

CORTISOL AND C-REACTIVE PROTEIN (CRP) LEVELS IN CHILDREN EXPOSED TO PHYSICAL AND SEXUAL VIOLENCE ATTENDING MENOUFIA UNIVERSITY HOSPITALS.

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ABSTRACT

BACKGROUND: Children maltreatment is a common problem worldwide which needs proper evaluation for better management and prevention. **OBJECTIVES:** This study aimed to investigate whether violence (physical and sexual) in children is associated with changes in cortisol hormone and C-reactive protein (CRP) levels and their potential role in evaluating type, frequency, severity, and outcome of such violence. **METHODOLOGY:** This study included all children presented to Menoufia university hospital suffering from physical or sexual violence during the period of study, from the 1st of December 2016 to the 30th of November 2018. A clinical sheet was pre-designed and fulfilled for the cases. Injured Patients were classified according to injury severity score (ISS). Blood samples were taken from case and controls groups for estimation of Cortisol and CRP levels. **RESULTS:** The study included 75 children who were victims of violence (physical or sexual) with girls' predominance mostly from rural areas. Physical violence outnumbered sexual violence and violence was predominantly repeated. Contusions were the most presented external injuries while fractures were the commonest in internal injuries. According to ISS more than half of victims were of serious degree. The mortality rate was 8%. Violence against children was associated with changes in cortisol and CRP levels in comparison to controls. Cortisol levels changes were strongly connected to the type, frequency, and severity of violence, as well as the outcome of the cases, whereas changes in CRP levels were significantly related to the type and frequency of violence, and outcome of the cases. **CONCLUSION:** These markers could help physicians in early diagnosis and evaluation of children's physical and sexual maltreatment as evidence of stress and inflammation especially in cases with vague history of abuse and vague physical signs that are not conclusive for assault.

Keywords: Children, violence, cortisol, CRP.

INTRODUCTION

As a result of their small size and inability to defend themselves, infants and young children are being harmed by others (Child Welfare Information Gateway, 2020).

For infants and younger children, violence mainly involves child maltreatment (i.e., physical, sexual, and emotional abuse and neglect) at the hands of parents and other authority figures. As children reach adolescence, peer violence, and intimate partner violence, in addition to child

maltreatment, become highly prevalent (WHO, 2016).

Violence against children occurs at multiple levels (individual, household, institutional, and societal) (Hillis et al., 2016).

Research showed that most children grow up in environments that routinely expose them to violence. Their safety and well-being are not just compromised in their homes and families, but also in schools, workplaces, childcare institutions, the justice system, and in different places in the communities in which they live (NCCM, 2018).

Egypt Demographic and Health Survey (EDHS) showed that in the month preceding the study, 93 percent of children aged one to fourteen were subjected to aggressive disciplinary behaviors at home, comprising both psychological abuse and physical assault. Additionally, 43% of them were subjected to harsh punishment through physical force, such as hitting or slapping on the head, face, or ears, repeated beating, and hitting with hard objects, such as a stick, belt, wooden cane, or whip (Ministry of Health and Population, 2015).

There is a well-established link between exposure to childhood maltreatment and the development of psychiatric and physical disorders across the lifespan (Delahanty et al., 2005).

This link is, in part, mediated by persistent changes in neuroendocrine stress response and immune systems (Bucci et al., 2016).

It was hypothesized that the innate inflammatory response would be activated through stress hormones and sympathetic nervous system activation in children that exposed to violence this activation would persist for many hours after the trauma (Bucci et al., 2016).

Traumatic events can increase allostatic load by activating the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic nervous system. This dysregulation can be manifested with elevated or abnormally low levels of cortisol (Kendall et al., 2000).

Since CRP is released in response to IL-6 and TNF- α liberation, it is widely used as inflammation marker. Furthermore, CRP is one of the components of the innate humoral immune system, facilitating pathogen detection and killing via complement activation or the neutrophils and macrophages recruitment. (Kingsley and Jones, 2008).

Measurement of C-reactive proteins aids in the evaluation of stress, trauma, infection, inflammation, surgery, and associated diseases (Povoa et al., 2005).

However, the immediate effects of violence exposure on these systems are not studied enough. Therefore, this study aimed to investigate whether violence (physical and sexual) in children is associated with changes in cortisol hormone and C-reactive protein (CRP) levels and their potential role in evaluating type, frequency, severity, and outcome of such violence.

SUBJECTS AND METHODS

Subjects:

Cases: This prospective case control study included all children presented to Menoufia university hospital suffering from physical or sexual violence during the period of study, from the 1st of December 2016 to the 30th of November 2018.

Inclusion criteria:

1-Children arrived at Menoufia University hospital with allegations of physical and sexual violence.

2-Cases whose legal guardian signed informed written consent.

Exclusion criteria:

1-Children with acute infections, hypertension, diabetes mellitus, inflammation-related illnesses such as autoimmune disease, and malignancies. These conditions may have high CRP levels because they can flare up and activate the immune system.

2-Children with history of brain diseases or injuries, epilepsy and endocrine disorders or taking medications that might affect the activity of HPA axis as angiotensin-converting enzyme inhibitors, lithium, beta blockers, psychotropic medications, amphetamines, levodopa, oral contraceptives, ketoconazole, spironolactone, aminoglutethimide, corticosteroids, danazol, phenytoin and metyrapone.

Control healthy group: for estimation of C - reactive protein and cortisol levels. This group consisted of 75 healthy children, with no history of exposure to physical and sexual violence or any trauma at the time of blood sampling and their guardian signed written informed consent. They had no history of the above diseases, were not under the treatment of any of the above drugs and were of comparable age and gender.

Positive control group: for estimation of C - reactive protein and cortisol levels. The group consisted of 75 children, who presented to Menoufia university hospital suffering from accidental trauma and their guardian signed written informed consent. They had no history of the above diseases, were not under the treatment of any of the above drugs and were of comparable age, gender, and injury severity score.

Ethical considerations: this study was done after approval of the Institutional Review Board of the Ethical Committee of Faculty of Medicine, Menoufia University (IRB No. 12/2016FORE). Guardians of children provided informed, signed consent.

Methods: For the cases, a clinical sheet with sociodemographic characteristics, history of violence and circumstances, clinical assessment (general examination, injuries examination and

local examination of the cases subjected to sexual assault), injury type, site, and severity, complications, and outcome at discharge time from hospital, and follow up, had been predesigned and completed.

Patients' injuries were classified by injury severity score (ISS) depending on anatomical distribution and injury severity and based on Abbreviated Injury Scale (AIS). AIS is a system of anatomical coding which categorizes injuries in each of six regions of the body (head/neck, face, chest, abdominal/pelvic contents, extremities, and external injuries) using 1-6 ordinal scale. One is given for the cases not needing any treatment, 2 for outpatient treatment cases, 3 for cases needing non-ICU admission, 4 for cases that need basic treatment and observation in ICU, 5 for cases needing support of blood pressure intubation and mechanical ventilation and 6 for cases with unsurvivable injuries (Stevenson et al., 2001). The ISS is computed by calculating the squares of the highest AIS value (up to five) for each of the three most severely injured areas of the body. If any of the three values is 6, the score is automatically considered as 75, consequently, ISS values range from 1 to 75 (Brown et al., 2017).

Cases with score 1-8 were categorized as minor, 9-15 as moderate, 16-24 as serious, 25-49 as severe, 50-74 as critical and 75 as unsurvivable (Cordovilla-Guardia et al., 2017; El-Farouny and Habib, 2019).

All needed investigations (laboratory, radiological, nerve conduction velocity, and ophthalmoscope) were done for each case as indicated.

Blood samples were taken from all the cases and positive control group on admission and from control healthy group for measurement of C-reactive protein and cortisol levels.

Cortisol Sample: 5 cm blood samples were taken in clean sterile plastic container (sodium heparin, EDTA) with plastic cap and preserved in a refrigerator. Cortisol levels were determined through Enzyme Linked Fluorescent Assay (Hawley et al., 2016).

CRP samples: 5cm blood samples were taken in clean sterile plastic containers and placed into plain bottles for estimation of CRP with no preservatives with plastic cap and preserved in a refrigerator. CRP levels were determined through AGAPPE misSPA-i2 device for c-reactive protein detection and reagent1 (Glycine buffer solution), Reagent 2 (Latex suspension coated with anti CRP antibodies 'rabbit polyclonal antibody") and smartcard. This reagent is intended for quantitative

in-vitro determination of CRP in human plasma or serum (Senju et al., 1986).

Statistical Analysis: data were statistically analyzed after collection and tabulation using SPSS version 22(SPSS, Inc., Chicago, Illinois, USA). Qualitative data were presented in the form of numbers and percentages. The Chi (X^2) test was used for comparison of two or more in dependent qualitative normally distributed variables. Kruskal-Wallis's test which is a significance test was used to compare more than two groups with non-normally distributed data while Mann-Whitney test (nonparametric test) was used for comparison between two groups with non-normally distributed data.

RESULTS

This prospective study included 75 children who were victims to physical or sexual violence, 78.67% of them were girls and mostly from rural areas (57.33%). More than half of the cases aged ≤ 10 years (54.67%), 89.33% were singles and 58.67% were students. Low socio-economic standard cases represented the highest percentage (38.67%) and about two third of the victims were from families which contains more than 5 members (65.33%) (Table 1).

Physical violence was found in most of the children included in this study (76%) while only (24%) of them were sexually maltreated and violence was predominantly repeated (50.67%) (Fig. 1).

Rape was the commonest among sexual violence cases (50%), followed by sodomy (33.3%) and then buggary which represented 16.7%. Type of injuries in sexual assault cases ranged from vaginal contusions and abrasions, hymen tears, deep tear reaching to anus and dilatation of the anus (Fig. 2).

Abdomen and pelvis including genitalia were the most commonly represented site of injuries (30.7%), followed by the upper limbs (24%) while 18.7% of the cases had injuries in the head and neck (Table 2).

The most common type of the external injuries were contusions (22.7%) followed by contused wounds (16%). Thermal burn and cut wounds represented 12% and 10.7% respectively and the least were firearm wounds (1.3%) (Table 3).

Brain contusions and hemorrhages were the most common internal soft tissue injuries (15.9%) followed by eye rupture with retinal affection (12.3%). Intraabdominal injuries (peritoneal fluid collection and rupture spleen), intrathorathic injuries and spinal and nerve injuries

represented 10.5%, 7% and 7% respectively. Bones fractures were the commonest in internal injuries as they occurred in 40 cases. The most common site of fractures was upper limb (24.6%) followed by chest bones (ribs or sternum) (12.3%). Fracture vertebrae and fracture skull represented 7% for each (Table 4).

The majority of the cases were cured without disfigurement or permanent infirmity (54.6%) while 26.7% of the them were cured with permanent infirmity or disfigurement. Disfigurement was in the form of ugly scars after healing of wounds in the face, neck, and upper limbs. Permanent infirmity was in the form of skull bone defects, loss of vision in one eye after the destruction of its tissue or rupture globe due to direct trauma or firearm, and limitation of hand movement. Unknown outcome was found in 10.7% of cases as follow up was not completed as those patients didn't complete their treatment and runaway. Death was in 8% of cases. They were six cases ,3 cases died due to severe head injuries, 2 cases were due to burn and one case due to violent asphyxia(strangulation by rope)(Fig. 3).

Cases were classified according to injury severity score (ISS) where more than half of them were of serious degree (58.7%), followed by moderate degree (24%) while unsurvivable degree cases were 8% (Fig. 4).

Highly significant difference was detected in cortisol level between cases and controls ($P < 0.001$) as the levels were higher in victims than control healthy children and positive control children. CRP levels also were statistically higher in cases than both controls ($P < 0.05$)(Table 5).

Cortisol and CRP levels in relation to the type of violence was significant ($P < 0.05$) as both was higher in physical violence than in sexual violence (Table 6).

Regarding the relation between the cortisol levels and injury severity score, the highest levels were detected in severe and critical degrees followed by serious degree while unsurvivable cases had the lowest levels of cortisol and the difference was statistically significant ($P < 0.05$). On the other hand there was no significant difference in the mean level of CRP between different degrees of injury severity score ($P > 0.05$) (Table 7).

The relation between cortisol and CRP levels and outcome was significant ($P < 0.05$) as cured cases with permanent infirmity or disfigurement showed highest mean levels of both markers while deaths were related to lowest levels detected in the cases (Table 8).

Cases with repeated violence showed higher levels of cortisol and CRP and the difference was statistically highly significant ($P < 0.001$) (Table 9).

Table (1): Distribution of victim children as regards demographic data (n=75).

Demographic data	Cases (n=75)	
	n	%
Gender:		
Male	16	21.33%
Female	59	78.67%
Residence:		
Urban	32	42.67%
Rural	43	57.33%
Age groups in years:		
10 or less	41	54.67%
>10-18	34	45.33%
Marital status:		
Single	67	89.33%
Married	8	10.67%
Occupation:		
Preschool & not working	25	33.33%
Student	44	58.67%
Worker	6	8%
Socio-Economic Standard:		
High	18	24%
Middle	28	37.33%
Low	29	38.67%
Family size:		
5 members or less	26	34.67%
More than 5 members	49	65.33%

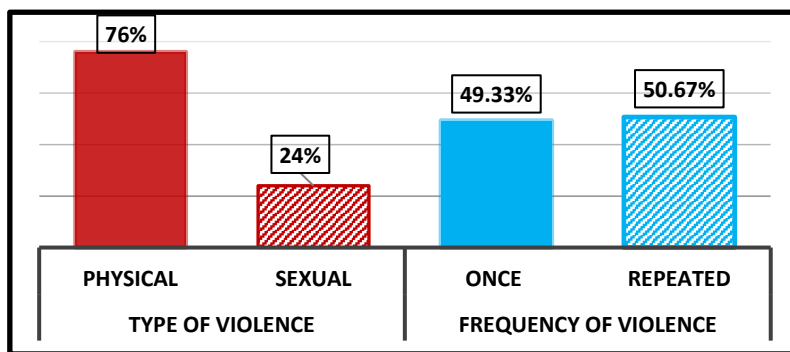


Figure (1): Frequency distribution of type and frequency of violence among the studied cases (n=75).

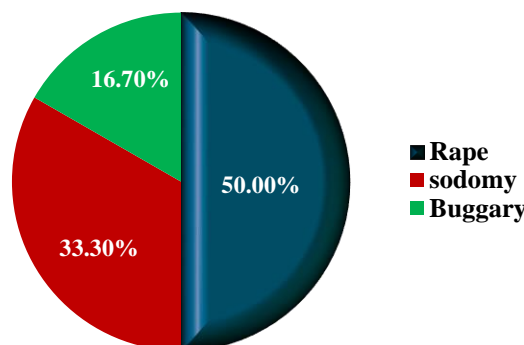


Figure (2): Frequency distribution of type of sexual assault in children exposed to sexual violence(n=18).

Table (2): Distribution of site of injuries in the studied cases (n =75).

Site of wounds	n =75	%
Face	5	6.7%
Head and neck	14	18.7%
Upper limbs	18	24%
Chest	4	5.3%
Abdomen and pelvis	23	30.7%
Lower limbs	2	2.7%
Multiple sites	9	12%

Table (3): Distribution of the victims as regards the type of external injuries (n =75).

Type of injury	n =75	%
Abrasions	2	2.7%
Contusions	17	22.7%
Contused wounds	12	16%
Punctured wounds	5	6.7%
Cut wounds	8	10.7%
Stab wounds	4	5.3%
Firearm wounds	1	1.3%
Thermal burn	9	12%
Combined injuries	12	16%
Dilatation of the anus	5	6.7%

Table (4): Frequency distribution of internal soft tissue injuries and fractures in physical violence cases (n=57).

Internal soft tissue injuries	n	%
Eye rupture with retinal affection	7	12.3%
Brain contusion and hemorrhage	9	15.9%
Spinal cord contusions/Nerve injury	4	7%
Intraabdominal injuries (peritoneal fluid collection and rupture spleen)	6	10.5%
Intrathorathic injuries	4	7%
None	27	47.3%
Total	57	100%
Fractures	n	%
Skull	4	7%
Face (nasal bones, mandible and teeth)	4	7%
Chest bones (ribs or sternum)	7	12.3%
Upper limb bones	14	24.6%
Vertebrae	4	7%
Lower limb bones	2	3.5%
Multiple sites	5	8.8%
None	17	29.8%
Total	57	100%

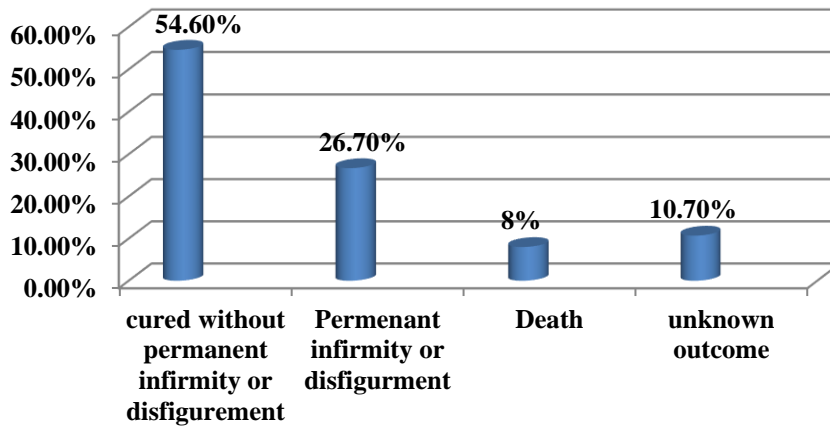


Figure (3):Frequency distribution of outcome of physical and sexual violence in children(n=75).

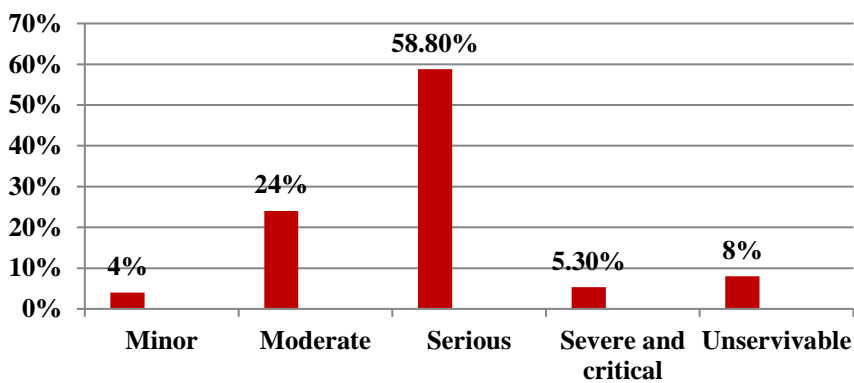


Figure (4):Frequency distribution of the cases according to injury severity score(n=75).

Table (5): Relation of plasma cortisol and CRP levels among children violence cases and controls (healthy control and postive control children).

	Cases n=75	Healthy Controls n=75	Postive Controls n=75	K test	P value
Cortisol level Mean ±SD (mcg/dl)	26.76±16.82	11.33±10.34	14.34±12.40	32.79	< 0.000** k1,k2
CRP level Mean ±SD (mg/l)	18.02±22.67	6.73±6.03	6.94±5.85	8.47	0.01* k1,k2

n=number K test:- Kruskal-Wallis test

K1: post hoc of Kruskal Wallis test is significant between cases and healthy controls.

K2: post hoc of Kruskal Wallis test is significant between cases and postive controls

*P value <0.05 = significant

**P value <0.001 = highly significant

Table (6): Distribution of plasma cortisol and CRP levels in relation to type of violence in victims(n=75).

	Type of violence		U test	P value
	Physical (n=57)	Sexual (n=18)		
Cortisol level				
Mean \pm SD (mcg/dl)	29.99 \pm 15.98	16.51 \pm 15.62	3.23	0.001*
CRP level				
Mean \pm SD (mg/l)	21.31 \pm 24.65	7.63 \pm 9.21	1.97	0.04*

n=number U test = Mann-Whitney test

*P value <0.05 = significant

Table (7): Distribution of the plasma Cortisol and CRP levels in relation to injury severity score(n=75).

	Injury severity score					Kruskal Wallis test	P value
	Minor n=3	Moderate n=18	Serious n=44	Severe and critical n= 4	Unsurvivable n=6		
Cortisol level							
Mean \pm SD (mcg/dl)	19.2 \pm 13.0	20.1 \pm 13.2	30.1 \pm 15.6	47.6 \pm 28.5	12.06 \pm 4.83	19.98	0.001*
CRP level							
Mean \pm SD (mg/l)	11.7 \pm 9.8	21.0 \pm 17.3	19.5 \pm 26.5	12.4 \pm 17.7	4.78 \pm 0.95	2.61	0.63 ^{NS}

n=number *P value <0.05 = significant NS= non-significant difference, P >0.05

Table (8): Distribution of the plasma cortisol and CRP levels in relation to outcome of the studied cases(n=75).

Outcome	Cortisol level Mean \pm SD (mcg/dl)	CRP level Mean \pm SD (mg/l)
Cured without permanent infirmity or disfigurement (n=41)	21.14 \pm 14.59	12.49 \pm 11.94
Permanent infirmity or disfigurement (n=20)	40.20 \pm 13.71	37.91 \pm 32.86
Patient didn't complete his treatment and runaway (unknwon outcome) (n=8)	30.81 \pm 16.51	6.60 \pm 2.54
Death (n=6)	12.06 \pm 4.83	4.78 \pm 0.95
Test of significance	K=25.26	K=7.56
P value	<0.000**	0.04*

n=number * k = Kruskal Wallis test

*P value <0.05 = significant ** P value <0.001 = highly significant

Table (9): The plasma cortisol and the CRP levels in relation to frequency of violence(number=75).

	Frequency of violence		Mann-Whitney Test	P value
	Once number= 37	Repeated number=38		
Cortisol level Mean ±SD (mcg/dl)	17.91±15.71	35.37±13.08	4.38	<0.000**
CRP level Mean ±SD (mg/l)	8.73±14.39	27.07±25.62	4.66	<0.000**

** P value <0.001 = highly significant

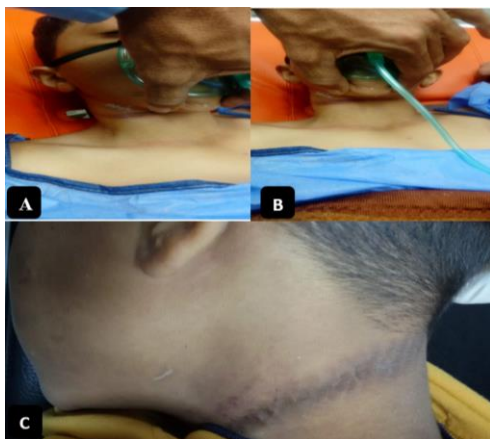


Figure (5): Show 11 year's old male child with violent asphyxia due to constriction of the neck by a ligature (rope) which is tied forcibly around the neck (strangulation by rope). The rope mark appears as a depression, along its edges there are areas of hyperemia and ecchymosis with minute abrasions and contusion, transverse, complete around the neck, symmetrical in depth (the force is equal all around the neck) (picture A, B & C).



Figure (6): Female patient 9 years old with history of repeated physical abuse with head of a belt by her stepfather. Blue purple contusion of forehead about 2x3cm (picture A). Purplish contusions over the chin and right cheeks about 2x4cm to 3x6cm (picture B) inflicted 2days before. Recent red contusions over the anterolateral surface of legs about 4x7cm (picture C) and red contusions over the anterior surface of the left thigh measuring 3x7cm (picture D).

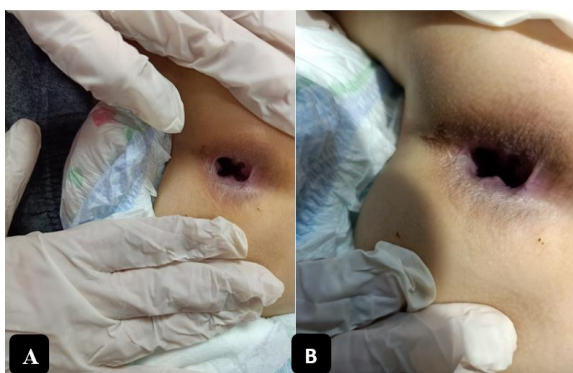


Figure (7): Shows local examination of 8years old boy with history of sexual abuse, it shows dilatation and gapping of anal orifice by bimanual lateral traction, with lax anal sphincter and stool incontinence and loss of subcutaneous fat around the anus (picture A & B).

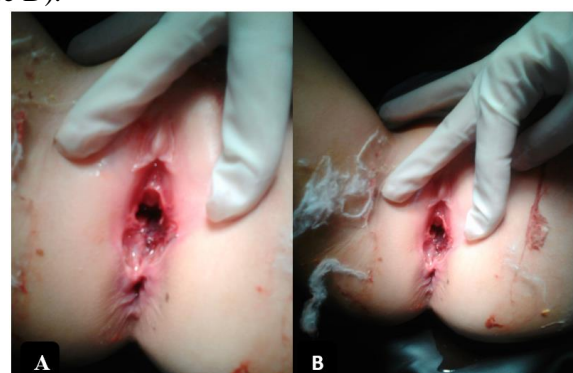


Figure (8): Shows local examination of 2 years old girl with history of sexual abuse, it shows rupture hymen and tear in posterior wall reaching upper border of anal sphincter (contused wound about 1,5cm) (picture A & B).

DISCUSSION

Violence against children is a major problem worldwide which affects community economic and social development, hence needs proper diagnosis and evaluation for proper management and prevention. It occurs when a child is maltreated physically, sexually, or emotionally, which may occur also through neglect. Western countries have formulated adequate and strict laws to deal with such issue, while in developing countries including Arabs, it is not yet regarded as a serious problem despite its growing incidence and significant complications.

Regarding demographic data of the cases in this study, it was found that most cases aged less than ten years, and this may be due to their small size and inability to defend themselves. Moreover ages 2-4 years are usually subjected to harsh physical discipline by the parents or the caregivers, and this is in accordance with UNICEF, (2020). Girls were predominant than boys, their weakness and helplessness associated with the society concept of females' inferiority might be the cause. Abdel Salam, (2005) conducted the same while Chandraratne et al., (2018) found that boys suffered more than girls as they may need more physical discipline due to their hyperactivity, also they are more resistant to obey commands and orders. Cases were mostly from rural areas as Menoufia is an agricultural governorate with predominance of rural places, in addition to the cultural concepts in such areas, low socioeconomic standards and large family size. Sedlak et al., (2010) showed similar results. The majority of the victims were single and students, as students are more subjected to violent discipline in schools or even at homes to study hard and do well in schools. Children with low socio-economic standard and large family size suffered more from physical and sexual violence. Family conflicts and financial difficulties rise with the size of family as conducted by World Health Organization, (2019). Harrell et al., (2014) also conducted that poverty and poor housing increase violence rate, moreover Veenema et al., (2015) found that violence against children is frequent in poor families lacking shelter and food supplies.

Most of the cases in this study were victims of physical assault. Parents, caregivers, and teachers consider physical punishment as a valid correctional method using it to control rude, stubborn, irritable, and disobedient children (UNICEF, 2015).

Physical violence also is more reported than sexual violence as most societies considers sexual assault as a sensitive issue and a taboo especially in

Islamic countries (Badawy et al., 2014). The violence in the current study was mostly repeated and Browne et al., (2002) concluded similar finding in his survey on Romanian households.

Sexual violence is one of the most violating disruptions of children's rights and in this study, rape was its commonest type, and this agrees with UNICEF, (2015) who reported that the National Child Helpline in Egypt has received reports of sexual assaults against children, and rape was the most prevalent.

Anal assault cases (sodomy and buggery) represented 50% of sexual violence cases and the same results were obtained by Elgendy and Hassan, (2013) .

As regards site of injuries, Abdomen and pelvis including genitalia were the most represented site of injuries as these areas include sites of sexual violence as well. Children also, are susceptible to intraabdominal injuries because of their thin less muscular abdominal wall, horizontal diaphragm and the more anterior liver and spleen, thus less protected by the ribs Maguire et al., (2013). Injuries to upper limbs were the second most common site. This could be due to that upper limbs are usually used for defense and to withdraw injury to other vital parts of the body. Head and neck came after upper extremities, and this could be explained by that assailants may intend to make injuries to victims in apparent parts of the body to offend the victims. These findings agree with Kemp et al., (2014), also Curca et al., (2012) revealed similar conclusions.

One of the classic quotes about violence against children was stated by Cameron et al., (1966) who said: 'The skin and bones tell a story which the child is either too young or too frightened to tell.' In the present study, the most common type of external injuries were contusions, and the least were firearm wounds as the perpetrator usually wants to control or terrify the child not to kill him, so he tends to use blunt instrument rather than more fatal ones as firearms. These findings were nearly in agreement with Cairns et al., (2005); Loder and Feinberg, (2008) and Saukko and Knight, (2016) who conducted that contusions were the commonest type of external injuries and could be seen almost anywhere on the victims' body.

Brain contusion and hemorrhages were the most common internal soft tissue injuries, this is in coincidence with Cheah et al., (1994) and Levin and Christian, (2010) which declared that the most common cause of serious traumatic brain injury in infants is intentional injury.

Eye rupture with retinal affection was the second internal soft tissue to be affected. This in agreement with Levin and Christian, (2010) who declared that violence against children can cause injury to the eye and commonly manifested with retinal hemorrhages.

Bones fractures occurred in 40 cases. The most common site of fractures was upper limb followed by chest bones (ribs or sternum). Upper limbs are the site of shearing strains across the metaphysis due to torsion and traction. Rennie et al., (2007) concluded that upper limb bones are the most common long bones to be affected in child abuse.

Rib fractures are common in young children who are gripped around the chest, compressed, and trembled and are highly indicative of child abuse. (Pandya et al., 2009).

Regarding the outcome of children's violence cases: Majority of the victims were routinely discharged and were cured without disfigurement or permanent infirmity. Their injuries were most likely less severe. This study shows that 26.7% of the cases were cured with permanent infirmity or disfigurement and these results coincide with Di Scala et al., (2000). The mortality rate was 8% of cases. Death motives were either, honor motives, sexual offences, inheritance, or revenge. Higher severity of injuries, delay in obtaining medical assistance owing to vague symptoms or signs, repeated assault by perpetrator before suspicion is verified, or the multiplicity of injuries that young babies are at risk for (intracranial injuries, lacerations of abdominal organ, and bone fractures) are all possible explanations for death in these cases. Furthermore, older children are more likely than younger children to report and seek medical assistance for physical abuse. (Allareddy et al., 2014).

Despite the number of proposed modifications and alternate scoring systems, Injury Severity Score (ISS) remains the most widely used to define severely injured patients (Huang et al., 2019).

In the current study cases were classified according to injury severity score (ISS) where more than half of them were of serious degree while unsurvivable degree cases were 8%. Mayer et al., (1980) stated that overall mortality was 14.5%. Both mortality and morbidity correlated linearly with increasing ISS score. The difference in value in mortality between the present study and Mayer et al., (1980) study was due to difference in site and type of injuries.

Results showed a highly significant difference in cortisol level between cases and controls (healthy or positive controls). The same results were obtained by Ouellet-Morin et al., (2019) who

stated that in comparison to controls, children who were maltreated had higher cortisol levels as a response to stress.

There was also a statistical difference in CRP level between cases and controls. The same results were obtained by De Punder et al., (2017) who stated that maltreated participant children showed significantly higher CRP levels than comparison children.

These results are contrary to that reported by Pamos et al., (2019) who concluded that maltreatment in children had no effect on inflammatory biomarker levels in either the subjects or the control group included in their study. This controversy may be due to the presence of a psychological disorder, difference in maltreatment type and pattern of the studied cases.

The higher levels of both markers in children exposed to violence than those of children with accidental trauma could be due the frequency of assault and the higher stress and inflammatory responses in physically and sexually maltreated children. This indicates that the presence of these high levels in children exposed to physical or sexual assault might help in diagnosis of such violences especially in cases with vague history of abuse and vague physical signs that are not conclusive for assault. The perpetrators sometimes use methods that leave no obvious physical signs on the child body, also the child may be terrified to give history of assault, so the use of these markers might be helpful in such cases. They also could be used for periodic checking of children in places in which they might be exposed to violence as in orphanages.

The relation between cortisol levels and type of violence was significant, as cortisol level was higher in physical abuse as severity and extent of injuries might be more in physical assault. There are several possible mechanisms behind this increased cortisol level in patients including high adrenocorticotrophic hormone (ACTH) release in response to physical injury stress, which then will binds to the receptor on the adrenal cortex plasma membrane, leading to activation of enzymes needed for the cortisol biosynthesis (Ghayee and Auchus, 2007). Hill et al., (2012) also linked it to the release of catecholamines from the sympathetic nerve terminals which will cause hypothalamic release of corticotrophin-releasing hormone, which then increase ACTH release, ultimately stimulating secretion of cortisol from adrenal cortex.

The same results were obtained by Saichan et al., (2016) while Cicchetti and Rogosch, (2001) found that physical assault was associated with lower cortisol responses. Trickett et al., (2011)

stated that both low and high cortisol reactivity may be present in child physical maltreatment.

These contradictory findings may be explained by the presence of differences in the severity and timing of the violence, methodological variation in collection of the samples as well as characters of the participants.

A significant relation between cortisol level and injury severity score was detected as the highest cortisol levels were in cases with severe and critical and serious degrees. The same results are obtained by Saichan et al., (2016) who concluded that the plasma cortisol levels may function as a noninvasive biomarker for injury severity and prognosis assessment. The results also showed that all unsurvivable cases had the lowest cortisol level detected in the victims. This might be due to acute hemorrhage and increased intracranial pressure that led to impaired blood flow to organs and a poor adrenal cortex response to ACTH stimulation (Hetz et al., 1996).

The relation between cortisol level and the outcome was significant; patients with permanent infirmity or disfigurement were related to a higher level of cortisol. A possible reason is associated severity and repeated violence in such cases which may cause persistent higher cortisol levels due to higher intensity of the stress or emergence of new stress responses. Our findings are consistent with the results of Cernak et al., (1999) Srinivas et al., (2010) and Saichan et al., (2016) as they found a significant association between plasma cortisol level and prognosis in injured patients.

The initial plasma cortisol level measurements may act as a predictor for the development of complications and permanent infirmity in such cases and so the need for extra efforts for their proper management. This was supported by Counts et al., (2022) who stated that cortisol exaggerated responses are manifested by higher-than-average cortisol levels, which may result in delayed return to normal and development of complications. They also added that previous study suggested that extreme responses may put the person at a higher risk for adverse health outcomes such as persistent illnesses and early death due to biologic wears and tears on the systems of the body.

Murphy et al., (2022) also concluded that toxic stress is defined as extreme negative experiences that last for longer periods, such in cases of physical and sexual violences. The HPA axis and the release of cortisol constitute the main neuroendocrine response to stress. This type of stress can cause long-term psychological and physiological problems in growing children. In turn, these toxic stressors and traumatic experiences

show a high correlation with multiple adverse health consequences in adulthood life as well.

The relation between CRP level and type of violence was significant: CRP levels were higher in physical abuse than in sexual abuse as the injuries in physical violence were more extensive and the violence was mostly repeated and so giving time for more complicating inflammations. Aas et al., (2017) stated that physical maltreatment was associated with elevated CRP levels, however, Tyrka et al., (2015) found that CRP was not significantly associated with childhood physical maltreatment. D'Elia et al., (2018) also, stated that higher CRP levels were found in children suffered from sexual assault. This controversy may be due to different assessment methods of abuse (through victims' direct examination or through only survey and questionnaire), frequency and time of infliction (D'Elia et al., 2018).

This study results demonstrate no statistically significant difference in mean level of CRP between the different degrees of injury severity score. The same results were obtained by Panagiotis, (1998) who found that there was no correlation with injury severity score. The explanation was given by Alper et al., (2016) who stated that CRP levels increased 6-12 hours post trauma, suggesting that this criterion may not be useful in determining the severity of trauma in the initial assessment of the cases.

Regarding the distribution of the CRP level in relation to outcome. The relation was significant as the highest levels were detected in cases with permanent infirmity as most of these cases suffered from repeated violence with more inflammatory response. All cases of death were related to lowest CRP levels detected in the affected children. This could be explained by Bishara, (2012) who stated that blood CRP levels were not usually raised during clinical symptoms, however there were delayed elevations 8 to 10 hours after the emergence of the physical manifestations. Pepys and Gideon, (2003) also, stated that blood CRP concentrations are getting higher about 6 to 8 hours after the injury and peak in 48 hours. All death cases in this study died sooner after they arrived at hospital and had not enough time for the serum concentration of CRP to be elevated. However high serum CRP levels could be used as a reliable predictor factor for systemic inflammatory response in injured patients Bomba et al., (2013).

Cases with repeated violence showed higher levels of both markers as frequency of violence could result in increased and persistent stress and inflammatory responses. Cortisol levels may be affected by maltreatment frequency, severity, and

extent, as reported by Gonzalez, (2013). Punder et al., (2017) also concluded that CRP levels directly correlated with the number of maltreatment incidents included in their study.

CONCLUSION

Cortisol and CRP markers could help physicians in early diagnosis of physical and sexual maltreatment as evidence of stress and inflammation especially in cases with vague history of abuse and vague physical signs that are not conclusive for assault. High levels were significantly related to the type and frequency of violence, and they could help in the prediction of the development of complications and permanent infirmity in such cases. However, cortisol level was more advantageous in evaluation of such violences as it may function as a noninvasive biomarker for injury severity assessment as well.

RECOMMENDATIONS

Violence against children is a global issue that requires everyone in the community to contribute to the development of long-term, viable solutions that address structural barriers that contribute to and perpetuate interpersonal violence.

Further research is required to measure serial measurements of CRP and Cortisol in different time points (from admission of children until discharge) to assess posttraumatic levels for better prediction of prognosis and outcome.

CONFLICT OF INTEREST

All the authors of the current study had declared that there is not any conflict of interest.

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الملخص العربي

مستويات الكورتيزول والبروتين التفاعلي "سى" في الأطفال المعرضين للعنف الجسدي والجنسي

الواردين إلى مستشفيات جامعة المنوفية

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قسم الطب الشرعى و السموم الإكلينيكية- كلية الطب- جامعة المنوفية

العنف ضد الأطفال مشكلة شائعة في جميع أنحاء العالم ويحتاج إلى تقييم مناسب لتحسين طرق التصدى والوقاية منه. لذلك هدفت هذه الدراسة إلى التحقق مما إذا كان العنف (الجسدي والجنسي) عند الأطفال مرتبطاً بالتغيرات في مستويات هرمون الكورتيزول والبروتين التفاعلي سى (CRP) ودورهما المحتمل في تقييم نوع وتكرار وشدة وحصيلة هذا العنف. وتضمنت هذه الدراسة جميع الأطفال القادمين إلى مستشفى جامعة المنوفية والذين تعرضوا للعنف الجسدي أو الجنسي خلال فترة الدراسة ، من 1 ديسمبر 2016 إلى 30 نوفمبر 2018. تم مسبقاً تصميم ورقة سريرية واستيفائها للحالات. تم تصنيف المرضى المصابين حسب درجة خطورة الإصابة (ISS). كما تم أخذ عينات الدم من الحالات والمجموعات المراقبة لتقدير مستويات الكورتيزول والبروتين التفاعلي سى. تضمنت الدراسة 75 طفلاً ممن تعرضوا للاعتداء الجسدي أو الجنسي غالبيتهم من الفتيات وكان معظم الحالات من المناطق الريفية. فاق العنف الجسدي عدد العنف الجنسي وكانت غالبية العنف من النوع المتكرر. كانت الكدمات أكثر الإصابات الخارجية ظهوراً بين الحالات بينما كانت الكسور هي الأكثر شيوعاً في الإصابات الداخلية. تم شفاء أكثر من نصف الاطفال ، وبلغ معدل الوفيات 8٪ وكان 58.7٪ من الجروح من الدرجة الخطيرة حسب تصنيف (ISS). كان العنف ضد الأطفال مرتبطاً بتغيرات في مستويات الكورتيزول والبروتين التفاعلي سى بالمقارنة مع المجموعات المراقبة. ارتبطت التغيرات في الكورتيزول بشكل كبير بنوع وتكرار وشدة العنف وحصيلة الحالات بينما كانت تغيرات البروتين التفاعلي سى مرتبطة بشكل كبير بنوع العنف وتكراره وحصيلة الحالات. لذلك يمكن أن تساعد هذه المؤشرات الحيوية الأطباء في التشخيص المبكر وتقييم سوء معاملة وتعرض الأطفال للعنف كدليل على التوتر والالتهاب خاصة في الحالات ذات التاريخ الغامض لسوء المعاملة والعلامات الجسدية الغامضة التي لا تكون قاطعة للدلالة على الاعتداء الجسدي أو الجنسي. ويتطلب العنف ضد الأطفال من كل فرد في المجتمع أن يلعب دوراً في تفعيل حلول مستدامة وطويلة الأجل تعالج الجوانب التي تسهم في استمرار العنف بين الأجيال. ويوصى بمزيد من الدراسات لقياس المستويات التسلسلية للبروتين التفاعلي سى و هرمون الكورتيزول في نقاط زمنية مختلفة (من الدخول الى الخروج من المستشفى) لتقييم مستويات ما بعد الإصابة من أجل التنبؤ الأفضل بحصيلة ومستخرجات هذا النوع من العنف.