

# Impacts of intake of bakery food chemicals, degraded water and psychiatric drugs on liver & renal functions of brain tumor patients

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**Abstract:** A chemically preserved food has raised mental health issues. Abnormalities in liver and kidney functions have been reported from mentally imbalanced individuals. This study was focused on finding anxiety issues and biochemistry alterations in brain tumor patients and in controls. The levels of liver & kidney enzymes were compared in both groups through Mann-Whitney U test. Kendall's tau-b correlation was conducted to determine that is there any relationship between anxiety levels and biochemistry parameters in both groups. There were more occurrences of severe anxiety levels (58%) in brain tumor patients. There were more mood swings in CG (64%) as compared to BP (48%). Less sleeping pattern was found in CG (42%) as compared to BP (37%). More patients (58%) were having severe anxiety levels as compared to CG (52%). 73% patients were having low levels of alkaline phosphatase (AP). 52% individuals in CG were having low levels of AP. AP was found significantly associated with anxiety levels in brain tumor patients only. A nutrient deprived food from preservation can reduce levels of alkaline phosphatase. This can impact metabolism of necessary minerals for proper brain function. This epidemiological study reports a significant association between anxiety and reduced AP levels.

**Keywords:** Alkaline phosphatase, anxiety, liver and renal functions, bakery food chemicals.

## INTRODUCTION

Food preservatives prolong the shelf life of bakery products by inhibiting microbial degradation. These processed items loaded with chemical preservatives which can induce genotoxic and cytotoxic effects on various (El Hefny *et al.*, 2017). A shift in diet from organic to processed bakery food has raised mental health concerns in the form of psychological disorders, depression or anxiety. Disturbances in liver and kidney functions have been reported from mentally imbalanced people. Everyone takes packed food such as bread, packed juices, jam, pickle, ketchups etc., which, contain artificial food colorants which can alter hepatic functions. This study was focused on finding the prevalence of mood-swings, sleeping time, intake of psychiatric medicines, sleeping drugs, anxiety levels, alteration in liver and kidney enzyme levels in brain tumor patients (BP) and in local population who were taking bakery food and degraded water, etc. Ahmad *et al.* (2001) found that in some rural areas of Pakistan, women (72%) and men (44%) of men suffered from anxiety. A 50.2% of Karachi people were suffering from generalized anxiety disorder (Khan *et al.*, 2013). Kidwai & Ahmed (2013) reported that out of total 1488 individuals, 31.3% reported the prevalence of sleep

problems. A higher frequency of insomnia in females (32.7%) was reported as compared to males (28.6%). A study was conducted by Bateman *et al.*, (2004) evaluated the hyperactive behavior or restlessness, anxiety in three years old children who were consuming sodium benzoate preservative based food. A significant association existed between unhealthy dietary habits and degraded mental state together with depressive disorder development (Puloka *et al.*, 2016). Administered high doses of artificial food color have resulted in an accelerated metabolism of serotonin in several brain regions accompanied with higher plasma corticosterone levels, to induce a hyperactive behavior (Dalal *et al.*, 2010). In a study, the effects of artificial food colors were assessed in children. The subject population exhibited hyperactive behavior owing to the consumption of food items loaded with food colorants and preservative benzoate (McCann *et al.*, 2007). Sodium benzoate is responsible for significant reduction in weight, cirrhotic and necrotic alterations in liver (Aktac *et al.*, 2003). It is a potent neurotoxin which exerted negative effects on learning and memory performance in laboratory animals (Khoshnoud *et al.*, 2017). Sodium benzoate and citric acid caused liver and kidney tissue damage in Wistar albino rats. Citric acid resulted in the up regulation of total Sialic acid levels in kidney tissues (Bakar & Aktac, 2014). Phosphorus

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preservatives have a widespread application in meat, soft drinks and beverages, dressings, bakery goods and cheese (Uribarri, 2007). A recent study found a positive correlation in the intake of unprocessed foods such as vegetables, fish and unrefined grains with the anxiety in adults (Gibson-Smith *et al.*, 2019).

## MATERIALS AND METHODS

### *Study design, clinical and background information*

This case-control epidemiological study was conducted through a detailed survey on a pre-designed, self-administered proforma under the supervision of a neurologist for background, clinical and anxiety assessments. The study focused on finding the prevalence of mood-swings, sleeping time, intake of psychiatric medicines, sleeping drugs, anxiety levels, alteration in liver and kidney enzymes levels in Asian Pakistani brain tumor patients (BP; n=71) and in matched local control group (CG; n=130) who were taking bakery food of artificial flavored food items and degraded water, etc. The brain tumor patients were targeted in this study as subjects from Jinnah Hospital, Lahore and Shaikh Zayed Hospital, Lahore.

### *Clinical information and anxiety test*

A generalized anxiety test (GAD-7) (Spitzer *et al.*, 2006) consisting of seven items was used to measure the anxiety. The participants scoring 5, 10 and 15 cut off points were grouped into mild, moderate and severe anxiety classes respectively. The information of anxiety test score was categorized as: mild, moderate and severe.

### *Blood sampling and measurements of liver & renal enzymes/proteins*

A blood samples of 2 ml from each individual from both groups (BP; n=71 and CG; n=130) were collected after taking written informed consents. The samples were obtained in serum separating tubes and were sent to laboratory immediately after its collection to perform liver function test (LFT) and renal function test (RFT) for both groups. After collection of the sample, the tubes were gently inverted to mix the blood with clot activator and then placed in vertical position for a few minutes until the light yellow colored blood serum layer was appeared. The measurement of LFT parameters, i.e., ALT (alanine aminotransferase) in U/L, AST (aspartate aminotransferase) in U/L and AP (alkaline phosphatase) in U/L was done by following Aeroset Abbott chemical kits: Aeroset ci800 7D56-20 and Aeroset 7D55-20 and 7D55-30. Bilirubin in mg/dl was measured from Abbott Aeroset 8G63-20. The measurement of RFT parameters, i.e., blood urea (BU) in mg/dl and creatinine in mg/dl from Abcam kits (ab83362) and (ab65340) respectively.

## STATISTICAL ANALYSIS

All included biochemistry parameters' mean values (ALT/SGPT, AST/SGOT, AP, BU, creatinine levels)

were calculated for all normal values which were found within the normal range, all values which were below the normal range and all values which were found above the normal range in both groups. *Chi Square tests* (a test of association) of independence were used to determine whether there is an association between each categorical variable that whether the variables were independent or related. *Shapiro-Wilk (W)* test was applied to determine the normalized or non-normalized distribution in each LFT/RFT depending upon the p-values obtained. *Mann Whitney (U) test* was applied to compare the above mentioned (LFT/RFT) parameters in both groups (BP & CG) and identified significant results. *Kendall's tau-b correlation* was conducted to determine that is there any relationship between anxieties and biochemistry (blood urea, creatinine, SGPT, SGOT, bilirubin, alkaline phosphatase) variables in BP patients as well as in CG. A p-value of less than 0.050 was considered significant.

### *Ethical approval*

A prior ethical approval was taken. Informed consents were obtained from all patients included in the study. The study is conformed to the institutional ethical standards. The author reports no conflict of interest.

## RESULTS

### *Background information*

There were 15 (21.13%) patients from rural areas, 48 (67.71%) from urban areas and 8 (11.27%) from suburban areas of Lahore. In the CG, there were 11 (8.46%) individuals from rural areas, 106 (81.52%) from urban areas and 13 (10%) from suburban areas of Lahore. There were 28 (39.44%) patients were in the age group 8-32 years, 30 (42.25%) were in the age group 33-57 years and 13 (18.31%) were in the age group 58-82 years. In the CG, there were 86 (66.15%) individuals were in the age group 8-32 years, 40 (30.77%) were in the age group 33-57 years and 4 (74.62%) were in the age group 58-82 years. There were 37 (52.11%) male patients and 34 (47.89%) female patients and in the CG, there were 97 (74.62%) males and 33 (25.38%) females. There were 45 (63.38%) patients were in poor status, 26 (36.62%) were from middle class family and there was no patient from upper class family status. There were 29 (22.31%) individuals were poor, 101 (77.69%) were from middle class family in CG. There was no one from an upper class family in a CG as well. There were 5 (7.04%) patients were farmers, 13 (18.31%) were field workers, 4 (5.63%) were shopkeepers, 30 (42.25%) were housewives, 6 (8.45%) were students, 5 (7.04%) were teachers and 4 (5.63%) were office workers. In the CG, there were 7 (5.38 %) patients were farmers, 20 (15.38%) were field workers, 20 (15.38%) were shopkeepers, 18 (13.85%) were housewives, 25 (19.23 %) were students, 20 (15.38%) were teachers and 20 (15.38%) were office workers.

**Table 1a:** Association between occurrence of intake of sleeping pills & intake of psychiatric medicines in brain tumor patients and Controls

Groups	Intake of Sleeping Pills		Total	Chi Square	p-value
	Yes	No			
Brain Tumor Patients (n=71)	2	69	71	0.0491	0.82466
Controls (n=130)	3	127	130		
Total	5	196	201		
	Intake of Psychiatric Medicine				
	Yes	No			
Brain Tumor Patients (n=71)	0	71	71	Chi-square cannot be calculated	-
Controls (n=130)	0	130	130		
Total	0	201	201		

**Table 1b:** Association between 'mood swing per day', 'daily sleeping hours' & Anxiety Levels in brain tumor patients (BP) and controls (CG)

Groups	Mood Swing Frequency			Total	Chi Square	p-value
	2-4 times/day	5-7 times/day	>7 times/day			
Brain Tumor Patients (n=71)	34	24	13	71	4.8195	0.089839
Controls (n=130)	83	31	16	130		
Total	117	55	29	201		
	Daily Sleeping Hours					
	<8 hours	8 hours	>8 hours			
Brain Tumor Patients (n=71)	26	30	15	71	5.5889	0.06115
Controls (n=130)	55	63	12	130		
Total	81	93	27	201		
	Anxiety Test Scores					
	Mild	Moderate	Severe			
Brain Tumor Patients (n=71)	10	20	41	71	51.4501	<0.0001† († highly significant)
Controls (n=130)	68	46	16	130		
Total	78	66	57	201		

**Table 1c:** Association between sources of water intake in brain tumor patients (BP) and healthy individuals (CG)

Groups	Drinking Water					Total	Chi Square	p-value
	Bore/ Well water	Boiled water	Tap water	Filtered water	Mineral water			
Brain Tumor Patients (n=71)	41	3	10	15	2	71	33.0561	<0.000001
Controls (n=130)	26	13	17	59	15	130		
Total	67	16	27	74	17	201		

**Clinical and surgical information**

There were 40 (56.34%) benign cases and 26 (36.62%) were malignant cases. All of the patients had gone through chemotherapy treatments, whereas, 29 (40.85%) had gone through the radiotherapy treatment with maximum sessions 25 and minimum sessions 8. Sixty five (91.55%) patients did not take steroids and 70 (98.59%) did not take any antiepileptic drug. No family history of cancer was found in majority of patients, (60; 84.5%) and in controls (103; 79.23%).

**Psychiatric health and anxiety level assessments**

Most of the patients (69; 97.18%) and CG (127; 97.69%) were not taking sleeping drugs. Similarly, most of the

patients (64; 90.14%) and CG individuals (127; 97.69%) were taking anti-depressants. No one was found with an intake of psychiatric medication in both groups. Most of the patients (34; 47.88%) and most of CG individuals (83; 63.85%) were found with mood swing 2-4 times per day. The 26 (36.62%) patients and 55 (42.31%) control individuals were having sleep less than 8 hours, whereas most of them were having sleep equal to 8 hours of sleep (BP: 30; 42.25%, CG: 63; 48.46%). Following are the results of anxiety test: there were 10 (14.08%) patients with mild level anxiety (score: 5), 20 (28.17%) were with moderate level anxiety (score: 6-10) and majority i.e., 41 (57.75%) patients with severe level anxiety (score: 11 and greater). In CG: there were majority, i.e., 68 (52.31%)

patients with mild level anxiety (score: 5), 46 (35.38%) were with moderate level anxiety (score: 6-10) and 16 (12.31%) patients with severe level anxiety (score: 11 and greater).

#### **LFT & RFT -Mean values and comparisons**

Sixty four (91.14%) BP patients were having normal blood urea (BU) levels (mean: 26.54 mg/dl), whereas, 126 (98.44%) controls were having normal BU levels (mean: 26.833 mg/dl). There were only 2 (2.82%) patients with BU levels above the normal range (mean: 60.5 mg/dl), whereas, there was no control group person with high levels of BU levels. There were 5 (7.04%) patients with BU levels below the normal range (mean 7.14 mg/dl), whereas, there were 2 (1.56%) controls were having BU levels below the normal range (mean: 8.7 mg/dl). Sixty eight (95.77%) BP patients were having normal creatinine levels (mean: 0.876 mg/dl), whereas, 115 (89.84%) controls were having normal creatinine levels (mean: 0.932 mg/dl). There were only 2 (2.82%) patients with creatinine levels above the normal range (mean: 3.2 mg/dl), whereas, there were 5 (3.91%) controls with high levels of creatinine levels (mean: 1.74). There was only 1 (1.14%) patient with creatinine levels below the normal range (mean: 0.5 mg/dl), whereas, there were 8 (6.25%) controls who were having creatinine levels below the normal range (mean: 0.4 mg/dl). Fifty seven (80.28%) patients were having normal SGPT levels (mean: 30.47 U/L), whereas, 113 (88.28%) controls were having normal SGPT levels (mean: 25.41 U/L). There were 14 (19.72%) patients with SGPT levels above the normal range (mean: 63U/L), whereas, there were 15 (11.72%) controls with high levels of SGPT levels (mean: 68). There was no patient and CG individual with low levels of SGPT as compared to the normal range. Fifty nine (83.1%) BP patients were having normal SGOT levels (mean: 25.88 U/L), whereas, 114 (89.06%) controls were having normal SGOT levels (mean: 26.84 U/L). There were 12 (16.9%) patients with SGOT levels above the normal range (mean: 49.66 U/L), whereas, there were 16 (12.5%) controls with high levels of SGOT levels (mean: 49.31 U/L). There was also no patient and CG individual with low levels of SGOT as compared to the normal range. Seventy (98.59%) patients were having normal bilirubin levels (mean: 0.544 mg/dl), whereas, 117 (91.41%) controls were having normal bilirubin levels (mean: 0.633 mg/dl). There was only 1 (1.41%) patient with bilirubin levels above the normal range (mean: 49.66 mg/dl), whereas, there were 11 (8.6%) controls with high levels of bilirubin levels (mean: 1.71 mg/dl). There was also no patient and CG individual with low levels of bilirubin as compared to the normal range. 11, 8.59%). Only nineteen (26.76%) patients were having normal alkaline phosphatase (AP) levels (mean: 128.4 U/L), whereas, 60 (46.88%) controls were having normal AP levels (mean: 144.32 U/L). There was no patient with AP levels above the normal range, whereas, there were 2

(1.56%) controls with high levels of AP levels (mean: 302 U/L). There were 52 (73.24%) patients with low levels of AP (mean: 72.92 U/L) and there were 66 (51.56%) CG individuals with low levels of AP (mean: 75.83 U/L).

#### **Chi-square tests-association of relative significance**

A significant association ( $p < 0.0001$ ) was found in occurrences of three levels of anxiety (mild, moderate & severe) between brain tumor patients and CG. The two were significantly different ( $p < 0.000001$ ) relative to different drinking water sources (tables 1a-1c).

#### **Mann-Whitney (U) test and kendall's tau-b correlations**

Following were found significant: SGPT levels (Z score: -3.45664; p value: 0.00054), bilirubin (Z score: 4.2659; p value: 0.00001) and AP (Z score: 3.74583; p value: 0.00018), blood urea (Z score: 4.2659; p value: 0.00001). All correlations were insignificant except alkaline phosphatase (AP) in brain tumor patients at p-value 0.007 with Kendall's tau-b coefficient -0.311. There was no significant correlation in any variable in control group individuals.

## **DISCUSSION**

The exposure to food additives, chemicals in the human body comes from the consumption of various bakery foods. Such chemicals can trigger anxiety, cognitive deficits, and behavioral disorders. Some food additives like monosodium glutamate and aspartate have a widespread use in different foods as aroma or flavor enhancers. They are considered as excitatory neurotoxins (Yonden *et al.*, 2016). We evaluated a correlation between anxiety levels and all biochemistry levels. Seddighi *et al.*, (2015) reported a 14.7% prevalence of anxious behavior in brain tumor male patients before surgery. The anxiety rate in female brain tumor patients was 28.7% preoperatively. 73% patients were having low levels of AP, whereas, 52% individuals of CG were having low levels of AP. Only, alkaline phosphates (AP) was found significantly associated (p-value 0.007) with anxiety levels in brain tumor patients. A poor quality processed bakery and fast food items are significantly associated with mental anxieties (Jacka *et al.*, 2010). Methylcellulose is used as an emulsifier, flavor enhancer and stabilizer in a processed foods such as ice creams, baked goods, milk and processed meat. Animal models have demonstrated a positive correlation between MSG and neuronal damage (Farombi & Onyema, 2006). Butylated hydroxyanisole (BHA) is used as an antioxidant in cheese, oil, margarines, crisps and soup mixes to prevent oil from oxidation and rancidity. The neoplastic changes have been observed in rats fed with BHA diet (Ito *et al.*, 1983). Sunset Yellow is used in processed and packaged diet like ice creams, biscuits, soft drinks, cheese, margarines and candies. It is proved to induce headaches, behavioral changes, sleeping disorder, high

blood pressure, mental degradation, carcinogenic effects and damage to kidneys & adrenal glands. Dietary toxicity of Sunset Yellow was investigated in male rats and a significant high level of alanine transaminase, aspartate transaminase, alkaline phosphatase, creatinine and urea were found in subjects as compared with the controls (Elhalem *et al.*, 2016). Most (58%) of brain tumor patients in our study were found with severe anxiety levels, whereas, most (52%) of our CG individuals were found with a mild level of anxiety. Sleeping time was found less than 8 hours in 37% patients and 42% of control group individuals in our study. A chronic sleep deprivation can alter the neurotransmitter receptor and neuroendocrine stress systems (Novati *et al.*, 2008). A study examined sleep patterns in children and found that > 80% had at least one sleep-related problem, and > 50% had three or more sleep disturbances in the form of insomnia (Alfano *et al.*, 2007). Sleep disturbance in children was also linked with anxiety (Gregory *et al.*, 2005). Yetimalar *et al.*, (2007) also provided the evidence of a link between psychological symptoms such as psychomotor agitation, decreased sleep and brain tumor. Zwinkels *et al.*, (2016) reported changes in behavior in Glioma patients. We found a significant associated between anxiety levels and AP in brain tumor patients only. Kaplan *et al.* (1940) mentioned that patients of Glioma or Medulloblastoma can have raised AP levels. Loss of AP has been observed in high-grade Meningiomas (Niedermayer *et al.*, 1997). Ray *et al.*, (2017) reported that Zn and Mg deficiencies are important to cause lower AP activity. A positive correlation was found between these minerals and AP alterations. The use of antipsychotic medication can have a direct correlation between hypokalemia (Hafez *et al.*, 1984). Bilirubin is an antioxidant in the antioxidant brain networks (Mancuso, 2004). The low bilirubin levels have been found to be associated with a high prevalence of cerebral deep white matter lesions (Higuchi *et al.*, 2018). A degraded water intake can also impact brain. Many included patients (58%) in this study were using unsafe bore water/well-water or ground water for drinking. There are higher levels of heavy metal and biological contaminants in some groundwater of Pakistan (Waseem & Arshad, 2016). Mueller *et al.*, (2004) reported a positive association between the risks of Astrocytoma in the babies of pregnant women, who were exposed to increased levels of nitrite in tap water. There is also a link between high nitrate levels of water and brain cancer (Ho *et al.*, 2011). Heavy metals can induce oxidative stress and neuroinflammation (Matés *et al.*, 2009).

## CONCLUSION

Abnormal levels of AP can impact metabolism and absorption of necessary minerals and nutrients which are necessary for proper brain function. We found a significant associated between anxiety level and AP in

brain tumor patients. A nutrient deprived food from preservation can develop malnutrition states. Low levels of AP are usually not marked as high levels, we recommend to evaluate low levels especially in patients.

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