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Anxiety and plasma oxytocin levels in mothers having CP children

Alamzeb Jadoon^a, Ayesha Gohier^b

^a Associate Professor, Department of Physiology, Nowshera Medical College, Nowshera.

^b Assistant Professor, Department of Physiology, Rai Medical College, Sargodha.

Correspondence: * ayeshagohier@gmail.com

ABSTRACT

BACKGROUND & OBJECTIVE: Children with cerebral palsy (CP) experience several medical, social, and psychological problems, and their families, especially mothers, face considerable economic and psychosocial difficulties. The current study aimed to estimate the levels of anxiety in mothers caring for children who are severely affected by CP, compare these scores with those of mothers of healthy children and assess the correlation between anxiety scores and plasma oxytocin levels.

METHODOLOGY: The cross-sectional comparative study included a total of 42 mothers with first group of 21 mothers who had children with severe CP and a second group of 21 controls after obtaining written informed consent. All participants were younger than 40 years. Anxiety was assessed using the Beck Anxiety Inventory (BAI). Oxytocin was measured using Enzyme-Linked Immunosorbent Assay (ELISA).

RESULTS: No significant difference was observed between the means of the anxiety scores and plasma oxytocin levels of the two groups. Spearman correlation analysis showed, a significant negative correlation of BAI score with the plasma oxytocin levels was observed.

CONCLUSION: The results of this study revealed no significant difference in anxiety in mothers having CP children. The significant negative correlation between plasma oxytocin levels and anxiety scores suggests a possible role of oxytocin in anxiety.

KEYWORDS: Anxiety, Oxytocin, Cerebral Palsy.

INTRODUCTION

Approximately 3.6 % of the world population, i.e. 264 million, is suffering from anxiety disorders and an increase of 14.9 % was observed in the last decade globally^[1]. Cerebral Palsy (CP) is a non-communicable disease and a leading cause of disability in children, caused by hypoxic insult to the brain, with a global prevalence of 1.4 to 4 per 1000 live births^[2]. In Pakistan, District Swabi, KPK, its prevalence is approximately 1.22/1000 live births^[3].

A survey revealed CP as the leading cause of abnormalities related to posture, tone, and movement^[4]. Factors that can increase the risk of CP include intrauterine infection, developmental abnormalities, multiple gestation, placental abnormalities, retarded growth of the fetus, prolonged labour, preterm delivery and instrumental delivery^[5]. The economic burden of children with CP far exceeds the needs of healthy children, adding to the physical and mental stress on their parents^[6,7]. Parents, particularly mothers of children with cerebral palsy (CP), may experience psychological and emotional challenges. Several studies have investigated anxiety and assessed the impact of caring for children with CP on maternal quality of life (QOL)^[8,9].

Oxytocin hormone is synthesized in the hypothalamus and released from the pituitary. It is strongly associated with

social behavior, trust and stress^[10,11]. Basal plasma level in non-pregnant, non-lactating females is 200-359 pg/ml^[12]. Plasma oxytocin concentrations are positively related to CSF oxytocin levels and negatively related to anxiety^[13,14]. We conducted this study to assess anxiety in mothers caring for children with cerebral palsy (CP) and to determine the correlation between BAI scores and plasma oxytocin levels. The study aimed to investigate the effects of CP on maternal anxiety and plasma oxytocin levels and compare their scores with those of healthy controls. The results achieved emphasize on the need for psychiatric support to improve and enhance the quality of life of the child, his or her parents and family.

METHODOLOGY

This cross-sectional comparative study was conducted from 1st January 2020 to 31st December 2020. The Ethical Review Committee of the University of Health Sciences Lahore reviewed and approved the study on 23rd May 2019 (UHS/REG-19/ERC/1863). The Institutional Review Board (IRB) of Children Hospital/Institute of Child Health, Lahore, reviewed and approved the study on 18th July 2019 (2019-37-CHICH).

The study was carried out in Lahore, Punjab province, Pakistan. Researchers recruited subjects from a specialized

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tertiary care hospital of Lahore. The study included 42 mothers aged up to 40 years (21 in each group). Mothers younger than 40 years and having a child suffering from severe CP were considered eligible for this study. The Gross Motor Functional Classification System (GMFCS) was used as a diagnostic tool, and level V of the classification was considered severe CP in children^[15,16]. We calculated the sample size using the WHO calculator version 2.021; estimates were based on previous literature^[17]. All lactating and pregnant women, mothers on steroid or other hormonal therapy, oral contraceptive pills or medication for depression, and mothers having chronic liver and kidney diseases based upon history and investigations were excluded from the studies. The purposive sampling technique was used keeping in view the inclusion and exclusion criteria as described earlier.

A well-recognized self-report questionnaire with acceptable psychometric properties was used after consultation with the psychiatrist already working in the same tertiary care hospital for children in Lahore. Anxiety level was estimated by using the BAI^[18,19]. The recorded participants' demographic details of participants, past medical, surgical, or drug history, and family history on specially structured datasheets. Details about antenatal visits, investigations, duration of pregnancy, risk factors or diseases in pregnancy, mode of delivery, the delayed cry of the newborn, neonatal infections and family history of CP were also noted to find out the cause of CP.

Antecubital venous blood samples were collected between 8 am and 11 am to avoid fluctuations due to the circadian rhythm of the hormone^[20]. Estimation of oxytocin was performed within 10 days of sampling on unextracted plasma samples with the commercially available ELISA kit (Elabscience Biotechnology Inc. USA).

All the details were entered into a Microsoft Excel data sheet. Data were analyzed using the Statistical Package for

Social Sciences 25.0. Descriptive statistics were used to analyze the demographic data and other parameters. Mean $\pm$ S.D. or median + interquartile range was given for the quantitative variables. Frequencies and percentages were used for qualitative variables. Graphs were presented for the variables. Normality of data was checked by the Shapiro-Wilk test. Spearman correlation test was applied to assess the association of the oxytocin levels with BAI scores. Student's T-test was used to compare random blood sugar (BSR) and alanine aminotransferase (ALT) levels between group I and group II. The Mann-Whitney test was used to compare body mass index (BMI), serum creatinine, Glomerular filtration rate (GFR), total serum protein, serum bilirubin, anxiety scores, and plasma oxytocin levels between group I (mothers with children with CP) and group II (mothers with healthy children). A p-value of ≤ 0.05 is considered statistically significant.

RESULTS

This study included a total of 42 mothers, equally divided into two groups of 21 each. Group I included mothers of children with CP, and group II included mothers of healthy children. There was no significant difference between the ages of group I (mothers having children with CP) and group II (mothers having healthy children) ($p = 0.103$).

Anxiety score and plasma oxytocin levels were measured among the study participants. All participants were screened for chronic illness based on history and investigations such as BMI, serum creatinine, GFR, ALT, total serum protein, and serum bilirubin. All the participants of the study belonged to the middle-class socioeconomic status. Details noted revealed that among Group I, only 2 children reported CP in their first-degree relatives. 12 of the Group I mothers gave a positive history of prolonged labour, and 9 children had home delivery supervised by a midwife.

Table-I: Comparison of age in group I and group II.

Parameters	Mothers having children suffering from CP(n=21)		Mothers having apparently healthy children(n=21)	P-value
Age (years)	Mean $\pm$ SD	29.14 $\pm$ 6.79	32.52 $\pm$ 4.31	0.103 ^a
	Median (IQR)	30 (24-35)	31 (29-37)	

^a Mann-Whitney U test.

*P-value < 0.05 is considered statistically significant.

Group I and II were compared for the parameters included in the study. No significant difference was observed between the means of BMI, serum creatinine, GFR, ALT, total serum protein and serum bilirubin of both groups. However, the difference in BSR levels between the two groups was statistically significant, with a p-value of 0.024. The BAI scores for group I, having mothers of children with CP, were higher as compared to group II, but this difference was not statistically significant ($p = 0.176$, Mann-Whitney U test).

In group I (mothers having children suffering from severe CP), the plasma oxytocin was lower than the group II (mothers of apparently healthy children). Still, this difference was not statistically significant ($p = 0.571$, Mann-Whitney U test).

Among group I, all 21 mothers were diagnosed with mild anxiety. However, in group II, mothers having healthy children, 19 mothers had mild anxiety and 2 mothers had moderate anxiety.

By applying the Spearman rho correlation test, anxiety scores showed a significant negative correlation with the plasma oxytocin levels in both groups. Group I, mothers with children having CP, anxiety scores had a significant negative correlation with plasma oxytocin levels ($p = 0.037$, $r = -0.457$). In Group II (mothers with healthy children), a significant negative correlation was observed ($p = 0.001$, $r = -0.764$) (Table-V).

Table-II: Comparison of study parameters measured in cases and control groups.

Parameters	Mothers having children suffering from CP(n=21)		Mothers having apparently healthy children(n=21)	P-value
BMI (kg/m ²)	Mean ±SD	23.40±2.51	24.79±3.82	0.159 ^a
	Median (IQR)	22.70 (21.52-24.40)	24.59 (21.4-27.23)	
Serum creatinine (mg/dl)	Mean ±SD	0.57±0.09	0.61±0.10	0.351 ^a
	Median (IQR)	0.60 (0.5-0.65)	0.60 (0.5-0.7)	
GFR (ml/min/1.73m ²)	Mean ±SD	136.61±26.51	123.95±23.77	0.195 ^a
	Median (IQR)	131 (117-151)	124 (100-148.5)	
ALT (U/L)	Mean ±SD	19.19±4.13	17.61±3.76	0.205 ^b
	Median (IQR)	18 (16.5-21.5)	17 (14-20.5)	
Total Serum Protein (g/dl)	Mean ±SD	7.37±0.19	7.28±0.26	0.291 ^a
	Median (IQR)	7.40 (7.20-7.55)	7.30 (7.10-7.50)	
Bilirubin (mg/dl)	Mean ±SD	0.46±0.12	0.48±0.13	0.747 ^a
	Median (IQR)	0.50 (0.35-0.60)	0.50 (0.5-0.6)	
BSR (mg/dl)	Mean ±SD	103.52±8.57	97.76±7.32	0.024 ^{b*}
	Median (IQR)	103 (98-107)	98 (92.5-104)	
BAI score	Mean ±SD	8.81±6.52	7.38±7.35	0.176 ^a
	Median (IQR)	6 (4-17)	4 (3-8)	
Plasma Oxytocin (pg/ml)	Mean ±SD	115.60±40.30	139.92±70.11	0.571 ^a
	Median (IQR)	123.11 (82.32-148.80)	114.11 (84.71-190.68)	

a Mann-Whitney U test.

b Student T-test.

***P-value < 0.05 is considered statistically significant.**

Table-III: Comparison of BAI scores and plasma oxytocin levels in cases and control groups.

Parameters	Mothers of children suffering from CP(n=21)		Mothers with apparently healthy children(n=21)	P-value
BAI score	Median (IQR)	6 (4-17)	4 (3-8)	0.176 ^a
	Mean ± SD	8.81±6.52	7.38±7.35	
Plasma Oxytocin	Median (IQR)	123.11 (82.32-148.80)	114.11 (84.71-190.68)	0.571 ^a
	Mean ± SD	115.60±40.30	139.92±70.11	

a Mann-Whitney U test.

***P-value < 0.05 is considered statistically significant.**

Table-IV: Frequency and percentage of anxiety in mothers taking care of CP children and mothers of apparently healthy children.

Variables	Mothers of children with severe CP (n=21)		Mothers having healthy children(n=21)
Anxiety grades	Mild	21 (100)	19 (90.47)
	Moderate	0	2 (9.52)
	Severe	0	0 (0)

Table-V: Correlation of anxiety scores and plasma oxytocin levels.

Parameters	Mothers having healthy children (n=21)		Mothers having CP children (n=21)		All mothers included in the study (n=42)	
	BAI	Plasma Oxytocin	BAI	Plasma Oxytocin	BAI	Plasma Oxytocin
R	1.00	-0.764	1.00	-0.457	1.00	-0.652
P value	0.001*		0.037*		0.001*	

Spearman's Rho correlation coefficient was used to generate the correlation coefficient (rho) and p-values.

*** P-value < 0.05 is considered statistically significant.**

DISCUSSION

This study included two groups, group I with 21 mothers looking after children with severe CP and group II with 21 mothers with healthy children. Almost all 42 the mothers reported mild anxiety irrespective of groups. When further compared, no significant difference was noted between plasma oxytocin levels and anxiety scores of the two groups.

Anxiety and depression usually overlap in symptoms and treatment. Anxiety was measured based on the BAI score. In our study, mothers having children with CP had higher anxiety scores than the mothers having healthy children, but the difference was not statistically significant. Multiple studies have been conducted worldwide to assess anxiety in mothers having children with CP. Results suggest that mothers with children with CP have significantly higher anxiety scores as compared to mothers having healthy children^[21,22]. Some of the studies found no difference between the anxiety scores of the mothers having children with CP and the control group^[23]. One possible explanation could be the fact that anxiety symptoms typically arise during acute events and that chronicity of the state predisposes these mothers to depression rather than anxiety^[23].

In our study, plasma oxytocin levels showed a significant negative correlation with BAI scores in both group I and group II. In Group II (mothers having healthy children), there are multiple other factors like social factors, financial problems, household problems, family issues and hormonal imbalance that could be possible causes of anxiety and depression in them.

Scarce literature is available to correlate plasma oxytocin levels in mothers having children with CP. The present study helped us to correlate depression and anxiety with the plasma oxytocin levels in mothers having CP children. It highlighted the necessity of psychological support and social help for the mother of children with CP. It emphasised the need of proper medical services for the mother during the antenatal, natal, and postnatal periods. The study may help future advancements about oxytocin and its use as a biomarker for prediction, prognosis and treatment of depression.

RECOMMENDATIONS:

Proper, regular antenatal checkups and deliveries in a tertiary care hospital are mandatory to decrease the incidence of CP. Plasma oxytocin may play a role in assessing the prognosis of anxiety during treatment and can be part of treatment as adjuvant therapy.

Expectant mothers should have proper medical evaluation during pregnancy and even after delivery. The immediate assessment of the newborn is also of prime importance. Further studies with large sample size are recommended to highlight the role of oxytocin in anxiety. Education to the family and society about the requirement for psychological support and the need of social and family care, especially for the mother having a child, is highly recommended.

LIMITATIONS:

The study was a cross-sectional study conducted on a relatively smaller number of subjects due to financial and the time constraints; therefore, it is hard to establish the exact cause-and-effect relationship. Furthermore, this report applies only to oxytocin measured by ELISA using unextracted plasma, which is more prone to cross-reactivity. Different approaches measure the hormone, and each technique has different reference ranges and potential drawbacks. We included a limited number of parameters due to financial constraints and lack of funds.

CONCLUSION

All mothers visiting the hospital have mild anxiety irrespective of the CP disease. Mothers taking care of CP children are not more prone to depression and anxiety as compared to the mothers of healthy children. The significant negative correlation of plasma oxytocin with anxiety suggests some role in depression.

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Alamzeb Jadoon : Interpretation , Drafting the work and reviewing it critically for important intellectual content.

Ayesha Gohier : Substantial contributions to the conception , design and analysis of data for the work.

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