

Clinical Evaluation of Immunological and Hepatic Alterations in Amphetamine-Dependent Patients

Mahdi Salih Talib

Department of Chemistry, Faculty of Science, University of Azarbaigan Shahid Madani, Tabriz, Iran.

ABSTRACT: Amphetamine is a chemical compound that changed into synthetic through the Romanians inside the year 1887. This compound has a very robust effect on the nervous and mental system and has bad consequences on the cardiovascular system, in addition to bad consequences on the heart, liver, kidneys, and different organs of the body. Amphetamine is a useful psychostimulant, but when abused, it damages serotonin and dopamine receptors. Among the most significant side effects of amphetamine usage are weakened immunity and increased inflammation. Lipoxin, an immunological and anti-inflammatory indicator, was selected as one of the biochemical parameters because its results indicated a drop in the blood level of amphetamine abusers. In this study, sixty participants served as a case study, while sixty others served as a control group. All of the samples were obtained from the Basra Governorate's Al-Fayhaa Hospital. The study concentrated on the liver enzymes AST, ALP, GGT, and TSB, as well as the immunological factor represented by lipoxin. For lipoxin, the concentrations were determined using the ELISA method; for the remaining biochemical parameters, spectrometry was used. There was no discernible difference between the amphetamine abusers and the control group, according to the findings of the search for liver enzymes, GGT, and TSB. This may be attributed to the duration of the abusers' use as well as the dosage concentration. However, the findings indicate that the case group's lipoxin levels were much lower than those of the control group. We determine that the reaction of liver enzymes, bilirubin, and GGT, is less responsive to lipoxin than the immunological and inflammatory response. We advise carrying out a more accurate laboratory survey of drug users, accounting for the user's age and weight, the concentration administered, and the duration of usage.

KEYWORD: Amphetamines, Immunological, Lipoxine, Bilirubin

INTRODUCTION

In 1887, Romanian scientist Lazar Edeleanu synthesized amphetamines from the Chinese chemical compound Ma-Huang. In the 1920s, amphetamines were used to treat colds, hay fever, and inflammation by expanding the lungs' bronchial sacs. Benzedrine inhalers were popular over-the-counter medications when they were first introduced in 1932. ^[1] Amphetamine is a potent sympathomimetic and psychostimulant that has detrimental effects on the user's body, both physically and neurologically. In addition to decreasing hunger, consumption raises body temperature, blood pressure, heart rate, and alertness.^[2] Because amphetamine causes altered neuronal function, addiction, and cellular death, few studies have examined its effects on peripheral organs or the central nervous system. Dopamine and serotonin terminals are permanently harmed by amphetamine, a psychostimulant that is often abused. However, instances of liver and other organ damage have also been connected to amphetamine use. ^[3] Most studies found that amphetamine either immediately caused hyperthermia-dependent liver damage that lasted for at least 24 hours after drug administration, or it raised blood levels of AST, ALT, and ALP. Additionally, it produced hepatotoxicity by inducing cell cycle arrest and death.^[4] The brain and central nervous system are clearly affected by amphetamine abuse, leading to neurological system damage and inflammation. The immune system and the response of immunological parameters, such as lipoxin and interleukins in general, are negatively impacted by this. ^[5] There is an inverse relationship between cognitive impairment and the activity of the immunological markers lipoxin and interleukins in amphetamine users. ^[6] The term "lipoxin" describes the byproducts of interactions between lipoxygenases. LXA4 and LXB4 are the two main lipid mediators that mammals make. ^[11] The identification of four LXs may create new avenues for the treatment of chronic inflammatory illnesses since host defense and inflammation control are important in human immunological disorders. ^[10] It was only recently discovered that human leukocytes contain lipoxins (LX), a special family of arachidonic acid metabolites. The biological activities of lipoxins suggest that they may function as inflammation regulators or mediators. LXA 4 (5S, 6R, 15S-trihydroxy-7,9,13-trans-I 1-cis-eicosatetraenoic acid) induces vasodilation, activates protein kinase C, and enhances leukocyte secretion in the hamster cheek pouch and kidney. ^[11] Lipoxins (LXs) are the first class of endogenous inflammatory braking signals to be identified. These compounds can help reduce inflammation by

Clinical Evaluation of Immunological and Hepatic Alterations in Amphetamine-Dependent Patients

preventing the generation of dangerous chemicals like ROS and pro-inflammatory cytokines. Lipoxin A4 (LXA4), one of the most important LXs, may bind in vivo to the LXA4 receptor (ALXR), a specific G-protein-coupled receptor (GPCR).^[12]

Methamphetamine (METH) is a psychostimulant that is often misused and causes irreversible damage to the liver and other organs. Long-term dopamine and serotonin depletion, elevated brain and peripheral ammonia, and liver damage from METH have all been connected in studies, highlighting the significance of peripheral organ damage in mediating the drug's neurotoxicity. The hepatocellular damage caused by METH has not been thoroughly investigated in vivo despite these findings. This is significant since METH's well-known neurotoxicity tends to be influenced by its hepatotoxicity.^[14] The following tests can help identify the site of liver damage: lactate dehydrogenase, total protein, globulins, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), 5'-nucleotidase, conjugated (direct) and unconjugated (indirect) bilirubin, and the elevation pattern can help organize a differential diagnosis.^[13] Gamma-glutamyl groups are transferred to other amino acids by peptides. It is more selective for biliary illness than alkaline phosphatase since it is abundant in many other organs, such as the kidney, pancreas, gut, prostate, testicles, spleen, heart, and brain. Serum Although GGT from the kidney, urine, and pancreas is different from GGT from the liver enzyme in terms of electrophoretic mobility and lectin-affinity reaction, reports indicate that obstructive liver disease causes an average 12-fold increase in GGT levels compared to a 3-fold increase in ALP levels, making GGT slightly more sensitive than ALP in this regard. GGT activity levels in children may be a reliable marker of bile duct damage.^[15]

SUBJECTS AND METHODS

1) SUBJECTS:

Patients

In the current study, sixty addicts between the ages of 15 and 45 have taken part. The samples were taken between September and December of 2025 from the Al-Basrah Rehabilitation Center for Addiction in the Al-Fayhaa Teaching Hospital in the Basrah Governorate of Iraq.

Controls

As a control group, sixty individuals who appeared to be in good health were chosen. participated in the Al-Fayhaa Teaching Hospital's outpatient clinical. Five milliliters of venous blood were drawn from each patient and control using plastic syringes and disposable needles. After the samples were transferred into a brand-new plain tube, the blood was centrifuged for five minutes at 3000 rpm to separate the serum, allowed to coagulate for fifteen minutes at room temperature, and then transferred into brand-new disposable Eppendorf tubes. [7, 8, 9]

METHODS

Since the Elisa Kit employed lipoxin from Sunlong Company, the lipoxin biomarker served as a benchmark for immunity and inflammation in this study. (www.sunlongbiotech.com) (Catalog Number: SL1086Hu), while bilirubin, gamma-glutamyl transferase, ALT, AST, and ALP were evaluated using a spectrophotometer in accordance with Biolabo's methodology.

RESULT AND DISCUSSION

Table (1): The study sample was distributed based on the biochemical characteristics.

Parameters		Amphetamine addicts n= 60 (mean ± SD)	Healthy Control n= 60 (mean ± SD)	P-value*
LFT	TSB (mg/dl)	0.6± 0.52	0.7± 0.35	p =0.86
	S.ALT (U/L)	19.12± 9.9	18.88± 10.7	p =0.915
	S.AST (U/L)	21.56±10.5	18.26± 6.3	p =0.384
	S.ALP (U/L)	63.9± 12.7	57.19± 13.6	p =0.08
	S.GGT (U/L)	22.4± 26.3	20.07± 17.2	p =0.629
	Lipoxin	2.54± 2.05	2.92± 0.09	p =<0.001

Clinical Evaluation of Immunological and Hepatic Alterations in Amphetamine-Dependent Patients

Table 1 exhibits the liver enzymes; ALT, AST, ALP, TSB, and GGT did not significantly differ between amphetamine addicts and controls ($p \geq 0.05$). Numerous studies, or even the majority of studies that examined how addiction affects the liver through its enzymes, confirm that drugs have a detrimental effect on the liver because all drugs cause damage to liver cells and because liver enzymes dramatically increase with the duration of abuse. ^[16]This research contradicts the current study. The research conducted by the scientists clearly demonstrated that the effects of liver enzymes, GGT, and bilirubin are evident if the effector is from inside the liver; however, if the effector is from outside the liver, the sensitivity of the liver enzymes towards the effect is gradual. The scientists explained that amphetamine has a significant effect on the liver, but it takes a certain amount of time. ^[17]

Others have demonstrated that the duration of misuse and the dosage administered determine the increase in liver enzymes. ^[18] Despite the influence of some other criteria, such as happiness hormones and neurotransmitters, the results of the search for liver enzymes in the aforementioned research show that the results of liver enzymes are not significant for new drug users. Scientists have explained that this is because the neurotransmitters and happiness hormones are affected more rapidly than the liver during the initial periods of drug use. ^[19,20]

Since studies have shown that low concentrations of intoxicants and narcotics do not significantly influence liver enzymes over short periods of time, the amount of narcotic substance that enters the body has a significant impact on how well the liver functions. ^[19]

The findings of the present study are exactly the same as those of the previously cited studies.

According to the current study's findings, lipoxin levels significantly decline in drug abusers. These findings are consistent with the majority of studies that examined the connection between lipoxin and infections and immune responses, as most studies found that individuals with inflammation or immune disorders had low blood lipoxin levels ^[21]. Multiple research studies pertaining to the study of lipoxin demonstrate that its levels decrease when the body is impacted by oxidative stress or inflammation. This is because lipoxin stimulates the production of prostacyclin by endothelial cells and nitric oxide by vascular endothelial cells, which causes lipoxin to be absorbed quickly ^[22]. However, research has demonstrated that drug abuse exposes the user to inflammation and a lack of immunity ^[23]. Based on the aforementioned findings, it can be concluded that the drop in lipoxin levels is a reaction to the inflammation brought on by drug abuse, which in turn causes a decrease in immunity and an increase in oxidative stress, which in turn stimulates the body to consume lipoxin in order to increase antioxidants, which is consistent with the findings of our current study. Because of the anti-inflammatory properties of lipoxin receptors, which are produced from LTA4 through metabolism, we can conclude that lipoxin stays at low levels during inflammation due to the role it plays in reducing white blood cell infiltration through adhesion to cells, removing phagocytes from cells, and achieving the production of cytokines. ^[26] However, studies that corroborate the current findings demonstrate that a particular cytochrome (CYP4F3A) has a strong affinity for LXA4 AND LXB4 during the inflammatory phase when the hydroxylation process occurs. ^[27] Short-lived endogenously generated nonclassical eicosanoids, lipoxins (LX) are a family of anti-inflammatory mediators whose emergence in inflammation indicates the resolution of inflammation ^[24]. The results of the current study are validated and supported by another study, which showed that the dissociation rate of LTA4 is several times higher than the dissociation rate of LTB4. ^[25] Lipoxin is distributed to amphetamine addicts based on how long they have abused the drug.

Table (2) showed the distribution. The current study's findings showed that amphetamine addicts with a length of more than a year ($1.73+1.91 \mu\text{mol/l}$ and $2.57+2.0 \mu\text{mol/l}$) had mean lipoxine levels that were not significantly different from those with a duration of less than a year ($1.64+0.32 \mu\text{mol/l}$ and $2.55+2.23 \mu\text{mol/l}$) ($p > 0.05$).

Table (2): Lipoxine is distributed based on the duration of amphetamine usage.

Parameter	Lipoxin (Mean \pm SD) (ng/l)	P-value*
Duration of abuse	≤ 1 year 26.6%	2.55 \pm 2.23
	>1 years 73.4%	2.57 \pm 2.0

As seen in the table above, there is no substantial variation in lipoxin levels between the two periods, because the action of amphetamine manifests within a relatively brief duration. ^[28]

Table (3): Lipoxine distribution among research participants based on their BMI

BMI (Kg/m ²)	Lipoxin (Mean \pm SD) (ng/l)		P-value*
	Amphetamine addicts n= 60	Healthy Control n= 60	
Normal weight 18.5-24.9	2.09 \pm 1.5	4.52 \pm 1.13	$p = < 0.001$
Overweight	2.89 \pm 0.83	4.43 \pm 0.5	$p = < 0.001$

Clinical Evaluation of Immunological and Hepatic Alterations in Amphetamine-Dependent Patients

25-29.9			
Obese ≥ 30	2.8 \pm 2.61	4.0 \pm 1.65	p = <0.001

When compared to the healthy group, Table 3 shows a substantial shift in all phases of BMI addicts. Because body mass influences the effects of drugs on the body, the results of most studies that consider the body mass index and how drug misuse affects that index vary significantly. ^[29]

The current research collected samples at random without considering the concentration, duration of the abuse, user age, and kind of misuse, which accounts for the disparity between its findings and those of previous studies.

CONCLUSION

Lipoxin is a highly sensitive immunological marker for amphetamine addiction, showing a significant decrease in abusers regardless of duration.

Hepatic enzymes (AST, ALT, ALP, GGT) and TSB levels show no immediate significant changes, suggesting they are less responsive than inflammatory markers in early-stage abuse.

Amphetamine abuse triggers rapid oxidative stress and inflammation, leading to the depletion of Lipoxin as the body attempts to neutralize these effects.

Significant alterations in Lipoxin levels occur across all BMI categories in addicts, confirming that body mass influences drug-induced physiological responses.

REFERENCES

- 1) Risan, T. Z., & Ali, B. M. (2024, March). Study the effect of amphetamine on neurotransmitter factors in abusers individuals. In AIP Conference Proceedings (Vol. 3092, No. 1, p. 030005). AIP Publishing LLC.
- 2) Auda, F. M., Ali, B. M., Al-Andaleb, M., Abidali, M. K., & Dhyaa, S. (2021). Estimation of hepcidin and sexual hormones levels in patients with atherosclerosis in Al-Najaf City/Iraq. *Indian Journal of Forensic Medicine & Toxicology*, 15(3), 5235-5239.
- 3) Cruickshank, C.C., Dyer, K.R., A review of the clinical pharmacology of methamphetamine and 3,4-methylenedioxymethamphetamine (MDMA): neurotoxicity and implications for treatment, *Drug Alcohol Rev.* 2021; 40(1), 13–25.
- 4) Ali, B. M., Alassadi, P., Iqbal, J., & Zearah, A. P. (2020). Study the effect of antioxidants and oxidative products and their genetic effect on methionine synthase in people with autism spectrum disorder. Proff. Sameerah Ahmed, Study the Effect of Antioxidants and Oxidative Products and Their Genetic Effect on Methionine Synthase in People with Autism Spectrum Disorder (March 23, 2020).
- 5) Fan, Runyue, et al. "The effect of the NLRP1 inflammasome on methamphetamine-induced cognitive impairment in rats." *Drug and Alcohol Dependence* 237 (2022): 109537.
- 6) Ali, B. M. (2014). Evaluate some biochemical changes associated with chronic renal failure patients undergoing hemodialysis in al najaf al ashraf governorate.
- 7) Auda, F. M., & Rehman, A. (2025). Evaluation of midkine, cortisol, and other biochemical indicators in patients with atherosclerosis. *Anaesthesia, Pain & Intensive Care*, 29(1), 40-46.
- 8) Al-Zurfi, S.K.L., Al-Hashimi, A.R., Al-Kubaisi, M.A., Assessment of heavy metals levels in maternal blood and breast milk: comparative analysis across central Iraqi governorates, *Rasayan J. Chem.* 14.4 (2021): 1832–1839.
- 9) Aziz, D. Z., Mahdi, R. A., Mahdi, M. A., Talib, Z. M., Mohsin, A. H., & Dayea, E. Z. Assessment of some hematological and biochemical parameters in patients with renal failure in Al-Najaf province, *J. Res. Chem.* 4.1 (2023): 31–34. DOI: 10.22271/reschem.2023.v4.i1a.77.
- 10) Ali, B. M., Moein, F., Al-Andaleb, M., Hussein, Z., Abidali, M. K., & Dhyaa, S. (2021). STUDY OF SOME FACTORS AFFECTING IN MYOCARDIAL INFARCTION. *Annals of the Romanian Society for Cell Biology*, 25(6).
- 11) Wolpe, Abigail G., et al. "Polarized proteins in endothelium and their contribution to function." *Journal of Vascular Research* 58.2 (2021): 65-91.
- 12) Kollareth, D. J. M., Leroy, V., Tu, Z., Woolet-Stockton, M. J., Kamat, M., Garrett, T. J., Atkinson, C., Lipoxin A4/FPR2 signaling mitigates ferroptosis of alveolar epithelial cells via NRF2-dependent pathway during lung ischemia-reperfusion injury, *FASEB J.* 39(8) (2025): e70545. DOI: 10.1096/fj.202401475R.
- 13) Banerjee, P., A. Goswami, S. Bhunia and S. Basu (2021). "Determination of Causal Relationship Between Bilirubin and Other Liver Biomarker in Case of Hepatitis C." *Biomed. Stat. Informatics* 6(2): 23-31.
- 14) Ali, L. B. M., Alasadi, I. J. B., & Zearah, S. A. (2020). Determination of Some Biomarkers that affect in Behaviors of Autism Spectrum Disorder Individuals in Iraq. *Indian J. Forensic Med. Toxicol*, 14, 1681-1686.

Clinical Evaluation of Immunological and Hepatic Alterations in Amphetamine-Dependent Patients

- 15) Akaydin, S. Y., E. M. Salihoğlu, D. G. Güngör, H. Karanlık and S. Demokan (2020). "Correlation between gamma-glutamyl transferase activity and glutathione levels in molecular subgroups of breast Cancer." *European Journal of Breast Health* 16(1): 72.
- 16) Almohanna, T., Auda, F. M., & Ali, B. M. (2025). Early detection of digestive system cancers: Insights from enzymatic and non-enzymatic tumour markers. *Journal of Medical Biochemistry*, 44(3), 631.
- 17) Coté, C. J., Lerman, J., Todres, I. D. *A Practice of Anesthesia for Infants and Children*, 7th Edition E-book, Elsevier Health Sciences, 2022.
- 18) Niesters, M., Martini, C., Dahan, A., Ketamine for chronic pain management: updated evidence on efficacy and safety, *Br. J. Clin. Pharmacol.* 88(5) (2022): 2103–2115. DOI: 10.1111/bcp.15210.
- 19) Ali, B. M., Moein, F., Maha Al-Andaleb, L., & Dhyaa, S. (2021). A field study dealing with biometrics of some clinical variables for hepatitis C patients. *Magazine of Al-Kufa University for Biology*, 13(2).
- 20) Kim, D., Kim, W. R., Kim, H. J., Therneau, T. M., Association between abnormal liver function tests and long-term outcomes in asymptomatic adults: a contemporary cohort study, *N. Engl. J. Med.* 388(5) (2023): 453–463. DOI: 10.1056/NEJMoa2211425.
- 21) Ali, A. B. M. (2016). Study effect of blood glucose level on renal failure in peoples suffering from diabetes. *International Journal of Science and Research*, 5(5), 2033-2038.
- 22) Andrews, D., & Godson, C. (2021). Lipoxins and synthetic lipoxin mimetics: Therapeutic potential in renal diseases. *Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids*, 1866(8), 158940.
- 23) Hashim, Z. H., & Ali, B. M. (2026). A Proportional Analysis of Lung Cancer Patients via Elucidating the Roles of NAMPT and SIRT6 in Metabolic Pathways. *Egyptian Journal of Medical Microbiology*.
- 24) Shaker, S. A., Ali, B. M., & Audah, F. M. Estimation the level of zonulin, antioxidant factors and some biochemical parameters in renal failure patients. *International Journal of Health Sciences*, 6(S4), 10761-10772.
- 25) • Nakamura, M., Shimizu, T. Recent advances in function and structure of two leukotriene B₄ receptors: BLT1 and BLT2, *Biochem. Pharmacol.* 203 (2022): 115178.
- 26) Ali, B. M., Auda, F. M., & Hassooni, F. A. (2025). Transformative Approaches to Biomarker Assessment and Clinical Profiles in Pulmonary Hypertension Patients. *Galen Medical Journal*, e4132-e4132.
- 27) Abbas, Z. K., Auda, F. M., Abbas, J. K., & Ali, B. M. Positive Correlation Between Parathyroid Hormone-related Protein (PTHrP) and Vitamin D Bind Protein (VDBP) in Osteoporosis and Osteopenia Patients in AL-Najaf City/Iraq. *International Journal of Health Sciences*, 6(S6), 8498-8505.
- 28) Fredriksson, I., Venniuro, M., Reiner, D. J., Chow, J. J., Bossert, J. M., & Shaham, Y. (2021). Animal models of drug relapse and craving after voluntary abstinence: a review. *Pharmacological Reviews*, 73(3), 1050-1083.
- 29) ULA, J. M., & BASIM, M. (2024). Following up on the repercussions on patients with high blood pressure and diabetes, including atherosclerosis. *JOURNAL OF KUFA FOR CHEMICAL SCIENCES Учредители: University of Kufa*, 3(3), 407-424.