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Issue I

MEDICAL RESEARCH BULLETIN

Georgian Research Ecosystem
Innovate and Create



Volume II

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***Medical Research Bulletin :
Georgian Research Ecosystem
Innovate and Create***



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Lucknow, Uttar Pradesh*

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14 July, 2023

Message

I am glad to know that King George's Medical University is going to release the 2nd Edition of '**Medical Research Bulletin-Georgian Research Ecosystem-Innovate and Create.**'

Sharing knowledge and fostering collaboration within the medical community is truly commendable. By making your research accessible through this bulletin, you are promoting the exchange of ideas, facilitating discussions, and encouraging further investigations into critical medical issues. I hope that this initiative will undoubtedly contribute to advancing medical knowledge and improving patient care.

I extend my best wishes on the release of the bulletin.

Anandiben Patel
(**Anandiben Patel**)

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Finerenone-A Novel Mineralocorticoid receptor antagonist for reduction of the progression of CKD and cardiovascular events in patients with CKD and T2DM- a review of the FIDELIO-DKD trial

Umesh Tripathi, Akshyaya Pradhan*

Many individuals diagnosed with type 2 diabetes are prone to developing chronic kidney disease in the current global situation. This condition, known as diabetic kidney disease, is characterized by a progressive deterioration of renal health and also has a negative impact on cardiovascular health. It has been observed that controlling high blood sugar levels and hypertension can effectively slow down the progression of this disease. To achieve this, various pharmacological agents, such as RAAS inhibitors, ARBs, and more recently, SGLT2 inhibitors, have been utilized. Despite the use of these agents, there is still a risk of diabetic kidney disease progressing, necessitating the need for newer therapies.

There is growing evidence supporting the role of overactive mineralocorticoid receptors in cardiorenal diseases, including chronic kidney disease and diabetes. These receptors contribute to inflammation and fibrosis, leading to progressive dysfunction in the kidneys and cardiovascular system. A meta-analysis demonstrated a 31% reduction in urinary protein or albumin excretion when patients with chronic kidney disease were treated with a steroidal mineralocorticoid receptor antagonist. However, there is still a lack of data regarding the impact of these treatments on tangible clinical outcomes.

Finerenone

The development of a novel non-steroidal selective MRA Finerenone with enhanced anti-proliferative and antifibrotic effects.[1] In CKD patients receiving a RAS blocker, finerenone has been found to lower the urinary albumin-to-creatinine ratio while impacting serum potassium levels less than spironolactone.

The Trial

The FIDELIO-DKD trial aimed to determine if Finerenone could slow down the progression of chronic kidney disease (CKD) and reduce cardiovascular problems in patients with advanced CKD and type 2 diabetes [2]. The trial involved randomly assigning eligible patients to receive either Finerenone or a placebo. The primary outcome measured was a combination of kidney failure, a significant decrease in kidney function, or death from kidney-related causes. The secondary outcome assessed included death from cardiovascular causes, heart attack, stroke, or hospitalization for heart failure. The trial showed that Finerenone resulted in a lower incidence of kidney failure and reduced the risk of cardiovascular events compared to the placebo. The drug also reduced the urinary albumin-to-creatinine ratio and had modest effects on blood pressure. Adverse events were similar between the groups. However, the trial had limitations, such as excluding non-diabetic and non-albuminuric CKD patients, which limits the generalizability of the findings. The ongoing FIGARO-DKD trial will provide further insight into the effectiveness and safety of Finerenone in patients with less advanced CKD and type 2 diabetes [3, 4].

Conclusion

Finerenone is poised to demonstrate itself as a superior option compared to current mineralocorticoid receptor antagonists (MRAs), particularly in individuals with diabetic kidney disease. It carries a reduced risk of hyperkalaemia and exhibits a heightened ability to slow down the advancement of renal dysfunction. Moreover, it manifests diminished cardiovascular effects in patients with advanced chronic kidney disease (CKD).

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Bundling Up for Success: Reducing Catheter Associated Urinary Tract Infections in the Paediatric Intensive Care Unit

Anju Shukla, Anugrah Charan*

Catheter-associated urinary tract infection (CAUTI) is a prevalent medical issue among hospitalized children. According to the global burden of disease study in 2019, the incidence of CAUTI in children worldwide ranges from 13.7% to 23.5%. Similarly, in India, the National Healthcare Safety Network and healthcare-associated infection surveillance reported an incidence rate of CAUTI between 8.3% and 12.1% among paediatric patients [1-3]. The use of catheters accounts for over 80% of all acquired urinary tract infections. The primary culprits for CAUTI are typically E. coli, Klebsiella, Staphylococci, Candida parasitosis, and Candida tropicalis [1-3].

In their study published in the Clinical Nurse Specialist journal in 2016, Düzkeya DS, Bozkurt G, Uysal G, and Yakut T examined the effects of bundles on catheter-associated urinary tract infections in the pediatric intensive care unit. The objective of this research study was to assess the rates of catheter-associated urinary tract infection (CAUTI) over a period of two years in a Pediatric Intensive Care Unit (PICU) where a CAUTI prevention bundle was implemented. Children affected by CAUTI experience various difficulties in their daily activities and exhibit symptoms such as frequent urination, urgency, bedwetting, dribbling, and foul-smelling urine. Complications in children due to urinary tract infections may include irritability, fever, abdominal pain, loss of appetite, blood in urine, and vomiting. Consequently, the researchers recognized the need to effectively implement the CAUTI prevention bundle in order to enhance healthcare quality and minimize the risk of infection among children.

The study was conducted for a duration of two years, from July 2013 to July 2015, involving 390 patients in the PICU of Istanbul Faculty of Medicine, Turkey. Patients between the ages of one month and 18 years, who stayed in the PICU for more than 48 hours and showed no symptoms of UTI, were included in the study.

The research consisted of two phases:

Phase 1: PICU nurses were briefed about the research study and gave their consent to participate. They underwent a two-hour training session on the CAUTI prevention bundle.

Phase 2: Demographic data forms were completed for each patient within 24 hours, and the patients were provided with daily care using the CAUTI prevention bundle by nurses. Subsequently, the infection status was evaluated.

Findings & Implications:

Prior to the implementation of the CAUTI prevention bundle, the majority of samples, 95.3% (272 patients), were found to be sterile, while the remaining 4.7% (18 patients) were infected. Following the implementation of the CAUTI prevention bundle, the majority of samples, 97.7% (382 patients), were found to be sterile, with only 2.3% (9 patients) remaining infected [1]. It is important to note that the results of this study cannot be generalized as they were obtained from a single ICU.

CAUTI has a significant impact on morbidity, mortality, and healthcare costs, and clinical nurses play a crucial role in reducing CAUTI rates through proper urinary catheter care [1, 3]. Nurses should be encouraged to read research articles and journals and engage in nursing research. In-service education can be provided to all nursing personnel to enhance their knowledge and skills.

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Plastic Surgery: Blurring the Boundaries of Reality and Science Fiction

Mehul Saxena, Shubhajeet Roy, Harsha Vardhan*

It was the year 1997. "Face/Off" a motion picture, released by Paramount, was on its way to become a blockbuster. It depicted the rivalry between an FBI special agent played by Nicolas Cage and a homicidal sociopath played by John Travolta, two of the biggest stars of the time. In the movie, they undergo 'facial transplantation', with their faces being exchanged, leading to one assuming the identity of the other. It earned rave reviews and was awarded for scriptwriting in the science fiction genre [1]. Little did the world know, this science fiction would be a reality by the end of the next decade. As the scriptwriters were imagining the script of this movie in Hollywood California, about 2500 miles away, across the American continent, doctors at the Cleveland clinic, Ohio, USA, were working on face transplantation. Groundwork for the first face transplant was being laid with cadaveric dissections, refinements in immunosuppression and deliberating ethical considerations. Ethical approval was finally received in 2004 and in 2008, the first face transplant was performed in the world. This was reported in The Lancet journal in 2009 [2].

The first face transplant was performed in a 45-year-old female after a post gunshot deformity of the face with multiple failed attempts at facial reconstruction. A composite allograft consisting of bones, soft tissue, facial nerve and parotid gland was transplanted from an age, gender and racially matched brain-dead donor. The procedure was performed on 8th December 2008. A team of eight surgeons, divided themselves into two teams and performed the procedure. The procedure lasted 22 hours. This involved disconnecting and connecting on the patient, the bones, muscles, nerves, and the blood vessels. The patient was started on immunosuppressive therapy, the risks of which, the patient was already explained about. In addition to medical care the patient under psychological care constantly. The recovery was uneventful, with the patient going back to feeding, something she had been unable to do since her injury. She was also happy with the cosmetic appearance of her new face, with this surgery being nothing short of a miracle.

Plastic surgery has been at the forefront of the transplant revolution. The first attempts at transplant were performed by plastic surgeons. In-fact, Dr Joseph Murray, the only plastic surgeon to win the Nobel prize, received it for performing the first renal transplantation in the world [3]. Limb transplantation was first performed in the early 90s in France, with the world catching up soon and almost 200 being performed so far [4]. Hand transplants have been performed in India as well, with the first being performed at the Amrita Institute of Medical Science, Kochi. Around 20 upper limb transplants have been performed in India so far in multiple centres across the country. Face transplant is a much riskier procedure, done with much lesser frequency. The mortality in face transplants has been also higher than limb transplants. For this multitude of reasons, face transplant is yet to be performed in India.

Unlike solid organs, composite tissue transplantation is not a life-threatening indication. It is however a life altering one. Even after being explained in detail, regarding the risks of undergoing this

sort of surgery, the patients agree, as the alternative is to live a life dependent upon others for basic activities of eating and maintaining hygiene.

We are at a precipice of a scientific revolution. The only pre-requisite is the immunosuppressive therapy. The transplant program will become much more successful if the immunosuppressive therapy becomes safer. The need of the hour is to improve the awareness regarding the transplant program, informing the population regarding the need, possibilities, and the advantages of a transplant program.

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Revitalizing the Mind: Exploring Cognitive Remediation for Schizophrenia

Huma Fatima, Sujita Kumar Kar*

Recovery is about progression, not perfection!

-Unknown

Cognitive deficits are one of the core symptoms of schizophrenia. Vita et al. (2021), in their paper titled “Effectiveness, Core Elements, and Moderators of Response of Cognitive Remediation for Schizophrenia- A Systematic Review and Meta-analysis of Randomized Clinical Trials” discussed the important determinants of cognition in Schizophrenia and Relevance of Cognitive Remediation (CR) in schizophrenia (1). In this systematic review and meta-analysis, 194 reports from 130 studies published between 2011 to 2020 were included, which covered 8851 participants with schizophrenia who received CR.

Main outcomes and measures in this study were changes in global cognition and overall functioning from baseline to after treatment, subsequently investigated through meta regressions, subgroup, and sensitivity analyses based on prespecified hypotheses, i.e., to identify potential moderators of response associated with treatment modality and patient characteristics.

They found a small to moderate effect of CR on primary outcomes, i.e., global cognition and global functioning. (Global cognition: $d, 0.29$ [95% CI, 0.24-0.34]; $P < .001$; 135 comparisons; global functioning: $d, 0.22$ [95% CI, 0.16-0.29]; $P < .001$; 95 comparisons)

Along with the primary intervention, moderators viz. active and trained therapists, structured development of cognitive strategies lead to more effectiveness for CR; additionally, in the part of subjects, fewer years of education, lower premorbid IQ, higher baseline symptom severity were associated with more significant improvements on primary outcomes (1).

Implications

- *Another recent meta-analysis by Cella et al. (2020) reported consistent effectiveness of CR interventions among inpatients, who usually present a more severe clinical condition. (2). It showed a substantial relationship between premorbid IQ, education, and symptom severity, demonstrating that clinically compromised patients can still be considered for CR. The fact that age and duration of illness did not emerge as important factors suggest that CR might be made available to all participants, independent of their age and medical history. (1)*
- *When CR combined with Structured Rehabilitation Therapy (SRT), Buonocore et al. maintained that effectiveness in cognitive and functional domains is still preserved ten years after the end of the treatment. (3) It is also true for verbal memory, one of the skills most susceptible to cognitive decline. (4)*
- *These results provide a strong basis for routinely including CR in national and international treatment recommendations. It is an evidence-based therapy that could replace an optional intervention aimed at a selected group of people with a component of standard care. Widespread use of CR could be a game-changer for attaining the patient's individual recovery goals because pharmacological treatment has limited*

effects on cognitive deficits, and clinical remission does not always lead to functional recovery. Notably, combining CR with structured psychiatric rehabilitation improves the transfer of cognitive improvements into real-world contexts. (5)

To summarize, the efficacy of CR on both cognitive and functional outcomes in individuals diagnosed with schizophrenia has been confirmed by several research. It is recommended widely to use this evidence-based intervention as a standard treatment. An active and trained therapist, structured development of cognitive strategies, and integration with rehabilitation are crucial ingredients of efficacy. Optimal candidates for this intervention were found to be those with fewer years of education, lower premorbid IQ, and higher baseline symptom severity. It is imperative that cognitive remediation be utilized for all patients, including those most severely affected. Additionally, in resource-scarce settings (like developing and underdeveloped countries), the gap between demand for CR and the availability of resources and manpower is high. In such situations, online cognitive remediation, group cognitive remediation and home-based CR (by training a caregiver) may be beneficial.

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Powerful Sparks: Unleashing the Efficacy of Neurostimulation in Mental Disorders

Huma Fatima, Sujita Kumar Kar*

The brain is truly wonderful and complex, seamlessly and apparently effortlessly able to attend to multiple tasks at the same time. However, the human brain, via religion or science, art or technology, has yet to figure itself out.

*John S. Allen (from *The Lives of the Brain*, 2009)*

Non-Invasive Brain Stimulation (NIBS) is very relevant for mental disorders. Hyde et al. (2022), in their paper titled "Efficacy of neurostimulation across mental disorders: a systematic review and meta-analysis of 208 randomised controlled trials", discussed the Transcranial magnetic stimulation (TMS) and transcranial Direct Current Stimulation (tDCS), two types of NIBS (1). In this systematic review and meta-analysis, they conducted a series of random effects meta-analyses based on 208 RCTs to evaluate the effectiveness of NIBS compared to sham for core symptoms and cognitive functioning across a wide range of mental illnesses.

Change in core symptom severity in each mental disorder was the primary outcome. Secondary outcomes were score changes in standard cognitive functioning tasks which included modifications in the intensity of the main symptoms and improvements in cognitive functions.

Implications:

- *NIBS proved to be an effective intervention for various psychiatric illnesses. The bilateral DLPFC or unilateral left (L) or right (R) dorsolateral prefrontal cortex (DLPFC) was the most frequently stimulated TMS/tDCS location, with 10–20 TMS/tDCS sessions typically the most efficient for lowering symptoms (1).*

Although labour-intensive, patients have shown great safety and tolerance towards neuromodulation. Antipsychotic medication unquestionably reduces overall and positive symptoms, but electroconvulsive therapy remains the preferred treatment for catatonia associated with schizophrenia, mood disorders, and non-psychiatric illnesses. The use of TMS/tDCS, along with ECT, medication, and psychotherapy, is facilitated by its low-risk nature and tolerability. These methods have emerged as potential treatments for negative symptoms and auditory hallucinations resistant to medication (2).

- *Certain psychological disturbances and psychiatric disorders can benefit greatly from using brain stimulation therapies as biologically based treatment modalities. Together with various forms of psychotherapy and pharmacotherapy, they have been successfully implemented in the mental health field. These therapies show promise for treating some mental diseases that do not respond to other treatments while being less commonly utilised than medicine and psychotherapy. These have included dementia, Alzheimer's disease, posttraumatic stress disorder, anxiety disorders, and depression (3).*
- *The most well-known method for treating brain diseases is transcranial magnetic stimulation (TMS), and recurrent TMS is a recognised treatment for depression that has not responded to medicine. The electrical stimulation approaches have the advantage of reduced cost, portability, applicability at home, and ease of combining with training or rehabilitation, despite*

evidence that the clinical efficacy of the other stimulation modalities is more restricted. To maximise the clinical benefits of neuromodulation, additional research is required (4).

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Unlocking the Enigma: Unveiling the Connection between Neurological Soft Signs and Schizophrenia ***Saalya Chak, Sujita Kumar Kar****

In a recent review Tsapakis et al. (2023) discussed about the neurological soft signs (with reference to different variables like antipsychotic medication, neurocognition, brain imaging) in schizophrenia [1]. The authors also described these measures with reference to first-degree relatives of schizophrenia and healthy controls¹. The highlights of this review are:

- 1. Neurological soft signs (NSS) suggest abnormal neurodevelopment and neural connectivity.*
- 2. NSS could serve as an objective measure for assessing serious psychiatric disorders in various stages.*
- 3. NSS are independent of antipsychotic treatment and are a trait symptom.*
- 4. Possible structural substrates of NSS are somato-motor and somatosensory regions, spatial orientation, and visual processing areas, cerebellum, and basal ganglia.*
- 5. NSS may help identify individuals at risk of developing schizophrenia later in life and may not be unique to schizophrenia but extend across the schizotypy continuum.*

Psychiatric comorbidities such bipolar illness, depression, anxiety disorder and obsessive-compulsive disorder have not been completely ruled out in the studies cited by Tsapakis et al. While the studies included, acknowledges the fact that neurological soft signs play a significant role in schizophrenia, it is well known that these psychiatric conditions can also significantly impact the grading of neurological soft signs. Additionally, a study showed that bipolar disorder is marked by a significant number of neurological soft symptoms, which is only slightly less than schizophrenia [2]. Both illnesses share increased neurological soft symptoms as a common trait. Neurological soft signs may be impacted by other severe illnesses like tuberculosis and meningitis, medicine use (for any prior chronic illness), neurological conditions like epilepsy, and migraine. The impact of a patient with schizophrenia having previously experienced psychiatric conditions like depression on the assessment of neurological soft signals has not been evaluated. Future research on schizophrenia and neurological soft indicators must also take into account the length of the condition, its mode of onset (acute or chronic), and its severity. Due to the lack of a strong correlation between antipsychotic medication and neurological soft signs, neurological soft signs have traditionally been viewed as independent of illness stage and medication. However, a study found that the severity of neurological soft signs was significantly higher in non-remitters than remitters, which may establish a link [3]. Since schizophrenia is a persistent mental condition, there is no evaluation of neurological soft symptoms in various stages of the illness and its relapsing episodes in the review.

Implications

It is important to understand whether

- a. Neurological soft sign is a state factor or trait factor*
- b. Family history (genetics) of any psychiatric disorder other schizophrenia influence the*

presence of neurological soft signs in patients with schizophrenia

- c. *Neurological soft signs improve with neuromodulation and antipsychotic treatment in schizophrenia*
- d. *Symptom severity of schizophrenia in any way related to the neurological soft signs*
- e. *Any specific symptom of schizophrenia (cognitive deficits or positive symptoms like delusion or hallucination) is associated with neurological soft signs*

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Effect of periodontal therapy on inflammatory biomarkers in patients with metabolic syndrome: a randomized controlled clinical trial

Pushpendra Singh, Saumyendra Vikram Singh*

The metabolic syndrome (MetS) is a combination of cardiovascular risk factors that includes dyslipidemia, obesity, hypertension, elevated glucose, and prothrombic and proinflammatory states, all of which can lead to atherogenesis due to inflammatory processes. Recent evidence suggests that there is an association between periodontitis and atherosclerotic vascular disease, as well as metabolic syndrome. The long-term, low-grade state of systemic inflammation accompanying both periodontitis and metabolic syndrome may be the underlying factor linking these conditions with an increased risk of atherosclerosis. The authors conducted a one-year study to determine whether lowering systemic inflammation can reduce the risk of cardiovascular disease (CVD) by eliminating periodontitis in patients with MetS. The authors selected patients with a diagnosis of MetS who were attending for treatment to reduce CVD risk based on inclusion and exclusion criteria. After educating them and signing the consent form, they were divided into an experimental group and a control group, with both groups having 60 subjects each [1].

Patients in the experimental group received supragingival and subgingival scaling, root planning, crown polishing and a course of metronidazole and amoxicillin, while the patients in the control group received supragingival scaling, crown polishing and two placebo tablets. Blood samples were collected after the treatment to measure biochemical markers, including high sensitive-CRP (C-reactive protein), serum lipoproteins, cholesterol and total leukocytes count (TLC) at baseline and 9 months. The baseline characteristics of both groups were similar [1].

The results showed a significant reduction in serum CRP and improvement in periodontal inflammation in the experimental group compared to the control group. Since no significant changes in habits or lifestyle were observed during the study, this indicated an improvement in the CRP values may be due to the reduction of periodontal inflammation in the subjects.

In addition, the experimental group showed a significant decrease in serum lipoproteins like high-density lipoprotein (HDL), cholesterol levels, very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), as well as a significant decrease in TLC compared to a control group from baseline to 9 months. Other studies showed that increased TLC increases the risk of CVD. Also, measuring TLC can predict coronary artery diseases independent of other risk factors, such as elevated lipid levels.

Implications

- 1. A significant reduction in CRP and improvement in periodontal inflammation contribute to decreased risk of cardiovascular disease, which can be achieved with a simple periodontal treatment.*
- 2. Periodontal treatment may have a delaying effect on this chain of events because an increase in systemic inflammation in response to periodontitis may exacerbate the metabolic changes in patients with MetS, accentuating insulin resistance as well as dyslipidemia and increasing risk of cardiovascular accidents.*

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Obituary - I

Prof. Divya Mehrotra, Department of Oral and Maxillofacial Surgery, King George's Medical University Lucknow

Pushendra Singh, Saumyendra Vikram Singh*



Dr. Divya Mehrotra was a distinguished clinician, researcher and teacher in the field of Oral and Maxillofacial Surgery. She was born on 31st March 1968 in Lucknow, Uttar Pradesh, India. She obtained her Bachelor of Dental Surgery (BDS) degree with honours in various subjects in 1992.

Later, she completed her Master of Dental Surgery (MDS) in 1995 from the same university, King George's Medical University (KGMU), Lucknow.

Dr. Mehrotra joined the Department of Oral and Maxillofacial Surgery, KGMU, Lucknow, as a senior resident in 1996, and after four years, she became an Assistant Professor at KGMU in 2002. Over the years, she progressed through the academic ranks and was appointed as a full Professor in 2010.

Dr. Mehrotra academic accomplishments are remarkable, with numerous fellowships and awards to her credit. She was a fellow of several prestigious organizations, including FDS RCPS (Glasgow, England), FFD RCS (Ireland), FAMS, FBADI, BDS, MDS, AO Fellow, and UICC Fellow. She received awards such as the KGMU Research Award, Best Teacher Award, NAMS Dental Public Health Award, TC White Visiting Scholarship, Women's Award for Dynamism & Innovation by Indian Express & UP Govt, Dental Public Health Award, Devi Award, various International Travel Grants from ICMR, CSIR & DST. Dr. Mehrotra was an accomplished researcher with an impressive publication record. She authored 155 scientific articles and had handled research projects from DHR, DBT, DST, UPCST. She contributed chapters in eleven books, edited two books and filed three patents. She was serving as editor-in-chief for the Journal of Oral Biology & Craniofacial Research and was a reviewer/editorial board member in more than 30 journals, she was an international faculty member and delivered more than 75 keynote and guest lectures; her contributions to the field were recognized by her inclusion in the top 2% of Indian scientists in her field, according to the Sanford University Ranking.

Dr. Mehrotra's contributions to academia and research were exceptional. She established a multidisciplinary research unit (DHR-MRU) at KGMU and served as its faculty-in-charge and nodal officer. She was also the Dean of quality planning and accreditation at her university until February 2023, leading KGMU through its first accreditation.

In addition to her research work, Dr. Mehrotra was an exceptional clinician, specializing in TMJ ankylosis, facial deformity correction technologies, Maxillofacial Trauma & Tumor, Cleft Lip & Palate Repair, Distraction Osteogenesis, Cosmetic & Orthognathic Surgery, Precancer, TMJ Surgery Dental & Craniofacial Implant Tissue Engineering. She was skilled in Oral & Maxillofacial Surgery, Epidemiology, Lecturing, Healthcare, Medical Education.

Dr. Mehrotra served in several administrative roles at the university. Also, she was a member of various associations, including IDA, AOMSI, AO-CMF, UP-AOMSI, SOAR, BAOMI, and many more.

Dr. Mehrotra was actively involved in various community health initiatives, organizing free health checkups in several cities in India with Rajeev Gandhi Foundation & Impact India Foundation. She also mentored and guided many students, serving as an external examiner for MDS and BDS exams. Truly, she was an exceptional talent cut

short by the cruel hands of fate, and her loss is irreplaceable to this University. Her colleagues and students remember her as a brilliant researcher, dedicated teacher, and kind friend who left a lasting legacy in her field.

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Obituary - II

Prof. Vishnu Dev Sharma, Department of Orthopaedic Surgery, King George's Medical University Lucknow.

Prof. Vishnu Dev Sharma was a distinguished clinician, researcher and teacher in the field of Orthopaedic Surgery. He was born on 23rd March 1947 and obtained his Bachelor of Medicine, Bachelor of Surgery (MBBS) degree with honours in various subjects in 1968 from S.N. Medical College, Agra.

Later, he completed her Masters in Surgery (MS) in 1972 from the prestigious King George's Medical University (KGMU), Lucknow.

Dr. Vishnu worked in the Department of Orthopaedic Surgery, KGMU, Lucknow, as a lecturer from 12 years at KGMU, since 1973 till 1985. Over the years, he progressed through the academic ranks and was appointed as a full Professor in 1997. He headed the department with lots of enthusiasm and love since September 2003 till January 2009 and also gave his expertise and valuable teachings in the department as a contractual professor from 2009 to 2011

Dr. Vishnu's academic accomplishments are remarkable, with numerous fellowships and awards to his credit. He was a fellow of several prestigious organizations, including Prof B.N. Sinha gold medal in 1972

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Obituary - III

Prof. Anand Narain Srivastava, Department of Pathology, King George's Medical University Lucknow.

Prof. Srivastava was a distinguished clinician, researcher and teacher in the field of Pathology. He was born on 13th June 1946 and obtained his Bachelor of Medicine, Bachelor of Surgery (MBBS) degree with honours in various subjects in 1969 from G.S.V.M. Medical College in Kanpur.

Later, he completed his Diploma in clinical pathology (DCP) in 1973 from the prestigious King George's Medical University (KGMU), Lucknow and Doctor of Medicine (MD) in pathology and bacteriology from the same institute in 1976

Dr. Srivastava was a lecturer in department of pathology, KGMU, Lucknow for a period of over 4 years and was appointed as a Professor in May 1997. He contributed to the department with lots of enthusiasm and love and also gave his expertise and valuable teachings to his numerous students before retiring in March, 2009.

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Research Reports

A Prospective Study to Evaluate the Efficacy of Single versus Double Drains in Breast Cancer patients undergoing Modified Radical Mastectomy.

Pooja Ramakant, Shubhajeet Roy, Shikhar S Gupta, Rohit Anand, Utkarsh Singh, Ganesh Bhat, Rizhin Sooraj, Rahalkar Ashwinee, Mithun Raam, Kul Ranjan Singh, Anand Mishra

There has been a major rise in the incidence of breast cancer in the last decade. More than 2 billion cases of breast cancer were diagnosed in 2020 with a global death record of 6,85,000 patients [1]. Although there have been many advancements in the treatment of breast cancer, staging of the disease plays an important role in determining the outcome as well as the response to various treatment modalities to be offered to the patient. The lifesaving surgical options offered to the patients include breast conservation surgery with or without oncoplasty procedures, and Modified Radical Mastectomy (MRM) [2]. Postoperative seroma formation is one of the most common sequels of axillary dissection in MRM. Seroma is a collection of serous fluid under the skin flaps or in the axillary dead space following axillary dissection. Seroma formation can lead to pain, infection and delayed healing, due to which doctors use surgical site drains to prevent it. Many conflicting results regarding the use of single drain versus double drains are available in the literature. One drain is always placed in the axilla, and the another one under the mastectomy flap in case of a double drain procedure [3]. Thus, it becomes important for surgeons to consider the use of drains accordingly, to benefit the patients as well as to reduce the complications.

This prospective randomised dual-arm study was conducted over a period of 6 months on all breast cancer patients who underwent Modified Radical Mastectomy in the Department of Endocrine Surgery, King George's Medical University, Lucknow. We randomised the patients into two groups, each comprising 40 patients, using a random number generator. Patients from one group were put on a single drain (axillary drain) and those of the other group on double drains (one in the pectoral area and the other in the axillary area). After surgery, excised breast masses were weighed and sent for histopathological evaluation. The patient's particulars and the weight of the mass excised along with the operative details were documented. Drainage volume was recorded daily and the drain was removed when the drain volume was less than 30mL/24hrs for 2 consecutive days. A complete record of the period of drain placement, Volume of drainage, Volume of seroma (if formed), and complications, was maintained.

The study concludes that:

Significant p-value (difference between the two groups is significant)

- Although average total drain volume of single drain group was more than that of double drain group, the difference wasn't significant.
- Although number of patients in whom seroma formation had occurred was more in the double drain group, the difference wasn't significant. But, average volume of aspirated Seroma fluid was insignificantly more in the single drain group.
- The only other complication noticed was flap necrosis— in 5% patients of the double drain group.

Parameters	Single Drain Group(n ₁ =40)	Double Drain Group(n ₂ =40)	p-value
Age (in years)	46.58±10.64	52.58±13.21	0.01*
Weight (in kg)	55.81±11.06	57.04±15.41	0.34
Height (in cm)	152.10±5.52	151.65±6.77	0.37
BMI (in kg/m ²)	24.19±5.09	24.72±5.97	0.34
Weight of excised mass (in g)	533.975±199.99	631.58±306.58	0.049*
Postoperative Day of Pectoral Drain Removal	N/A	5.05±0.44	
Postoperative Day of Axillary Drain Removal	11.95±3.04	13.50±3.03	0.01*
Total Drain Volume (mL)	583.13±289.79	566.65±271.79	0.40
Number of patients with Seroma formation	4(10%)	5(12.5%)	0.72
Volume of seroma fluid aspirated (in mL)	57.50±8.29	55±34.93	0.40
Number of aspirations	1±0	1.2±0.4	0.27
Number of patients with Flap Necrosis	0	2(5%)	

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Research Reports

Characterization of a Novel Cancer Biomarker “PP1 γ 2” for Cervical Cancer

M. L. B. Bhatt, Rajeev Gupta, Kirti Srivastava, Rekha Sachan,
Monika Sachdev, Saurabh Kumar Agnihotri

Tumor cells frequently express genes that are normally restricted to the testis, known as Cancer Testis (CT) Antigens. Aberrant ectopic expression of these genes in somatic cells may contribute to the activation of malignant pathways. The restricted expression of CT molecules makes them ideal candidate for early diagnosis and cancer immunotherapy. Similarly, expression of germ cell protein-Protein Phosphatase 1 Gamma 2 (PP1 γ 2) has been reported as testis-specific isoform. This study aimed to characterize PP1 γ 2 as a potential biomarker for cervical cancer.

In vitro experiments with various cervical cancer cell lines (CaSki, HeLa & C33A) were performed using standard cell culture methods. Clinical samples were collected from the patient undergoing treatment at the various stages of the cancer and were screened for the expression of the PP1 γ 2. Samples were processed and analyzed using various molecular biology techniques and assays (RT-PCR, Western Blotting, Immunohistochemistry and ELISA etc). The statistical analysis was performed using the GraphPad Prism software. Various statistical tests like the student t-test (2- tailed) for comparisons between 2 groups, one-way analysis of variance for multiple groups of data were used to evaluate the experimental data's statistical significance which were further correlated with the clinic-pathological stages of the subjects.

The study concludes that Spatio-Temporal distribution of PP1 γ 2 was observed between spindle poles in dividing cervical cancer HeLa Cells and which might play role in cell cycle dynamics of cervical cancer. Real Time Polymerase Chain Reaction (RT-PCR) and Western Blotting analysis of patient's cervix biopsy samples demonstrated that PP1 γ 2 is expressed in precancerous, early and advanced stages of cervical cancer patients. Whereas High risk HPV infected cervical cases were also positive for the expression of PP1 γ 2. PP1 γ 2 transcript and antigen have been detected in the cervico-vaginal fluid of cervical cancer patients. Urine samples of the cervical cancer patients have shown the presence of secretory PP1 γ 2 protein as well as patients have shown humoral immune response against PP1 γ 2. Lentivirus mediated RNAi interference can effectively downregulate expression of PP1 γ 2 in cervical cancer cells in vitro and it may lead to suppression of cell proliferation; induction of apoptosis; inhibition in growth and metastasis in cervical cancer cells in vitro. Study findings demonstrate that PP1 γ 2 has enormous potential to be explored further for early diagnostic biomarker of cervical cancer. The leads generated though the present study might contribute in better understanding of cervical tumorigenesis and it may open new vista for the early diagnosis and potential for devising better therapeutic strategies in cervical cancer.

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Research Reports

Effect of dexmedetomidine infusion on post operative cognitive dysfunction in elderly patients after oral cancer surgery: A double blinded randomized controlled study.

Swati Srivastava, Rajni Gupta, Reetu Verma, Nitu Nigam, Jitendra Kushwaha, Sameer Gupta

Post operative cognitive dysfunction is a common complication after general anesthesia in elderly patients. The objective of this study was to explore the efficacy of dexmedetomidine in reducing post operative cognitive dysfunction in elderly patients after oral cancer surgeries.

In this study 64 adult patients planned for oral cancer surgery between the age group 50- 75 years were randomized into 2 groups. Group A received dexmedetomidine infusion (loading at 0.5 mcg/kg for 10 minutes followed by infusion at 0.2 mcg/kg/min till 20 mins before extubation and group B received fentanyl infusion (1.5 mcg/kg loading at induction followed by infusion 10 mcg/ml at 5 ml/hour till 20 mins before extubation) .MMSE score and CAM score were assessed on day 1,3,7 . Additionally hemodynamic stability, propofol requirement during induction, intraoperative inhalational requirement and post operative opioid requirement was assessed between the two groups.

Results from this study showed that patient demographics were similar between the two groups. MMSE score was significantly higher in the dexmedetomidine group ($p < 0.001$) (Day 1,3,7 mean score was 27.53 +/-0.72, 28.28 +/- 0.68, 28.59 +/-0.56 for dexmedetomidine group vs 25.72 +/-0.46, 23.06 +/-0.80, 22.00 +/-0.00 for fentanyl group. Dexmedetomidine group had improved hemodynamic stability, reduction of dose of propofol for induction by 40 % and decreased inhalational requirement intraoperatively and decreased requirement of opioid post operatively. This study concluded that Dexmedetomidine reduces the incidence of post operative cognitive dysfunction in elderly patients after major surgeries.

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An observational prospective analysis of suspected poisoning cases admitted in Medicine and Paediatrics departments of a North-Indian teaching medical university.

Yashita Khulbe, Yash Chandani, Raja Rupani, KK Sawlani, Arpita

Poisoning may occur due to various causes, most common of which include intentional ingestion, accidental exposure, iatrogenic administration of erroneous drugs or significantly high doses during treatment or self-administration of medicines with or without prescription. Recent years have seen a rise in accidental and incidental poisoning in developing countries such as India.

Appropriate knowledge about poisoning patterns can lead to discernment of risk factors, early diagnosis and correct management of its treatment, thereby reducing morbidity and mortality rates. The demographic and etiological trends observed in poisoning cases may differ among different geographical regions of the same country. Hence, it is essential for each country to characterise its own poisoning profile and take measures required against prevention of possible risks and threats.

Demographics and details of patient investigations and treatment was collected from patients of suspected poisoning and snake bite admitted in Medicine and Pediatrics department in KGMU for a period of 6 months (April to September). A total of 145 patients were enrolled in the study after obtaining informed consent and assent (where applicable). Statistical analysis was done using SPSS version 22. Descriptive and correlation analysis were performed using Chi-square test and Analysis of Variance (ANOVA) test.

This study concludes that More incidence of poisoning was found among males (64%) and age group 16-24 years (28.9%). Snake bite and organophosphate poisoning were the most common cause of poisoning in both Medicine and Pediatrics departments. Incidence of suicidal (n=53, 45.7%) and accidental (n=56, 48.3%) poisoning was comparable in Medicine department, while all cases in Pediatrics department were allegedly accidental. Laboratory investigations revealed Electrolytes – hyponatremia was found in cases of dhatura and rat poison consumption. Hypokalemia was found in a singular case of sulfonylurea poisoning. Kidney panel – increased blood urea levels were found in cases of diesel, insecticide and herbicide poisoning. Increased blood creatinine levels were found in dhatura poisoning. Liver function tests – increased total bilirubin levels were found in sulfonylurea and fungicide poisoning. SGPT and SGOT levels were markedly increased in herbicide poisoning. Mean duration of hospital stay was 4.7 + 5.3 days, maximum being in case of diesel poisoning (18 days) followed by herbicide poisoning (10 days). Ventilatory support was required in cases of snake bite and organophosphate and corrosive poisoning. Average mortality rate was 7.7%, with maximum mortality, with organophosphates having maximum mortality among adults (13.8%) and corrosive having maximum mortality among children (20%).

Results showed that Poisoning is more common in young males, with high rates of suicidal incidences among adults. Organophosphate poisoning, which is easily accessible through pesticides, is one of the most common causes of suicidal poisoning. Snake bites are also very common in rural areas. Organophosphate and corrosive poisoning had the maximum mortality rate among adults and children respectively. Appropriate measures must be adopted at peripheral healthcare institutions to

promote safe use of potential poisons like pesticides and insecticides, and to provide adequate treatment and ventilatory support to patients of poisoning.

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Research Reports

Validation of smartphone photographs as a screening tool for detection of ocular morbidity in children of central Uttar Pradesh

Siddharth Agrawal, Shally Awasthi, Apjit Kaur, Rajat M Srivastava, Vishal Katiyar, OP Singh

Childhood blindness and visual impairment (VI) is a global concern. Considering the high burden of childhood visual impairment, and limited trained resources in India, school eye screening by ophthalmologists and optometrists has not been a feasible model. Assessing visual acuity for screening has been the traditional method since the inception of school screening. Smartphone photographs capturing Bruckner's reflex have demonstrated reliability in identifying amblyogenic conditions in children. However, phone photographs have not been used as a screening tool. This study aimed to assess the reliability of smartphone photographs in detecting ocular morbidities in school children and to compare it with traditional vision screening.

Methodology of the study includes Two thousand five hundred and twenty school children underwent vision screening and smartphone camera photography by a trained research assistant followed by a comprehensive eye examination of all children by an ophthalmologist. Children with unaided visual acuity less than 6/12 in either of the eyes were graded as abnormal. Based upon the characteristics of the Bruckner's reflex, the photographs were graded as normal or abnormal by two investigators blinded to the clinical findings. Statistical analysis was performed to compare the sensitivity and specificity of traditional vision screening and photograph-based screening, considering comprehensive eye examination as the gold standard.

In this study a total of 262 (10.61%) students were found to be visually impaired by the evaluator and suffered with some ocular morbidity. The most common ocular morbidity detected by the evaluator among screened children was refractive error followed by strabismus. The positive predictive value and negative predictive value for screening with photographs were 90.67% and 99.37% respectively. The sensitivity and specificity of vision screening was 81.88% and 97.35% whereas for photographs it was 94.69% and 98.85% respectively. When the two methods were compared, the p value was <0.05. We thus concluded that smartphone photography is better than traditional vision screening for detecting ocular morbidities in school children.

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Research Reports

Clinical and echocardiographic parameters of neonates of diabetic and non-diabetic mothers and its correlation with cord blood insulin like growth factor 1 levels and maternal HbA1c levels-a case control study.

C. Tharuna, Shalini Tripathi, Ashish Tiwari, Gyanendra Sonkar,
Smriti Agarwal, Mala Kumar, S.N. Singh

Infants of diabetic mothers (IDMs) develop interventricular septal hypertrophy (ISH) (> 6 mm). The proportion of IDMs developing ISH varies from country to country. Maternal HbA1c and cord blood Insulin like growth factor-1 (IGF-1) levels have been found useful to predict ISH. This was a case-control study of term neonates of diabetic mothers (cases) and of non-diabetic mothers (controls) to evaluate echocardiographic (ECHO) differences among cases and controls and to find the correlation of interventricular septal thickness (IVS) thickness with maternal HbA1C and cord blood IGF-1 levels.

Results revealed that of 32 cases and 34 controls (mean gestational age 37.7 ± 0.9 weeks), 15 (46.8 %) cases, no control developed ISH. Septal thickness was more (6 ± 0.15 cm vs 3 ± 0.06 cm; $p = 0.027$) in cases than controls. Functional ECHO parameters including left ventricle ejection fraction were comparable ($p = 0.9$) among the two groups. Maternal HbA1C levels were higher ($6.5 \% \pm 1.3$ vs $3.6 \% \pm 0.7$; $p = 0.001$) with a positive correlation with IVS (Pearson's coefficient 0.784, $p < 0.001$). Cord blood IGF1 levels were too higher in cases (99.1 ± 6.09 ng/ml vs 37.1 ± 2.99 ng/ml; $p < 0.001$) with moderate correlation with IVS thickness (Pearson's coefficient 0.402; $p = 0.00$). Receiver operator curve analysis showed, that at a cut-off of 72 ng/ml, cord blood IGF1 predicted ISH with 72 % sensitivity; 88 % specificity and at a cut-off of 7.35 %, maternal HbA1c predicted ISH with sensitivity; specificity of 93.8 % and 72.1 % respectively. ISH was present in 46.8 % of cases as compared to none in controls. IVS thickness correlated well with maternal HbA1C and moderately with cord blood IGF-1 levels. Functional parameters on ECHO were unaffected by maternal diabetic control. At the cut-off of maternal HbA1c of 7.35 % and cord blood IGF-1 of 72 ng /ml, babies need to be monitored clinically with ECHO to look for ISH.

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Effect of Beet root juice rinse on oxidative stress and microbial profile of patients with Oral Lichen Planus

Snehlata Kaushik, Rameshwari Singhal, Nand Lal, Pavitra Rastogi, Vikram Khanna, Abbas Ali Mahdi, Prashant Gupta.

Patients with Oral Lichen Planus (OLP) have severe erythema, ulceration and desquamation, making oral hygiene practices difficult. OLP gingival involvement is very frequently observed with wide variations in clinical appearance and symptoms. Chlorhexidine mouthwash being the gold standard for chemical plaque control agents with the downside it irritates the mucus and cannot be used in the long run. Adjunctive use of beetroot juice as chemical plaque control agents that are non-irritating, medicinal for oral lesions and can be used in the long run. Aim is to compare and evaluate the effect of beetroot juice rinse with chlorhexidine mouthwash in oral lichen planus and gingivitis patients on the basis of clinical parameters, microbial concentration and salivary antioxidant levels.

32 Gingivitis patients with OLP and without OLP were randomly allocated into 4 groups(n=8), 2 test and 2 control groups.

Group 1-Gingivitis with OLP received CHX and

Group 2 received beetroot rinse. Similarly Group 3 Gingivitis received CHX and Group 4 received beetroot. Samples were taken at 3time intervals- baseline, Scaling and Root planning with interventions and 1 week after follow up. Change in clinical parameters which are Gingival Index (GI) and Plaque Index (PI), Plaque and Saliva samples were measured at all 3 intervals and Visual Analogue Scale and Lichen Planus Score at baseline and follow up.

Results showed As Sig. value(p-value) more than 0.05. It is concluded statistically there is no difference between Group 1-2 and Group 3-4, in certain parameters such as PI, GI, LPS. Streptococcus species count- The mean value of streptococcus species at baseline was 1.59. After intervention- no significant difference between Group 1-2 and Group 3-4 was seen. After one week follow-up, reduction in number of bacterial colonies is seen within the group after 1 week followed with mean difference:

Group 1: 0.191

Group 2: 0.015

Group 3: 1.155

Group 4: 0.031

Hence, more decrease in colonies is seen in CHX patients.

Nitric oxide level-After immediate intervention:

Group 1- there is a decrease in NO level with a mean range of -0.371

Group 2- there is less decrease of 0.029

Group 3 and 4: NO level was seen increasing equally.

After one week follow-up, difference in levels is:

Group 1= -0.53

Group 2= 0.023

Group 3 = -0.178

Group 4=0.110

Hence, decrease in NO level is seen in CHX patients and increase in level is seen in beetroot rinse.

To the best of our knowledge, this is the first study to see the effect of beetroot juice rinse on Oral Lichen Planus patients. It was concluded that beetroot juice was a better antioxidant agent in improving gingival health of patients which causes rapid healing, inhibit growth of bacteria, thereby increasing effectiveness of treatment but was less effective as anti-microbial agent compared to Chlorhexidine mouthwash. It also came out to be an effective treatment in OLP patients by performing the dual function as an adjuvant to medication by acting as an anti-oxidant and also by acting as a plaque control measure.

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Research Reports

Evaluation of MGMT gene promoter region SNPs in association with MGMT methylation status and prognosis in glioblastoma

Krachi Agarwal, Shivanjali Raghuvanshi

Eighty percent of malignant brain tumours are gliomas. The updated glioma classification usages molecular markers to subgroup tumours, which better correlates with tumour biology and behaviour and patient prognosis than the previous histology-based classification system. O6-methylguanine-DNA methyl-transferase (MGMT) on chromosome 10q repairs DNA. Alkylating chemotherapeutic response is strongly predicted by this gene's methylation in 50% of grade IV gliomas. Temozolomide (TMZ) fails to repair DNA alkylation because MGMT gene promoter methylation suppresses the gene. Thus, TMZ was found to be most effective in glioblastoma patients with MGMT gene silencing.

The main structure, expression, and DNA repair activity of MGMT gene polymorphism are affected. rs1625649 is the sole polymorphic SNP discovered in 37.5% of glioblastomas in the MGMT promoter region. TMZ-treated glioblastoma patients' MGMT protein expression is downregulated by SNP rs1625649.

Glioblastoma patients' MGMT gene promoter methylation is the best predictive sign, thus we must stratify our setup to identify treatment responders. Indian researchers haven't studied MGMT gene promoter SNPs either. Therefore, this study was planned to-

1. examine glioblastoma MGMT gene promoter area methylation and analyse the MGMT gene promoter SNP rs1625649 in glioblastoma cases and
2. understand the association of SNP rs1625649 with MGMT gene promoter methylation and know the link MGMT methylation status and SNP to survival and treatment response.

The study was carried out in the Dept of Pathology. Consenting glioblastoma patients with tissue suitable for molecular analysis and a histopathologically confirmed diagnosis were investigated. The study excluded patients who declined to participate, those with additional concurrent malignancy, and those with insufficient material for molecular evaluation.

Ethical clearance for this study was obtained from the Institutional Ethics Committee (Ref. Code: VIII-PGTSC-II B IMR-R/P5).

Applying these criteria all cases of glioblastoma diagnosed through histomorphology were included in the study. Patient's surgical and chemoradiotherapy history and follow-up information, were obtained. DNA was extracted from FFPE tissue blocks from Pathology Department archives. PCR and PCR-RFLP were used to evaluate SNP rs1625649 in the promoter region of the MGMT gene.

Obtained data was entered on excel sheet and statistical analysis was done and subsequent findings are presented.

Results showed A total of 66 glioblastoma instances met inclusion criteria. Mean age of studied patient

was 43.50 ± 16.11 years, with a male:female ratio of 1.6:1. 37 glioblastomas (56.1%) had methylation in SNPrs1625649 gene polymorphism

Most prevalent CC (62.1%)

Least common AA (15.2%).

It was observed that CC genotype was found in most unmethylated (72.4%) and methylated (54.1%) glioblastomas. Compared to unmethylated instances, methylated subjects had CA and AA genotypes. SNPrs1625649 was not linked with methylation. Methylated cases had longer progression-free survival (PFS) and overall survival (OS) (41.8 vs. 86.3 days) than unmethylated cases (17.3 vs 35.0 days) with $p < 0.001$. The progression-free survival of AA genotype cases was substantially greater than CA and CC genotype cases (63.20 ± 19.21 vs. 32.80 ± 7.89 & 22.93 ± 3.26 days) $p = 0.026$.

Overall survival of AA genotype cases was considerably greater than CA and CC genotype cases (130.80 ± 28.21 vs. 64.18 ± 17.15 & 46.97 ± 5.11 days) $p = 0.002$.

In unmethylated instances, AA genotype cases had a longer progression-free survival (19.33 ± 12.84 vs. 16.20 ± 4.68 & 16.29 ± 3.84 days) than CA and CC genotype cases. Overall survival of unmethylated AA genotype individuals was higher than CA and CC genotype cases (61.00 ± 44.51 vs. 23.20 ± 4.79 & 31.95 ± 5.39 days).

In 14 chemoradiotherapy patients, MGMT methylated patients had longer PFS and OS than unmethylated patients. MGMT promoter homozygous SNP rs1625649 (AA genotype) was associated with improved PFS and OS in MGMT-methylated glioblastoma.

The present study was carried out with the aim to evaluate the single nucleotide polymorphism in the MGMT gene promoter region and its correlation with MGMT methylation status and prognosis in glioblastoma. In this study, 66 cases were enrolled, and a prospective and retrospective study was performed. Among the patients with MGMT methylated glioblastoma (56.1%), those with homozygous rs1625649 (AA genotype) were associated with better progression free survival and overall survival. According to reports, individuals diagnosed with MGMT methylated glioblastoma who possess the homozygous rs1625649 (AA genotype) exhibit a notable correlation with the absence of MGMT protein expression and a superior progression-free survival (PFS) in comparison to those with the wild type rs1625649 (CC genotype) or heterozygous rs1625649 (CA genotype) corroborate with our study findings . Thus, MGMT promoter SNP rs1625649 has prognostic impact on patients with MGMT methylated glioblastoma and methylation status is a predictive biomarker for response to temozolomide.

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Research Reports

Sanger sequencing analysis of BRAF, TERT, and NRAS gene mutations and their clinicopathologic association in papillary thyroid carcinoma

Isha Makker, Chanchal Rana

This is reported that thyroid cancer is among the most prevalent forms of endocrine neoplasms, and its global incidence has been progressively increasing in recent decades . Probably mutations in the genes BRAF, TERT, and NRAS may function as potential prognostic factors . In this investigation, the clinical and pathological correlations of single or combined mutations in the BRAF, TERT, and NRAS genes in papillary thyroid carcinoma were explored using the Sanger sequencing technique. All of these genes have demonstrated involvement in the advancement of the ailment. The focus of this investigation pertains to the examination and importance of these alterations.

The study was done in the Dept of Pathology. FFPE blocks of histologically proven PTC cases retrieved from the departmental storage facility. Clinical and biochemical details were collected from patient record files and departmental archives. The DNA quality assessment was done using a spectrophotometer along with gel electrophoresis. Sample with purity ratio more than or equal to 1.8 were processed for further analysis. Relevant exons of BRAF, NRAS and TERT genes were amplified, under a controlled thermal profile and PCR products obtained were purified. Following set of primers were used (reverse and forward):

- **BRAFV600E:** Forward-5'-CTAGTAACTCAGCAGCATCTC TCTCACCTCATCCTAACAC-3'
- **NRAS : Forward-5'-CCT GTT TGT TGG ACA TAC TG-3'**
Reverse- 5'-CCT GTA GAG GTT AAT ATC CG-3'
- **TERT:** Forward-5'-TCTGAGTGACCTTTCACC-3'
Reverse- 5'-TTCCACATACCGCTACTC-3'

Sanger sequencing was performed using Applied Biosystems 3500 genetic analyser. A controlled thermal profile was used for all the three mutations to be analysed. Statistical analysis was done applying SPSS 24.0 version.

The sample comprised of 48 papillary thyroid cancer including 9 hemi thyroidectomies and 39 complete thyroidectomies. With a 1:5 male-to-female ratio, 83.33% of patients were female. Age range was between 14–70 years and average age was 36.6 ± 14.6. Majority of (45.8%) patients were between 20-40. These 48-sample included 13 follicular variants, 2 solid variants, 1 hobnail variant, 1 diffuse sclerosing variant, 1 cribriform morula variant, and 1 columnar variant of PTC. 29 traditional PTCs remained.

Age, tumor size, location, lymph node metastasis, extrathyroidal extension, distant metastasis, and tumor recurrence were used to categorize individuals. Only 10 (20.8%) instances had multifocal tumors, 15 (31.25%) instances had capsular invasion, 13 (27.1%) had extrathyroidal extension.

The study concluded that the prevalence of BRAF V600E mutation in our study population was 45.8%. Reports reveal BRAF V600E mutation was correlated with more aggressive and iodine-resistant

phenotypes, providing valuable prognostic information for thyroid cancer –. In this study BRAF V600E mutation status showed statistically significant correlation with >55 years of age at diagnosis, CVPTC, extrathyroidal extension, lymph node metastasis and recurrence. 50% of BRAF V600E positive cases were of advanced T (T3) stage. TERT mutation is significantly correlated with distant metastasis, recurrence and poor clinical outcome. Although there was a clear tendency towards increased prevalence of TERT promoter mutation in individuals with older age, large tumor size, capsular invasion, extrathyroidal extension, LNM, LVI, advanced T stage, the correlation was not statistically significant. TERT promoter mutation occurred concomitantly with BRAFV600E in 2 cases, both of these patients presented with advanced disease (recurrence and distant metastasis) that resulted in death of diseased. The association of TERT promoter mutations with the BRAF V600E mutation, and the synergistic effect of the two mutations resulting in aggressive clinico-pathological outcomes of PTC, particularly tumour recurrence and patient mortality, demonstrates the necessity of early molecular classification of PTC patients, who must be constantly monitored, even after total thyroidectomy and radiotherapy. NRAS mutation was not found to coexist with any other mutation and was not significantly correlated to any of the clinico-pathological factors, which is similar to a previous finding . There is a need to identify and study a group of cases and controls, multicentric research, long term follow-up and prospective research. Such study would be helpful in investigating predictive, diagnostic/prognostic, and therapeutic molecular values of these three gene mutations for PTCs.

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Research Reports

Molecular Predictive Biomarkers in Head and Neck Squamous Cell Carcinoma (HNSCC) patients undergoing radiotherapy

M.L.B. Bhatt, Rajeev Gupta, Anupam Mishra, Vijay Kumar, Smrati Bhadauria, Parul Dubey

Head and neck squamous cell carcinoma (HNSCC) arise from epithelial cell lining the mucosal surfaces of head and neck region. It is a significant health concern due to its high incidence and associated morbidity and mortality. One emerging area of research in HNSCC is the role of cancer stem cells (CSCs) in tumor initiation, progression and treatment resistance. CSCs are a small population of cells within a tumor that possess self-renewal and differentiation capabilities, contributing to tumor heterogeneity and therapeutic resistance. Understanding the molecular mechanisms underlying CSCs in HNSCC is crucial for improving the efficacy of radiotherapy which is the primary treatment modality for many HNSCC patients, and ultimately enhancing patient survival rates.

Study involved 90 histo-pathologically confirmed inoperable non-metastatic patients with HNSCC. Patients underwent standard radiotherapy treatment along with concurrent cisplatin chemotherapy. Treatment response was assessed after one month of completing the treatment, as per the Response Evaluation Criteria in Solid Tumours (RECIST guidelines). Immuno-histochemistry was conducted to evaluate the expression of CSC markers, including CD44, ALDH1 and CD133. Statistical analysis was performed to evaluate the association of CSC markers expression with clinico-pathological parameters, treatment response and survival.

Results showed that All patients exhibited expression of CSC markers, CD44, ALDH1 and CD133 albeit at varying intensities. The analysis revealed significant association between the expression of these CSC markers and several factors including treatment response, alcohol consumption, tumour size and stage. Notably, alcohol consumption and the expression of all three CSC markers were identified as independent predictors of treatment response. Kaplan-Meier curves depicting the 2-year overall survival rates demonstrated significant association with tumour size, lymph node metastasis, stage, tumour grade, ALDH1 and CD44 expression. Cox-regression analysis was performed to identify independent predictors of overall survival, which revealed tumour grade, lymph node metastasis, recurrence and CD44 expression as significant predictors.

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About The Journal

- Medical Research Bulletin: Georgian Research Ecosystem – Innovate and Create

Why this research bulletin?

- 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 7th March 2022. (National Medical Commission, 2022). After finishing their MBBS course, the majority of MBBS students intend to continue higher study (post-graduation and super-specialization). Many MBBS students choose to study overseas to receive in-depth training in a particular discipline. Other recent medical school grads have a propensity towards academic medicine and research. All of these tendencies and interests call for a research-oriented mindset because all of 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 the undergraduate as well as postgraduate medical / dental / paramedical students to
 - Develop / Enhance their understanding about 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, who are inclined towards research.

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

What this research bulletin will contain?

This research bulletin will contain small articles related to latest developments in medical science, impactful research works that have significant practice implications. Additionally, the bulletin 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 in reference to published impactful research in an indexed reputed journal of the field. It should contain 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 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

 Reference style: NLM (National Library of Medicine) style of reference
Source: <https://www.ncbi.nlm.nih.gov/books/NBK7256/>

 Authorship criteria:

A student will be a lead author of the article. The student writing the

article, need to have a faculty mentor (from any department of King George's Medical University, Lucknow, U.P). The faculty mentor will be the last (second / Third) author and corresponding author.

An article may have up to two student authors and one faculty author.

If, two students contribute to the article, student with more contribution will be the lead author, followed by the second student as author. The faculty member will be the third author.

Always, the faculty mentor will be the corresponding author.

Submission Procedure:

All submission should be mailed to the Editor-in Chief through E-mail.

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Submission document: The manuscript to be submitted as a single document containing:

1. Covering Letter
2. Title page (mentioning the article type, Author's details, Corresponding author)
3. Manuscript

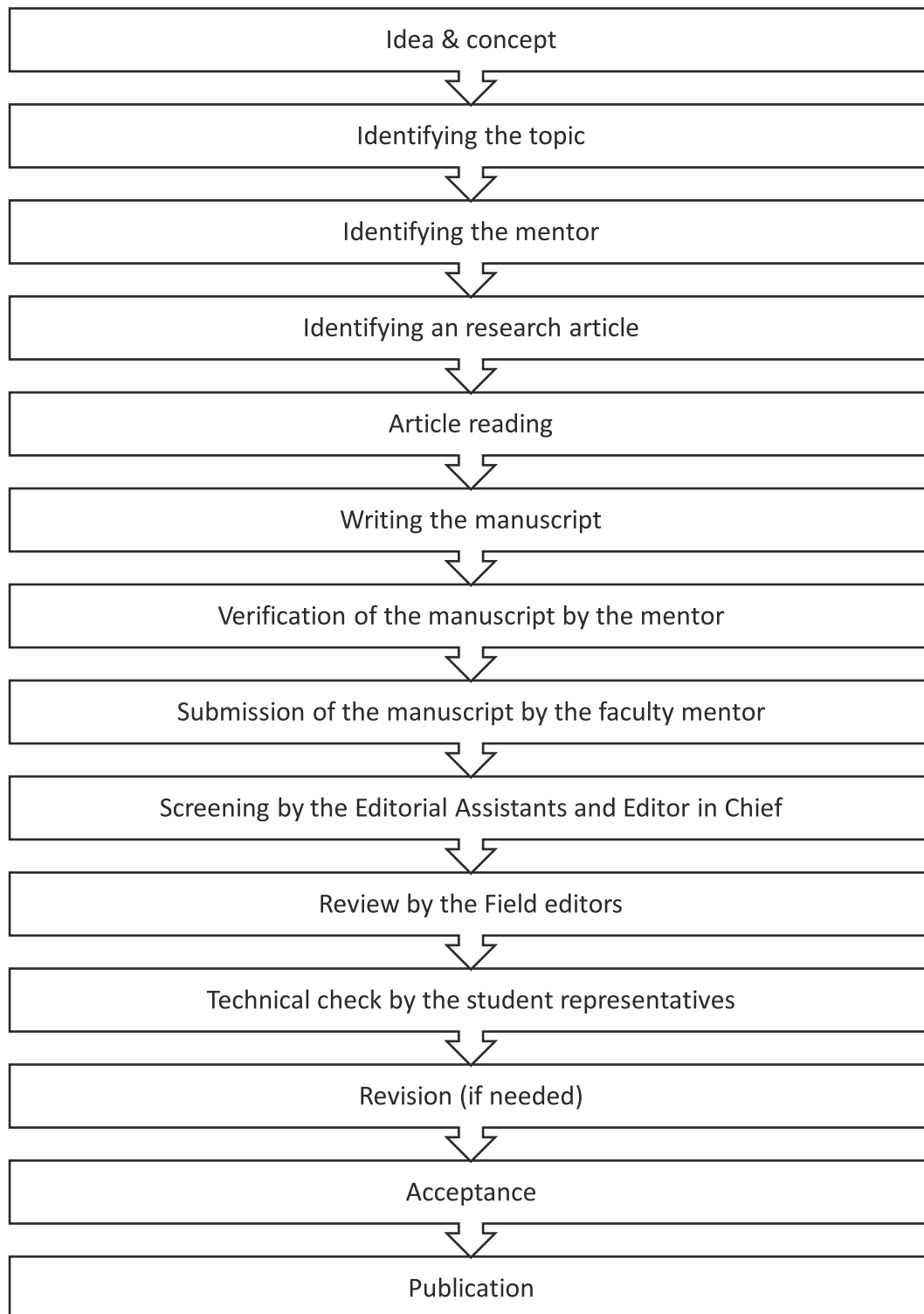
Manuscript should be typed in TIMES NEW ROMAN font style with 12 font size, with double line spacing

 Similarity index of more than 10% will not be considered.

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 **The journey from idea to publication**



Art Gallery



Art Gallery





The front cover of the journal is designed by Mr. Timil Suresh (MBBS student 2020 batch) and the back cover is designed by Dr. Farzana Rizvi (PG resident - Psychiatry).