

Aggression Assessment and Plasma Serotonin Level amongst Pakistani Youngsters

SUMAIRA RIFFAT¹, SAHAR ZAHID², MUSHTAQ HUSSAIN³, RAZA UR REHMAN⁴, MASOOD ANWAR QURESHI⁵

¹Research Associate, Bioinformatics and Molecular Medicine Research Group, Dow Research Institute of Biotechnology and Biomedical Sciences, Dow College of Biotechnology, Dow University of Health Sciences, Karachi, Pakistan. Lecturer, PhD Scholar, Department of Physiology, Sindh Medical College, Jinnah Sindh Medical University, Karachi, Pakistan

²Research Associate, Bioinformatics and Molecular Medicine Research Group, Dow Research Institute of Biotechnology and Biomedical Sciences, Dow College of Biotechnology, Dow University of Health Sciences, Karachi, Pakistan

³Assistant Professor (Genetics, Genomics and System Medicine) Bioinformatics and Molecular Medicine Research Group, Dow Research Institute of Biotechnology and Biomedical Sciences, Dow College of Biotechnology, Dow University of Health Sciences, Karachi, Pakistan.

⁴Professor, Bioinformatics and Molecular Medicine Research Group, Dow Research Institute of Biotechnology and Biomedical Sciences, Dow College of Biotechnology, Dow University of Health Sciences, Karachi, Pakistan.

⁵Principal, Professor, Bioinformatics and Molecular Medicine Research Group, Dow Research Institute of Biotechnology and Biomedical Sciences, Dow College of Biotechnology, Dow University of Health Sciences, Karachi, Pakistan.

Correspondence to: Sumaira Riffat, Email: sumaira.riffat@jsmu.edu.pk

ABSTRACT

Background: Aggressive behavior is a multifaceted construct involving various physiological modulators and genetic factors with a variable frequency in different populations. Of multiple genetic factors, serotonin is known to have profound role with disagreement exists in relation to its expressional alignment with the intensity of aggression. The existing study is designed to develop alignment of the psychological scale of aggression with the plasma serotonin levels.

Methodology: Buss Perry Aggression Questionnaires (BP-AQs) were distributed among male and female students of different universities of Karachi. Among those, 2000 properly filled questionnaires were selected to be scrutinized and scored which led to selection of 80 students each of score lower than 60 (least aggressive individuals) or higher than 100 (most aggressive individuals). Plasma serotonin levels of the 160 individuals were then measured by ELISA.

Results: Cumulatively, males tend to have higher BP-AQ score than females (79.14+16.22 vs. 75.28+16.97) and also in physical aggression (23.81+6.44 vs. 21.05+6.17) statistically significant difference of $p=0.0011$ and $p<0.0001$, respectively. All scores of different forms of aggression were found positively correlated with each other and with strong statistical significance. Level of serotonin was found significantly higher ($p=0.0004$) in females (244ng/ml) compared to males (70.39ng/ml). Plasma serotonin levels were negatively correlated with BP-AQ scores especially in females ($p=0.0222$) and in whole of the assessed subjects ($p=0.0069$).

Practical implication: In order to facilitate a better understanding of aggressive behaviour, this study helps to align a physiological biomarker with psychological tools. Additionally, serotonin can be used as a biomarker to comprehend the physiological underpinnings of aggression, and future studies can be planned that use serotonin or its receptors in relation to aggressive behaviour. And it will positively impact the mental health of any society.

Conclusion: The findings in total suggest male holds more aggressive behavior especially physical aggression compared to females. Additionally, the aggression in female is more profoundly associated with the low plasma serotonin level.

Keywords: Aggression, Behavior, Hostility, Adolescents, Neurotransmitters, Serotonin,

INTRODUCTION

Aggression can be defined as the behavior deviant from the societal norm, which is particularly intended to be destructive to self or other¹. Based on different forms of manifestation and approaches, aggression can be divided into several subtypes including anger, hostility, physical and verbal aggression². In evolutionary terms, aggression is inarguably productive, but the development of social and civil system in Homo sapiens, have set another threshold for the accommodation of such behavior and its exhibition is often demonstrated to be counterproductive. In fact a study in United States concluded that financial losses of up to 92 billion USD only in the year 2000 were associated with drop in productivity underpinned by aggressive and/or violent behaviour³. Since youngsters are the group of population where economic and social progress bred for the impending future, this population subset may in turn hold profound importance for a nation and/or country.

Globally, prevalence of aggression varies in different age groups, genders and in different demographics. For example, 23% to 40% of the global population of children are shown to exhibit variable clinical signs of aggression⁴. In comparison, the prevalence of aggression in Pakistani children and adolescents is reported to be 36.5% and 44%, respectively^{4,5}. In low and middle income countries, adults are seemingly more prone to exhibit aggressive behavior where its prevalence is found to be 2.68 times higher in males than females⁵.

Physiologically, aggression is as complex if not more as its psychology, with an array of genes and/or encoded protein mutations and expressional dysregulation of hormones, proteins

and neurotransmitters have been found associated with the behaviour⁶. Amongst neurotransmitter a homeostasis of dopamine and serotonin noticeably impact the incidence and/or progression of aggressive behavior^{7,8}. Paradoxically, constitutive serotonin expression has been found both positively and negatively correlated with aggression⁹⁻¹⁵. These variations could be because of the study design, techniques employed in the measurement of serotonin or population under study. Thereby, this demands the need for further investigations in a different population sets with a distinct and/or standardized study design.

Since Pakistani population constitute nearly 2.83% of total world population, where almost 30% of the country's population comprises of youth, which indeed makes the backbone of the progress of the developing nation¹⁶. The present study aims to investigate the prevalence of aggression amongst Pakistani youngsters between the ages of 18 to 25 years employing BP-AQ. Moreover, alignment of plasma serotonin level with the scoring of BP-AQ has been attempted and discussed.

MATERIAL AND METHODS

Standardization of BP-AQs: Standard BP-AQs was first translated in Urdu and then retranslated in English by linguistic experts. The questionnaire was distributed among 200 each male and female undergraduate students of different universities of Karachi with guidance over provisional filling of questionnaire. The scores were later compared to assess the standardization of translation.

Assessment for Prevalence of Aggression: The standard BP-AQs was distributed among 2200 male and female undergraduate

students of different universities of Karachi with guidance over provisional filling of questionnaire with prior consent for the study. Of these, only 2000 forms were selected accounting consent and proper filling of forms. The properly filled questionnaires were then used to score the level of aggression holistically and in four different categories including hostility, anger, verbal aggression and physical aggression. From the assessed scores, 40 of each male and female students with BP-AQ score lower than 60 (least aggressive individuals) and 40 of each male and female student with BP-AQ score higher than 100 (most aggressive individuals) were recruited for further studies.

Estimation of Serotonin: The blood samples were taken from the selected least and most aggressive individuals in EDTA containing sterilized vacutainers and centrifuged at 2000g for 10 minutes to separate plasma, which was then pipetted out into pre autoclaved tubes. The plasma samples were stored at -80°C with proper coding and labeling until the performance of ELISA through Abcam's Serotonin Elisa Kit (Cat No: ab133053) in accordance with the protocols recommended.

RESULTS

Standardization of translated and reverse translated questionnaire did not reveal any statistically significant differences between BP-AQs scores in total and in different categories, that is; physical aggression, verbal aggression, anger and hostility (Fig. 1).

Out of total 2200 BP-AQs that were distributed among University students, 200 forms were excluded that did not seem to be properly filled. The remaining recruited questionnaires comprised of 806 males and 1194 females showed BP-AQ scores ranging from 39-137 and 29-128, respectively. Over all, male students seem to be more aggressive with BP-AQ score of 79.14 ± 16.22 than female having BP-AQ score 75.28 ± 16.97 , and the difference was found to be statistically significant ($p=0.0011$) (Fig. 2A).

Besides overall scores, the distinct scores relating to individual subtype of aggression also reflect interesting characteristics. Like in physical aggression the scores of male participants range from 9-45 compared to female scores of 9-43 where mean score is 23.81 ± 6.438 and 21.05 ± 6.168 , respectively with statistically significant difference ($p<0.0001$). The other three forms of aggression, anger, hostility and verbal aggression did not show any noticeable difference between both genders (Fig. 2B-E).

In addition, the different correlation analysis among hostility and anger, anger and verbal aggression and verbal to physical aggression when performed showed positive correlations ($p<0.0001$) between each of the two compared categories, irrespective to the genders (Fig. 3). Subsequently, the serotonin levels were when measured of most and least aggressive individuals found to be in range of 1.363-779.8ng/ml ($118.2 \pm 179.10\text{ng/ml}$) for individual with BP-AQ score equal to or greater than 100 and 6.320-1301ng/ml ($186.4 \pm 246.10\text{ng/ml}$) of individuals with scores equal to less than 60 with the marginal statistical difference found between them ($p=0.0438$) (Fig. 4A). In male participants, with BP-AQ scores > 100 , range of plasma serotonin was found to be 1.363-210.6ng/ml ($44.41 \pm 45.96\text{ng/ml}$) and with BP-AQ scores < 60 the plasma serotonin level was within 9.227-562.0ng/ml range ($93.36 \pm 129.6\text{ng/ml}$). The difference between the serotonin levels of least and most aggressive males was found to be statistically insignificant ($p=0.3297$). Similarly the difference between serotonin levels of female with BP-AQ scores $> 1301\text{ng/ml}$ ($273.3 \pm 294.6\text{ng/ml}$) was also found to be statistically insignificant ($p=0.1210$) (Fig. 4B). Furthermore, correlation analysis between plasma serotonin and total BP-AQ scores showed negative association between the two variables ($p=0.0069$; $r=-0.2129$) (Fig. 5A). However, such association dwindles when the comparison was made with reference to males but marginally remained linked in case of females ($p=0.022$; $r=-0.2570$) (Fig. 5B and 5C). Plasma serotonin levels and BP-AQ scores of physical Aggression were found negatively correlated in total ($p=0.0486$, $r=-0.1562$) and in case of males ($p=0.0364$, $r=-$

0.2329) whereas no significant score100 ranges from 1.424-779.8ng/ml ($203.3 \pm 231.9\text{ng/ml}$) and BP-AQ scores < 60 ranges from 6.320-correlation was found in case of females (Fig. 5D). In contrast the correlation analysis when performed between BP-AQ scores of all other categories of aggressions and plasma serotonin levels showed no potential association (Fig. 5E-G).

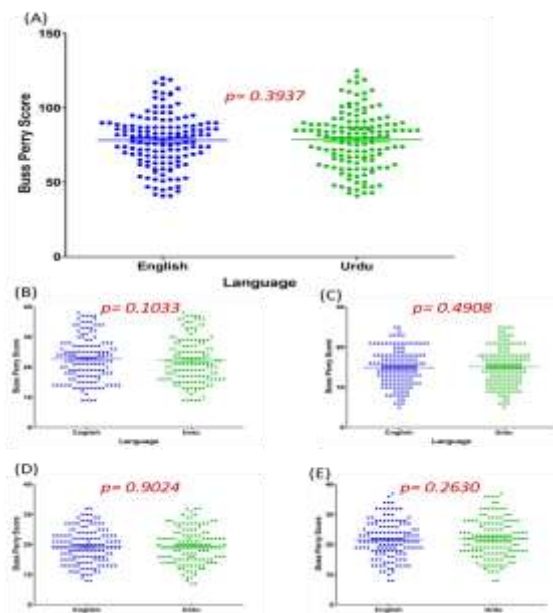


Figure 1: Standardization of Buss Perry Aggression Questionnaire. Comparison between total scores of Buss Perry questionnaire (A), scores of physical aggression (B), scores of verbal aggression (C), anger (D) and hostility (E) in English (blue) and Urdu (green) are shown here. Mean scores and standard deviation are represented by large and small horizontal bars, respectively.

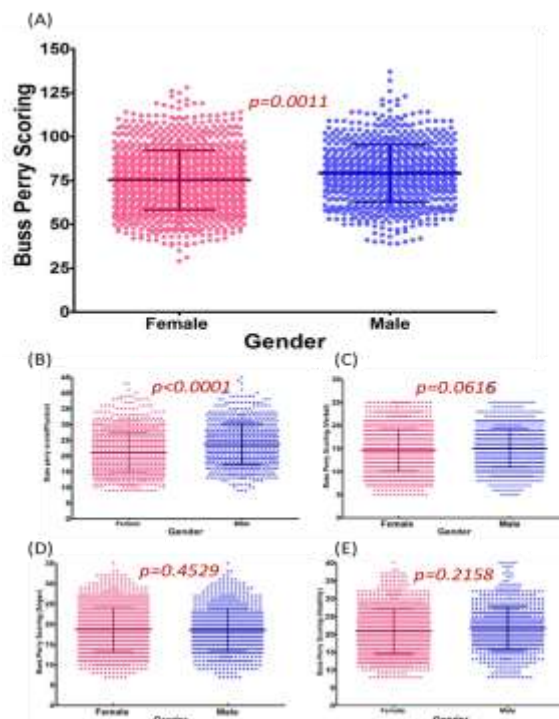


Figure 2: Buss Perry Aggression Questionnaire Scores. Comparison between total scores of Buss Perry questionnaire (A), scores of physical aggression (B), scores of verbal aggression (C), anger (D) and hostility (E) in male (blue) and female (pink) are shown here. Mean scores and standard deviation are represented by large and small horizontal bars, respectively.

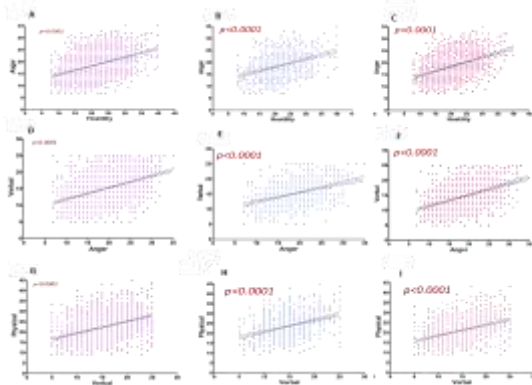


Figure 3: Correlation between different types of Aggression. Correlation between anger and hostility scores on Buss Perry Aggression Questionnaire is shown in both male and female individuals (A), male (B) and female participants (C). Correlation between verbal aggression and anger scores on Buss Perry Aggression Questionnaire is shown in both male and female individuals (D), male (E) and female participants (F). Correlation between physical and verbal scores on Buss Perry Aggression Questionnaire is shown in both male and female individuals (G), male (H) and female participants (I). In all cases, the regression line and 95% confidence interval bands are shown with solid and dotted lines, respectively.

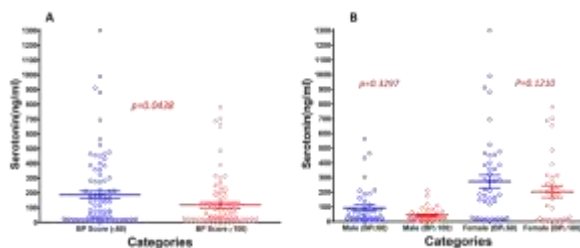


Figure 4: Comparison of Plasma Serotonin Levels. Comparison of plasma serotonin levels among least aggressive individuals ($bp < 60$) (blue dots) with the serotonin levels in highly aggressive individuals ($bp > 100$) (red dots) is shown here (A). Comparison of serotonin levels among least aggressive males and females ($bp < 60$) with the serotonin levels in highly aggressive males and females ($bp > 100$) is shown. The least aggressive individuals are coloured blue, whereas highly aggressive participants are represented by red colour. (B) Mean value scores and standard deviations are represented by large and small horizontal bars, respectively.

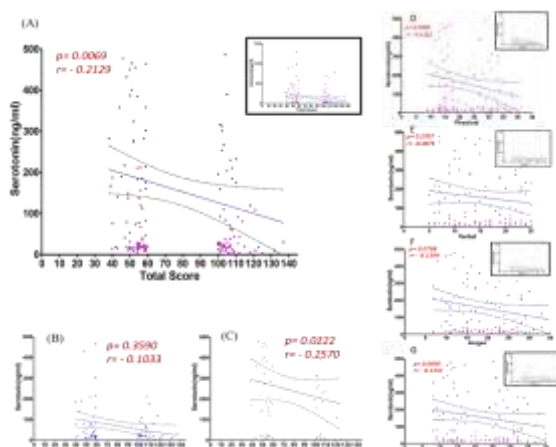


Figure 5: Correlation between Buss Perry Scores and Plasma Serotonin level. Correlation between Buss Perry scores (total) and serotonin level in least and highly aggressive males and females (A) represented by purple dots, males (B) represented by blue dots and females (C) represented by pink dots are shown. Correlation between Buss Perry scores (Physical) and serotonin levels in least and highly aggressive individuals both males and females (D). Correlation between Buss Perry scores (Verbal) and serotonin levels in least and highly aggressive individuals both males and females (E). Correlation between Buss Perry scores (Anger) and serotonin levels in least and highly aggressive individuals both males and females (F). Correlation between Buss Perry scores (Hostility) and serotonin levels in least and highly aggressive individuals both males and females (G). In all cases, the regression line and 95% confidence interval band are shown with solid and dotted lines respectively. The insets show the full scaled graphs.

DISCUSSION

The standardization of BP-AQ shows insignificant difference between the translated BP-AQs, showing the validity of the BP-AQ for the indigenous population (Fig. 1). BP-AQ has been translated and used in almost all major languages and have showed its validity in multiple ethnic populations¹⁷. However, there are limitations of employing BP-AQ since its being designed and validated only in the population with age range of adolescents and early adulthood². Thus, the present validation is restricted to only youngsters but not the whole population in general. It is though worth mentioning here that Pakistan is amongst the very few countries where the youngsters constitute almost 1/3rd proportion of the total population¹⁸ which by and large considerably different from countries like Japan and most European nations where middle and old aged individual forms a significantly high proportion of the population¹⁸. Therefore, the present analyses hold significant importance to obtain a better idea in relation to the prevalence of aggressive behavior for the country.

Out of 2000 assessed individuals in the study, 40.3% were males and 59.7% were females. Greater number of recruited males (10.66%) scored high on aggression questionnaire compared to females (9.69%) with statistically significant difference (Fig. 2A). Categorically, male participants scored more on aggression questionnaire in terms of physical aggression (Fig. 2B).

Whereas statistically insignificant differences were observed in relation to verbal aggression, anger and hostility between both genders (Fig. 2C-E). This data is in alignment with the estimation of higher prevalence of physical aggression (47.8%) in males than females (25.0%) across North America and Czech Republic where physical aggression was found to be prevalent in 69.1% in males and 26.7% females¹⁹. In South Asia, a study conducted in India on 5476 individuals found that in addition to higher prevalence of aggressive behavior in male, youth and adolescents also experiences more bouts of aggressive behavior than adults²⁰. Similarly, the study conducted in school going boys and girls of Iran also found higher occasion of physical aggression in boys (15.6%) than girls (6.3%) whereas the verbal aggression score was found higher in girls (7.0%) than boys (2.9%)²¹. Such studies also attempt to associate these gender differences with various physical, environmental and psychological factors. A well-established link exist between testosterone, the male sex hormone, and aggression; levels of which also seem to peak at puberty and decrease thereafter²²⁻²³ a pattern of physical aggression that is suggested in present study and was previously known as “Young Male Syndrome”²⁴. In addition the correlation analysis in present study shows strong positive correlation between the scores of hostility and anger, anger and verbal aggression and verbal and physical aggression (Fig. 3) in both genders. This points to the transition of hostile thoughts into verbal and in turn execution of physical action of aggression, which is consistent with the earlier studies demonstrating link between physical and verbal aggression^{25,26}.

Aggressive behavior is mostly underpinned by homeostasis between two bio molecules namely serotonin and dopamine^{7,10,14} where former is regarded as the most studied neurotransmitter because of its broad-spectrum influence on major neuronal pathways regarding mood regulation^{1,8,12-14}. There are number of neurobiological studies depicting the plasma or serum serotonin levels as a peripheral biomarker for various mental and/or psychiatric disorders like depression, schizophrenia, attention deficit hyperactivity disorder (ADHD), autism as well as its association with aggressive behavior. The later yields paradoxical results regarding serotonin levels and its metabolite 5-HIAA in highly aggressive people compared to non-aggressive individuals^{14,27,28}. But it is worth mentioning here that serotonin or its metabolite levels in CSF (especially spinal tap) is not a direct and clear cut index of post-synaptic neuronal serotonin activity. Thus, in this study we decided to use plasma levels of serotonin based on multiple previous evidences that storage, uptake and

release of serotonin in platelets is identical to that occurring in brain serotonergic neurons²⁹⁻³¹.

In the present study, the more aggressive individuals who scored higher on BP-AQ were found to have low serotonin level compared to less aggressive individuals (Fig. 4A) which is consistent when study groups are plotted on graph showing both males and females with BP-AQ scores >100 (less serotonin) compared to high serotonin found in both genders having BP-AQ <60 (Fig. 4B). This negative correlation between BP-AQ score and plasma serotonin levels is in accordance with most of the studies conforming the "Serotonin Deficiency Hypothesis" in relation to aggressive behavior³². Consequently, females were found to be less aggressive over all, in consistence with several previous studies, also found to have more serotonin compared to males (Fig. 4B). The higher serotonin in female can be due to the influence of estrogen on serotonergic pathways as well as mood changes³³. Though the lack of statistical significance between the serotonin level and BP-AQ could be due to variety of reasons like hypo critic filling of Buss Perry questionnaire, multifactorial physiological etiology of anger and nature of anger³². The later seems plausible as negative correlation was observed between serotonin and physical aggression and anger in males but not cumulatively (Fig. 3). This might be seen in parallel to the predictions from the taxonomic theory of life-course which depicts exhibition of externalizing behavior like aggression by male is more pronounced compared to women who tend to show internalizing disorders like depression³⁴. The mediator role of serotonin in testosterone dependent regulation of aggression is yet another link which may be helpful in explaining gender differences in plasma serotonin level found in our study²². Finally, it is also possible that the binding of serotonin with its different receptors may lead to different consequences which may explain variation in the studies exploring the link between serotonin and aggression³⁹. Indeed, there are structural differences in different serotonin receptors. In addition, spatial orientation of functionally important residues also varies subtly³⁵. This in turn may reflect different affinities to the ligand for the receptors and ensuing downstream cascade of molecular events⁴.

CONCLUSION

The present data is the first to explore the frequency of the aggressive behavior and its different forms and shape amongst Pakistani youngsters. The findings in total suggest males hold more tendencies towards aggressive behavior especially physical aggression compared to females. Additionally, aggressive behavior in females and in particular physical aggression in males has been linked with the decrease level of plasma serotonin.

Conflicts of Interests: The authors declare no conflict of interest

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