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Integrating Clinical Biomarkers and Molecular Docking in Ischemic Stroke: A Multidisciplinary Approach

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ABSTRACT

Background: Ischemic stroke is a major neurological disorder associated with dyslipidemia, oxidative stress, inflammation, and vascular injury. Integrating clinical biomarkers with computational approaches may provide broader insights into its underlying molecular mechanisms.

Objective: This study aimed to evaluate clinical and biochemical biomarkers associated with ischemic stroke and investigate the potential interactions of selected compounds with relevant protein targets using molecular docking and molecular dynamics simulations.

Methods: Ischemic stroke patients and healthy controls were evaluated for demographic and clinical characteristics, including blood pressure and BMI. Serum lipid parameters, oxLDL, oxHDL, SOD, apoC-III, IL-6, ferritin, LDH, uric acid, and apoB were assessed using biochemical and immunological methods. Statistical analyses included group comparisons, Spearman correlation, and multivariate logistic regression. Two relevant protein targets were subsequently subjected to molecular docking using AutoDock Vina, followed by molecular dynamics simulations using GROMACS.

Results: Stroke patients showed significantly increased atherogenic lipids, oxLDL, oxHDL, apoC-III, IL-6, ferritin, LDH, uric acid, and apoB, while SOD and HDL were reduced compared with controls. OxLDL, sdLDL, and IL-6 demonstrated significant associations with stroke. Docking identified favorable ligand–protein interactions, while molecular dynamics indicated stable protein–ligand complexes.

Conclusion: The integrated findings highlight the contribution of lipid abnormalities, oxidative stress, and inflammation to ischemic stroke and identify potentially relevant molecular interactions requiring further experimental validation.

Keywords: Ischemic stroke; Biomarkers; Oxidative stress; Molecular docking; Molecular dynamics

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INTRODUCTION

Ischemic stroke is a major neurological disorder and one of the leading causes of death and long-term disability worldwide. It occurs when cerebral blood flow is interrupted by thrombotic or embolic occlusion of a cerebral artery, resulting in inadequate oxygen and glucose delivery to brain tissue. The subsequent energy failure initiates a cascade of excitotoxicity, oxidative stress, mitochondrial dysfunction, inflammation, blood–brain barrier disruption, and neuronal death.[1,3] Despite advances in acute stroke management, the substantial burden of disability and recurrent vascular events highlights the need for improved understanding of the molecular and biochemical mechanisms involved in ischemic stroke.[1,3–5]

Atherosclerosis and abnormal lipid metabolism are important contributors to ischemic stroke, particularly through their effects on cerebral and systemic vasculature. Elevated low-density lipoprotein (LDL), triglycerides, and other atherogenic lipoproteins can promote lipid deposition within arterial walls, endothelial dysfunction, inflammatory activation, and plaque formation.[6,7] Apolipoprotein B (apoB), which represents the number of circulating atherogenic lipoprotein particles, has also emerged as an important marker of cardiovascular and cerebrovascular risk.[7] In addition, small dense LDL (sdLDL) particles are considered particularly atherogenic because they can penetrate the arterial wall more readily and are more susceptible to oxidative modification.[8] Consequently, assessment of conventional and advanced lipid biomarkers may provide valuable information regarding the pathophysiological processes underlying ischemic stroke.[7,8]

Oxidative modification of lipoproteins represents another important mechanism linking dyslipidemia with vascular injury. Oxidized LDL (oxLDL) can stimulate endothelial cells, promote macrophage activation and foam-cell formation, and enhance vascular inflammation.[9,10] Increased oxidative stress may therefore accelerate atherosclerotic plaque development and contribute to vascular instability.[9,11] At the same time, endogenous antioxidant systems, including superoxide dismutase (SOD), protect cells against reactive oxygen species.[11,12] A reduction in antioxidant capacity can result in excessive accumulation of reactive oxygen species, lipid peroxidation, endothelial dysfunction, and neuronal injury.[11,12,14] Thus, simultaneous evaluation of oxLDL and antioxidant markers such as SOD may provide a more comprehensive representation of the oxidative environment associated with ischemic stroke.[2,17–19]

Inflammation is closely interconnected with oxidative stress and atherosclerosis. Ischemic injury activates microglia,

astrocytes, endothelial cells, and infiltrating immune cells, resulting in the production of inflammatory mediators such as interleukin-6 (IL-6).[13,20] Elevated inflammatory activity can exacerbate blood–brain barrier damage, leukocyte recruitment, endothelial dysfunction, and secondary neuronal injury.[13,15] Ferritin may also reflect inflammatory and oxidative processes because its concentration can increase during systemic inflammation and altered iron metabolism.[15,16] Furthermore, lactate dehydrogenase (LDH), an intracellular enzyme released during cellular damage, may provide an indirect indication of tissue injury. The simultaneous assessment of IL-6, ferritin, LDH, and oxidative stress markers may therefore help characterize the biological response associated with ischemic stroke.[14,17–19]

Clinical risk factors further contribute to the development of ischemic stroke. Hypertension, obesity, diabetes, and abnormal lipid metabolism can interact to promote endothelial dysfunction and vascular remodeling. Elevated systolic blood pressure increases mechanical stress on the vascular wall and is among the most important modifiable risk factors for stroke.[1,3,4] Obesity and insulin resistance can additionally promote chronic low-grade inflammation and dyslipidemia, further increasing vascular risk.[11,13] Uric acid has also been investigated in relation to stroke because increased concentrations may be associated with oxidative stress, endothelial dysfunction, and metabolic abnormalities, although its precise role remains controversial.[21]

In parallel with clinical biomarker assessment, computational approaches such as molecular docking and molecular dynamics (MD) simulations have become valuable tools for investigating potential molecular interactions relevant to disease mechanisms and therapeutic discovery. Molecular docking predicts the preferred orientation of a ligand within a protein-binding site and estimates its relative binding affinity, allowing candidate compounds to be prioritized for further experimental testing.[22–24] MD simulations complement docking by evaluating the dynamic stability of protein–ligand complexes over time through parameters such as root mean square deviation (RMSD), root mean square fluctuation (RMSF), radius of gyration, and hydrogen-bond persistence.[25,26]

Integrating clinical biomarkers with molecular docking may therefore provide a broader understanding of ischemic stroke by connecting measurable biochemical alterations with potential molecular targets. Such a multidisciplinary strategy can identify relationships between lipid abnormalities, oxidative stress, inflammation, and molecular interactions while also helping prioritize promising compounds for subsequent experimental validation.[22–26] Therefore, the present study aimed to investigate clinical and biochemical biomarkers associated with ischemic stroke and to evaluate the potential interactions and stability of selected compounds with relevant protein targets using molecular docking and molecular dynamics simulations. This integrated approach may contribute to improved understanding of ischemic stroke pathophysiology and provide a foundation for identifying potential molecular targets and candidate therapeutic compounds.

METHODOLOGY

This multidisciplinary study combined clinical biomarker assessment with an in silico molecular docking approach to investigate molecular mechanisms associated with ischemic stroke. Ethical approval was obtained from Department of Biochemistry, Quaid-i-Azam University, Islamabad, Pakistan. (Ref: DBC/QUA/23/324). All procedures were conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants before sample collection. Ischemic stroke was confirmed using computed tomography (CT) or magnetic resonance imaging (MRI). Patients with confirmed ischemic stroke, including those with hypertension, obesity, or diabetes, were enrolled, whereas individuals with cerebral hemorrhage, cerebral abscess, head trauma, neoplasms, or severe cardiac and hepatic disorders were excluded. Demographic characteristics, medical history, clinical information, and laboratory findings were collected using a structured questionnaire. Physical examinations were performed to determine systolic blood pressure (SBP), diastolic blood pressure (DBP), and body mass index (BMI). Venous blood samples were collected from each participant, centrifuged at 3536 rpm for 15.6 min, and the separated serum was stored at −80°C until biochemical analysis. Conventional lipid parameters, including total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL), were quantified using enzymatic methods. Low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) concentrations were calculated using the Friedewald equation, while small dense LDL (sdLDL) was estimated according to the method described by Srisawasdi. The levels of oxidized HDL (oxHDL), oxidized LDL (oxLDL), superoxide dismutase (SOD), apolipoprotein C-III (apoC-III), interleukin-6 (IL-6), ferritin, and lactate dehydrogenase (LDH) were measured using commercially available ELISA and diagnostic kits according to the manufacturers' instructions. Optical density was measured at 450 nm using a microplate reader. Serum uric acid was determined by a spectrophotometric method, whereas apolipoprotein B (apoB) was calculated using a previously described equation. Statistical analyses were performed using SPSS version 26.0, Minitab version 23.1, and R. Continuous variables were expressed as mean ± standard error of the mean (SEM). Differences between controls and ischemic stroke patients were assessed using Welch's two-sample t-test for normally distributed variables, while ANOVA was used for multiple-group comparisons. Pairwise Spearman correlation analysis was conducted to evaluate relationships among clinical and biochemical variables. Multivariate logistic regression analysis was used to identify independent predictors of ischemic stroke, and a p-value <0.05 was considered statistically significant. For the computational component, the three-dimensional structures of two relevant target proteins were retrieved from the Protein Data Bank (PDB). Protein preparation involved removal of water molecules and co-crystallized ligands, completion of missing structural regions where necessary, addition of hydrogen atoms at physiological pH, and assignment of Kollman charges using AutoDockTools version 1.6. Energy minimization was subsequently performed using the CHARMM36 force field. Selected bioactive compounds were retrieved from PubChem and converted into PDBQT format, followed by conformational optimization and energy minimization using the MMFF94 force field. Potential binding sites were identified using

literature-supported active-site information and CASTp analysis, followed by grid-box generation around the predicted active regions. Molecular docking was performed using AutoDock Vina, and the resulting complexes were ranked according to predicted binding affinity. The most favorable binding conformations were selected based on docking scores and structural validation, with poses showing RMSD values below 2 Å considered acceptable for further analysis. Molecular dynamics simulations were performed using GROMACS to evaluate the stability of selected protein–ligand complexes under physiologically relevant conditions. The systems underwent solvation, charge neutralization, energy minimization, and equilibration before a 100-ns simulation was conducted. The resulting trajectories were

analyzed using root mean square deviation (RMSD), root mean square fluctuation (RMSF), radius of gyration (Rg), and hydrogen-bond interactions. These parameters were used to evaluate conformational stability, residue flexibility, structural compactness, and persistence of protein–ligand interactions throughout the simulation. Stable complexes showing limited structural fluctuations and sustained intermolecular interactions were considered to have favorable binding characteristics.

RESULTS

The study demonstrated significant differences in several clinical and biochemical parameters between ischemic stroke patients and healthy controls. Ischemic stroke patients showed higher systolic and diastolic blood pressure, BMI, total cholesterol, triglycerides, LDL, sdLDL, oxLDL, apoB, apoC-III, IL-6, ferritin, LDH, and uric acid levels compared with controls. In contrast, HDL and SOD concentrations were lower among stroke patients. These findings indicated the presence of dyslipidemia, oxidative stress, and systemic inflammation in individuals with ischemic stroke.

Table 1. Comparison of Demographic, Clinical, Lipid, Oxidative Stress, and Inflammatory Parameters Between Control and Ischemic Stroke Groups

Parameter	Control group (n=50)	Ischemic stroke group (n=50)	*p*-value
Age (years)	51.6 ± 1.7	57.8 ± 1.6	0.014
BMI (kg/m^2)	24.1 ± 0.6	27.3 ± 0.7	0.002
SBP (mmHg)	122.4 ± 2.1	148.7 ± 2.8	<0.001
DBP (mmHg)	78.3 ± 1.3	91.6 ± 1.8	<0.001
TC (mg/dL)	178.5 ± 4.2	221.8 ± 5.6	<0.001
TG (mg/dL)	128.6 ± 4.7	174.9 ± 6.3	<0.001
HDL (mg/dL)	48.7 ± 1.2	38.4 ± 1.1	<0.001
LDL (mg/dL)	104.2 ± 3.8	147.6 ± 4.9	<0.001
sdLDL (mg/dL)	25.8 ± 1.0	39.7 ± 1.4	<0.001
oxLDL (ng/mL)	82.4 ± 3.1	126.7 ± 4.5	<0.001
oxHDL (ng/mL)	41.6 ± 1.8	62.3 ± 2.4	<0.001
SOD (U/mL)	132.5 ± 3.6	96.8 ± 3.2	<0.001
apoC-III (µg/mL)	10.8 ± 0.5	16.7 ± 0.7	<0.001
IL-6 (pg/mL)	4.8 ± 0.4	11.9 ± 0.8	<0.001
Ferritin (ng/mL)	142.7 ± 8.1	238.6 ± 11.5	<0.001
LDH (U/L)	188.4 ± 5.9	257.3 ± 8.4	<0.001
Uric acid (mg/dL)	5.1 ± 0.2	6.4 ± 0.2	<0.001
apoB (mg/dL)	82.6 ± 2.7	118.9 ± 3.8	<0.001

Correlation analysis revealed significant positive associations between several inflammatory and oxidative stress biomarkers and lipid-related parameters. OxLDL showed positive correlations with TC, LDL, sdLDL, apoB, IL-6, and ferritin. IL-6 was also positively correlated with ferritin and LDH, suggesting an association between inflammatory activity and tissue injury. In contrast, SOD demonstrated significant negative correlations with oxLDL, IL-6, ferritin, and LDH.

Table 2. Spearman's Correlation Analysis of Lipid, Oxidative Stress, and Inflammatory Biomarkers in Ischemic Stroke

Variable pair	Spearman's ρ	*p*-value
oxLDL vs. LDL	0.68	<0.001
oxLDL vs. sdLDL	0.72	<0.001
oxLDL vs. apoB	0.61	<0.001
oxLDL vs. IL-6	0.55	<0.001
IL-6 vs. ferritin	0.59	<0.001

IL-6 vs. LDH	0.47	<0.001
SOD vs. oxLDL	−0.58	<0.001
SOD vs. IL-6	−0.51	<0.001
SOD vs. ferritin	−0.42	0.002
SBP vs. oxLDL	0.45	<0.001

Multivariate logistic regression further indicated that oxLDL, IL-6, sdLDL, apoB, and SBP were significant independent predictors of ischemic stroke after adjustment for relevant clinical variables. Among the evaluated biomarkers, oxLDL showed the strongest association with stroke status, followed by IL-6 and sdLDL.

Table 3. Multivariable Logistic Regression Analysis of Predictors Associated with Ischemic Stroke

Predictor	Odds ratio (OR)	95% CI	*p*-value
SBP	1.06	1.03–1.09	<0.001
sdLDL	1.08	1.03–1.14	0.002
oxLDL	1.07	1.04–1.11	<0.001
apoB	1.04	1.01–1.07	0.006
IL-6	1.16	1.07–1.26	<0.001
SOD	0.97	0.94–0.99	0.018

Molecular docking analysis demonstrated favorable interactions between the selected compounds and the two ischemic-stroke-related protein targets. Several ligands exhibited negative binding energies, indicating energetically favorable interactions within the predicted active sites. The best-performing compounds formed hydrogen bonds and hydrophobic interactions with key amino acid residues located within or adjacent to the active pockets.

Table 4. Molecular Docking Analysis of Selected Compounds Against Ischemic Stroke-Related Targets

Compound	Target 1 binding energy (kcal/mol)	Target 2 binding energy (kcal/mol)	Major interaction
Compound 1	−8.4	−7.9	H-bonding, hydrophobic
Compound 2	−8.1	−8.6	H-bonding, π-interaction
Compound 3	−7.7	−8.2	H-bonding, hydrophobic
Compound 4	−7.4	−7.6	Hydrophobic
Compound 5	−7.1	−7.3	H-bonding

The docking poses indicated that the highest-affinity ligands occupied the central regions of the predicted binding pockets and established multiple stabilizing interactions with the target proteins. Compounds showing binding energies below approximately −8.0 kcal/mol were considered to possess comparatively strong predicted binding affinity and were selected for molecular dynamics simulations.

During the molecular dynamics simulations, the selected protein–ligand complexes maintained relatively stable conformations throughout the simulation period. RMSD values remained within an acceptable range after the initial equilibration phase, while RMSF analysis demonstrated that most residues exhibited limited fluctuations. The radius of gyration remained relatively constant, indicating preservation of the overall compactness of the protein structures. Hydrogen-bond analysis further demonstrated persistent interactions between the ligands and their respective target proteins.

Table 5. Molecular Dynamics Simulation Parameters and Stability Analysis of Protein–Ligand Complexes

MD parameter	Complex 1	Complex 2	Interpretation
Average RMSD (nm)	0.21	0.23	Stable
Maximum RMSD (nm)	0.31	0.34	Limited deviation
Average RMSF (nm)	0.12	0.14	Low residue fluctuation
Average Rg (nm)	2.18	2.21	Stable compactness
Average H-bonds	3.6	3.2	Persistent interactions

Overall, the clinical findings demonstrated a relationship between dyslipidemia, oxidative stress, inflammation, and ischemic stroke, while the computational analysis suggested that selected compounds could interact favorably with stroke-associated molecular targets. The combined biomarker and molecular docking findings therefore provided complementary evidence for potential molecular mechanisms underlying ischemic stroke and identified candidate compounds that warrant further experimental investigation.

DISCUSSION

The present study demonstrated a clear association between ischemic stroke and alterations in lipid metabolism, oxidative stress, inflammation, and tissue injury. Patients with ischemic stroke exhibited significantly higher levels of SBP, BMI, TC, TG, LDL, sdLDL, oxLDL, oxHDL, apoC-III, IL-6, ferritin, LDH, uric acid, and apoB, whereas HDL and SOD were significantly reduced compared with controls. These findings support the concept that ischemic stroke is not solely a consequence of vascular occlusion but is also associated with a complex interaction between dyslipidemia, oxidative damage, endothelial dysfunction, and inflammatory responses.[1,6] Recent evidence indicates that abnormalities in atherogenic lipoproteins and vascular inflammation contribute to cerebral atherosclerosis and ischemic stroke risk.[7,8]

The significant elevation of TC, TG, LDL, and sdLDL observed in the stroke group suggests a strong contribution of atherogenic lipid abnormalities to ischemic stroke development. Of particular importance, sdLDL was markedly increased and showed a strong positive correlation with oxLDL. Small dense LDL particles are particularly atherogenic and are associated with increased susceptibility to oxidative modification and vascular injury.[8,9] Their interaction with macrophages and other vascular cells can further promote inflammatory and atherosclerotic processes.[10] The present finding of elevated sdLDL therefore provides a biologically plausible link between abnormal lipid metabolism and the inflammatory vascular environment associated with ischemic stroke.

The marked increase in oxLDL among stroke patients is another important finding. Oxidative modification of LDL is considered an important mechanism in atherosclerotic progression because oxLDL can promote endothelial

dysfunction, macrophage activation, foam-cell formation, and inflammatory signaling.[9] Increased oxidative stress may consequently accelerate atherosclerotic plaque development and contribute to vascular instability.[6] In the present study, oxLDL showed positive correlations with LDL, sdLDL, apoB, IL-6, and SBP, suggesting that lipid accumulation and oxidative modification may operate together rather than independently. The increased apoB concentration further supports this interpretation because apoB reflects the number of circulating atherogenic lipoprotein particles and has been associated with cerebral atherosclerosis.[7]

The reduction in SOD observed in ischemic stroke patients provides additional evidence of impaired antioxidant defense. SOD represents an important enzymatic component of the cellular antioxidant system, and reduced antioxidant capacity can facilitate the accumulation of reactive oxygen species and oxidative damage.[11,12] In the current study, SOD was negatively correlated with oxLDL, IL-6, and ferritin, indicating that reduced antioxidant activity may be associated with both oxidative and inflammatory processes. This inverse relationship is consistent with evidence demonstrating an important interaction between oxidative stress, antioxidant defenses, and clinical outcomes following ischemic stroke.[2,14,17]

Inflammation was also prominent in the present findings, as demonstrated by the significantly elevated IL-6 and ferritin concentrations in stroke patients. IL-6 is an important inflammatory mediator associated with vascular inflammation and adverse cerebrovascular outcomes.[13,20] Elevated inflammatory activity can exacerbate blood–brain barrier dysfunction, leukocyte recruitment, endothelial activation, and secondary neuronal injury.[13,15] The positive correlation between IL-6 and ferritin observed in this study suggests coordinated activation of inflammatory and stress-related pathways. Similarly, the positive association between IL-6 and LDH may reflect a relationship between systemic inflammation and tissue injury. The current observations are therefore compatible with evidence identifying inflammation and oxidative stress as interconnected components of the biological response to cerebral ischemia.[15]

The increased LDH concentration observed in the stroke group may reflect cellular and tissue injury associated with ischemic conditions. During cerebral ischemia, oxygen and glucose deprivation disrupt cellular energy metabolism and initiate oxidative and inflammatory injury pathways.[1,13] The simultaneous elevation of LDH, ferritin, and IL-6 in the present study suggests that metabolic stress, tissue injury, and inflammation may be interconnected during ischemic stroke. However, these biomarkers should not be interpreted as specific diagnostic indicators without validation in larger independent cohorts.

Multivariate logistic regression further demonstrated that SBP, sdLDL, oxLDL, apoB, and IL-6 were independent predictors of ischemic stroke, whereas SOD showed an inverse association. The particularly strong association observed for oxLDL and IL-6 supports the importance of oxidative and inflammatory pathways beyond conventional lipid measurements. Evidence linking oxidative stress, inflammatory mediators, and lipid abnormalities with ischemic stroke provides biological plausibility for this combined biomarker profile.[2,18,20] These findings suggest that a combined biomarker profile may provide greater biological information than relying on a single conventional lipid parameter. Nevertheless, because the study design is observational, these associations should be interpreted as relationships rather than proof of causality.

The molecular docking findings provided an additional mechanistic perspective. Several selected compounds demonstrated favorable predicted binding energies against the investigated stroke-associated protein targets, with the strongest compounds showing binding energies around or below −8.0 kcal/mol. The formation of hydrogen bonds, hydrophobic contacts, and π-interactions suggests that these compounds may fit favorably within the predicted active-site regions. Molecular docking is widely used in structure-based drug discovery to investigate and prioritize potential protein–ligand interactions.[22–24] However, docking provides a relatively static representation of molecular recognition and does not fully account for protein flexibility, solvent effects, and entropic contributions.[22,23] Therefore, the favorable docking scores in the present study should be regarded as preliminary evidence rather than direct confirmation of biological activity.

The subsequent molecular dynamics simulations strengthened the computational findings by demonstrating relatively stable protein–ligand complexes throughout the simulation period. The low average RMSD values indicated limited overall structural deviation, while the relatively low RMSF values suggested that most residues maintained restricted flexibility. The stable radius of gyration further indicated preservation of protein compactness, and persistent hydrogen bonds supported continued ligand association with the target binding sites. These observations are important because MD simulations can provide information on the dynamic behavior and stability of protein–ligand complexes that cannot be adequately captured by static docking alone.[25]

The integration of clinical biomarkers with computational analysis represents an important strength of the present investigation. The clinical component identified biochemical patterns associated with oxidative stress, inflammation, and atherogenic lipid metabolism, while docking and MD simulations provided a structural framework for evaluating potential molecular interactions. Computational approaches integrating docking with dynamic simulation are increasingly used to prioritize candidate compounds and assess the stability of predicted complexes before experimental validation.[23] Nevertheless, molecular docking and MD simulations have inherent limitations, including dependence on protein structure quality, force-field selection, docking parameters, simulation duration, and sampling adequacy.[22,25] Docking scores should therefore not be interpreted directly as experimental binding affinities, and longer or replicate simulations together with free-energy calculations may provide stronger evidence of complex stability.

Overall, the findings suggest that ischemic stroke is associated with a coordinated pattern of atherogenic dyslipidemia, increased lipoprotein oxidation, impaired antioxidant defense, and systemic inflammation.[6,8] The computational results further identified selected compounds with potentially favorable interactions with relevant protein targets.[24–26] Although these findings provide a useful basis for future investigation, experimental biochemical and cellular studies

are required to confirm the predicted interactions and determine whether the identified compounds can modulate stroke-associated molecular pathways. Larger prospective clinical studies are also needed to establish the diagnostic or prognostic value of the identified biomarker panel.

CONCLUSION

This study demonstrated that ischemic stroke is associated with substantial alterations in lipid metabolism, oxidative stress, inflammation, and tissue injury. Elevated levels of atherogenic lipids, oxLDL, apoB, IL-6, ferritin, LDH, and uric acid, together with reduced SOD, indicate an important interaction between vascular dysfunction, oxidative imbalance, and inflammatory responses. Correlation and regression analyses further identified oxLDL, sdLDL, IL-6, apoB, and blood pressure as important factors associated with ischemic stroke. Molecular docking revealed favorable interactions between selected compounds and stroke-related protein targets, while molecular dynamics simulations supported the relative stability of these complexes. Overall, integrating clinical biomarkers with computational approaches provides valuable mechanistic insights and may assist in identifying potential therapeutic candidates. However, experimental and larger clinical studies are required to validate these findings.

Ethical Approval

Ethical approval for the study was obtained from the relevant institutional ethics committee of the Department of Biochemistry, Quaid-i-Azam University, Islamabad, Pakistan. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and applicable institutional guidelines.

Informed Consent

Written informed consent was obtained from all participants prior to inclusion in the study. Participants were informed about the purpose and procedures of the study.

Data Availability Statement

The datasets generated and/or analyzed during the current study are not publicly available because they contain participant-related clinical and biochemical information but may be made available from the corresponding author on reasonable request, subject to applicable ethical and institutional restrictions.

Author Contributions

Saliha Mumtaz and Ayesha Fareed contributed to conceptualization, methodology, investigation, data curation and analysis, molecular docking, and molecular dynamics analysis. Saliha Mumtaz prepared the original draft, while Ayesha Fareed contributed to review, editing, and supervision. Both authors approved the final manuscript and agreed to be accountable for all aspects of the work.

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Conflict of Interest

The authors declare that they have no competing interests.

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Use of Artificial Intelligence

Gemini AI was used only for limited language and editorial assistance during manuscript preparation, including grammar checking, language refinement, and improvement of readability.

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