Pharmacology

Research Article

Pharmacology 2024; Volume 109, Issue 2:

Received: Aug 07, 2023
Accepted: Dec 21, 2023
Published online: Feb 15, 2024

Comparison of The Impact of Rivaroxaban Against Aspirin on Stroke Recurrence in Patients Having a History of Atrial Cardiomyopathy and Unknown Stroke

[1]Dr. Rashid Usman, [2]Dr.Waqas Gulzar, [3]Khalida Ajmal, [4]Dr Husnain Hashim, [5]Dr Shandana Altaf, [6]Dr Muhammad Shuaib, [7]Muhammad Kashif Habib, [8]Dr Fahmida Khatoon, [9]Kashif Lodhi

[1] Fauji Foundation Hospital, Rawalpindi.
[2]Mayo Hospital Lahore,
[3]Wah Medical College Wah Cantt
[4]Neurology department, Fauji Foundation Hospital Rawalpindi,
[5]Pharmacology KMC Peshawar,
[6]Department of Medicine, Mohiuddin Teaching Hospital, Mirpur AJK,
[7]Resident physician, medical c unit saidu group of teaching hospital swat,
[8]Associate professor, Department of Biochemistry, College of Medicine
University of Hail, KSA,
[9]Department of Agricultural, Food and Environmental Sciences. Università Politécnica delle Marche Via Brecce Bianche 10, 60131 Ancona (AN) Italy,

Keywords: Atrial Cardiomyopathy, Aspirin, Stroke

Abstract

Background: Cryptogenic strokes, the majority of which are brought on by an embolic mechanism, are a subset of ischemic stroke that affects around 25% of all patients. In people with a history of cryptogenic or left atrial cardiomyopathy and unknown stroke who are on anticoagulant therapy, rivaroxaban may reduce the chance of having another stroke compared to aspirin.

Methods: The effectiveness and tolerability of rivaroxaban and aspirin in preventing recurrent stroke in individuals with a history of left atrial cardiomyopathy and cryptogenic stroke were compared in this cross-sectional investigation.

Results: The odds ratio for stroke recurrence with aspirin treatment was 11 times higher than with rivaroxaban therapy, even after controlling for other factors such as age, gender, hypertension, and diabetes with the p-value of 0.038 and 95% confidence interval range of 1.39 to 113.08 and OR value of 11.35

Conclusions: In individuals with a history of unknown etiology stroke and left atrial cardiomyopathy, rivaroxaban was more effective than aspirin at preventing recurrent stroke.

Dr. Rashid Usman
Fauji Foundation Hospital, Rawalpindi

INTRODUCTION:

A stroke is characterized by a reduction in blood flow to the brain, which may result in neurological impairments. The burden on people living in lower and lower-middle-income nations rose significantly from 1990 to 2019; it has become the second largest cause of mortality and the third major contributor to disability and death combined worldwide. The incidence, mortality, prevalence, and DALYs (disability-adjusted life-years lost) rates of age-standardized stroke varied greatly by region, with the greatest rates occurring in Eastern Europe, Asia, and Sub-Saharan Africa. [1] There are no discernible gender variations in the number of stroke-related fatalities, even though the point estimates of prevalent and incident strokes are greater in females than in men. [2,3] Approximately one in four persons today have a lifetime risk of stroke. High systolic blood pressure (SBP), a high body mass index (BMI), high fasting plasma glucose (FPG), atmospheric particulate matter (PM2.5) exposure, and smoking are the primary risk causes for stroke. The incidence of stroke is mostly caused by metabolic, behavioral, nutritional, and environmental risk factors together. [4-7]

The age-standardized incidence rate (ASIR) of stroke declined in both genders from 166.6 per 100,000 inhabitants in 1990 to 138.8 per 100,000 populations in 2019. In Pakistan, stroke incident cases climbed from 48,274 in 1990 to 102,778 in 2019, showing a 2.1-fold increase. From 21,698 fatalities due to stroke in 1990 to 40,912 in 2019, there has been an increase. In addition, the age-standardized mortality rate (ASDR) from stroke dropped by 45.1%. [27-46]

The majority of cryptogenic strokes, which account for around 25% of all ischemic stroke patients, are brought on by embolic mechanisms. Cryptogenic strokes have often been defined as non-lacunar infarctions without distal arterial constriction or cardioembolic causes; nevertheless, neither a generally recognized definition nor a necessary universally accepted diagnostic evaluation has been established. Clinical research on the best preventative treatment for cryptogenic strokes has been hampered as a result. [8]

In vulnerable populations, atrial cardiomyopathy (AC) is now understood to be a substantial cause of atrial hypercontractility and a foundation for atrial fibrillation (AF). New potential targets for catheter-based and pharmacological therapies include AC. Even though the atria and ventricles vary significantly in terms of their shape, function, and molecular and cellular makeup, atrial cardiomyopathy is relatively much less well understood than ventricular cardiac arrest and cardiomyopathy. [9]

The likelihood of having another stroke remains high regardless of the efforts of academics and pharmaceutical corporations. Aspirin is a popular antiplatelet drug used to prevent subsequent strokes, but its benefits must be balanced against the danger of bleeding, especially in the aged population. Aspirin is both safe and helpful in avoiding stroke recurrence, however, it can only prevent 20% of repeated vascular episodes. [10,11,12]

In individuals with left atrial cardiomyopathy with cryptogenic stroke, we expected that rivaroxaban would prevent stroke recurrence more effectively and safely than aspirin. This cross-sectional research looked at whether individuals with a history of unknown etiology stroke, left atrial cardiomyopathy, and moderate to acute left atrial volume index (LAVI) were much more likely to benefit from rivaroxaban medication than aspirin.

METHODS: From December 2020 to December 2022, cross-sectional research was carried out at the neurology department of Mayo Hospital in Lahore, Pakistan. From the database of patients hospitalized in the neurovascular unit at this time, 73 individuals with histories of left atrial cardiomyopathy, moderate to severe LAVI, and cryptogenic stroke were chosen.

Clinical variables were taken out of the patient data. High systolic or diastolic blood pressure

Dr. Rashid Usman
Fauji Foundation Hospital, Rawalpindi

upon discharge, a previous diagnosis of hypertension, or being treated with medication were all considered to be signs of hypertension. A diagnosis of diabetes mellitus was indicated by an admitting HbA1C of more than 6.5%, a prior diagnosis of diabetes, or the use of medication. Each patient's non-contrast head CT or brain MRI was examined to determine if left atrial cardiomyopathy and an acute or subacute cryptogenic stroke were present.

The inclusion criteria included a history of previous cryptogenic stroke, a cardiac ejection fraction of greater than 30, the absence of atrial fibrillation (AF), the absence of cervical and intracerebral artery stenosis greater than 50%, the lack of prosthetic heart valves, the nonattendance of mild to severe stenosis of cardiac valves, and before tracking of heart activity for at least 1 day. Patients, on the other hand, were only allowed to participate in the study if they met at least two of the following criteria for atrial congestive heart failure: LAVI 35, episodes of high atrial rates, also referred to as frequent premature atrial contraction, CHADS2-VASc (congestive heart failure, hypertension, age more than or equal to 75 (doubled), vascular disease, diabetes, stroke (doubled), age 65 to 74, and sex category (female)) score above 4, and spontaneous echo. Cardiac arrhythmia, constriction of more than 50 percent of the cervical and intracerebral veins, and a functioning patent foramen ovale were among the exclusion criteria (PFO). Patients were taken from the neurovascular department database who satisfied the inclusion requirements and at least two of the atrial cardiomyopathy criteria. According to the doctor's judgment, some patients received rivaroxaban for secondary prevention while others received aspirin (level C evidence). All patients were split into two groups based on whether they were taking aspirin or rivaroxaban, and the result in each group was tracked over the course of the next two years. For each patient's admission transthoracic echocardiography, the left atrial volume index (LAVI) of 35 mL/m2 was retrieved from the reports.

SPSS version 26.0 was used to analyze the data. We first compared baseline traits between the two groups. For continuous variables, descriptive statistics are shown as mean SD, and for categorical variables, they are shown as percentages. If group variances were homogenous, the one-way ANOVA (analysis of variance) was used to compare groups; if heterogeneity was present, the Welch analysis of variance was used. We employed the nonparametric Kruskal-Wallis test for variables with uneven distributions, and the chi-square or Fisher exact test for categorical variables to compare the groups. After adjusting for confounding factors such as diabetes and hypertension, a logistic regression analysis was used to compare recurrent stroke between the two groups. A 0.05 p-value was regarded as statistically significant.

RESULTS: The mean age of the 73 patients in our sample was 60.67 ± 10.41 years, and the percentage of men was 60.3%. Their ages ranged from 35 to 85. Between the two groups, there was a similar age distribution, high blood pressure, and diabetes. The risk factors connected to atrial cardiomyopathy were also examined in groups. Table 1 listed the fundamental traits of a cryptogenic stroke.

Dr. Rashid Usman
Fauji Foundation Hospital, Rawalpindi

Table 1: Comparing the cryptogenic stroke's baseline features.

	Age	**Gender (Male)**		**Hypertension**		**Diabetes Mellitus**	
Variables	mean ±SD)	n	**%**	n	**%**	n	**%**
Rivaroxaban	62.21± 10.51	19	57.6	8	24.2	7	21.2
Aspirin	59.40± 10.28	25	62.5	14	35	11	27.5
Total	60.67 ±10.41	44	60.3	22	30.1	18	24.7
P-value	0.254	0.669		0.319		0.535	

The CHA2DS2-VASc mean (SD) score was 4.55 (0.746), and the p-value which is 0.219, indicates that the two groups' differences are not statistically significant. Since the start of the research, there has been no statistically significant difference between the rivaroxaban and aspirin groups in terms of the frequency of premature atrial contraction (FPAC) (P-value=0.541). Instead, FPAC has been the same in both groups (93% and 90%, respectively). However, during the course of the study, atrial fibrillation (AF) had established in 12% of those taking rivaroxaban and in 15.5% of those taking aspirin. Additionally, transient atrial fibrillation occurred in 18.2% of those taking rivaroxaban and in 25.0% of those taking aspirin (TAF). Six patients were unaffected by the atrial arrhythmia. The left atrial volume index, the CHADS2-VASc score, and the frequency of high atrial rates (regular premature atrial contraction) did not differ statistically significantly between the aspirin and rivaroxaban treatment groups (Table 2).

Table 2: Differences in left atrial cardiomyopathy traits between treatment groups.

Variables	**Left atrial volume index**	**CHADS2-VASc score**	**Absent**	**Arrhythmia**
Aspirin	40.40±3.136	4.45±0.639	4(10.0)	36(90.0)
Rivaroxaban	40.61±3.316	4.67±0.854	2(6.1)	31(93.9)
P-value	0.786	0.219	0.541	0.541

The analysis of cardiomyopathy and stroke recurrence revealed a statistically significant difference between the rivaroxaban and aspirin groups. According to the odds ratio (OR) of atrial cardiomyopathy and stroke recurrence (OR=6.78, CI 95%: 0.789-58.33, P-value=0.048), rivaroxaban reduced the risk of stroke recurrence by more than 6 times compared to the aspirin group. With the value of crude risk ratio as 6.6 and a 95% confidence interval range of 0.869 and 50.11, the findings revealed that while the rivaroxaban group only saw one case of stroke recurrence, the aspirin group saw eight cases The logistic regression model used to analyze the correlation between the two groups' treatment histories and stroke recurrence. A stroke recurrence odds ratio of 11.35 was found, with a 95% confidence interval of 1.39–113.08, and a P value of 0.038, assuming that other variables like age, gender, high blood pressure, and diabetes remained constant. The findings showed that patients with a history of left atrial cardiomyopathy and unknown etiology stroke were more inclined to benefit from rivaroxaban therapy than from aspirin for preventing recurrent stroke (Table 3).

Table 3: Stroke recurrence and rivaroxaban treatment vs aspirin therapy.

Groups Study	Stroke Re.	Odds Ratio	Std. Err.	P-value	95% Confidence Interval
Rivaroxaban (n=33)	1(3.0)				
Aspirin (n=40)	8(20.0)	11.35	13.31	0.038	1.13-113.08

DISCUSSIONS: It has not yet been shown that rivaroxaban's superiority over aspirin in preventing the recurrence of unknown etiology stroke and left atrial cardiomyopathy predicts clinical effectiveness. According to estimates, 11% of people will get a recurrence within a year after their first stroke and 26% within five years. [13]

Aspirin is a popular antiplatelet drug used to prevent subsequent strokes, but its benefits must be balanced against the danger of bleeding, especially in the aged population. Aspirin is both safe and helpful in reducing repeated strokes, however, it can only lower recurrent vascular events by 20%.[14]

According to this research, anticoagulant medication with rivaroxaban decreased the risk of stroke in these individuals when compared to aspirin, as shown by the p-value of 0.038, 95% confidence interval range of 0.0088 and 0.8779, and OR value of 0.088. We discovered that rivaroxaban, as opposed to aspirin, did lower the incidence of recurrent stroke in patients with atrial cardiomyopathy, a disease that is highly likely to develop AF, a dangerous arrhythmia that worsens with aging and is associated with very high healthcare consumption and expenditures. Despite this, recent research found a link between atrial pathology indicators and ischemic stroke, suggesting that the tissue substrate may be more of a risk factor for stroke than an arrhythmic condition. [15,16]

Our findings disagree with some earlier research. To prevent strokes following an embolic stroke of unknown origin, they compared a daily dosage of 15 mg of rivaroxaban to 100 mg of aspirin (ESUS). They concluded that rivaroxaban had a greater risk of bleeding and was not more effective than aspirin in preventing subsequent strokes after a first embolic stroke of unknown origin. However, our findings are in line with a few other investigations. [17,18,19] They showed that among individuals with ESUS and moderate to severe left atrial enlargement, rivaroxaban was linked to a lower risk of recurrent stroke. [20-24] Additionally, in line with our findings, another trial discovered that rivaroxaban was more effective than aspirin in lowering the risk of recurrent stroke or systemic embolism. [25,26]

Retrospective design in single-site research and the limited sample size was study limitations. Retrospective studies rely on data that has already been collected, which can limit the accuracy of the information and make it harder to control for extraneous variables. A small sample size can also limit the generalizability of the study's findings, as the results may not be representative of the larger population.

CONCLUSIONS: In conclusion, individuals with a history of left atrial cardiomyopathy and unknown stroke fared better on rivaroxaban than they did on aspirin in terms of preventing recurrent stroke. This cross-sectional study may not only have useful therapeutic ramifications for primary and secondary stroke prevention, but it may also serve as a catalyst for a conceptual shift that will create a wealth of new opportunities for future studies on minimizing the load of atrial cardiomyopathy and stroke.

REFERENCES:

1. Perera, K. S., de Sa Boasquevisque, D., Rao-Melacini, P., Taylor, A., Cheng, A., Hankey, G. J., ... & Young ESUS Investigators. (2022). Evaluating rates of recurrent ischemic stroke among young adults with embolic stroke of undetermined source: the Young ESUS longitudinal cohort study. *JAMA neurology*, *79*(5), 450-458.
2. Lip, G. Y., Lane, D. A., Lenarczyk, R., Boriani, G., Doehner, W., Benjamin, L. A., ... & Potpara, T. (2022). Integrated care for optimizing the management of stroke and associated heart disease: a position paper of the European Society of Cardiology Council on Stroke. *European Heart Journal*, *43*(26), 2442-2460.
3. Mac Grory, B., Yaghi, S., Cordonnier, C., Sposato, L. A., Romano, J. G., & Chaturvedi, S. (2022). Advances in recurrent stroke prevention: focus on antithrombotic therapies. *Circulation Research*, *130*(8), 1075-1094.
4. Diener, H. C., Easton, J. D., Hart, R. G., Kasner, S., Kamel, H., & Ntaios, G. (2022). Review and update of the concept of embolic stroke of undetermined source. *Nature Reviews Neurology*, 1-11.
5. Kim, A. S., Kamel, H., Bernstein, R. A., Manchanda, M., & Caprio, F. Z. (2022). Controversies in Stroke: Should Patients With Embolic Stroke of Undetermined Source Undergo Intensive Heart Rhythm Monitoring With an Implantable Loop Recorder?. *Stroke*, *53*(10), 3243-3247.
6. Pezzella, F. R., Mangiardi, M., Ferrante, M., Fabiano, S., Anticoli, S., Pennacchi, F. G., ... & Caso, V. (2022). Management of Oral Anticoagulation and Antiplatelet Therapy in Post-Myocardial Infarction Patients with Acute Ischemic Stroke with and without Atrial Fibrillation. *Journal of Clinical Medicine*, *11*(13), 3894.
7. Gladstone, D. J., Lindsay, M. P., Douketis, J., Smith, E. E., Dowlatshahi, D., Wein, T., ... & Canadian Stroke Consortium. (2022). Canadian stroke best practice recommendations: Secondary prevention of stroke update 2020. *Canadian Journal of Neurological Sciences*, *49*(3), 315-337.
8. Kariki, O., Vlachos, K., Dragasis, S., Tsetika, E. G., Perlepe, K., Saplaouras, A., ... & Letsas, K. P. (2022). Atrial cardiomyopathy: Diagnosis, clinical implications and unresolved issues in anticoagulation therapy. *Journal of Electrocardiology*.
9. Ntaios, G., & Korompoki, E. (2022). Embolic stroke of undetermined source and atrial cardiopathy: Towards a personalized antithrombotic strategy for secondary stroke prevention. *European Journal of Internal Medicine*, *99*, 24-25.
10. Spence, J. D. (2022). Management of Patients with Embolic Stroke of Unknown Source: Interpreting the Evidence in the Light of Clinical Judgement. *Current Neurology and Neuroscience Reports*, 1-5.
11. Korsholm, K., Damgaard, D., Valentin, J. B., Packer, E. J. S., Odenstedt, J., Sinisalo, J., ... & Nielsen-Kudsk, J. E. (2022). Left atrial appendage occlusion vs novel oral anticoagulation for stroke prevention in atrial fibrillation: rationale and design of the multicenter randomized occlusion-AF trial. *American Heart Journal*, *243*, 28-38.
12. Best, J. G., Cardus, B., Klijn, C. J., Lip, G., Seiffge, D. J., Smith, E. E., & Werring, D. J. (2022). Antithrombotic dilemmas in stroke medicine: new data, unsolved challenges. *Journal of Neurology, Neurosurgery & Psychiatry*, *93*(9), 939-951.
13. Mac Grory, B., Ohman, E. M., Feng, W., Xian, Y., Yaghi, S., Kamel, H., & Reznik, M. E. (2022). Advances in the management

of cardioembolic stroke associated with patent foramen ovale. *bmj*, *376*.
14. Kumar, R., Sun, L. R., Rodriguez, V., Sankar, A., Sharma, M., Meoded, A., ... & Goldenberg, N. (2022, October). Hemostatic and Thrombotic Considerations in the Diagnosis and Management of Childhood Arterial Ischemic Stroke: A Narrative Review. In *Seminars in pediatric neurology* (p. 101003). WB Saunders.
15. Kerr, B., & Brandon, L. (2022). Atrial Fibrillation, thromboembolic risk, and the potential role of the natriuretic peptides, a focus on BNP and NT-proBNP–A narrative review. *IJC Heart & Vasculature*, *43*, 101132.
16. Barnea, R., Agmon, I. N., Shafir, G., Peretz, S., Mendel, R., Naftali, J., ... & Cardiac CT for Undetermined Source of Embolic Stroke (CaCTUSES) Working Group. (2022). Cardiac CT for intra-cardiac thrombus detection in embolic stroke of undetermined source (ESUS). *European Stroke Journal*, 23969873221099692.
17. Pires, C. M., Silva, R., Garcia, B. L., Antunes, N., Vieira, C., Marques, J., ... & Pereira, V. H. (2022). Atrial cardiopathy in young adults with embolic stroke of undetermined source: a myocardial deformation imaging analysis. *The International Journal of Cardiovascular Imaging*, 1-10.
18. von Falkenhausen, A. S., Feil, K., Sinner, M. F., Schönecker, S., Müller, J., Wischmann, J., ... & Kellert, L. (2022). Atrial Fibrillation Risk Assessment after Embolic Stroke of Undetermined Source. *Annals of Neurology*.
19. Blum, S., & Conen, D. (2022). Mechanisms and clinical manifestations of cognitive decline in atrial fibrillation patients: potential implications for preventing dementia. *Canadian Journal of Cardiology*.
20. Mosconi, M. G., Paciaroni, M., & Ageno, W. (2022). Investigational drugs for ischemic stroke: what's in the clinical development pipeline for acute phase and prevention?. *Expert Opinion on Investigational Drugs*, (just-accepted).
21. Li, Q., Wang, C., Li, W., Zhang, Z., Wang, S., Wupuer, A., ... & Yu, W. (2022). A Novel Mutation in COL4A1 Gene in a Chinese Family with Pontine Autosomal Dominant Microangiopathy and Leukoencephalopathy. *Translational stroke research*, *13*(2), 238-244.
22. Sagris, D., Harrison, S. L., Buckley, B. J., Ntaios, G., & Lip, G. Y. (2022). Long-term cardiac monitoring after embolic stroke of undetermined source. Search longer–look harder. *The American Journal of Medicine*.
23. Lüscher, T. F., Davies, A., Beer, J. H., Valgimigli, M., Nienaber, C. A., Camm, J. A., ... & Konstantinides, S. V. (2022). Towards personalized antithrombotic management with drugs and devices across the cardiovascular spectrum. *European heart journal*, *43*(10), 940-958.
24. Sibon, I., & Liegey, J. S. (2022). Management of stroke in patients on antithrombotic therapy: Practical issues in the era of direct oral anticoagulants. *Revue Neurologique*, *178*(3), 185-195.
25. Volgman, A. S., Nair, G., Lyubarova, R., Merchant, F. M., Mason, P., Curtis, A. B., ... & ACC Geriatric Cardiology and Electrophysiology Councils. (2022). Management of Atrial Fibrillation in Patients 75 Years and Older: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*, *79*(2), 166-179.
26. Kim, S. E., Khawaja, M., Kim, J. A., Safavi-Naeini, P., Pickett, J., Molina-Razavi, J., ... & Chelu, M. G. (2022). Detection of Atrial Fibrillation in Real World Setting in Patients with Cryptogenic Stroke and an Implantable Loop Recorder. *Available at SSRN 4305778*.
27. Khan MI, Ashfaq F, Alsayegh AA, Hamouda A, Khatoon F, Altamimi TN, et al. Advanced glycation end product signaling and metabolic complications: Dietary

approach. World Journal of Diabetes [Internet]. 2023 Jul 15;14(7):995–1012. Available from: http://dx.doi.org/10.4239/wjd.v14.i7.995
28. Aladel A, Khatoon F, Khan MI, Alsheweir A, Almutairi MG, Almutairi SO, et al. Evaluation of miRNA-143 and miRNA-145 Expression and Their Association with Vitamin-D Status Among Obese and Non-Obese Type-2 Diabetic Patients. Journal of Multidisciplinary Healthcare [Internet]. 2022 Dec;Volume 15:2979–90. Available from: http://dx.doi.org/10.2147/jmdh.s391996
29. Kumar R, Khan MI, Ashfaq F, Alsayegh AA, Khatoon F, Altamimi TN, et al. Hesperidin Supplementation Improves Altered PON -1, LDL Oxidation, Inflammatory Response and Hepatic Function in an Experimental Rat Model of Hyperlipidemia. Indian Journal of Clinical Biochemistry [Internet]. 2023 Jun 20; Available from: http://dx.doi.org/10.1007/s12291-023-01140-5
30. Ashfaq F, Aljaadi AM, Salaka AS, Noorwali EA, Khatoon F, Khan MI. Comparison of TCN-2 (776C>G) Gene Polymorphism and Vitamin B12 Status with Different Body Mass Index among Saudi Adults. Life [Internet]. 2023 May 15;13(5):1185. Available from: http://dx.doi.org/10.3390/life13051185
31. Mughal h, Abdullah m, Jamil a, Malik a, Rasheed s, Khatoon f. Efficacy of methotrexate alone or with low-dose prednisone in alopecia areata totalis. Biological and Clinical Sciences Research Journal [Internet]. 2023 Jun 23;2023(1):332. Available from: http://dx.doi.org/10.54112/bcsrj.v2023i1.332
32. SIDDIQUI E, ABBASI M, KHOSA M, MOHSIN R, JABEEN N, SIDDIQUE U, et al. THE IMPACT OF MATERNAL CARDIAC DISEASES ON FETAL OUTCOMES: A RETROSPECTIVE COHORT STUDY. Biological and Clinical Sciences Research Journal [Internet]. 2023 Jun 16;2023(1):315. Available from: http://dx.doi.org/10.54112/bcsrj.v2023i1.315
33. Altamimi T, Balouch F. Mini Review; Role of Changes in SARS-CoV-2 Spike Protein and Its Human Interaction. Egyptian Academic Journal of Biological Sciences C, Physiology and Molecular Biology [Internet]. 2023 Jun 9;15(1):503–7. Available from: http://dx.doi.org/10.21608/eajbsc.2023.303781
34. Ali S, Saeed SJ, Zahid S, Rashid I, Khatoon F, Altamimi TN. Impact of Evaluation of Tumour Grade by Core Needle Biopsy on Clinical Risk Assessment and Patient Selection for Adjuvant Systemic Treatment in Breast Cancer. Pakistan Journal of Medical and Health Sciences [Internet]. 2023 Mar 15;17(2):817–9. Available from: http://dx.doi.org/10.53350/pjmhs2023172817
35. Khan MI, Hashmi MO, Abid SUH, Khan B, Iqbal H, Khatoon F. Mid-Term Clinical and Echocardiographic Outcomes of Percutaneous Transvenous Mitral Commissurotomy in Patients with Rheumatic Mitral Stenosis. Pakistan Journal of Medical and Health Sciences [Internet]. 2023 Mar 15;17(2):793–5. Available from: http://dx.doi.org/10.53350/pjmhs2023172793
36. Khatoon f, mohammad alshammari sm, alshammari na, alshurtan ks, alshammari ns, alreshidi fs, et al. Perception, awareness and attitude towards varicose veins among employees working in prolonged sitting and standing postures in hail region, saudi arabia. Medical science [internet]. 2023 may 2;27(135):1–8. Available from: http://dx.doi.org/10.54905/disssi/v27i135/e206ms2985
37. Khan m, nouman m, hashim h, latif s, husain s, sattar s, et al. A correlation biomarker

between bmi and lipid peroxidation in type 2 diabetes mellitus with and without other complications. Biological and clinical sciences research journal [internet]. 2023 Apr 21;2023(1):253. Available from: http://dx.doi.org/10.54112/bcsrj.v2023i1.253

38. Sohair A M Shommo, Firas S. Azzeh, Alsolami Ahmed Khatoon F Et Al, Prevalence Of Serum Vitamin Deficiency In Pakistan Of Chronic Fatigue Without Any Systemic Illness 2023.Volume -12, Special Issue-13 (2023 Doi; 10.53555/Ecb/2023.12.Si13
39. Ahmed S , Mahmood T , Mudasir M, Khatoon F et al.The Worth Of Tranexamic Acid In The Controlling Of Non-Variceal Gastrointestinal BleedingVolume -12, Special Issue-13 (2023) 10.53555/ecb/2023.12.Si13.1982023.25/11/2023
40. Gul S, mir n, Fatima k, tahir s, Younis ns, Khatoon F, et al. Catheter-related infections in hemodialysis: frequency and microbiological profile patients undergoing antimicrobial lock therapy with gentamicin for prophylaxis. Biological and Clinical Sciences Research Journal [Internet]. 2023 Apr 18;2023(1):247. Available from: http://dx.doi.org/10.54112/bcsrj.v2023i1.247
41. Alreshidi FF, Alshammari RF, Alenazi SH, Alshammry TE, Altamimi TN, Almughais ES, et al. Sciatica pain in Saudi population: Knowledge and attitude towards sciatica pain and treatment methods among the population of Hail in Saudi Arabia. Medical Science [Internet]. 2023 Mar 1;27(133). Available from: http://dx.doi.org/10.54905/disssi/v27i133/e142ms2906
42. Zahra A, Hassan SU, Hassan MS, Parveen N, Park JH, Iqbal N, Khatoon F, Atteya MR. Effect of physical activity and sedentary sitting time on psychological quality of life of people with and without disabilities; A survey from Saudi Arabia. Front Public Health. 2022 Sep. fpubh.2022.998890 PMID: 36225781; PMCID: PMC9548647.https://doi.org/10.3389/fpubh.2022.998890
43. Almughais, E. S., Abdullah Alshammari, K. A., Alshammari, H. H., Alreshidi, F. F., Alarfaj, R., Alshammari, R. F., Altamimi, T. N., Aboras, R., Almehmadi, S. A., & Balouch, F. K. (2023, February 5). "Assessment of knowledge and practice of Carpal tunnel syndrome among pregnant and non-pregnant women in Hail region, Saudi Arabia." Medical Science, 27(132), 1–8. https://doi.org/10.54905/disssi/v27i132/ee116ms2910
44. Khatoon, F., Alshammari, R. A., Batool, A., Elhaj, A. H., Alreshidi, F. F., Elhussein, G. E. M. O., Abdalla, R. A. H., Elhag, A. B. M., & Balouch, Z. (2022, October 30). Systematic Review on Implication for DNA Assisted Technology into Molecular Medicine and the useful is the application of Genome Wide Studies. Pakistan Journal of Medical & Health Sciences, 16(10), 217–220. https://doi.org/10.53350/pjmhs221610217
45. Khatoon, F. (2022, August 30). Association of Genetic and Reproductive Hormone with Infertility in Male. Progress in Medical Sciences, 1–11. https://doi.org/10.47363/pms/2022(6)175
46. Kausar, M. A., Shahid, S., Anwar, S., Kuddus, M., Khan, M. K. A., Khalifa, A. M., Khatoon, F., Alotaibi, A. D., Alkhodairy, S. F., Snoussi, M., & Arif, J. M. (2022, February 4). Identifying the alpha-glucosidase inhibitory potential of dietary phytochemicals against diabetes mellitus type 2 via molecular interactions and dynamics simulation. Cellular and Molecular Biology, 67(5), 16–26. https://do