59.39 57.02	60.00 50.00	151

The Polymerase Chain Reaction: PCR is a rapid technique for *in vitro* amplification of a specific DNA fragment by use of two short single stranded primers flanking this segment. The component of PCR reaction and their quantities in 50 µl total volume. The PCR reaction was done in a sterile 0.5 ml tube, the reaction mix was made in the following order (Yang *et al*., 2007; Dollynee *et al*., 2000).The thermo cycling program was set to run 35 cycles according to the following parameters as indicating in below (Dollynee et al., 2000).

Table 3.5. The component of PCR reaction and their quantities in 50 µl total volume

Component	Vol./ reaction
Taq 2x Master mix	25 µl
Forward primer (10µM）	1 µl
Reverse primer（10µM）	1 µl
Template DNA	2 µl
Sterile water	21 µl
Total volume	50 µl

3.3. Agarose Gel Electrophoresis

Agarose gel electrophoresis adopted to the extracted genomic DNA to detect the presence of the genomic matter. Amplification and the band sizes of all the PCR reactions were confirmed by visualizing products on a 1% (w/v) gel as following;

Table 3.6. Condition of gradient PCR reaction for MAOA gene (exon8)

PCR step	Temperature (C)	Time
Initial Denaturation	94	4 min
Denaturation	94	30 sec
Annealing	56,5	30 sec
Extension	72	30 sec
Final Extension	72	2 min
Hold	4	0.00 min
Cycle number.	35	Cycle

1. A glass board with suitable dimension of gel electrophoresis tank was prepared. The edge of board was surrounded by strong tap in which a special comb was fixed to make wells in one side of the gel.

2. Agarose was made in 2% by dissolving one gram of agarose in 10 ml of 10x TBE buffer and the volume completed to 100 ml of distilled water and boil continuously with striking then left to cool to 55°C.
3. The formula was poured gently, continuously and quiet and left to solid, the tip and comb were removed and immersed the gel in 1x TBE solution, the gel was put in electrophoresis tank which contain 1x TBE buffer.
4. Sample of DNA (7 ul) were mixed with (2 ul) loading dye buffer and added to the gel wells (Albrts *et al*., 2002; Sulaiman, 2013).

3.3.1. Running the Gel

The lid of the gel apparatus with the adjoining electrophoresis were attached making sure that the negative one is on the same side as the wells. For a better resolution power supply of 45 volts was applied for 15 minutes until the DNA left the wells and moved towards the positive electrical, then the voltage was increased to 135 volts and the electrophoresis was allowed to proceed for sufficient time usually between 70-80minutes; (Sambrook and Russell, 2001).

After electrophoresis completed the gel was put in bath contain Ethidium bromide to staining for 40 to 60 minutes, by immersing the gel in distilled water containing the dye of a final concentration 0.5 mg/ml, DNA band were visualized by UV illumination at (240-366 nm) wave length on UV trans illuminator (Sambrook and Russell, 2001).

3.4. PCR Product Sequencing

PCR products are analysed by a 96 capillary automated sequencer (Applied Bio systems 3500 Series Genetic Analysers) based on the Sanger method. The sequence was done in the Genomics Institute at Tehran.

3.4.1. Sequencing Reaction System

Cocktail of sequencing reaction are given on Table 3.7.

Table 3.7. Sequencing reaction mixture of exon 8 of MAOA gene

DNA (Purified PCR product)	3 µl（30-50 ng）
Primer (3 pM)	1 µl
Big dye	0.5 µl
ddH2O	0.5 µl
Total	5 µl

3.4.2. Sequencing Reaction Mixture of Exon 8 of MAOA Gene

Cocktail of sequencing reaction are given on Table 3.8.

Table 3.8. Sequencing reaction procedure MAOA gene exon 8

PCR step	Temperature	Time
Initial Denaturation	95˚C	2 min
Denaturation	95˚C	10 sec
Annealing	55.45˚C	10 sec
Extension	60˚C	190 sec
Final Extension	12˚C	Forever
Hold	4˚C	0.00 min
Cycle number	25	Cycle

4. RESULTS

4.1. Analysis of Crimes Comparing to Age, Married state and Education levels

The relation between age and crime of blood samples of 30 prisoners are shown on Figure 4.1. Our results show that the rate of offending crimes were declined sharply with age. The highest crimes found in the age of 31 to 40.

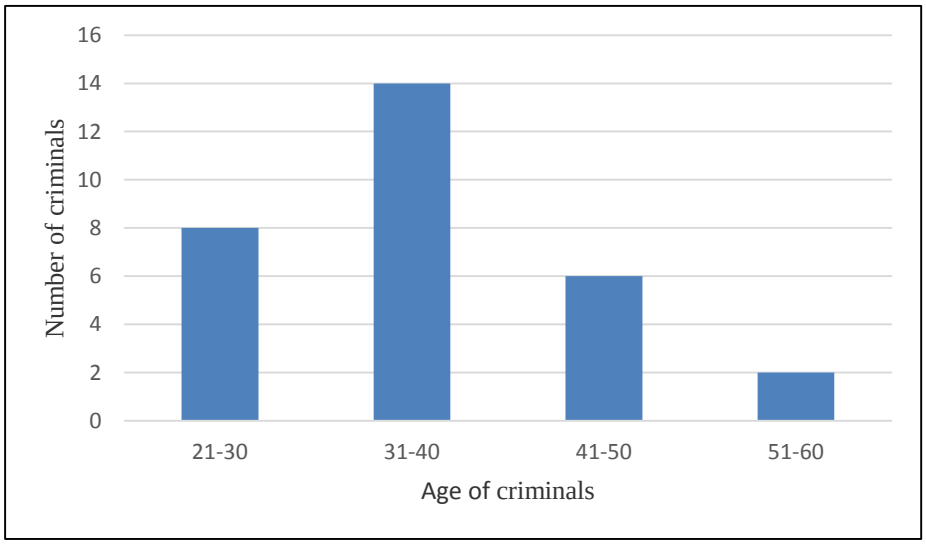


Figure 4.1. Shows the relationship between age and crime

Age also makes a difference in criminal behavior. Offending rates are highest in the late teens and early twenties and decline thereafter. More to the point and as Shoemaker (2010) argues that there are three major factors play an important role for this sort of crime and criminal behavior. First, peer relationships matter more during this time of one's life than later, and peers are also more likely during this period than later to be offenders themselves. For both reasons, the peer relationships during the teens and early twenties are more likely than those in the later years to draw us in to crime. Second adolescents and young adults are more likely than older adults to lack full-time jobs.

For this reason, they are more likely need money and thus to commit offenses to obtain money and other possessions. Third, at the early twenties, the ties to conventional society increase (Shoemaker 2010). Generally speaking, when people got married and have children, and get a full-time employment, they become more reasonable and wise. These events and bonds increase our stakes in conformity to use some social science jargon, and thus reduce the desire to break the law (Laub *et al*., 2006).

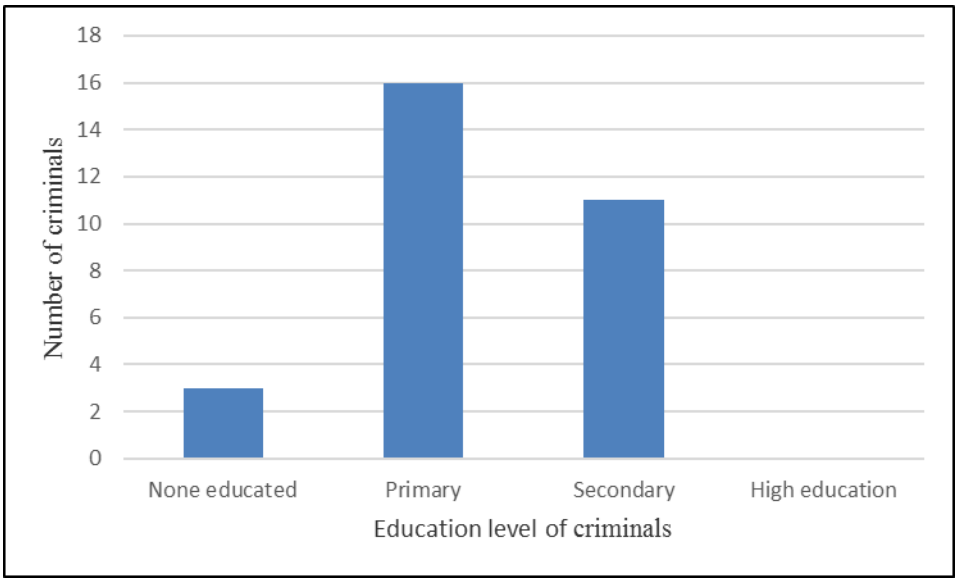


Figure 4.2. Education level and crime

Another aspect of our finding is the correlation between education and offending. It's evident that the majority of the samples chosen are not very educated as 16 cases (53%) of them holds primary school qualifications. Many had regularly truanted from school and school levels hold secondary school qualifications, as it's seen in Figure 4.2.

There is an important link between offending and education which has been found in many empirical studies (Rutter 1979; Thornberry *et al*., 1985). Focusing on the importance of completing school, Lochner (1999) found that high school graduation reduced criminal participation among young males in the USA, even after differences in ability were controlled for. He also reported that young male high school graduates were 30% less likely to earn an income from crime than those who did not graduate.

Moreover, high school graduation reduced the probability of being arrested by around 60% and incarceration by between 85 to 95%. In the UK, Farrington *et al* (1986) found offending was slightly lower amongst youths still at school. Perhaps more importantly, education allows children to develop skills and acquire knowledge and training which will affect their future success in life. Their ability to communicate and forge relationships, their post compulsory educational choices, the jobs they will get and the wages they will receive over the life cycle potentially depend on the skill formation and human capital accumulation whilst still at school.

There are many reasons to believe that education can reduce criminal activity. First, schooling increases the returns to legitimate work, raising the opportunity costs of illegal behavior. Additionally, punishment for criminal behavior often entails incarceration. By raising wage rates, schooling makes any time spent out of the labor market more costly. Second, schooling may directly affect the financial or psychic rewards from crime itself. Finally, schooling may alter preferences in indirect ways, which may affect decisions to engage in crime (Lance and Enrico, 2004).

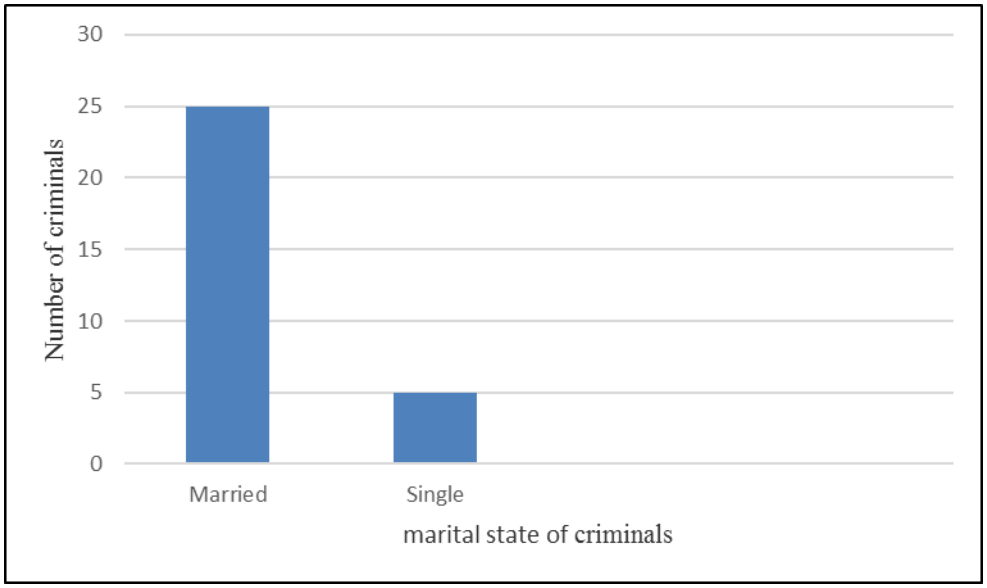


Figure 4.3. Shows the relationship between marital status and crime

Regarding the relationship between marital status and crime as shown in Figure 4.3, the number of crime among married status were higher than the single, 25 (83%) were

married and 5 (17%) were single. The relation of marriage with crime among men has been widely reported in both quantitative and qualitative studies. First, a change in criminal behavior may occur in response to the attachment or social bond that forms as a result of marriage. This notion reflects a classical social control or "social bonding" perspective (Hirschi, 1969) wherein the social relationship of marriage is important because it creates interdependent systems of obligation, mutual support, and restraint that impose significant costs for translating criminal propensities into action (Sampson and Laub, 1993). A second reason, marriage might influence desistance because it leads to significant changes in everyday routines and patterns of association with others. It is well obvious that lifestyles and routine activities are a major source of variation in exposure to crime and victimization. Consistent with this theme, Osgood and colleagues (1996) showed that unstructured socializing activities with peers increased the frequency of deviant behaviors among those ages 18 to 26. Marriage has the potential to change such routine activities, especially with regard to deviant peer groups.

According to Skoczylas and Binczycka (2005), the most common risk factors for violence among children and adolescents include improper parental conduct, failures at school, health-threatening behaviors, violent scenes seen by young people in television programs and films (Skoczylas and Binczycka, 2005). It is important to ask about the reasons why teenagers begin to use violence and derive satisfaction and pleasure from the suffering and humiliation of others. The major causes of the aggressive behavior stem from the unfavorable family environment, unhealthy peer group, unsatisfactory attitude regarding educational institution and rigid behavior regarding religious sect. More to the point, the unsatisfactory relationships with peer group have been found a more significant factor in causing aggression among youth (Imtiaz *et al*., 2010).

4.2. Study of Patients having Aggressive Behavior and Mutation MAOA Gene in Exon 8

A key objective of my study was to investigate the association between mutation of exon 8 MAOA gene and aggressive behavior in criminals, to determine mutation in Exon 8 of MAOA gene, the DNA extracted from 30 criminals and 5 normal persons age group of

20-60 years in Erbil city. Analysis of DNA quantity and purity was performing using a nanodrop-spectrophotometer (Nanodrop-Thermo Scientific. UK).

The sample genomic DNA was amplified by Polymerase Chain Reaction (PCR). PCR conditions were standardized. The amplified PCR product was checked on 2% agarose to verify the amplification of target region. The amplified sizes were estimated at 151 bp for exon 8.

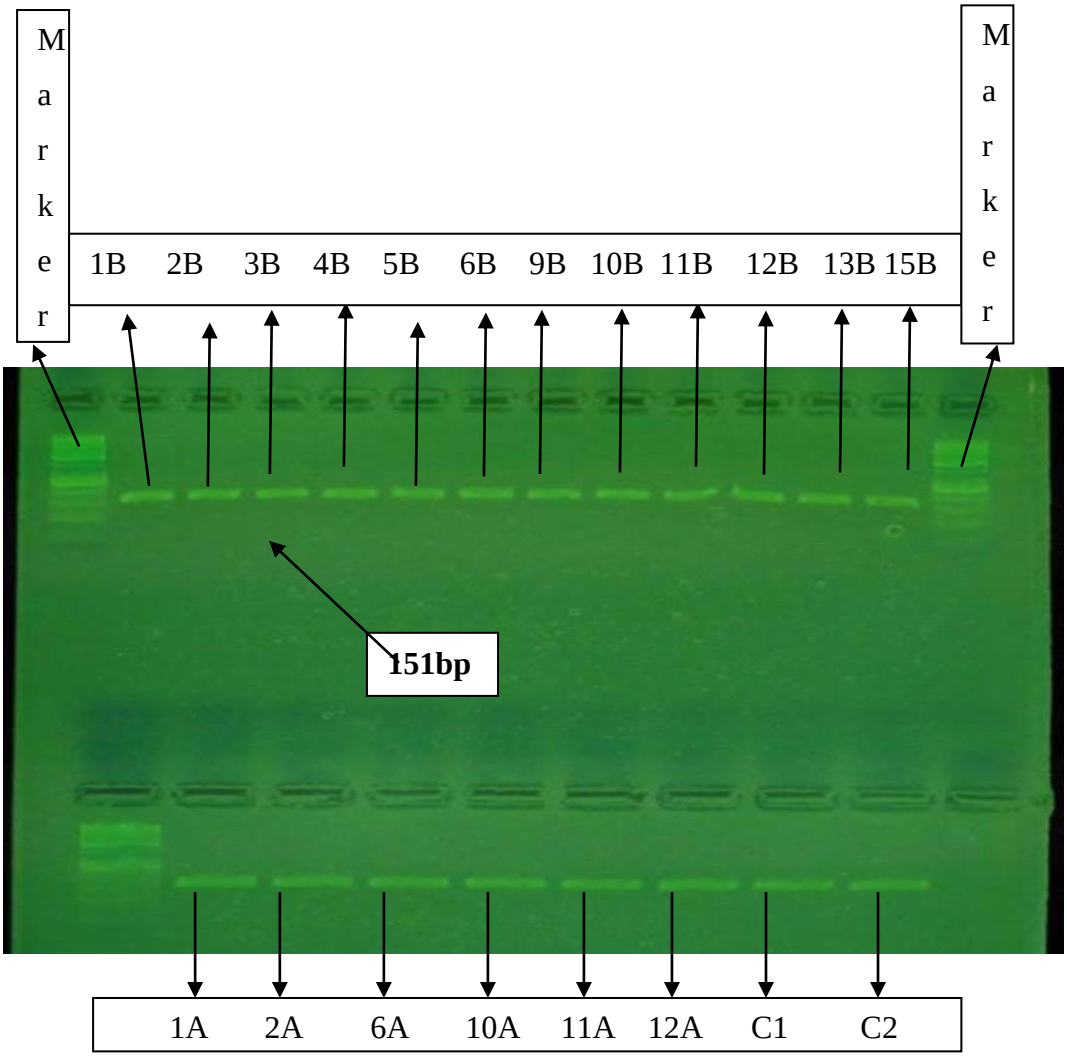


Figure 4.4. 2% agarose gel showing amplified PCR product of Exon (D=8) length product exon arrows point to 151 brands (8=151)

Cycle sequencing reactions were performed using MAOA gene exon 8 primers then; finally the coding DNA sequence of MAOA gene was aligned with the reference

sequence using the Sequence Finch TV Software Program. We observed two mutations substitution and insertion.

Sequence analysis revealed 3 SNPs in the coding (exonic) region of MAOA gene given on coding DNA Sequences of exon 8 MAOA gene were conceptually translated and compared with those of MAOA gene reported sequences (NCBI Accession number EU 386358, Table 4.1.). At position 2326 nt of exon 8, only one SNP (G to T) has been identified which has resulted in a substitution of lysine to asparagine in case of 1B, 5B, 6B, 8B, 9B, 10B, 11B, 15B, 1A, 2A, 11A and 12A caused Missense mutation. Exon 8 of cases 2B, 4B, 12B, 13B, 6A, and 10A did not show any change in base sequence. However, a total of 3 SNPs have been identified in exon 8 case of 3B. At position 2326 nt of exon 8, SNP (G to T) has been identified which has resulted in a substitution of resulting in a lysine to asparagine exchange in codon 32, and G to C transversion at nucleotide position 2276 resulting in a arginine to arginine exchange in codon 15 caused nonsense mutation and insertion (C) at position 2301 leading frame shift and a premature stop codon or protein truncation.

A number of control individual C1 and C2 were also screened for mutations. The sequence analysis confirmed that no mutations had gone and all samples were mutations free and sequencing showing the normal wild type sequence in MAOA gene exon 8 and the DNA sequence that obtain from NBCI website.

Table 4.1. SNPs identified in MAOA gene (Exon 8)

Region	Position	Base change	Amino acid substitution
Exon 8	2326	G–T	Arginine to Arginine
	2276	G-C	lysine to Asparagine
	2302	Inse (C)	frame shift change all amino acid

4.3. Sequence Change of MAOA Gene Exon 8 on Chromosome X

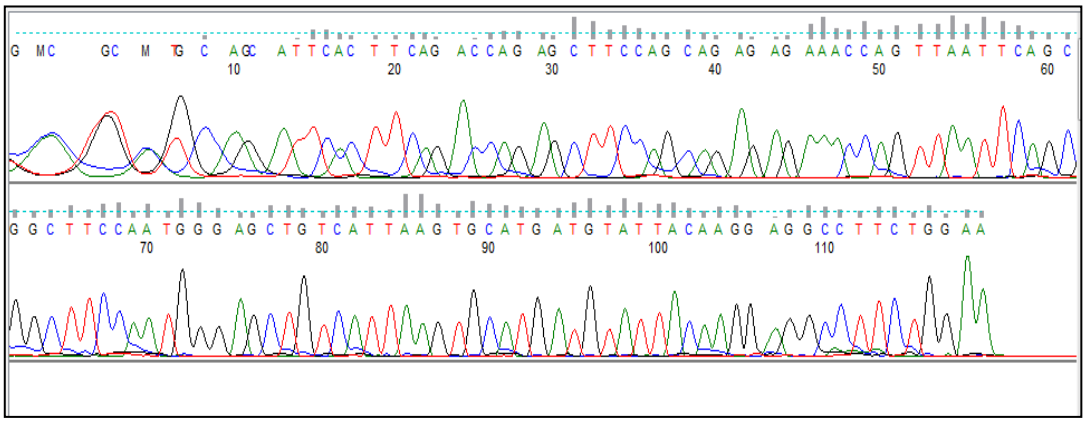
A

2221 acattatgagtgcaaatacgtaattaatgcgatccctccgaccttgactgccaagattca
2281 cttcagaccagagcttccagcagagagaaaccagttaattcagcggcttccaatgggagc
2341 tgtcattaagtgcatgatgtattacaaggaggccttctggaagaagaag

B

2221 acattatgagtgcaaatacgtaattaatgcgatccctccgaccttgactgccaacattca
2281 cttcagaccagagcttccacgcagagagaaaccagttaattcagcgtcttccaatgggagc
2341 tgtcattaagtgcatgatgtattacaaggaggccttctggaagaagaag
(a, normal sequence b, different SNPS and Amino acid)

21-C1



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Query 73    GGAGCTGTCATTAAGTGCATGATGTATTACAAGGAGGCCTTCTGGAA 119
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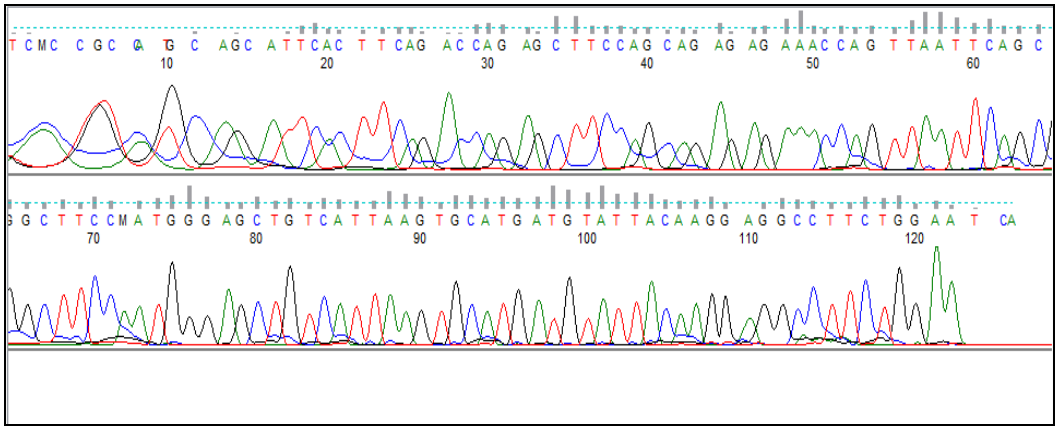
24-C2



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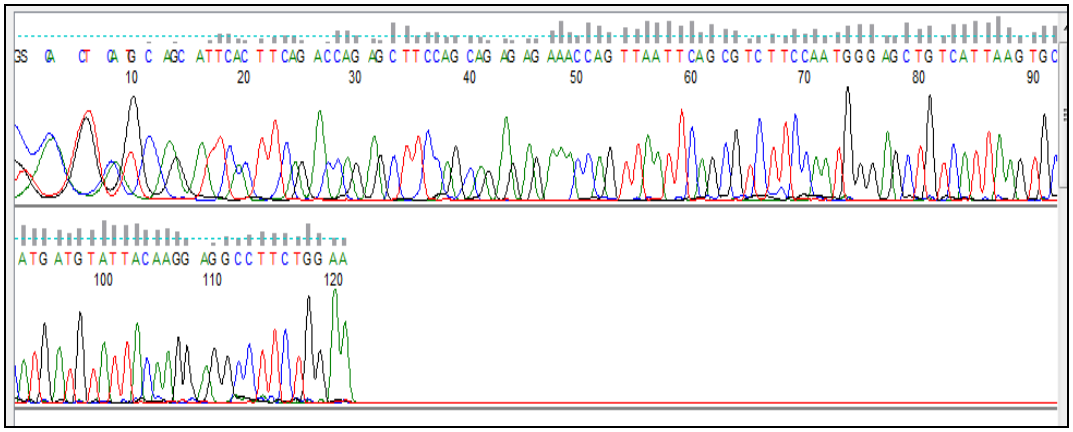
1B



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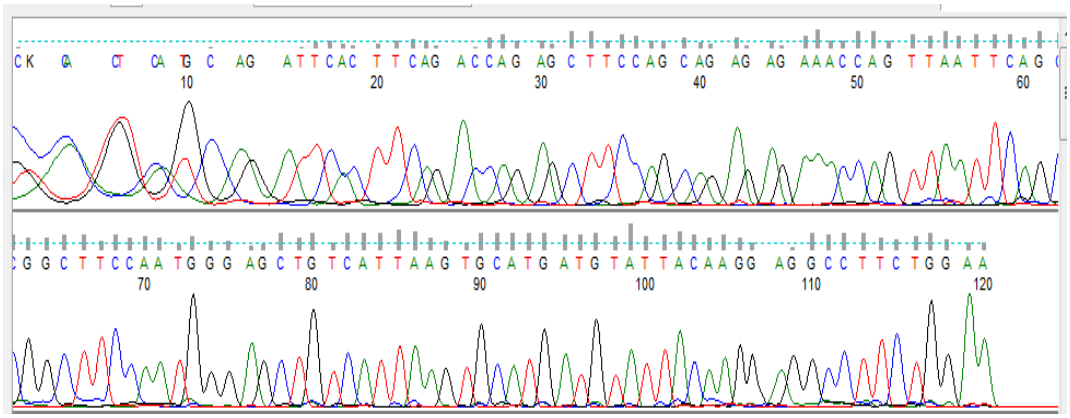
2B



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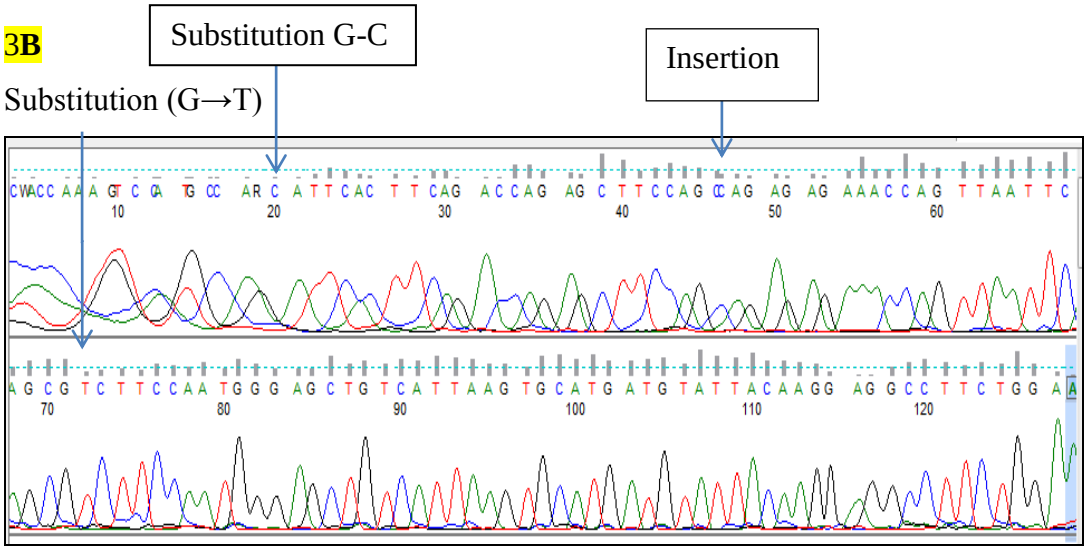
3B

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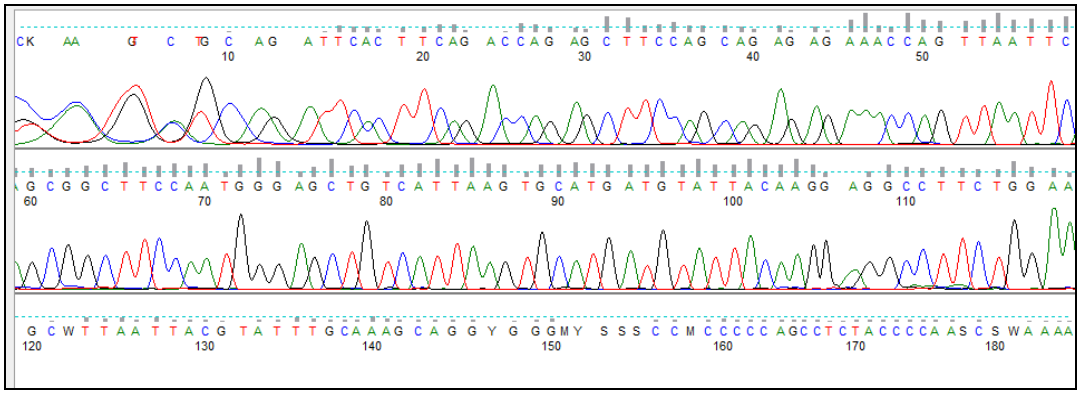
4B



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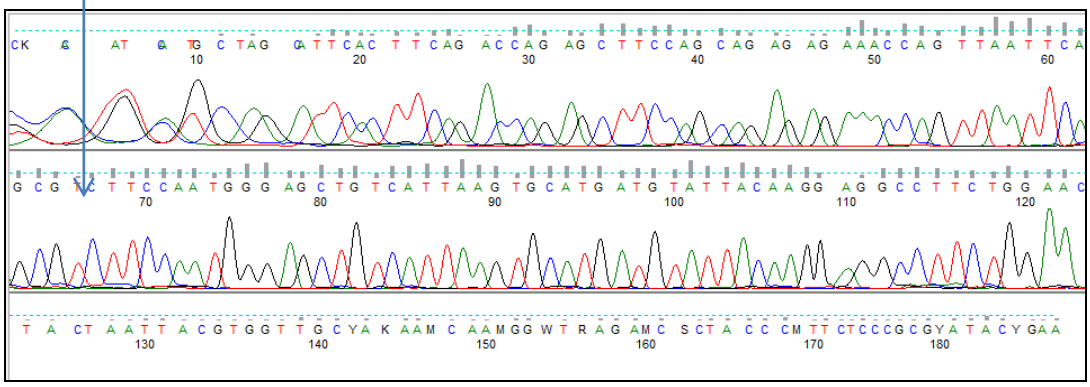
```

5B

Substitution (G→T)



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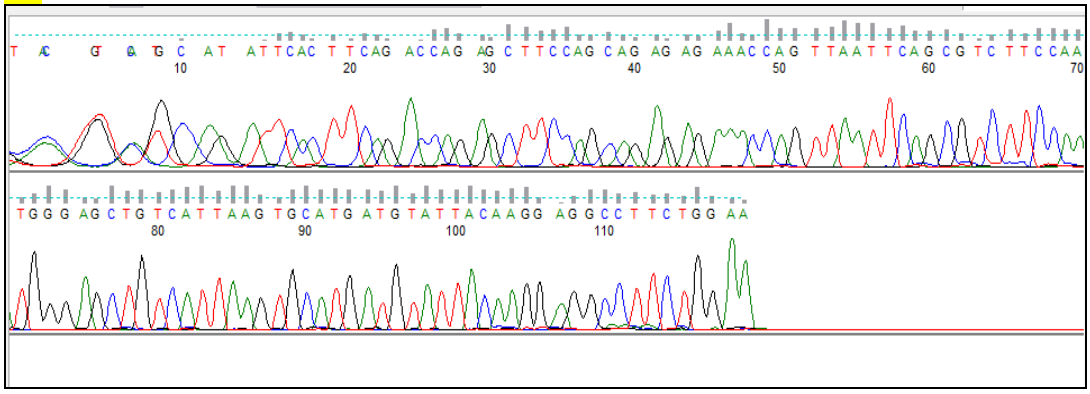
6B



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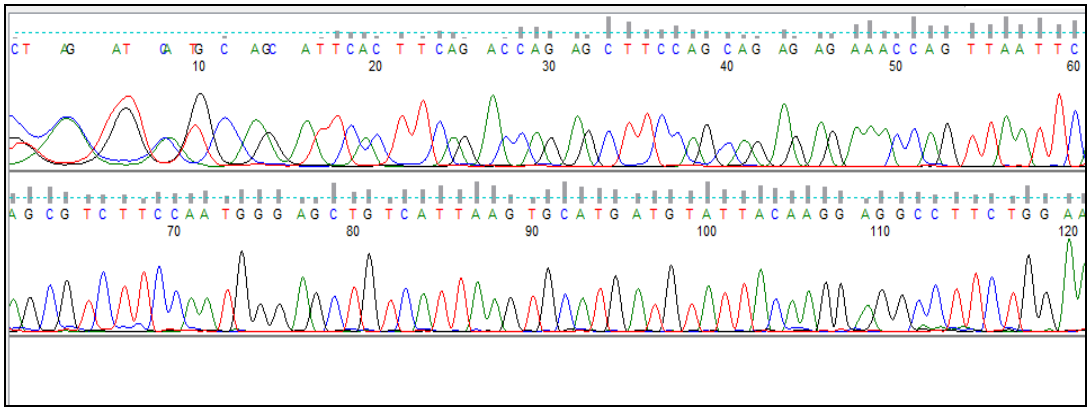
9B



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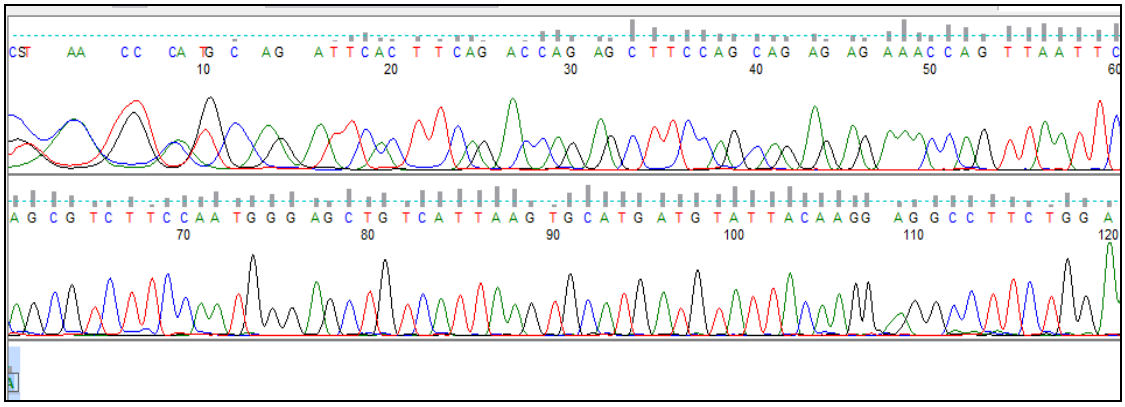
10B



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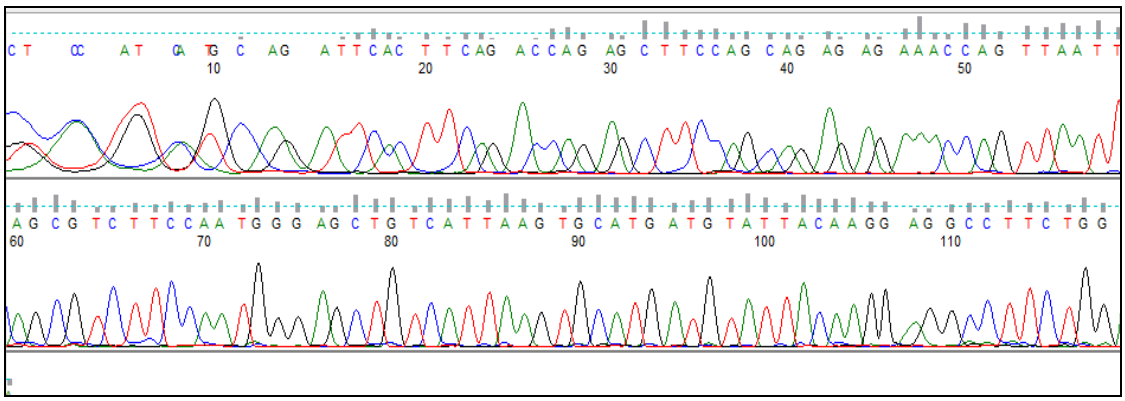
11B



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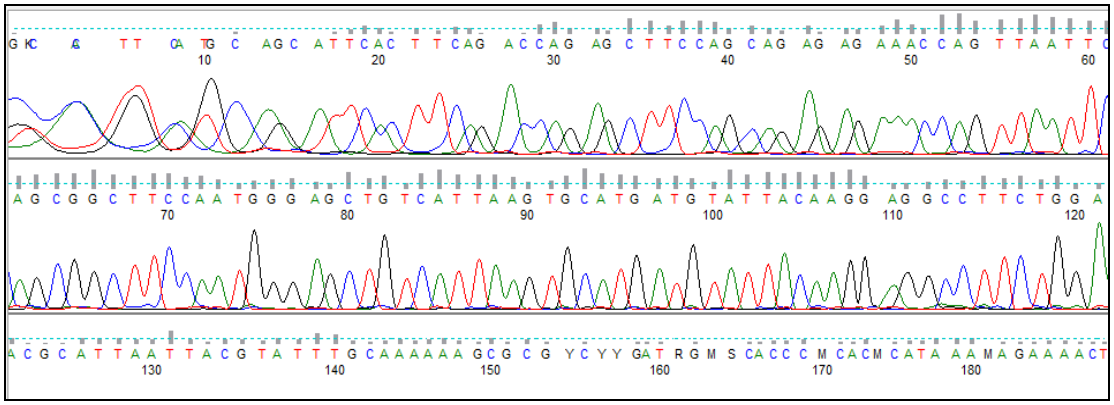
12B



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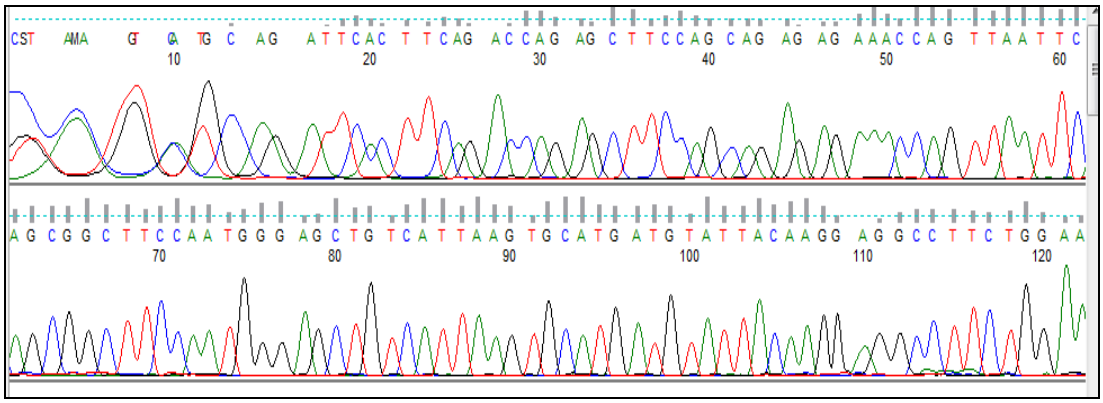
13B



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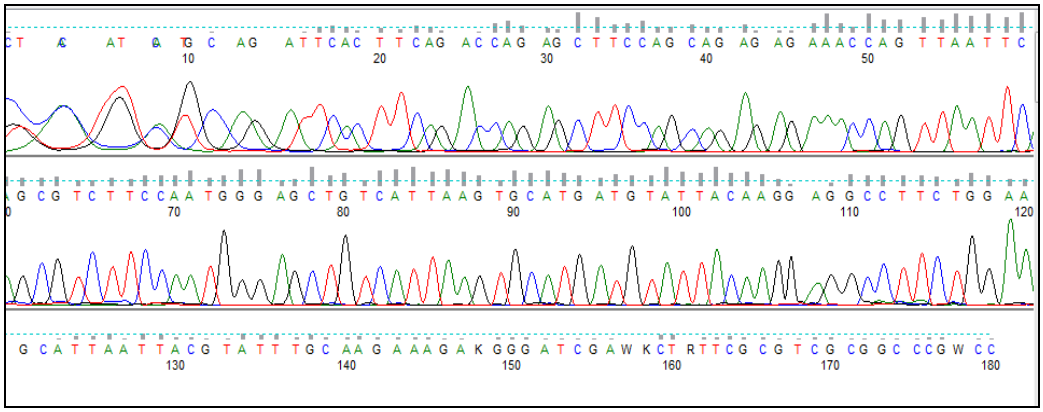
15B



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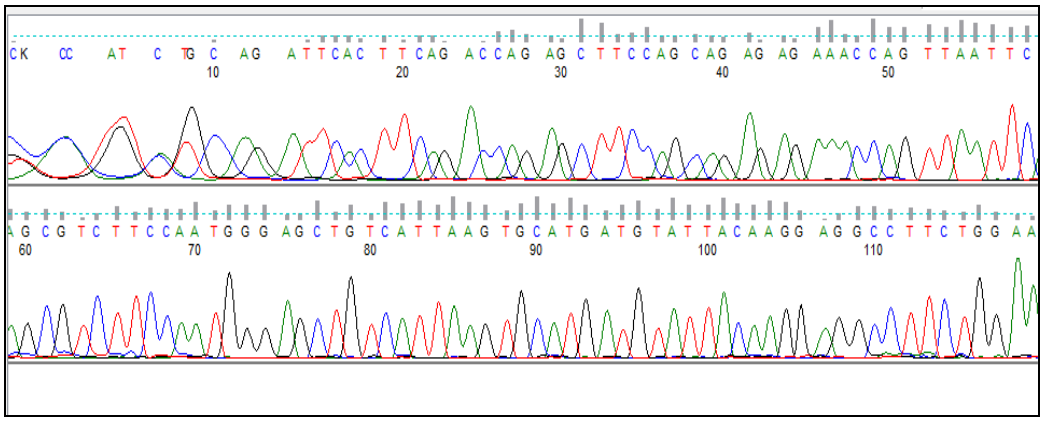
1A



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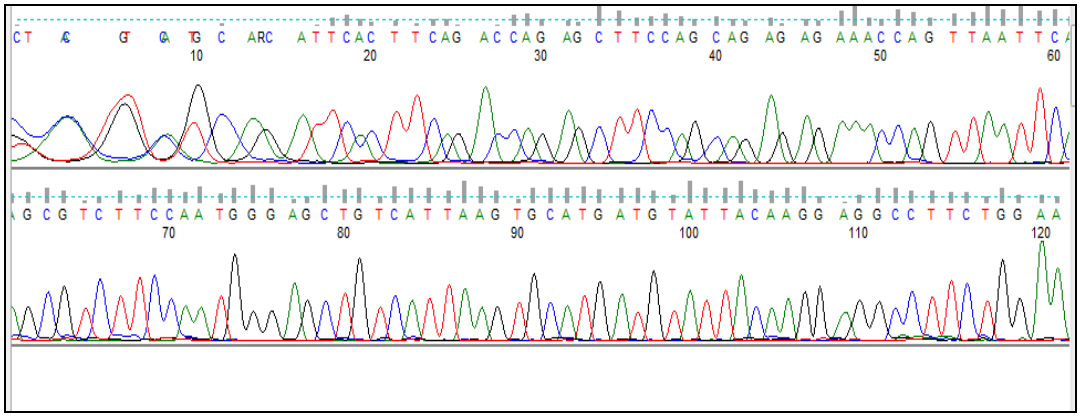
2A



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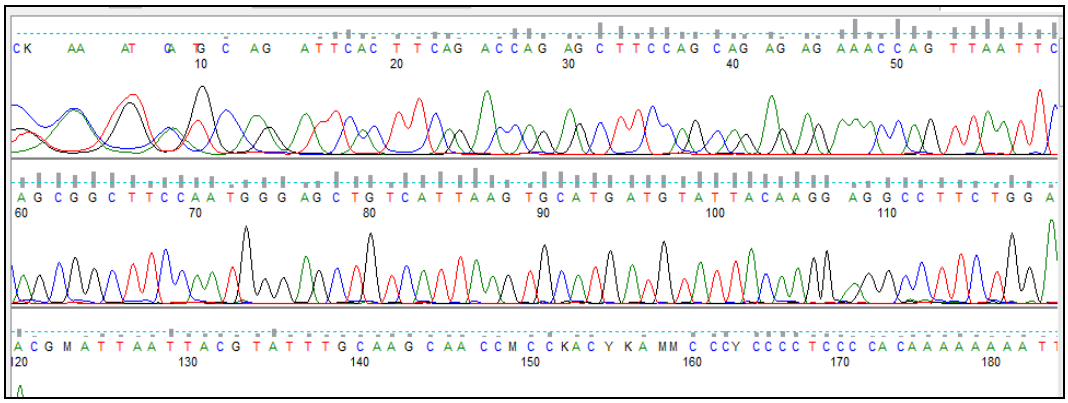
6A



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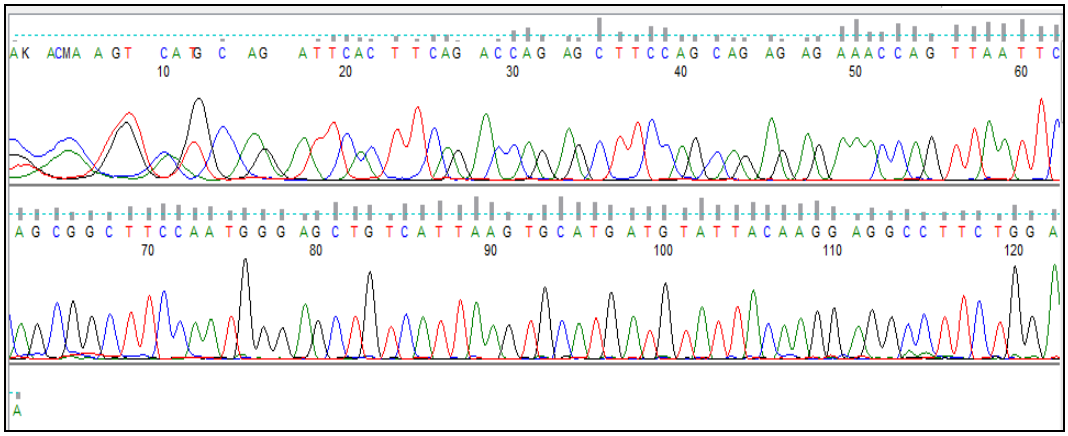
10A



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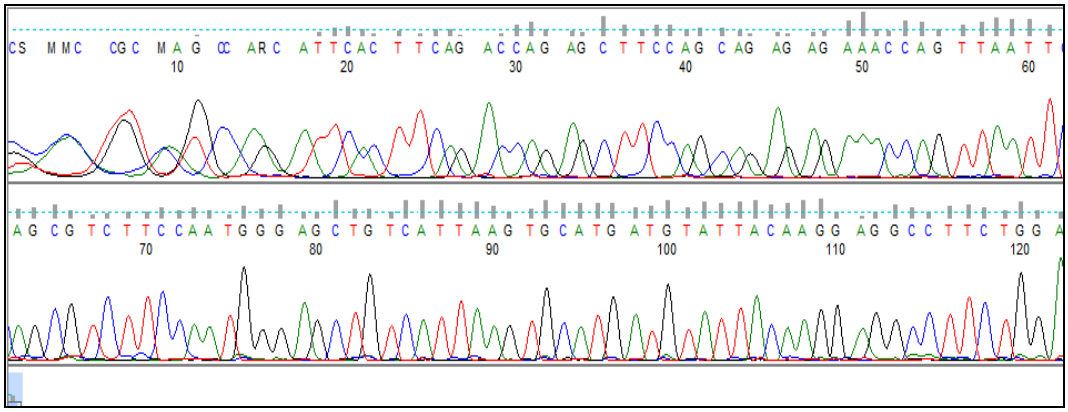
11A



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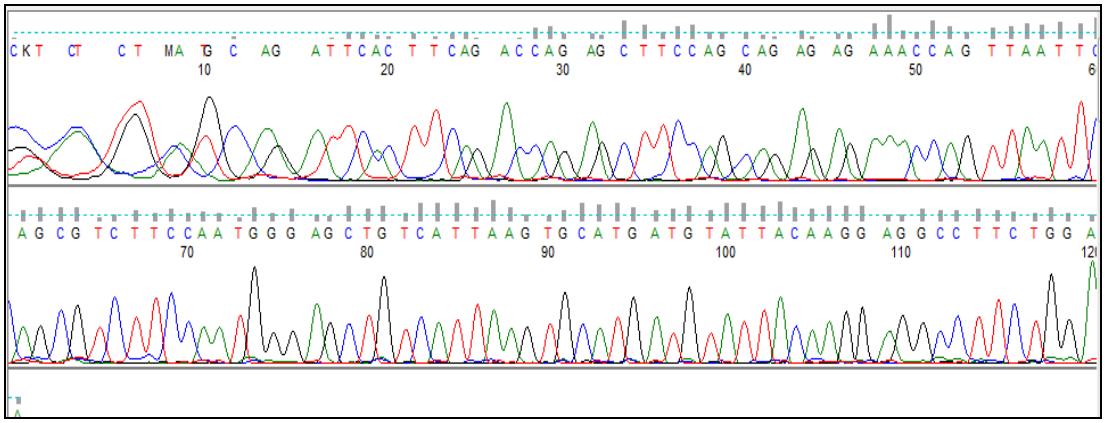
12A



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```

Figure 4.5. Sequence analysis of Exon 8 of the MAOA gene for case of 21-c1, 24-c2 (control), and case of 1B, 2B, 3B, 4B, 5B, 6B, 9B, 10B, 11B, 12B, 13B, 15B, 1A, 2A, 6A, 10A, 11A and 12A (criminal cases)

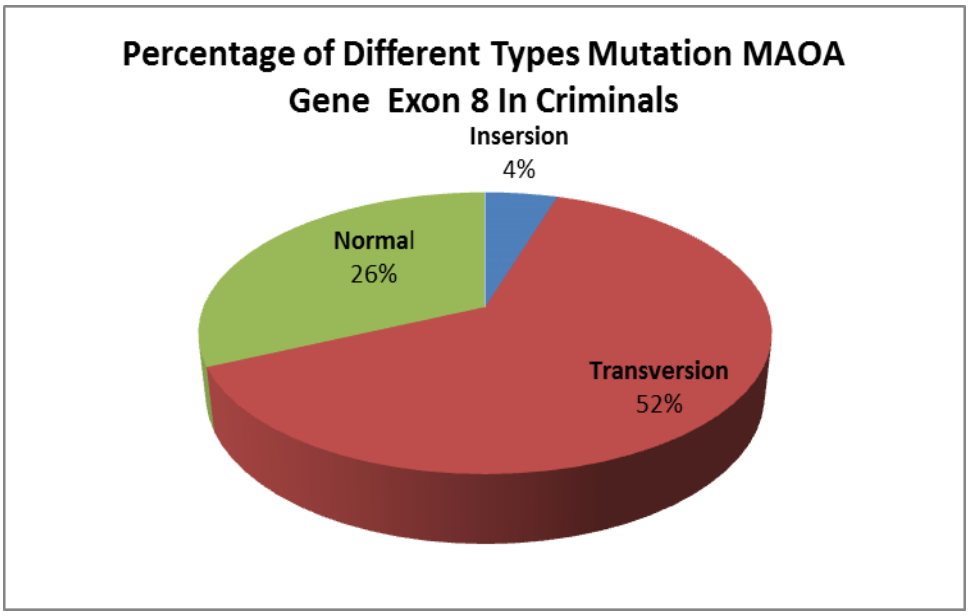

Figure 4.6. Show the percentage and the common type of mutation in exon (8) in MAOA gene of criminals. The percentage of the common mutation in exon 8 was 52% by substitution at position 2326 nt of exon 8, that SNP (G to T) and 26% G to C transversion at nucleotide

5. DISCUSSION

In various recent studies that genetics do influence criminal or antisocial behavior. Researchers agree on the point that genes influence personality traits and disorders, such as the ones just mentioned. However, there is an agreed argument among scholars that there is an environmental component that needs to be examined. Environmental influences such as family and peers will be discussed, as well as a look into the social learning theory. In case of 1B, 3B, 5B, 6B, 9B, 10B, 11B, 15B, 1A, 2A, 11A and 12A we detected different types of point mutations. Similar results were obtained in experiments on humans also show that the effect of individual genes on aggressive behavior strongly depends on the genetic background (Kudryavtsevaa *et al*., 2015). In several men of the family showed mental retardation and inclination to violence, manifesting itself in impulsive violent acts, arsons, attempts at rape, and exhibitionism. These men had reduced activities of MAOA as a result of a point mutation in exon 8 of the MAOA gene which produced a termination codon. Subsequent studies confirmed the association between MAOA polymorphism and aggression in humans (Manuck *et al*., 2000; Huang *et al*., 2004).

Monoamine oxidase A (MAOA) is a mitochondrial enzyme involved in deamination of excess monoamines. As impulsivity, mood swings, aggression, sleep disorders, depression and sexually deviant behavior have been noted in MAOA deficient individuals and MAOA gene variants have been hypothesized in development of violent criminal behavioral patterns. Brunner *et al*. (1993) examined males in a large Dutch family with a history of borderline mental retardation and abnormal behavior (impulsive aggression, rape attempts, arson, and Exhibitionism). Five persons exhibiting the behavior possessed MAOA deficiency *in vitro* due to a missense C936T mutation in exon 8. Although the genetic basis for the in ability to control impulsive anger has been proposed, this rare single nucleotide polymorphism (SNP) has not been reported since. Yet, rodent studies report higher aggression rates, as well as maladaptive defensive reactivity and enduring

responses, in MAOA deficient mice (Bortolato and Shih, 2011; Cases *et al*., 1995; Teodorović *et al*., 2015).

Monoamine oxidase (MAO) is an enzyme that has been shown to be related to antisocial behavior. Specifically, low MAO activity results in disinhibiting which can lead to impulsivity and aggression (Elliot, 2000). The Brunner *et al*. (1993) study is the only one to report findings of a relationship between a point mutation in the structural gene for MAOA and aggression, which makes the findings rare. However, there has been other evidence that points to the conclusion that deficiencies in MAOA activity may be more common and as a result may predispose individuals to antisocial or aggressive behavior (Brunner *et al*., 1993). MAO is associated with many of the neurochemicals that already have a link to antisocial or criminal behavior. Norepinephrine, serotonin, and dopamine are metabolized by both MAOA and MAOB (Elliot, 2000). While, according to Eysenck (1996), MAO is related to norepinephrine, epinephrine, and dopamine, which are all related to the personality factor of psychosis dopamine is a neurotransmitter in the brain that is associated with pleasure and is also one of the neurotransmitters that is chiefly associated with aggression. Activation of both affective (emotionally driven) and predatory aggression is accomplished by dopamine (Elliot, 2000). Genes in the dopaminergic pathway have also been found to be involved with Attention Deficit Hyperactivity Disorder (ADHD; Morley and Hall, 2003). Morley and Hall (2003) cited that a relationship was found between the genes in the dopaminergic pathway, impulsivity, ADHD, and violent offenders. Obviously, from this list of neurochemicals it seems plausible that there is a genetic component to antisocial or criminal behavior.

What drew scientists to study this family was the discovery that the affected men had an unusual version of a gene controlling an enzyme that helps break down important neurotransmitters, an enzyme known as monoamine oxidase. This family suffered from a particularly rare mutation in this gene that essentially eliminates the production of one form of monoamine oxidase (known as MAO-A). Several other studies have implicated variants of genes regulating monoamine oxidase activity as a contribution to criminal behavior, at least among males (Ellis 1991; Sjoberg *et al*., 2008).

In a recent New Zealand study, a gene coding for low MAOA activity was found to be associated with violent and antisocial behavior if individuals also suffered substantial maltreatment as children. Individuals with the same genetic variant but who were not abused as children were not unusually prone to antisocial conduct (Caspi *et al*., 2002). The researchers interpreted this finding as suggesting that both genetic and family environmental factors must often interact to affect criminality. Overall, this line of research on MAOA suggests that the way genes alter the breakdown of neurotransmitters may help in the understanding of antisocial behavior.

Although the present study was unable to find a strong association of aggressive behavior with MAOA variants in the criminal cases of 2B, 4B, 12B, 13B, 6A and 10A. Our finding has shown that one third of school going children had aggressive behavior directly related to family structure and family environment in a rural community of a developing country (Khan *et al*., 2014). Schimtz (2003) suggested that relationship between family environment and child behavior characterizes a child's wellbeing with a positive and caring parent-child relationship, a stimulating home environment, and consistent disciplinary techniques. Families with poor communication and weak family bonds have been shown to have a correlation with children's development of aggressive/criminal behavior (Garnefski and Okma, 1996). Therefore it obvious to conclude that those families who are less financially sound, perhaps have more children, and who are unable to consistently punish their children will have a greater likelihood of promoting an environment that will influence antisocial or delinquent behavior. Another indicator of future antisocial or criminal behavior is that of abuse or neglect in childhood. Holmes *et al*. (2001) reported that 50% of children are at greater risk of engaging in criminal acts if they were neglected or abused. This has been one of the most popular arguments as to why children develop antisocial or delinquent behaviors.

CONCLUSION AND RECOMMENDATION

The following conclusions could be considered from the results of present study.

1. The age and level of education are very vital variables. It seems that the young offender's crime peaks between the ages of 21 to 30 and 31 to 40 year old. The rate of crime decline sharply with elder age, in regard to education we found that 16 out of 30 (53%) had only primary school qualification. 11 out of 30 which represent (36%) of the sample had a secondary school qualification. Furthermore, it seems that the marriage as a variable didn't have any effect, because we expected that the offending crimes would be less among married people, comparing with single persons. Therefore, 25 out of 30 (83%) were married whereas 5 out of 30 (17%) were single.
2. Primers for MAOA gene in Exon 8 were designed.
3. We observed two mutations substitution and insertion, by direct sequence analysis in the exon 8 in MOAO genes.
4. The result show common mutation in exon 8 in MAOA genes of Criminals. The percentage of the common mutation in exon 8 was 52% by substitution at position 2326 nt of exon 8, that SNP (G to T) change arginine to arginine (nonsense mutation) and 26 % G to C transversion at nucleotide position 2276 change lysine to asparagine (missense mutation) and 4% insertion (C) at position 2302 leading frame shift change all amino acid.

The following recommendations could be withdrawn;

1. Further studies are needed to classify all DNA mutations in Iraqi population and studies on more samples are needed to better understand the role of MAOA gene.
2. More prospective studies are required to explain the relationship between maternal MAOA gene and criminals.
3. Further studies needed for the whole genes (molecular study) of MAOA gene in Iraq.

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CURRICULUM VITAE

I was born in Erbil on the 16th of April 1974. I studied Primary and secondary school in Erbil. I began undergraduate education at Salahaddin University, College of education, and department of biology and graduated in 2001. In 2002, I registered for a 6 months police officer course, then I worked as police officer for about 15 years till date, and then in 2014, I registered for one year at Cyprus International University institute of graduate studies and research, environmental sciences department to continue my masters studying. In 2015, I registered at Bingol University, Biology department, the graduate program. Iam married and have 2 children. I speak Arabic fluently.