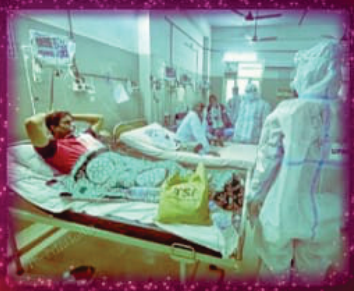
Volume I December 2022 Issue I

MEDICAL RESEARCH BULLETIN

Georgian Research Ecosystem
Innovate and Create



Volume I December 2022 Issue I

Medical Research Bulletin: Georgian Research Ecosystem Innovate and Create

King George's Medical University
Lucknow, Uttar Pradesh

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(Additional Professor of Psychiatry)

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Medical Research Bulletin:
Georgian Research Ecosystem Innovate and Create

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KING GEORGE'S MEDICAL UNIVERSITY
U.P., LUCKNOW
किंग जार्ज चिकित्सा विश्वविद्यालय, उ०प्र०
लखनऊ

MESSAGE

King George's Medical University is a renowned institute with a history of more than a hundred years in the field of Medicine. Its alumni are spread across the globe and continue to add to the rich basket of accolades and milestones of the university. In an endeavour to further expand the horizons in terms of research, the institute has decided to begin an independent journal for articles by the students of undergraduate and postgraduate courses. We hope that this new step in the history of the university will help in promoting research and giving an early platform to the upcoming leaders in the field. With immense pleasure and pride, I take this chance to give my best wishes to the teachers and students of the university. May this be the beginning of another chapter in the legacy of this institution.

(Lt. Gen. (Dr.) Bipin Puri)
Vice Chancellor

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किंग जार्ज चिकित्सा विश्वविद्यालय, उ0प्र0, लखनऊ
KING GEORGE'S MEDICAL UNIVERSITY, U.P., LUCKNOW

प्रोफेसर विनीत शर्मा
प्रति-कुलपति
Professor Vineet Sharma
Pro-Vice Chancellor

Message

King George's Medical University prides itself in academic excellence and in the notable contributions made by its esteemed alumni in various arenas of medical science and research. However, the field of undergraduate research, as of now had been an underutilized area in our institute.

With the inauguration of this upcoming research journal we wish to change that.

With this research journal we wish to inculcate an inherent sense of intrigue and curiosity and a desire to delve into the field of research in the undergraduate students.

I applaud the editorial board for taking this incentive first time in the history of K.G Medical University and congratulate them on the inaugural issue of this research journal.

(Prof Vineet Sharma)
Pro-Vice Chancellor

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किंग जार्ज चिकित्सा विश्वविद्यालय, उ0प्र0, लखनऊ
KING GEORGE'S MEDICAL UNIVERSITY, U.P., LUCKNOW

Prof. A. K. Tripathi

Dean - Academics

Message

It gives me immense pleasure to witness the release of inaugural issue of "Medical Research Bulletin: A Spirit of the Georgians". Over the years the research interest among medical graduates is increasing. The Indian Council of Medical Research is also promoting the research of medical graduates by giving them short-term research grants. When students are planning to pursue higher education abroad, their research exposure during medical graduation becomes an important criterion to get selected. Hence, in the current scenario, promoting research among the medical students is important. To facilitate this, the step taken by the prestigious King George's Medical University is a land mark step of its own kind. The Honorable Vice Chancellor of this institute has taken the initiative to start a medical research bulletin to promote research among medical, paramedical students of the institute, which will be remembered in the glorious history of King George's Medical University. I must congratulate the editorial team, particularly the medical graduates who actively involved in contributing articles to the inaugural issue to make it a success. I hope the journal will disseminate knowledge, promote research and will give platform to publish student's research.

Long live the spirit of Georgians.

(Prof. A.K. Tripathi)
Dean-Academics

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King George's Medical University, U.P., Lucknow

Office of the Dean, Research & Development

Prof. Shally Awasthi
Dean

No.: 1432/R-Cell-22
Date: 14/12/2022.

Message

King George's Medical University (formerly, King George's Medical College) has a long history of scientific research and innovation. This institute is one of the most prestigious medical institutions in the country with international repute. There is growing interest among medical graduates towards research, however many of their ideas remain undocumented as most of them do not get a good platform to publish them. The initiative taken by King George's Medical University, to promote the research attitude of medical and paramedical students is very unique and first of its kind in the country. Many medical institutions run scientific journals; however, to the best of my knowledge, none of them are exclusively meant to promote student initiated research. I hope this journey will go long and will keep on igniting young minds to work on innovations. My best wishes to the editorial team and the students.

Prof. Shally Awasthi
Dean, Research and Development
& Head, Department of Pediatrics
King George's Medical University, U.P.,
Lucknow

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Editorial

Journey of a journal: Identity crisis to the establishment of identity

Sujita Kumar Kar

There is an exponential growth in the number of journals, including scientific journals, globally. Journals aim to disseminate information. Scientific journals allow researchers and academicians to publish their ideas, opinions and research. The scope of the journals is diverse. Many journals publish literature from a variety of disciplines, whereas some others limit their scope to specific domains. Similarly, all types of articles are allowed for submission in several journals, whereas several other journals restrict their content to publishing a particular type of article only. For example, many journals publish review articles only (e.g., International Review of Psychiatry) or case studies exclusively (e.g., BMJ case reports).

Many journals die premature death (untimely discontinuation). Lack of initiative and enthusiasm, merging with a major journal, conflict in the society/organization publishing the journal and financial constraints are the primary reasons for the untimely discontinuation of the journals. Many journals starve to find articles or reviewers. As a result, the number of articles published in an issue becomes few. The journals also need help in getting published on time. Sometimes, regular journal issues are dropped from publication leading to an interruption of the publication process. As a result, the journal faces challenges in indexing in indexation databases. Readers also lose interest and trust in the journal if the journal is published irregularly. It may affect the citation of the published articles in the journal adversely. A study evaluated the discontinuation of 140 Australian journals and found the mean death age of the journals to be 19.7 years [1]. More than half (54%) of the total journals discontinued were published under the aegis of educational institutions [1]. Approximately three fourth of the discontinued journals were from social sciences, humanities and arts; non-availability of the fund is the primary reason for the discontinuation of journals. The inadequate quality of submitted articles and poor support from the organization are other factors responsible for the premature discontinuation of the journals [1].

Evidence suggests a disparity in the representation of disciplines, gender, and professionals in scientific publications [2]. The student population, though very large, has little contribution to research publications. Mostly the contribution of the students is limited to developed countries and some institutions. Unawareness, lack of motivation, different priorities, and lack of mentorship might be the reasons why students publish less research. The unavailability of a suitable platform for submission might be another obstacle for the students. To promote research by the students, the Indian Council of Medical Research is providing short-term student research grants. Students engaged in research and making publications are more likely to match the needs of academic appointments [3]. Because of their unawareness, many students fall into the trap of predatory journals, and all their efforts lose scientific credibility.

Survival of a journal needs adequate and continuous nurturing through good mentoring, organizational support, good quality submissions, adequate peer review support, and good microplanning. When the journal is solely meant for the student population, the majority need to be more proactive in research, and even if they are proactive, the majority do not get an opportunity; committed and consistent effort needs to be made to mentor and motivate the students for research. This may help the journal to travel a long journey. I wish the "Medical Research Bulletin: A Spirit of the Georgians" to initiate this challenging journey and create milestones.

Let the spirit of the Georgians never fade.

Let the science grow.

Let the students flourish in their academic ventures.

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Abnormal Potassium Homeostasis in Heart Failure- Identify the Warmongers!

Sahil Chaudhary, Vibhor Agrawal, Akshyaya Pradhan*

According to the Global Health Data Exchange registry, the worldwide prevalence of heart failure (HF) as of 2020 is 64.34 million cases (8.52 per 1,000 inhabitants). HF produces the most significant burden after 60 years of age, and its prevalence has increased by 3.9% in older adults in the last three decades [1]. The treatment protocol for HF includes drugs like thiazide diuretics and steroidal mineralocorticoid receptor antagonists (MRAs), which are known to cause significant dyskalemia. Since potassium levels in plasma lie in a very narrow range, it becomes essential to monitor the serum potassium levels throughout the treatment.

Serum potassium levels play a crucial role in maintaining the membrane excitability of cardiac muscle fibres, affecting the heart's contractility. Hypokalemia and hyperkalemia can both affect the membrane potential, which mainly manifests as an arrhythmogenic rhythm of the heart and is, therefore, linked to increased morbidity and mortality. According to a meta-analysis, the association between serum potassium concentrations and adverse outcomes in patients at risk for HF is a U-shaped curve establishing that both hypokalemia and hyperkalemia are associated with adverse events [2].

A recent study by Mozo et al. tried to investigate the factors associated with dyskalaemia in people at increased risk of developing HF who were assigned to receive spironolactone or not in the Heart 'OMics' in AGEing (HOMAGE) trial [3,4]. The HOMAGE trial was a prospective, randomized, open-labelled, blind-endpoint trial that compared the use of spironolactone to standard care for up to 9 months in people with clinical risk factors for developing HF [3]. Serum potassium in the patients was assessed every 1 and 9 months after randomization. Doses of spironolactone were initiated at 25 mg/day and were increased, decreased, or discontinued, with or without restarting, according to their serum K+ levels and renal function, intending to keep the levels of potassium in the range of 4.5-5.4 mEq/L. In the HOMAGE cohort, hypokalemia and hyperkalemia levels were set at <4.0 mEq/L and >5.0 mEq/L, respectively [3,4].

Hypokalemia can lead to fatal conditions like ventricular arrhythmias, electrolyte disturbances, sudden cardiac death, ischemic substrates, and reduced ejection fraction. A Danish study established a three-fold increase in the risk of death in patients with potassium levels below 3.5 mEq/L compared to those between 4.2 to 4.4 mEq/L [5]. This relationship is also evident in the TOPCAT study [6]. An important conclusion was that the correction of hypokalemia nullifies this increased risk. In the MRIFT trial, a decrease in serum potassium levels by 1.0 mEq/L increased ventricular arrhythmias by 28%. Its data also indicated that hypokalemia is linked with an increased risk of sudden cardiac death in patients with high blood pressure on therapy with thiazide diuretics [7]. Hyperkalemia can also lead to fatal conditions, like sudden ventricular arrhythmias, and is a cause of mortality and morbidity in the population. One of the major causes that result in hyperkalemia is the pharmacotherapy with renin-angiotensin-aldosterone system inhibitors, which include angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and MRAs [8]. Hyperkalemia is also associated with conditions such as diabetes mellitus and chronic kidney disease and pharmacotherapy with drugs like MRAs. As the levels of potassium increase, the prognosis becomes poorer, which is also evident from the U-shaped curve described earlier.

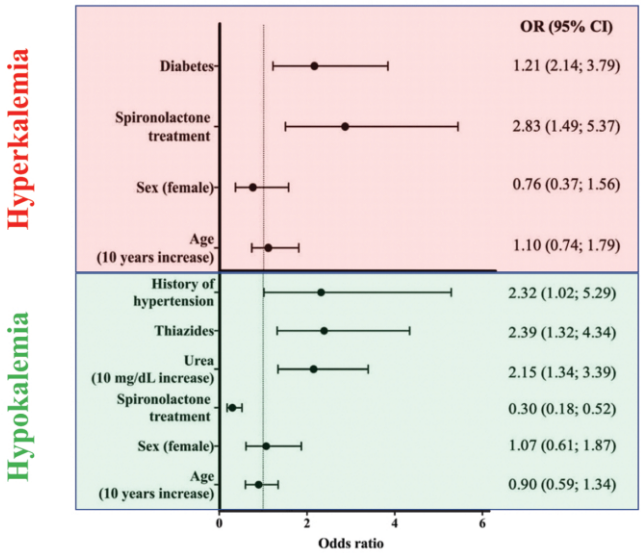

Figure 1: Forest plot of odds ratio for the predictors of hyperkalaemia and hypokalaemia as described in the HOMAGE Trial

During the trial, potassium levels <3.5 mEq/L were found only in 1.2% of patients (only 1 in the spironolactone group while 5 in the control group), and potassium <4.0 mEq/L was found in 46.9% (only 7 in spironolactone group while 39 in the control group), and potassium levels >5.5 mEq/L were found only in 1.0% (4 in spironolactone group and 1 in control group). It is evident from this that the participants who developed hyperkalemia were more likely to be treated with spironolactone compared with normokalaemic and hypokalaemic subjects. Following the results of the trial, spironolactone (daily dose 33.8 ± 13.9 mg) increased serum K+ only by 0.23 mEq/L. Risk factors for developing K+ >5.0 mEq/L included the presence of diabetes mellitus and randomization to spironolactone, while the factors for developing potassium levels <4.0 mEq/L included the use of thiazides, blood urea concentration, history of hypertension but was inversely related to the use of spironolactone (Figure 1) [3,4].

In conclusion, for people at risk of developing HF and with relatively normal renal function, using spironolactone or MRAs reduces the risk of developing hypokalemia and overall mortality and morbidity. Steroidal MRAs like spironolactone, mostly at doses 25-50 mg/day, only slightly increase the serum K+ levels, with a shallow risk of developing clinically significant hyperkalemia. Altogether, this efficacy and safety profile sets the stage for trials of MRAs aiming to reduce cardiovascular and renal morbidity and mortality in patients at risk of HF.

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Different Potential Mitochondrial Drug Targets in Oral Carcinogenesis

*Ekta Raphael Anthony, Rahul Pandey, Divya Mehrotra**

While mitochondrial drug targets in oral carcinogenesis are widely recognized as essential considerations in health research, the presence of these and other critical determinants of health in research findings remains quite variable in published literature. In an effort to close this knowledge gap concerning the implications of mitochondrial drug targets in oral carcinogenesis in health research is evidence base, the Polymorphism Journal has recently adopted an editorial policy requiring authors to ensure that their manuscripts speak to these concepts, where applicable.

Cancer is a genetic disease that chiefly consists of unregulated cell growth and division caused by changes to genes or damage to DNA. In cancer, a cell divides and grows uncontrollably, forming malignant tumours and invading nearby body parts. Cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Oral cancer is currently a major global health issue [1] and is most commonly found in many underdeveloped South Asian countries, especially among men in comparison to women. In India, considering the mortality rate among various cancers, the primary reason for death in men is due to oral cancer [2]. Oral Squamous cell carcinoma (OSCC) occurs at the lips, hard palate, upper and lower alveolar ridges, anterior two-thirds of the tongue, sublingual area, buccal mucosa, retromolar trigone, and the floor of the mouth [3] and is the most common subtype of Head and Neck Squamous Cell Carcinoma. Globally, the incidence of OSCC was increasing and accounted for 8.8 million deaths in the year 2015 [https://www.who.int/en/news-room/factsheets/detail/cancer] [4]. A high prevalence of tobacco and alcohol consumption and the Human Papilloma Virus (HPV) are some of the causative agents of the OSCC [5]. The late diagnosis and lack of clinical interventions are some of the salient reasons for the high mortality rate due to OSCC. Diagnosis of oral cancer at later stages implies that the neoplastic cells become aggressive and become resistant to standard therapeutics [2]. Despite the vast amount ofresearch and several conventional therapeutics advancements for oral cancer patients, many drawbacks have to be addressed, like surgical resection leads to constant defacement, altered individuality, and devitalizing physiological consequences. Similarly, chemotherapies and radiotherapies result in toxic effects, thus affecting the welfare and quality of patient life [6]. Therefore, the prognosis for the OSCC patient remains a poor and burdensome task with a five-year survival rate that encourages further research on the factors which modify the disease outcome [5, 7].

Previous studies account for the inter-relation of mtDNA mutation and apoptosis in various types of cancer. There are many pathways through which apoptosis is dysregulated in the mitochondria of cancerous cells. One mechanism is free radical-induced cell death, where defective mitochondria overproduce free radicals. There are many genes involved in the apoptotic pathway. Mechanisms for a few genes like the B cell Lymphoma-2 (BCL-2) and B cell Lymphoma-2 Associated X, Apoptosis Regulator (BAX) are understood, but still, there are many whose roles and exact function is still poorly understood. In the mechanism of apoptosis, the caspases play a central role as they are both the initiators and executioners. The apoptotic pathway has three critical pathways Extrinsic Apoptotic Pathway (Death Receptor Pathway), Intrinsic Apoptotic Pathway (Mitochondria Pathway), and Initiation Pathway (Intrinsic Endoplasmic Reticulum Pathway). The dysregulation of the apoptotic pathway leads to cancer. In cancer, during oncogenesis, there is an over-expression of antiapoptotic proteins while a down-expression of proapoptotic proteins. There is a proliferative expression of Inhibitors of Apoptotic Proteins (IAPs).

Caspase expression decreases while TP53 expression increases. In an impaired receptor signalling pathway, there is a reduced expression of the death receptor and signals [8, 9]. Thus, we see various genes that are either drivers or followers during oncogenesis. Because there is difficulty in identifying which genes are drivers and which are followers, the search for an ideal drug target in oral cancer up till now has been unfruitful. The present study focuses on the potential therapeutic drug target to trigger mitochondrial-dependent cell death in oral carcinogenesis. The present study's novelty has been identifying potential therapeutic drug targets to start mitochondrial-dependent cell death involved in cellular apoptosis in oral carcinogenesis using a bioinformatics approach. The main objective of the present study is to identify suitable therapeutic drug targets that trigger mitochondrial-regulated cell death, which is the first study of this type.The initial effort to address the

mitochondrial drug targets in oral carcinogenesis in the Polymorphism Journal has adopted an editorial policy that asks the authors to address the relevance of the role of mitochondrial drug targets in oral carcinogenesis. While this most recent policy shift focuses specifically on finding mitochondrial drug targets in oral carcinogenesis in cancer research findings, the importance of other exciting factors in advancing our understanding of the health of populations cannot be ignored. The first step with the new Polymorphism Journal policy will require authors to speak to how the mitochondrial drug targets in oral carcinogenesis are presented in their studies. Specifically, the Polymorphism Journal Board now requires all authors to answer the following questions as part of the manuscript submission process:

1. *More datasets should be used for the study. Yes/No*
2. *For the construction of Protein-Protein Interaction, Bioconductor should be used. Yes/No*
3. *If No, please describe why only one dataset should be used.*
4. *If No, please describe why Cytoscape is an excellent software for constructing the Protein-Protein Interaction.*

This shift will require both authors and reviewers to consider the complex ways in which the determinants of health contribute to advancing the evidence based on mitochondrial drug targets in oral carcinogenesis.Authors:

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INVICTUS TRIAL: Bringing Rivaroxaban into our Clinics

Vaishali Singh, Shubhajeet Roy, Gaurav Chaudhary

Background:

Vitamin K antagonists have been shown in randomized trials to be effective for stroke prevention in patients with atrial fibrillation [1]. Vitamin K antagonist therapy is difficult to administer due to numerous dietary and pharmacologic interactions, and regular blood sampling is required to monitor anticoagulation status with the international normalized ratio of prothrombin time (INR). The need for non-monitored drugs led to the development of dabigatran, a direct thrombin inhibitor, and the factor Xa inhibitors rivaroxaban, apixaban, and edoxaban. There has been little testing of factor Xa inhibitors for preventing cardiovascular events in patients with rheumatic heart disease-associated atrial fibrillation, so this trial was conducted.

Trial Summary:

The intention-to-treat analysis included 4531 patients, with 2275 assigned to the rivaroxaban group and 2256 assigned to the vitamin K antagonist group [1]. The primary efficacy outcome was a composite of total stroke or systemic embolism, and the key secondary outcomes were myocardial infarction and death from vascular (cardiac or non-cardiac) causes.

The primary outcome event occurred in 560 of 2275 (24.6%) patients in the rivaroxaban group and 446 of 2256 (19.8%) patients in the vitamin K antagonist group over a mean of 3.1 ± 1.2years (proportional-hazards ratio, 1.25; 95% CI, 1.10 to 1.41; P<0.001). The rivaroxaban group had a restricted mean survival time of 1599 days, while the vitamin K antagonist group had a time of 1675 days (difference, 76 days; 95% CI, 121 to 31 days; P<0.001 for superiority). More patients in the rivaroxaban group had a stroke than in the vitamin K antagonist group (90 vs 65 patients). In the rivaroxaban group, 552 patients died, while 442 died in the vitamin K antagonist group (95% CI). The rate of hospitalization for heart failure did not differ between groups. There was no significant difference in valve replacement surgery rates or mitral valvuloplasty rates between the two groups. The between-group differences in stroke and death rates were similar in the on-treatment and intention-to-treat analyses. There was no significant difference in major bleeding rates between treatment groups. On the other hand, rivaroxaban had a lower risk of fatal bleeding than vitamin K antagonists.

Summary:

Compared to rivaroxaban therapy, vitamin K antagonist therapy significantly reduced the risk of a composite of cardiovascular events or mortality without increasing the risk of bleeding in individuals with atrial fibrillation associated with rheumatic heart disease, thereby supporting current guidelines.

Critical Remarks:

The use of rivaroxaban or other factor Xa inhibitors for stroke prevention is non-inferior to warfarin therapy, with a significant reduction in the risk of hemorrhagic stroke in patients with atrial fibrillation unrelated to rheumatic heart disease. The patients in this INVICTUS trial [1] were much younger (mean age, 50.5 years) and more likely to be female (72% of the patients) than in previous trials that only included patients without rheumatic heart disease. This trial had a lower percentage of hypertensive patients (23%) than previous trials. Previous studies, however, predicted a similar or higher risk of stroke because mitral stenosis is associated with an increased risk of stroke. A randomized trial comparing rivaroxaban to vitamin K antagonist

therapy in patients with atrial fibrillation and bioprosthetic mitral valves found a lower risk of stroke with rivaroxaban but no significant difference in mortality. As a result, the current trial's findings were unexpected. Due to the requirement for monthly INR control monitoring, patients in the vitamin K antagonist group interacted with medical personnel more frequently than those in the rivaroxaban group. This may have improved general healthcare, decreased stroke-related fatalities, and improved general healthcare. There was little difference between the vitamin K antagonist and rivaroxaban groups during the first 12 to 18 months of follow-up. Following that, it was clear that the vitamin K antagonist group had a lower rate of the primary composite outcome than the rivaroxaban group, and this difference remained significant three years later. The Warfarin versus Aspirin in Reduced Cardiac Ejection Fraction (WARCEF) trial also found a delay in the onset of a benefit from vitamin K antagonist therapy. The WARCEF trial investigated whether warfarin therapy reduced the risk of death or stroke compared to aspirin in patients with heart failure due to a reduced ejection fraction but no atrial fibrillation. The trial found no overall benefit, but a time-varying Cox analysis revealed the use of warfarin therapy that emerged only later in the follow-up period, as in the INVICTUS trial [1]. Rivaroxaban treatment significantly reduces mortality in patients with atherosclerotic vascular disease. Thus, the findings of INVICTUS trials [1] support the hypothesis that vitamin K antagonist therapy lowers the risk of death from vascular causes in patients with rheumatic heart disease; this effect appears to be independent of atrial fibrillation-related stroke prevention and suggests a direct impact on the disease process of rheumatic heart disease. Compared to rivaroxaban, vitamin K antagonist therapy resulted in a lower rate of ischemic stroke and lowered mortality due to vascular causes in patients with rheumatic heart disease-associated atrial fibrillation without significantly increasing the rate of significant bleeding.

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Impact of Antimicrobial Resistance on Global Public Health

*Shailendra Kumar Yadav, Dandu Himanshu Reddy**

Introduction:

Around 1.27 million people die yearly due to Antimicrobial resistance, which is less than deaths by HIV (8,64,000 deaths) or malaria (6,43,000 deaths) every year, So antimicrobial resistance is a significant cause of mortality. It is increasing the mortality rate in patients. Superbugs are the most common antimicrobial resistance microorganisms. Viruses, bacteria, fungi and parasites can evade the effect of antimicrobials used to treat the infection. Superbugs are spreading infection in humans and becoming the primary cause of mortality, antimicrobial resistance and increasing financial burden on society. Antimicrobial resistance is a significant problem for healthcare professionals. Microorganisms have a unique ability to modify their genes and biochemical functionality to survive against antimicrobial drugs. This is also a fundamental cause of the development of antimicrobial resistance in microorganisms. Many factors are involved in developing antimicrobial resistance; a single therapeutic strategy cannot prevent it. Some of the microorganisms don't require antimicrobial drugs for the development of resistance. Sometimes the surrounding environment also facilitates the development of resistance. Continuous misuse of antibiotics by healthcare professionals and their extensive use in meat and food production is causing considerable risk to human health. Due to low interest and lack of research resources for developing newer antibiotics are also contributing to the evolution of superbugs and their growth. With proper collaboration in all countries, antimicrobial resistance will be manageable. World Health Organization assembly adopted a global action plan to overcome antimicrobial resistance, increasing awareness about antimicrobial resistance to decrease the misuse of antibiotics [1].

Inappropriate prescribing of antibiotics:

Many studies showed that 50% of antibiotics are prescribed unnecessarily in clinical practice, which is the primary cause of the development of antimicrobial resistance. There should be proper antibiotic policies in every hospital for the appropriate use of antibiotics, and the antibiotic policy should be implemented appropriately with antibiotic audits [2].

Overuse of Antibiotics in Livestock:

A large number of antibiotics are used in the maintenance and growth of livestock. Antibiotics are also used in fish farming which is an important cause of antimicrobial resistance. Antibiotics used for livestock and fish farming should be minimized to overcome antimicrobial resistance [3].

Poor Infection Control in healthcare settings:

There should be a proper strategy to control the infection. Every hospital should have its antibiotic policy for properly using antibiotics. Antibiotic prescription audits should be conducted timely to overcome the misuse of antibiotics. The hospital infection committee plays a vital role in overcoming the infection.

Poor Hygiene and Sanitation:

Microorganisms spread quickly when there is a lack of hygiene and sanitation. It's essential to maintain hygiene and sanitation, especially in healthcare settings. Proper disinfectants should be used by the cleaning staff.

Antimicrobial Stewardship:

An antimicrobial stewardship program is the most effective way to overcome antimicrobial resistance and to educate healthcare workers in a healthcare setting. It improves the use of antibiotics and minimizes the misuse of antibiotics. Implementation of the Antimicrobial Stewardship Program is most important [4].

Summary:

Antimicrobial stewardship program is a vital tool to reduce antimicrobial resistance in hospitals. It will reduce the mortality rate in healthcare settings. It reduces the unnecessary use of antibiotics in hospitals, and it reduces the treatment cost for the patients. There is a need to develop more potent antibiotics and therapeutic strategies to reduce antimicrobial resistance. There is a need for huge collaboration of national, international government and private agencies to facilitate this Global health problem [5].

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COVID-19 Associated Mucormycosis in India - A Dreaded Sequelae

*Vinay Suresh, Hardeep Singh Malhotra**

COVID-19 is a pandemic that has been detrimental to all facets of human life. The second wave, particularly, strained the economy and infrastructure of developing countries like India. The pandemic exposed several bottlenecks in the health infrastructure, such as poor planning, lack of resources and poor planning.

Amidst this second wave of the COVID-19 pandemic, we saw an endemic of mucormycosis or the 'black fungus'. The numbers were staggeringly high in India. A number of theories were proposed to explain plausible causes of this surge. Unchecked use of steroids, overloading of zinc, monoclonal antibodies, COVID-19-associated low immunity, diabetes and other comorbid conditions of patients lead to an increased risk of mucormycosis [1]. One explanation pointed out the use of unsterile water to dehumidify oxygen [1].

Mucormycosis, also known as zygomycosis, is widely dispersed in the environment; hence, the risk of exposure is substantially high. The implicated fungal species in COVID-19-associated mucormycosis is primarily R. arrhizus, followed by Rhizopus spp. and Rhizopus microsporus [2]. The infection usually targets the brain, lungs and sinuses. However, in India, the lungs' involvement was surprisingly less compared to the sinus involvement, followed by an extension to the brain. It can present either as a widely disseminated condition or as rhinocerebral, pulmonary, cutaneous and renal mucormycosis [3]. Many states in India declared mucormycosis as a notifiable disease in May 2021.

John et al. reviewed 41 cases of COVID-associated mucormycosis and reported that pre-existing diabetes was present in 80% of patients, while steroid was administered in 90% of cases [4]. Multiple systematic reviews also report that diabetes mellitus seems to be a frequently reported condition associated with mucormycosis in India [2,5]. Interestingly, the review by Muthu V et al. also confirms that the case fatality rate of COVID-associated mucormycosis in India was significantly lower compared to the rest of the world [2].

One multicentric study analyzed a large sample of 2826 patients in India with COVID-associated mucormycosis [6]. They observed that most patients presented with severe facial pain, associated headache, eschar over the nose, ocular congestion, and proptosis followed by perforation at the palate [6]. Following initial localization in the nasal mucosa, the fungus trails up the sinuses and pools up in the sphenopalatine fossa. It then extends largely through the cavernous sinus (70%) and to a small extent via the cribriform plate (22%) and pterygopalatine fossa (12%) into the brain. One or more cranial nerves can get involved along the same side, which is also called Garcin syndrome. It can also cause orbital apex syndrome and cavernous sinus syndrome. Vascular complications such as intracranial haemorrhage and occlusion or stenosis of vessels were also seen as complications. Early clinical diagnosis and prompt treatment provide a much better prognosis in these patients.

COVID-associated mucormycosis is thus a severe and potentially life-threatening condition. Adequate measures, such as medication restrictions like corticosteroids, must be efficiently implemented at all levels of COVID-19 care.

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Derivation of a bedside score (MASH-P) to predict 6-month mortality in tuberculous meningitis

*Yashita Khulbe, Imran Rizvi**

Tubercular meningitis (TBM) is considered as the most lethal and disabling form of tuberculosis. An estimated 100,000 new TBM cases are reported every year, out of a total of 10.4 million new tuberculosis cases each year as stated by World Health Organisation (WHO) [1]. Traditionally, the British Medical Research Council (MRC) staging system has been used to determine the severity of TBM patients since 1948. More recent studies have shown that scales such as Glasgow Coma Scale (GCS) and Acute Physiology and Chronic Health Evaluation (APACHE)-II are better at predicting outcomes in adult TBM patients [2]. Hence there is a need for a simple yet comprehensive scale which encompasses all significant factors affecting the prognosis of tubercular meningitis.

The update on the development of such a scale by Rizvi et al is an essential step in evaluating the factors that have and have not been included until now in determining TBM cases' prognosis. The authors utilized data from 721 patients with tuberculous meningitis between October 2012 and September 2018. Baseline clinical variables, neuro-imaging variables and cerebrospinal fluid parameters were used as predictors of death. The goal was to develop a simple score which can be used easily at the bedside to predict the prognosis of tuberculous meningitis. After multivariate analysis, the model was internally validated using the bootstrap technique. The findings were very encouraging, with the confidence intervals of regression coefficients being narrow for the set of significant predictors. Finally, rounding the regression coefficients was done to produce a bedside prognostic score for 6-month mortality in TBM. The score showed good discrimination with an AUC of 83.1% (95% CI = 79.5%–86.7%, P < .001). The score has been given the acronym MASH-P, which is short for its components - baseline MBI (M), age (A), stage (S), hydrocephalus (H) and papilledema (P). The score can range from 0 to 10; a score of 0 carries a low probability of mortality (1.7%), whereas a score of 10 carries a high likelihood of mortality (65%).

The score has several practical implications –

- *None of the variables used in the score requires specific procedures or investigations, with age, stage, papilledema and MBI being obtainable by a simple bedside history and examination and hydrocephalus easily diagnosed on neuroimaging. Hence the score can easily be used at the bedside.*
- *In comparison, the MASH-P score performed better than the MRC stage alone in predicting death, as shown in the article.*
- *In a unique attempt, the authors have used the Modified Barthel index (MBI) as an indicator of disability status at the baseline, which was found to be a significant predictor of death.*
- *The authors have also developed an excel score sheet, which can be used to estimate the prognosis digitally within a minute (e-component, MASH-P Prediction e-Calculator). This will serve as a user-friendly approach for the masses to understand the prognosis of their respective cases.*

This model is an improvement over the model by Thao et al., which was dependent on extensive history, treatment protocols and CSF investigations. Hence it made prognosticating TBM cases a very exhaustive and cumbersome process [3]. This score also does not use parameters such as vasculitis, immunosuppression, or diabetes mellitus, used in the HAMSI score, which removes the multidimensional impact of these disorders that is unspecific in the prognosis of any particular disease [4].

With this in mind, the scale is manageable. Due to the limited participation of HIV co-infected patients in the study (2.8%), the score is not applicable in prognosticating cases with HIV co-infection. Similar is the case of drug-resistant patients (1.7% in the given study). Hence it can only be used in drug-sensitive cases. Moreover, the score is helpful in predicting mortality only; it is not valid in predicting disability.

The authors should be commended for this study, which provides a comprehensive yet feasible method to determine the prognosis of TBM cases. With appropriate external validation, the MASH-P score has the potential to become one of the leading prognostic tools of TBM. This will make it easy for the clinician to estimate the intensity of treatment to be provided to each patient and for the patient's relatives to understand the prognosis of the case.

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Deep phenotyping of CVD risk factors and added mobile, digital measurements to the FHS in cohorts of middle-aged people via the new e-FHS mobile application

*Rashmi Shrivastava, Narsingh Verma**

Eric et al. report the results of the eFHS study, consisting of eligible participants recruited from 3 cohorts embedded within the FHS that were initially enrolled from 2002 to 2005: the Third-Generation cohort (n=4095); the Omni 2 cohort (n=410; multiethnic cohort); and the New Offspring Spouse cohort (n=103) and were assessed for the usability of the new app using two domains (functionality, aesthetics) of the Mobile App Rating Scale (MARS) [1]. As per the key results, participants rated the new, enhanced eFHS app positively overall. Mobile app survey completion rates were high, consistent with positive in-app ratings from participants.

The objective of this editorial comment is to assist in finding the importance of remote monitoring through mobile technology concerning new e-FHS mobile applications, many of them cited by Eric et al.[2], into a more comprehensive context according to the following points.

- *There is evidence that in the era of the coronavirus disease 2019 (COVID-19) pandemic, the importance of remote monitoring through mobile technology has been highlighted by increasing reliance on telemedicine.*
- *It also illustrates the need for more robust research incorporating and implementing these technologies into longitudinal studies.*
- *The ubiquity of personal smart devices has enabled new modalities for questionnaire-based data collection through app-based survey administration.*
- *The studies in recent years have aimed to optimize the above mode of data collection and to understand its validity compared to traditional methods [3-5].*

The points mentioned above might support the findings by Eric et al. as the study sample is derived from one of the most scientifically rigorous and longest-standing longitudinal studies focused on cardiovascular health. It deploys a novel, multifaceted mobile health system in this cohort. We must recognize the possibility that people's health and education levels may have inflated the assessed usability ratings by influencing how they perceive the study's health technology.

In conclusion, the generalizability of results to other geographical places, races/ethnicities, and age groups is questionable because unique location, race, and ethnicity can also have an impact. Additionally, the in-person enrollment processes and possibly established longitudinal relationships that FHS participants may have with the research could be sources of bias, resulting in slightly higher observed adherence and usability measures. Last but not least, because they were not the main focus of the MDH app, the engagement and information subscales of the MARS were not evaluated as part of the study; nonetheless, including these items may have provided additional, intriguing insights into overall perceptions of the app. Because the study is observational and the data collected by the MARS were self-reported, it is impossible to rule out response misclassification and establish causal relationships.

List of abbreviations:

CVD-cardiovascular disease

FHS- Framingham Heart Study

e-FHS- electronic Framingham Heart Study

COVID-Corona Virus Disease

MDH-My Data Helps

MARS- Mobile App Rating Scale

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Spinal Cord Stimulation Therapy for gait disturbances in Parkinson's Disease: Where are we?

*Shakti Katiyar, Vibhor Agrawal, Shweta Pandey**

According to the Global Health Data Exchange registry [1], the prevalence of Parkinson's disease (PD) worldwide is as high as 10 million. Adams et al., in their book 'Principles of Neurology [2], define PD as "a progressive, degenerative neurologic disease characterized by tremors that are maximal at rest, retropulsion, rigidity, stooped posture, slowness of voluntary movements, and a masklike facial expression." These symptoms can be relieved by dopamine replacement therapy in the early stages. Still, axial symptoms like gait disturbances, posture, and freezing of gait, which are seen in advanced PD, are often resistant to treatment. Conventional therapies for PD have substantial constraints, with patients presenting with refractory symptoms despite continued efforts.

Spinal Cord Stimulation (SCS) arose as a potential alternative therapy for advanced PD in the last decade. SCS is based on tonic stimulation by a small current via leads implanted in the spinal cord. The drawback here is that paraesthesia is produced corresponding to the stimulated areas; However, a recent advancement is the burst stimulation paradigm, under which multiple pulses of high-frequency rapid action potentials are delivered, followed by a passive recharge phase of low frequency. This does not produce paraesthesias, making therapy imperceptible to the patient [3].

We searched the PubMed database for clinical trials, including randomized controlled trials, using the strategy ("Spinal Cord Stimulation"[Mesh]) AND "Parkinson's Disease"[Mesh]). The date range was from inception to October 30, 2022. A total of 4 results were retrieved, and the search was not limited by the year of publication or language. Upon reviewing each, we found that all of these studies were conducted in small cohorts, either single-blinded or unblinded. Second, although these studies have shown that SCS can improve gait in PD, the outcomes are heterogenous, as some patients did not respond well to the treatment. Third, there was a lack of clinical phenotyping, like gait characterization and selection of patients in these studies, which could have been responsible for the heterogeneous outcomes. Fourth, the mechanism of action of SCS needed to be better elucidated in these papers.

Thus, to produce conclusive evidence of whether SCS is efficient in improving gait disturbances in PD, a double-blinded, prospective clinical trial with well-characterized patients and a scientifically coherent study protocol are urgently required.

Hvingelby et al., [3] recently published a protocol for an open-label pilot study to gain proficiency in the technique and a double-blinded, prospective, randomized controlled trial on burst SCS therapy aimed to understand the mechanism of SCS, assess its safety, and investigate it as a treatment for gait problems. Using gait evaluations and clinical examinations, 14 patients will be evaluated, in total, at baseline, six and 12 months after SCS implantation. Two patients will be enrolled in an open-label pilot study for the first six months, while the remaining twelve will receive either a placebo or active treatment after randomization. For the following six months, the complete cohort will enter a phase of active treatment (open-label).

To our knowledge, this is the first double-blinded, randomized controlled trial with a placebo group with imaging modalities planned to explore SCS as a therapeutic alternative for PD patients with gait disturbances. This trial aims to obtain pivotal information to determine the feasibility of planning and conducting a large, multicentre trial. This study will provide information that will help us to :

- *Demonstrate the following indicators of feasibility: adherence of participants; tolerability; adverse events; rate of recruitment, consent rate and the rate of retention of participants.*
- *Estimate the standard deviation of the outcomes of burst SCS therapy to allow sample size collections for*

future trials.

- *Understand the effects of SCS on resting metabolic brain networks and cholinergic neurotransmission through 18F-FDG and 18F-FEOBV PET imaging before and after SCS treatment. This knowledge may help select the right group of patients for the trial.*
- *The imaging analysis may also divulge a subset of patients who benefit from SCS treatment. This will help us select the right population for future trials, thus avoiding unnecessary interventions.*
- *Assess the tolerability & safety of SCS treatment.*
- *Clearly define outcome measures to guide future studies.*

Interventions for PD have been dissatisfying, with significant response variability, primarily due to the heterogenicity of mechanisms of gait and postural abnormalities. However, SCS has shown promising results for these refractory symptoms. In addition, the emotional betterment of patients has also been documented [4]. Several studies have demonstrated other benefits of SCS treatment. Chronic pain decreases in patients and ameliorates PD symptoms after SCS insertion [5]. In the PD model of rats, SCS has also been found to exert neuroprotective effects [6]. Despite the compelling results of these studies, there's a need to explore, understand and elucidate the underlying mechanism of SCS in improving gait disturbances in the PD population before it can gain application in routine clinical practice.

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Relation between Frontal Pole Volumes and Cognitive Insight in Schizophrenia: Implications

*Shivangini Singh, Sujita Kumar Kar**

A significant characteristic of many mental diseases is the lack of insight. Studies show that between 40 and 80 per cent of schizophrenia (SCZ) patients exhibit insight deficiencies, making it one of the defining characteristics of the disease.

Clinical and cognitive dimensions of insight have both been studied. While cognitive insight refers to the capacity to "analyze and correct faulty ideas and misinterpretations," clinical insight mainly pertains "to the knowledge and awareness regarding the illness." While it may not be necessary to have excellent cognitive insight to have good clinical insight, other studies have found that good mental awareness somewhat depends on the clinical insight processes. And some studies have also found no correlation between cognitive understanding and clinical insight.

The two components of Beck's cognitive insight scale (BCIS), which is often used to assess mental insight, are Self-Reflectiveness (SR) and Self Certainty (SC). Self-Reflectiveness measures a person's capacity to evaluate their thought processes and consider other explanations. At the same time, Self-Certainty is the unshakable confidence in one's beliefs.

The Frontal Pole, also known as Broadman Portion 10 or FP, is the rostral-most region of the human brain and maybe the largest cytoarchitectonic area in the prefrontal cortex (PFC). Its volume has also been shown to have an inverse association with age in healthy volunteers. The frontal pole is related to the superior temporal gyrus (STG), amygdala, and anterior cingulate cortex (ACC), all of which are thought to play a role in the pathophysiology of schizophrenia. Examining the frontal pole's function in cognitive insight in schizophrenia is important, given that it is involved in self-referential activities.

FINDINGS-

There was a sizable gap in years of education and sex between Healthy Volunteers (HV) and SCZ, with SCZ being less educated and having noticeably more males. Although all individuals' MOCA scores were above 25, SCZ scores were much lower (p-0.001).

The BCIS ratings for SCZ and HV were similar, and there was no discernible difference between the groups regarding left FP volume.

In SCZ, the model showed age (=0.50; t=4.12; p=0.001) and left FP volume (=0.44; t=2.04; p=0.04) to be significant predictors of BCIS- composite score (R2=0.32; F=4.00; p=0.002). Age (=-0.33; t=-2.56; p=0.01) and ICV (=0.33; t=2.48; p=0.01) were significant predictors for BCIS-SC in the model (R2=0.22; F=2.42; p=0.03).

Years of education (=-0.49; t=-3.56; p=0.001) and sex (=-0.32; t=-2.11; p=0.04) were significant predictors of BCIS-SR in HV (R2=0.38; F=3.51; p=0.008).

There was no correlation between age, CDRS score, PANSS sub-score, SANS score, length of illness, or dose antipsychotic dose equivalent of olanzapine.

SUMMARY-

The BCIS-composite score was substantially correlated with left frontal pole volume in schizophrenia but not in healthy individuals. In patients with schizophrenia and healthy controls, there was no association between the size of the frontal pole and either age or BCIS-SR. In neither group was right frontal pole volume related to cognitive insight [1].

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Learning from "Neuropsychological and Behavioural Effects of Multisession Prefrontal tDCS and Concurrent Cognitive Remediation Training in patients with Autism Spectrum Disorder (ASD): A Double-Blind, Randomized Controlled fNIRS study"

*Kritika Chawla, Sujita Kumar Kar**

A little more than 45% of people have autism spectrum disorders. Despite having ordinary verbal and performance capabilities, people with disorders who do not have intellectual disabilities significantly struggle with social skills, including emotion recognition and social skills.

In ASD, executive functioning (EF) is compromised. It has been established that cognitive flexibility (CF) is essential for "cold" EF and leads to behavioural expression in people with ASD. (For instance, switching one's focus from one discourse to another). Cognitive flexibility deficits are associated with poor social interaction skills, which is regarded as "hot" Executive functioning (i.e., EF that involves affective processing). Global brain signalling is hampered by the excitation-inhibition (E: I) imbalance in the local neural networks supporting cognitive and affective processes; therefore, people with ASD may have trouble controlling voluntary movements.

There is proof that tDCS, which places the anode over the right supraorbital region, includes the right vmPFC and orbitofrontal cortex (OFC), and the cathode over the left dlPFC, social withdrawal, decreases irritability and hyperactivity and enhances processing speed and CF in adults with ASD. Additionally, computerized cognitive remediation training focusing on "cold" EF has been shown in numerous studies to have clinically and cognitively advantageous effects in ASD, as well as that tDCS, enhances the clinical effects of behavioural treatments and exhibits task-dependent effects on EF performance. Even though this combination was not researched in the ASD population, it is possible that tDCS could supplement traditional EF training for ASD.

AIM

The goal was to examine the positive effects of a combination of prefrontal tDCS (with the placement of anodes in the right supraorbital region and cathodes in the left dlPFC) given concurrently with computerized cognitive rehabilitation training on people with ASD [1].

FINDINGS

participant characteristics, tDCS safety, and blinding effectiveness

Participants were matched for age, sex, IQ, the severity of their initial ASD symptoms and handedness in the active and sham tDCS groups.

Short-term itching over the stimulation site was substantially more common in the active tDCS group than in the sham group (resolved within 10 minutes after each treatment session). Other adverse effects were not significantly different between participants in the active and sham groups.

tDCS effects on the primary outcome measure

Individuals in the active group experienced a significant decrease in SRS-2 total score, whereas participants in the sham group did not.

Individuals in the active group experienced a highly significant decline in (recurrent repetitive behaviour) RRB scores, whereas participants in the sham group did not.

Decrease in (social communication index) Individuals in the active group's SCI score had a highly significant

difference from participants in the sham group, who had no difference. Effects of tDCS on secondary outcomes.

The impact of TDCs on secondary outcome measures

Post hoc paired sample t-tests showed that the improvement in the Cognitive flexibility (CF) composite score was very significant in the active group and nonsignificant in the sham group.

Emotion recognition task (CANTAB ERT) was nonsignificant in both the active and sham groups.

Both the active and sham tDCS groups' improvements in the information processing efficiency (IPE) composite score were not statistically significant, according to post-hoc paired sample t-tests.

tDCS's effects on PFC and NFC

The 2x2 repeated-measures ANOVA showed that the right medial PFC and lateral PFCs did not see any alterations in resting state functional connectivity (rsFC), and the right medial PFC did.

The rise in rsFC was significant in the active tDCS group and nonsignificant in the sham tDCS group, according to post hoc paired t-tests for the proper medial PFC ROI.

After receiving active tDCS and a sham tDCS treatment, younger individuals' rsFC raw change in the right medial PFC showed more interindividual variability, according to visual assessment of individual rsFC data.

DISCUSSION

When used in conjunction with computerized cognitive remediation training for ten sessions, 1.5 mA tDCS significantly improved social communication. They decreased restricted, repetitive behaviours, leading to an increase in overall social functioning compared to sham tDCS [1].

The ability to recognize emotions more accurately was linked to this improvement.

Information processing efficiency (IPE), linked to increased CF and social communication, was optimized by tDCS but not by training alone.

Improvements in the rsFC of the right medial PFC appeared to be related to changes in information processing efficiency (IPE).

It can be concluded that the effect of tDCS with the placement of the cathode in the left dlPFC and the anode in the right supraorbital region on the "cold" EF network is task-dependent. At the same time, it is task-independent for "hot" EF network enhancement. Previous studies have shown that tDCS exhibits task-dependent effects on EF performance.

Right supraorbital area anode placement and left dlPFC cathode placement significantly improved rsFC of the right medial PFC but not the other ROIs, and the effect size was considerable. Only those who participated in the active tDCS group saw this impact.

In the active tDCS group but not in the sham tDCS group, this study discovered strong connections between information processing efficiency (IPE) and cognitive flexibility (CF) and between IPE and social communication.

IPE was linked to improved rsFC in the right medial PFC.

These results suggest that tDCS with the placement of the cathode in the left dlPFC and the anode in the right supraorbital region facilitates flexible and effective processing of social information relative to oneself within the right medial PFC, leading to improvements in clinically observable social functioning.

A prior study demonstrated that people with ASD had an elevated E: I ratio, especially in the medial PFC.

Relatedly, it was discovered that mice's social behaviour and synaptic information processing were both impaired by a more excellent E: I ratio in the medial PFC.

Therefore, it makes sense to hypothesize that the right supraorbital area anode location and left dlPFC cathode placement during tDCS would decrease the E: I ratio of the right medial PFC.

CONCLUSION

The procedure was a safe and effective treatment for adolescents and young adults with ASD, and the results showed that it might improve these individuals' general social functioning.

The improvement of the proper medial PFC's functional connectivity, a key node for flexible social information processing, is linked to this outcome, which allowed participants to process socially pertinent information more quickly in response to various social settings.

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Impact of ECT on Schizophrenia: Long-Term Relief

*Sushmita, Sujita Kumar Kar**

Schizophrenia is a split mind disorder characterized by symptoms in which the patient cannot think, feel and behave clearly. No confirmed aetiology is known for causing schizophrenia, but brain chemistry, structure, and other environmental factors play an essential role.

On one side, the treatment of choice in schizophrenia is antipsychotic drugs. On the other hand, ECT also shows a good impact or efficacy in treating schizophrenia.

Important Findings:

- *Analysis of 340 schizophrenic patients for efficacy or impact of ECT on negative symptoms shows significant improvement in 57.6% (196), no change in 15.5% (53) and deterioration in 26.7% (91) [1].*
- *Analysis of 12 patients for ECT response rate, out of 12, 11 patients' response rate was 91.7% in the phase I study. In study phase II, 7 out of 11 patients showed a 63.6% response rate after a one-year follow-up. Phase III of the study was also conducted, and after all three steps of the study, the result indicates that relapse cases were reported within one year in 4 patients out of 7 (57.1%); within 6-month relapse, cases were reported in 3 patients (42.9%); within three months relapsed cases were reported in 1 patient (14.3%) & no relapsed case was reported within one month [2].*
- *Analysis of a group of 2074 schizophrenic patients with the group of the same no of schizophrenic patients as a comparison group for an ECT impact in 1-year duration. A Group of schizophrenic patients who receive antipsychotics with ECT reduces the re-hospitalization rate compared to other groups who do not receive ECT [3].*

Summary:

Based on the above findings, we can say that ECT is effective among schizophrenic patients, but the effectiveness may vary from patient to patient. Every time in every case, we cannot be dependent on ECT.

So with the ECT, we need other supportive treatments (ex., drugs & therapies) for schizophrenic patients. So that may the patient get long-term relief.

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Efficacy of exposure therapy for the treatment of post-traumatic stress disorder in the adolescent

*Swati Rai, Sudha Mishra**

Post-traumatic stress disorder (PTSD) is a mental health condition triggered by a terrifying event, whether experiencing it or witnessing it. The significant range of symptoms linked with PTSD is poor concentration, confusion, emotional disability like depression, physical uneasiness, nausea, sleepiness and behavioural suspicion reactions. PTSD patients may experience constant or exaggerated negative thoughts together with horror, anger, shame and guilt.

Exposure therapy (ET) is one of the used techniques to treat patients with PTSD that can reduce flashbacks and nightmares. Exposure therapy lets the patients face stressful situations and memories until they are better at handling or coping with the situation.

Important findings:

- *Analysis of 39 veterans cases with chronic PTSD were randomly allocated to sessions of 90 minutes (n=19) or 60-minute (n=20) for exposure. Sixty-minute sessions were found to be least effective than 90-minute sessions in reducing PTSD symptoms, as the upper bound of the 95% confidence interval for the difference between conditions in the PTSD Symptom in Scale-Interview (post-treatment: 6.00; follow-up: 6.77) was below the predefined noninferiority margin (7.00) [1].*
- *In an analysis of 4 RCTs that include 431 participants, 50% are receiving CPT, and others are receiving prolonged exposure therapy; in both, exposure therapy accomplished meaningful results in the improvement of symptoms in PTSD [2].*

Summary :

- *based on the findings, we can say that exposure therapy can bring out significant effects on PTSD patients for the reduction in signs or symptoms and support its implication in treating PTSD. There is a need for improvement in remaining PTSD treatments and for developing and testing evidence-based practice in both trauma and non-trauma conditions.*

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Buerge's Allen Exercise improves circulation of the lower limb in a patient with a diabetic foot ulcer.

*Chetna Mishra, Sudha Mishra**

A diabetic foot ulcer is a skin sore with total thickness and skin loss on foot due to neuropathic and vascular complications in patients with type 1 or type two diabetes mellitus. Some medical genius at that time developed a postural treatment to improve circulation in the lower extremities. Buerger's exercises, or Buerger-Allen's exercises, were proposed by Leo Buerger and modified by Arthur Allen. Allen had frequently emphasized the value of these exercises, and many medical experts considered them crucial adjuvant treatment and postoperative care for circulatory disturbances in the extremities [1].

With 77 million patients, India has the second-highest number of patients after China. In India, the number of diabetic foot patients is increasing in both urban and rural settings, with 85% of amputations preceded by foot ulcers. Diabetic foot ulcers were found in 4.54% of patients newly diagnosed with type 2 diabetes mellitus in India; 46.1% had neuropathic, 19.7% had ischemic, and 34.2% had neuro ischemic foot ulcers [2].

Up to 25% of patients with diabetes with impaired sensation in their feet may develop a foot ulcer in their lifetime. 1 in 7 people with diabetes will develop a foot ulcer [3].

According to Pengzi Zhang, Jing Lu, and Yali Jing, global diabetic foot ulcer prevalence was 6.3% which was higher in males (4.5%) than in females (3.5%), and higher in type 2 diabetic patients (6.4%) than in type 1 diabetics (5.5%,) [4].

People with diabetes develop foot ulcers because of neuropathy, vascular insufficiency, and impaired wound healing. Foot ulcers preceded nearly 90% of diabetes-related lower limb amputations. In addition, conventional treatments such as operation and infection control to cure diabetic foot ulcers are often ineffective.

To promote Lower Extremity Perfusion whereby promoting the wound healing process and reducing Peripheral Neuropathy Symptoms among Diabetes Mellitus patients [5].

Technique to improve circulation in the lower limb:

Spinal cord stimulation is quite effective in relieving symptoms caused by claudication and increasing circulation through vasodilation [6].

Application of Royal Jelly by inducing vasorelaxation Royal jelly (RJ) has a variety of reported biological activities, including vasorelaxation and blood pressure-lowering effects [7].

Summary:

Most of the studies reported a positive effect of Buerger's exercises that can help in improving Peripheral circulation as well as help to increase the wound healing process among patients with Diabetes mellitus.

Some literature indicates that many diabetic patients had foot ulcers before their lower extremities were amputated. Hence, providing other diabetic care with Buerger's exercises would be beneficial for diabetic patients and also helps to reduce the burden on the health care system.

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Importance of Early Detection of Atherosclerosis

Victoria Angela Fernandez, Sudha Mishra*

According to data from the WHO and CDC, atherosclerosis is the leading cause of death orldwide. Diagnosing Atherosclerosis at an early stage is essential to decrease the morbidity and mortality rates of CVDs. As technological changes have evolved, many diagnostic methods can early diagnose the presence of Atherosclerosis, like IVU, miRNA, Carotid Intima-Media thickness, Arterial wall thickness. Among these, High-Spatial- Temporal-Resolution Invasive Angiography is the Gold standard and cost-effective diagnosis of Atherosclerosis.

Introduction:

Atherosclerosis is the leading cause of death all around the world. As atherosclerosis formation is a normal phenomenon of the body in which there is the formation of fatty streaks or plaques in the walls of arteries causing narrowing or obstruction in the blood flow, which can lead to severe cardiovascular disorders without showing any specific symptoms. While working in the cardiac ward, I have encountered many patients who do not have any past medical history of hypertension or diabetes but suffer from sudden cardiac arrest. After their diagnosis, it was found that they have >90% of blockage in one or more arteries.

Incidence and Prevalence:

According to WHO, "Cardiovascular diseases (CVDs) are the leading cause of death globally, taking an estimated 17.9 million lives each year." [1].

According to CDC, "About 697,000 people in the United States died from heart disease in 2020—that's 1 in every five deaths" [2].

Importance of Early Diagnosis:

A study by K.S Mathur et al. on atherosclerosis In India showed that atherosclerosis streaks start to form at a minimum age of 2.5 years and gradually increase in age [3].

As the world is changing and people are following a secondary lifestyle, the incidence of atherosclerosis formation is increasing. So it's essential to make an early diagnosis of Atherosclerosis to prevent mortality and morbidity related to cardiac disorders.

New Techniques:

According to an article published in the International Journal of molecular sciences on the New Progress of diagnosis of atherosclerosis. They explained that High-Spatial-Temporal Resolution Invasive Angiography is the gold standard and cost-effective method of early detection of the formation of atherosclerosis. Computed Tomography Cardiac Angiography (CCTA) is found to be very effective. According to the survey conducted, they found As compared to Intravascular Ultrasound, CCTA is more cost-effective and successful in early diagnosis [4].

The microRNA (miRNA), at the gene level, can help in the early detection of Cardiovascular disease as it plays an essential role in the lipid uptake, adhesion, proliferation and production of inflammatory mediators. It can be detected with the circulating blood test [4].

Carotid Intima-Media Thickness is also a method of assessing the Intima circumference of the arteries at an early age. It is related to age and high risk [5].

Arterial Wall Thickness is a method of analyzing the elasticity of the arterial walls using an echo tracking system by radiofrequency, which determines the diameter of the arteries [5].

Summary:

Thus, atherosclerosis can be diagnosed early by using different cost-effective and safe methods that can help reduce the morbidity and mortality of cardiovascular disorders worldwide. Currently, Blood markers, IVU, CCTA etc., are used, but New advancements in the medical field are getting new ways of detecting atherosclerosis in the early stage and treating it at the right time.

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Addressing The Family Burden Among Patients With Somatoform Disorders

*Rimmi, Sudha Mishra**

Patients with somatoform disorders experience discomfort, and their family members go through a degree of burden in their day-to-day life. Somatoform disorder patients proceed with various diagnostic investigations and are often misdiagnosed as having physical sickness, which leads to a lot of financial expenditure and an additional burden on the family members, which has been overlooked that needs to be given attention. It is a significant aspect that needs to be taken care of while providing the patient with the holistic care.

Patients with somatoform disorders experience various levels of discomfort, and their family members go through a degree of burden in their daily lives. Patients with somatoform disorder proceed with various diagnostic investigations and are pushed to multiple medical care facilities and are often misdiagnosed as having physical sickness; it most of the time leads to lots of expensive diagnostic tests that are to be done in a various cyclic manner new doctor ask the caregiver to get new diagnostic tests done for the patients [1]. The chronic nature of this illness makes the patient's daily functions challenging to perform [2]. It may also limit their daily activities, which they used to do earlier, it leads to extra burden on the caregiver that is to assist them in their activities of daily living in some cases and rest of the issues, it becomes stressful for a family in both economic and emotional aspect, as it is not easy to consider the physical symptoms of illness that comes up in somatoform disorder to be a psychiatric symptom. In our society, the stigmatization of psychiatric illness is far more than physical illness. After many diagnostic evaluations, mostly of physical findings, patients were referred to a psychiatrist [3]. It is challenging for a family to know about a fellow member's psychiatric illness, and with very minimal knowledge about the course of the disease, most of the time, families suffer a lot. It is very much essential to explore further the burdens faced by family members of patients with somatoform disorder to gain insight into their problems and to improve the treatment outcome as a whole; holistic care isn't provided without familial involvement. Most of the time, healthcare workers ignores and skips the basic need to educate the family member about the care of the patient at admission and homecare at the time of discharge that is to be followed for the betterment of the patient, which automatically increases the stress level of family members in order to how to keep the patient at home at ease without a hospital setup. A few previously done Indian studies had found that patients with somatoform disorder suffer a degree of disability and caregiver burden comparable to severe mental illness. Somatoform disorder in one family member leads to disruption of family interaction at some point, and it also affects the physical health of other members of the family [4]. Previously done studies have shown that the level of psychosocial disabilities in patients suffering from somatoform disorders was similar to those seen in other mental disorders such as depression, anxiety disorders, and affective disorders [5].

Summary:

Based on various studies, we have concluded that patients with somatoform disorders have experienced significant disabilities, i.e. in terms of physical, emotional, psychological, social and spiritual. Their caregivers and family members included experiencing various levels of burden comparable to severe mental illness. Hence, the difficulties faced by these individuals need to be addressed effectively to improve the treatment outcome, along with other strategies during the hospital stay/ hospital visit of the patient by psycho-educating them and by providing home-based care instructions to patients caregivers and family members for

the holistic care of the patient with somatoform disorder.

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Changing Face of Diabetes Prediction & Prevention: Through Artificial Intelligence

*Zoya Shakir, Wahid Ali**

High time to embrace more scientifically advanced routes to classify "Diabetes Diagnosis" and how to deal with diabetic patients. This is a wake-up call to recognize better resources, scientific models, timelines, and knowledge that march forward, and we should be quick to acknowledge this fact.

Clinicians use traditional diagnostic criteria of diabetes that are being fixed in stone. Instead, the time has changed to opt for more advanced approaches. Artificial Intelligence (AI), which uses machine learning, is a rapidly emerging field, and its application offers promise in Diabetes care [1]. This article aims to comprehend better how AI-based Computing Programs can be used to treat persons with diabetes, their clinicians, family, and caregivers.

AI is the simulation of human intelligence processes by machines. The purpose of AI is to make inferences based on a large amount of data. The mainstream technologies that brought a boom in AI in 2021 are Machine learning (ML) and Deep learning [2]. Machine learning automates analytical model building. It involves methods from neural networks (i.e. machine learning, which is inspired by human brain functioning. It's a computing system composed of interconnected units like neurons that processes information by reacting to external inputs) to find hidden insights in data without being explicitly programmed where to look or what to conclude [3].

In the case of diabetes, several AI-/ML – based medical devices regarding automatic retinal screening, clinical diagnosis support, and patient self-management tool have already been approved by the US Food and Drug Administration [2]. Many other advances will shower improvements in the accuracy of disease prediction models, while traditional methods use only statistical methods so far. Typical features of the current classification of Diabetes Mellitus (DM) includes patient with type 1 diabetes who have insulin resistance while patients with type 2 diabetes mellitus possess T-Cell mediated autoimmunity. Furthermore, it's essential to broaden our view of the causes of diabetes and its complications to incorporate standard pathophysiologic processes beyond "just metabolic" [4]. So, instead of just being stuck with these conventional methods of classification, we should excel in our diagnosis to better bio-mechanical tools to design algorithms to support predictive models for the risk of developing diabetes or its consequent complications. Digital therapeutics has proven to be a helpful intervention for lifestyle therapy in the monitoring and managing of diabetes. AI allows continuous and self-remote tracking of the patient's symptoms and biomarkers [1].

Hence, AI applications have the potential to transform diabetes care, help people to achieve better glucose control, and reduce diabetes comorbidities and other complications [5]. In the future, AI will establish a paradigm shift in diabetes care from conventional management strategies to designing targeted data-driven precision care.

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Can Below Knee Casts be Effective for Clubfoot Management in Walking Age Children? A Prospective Cohort Study: Implications

Mohd. Hassan Shakeel, Suresh Chand

To start with writing this commentary, the reader must have gone through this study by Agnihotri et al.[1]. First of all, I would like to mention that author used excellent methodology, had clear ideas and did well-structured research. The writing of the paper is also very concise, clear and comprehensive, and the conclusion is specific.

Although orthopaedics frequently use Below knee casting clinically in walking patients, there is yet to be available information regarding the superiority of the casting technique for clubfoot treatment. The only available study is by Manipuri SN et al. [2], which concludes a higher failure rate with below-knee casting in conjunction with Ponseti casting in neonates; thus, it does not recommend its use.

This study is a prospective interventional study, but the author did not mention the duration of the study. With this large number of patients and short term, the study can be a randomized control trial with lesser biases and more randomization. Also, previously intervened children can be more resistant to treatment and should also be randomized or should not include in the study for better clinically unbiased results.

The purpose of using the below-knee cast is ambulation of the patient and mobilization of the knee, but the author also did not mention whether the patient with below-knee cast was advised to remain bed-bound or allowed to walk and if only they are non-ambulatory, the result can be compared to above knee casting group.

With below-knee casting, there is an increased chance of wear and tear of the cast as compared to the Above-knee cast [3]. The condition of the cast should also be noted at the follow-up visit and, if possible, should be reinforced with hard fibreglass casting tape for better cast tolerance, durability and patient satisfaction3.

Biweekly is also a vague term and sometimes confusing; it could also mean twice in one week. The fortnight will be a better word.

In the end, this paper argues with the notion of putting below knee cast with the Ponseti technique, whether it may be an Orthopedician or concerned parents and put a full stop to all queries related to it. It was a much-awaited paper and solved the dilemma of both clinician and parents.

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Worldwide, a doctor's educational basis is their undergraduate medical education. Approximately 90,825 MBBS seats are available at 605 Indian medical institutions, according to website updates from the National Medical Commission (NMC) as of March 7 2022. (National Medical Commission, 2022). After finishing their MBBS course, most MBBS students intend to continue higher study (post-graduation and super-specialization). Many MBBS students study overseas to receive in-depth training in a particular discipline. Other recent medical school grads have a propensity towards academic medicine and research. These tendencies and interests call for a research-oriented mindset because these medical areas depend heavily on research. However, in the majority of the nation's medical institutions, medical graduates lack research understanding and direction. This research bulletin will encourage undergraduate as well as postgraduate medical/dental/paramedical students to

- *Develop / Enhance their understanding of research*
- *Develop / Enhance the scientific writing skills*
- *Develop / Enhance the skills to critically review a scientific article*
- *Facilitate the editorial skills*
- *Develop leadership qualities in the field of medical research*

Additionally, this process will facilitate mentoring to the students inclined towards research.

This research bulletin will be published online every four months. It will be freely available. There will not be any submission or publication fees.

What will this research bulletin contain?

This research bulletin will contain small articles related to the latest medical science developments, and impactful research works with significant practice implications. The publication will also include articles about researchers / Alumni of KGMU who contributed significantly to medical teaching and research.

Types of articles

Type of article	*Structure of the article*	*Word limits*	*References*
1. Commentary	*Abstract not required.* *It should be about published impactful research in an indexed reputed journal of the field.* *It should contain the practice implications of the research in 3 to 5 bullet points.*	*500*	*5*
2. Innovations	*Abstract not required.* *It should be any innovation in medical science with some practice implications.* *It should have a reasonable scientific basis.*	*700*	*5*
3. Georgian Biopic	*Abstract not required.* *It is about a brief biography of a Georgian Alumni who contributed significantly to teaching & research.*	*500*	*None*

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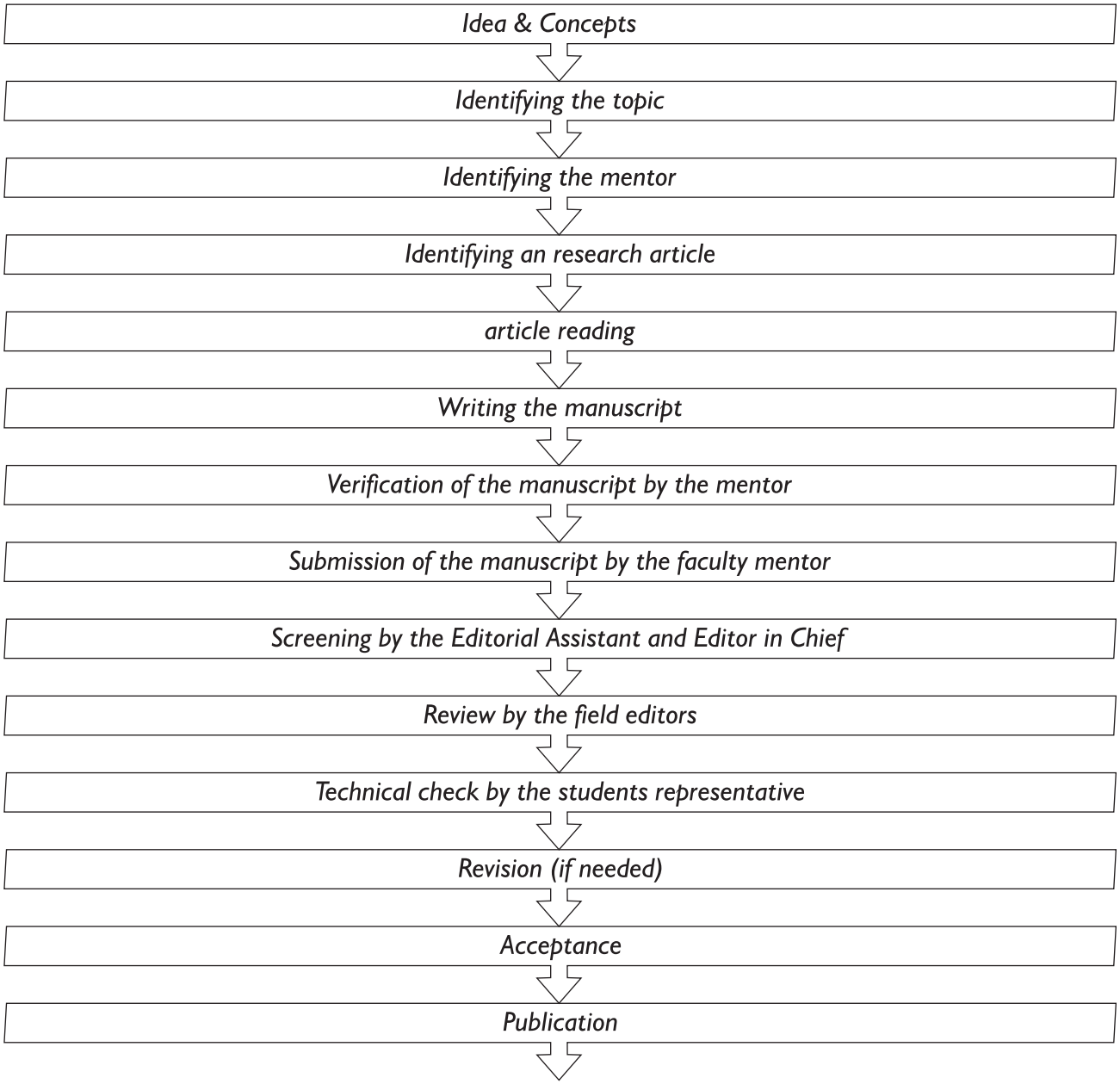

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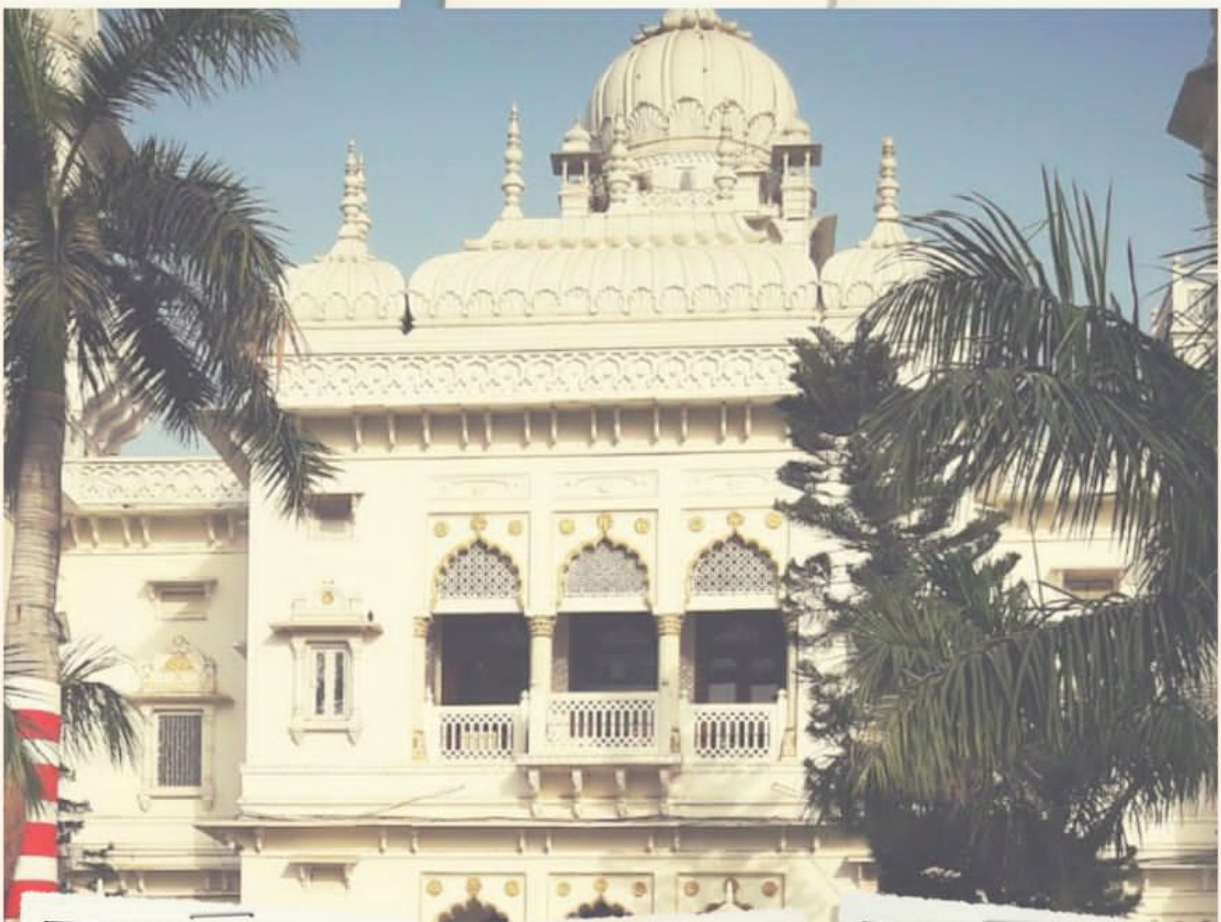

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