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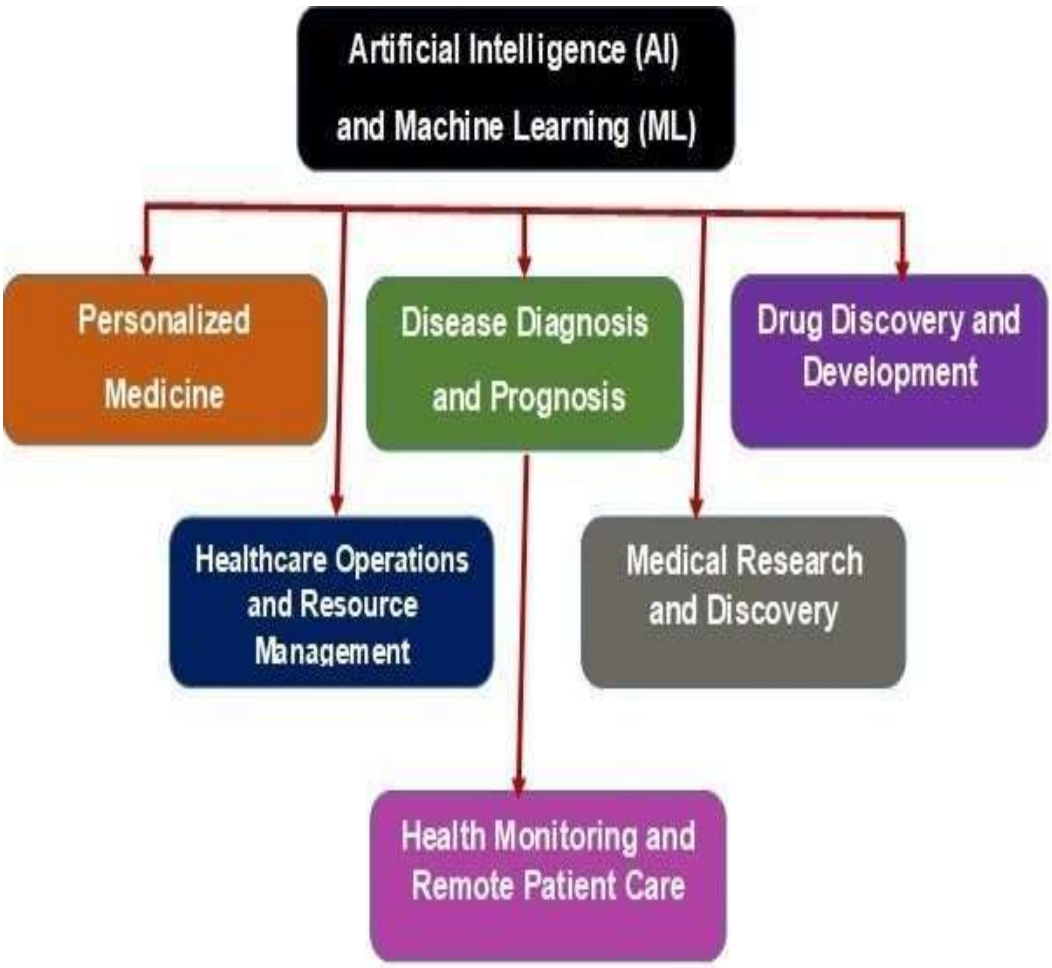
Transformative potential of AI and ML in medical sciences



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EDITORIAL

Artificial Intelligence and Machine Learning: Revolutionizing Medical Education, Training, and Practice

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Artificial Intelligence (AI) and Machine Learning (ML) have transformative potential in the field of medical sciences, offering numerous benefits that can revolutionize healthcare delivery, patient outcomes, and research. The integration of machine learning in clinical settings holds great promise for improving healthcare outcomes, enhancing diagnostic accuracy, and advancing medical research and innovation.

Machine learning algorithms, particularly convolutional neural networks (CNNs), have shown remarkable performance in various clinical applications, especially in fields like radiology, pathology, and dermatology. Applications of machine learning on clinical data are now conquering levels of performance that match or exceed those of human clinicians. Powerful diagnostic and predictive algorithms are built using a range of additional data, including electronic health records (EHR), -omics, monitoring signals, insurance claims, and patient-generated data.

Personalized Medicine

AI and ML algorithms can analyze large volumes of patient data, including genetic information, medical history, and lifestyle factors, to tailor treatment plans to individual patients. This approach, known as personalized medicine, enables healthcare providers to deliver more targeted and effective treatments, minimizing adverse effects and optimizing patient outcomes.

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Some Key Applications and Achievements (Figure 1)

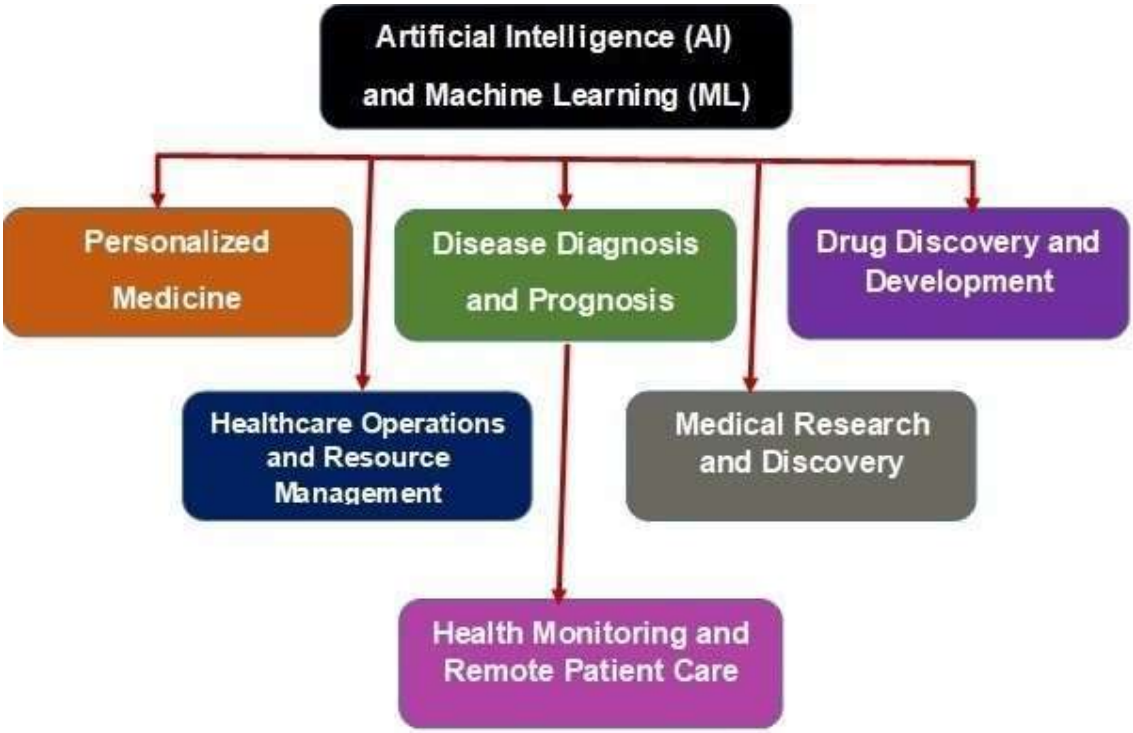

Figure 1. Transformative potential of AI and ML in medical sciences

Disease Diagnosis and Prognosis

ML models trained on medical imaging data, such as MRI scans, X-rays, and histopathology slides, can assist healthcare professionals in the accurate and timely diagnosis of various diseases, including cancer, cardiovascular disorders, and neurological conditions. Additionally, AI algorithms can analyze patient data to predict disease progression and identify individuals at high risk of developing certain conditions, facilitating early intervention and preventive measures.

Drug Discovery and Development

AI and ML techniques are increasingly being utilized in pharmaceutical research and drug discovery processes. These technologies can analyze molecular structures, predict drug-target interactions, and simulate biological processes, accelerating the identification of potential drug candidates and reducing the time and cost associated with traditional drug development pipelines. Moreover, AI-driven approaches enable the design of personalized therapies based on an individual's genetic profile, improving treatment efficacy and minimizing adverse reactions.

Healthcare Operations and Resource Management

AI-powered solutions can optimize healthcare operations and resource management, enhancing efficiency and reducing healthcare costs. For example, predictive analytics models can forecast patient admission rates, enabling hospitals to allocate resources effectively and streamline patient flow. Additionally, AI-driven chatbots and virtual assistants can

automate administrative tasks, facilitate patient scheduling, and providing personalized health recommendations, freeing up healthcare professionals to focus on patient care.

Medical Research and Discovery

AI and ML technologies play a crucial role in advancing medical research and driving scientific discovery. These tools can analyze large-scale biomedical datasets, uncover patterns, correlations, and identify novel biomarkers and therapeutic targets. Furthermore, AI algorithms can assist researchers in designing and conducting clinical trials, optimizing trial protocols, and identifying patient cohorts for specific interventions, ultimately accelerating the translation of research findings into clinical practice.

Health Monitoring and Remote Patient Care

The proliferation of wearable devices and IoT (Internet of Things) sensors has enabled continuous monitoring of vital signs and health metrics outside traditional healthcare settings. AI algorithms can analyze streaming data from these devices to detect anomalies, predict health-related events, and provide early warning signs of deteriorating health conditions. This facilitates remote patient monitoring and telehealth services, enabling healthcare providers to deliver proactive and personalized care to patients, particularly those with chronic diseases or limited access to healthcare facilities.

AI and ML hold tremendous promise for transforming the landscape of medical sciences, offering innovative solutions to enhance patient care, drive medical research, and improve healthcare delivery worldwide. As these technologies continue to evolve, their integration into clinical practice has the potential to revolutionize healthcare systems and contribute to the advancement of global public health.

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ORIGINAL ARTICLE

Intercountry Interactions to Reduce the Endemic Burden of Oral Cancer: An Exploratory Observership Model in India

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Abstract

Background: Lip and oral cavity cancers are the second most common cancers in India and Sri Lanka. Hence, there is a need to enhance partnership among countries and institutions to develop the capacity to ameliorate the huge burden of oral cancer in the SEAR region. **Methods:** An observership model was field tested with the inter-country collaboration from India and Sri Lanka in December 2018 on seven Sri Lankan dentists from National Cancer Control Program participated in the observership model conducted in India. **Results:** This model covered all the components of oral cancer prevention including awareness on oral cancer and oral potentially malignant disorder management training. **Conclusions:** This model emphasized the significance of inter-country handholding and strengthening of the existing cancer prevention activities.

Key words: Oral cancer, Cancer Prevention, Cancer Screening, Observership model, South-East Asia, Capacity Building, Health Promotion, Medical Education

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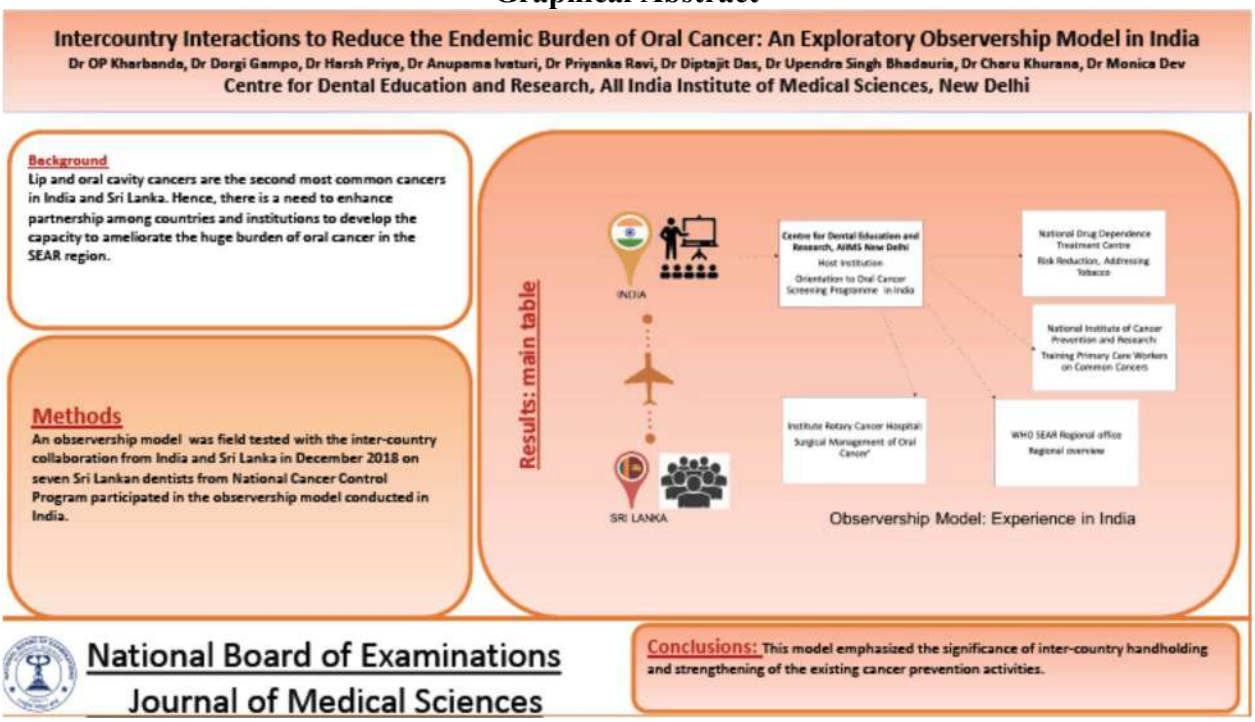
Graphical Abstract



Introduction

The Global Cancer Observatory (2018) [1] reports that the cancers of the lip and oral cavity are the second most common cancers in India (10.4%) and Srilanka (9.1%), high prevalence is seen among males in both India (16.1%) and Sri Lanka (14.8%). The prognosis represented as five year survival rate for early stage oral cancer is 60.2% and advanced stage is only 3.3% [2].

Most of the times the oral cancers are preceded by array of disorders that can be easily detected in the mouth because of an easy access of the site hence oral examination is possible; early identification and detection of these oral potentially malignant disorders is also possible during routine general health check-up or screening by physicians, dental professionals, healthcare workers and even by self-examination of one's oral cavity [3]. There is a dire need for improved and enhanced primary prevention measures, better quality diagnostic and treatment facilities and increased skilled workforce and their capacity building in the regions with high oral cancer burden [4].

The skillset of the primary health care team, pertaining to oral cancer early detection, in most of the South-East Asian Region (SEAR) Countries is fragmentary and there is a need to build capacities through concerted efforts. A leap forward was the development of the Training Module on early detection and prevention of oral cancer which is integrated into PEN (Package of Essential Non-Communicable Diseases).

International health organizations are committed to prevention of oral cancer through primary care and encourage national and international government associated health authorities, research institutions and agencies, non-governmental organizations and self-help groups and civil society groups and residential welfare associations to

strengthen their efforts for the effective and efficient control and prevention of oral cancer [5]. The inter country collaboration in this regard can serve as an ideal method for prevention of oral cancer and can serve as an integral measure in promoting oral cancer awareness across different countries where the countries can learn and adopt best practices on oral cancer screening and prevention. An exploratory observership model was thus conceptualized to train public health professionals in oral cancer screening and prevention.

Material and Methods

The structure of the proposed observership model was exploratory and takes into cognizance the burden of oral cancer, the risks endemic to this region, the similarities of the governance structures and the growing trend of a health policy change in this region. The cycle of events in the algorithm was need based. The crux of the model was the advocacy by the public health fraternity to the relevant governing bodies in the member states (Figure 1).

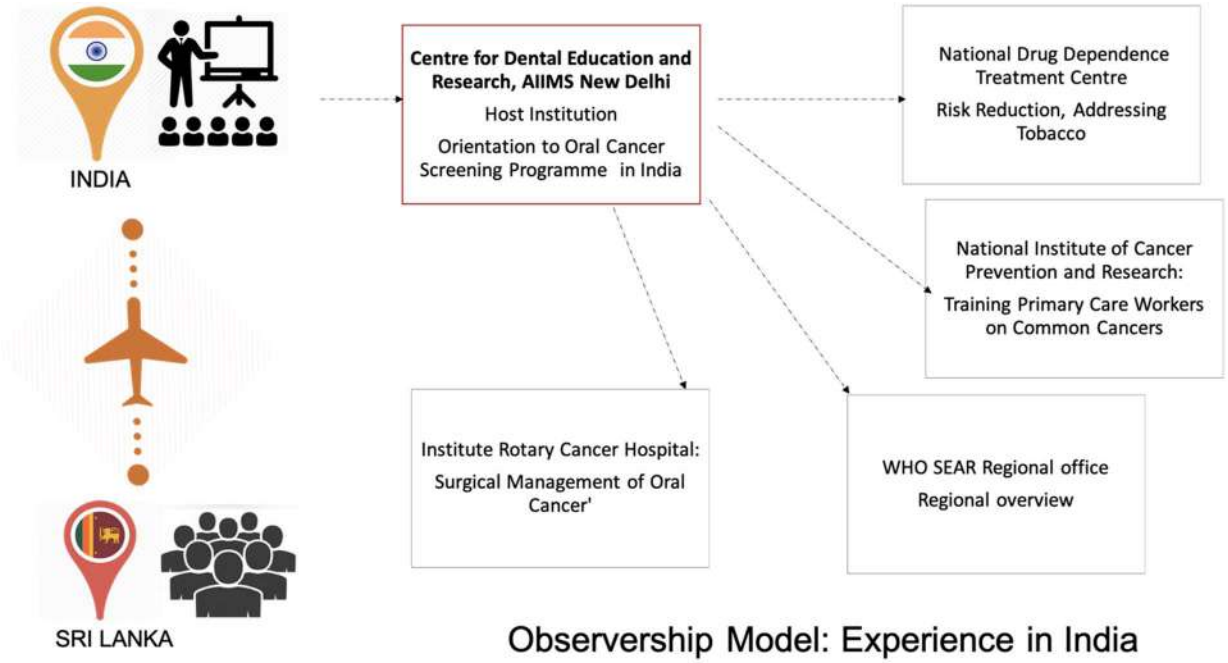


Figure 1. Observership Model

Approvals of the Ministries of Health, Home Affairs and External Affairs are important to ensure the entire capacity building plan for smooth run through validated channels. The needs and expectations of the trainees may then be gathered before formulation of an agenda.

The observership may involve participation of multiple institutions of a country along with field level activities. Handholding of nations with low capacities may be subsequently planned on the lines of the current model.

A blending of the didactics and field visits may be planned for achieving objectives which may spread across the following domains (Figure 1)

- Risk reduction
- Preventive Strategy
- Empowerment and Engagement
- Training
- Surveillance and Research
- Referral Pathways and Management Protocols.

Risk Reduction

Tobacco use along with excessive alcohol intake have been estimated to account for about 90% of the cancers in the oral cavity; the risk escalates when tobacco is used in combination with alcohol or areca nut [6]. The International Agency for Research on Cancer has provided evidence that smokeless tobacco causes oral cancer [7].

In the recent times federal and private agencies have been actively working in the concerted actions towards promoting oral cancer prevention, risk reduction, research and strategies in view of rising cost to treat oral cancer and its subsequent burden on the economy. Prevention on a large scale would be the optimal way to ultimately lower the physical, social, emotional, and financial burden as well as improve the overall quality of life of oral cancer survivors by reducing the risk of recurrence and provision of palliative care.

The common risk factor approach needs to be adopted by the oro-dental health programmes globally and integrate with broader health promotion rather than standalone oral health promotion [8]. It is clearly visible that the use of tobacco is a common risk factor between the majority of non-communicable diseases (NCDs) and oral disease burden. This forms a logical explanation regarding the integrative approach especially for tobacco control initiatives.

The aim of the WHO Oral Health Programme is to ascertain that oral health fraternity and oral health systems are directly, appropriately, continuously and consistently involved in influencing and benefitting patients and the masses to increase their awareness of the risks of tobacco use, and to decrease and be abstinent of use of all forms of tobacco. Management of tobacco dependence is a key feature of the tobacco control strategy indicated in the Article 14 of the WHO Framework Convention on Tobacco Control and MPOWER, where it is emphasized about “Offer help to quit tobacco use” [9]. Cessation support which can be either behavioural motivation to quit with or without cessation medications can increase the likelihood that a tobacco user will quit successfully.

Longitudinal studies with decade of follow-up have shown that educational and awareness creation interventions reduce tobacco use and dwindle incidence of oral potentially malignant disorders [10]. The main obstacles to provide tobacco cessation methods are lack of awareness, knowledge, skills and professional leadership. Hence, there is a need to integrate initiatives that are targeting tobacco cessation with programmes including oral health and train the professionals on the same. An inter country collaboration can aid in promoting targeted interventions which can significantly help in increasing awareness and skills ultimately leading to risk reduction.

Limiting the intake of alcohol, chronic irritation due to sharp tooth or denture and malnutrition are other modifiable risk factors, which can be prevented through capacity building (reference). Educating the public about the risk factors for cancer, prevention through risk-factor modification also play important roles in minimizing the impact of oral cancers.

Preventive Strategy

The survival rates of oral cancer are good, provided if they are detected and treated at the early stages. WHO [11] has developed a cost-effective Package of Essential Non-communicable (PEN) disease and health conscious lifestyle interventions for the SEAR. It contains a battery of validated, evidence-based easy to follow clinical blueprints and guidelines for clinical diagnosis and treatment of cardio vascular diseases, management of chronic respiratory diseases, suspected oral, breast and cervical cancers (the three most common cancers), recommendations on minimum requirements for essential medicines and inexpensive technologies, and standards and indicators to measure improvements. It also consists of agreement tools for behavioural interventions to talk about the main modifiable risk factors: cessation of tobacco habit, dietary modification, avoiding harmful use of alcohol and augmenting physical activity, which can be delivered by medical or non medical health-care workers.

Population based screening programmes also serve the purpose of increasing awareness in the community about cancers, risk factors and the need for periodic screening. It also enables an understanding of better health and avoidance of risk factors in the general community. Effective and accessible cancer screening program ensure early detection and increase in cancer survival rates. One of the best practices is the mobile screening and awareness building operation which was being carried out throughout Sri Lanka, where the common cancers of the country including oral cancer were screened. Training of health professionals is a cost-effective, evidence-based strategy for controlling tobacco use dependence. This will also help oral health care providers to perform their role as health communicators in the dental clinic setting [12].

Ministry of Health and Family Welfare, Government of India [13], provided the guidelines for common cancer screening which included a spectrum of health care professionals from doctors to primary health care workers including Accredited Social Health Activist (ASHA) and Auxiliary Nurse Midwife (ANM) to be trained in oral cancer

screening. The training included an algorithm for oral cancer screening for the health care workers and the referral system. Training the health care professionals on a similar model will help in channeling the cancer screening at the national level. It is important to train the dentist, doctors and other health care professionals in oral cancer screening. Oral visual examination of the mouth is an well-established method of screening to detect the oral potentially malignant disorders or very early stages of oral cancer with systematic visual inspection of the buccal and labial mucosa; gingivae; bucco-alveolar sulci; ventral, dorsal and lateral borders of the tongue; palate; and floor of mouth, by trained and calibrated caregivers under adequate sun or torch light with disposable instruments like wooden spatulas.

Empowerment and Engagement

Efforts to promote a mutual exchange of information, ideas and resources between the masses and the advocators of oral health are pertinent for prevention of oral cancer, ensuring appropriate dissemination of information, as well as adequate utilization of resources. A key component of empowerment and engagement model for oral cancer prevention included development of Information, Education and Communication (IEC) and Behavior Change Communication (BCC) materials Module for Multi-Purpose Workers (MPW) [14] - Female/Male on Prevention, Screening and Control of Common Non Communicable Diseases.

These materials aim to increase awareness, alter attitudes and bring about a change in specific behaviors like tobacco consumption, delay in reporting, use of home remedies for early signs of oral cancer, stigmatizing oral cancer and early onset of engaging in risk behaviors like chewing tobacco, smoking, alcohol consumption, among others. Sharing updated information and novel ideas in a way that is culturally sensitive and locally acceptable to the community, using appropriate social media platforms and channels would go a long way in prevention since it works at the societal level.

A campaign mode that involves relevant civil society groups, for instance, religious leaders invoking a ban on areca nut usage in Sri Lanka, was more relatable to the locals and yielded a better response to health communication that followed, addressing the socio-cultural barriers. This offered a pragmatic approach for advocacy in the political corridors too. Empowerment at both individual and community levels through thoroughly tested engagement activities that involved all the responsible societal groups created a supportive environment and strengthened community action. The proposed observership model thus accommodated a specific domain on empowerment and engagement paving way for enhanced outcomes of efforts to prevent oral cancer in this region.

Training

Building capacities of health and non-health professionals through training on early detection and referral of oral cancer is a significant step towards prevention in the SEAR. The diverse workforce in the eleven countries have similar responsibilities at the primary health care level thus making it possible to train this workforce on similar lines. This may involve didactics and demonstrations on Oral Visual Examination (OVE) and Mouth Self Examination in premiere teaching institutions at the individual and institutional level. Training may involve certain on-site field visits to provide a hands-on experience on working in low resource settings. Capacity building may also go the digital way. Multiple telemedicine and online avenues exist which may be exploited to reach out to a wide audience. The Extension for Community Health Outcomes (ECHO) is one such platform in vogue for educating medical professionals, dentists, nurses and primary workers dealing in health care on common cancer screening, early identification and detection, tobacco cessation and management of common cancers [15]. Observership is also one such method that may be tested for sustainability.

The professionals may be trained on a Training of Trainers model to build capacitates which may encompass the resources needed, budgeting, logistics and contingencies. An exemplary training programme may serve as a lead for adaptation in the regional countries based on the language, population and current service delivery mechanism perspectives.

Surveillance and Research

Surveillance and research are integral for effective and efficient cancer control programmes and monitoring and evaluating their stepwise and overall performance. A comprehensive surveillance and research system provides data on the magnitude of the oral cancer burden, trends in risk factors, and the effect of prevention, early detection, treatment and palliative care. These have been innovatively utilized in artificial intelligence solutions and precision modelling frameworks. Cancer registries are part of the surveillance system and there is a need for a registry on Oral Potentially Malignant Disorders. Research contributes to determining causes of cancer, evaluation of strategies for prevention, treatment and control.

Referral and Management

Cancer screening programmes require assured linkages at every level, with mechanisms in place for clinical handover and follow up, including high quality documentation processes that are accessible at any level of care at which the patient presents. There is a need to have a country wide uniform linkage referral system for effective and timely management of diagnosed oral cancer or oral potentially malignant cases up to the tertiary level. The oral cancer management should also be included as part of this model to ensure the health care professionals are familiar with the different treatment modalities/ protocol followed in other regions. Surgery, radiotherapy and chemotherapy methods should be sensitized to the health care professionals.

Results

National Cancer Control Program (NCCP), Sri Lanka expressed interest in oral cancer prevention activities in India and requested for an observership program. An observership model was developed by the Centre for Dental Education and Research (CDER), AIIMS, India. Seven dentists from the NCCP, Sri Lanka participated in the observership program, prior to the start of the program ethical and legal considerations were taken by gathering approval from the Ministries of Health, Home Affairs and External Affairs before the programme. Following this, the profile of the trainees was verified by the governing councils of the medical/dental education. The needs and expectations of the trainees (questionnaire google form) were gathered before formulating the agenda.

The exchange programme/ training involved participation of multiple institutions of the country, especially those at the premiere level of programme execution along with field level activities. The flow of events is depicted in Figure 2.

The primordial and primary prevention including tobacco and alcohol cessation counseling methods were discussed at the National Drug Dependence Treatment Centre. The National Institute of Cancer Prevention and Research was visited for the training on the national level oral cancer prevention research and tobacco control activities adopted in the India. As a part of the secondary prevention the oral potentially malignant disorder management training was given at CDER, AIIMS. The tertiary care prevention activities were briefed at the Dr. B.R.A Institute-Rotary Cancer Hospital – AIIMS where the oral cancer surgery and rehabilitative techniques were discussed. The program ended on a note to continue similar exchange programs in the future. A similar program based on the same module may be planned for other countries in the SEAR region. A visit to the WHO office strengthened the intercountry relation towards health care and an urgent need to involve other SEAR countries into similar initiatives.

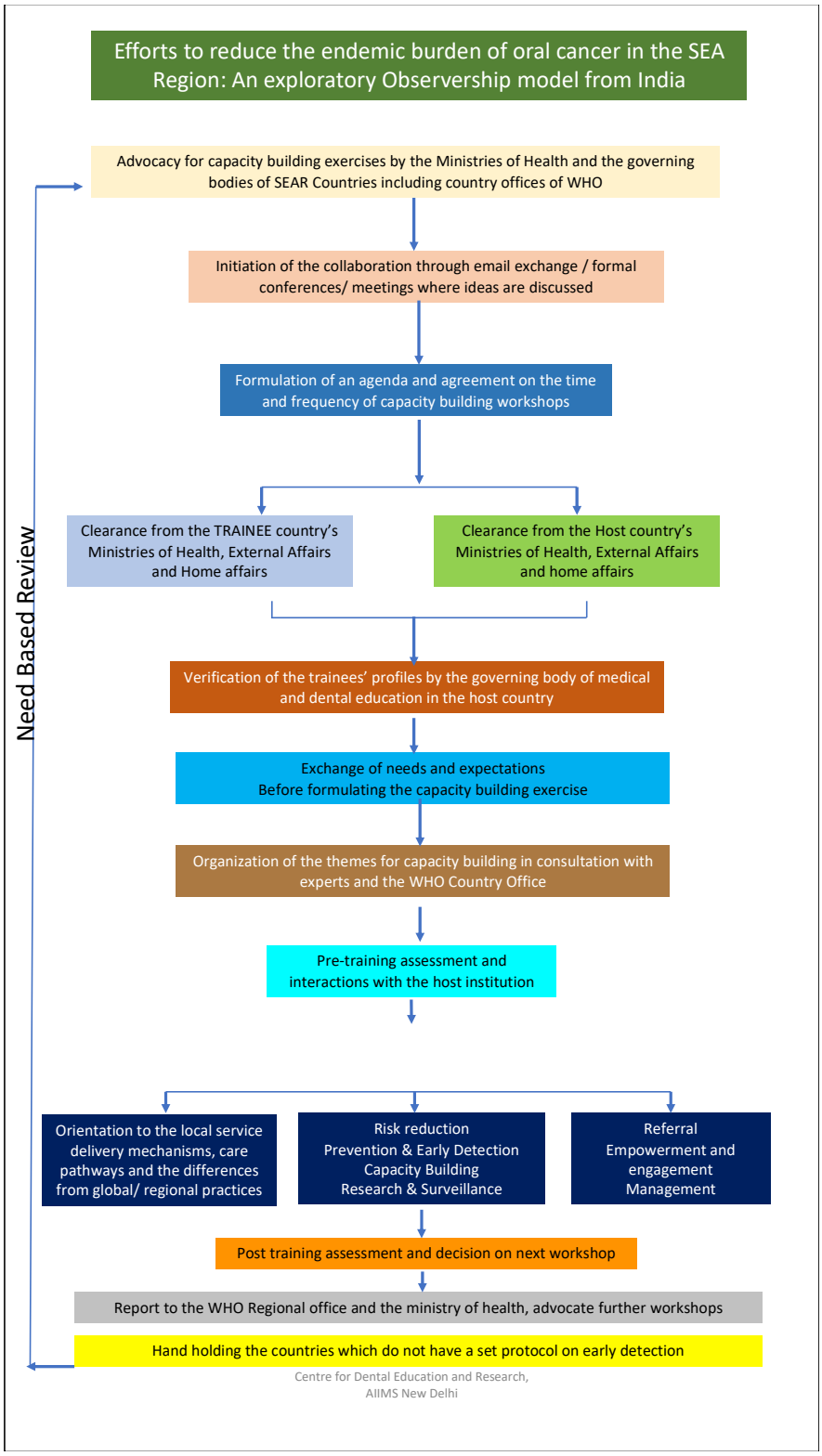


Figure 2. Efforts to reduce the endemic burden of oral cancer in the SEA region – A flow of events

Discussion

The observership of Sri Lankan delegates in India explored the possibility of inter country interactions in achieving cancer prevention. The method was holistic and involved visit of the delegation to tertiary level institutions. The delegates got an overview of institutional and national perspectives of oral cancer management from screening to surgery, budgeting cancer control programs to training primary health care workers. The team also visited the WHO regional office for a regional overview. The programme is itself a strength of the model and provides immense opportunities to interact, learn and adopt relevant practices, suited to the needs of their country. A healthy exchange of ideas leads to a pragmatic approach where countries come together and commit to reduce the endemic burden of oral cancer.

A National Cancer Screening Program under which the common cancers - oral, breast and cervical cancer are screened for, was operationalized by the Ministry of Health and Family Welfare, Government of India in 2017 [13]. A well designed framework which highlights the Dentist, medical officers and primary health care workers' duties in oral cancer screening and tobacco cessation are outlined.

National Cancer Control Programme, Sri Lanka [16] has adopted a risk factor model (RFM) for oral cancer screening, under their National Cancer Control Program. According to the RFM scores are calculated according to the individuals age, socioeconomic status, habit history such as tobacco smoking, betel quid chewing and alcohol consumption. Those individuals with a cut off score of 12 or more are referred for oral examination to a dental professional.

Ministry of Health, Timor-Leste [17] has included oral cancer screening at least once in lifetime under the National Strategy for prevention and control of NCD, Injury, Disabilities and care for elderly and NCD action plan 2014-2018. Currently, the oral cancer screening program is fragmented in other SEAR regions. Hence there is a need to appropriately channelize the screening system.

Conclusion

This model provides a road map for the observership program for oral cancer screening and prevention in the high oral cancer burden countries. This model may also include retraining assessments and exchange programme at young learner level. A similar model can be adopted for reduction of other common cancers such as breast and cervical cancer in the SEAR region. Future research should focus on evaluation of this model at various regions.

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tobacco addiction and its cessation. We are obliged to Dr SVS Deo, Professor, Surgical Oncology, Dr. BRA-IRCH for his permission and guidance at the operation theatre visit. We have huge appreciation for Ministry of Health And Family Welfare and Ministry of External Affairs, Government of India for timely clearances and permissions. We would also like to thank our technical support team of Mr. Ashish Jena, Data Entry Operator and Mr Kapil, Clerk for their logistic support.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

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ORIGINAL ARTICLE

Pattern of pulmonary function tests in subjects recovered from COVID 19 infection

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Abstract

Introduction and Aim: The pulmonary sequelae of COVID-19 have not been extensively studied in the Indian population. This study was taken up with the aim to assess the pulmonary function tests (PFT) in subjects recovered from COVID-19. **Material and Methods:** In this observational cross-sectional study PFT was assessed in 50 adults in the age group of 18-60years. Rapid Antigen Testing was performed to rule out active COVID-19 infection. Subjects with acute or chronic respiratory illnesses that could affect lung functions were excluded. **Results:** We performed PFT on 50 subjects, with a mean age and BMI of 36.09 years and 25.17 kg/m^2. Fatigue and/or breathlessness were the most common complaints present post-recovery. A normal PFT was found in 22 participants and 28 showed a restrictive pattern. Based on the severity of the disease they had experienced the study population was classified into three groups mild, moderate or severe COVID. The three groups were found to be comparable in their demographic parameters, the PFT parameters were significantly different between the groups with significantly lower values seen in subjects who recovered from severe COVID. **Conclusions:** Restrictive pattern on PFT was the common abnormality found in patients recovered from COVID-19. This finding emphasises the need for long-term follow-up and establishment of a plan of assessment and management in patients recovered from COVID-19.

Keywords: SARS CoV 2, coronavirus, lung function test, lung disease

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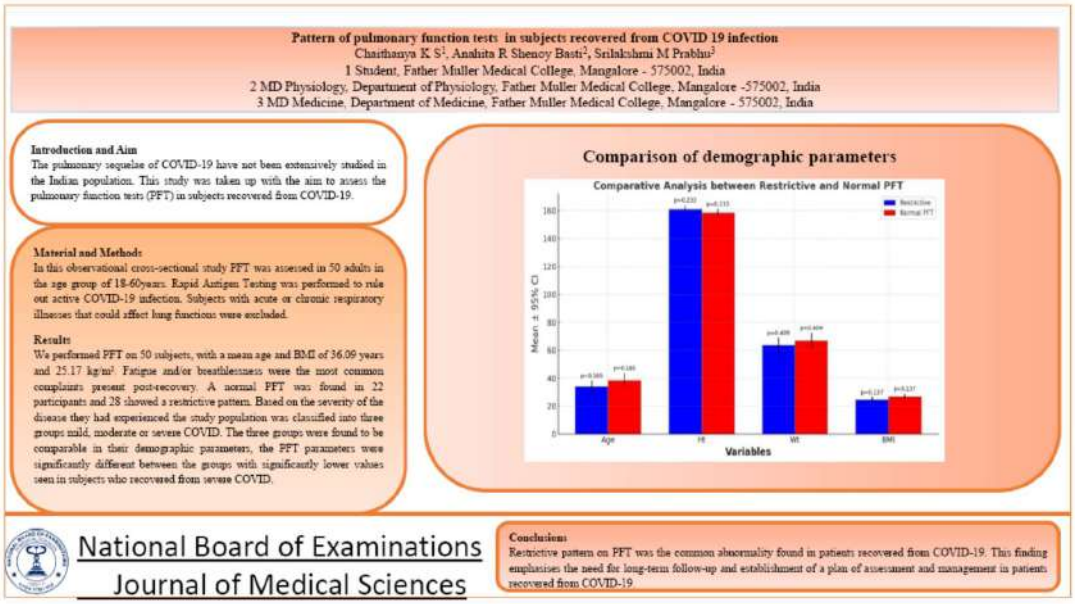
Graphical Abstract



Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS CoV-2) is the coronavirus that has led to the coronavirus disease 2019 (COVID-19) pandemic. 6,931,000 confirmed cases comprising 400,857 deaths globally were reported by 8th June 2020 [1]. With the onset of the second wave, an accumulative global surge of up to 141 million confirmed cases and 3.01 million global deaths as of April 2021 have been reported [2].

The most common symptoms include fever, fatigue, cough and expectoration accompanied by frequent muscle soreness, anorexia, chest tightness, dyspnoea, nausea, vomiting, diarrhoea and headache. The patients developing COVID-19 pneumonia had bilateral lung lesions and respiratory failure or acute respiratory distress syndrome (ARDS) [1,3].

Evidentiary studies have shown lungs to be the most common organ that is affected. Pulmonary injury following COVID-19 pneumonia occurs as a result of pathophysiological events like diffused alveolar epithelium destruction, hyalinisation of the membranes, capillary damage and bleeding, alveolar septal fibrous proliferation and pulmonary consolidation leading to pulmonary fibrosis and hypertension [4,5].

Although the pathophysiology of the disease has been determined to some extent, the long-term consequences and its effect on pulmonary function tests have not been studied in detail.

Evaluation of pulmonary function in recovered patients is important in assessing and understanding the prognostic attributes of the virus [6].

A wide spectrum of tools can be used to objectively assess functional respiratory parameters and the most commonly used tools are the pulmonary function tests such as spirometry, diffusion capacity and lung volumes, and evaluation of airway resistance or respiratory muscles. Epidemiological study report implicates that the above tools help in analysis of abnormalities which can lead to pulmonary fibrosis [4,7,8].

Reports have shown that short-term radiological and abnormal pulmonary functions are most likely to be evaluated in recovered patients' post-acute phase of infection. Little light has been thrown on long-term changes in the PFT which aids in understanding the recovery post-infection [1].

Thus, it is of utmost importance to determine pulmonary functions in the follow-up of patients recovered from COVID-19. This study was taken up with the objective of analysing pulmonary function tests (PFT) in subjects who have recovered from COVID-19 infection.

Methodology

This observational descriptive study recruited 50 adults in the age group of 18-60 years who survived mild, moderate or severe infection with COVID-19 virus.

Subjects who were previously diagnosed with COVID-19 by positive PCR on nasopharyngeal swab and/or presence of bilateral lung infiltrates on chest X-ray were included in the study. Baseline information regarding symptoms at initial presentation and severity of the disease was retrieved from medical records. Subjects underwent clinical examination and any persisting symptoms were noted. Rapid Antigen testing (RAT) was performed to exclude active COVID infection. Negative RAT was followed by performance of Pulmonary function test by a trained technician.

Subjects with acute or chronic respiratory illnesses that could affect lung functions were excluded.

PFT was conducted and interpreted using easy one connect software. The parameters assessed were Forced vital capacity (FVC), forced expiratory volume 1 second (FEV1), FEV1/FVC ratio, Forced expiratory flow (FEF) 25-75%, Peak expiratory flow (PEF).

Descriptive statistics were reported as mean ± standard deviation [SD]. Differences between the groups were analysed for statistical significance by chi-square or Fisher's exact test for categorical variables and by t-test or Wilcoxon rank sum test for continuous variables as applicable.

Results

In this study, we performed PFT on 50 participants majority of whom had complaints fatigue and/or breathlessness. Their mean age and BMI were found to be 36.09 years and 25.17 kg/m^2. Their demographic data is represented in Table 1. A normal PFT was found in 22 participants and 28 showed a restrictive pattern.

Table 1. Shows the demographic characteristics of the study population

n=50		Count (%)
Sex	F	39(78.0%)
	M	11(22.0%)
Presence of comorbidities	No	32(64%)
	Yes	18(36%)
Severity of COVID	Mild	32(64.0%)
	Moderate	15(30.0%)
	Severe	3(6.0%)
PFT	Restrictive pattern	28(56.0%)
	Normal pattern	22(44.0%)

A comparison of demographic parameters between subjects with restrictive pattern PFT and normal PFT has been depicted in Figure 1. The two groups were found to be comparable.

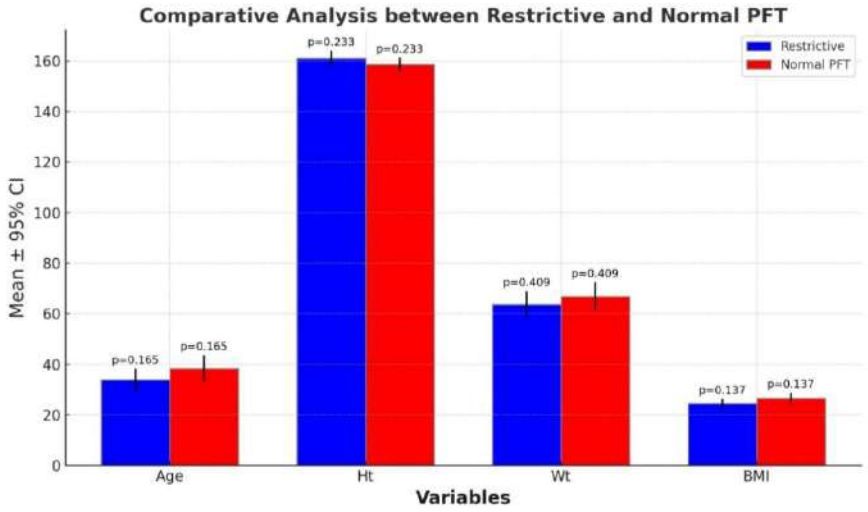


Figure 1. Comparison of demographic parameters between subjects with restrictive pattern PFT and normal PFT

Table 2 Compares the demographic data and PFT values between subjects recovered from mild, moderate and severe COVID-19. Based on the ANOVA p values, no statistically significant differences were found in age, height and weight between the three groups, indicating the groups were comparable in these aspects. However, there were highly significant differences ($p < 0.01$) in FVC, FEV1, FEV6, FEV1/FVC and FIVC values between the groups.

Table 2. Compares the demographic data and PFT values between patients recovered from mild, moderate and severe COVID-19

		n=50	Mean± Std. Deviation	ANOVA p
Age	Mild	32	35.19±11.31	0.497
	Moderate	15	35.67±12.10	
	Severe	3	43.67±16.50	
Ht	Mild	32	158.56±5.67	0.194
	Moderate	15	162.13±9.56	
	Severe	3	163.67±8.39	
Wt	Mild	32	65.44±13.42	0.441
	Moderate	15	62.80±12.99	

	Severe	3	73.33±8.33	
BMI	Mild	32	26.03±5.26	0.249
	Moderate	15	23.73±3.90	
	Severe	3	27.30±0.89	
FVC (% of predicted)	Mild	32	77.88±9.99	<0.001*
	Moderate	15	63.73±14.59	
	Severe	3	55.33±4.73	
FEV1 (% of predicted)	Mild	32	81.44±9.68	<0.001*
	Moderate	15	65.60±16.23	
	Severe	3	47.67±16.04	
FEV1/FVC (% of predicted)	Mild	32	105.63±7.69	0.008*
	Moderate	15	102.93±8.25	
	Severe	3	86.33±29.14	
FEV6 (% of predicted)	Mild	32	78.94±10.22	<0.001*
	Moderate	15	64.73±14.61	
	Severe	3	56.67±4.16	
FEF25-75 (% of predicted)	Mild	32	97.34±22.56	0.007*
	Moderate	15	74.47±33.19	
	Severe	3	56.67±48.69	
PEF (% of predicted)	Mild	32	91.13±12.52	0.004*
	Moderate	15	76.40±16.69	
	Severe	3	69.33±37.82	
FIVC (% of predicted)	Mild	32	75.69±12.03	0.003*
	Moderate	15	63.53±14.74	
	Severe	3	56.33±5.51	

*statistically significant

Table 3 Depicts Post hoc Bonferroni test performed for PFT between patients recovered from mild, moderate and severe COVID. On comparing the PFT values between the groups a significant difference was found in the PFT values between the mild and moderate, mild and severe group, however, no significant difference was found between moderate and severe group except in FEV1/FVC. P value < 0.05 was considered significant for all the parameters.

Table 3. Post hoc Bonferroni test performed for PFT between patients recovered from mild, moderate and severe COVID-19

Post hoc analysis-Bonferroni test			p value
FVC (% of predicted)	Mild	Moderate	0.001*
		Severe	0.006*
	Moderate	Severe	0.751
FEV1 (% of predicted)	Mild	Moderate	<0.001*
		Severe	<0.001*
	Moderate	Severe	0.077
FEV1/FVC (% of predicted)	Mild	Moderate	1.000
		Severe	0.006*
	Moderate	Severe	0.030*
FEV6 (% of predicted)	Mild	Moderate	0.001*
		Severe	0.007*
	Moderate	Severe	0.824
FEF25-75 (% of predicted)	Mild	Moderate	0.033*
		Severe	0.056
	Moderate	Severe	0.942
PEF (% of predicted)	Mild	Moderate	0.013*
		Severe	0.079
	Moderate	Severe	1.000
FIVC (% of predicted)	Mild	Moderate	0.011*
		Severe	0.045*
	Moderate	Severe	1.000

*statistically significant

Discussion

We performed PFT on 50 subjects, with a mean age and BMI of 36.09 years and 25.17 kg/m^2. Generalised weakness and/or breathlessness were the most common complaints present post-recovery. Among the 50 participants, 28 (56%) showed a restrictive pattern while the rest showed a normal PFT.

In a study done during the early convalescence phase found that abnormal pulmonary function tests especially impairment of diffusion capacity and the decline in FEV1/FVC ratio were detected in 43 (75.4%) patients. They also found that total lung capacity was significantly decreased in severe as compared to non-severe cases. However, in their study, only 12.3% of their subjects showed restrictive pattern and 10.5% showed obstructive pattern, as compared to 56% showing restrictive pattern in our study and none of our subjects showed obstructive pattern in PFT [9].

In another study that performed PFT on 100 post-COVID pneumonia subjects, found that restrictive pattern was present in 55% of the patients (N = 55), mixed pattern in 9% of patients (N = 9),

obstructive in 5% of patients (N = 5) with 31% (N = 31) having normal pattern [10].

A possible explanation for the absence of obstructive pattern in our study could be due to the exclusion of smokers and asthmatics who were included in the previous study [9]. Although a high percentage of our study population showed a restrictive pattern, majority (67%) had mild restriction. A higher percentage of restrictive pattern can also be attributed to the fact that the subjects included in our study were symptomatic with complaints of fatigue and breathlessness at the time of PFT recording. Our institution being a tertiary health care centre could also have contributed to a higher percentage of abnormal PFT. A high percentage (36%) of our study population also had comorbidities which could also be attributed to the presence of higher restrictive pattern on PFT.

In another study lung function was assessed in COVID-19 survivors more than 3 months after discharge. They compared patients who had been admitted to the intensive care unit and those who received ward treatments and found pulmonary restriction characterized by reduced vital capacity and/or alveolar volume in 65.4% of all participants. They found that 36.1% of patients had reduced transfer factor (TL_{CO}) but the majority (78.1%) had a preserved/increased transfer coefficient (K_{CO}), indicating an extrapulmonary cause. They attributed this to obesity, fatigue of the respiratory muscles, localized microvascular changes, or hemosiderosis from lung damage. They also concluded that this restrictive pattern was independent of whether or not the patients had received mechanical ventilation or had ward-based respiratory support [11].

A case series where 5 patients who were asymptomatic or had very mild symptoms of COVID-19 infection upon diagnosis and were not hospitalized for the same, were found to have interstitial lung disease four to eight weeks after a COVID-19 diagnosis [12].

In our study, 64% of the participants had recovered from mild COVID yet the percentage of participants showing restrictive pattern was high. As mentioned in the study by James A Stockley et al, other factors of extrapulmonary restriction could have been attributed to the restrictive pattern on PFT and should be considered while evaluating post-COVID sequelae.

We further classified the study population into three groups based on the severity of their disease into mild, moderate or severe COVID. Mild COVID was defined as patients with signs of upper respiratory tract infection without evidence of breathlessness or hypoxia. Moderate COVID was defined as pneumonia with no signs of severe disease, presence of clinical features of dyspnea and or hypoxia, fever, cough, including SpO2. Severe COVID was defined as Severe Pneumonia plus one of the following; respiratory rate >30 breaths/min, severe respiratory distress, SpO2. The three groups were found to be comparable in the demographic data however the PFT parameters were significantly different between the groups with lower values seen in subjects who recovered from severe COVID.

In a study with findings contradictory to ours no difference was found between mechanically ventilated patients for severe COVID pneumonitis and non-ventilated patients 3 months post-recovery [10]. In another cross-sectional follow-up study of 220 COVID-19 patients

performed 10 weeks post-COVID, found restrictive pattern to be prevalent in 38% of the study population. They found the TLC to be below normal in patients recovered from severe COVID [13].

In conclusion, varied abnormalities in pulmonary functions have been reported in different studies, with our study finding a high percentage of the study population having restrictive pattern. Thus, this study underscores the need for a long-term follow-up to understand the consequences of COVID-19 on pulmonary function and to help healthcare professionals and policymakers offer targeted therapies and rehabilitation for the large community of recovered patients.

Limitations

Pre-disease spirometry measurements of the study population were not available for analysis, thus the percentage of restrictive pattern could also be attributed to normal physiological variation, undiagnosed pulmonary or systemic disease.

The PFTs were performed at varied intervals post recovery from COVID, the interval varied from few days up to 14 months post-COVID recovery, this is also a limitation in interpreting the recovery pattern.

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Conflict of interest

The authors declare no conflict of interest

Ethical Approval

The study was initiated after ethical approval and written informed consent from the subjects.

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ORIGINAL ARTICLE

Assessment of teaching learning methods under CBME among second year medical students

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Abstract

Background: Medical institutions are progressively transforming their medical curriculum from a traditional approach to Competency-Based Medical Education (CBME), which is a student-centered curricular activity. Self-assessment of the teaching methods by the students is an important tool to ensure the best possible academic environment for the students. The main aim of the study was to assess the teaching learning methods under CBME among 2nd-year medical students based on student's feedback, in the Dept of Pharmacology. **Materials and methods:** A cross-sectional study was conducted using a questionnaire distributed to the 2nd year MBBS students who met the inclusion criteria. Data was analysed and expressed as percentages. **Results:** A total of 95 students met the inclusion criteria and all responded to the questionnaire. Majority responded positively towards the current teaching-learning methods. Small group discussion (SGD) seemed to be the preferred teaching learning method garnering a total of 67% vote. Most of the students mentioned their preference of learning in small groups but found the adult learning principles like Self Directed learning (SDL) to be less useful. **Conclusion:** Majority responded positively towards the current methods. It was evident from the study that facilitators need to focus on inclusivity in SGD. Incorporation of teaching learning methods suggested by the students would be an ideal tool to ensure the best academic environment for the students. Implementation of more problem based & critical thinking centric methods may encourage students to utilize the adult learning principles like SDL etc.

Keywords: Small group discussion, Competency based Medical Education, Self directed Learning

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Graphical Abstract

Title: Assessment of teaching learning methods under CBME among second year medical students

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Background: Medical institutions are progressively transforming their medical curriculum from a traditional approach to Competency-Based Medical Education (CBME), which is a student-centered curricular activity. Self-assessment of the teaching methods by the students is an important tool to ensure the best possible academic environment for the students. The main aim of the study was to assess the teaching learning methods under CBME among 2nd-year medical students based on student's feedback, in the Dept of Pharmacology.

Materials and methods: A cross-sectional study was conducted using a questionnaire distributed to the 2nd year MBBS students who met the inclusion criteria. Data was analysed and expressed as percentages.

Table : Students perception of new teaching modalities under CBME

Sl. no	Question	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
1.	CAL helps me understand ANS better	42%	43%	13%	2%	0%
2.	Injection practices on a mannequin gives me confidence to perform on a real patient	13%	49%	23%	14%	1%
3.	I find AETCOM modules helpful for MBBS curriculum	21%	38%	31%	7%	3%
4.	ADR reporting exercises gives me the confidence to report real cases in the Wards/OPDs	29%	58%	10%	2%	1%

Conclusion: Majority responded positively towards the current methods. Improvements suggested are now incorporated into our teaching learning methods. Focus should be on inclusivity in SGD and implementation of more problem based & critical thinking centric methods.

Introduction

Medical institutions are progressively transforming their medical curriculum from a traditional approach to Competency-Based Medical Education (CBME), which is a student-centered curricular activity. In India, the realm of medical education is currently in the midst of a significant transition, moving away from conventional frameworks towards competency-based medical education (CBME). This method places a strong emphasis on students acquiring tangible skills in a manner centered around the learner, fostering the growth of capable Indian Medical Graduates with a focus on metacognition. At the heart of CBME is the provision of skill-based training, with the overarching goal of preparing physicians who can effectively function as the primary healthcare provider for their community, all the while ensuring their global applicability [1]. Competency based medical education has been implemented by National Medical Commission since August 2019 in medical colleges all over India. The goal of NMC is to streamline medical education across India so that, quality is maintained irrespective of where a student may study. Apart from the conventional didactic lecture, certain teaching learning methods like self-directed learning and small group discussion has been emphasized in this new curriculum [2]. The practical classes also have received a complete make over. For Pharmacology subject, an entire new teaching aid like mannequin for practicing drug administration has been introduced. Students are now exposed to all the common types of injection techniques required for a normal hospital setting. Even the conventional method of learning drug effects using experimental animals has been replaced with Computer Assisted Learning (CAL), making the relevance of animal house obsolete for undergraduate teaching [3]. Since CBME has now been successfully implemented for two batches in the department of Pharmacology i.e. 2019 and 2020 batches, conducting an assessment to analyse how much the students have benefited with the new curriculum would help the department fill up gaps where it is required. Feedback is an important tool that can help assess the ground reality of newly introduced teaching methods. It will ensure that the department is driven in the right direction to achieve the learning outcome of the course [4]. Hence it is imperative for the department to have a self-assessment of the teaching methods by the students, in order to ensure the best possible outcome for the students. Conducting an assessment to analyse the teaching learning methods in the department of Pharmacology would help the department to identify the shortcomings and help improve the overall teaching method. Moreover, teaching method evaluation by the students in colleges is not a common practice, but is one that may help enormously in gap identification and introduction of new innovative methods in teaching for future batches [5].

Materials and Methods

A cross-sectional study was conducted in the Department of Pharmacology, Zoram Medical College after taking approval from the Institute's Research Committee (IRC No. G.28045/1/2021-ZMC/IRC/48) as well as from the Institutional Ethics Committee (IEC No. F.20016/1/18-ZMC/IEC/104). Questionnaire was framed in the department of Pharmacology by faculties, with a focus on the new teaching methods introduced under competency based medical education (CBME), where majority of the questions were framed on a Likert's scale with few being open ended. The questionnaire was then validated for its relevance and feasibility by

the Institutes research board, as well as Ethics committee. The questionnaire along with consent form was distributed at the end of the university practical exam. The students were not required to fill in their personal information and confidentiality was strictly maintained in an attempt to eliminate bias.

Inclusion criteria: 2020 batch students who were eligible to appear for university exam in 2023

Exclusion criteria: (i) 2020 batch students who were not eligible to appear for university exam in 2023 (ii) Repeater students from senior batch who were eligible to appear for university exam in 2023.

Data collected was entered and analysed using Microsoft Excel and expressed in frequencies and percentages.

Results

There were a total of 95 respondents who met the inclusion criteria. Among the current mode of teaching/learning method, majority (48%) preferred SGD (small group discussion) as compared to didactic lecture and SDL (Self-directed learning) (Table 1). Likert scale was used to evaluate students feedback on the newly implemented practical training module such as computer assisted learning (CAL) and Injection practices on a mannequin. Majority (85%) of the students agreed that CAL exercises helped them in understanding the Autonomic nervous system better while 13% were undecided. Regarding the route of drug administration exercises on a mannequin, 62% agreed that practicing injections like IV, IM, SC on a mannequin gives them the confidence to perform the skill on a real patient. As the department of Pharmacology is an ADR (Adverse drug monitoring) centre, ADR reporting exercises are given to the Phase 2 students, which also requires them to fill up the report in a PvPI (Pharmacovigilance programme of India) prescribed reporting format. This was included in the questionnaire and 89% agreed that the exercise would help them report real ADRs in the wards & OPDs. However, AETCOM module seems to be the least favourite among the newly introduced teaching aspect of CBME, where 41% of the students were either unsure or disagree with its relevance for their curriculum, (Table 2).

While 37% of the students agreed that the current lecture classes were good enough, 40% suggested the use of more videos, animations & mnemonics. 53% of the students also suggested that grading system after every small group discussion could be beneficial, in order to assess the individual contributions of each group member. Regarding Self-Directed Learning (SDL), only 9% were satisfied with the current method and 83% wanted an improvement either in the form of a more elaborate test, while some wanted more exam oriented topics to be included. (Figures 1-3).

Table 1. Preference of teaching learning methods by Phase II MBBS students

Sl no	Teaching/Learning method	Percentage
1.	Didactic lecture	35%
2.	Small group discussion	48%
3.	Self-Directed Learning	19%

Table 2. Students perception of new teaching modalities under CBME

Sl. no	Question	Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
5.	CAL helps me understand ANS better	42%	43%	13%	2%	0%
6.	Injection practices on a mannequin gives me confidence to perform on a real patient	13%	49%	23%	14%	1%
7.	I find AETCOM modules helpful for MBBS curriculum	21%	38%	31%	7%	3%
8.	ADR reporting exercises gives me the confidence to report real cases in the Wards/OPDs	29%	58%	10%	2%	1%

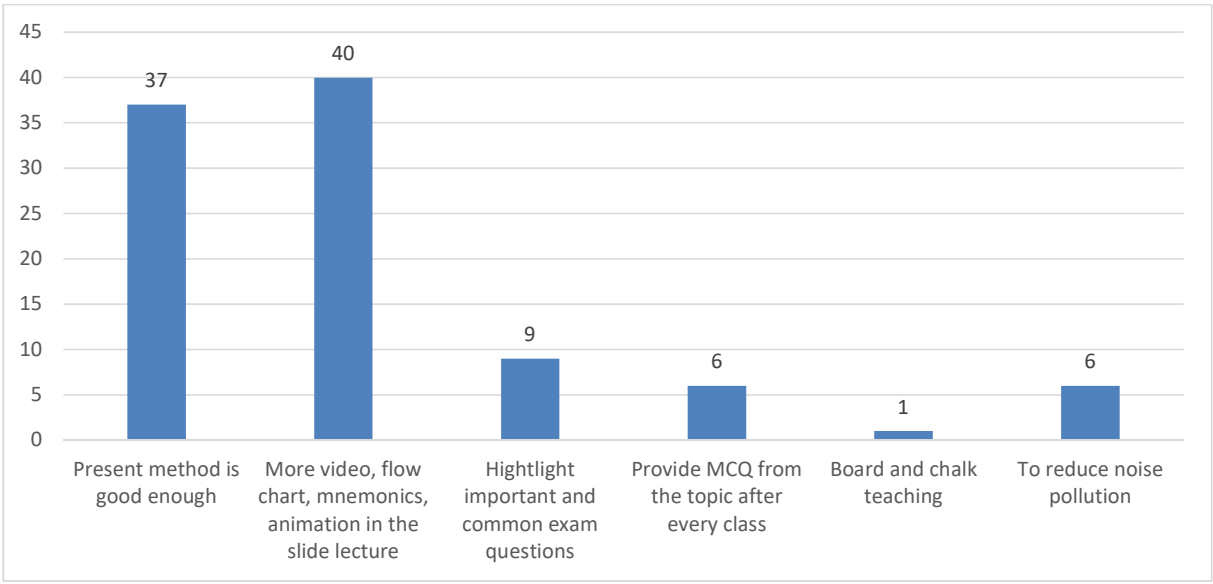

Figure 1. Students suggestion on how to improve Pharmacology theory classes

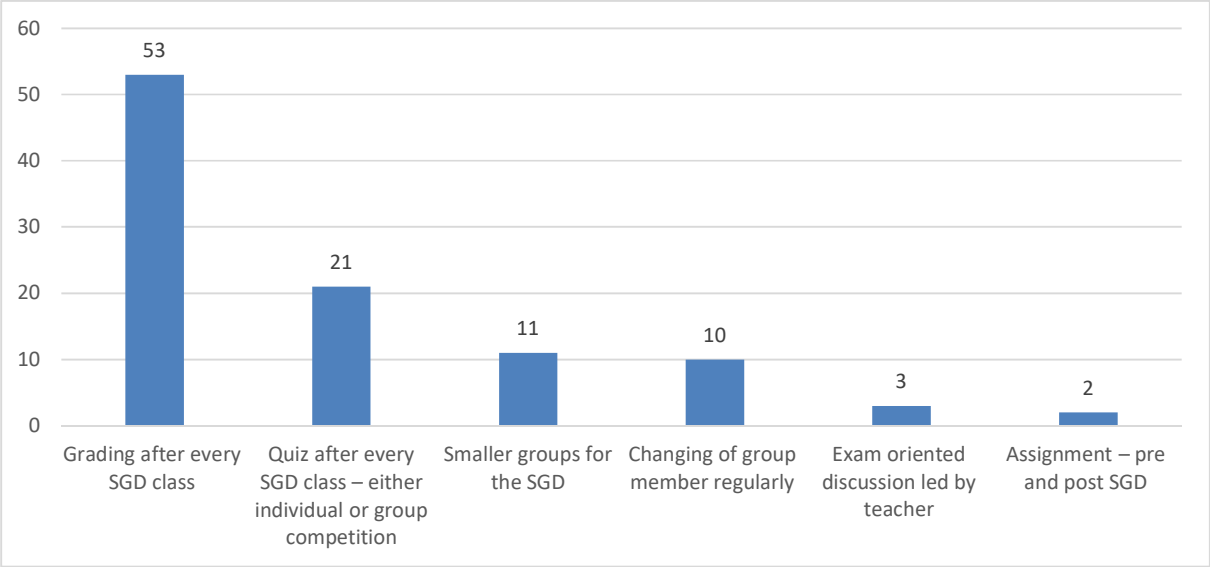

Figure 2. Students suggestion on how to improve SGD

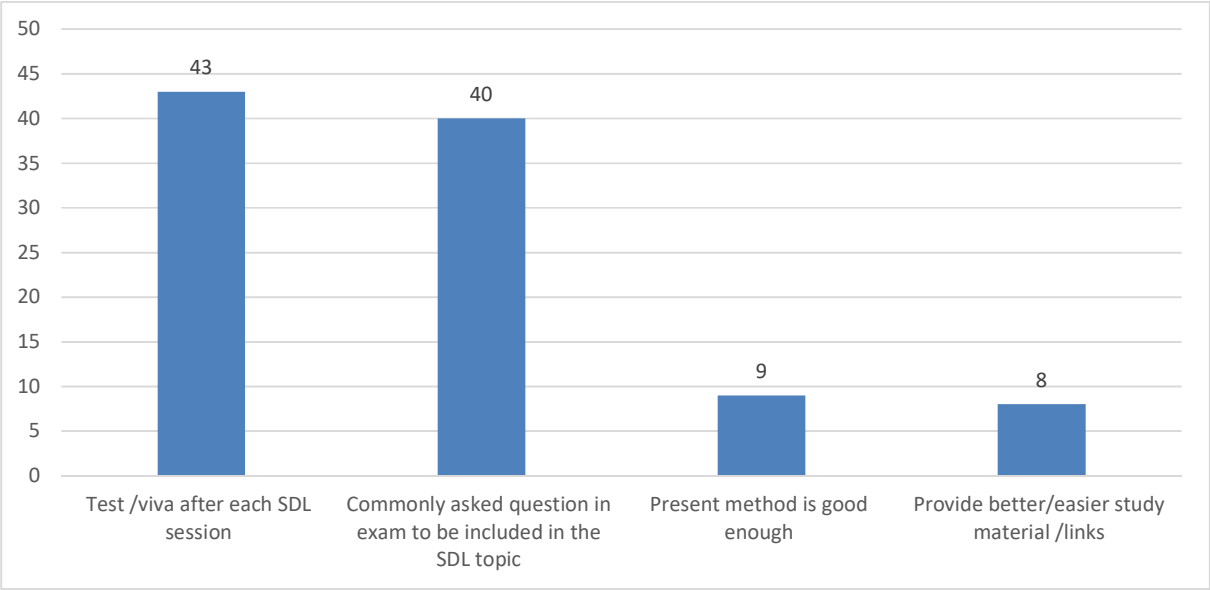

Figure 3. Students perception on Pharmacology SDL

Discussion

This cross-sectional study was conducted to assess the student's perspective on the teaching learning methods in the Department of Pharmacology, after the implementation of CBME. Assessment was done by distribution of questionnaires to Phase II MBBS students who met the inclusion criteria.

Small group discussion garnering a vote of 67% was observed to be the most appreciated method with some suggestions for improvement from the students themselves. Other studies like Thind et al. [6] and Ramanathan et al. [7] also observed that any form of teaching in a small group was ranked high by the students. Chelani & Mahajan [8] also pointed out that students appreciated sessions with direct interaction with teachers, where active participation from students was highly encouraged. Hence, from this study as well as similar ones mentioned, it is evident that students learn better in small groups as it provides a better environment to clear their doubts and spark interest for an extended period of time.

Self-Directed Learning was observed to be the least appreciated teaching-learning method as only 19% chose it as their preferred method. Similar findings were observed by Ramanathan et al. [7] where many students claimed SDL to be time consuming and felt it to be unnecessary for their curriculum. Regarding AETCOM, though roughly 60% of the students responded positively, about 40% were still not sure about the purpose of AETCOM in their curriculum especially during 2nd year, which is during phase II MBBS. However, proper faculty training and student sensitization workshops especially during their 1st year may alleviate some of the negative perceptions towards the adult learning principles incorporated in the new curriculum. Special emphasis has to be given to self-directed learning, especially with the assessment method used by the facilitator.

The major limitation of the study is that it was conducted among 2nd year MBBS students of a single medical college. Hence the findings regarding students' impression of CBME may have limitations in representation.

Conclusion

This cross-sectional study was conducted to assess the student's perspective on the teaching learning methods in the Department of Pharmacology, after the implementation of CBME. As this new curriculum has only been implemented recently, many medical colleges across India are yet to adhere strictly to all the guidelines. Hence, assessment studies on student's perceptions will be an important tool to facilitate the transition from the old to the new curriculum. It was also an important means for gap identification in the academic activities of the department. The innovative ideas suggested by the students are also planned for later incorporation in the departmental academic activities.

Conflict of interest

The authors declare they do not have conflict of interest

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ORIGINAL ARTICLE

Effect of Total Hemoglobin on Glycated Hemoglobin (HbA1c) in Type 2 Diabetes Mellitus

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Abstract

Background: Glycated hemoglobin (HbA1c) is a pivotal marker in the diagnosis, prognosis, and therapeutic monitoring of diabetes mellitus. Given the involvement of hemoglobin in non-enzymatic glycation reactions, it is hypothesized that total hemoglobin concentration might impact HbA1c levels alongside blood glucose concentrations. **Objectives:** This study aimed to estimate and compare plasma fasting glucose level and total hemoglobin level in type 2 diabetes mellitus (T2DM) patients with and without anemia. The study also aimed to estimate HbA1C and compare with calculated HbA1C using formula in T2DM patients with and without anemia and to correlate between total hemoglobin levels with directly measured HbA1c in T2DM patients with and without anemia. **Methodology:** This cross-sectional study, employing purposive sampling, investigated 30 anemic and 30 non-anemic Type 2 Diabetes Mellitus (T2DM) patients at the Central Diagnostic Laboratory. Total Hemoglobin, HbA1C, and Fasting Plasma Glucose were measured for the patients and the data was analyzed. **Results:** Independent 't' tests revealed significant differences ($p < 0.0001$) in estimated HbA1c, fasting blood sugar, calculated HbA1c, and Hb levels between the two groups. Subgroup analyses exhibited significant differences in estimated HbA1c for both groups individually ($p = 0.003$ for T2DM without anemia and $p<0.0001$ for T2DM with anemia). Pearson's correlation analysis indicated no significant correlation between HbA1c and hemoglobin in either subgroup. Similarly linear regression analysis treating HbA1c as the dependent variable yielded a non-significant p-value, suggesting that hemoglobin levels do not significantly influence HbA1c. **Conclusion:** In conclusion, regardless of anemia status, our findings suggest that hemoglobin is not a significant predictor of HbA1c levels in T2DM patients, offering valuable insights into factors influencing HbA1c variability in diabetic populations.

Keywords: glycated hemoglobin, type 2 Diabetes Mellitus, anemia in diabetes

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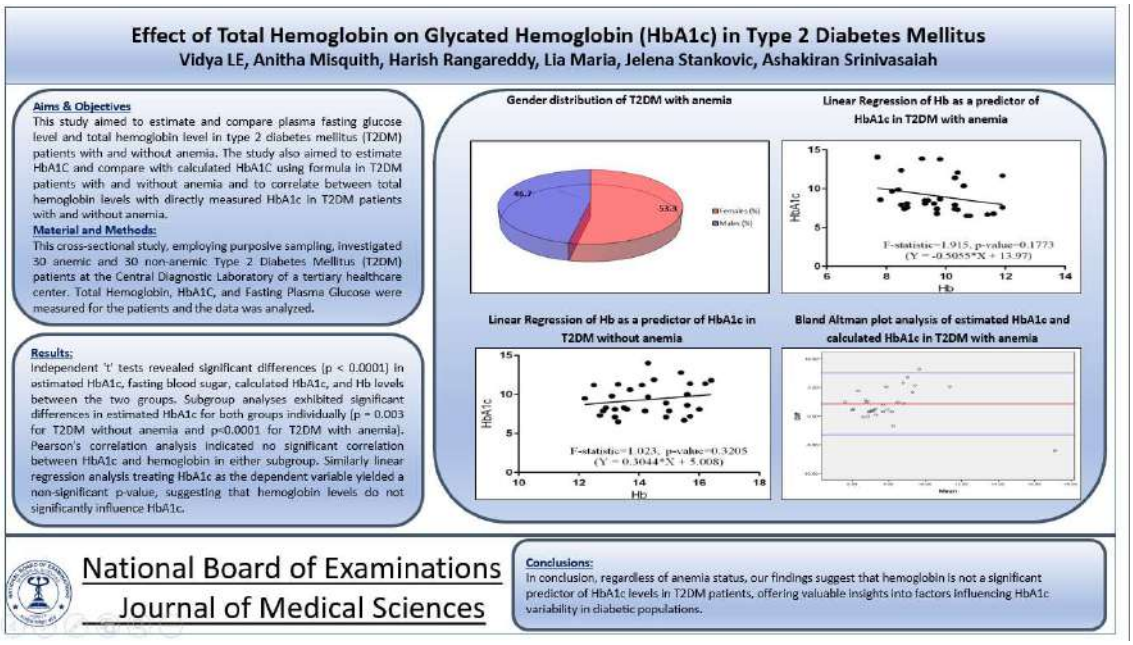
Graphical Abstract



Background

Glycated hemoglobins are hemoglobins that have a sugar moiety attached to them, forming the HbA1 fraction within the adult hemoglobin HbA [1]. The HbA1c fraction, in particular, serves as a predominant component of HbA1 and provides an estimate of an individual's blood sugar levels over the previous three months [2]. Studies have indicated that maintaining an HbA1c level below seven percent can decrease microvascular complications in diabetic patients [3,4]. Glycated hemoglobin (HbA1c) is a pivotal marker in the diagnosis, prognosis, and therapeutic monitoring of diabetes mellitus. However, it's crucial to note that HbA1c is influenced by factors beyond just blood sugar levels. Other variables also play a role in affecting HbA1c measurements [5]. HbA1c is dependent on the interaction between the concentration of blood glucose and the lifespan of the erythrocyte. Given the involvement of hemoglobin in non-enzymatic glycation reactions, it is hypothesized that total hemoglobin concentration might impact HbA1c levels alongside blood glucose concentrations [2]. This study aimed to estimate and compare plasma fasting glucose level and total hemoglobin level in type 2 diabetes mellitus (T2DM) patients with and without anemia. The study also aimed to estimate HbA1C and compare with calculated HbA1C using formula in T2DM patients with and without anemia and to correlate between total hemoglobin levels with directly measured HbA1c in T2DM patients with and without anemia.

Methodology

Study design

This cross-sectional investigation was conducted within the department of Biochemistry, employing purposive sampling to select previously diagnosed cases of Type 2 Diabetes Mellitus (T2DM) patients attending follow-up visits. The Institutional Ethics Committee approved

the study protocol and access to the database was strictly limited to analytical purposes, with personal information remaining inaccessible. Laboratory reports of T2DM patients from the Central Diagnostic Laboratory were gathered, ensuring data anonymization procedures were rigorously followed.

Sample size was calculated considering the mean differences of HbA1c measured by the National Glycohemoglobin Standardization Program (NGSP) certified immunoturbidimetric method in a study by Silva et al. [6]

$$n = (Z_{\alpha/2}+Z_{\beta})^2 * 2*\sigma^2 / d^2$$

where $Z_{\alpha/2}$ is the critical value of the Normal distribution at α/2 (for a confidence level of 95%, α is 0.05 and the critical value is 1.96), Z_{β} is the critical value of the Normal distribution at β (for a power of 80%, β is 0.2 and the critical value is 0.84), σ^2 is the population variance, and d is the mean difference. Sample size was estimated to be 26.

The study population comprised of already diagnosed 30 T2DM patients both with anemia and 30 T2DM patients without anemia, who were recruited from individuals visiting the Central Diagnostic Laboratory, after obtaining written consent. Exclusion criteria encompassed hemolysis, hemoglobinopathies, renal disorders, severe anemia (defined as hemoglobin levels <7g/dL), inadequate sample volume, mislabeling, illegible slips, and erroneous sample collection techniques.

Biochemical analyses were conducted under aseptic conditions, involving the collection of approximately 3 mL of blood into EDTA and sodium fluoride-containing vacutainers, followed by processing for Hemoglobin, HbA1C, and Fasting Plasma Glucose. Hemoglobin levels were assessed using the Automated Hemato Analyzer SYSMEX XNL 550, while HbA1C was measured via National Glycohemoglobin Standardization Program (NGSP) certified turbidometric inhibition immune assay [7]. Fasting plasma glucose (FBS) levels were determined using the Glucose Oxidase-Peroxidase method on VITROS 5600 [8]. Calculated HbA1c values were derived using the formula: HbA1c = 2.6 + 0.03 × Fasting Blood Sugar (mg/dL) [9].

Statistical analysis

Data was tabulated and entered in Microsoft excel. Kolmogorov-Smirnov test revealed that the data was normally distributed. Independent ‘t’ test was applied for HbA1c values in Type 2 Diabetes Mellitus Patients with anemia and checked for significant difference in comparison to the data obtained from Type 2 Diabetes Mellitus Patients without anemia. Pearson’s correlation analysis was performed to assess the relationship between HbA1c and total hemoglobin. Linear regression analysis was done with HbA1c as a dependent variable and total hemoglobin as a predictor. Statistical analysis was performed using SPSS v16, and significance was set at $p < 0.05$.

Results

The T2DM with anemia patients included 53.3% females and 46.7% males as shown in Figure 1. Independent 't' tests were employed to compare HbA1c, fasting blood sugar (FBS), calculated HbA1c, and hemoglobin concentrations between the two groups. The results revealed statistically significant differences in

estimated HbA1c, FBS, calculated HbA1c, and Hb levels ($p < 0.0001$) between T2DM patients with and without anemia as depicted in Table 1. Further subgroup analyses demonstrated significant differences in estimated HbA1c for both groups individually ($p = 0.003$ for T2DM without anemia and $p<0.0001$ for T2DM with anemia). Pearson's correlation analysis indicated no significant correlation between HbA1c and hemoglobin in either subgroup as depicted in Table 2. Linear regression analysis, with Hb as the predictor in T2DM with anemia yielded an F-statistic of 1.915 ($Y = -0.5055*X + 13.97$) with a non-significant p-value of 0.1773 as shown in Figure 2. Linear regression analysis, with Hb as the predictor in T2DM without anemia yielded an F-statistic of 1.023 ($Y = 0.3044*X + 5.008$) with a non-significant p-value of 0.3205 as shown in Figure 3.This suggests that hemoglobin levels do not significantly influence HbA1c. Calculated HbA1c relies on FBS levels and Bland Altman plot analysis was done in T2DM patients with anemia to check there was proportional bias between the means of estimated HbA1c and calculated HbA1c considering the possibility of decreased Hb in anemia to affect the estimated HbA1c values. However, the β coefficient was -0.172 and $p=0.364$ indicating that there was no proportional bias as shown in Figure 4. This further implies that though anemia may be having an impact on the HbA1c it may not be substantial.

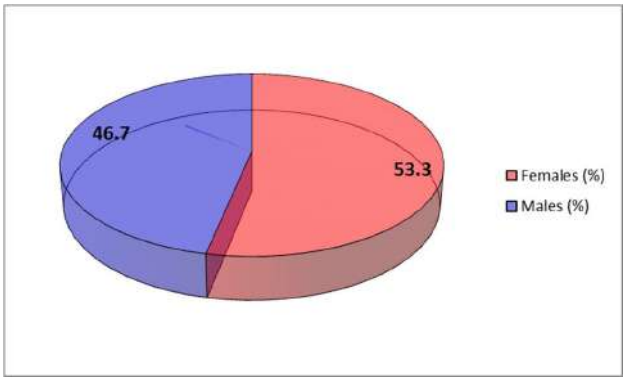


Figure 1. Gender distribution of T2DM with anemia

Table 1. Comparison of estimated HbA1C, FBS, Calculated HbA1C and Hb among type 2 diabetes mellitus with and without anemia

Parameters	T2DM without anemia, n=30 (Mean±SD)	T2DM with anemia, n=30 (Mean±SD)	p value
Estimated HbA1C (%)	9.3±1.2	9.1±2.3	<0.0001
FBS (mg/dL)	182.43±74.08	144.53±91.09	<0.0001
Calculated HbA1C (%)	8.1±2.2	6.9±2.7	<0.0001
Hb (g/dL)	14.3±1.2	9.7±1.2	<0.0001

p<0.05 statistically significant

Table 2. Pearson's correlation analysis of estimated HbA1c with Hb

	r	p value
T2DM without anemia n=30	0.188	0.321
T2DM with anemia n=30	-0.253	0.177

$p<0.05$ statistically significant

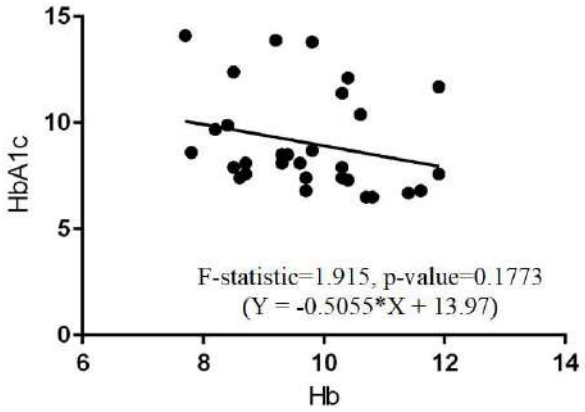


Figure 2. Linear Regression of Hb as a predictor of HbA1c in T2DM with anemia

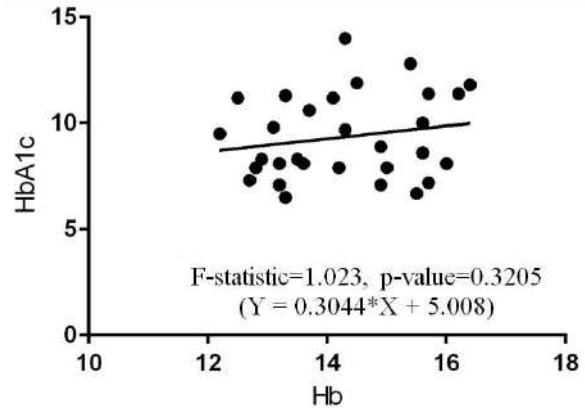


Figure 3. Linear Regression of Hb as a predictor of HbA1c in T2DM without anemia

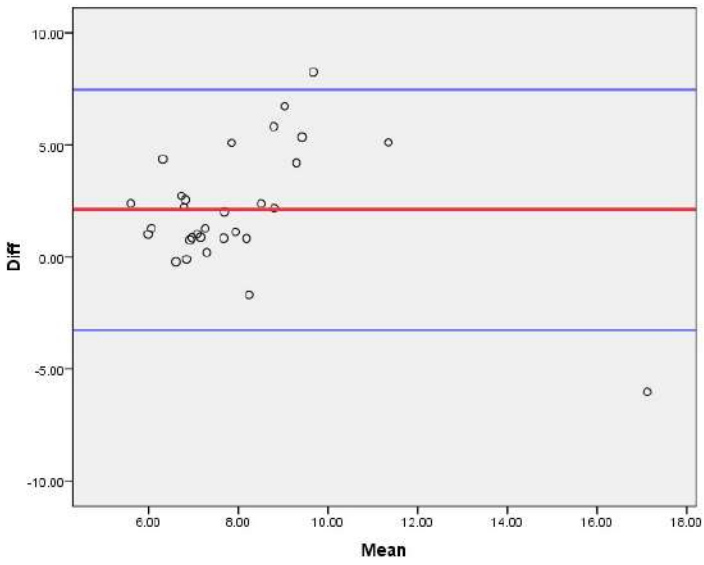


Figure 4. Bland Altman plot analysis of estimated HbA1c and calculated HbA1c in T2DM with anemia

Discussion

This study looked into how anemia affects glycated hemoglobin (HbA1c) levels in individuals with Type 2 Diabetes Mellitus (T2DM) and examined various factors that could influence HbA1c measurement. The study involved 30 patients with T2DM who had anemia and 30 who did not, with gender distribution of 53.3% females and 46.7% males in T2DM with anemia. The average age was 52.5±6.3 years in T2DM with anemia. This is similar to the prevalence study by Panda AK et al but in contrast in their study anemia was more common in males [10]. Anemia is recognized as a common condition that can have detrimental effects on their overall health. In a study by Hizomi Arani et al., it was found that a high number of patients with T2DM in northern Iran (around 22%) had anemia, which is linked to obesity, high levels of triglycerides, duration of T2DM, and chronic kidney disease [11]. Additionally, in a study by Sharif et al., observed that individuals with anemia tend to have comparatively shorter lifespan compared to individuals without anemia [12]. According to a research conducted by SC Thambiah et al., patients with anaemia showed elevated levels of serum urea, creatinine, and reduced FBS, estimated glomerular filtration rate (eGFR) when compared to patients without anaemia [13]. Patients with diabetes and nephropathy who were anaemic had a significantly lower level of haemoglobin than those without this complication (p=0.022). At a threshold eGFR value of 38.3 mL/min/1.73 m^2 with a maximum Youden index of 0.462, the accuracy to differentiate mild from moderate anemia was 66.7% for sensitivity and 79.5% for specificity. This research demonstrates that anemia is detected in T2DM patients when they first visit the specialist outpatient clinic and is closely linked to CKD [13]. However, in a prospective study by Mounika et al., found that diabetics even without kidney problems experienced a

high occurrence of anemia. Additionally, their research also indicated that inadequate blood sugar management and advanced age are linked to the development of anemia in diabetic individuals with unaffected kidney function [14].

In a study by Çetinkaya Altuntaş et al., it was observed in iron deficiency anemia individuals otherwise healthy without any other illness had low HbA1c levels and following iron administration as therapy the HbA1c levels increased; the possibility of hemoglobin affecting the HbA1c levels was highlighted [15]. In our study we selected T2DM with anemia patients and T2DM without anemia as the comparator group showed significant variations in estimated HbA1c, FBS, calculated HbA1c, and hemoglobin levels between T2DM patients with and without anemia, suggesting that anemia could affect these parameters. Further analysis of subgroups confirmed notable disparities in estimated HbA1c and calculated HbA1c levels within each group, indicating the diversity in HbA1c levels among various patient profiles.

In a study by Son et al., anemic individuals (n=112), their age and gender matched controls (n=217) suspected of diabetes were included. They underwent glucose tolerance and HbA1c tests. Mean HbA1c levels were compared for sensitivity and specificity in diabetes diagnosis. Clinical traits were similar. In normal glucose, HbA1c didn't differ significantly (P=0.580). Yet, anemic subjects with higher glucose showed slightly higher HbA1c levels. Anemia lowered HbA1c specificity in diabetes diagnosis ($p<0.05$) [16]. Our study results align with the findings of Solomon et al, indicating that diabetic patients with iron deficiency anemia (IDA) tend to have lower HbA1c levels compared to non-IDA diabetic patients [17].

In a prospective interventional case-control study conducted by Kalairajan et al., a significant correlation was found between Hb and HbA1c levels, with a coefficient of correlation of 0.26 and a p-value of less than 0.01 [18]. Urrechaga et al., study highlighted a positive association between HbA1c levels and iron deficiency [19]. In a study by Madhu SV et al, significant increase in HbA1c among patients with iron deficiency anemia (IDA) with a p-value of less than 0.001 was observed, and they also noted a substantial enhancement in HbA1c levels following oral iron supplementation [20]. Esfahani et al., observed a noteworthy enhancement in HbA1c levels following iron therapy treatment in patients with Type II diabetes and iron-deficiency anemia (IDA) [21]. This indicates that using only HbA1c to monitor T2DM anemia individuals could provide inaccurate information. Hence, healthcare providers and physicians need to take this into consideration prior to making treatment decisions.

In a study by Alsayegh et al., revealed a significantly elevated prevalence of anemia among diabetic patients ($p < 0.001$). Additionally, they found a frequent correlation between anemia and diabetic peripheral neuropathy as well as diabetic foot conditions. Interestingly, no significant association was observed between HbA1c and Hb levels ($p = 0.887$) [22]. Similarly in our study Pearson's correlation analysis revealed no significant relationship between HbA1c and hemoglobin in either subgroup, indicating that hemoglobin levels may not have a substantial impact on HbA1c values in T2DM patients.

Linear regression was also carried out to evaluate the association between Hb levels and HbA1c. The results showed that the F-statistics and p-values were not significant (F-statistic = 1.915, p = 0.1773 for T2DM with anemia; F-statistic = 1.023, p = 0.3205 for T2DM without anemia), suggesting that hemoglobin levels do not have a significant effect on HbA1c.

Moreover, the Bland-Altman plot analysis indicated no significant proportional bias between the mean values of estimated HbA1c and calculated HbA1c, indicating that while anemia could affect HbA1c levels to some extent, it may not have a considerable impact. These results add to our knowledge of the variables influencing HbA1c measurement in T2DM individuals and underscore the necessity for more studies to clarify the intricate connection between HbA1c and hemoglobin levels when anemia is present.

Conclusions

The comparative analysis between T2DM patients with and without anemia reveals substantial differences in estimated HbA1c, fasting blood sugar (FBS), calculated HbA1c, and hemoglobin concentrations. These results emphasize the importance of considering anemia status when interpreting HbA1c levels in diabetic individuals. Moreover, the subgroup analyses for T2DM patients with and without anemia individually highlight distinct patterns, further refining our understanding of the factors influencing HbA1c variability within these subpopulations. The lack of significant correlation between HbA1c and hemoglobin in both subgroups challenges previous assumptions, suggesting a more nuanced relationship between these variables.

A larger sample size may facilitate the exploration of potential confounding variables or modifiers that might have been overlooked in a smaller cohort. This step could contribute to a more comprehensive understanding of the complex dynamics between hemoglobin and glycemic control in diabetes. In conclusion, while the current study provides valuable initial insights, advocating for further exploration with a larger sample size is a prudent suggestion to strengthen the scientific validity and widen the applicability of the findings.

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Conflicts of Interest

The authors declare no conflicts of interest.

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ORIGINAL ARTICLE

Impact of Tobacco Consumption During COVID-19 Lockdown: Insights from Employees at a Government Medical College in Gujarat

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Abstract

Background: Tobacco consumption is consistently harmful to one's well-being, and for individuals with respiratory conditions, it can elevate the likelihood of contracting infections, raise the potential for complications, and enhance the probability of transmission. In this study awareness about the association and the impact of the lockdown on tobacco use among current tobacco users of Government Medical College, Gujarat was assessed. **Objectives:** To evaluate the level of insight regarding the connection between COVID-19 and tobacco use and to assess the influence of COVID-19 related lockdown measures on the rate of tobacco consumption among current tobacco users at Government Medical College, Gujarat. **Methods**: A study was conducted among Class 3 & Class 4 employees of Government Medical College using convenient sampling technique. Study population who was ready to participate in the study and had been actively engaged in the 10-month counselling program from January 2020 to November 2020. Data was gathered through a pre-tested closed-ended questionnaire. Statistical analysis was carried out using the SPSS software (version 22). Ethical approval was obtained from the Institute Ethical Committee, and written informed consent was acquired from all the participants. **Results:** A significant majority, comprising 68% of tobacco users, lacked awareness of the link between tobacco use and COVID-19. Among the 173 current tobacco users, 49 of them successfully abstained from tobacco use during the lockdown period. The primary reasons cited for this change were the unavailability and higher prices of tobacco products. **Conclusions:** The level of awareness regarding the connection between tobacco and COVID-19 played a crucial role in motivating tobacco users to discontinue their tobacco consumption.

Keywords: COVID-19, Lockdown, Counselling, Tobacco Cessation, Employees

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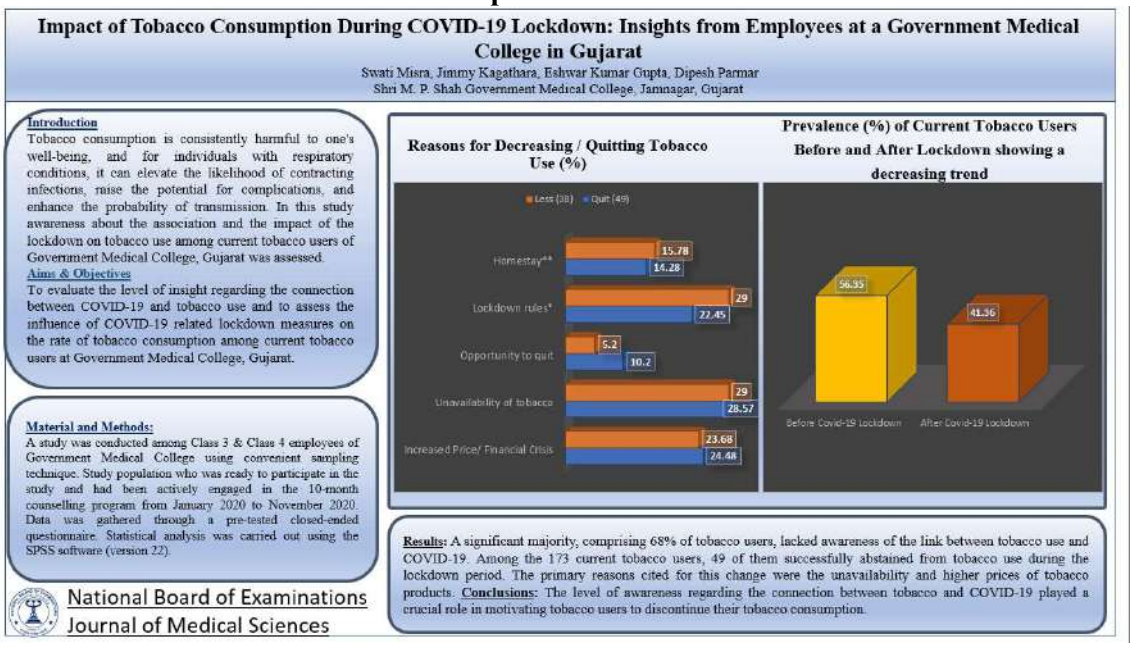
Graphical Abstract



Introduction

The outbreak of Coronavirus Disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, was initially identified at the close of 2019 in Wuhan, China [1] COVID-19 is an infectious illness caused by the highly contagious SARS-CoV-2 virus. It can lead to severe pneumonia, acute respiratory distress syndrome, and, in many cases, fatal outcomes, particularly among vulnerable populations. These at-risk groups include older adults and individuals with chronic medical conditions like cardiovascular disease, diabetes, respiratory issues, hypertension, and malignancies [2]. The importance of maintaining optimal respiratory health has been underscored by the COVID-19 pandemic. One noteworthy aspect that has received significant focus in the context of COVID-19 is the link between tobacco use, which includes both smoking cigarettes and using other tobacco products, and the heightened risk of contracting the virus and experiencing severe consequences. Understanding that COVID-19 primarily spreads through respiratory droplets released when an infected person coughs, sneezes, or talks is crucial. These droplets can be inhaled by individuals in close proximity, potentially leading to infection. Given that COVID-19 primarily targets the respiratory system, any factor that compromises lung health and the immune response can potentially increase the risk of severe illness. Tobacco use is recognized for its harmful impact on the respiratory system, with smoking being a significant contributor to respiratory conditions like chronic obstructive pulmonary disease (COPD) and lung cancer. Smoking causes damage to the lungs, diminishing their ability to function optimally. It also impairs the cilia, tiny hair-like structures in the airways that help remove mucus and particles, making it harder for the body to clear infections. In the context of COVID-19, this is concerning because individuals with compromised lung health may be less equipped to combat the virus. This had

affected severely the whole world resulting into implementation of 'lockdown' interventions at different degrees and at different times [3]. The Prime Minister of India initiated a nationwide lockdown as a measure to combat the COVID-19 pandemic on 24th march, 2020 [4]. While the COVID-19 pandemic and lockdown measures were linked to increased levels of anxiety, fear, sadness, adjustment problems, post-traumatic stress disorder, and suicidal tendencies, these psychological issues may raise the risk of engagement in and exacerbation of substance misuse as an unhealthy coping mechanism in various populations [5]. Columbia University [6] also conducted the study to know initial COVID-19 lockdown period witnessed a potential surge in tobacco use. However, quitting tobacco consumption has the potential to alleviate the burden of non-communicable diseases [7] and also respiratory diseases.

According to few studies [8-10], COVID-19 prevalence and its association with tobacco use have been extensively studied. According to those studies, the global prevalence of COVID-19 continues to fluctuate, with periodic surges in cases driven by variants, vaccination rates, and public health measures. However, ongoing research consistently highlights the association between tobacco use and adverse COVID-19 outcomes. Studies have shown that smokers are at a higher risk of severe illness, hospitalization, and death from COVID-19 compared to non-smokers. Additionally, tobacco use may exacerbate respiratory symptoms and impair the body's immune response, making individuals more vulnerable to respiratory infections like COVID-19. These findings underscore the urgent need for targeted interventions to address tobacco use, particularly in populations vulnerable to COVID-19 complications. By understanding the socio-demographic factors influencing tobacco consumption patterns, the study can provide valuable insights for public health initiatives aimed at reducing both tobacco use and the burden of COVID-19. According to Almu'atasim, Khamees et al. [8], the study found that the lockdown had a notable effect on individuals' lifestyles, particularly their smoking behaviors. The majority of smokers in our sample reported a shift in their smoking habits, with a predominant increase observed. Conversely, those who reported a decrease in smoking levels generally exhibited a healthier lifestyle in terms of nutrition and other facets.

Quitting tobacco is a critical step in reducing the risk of severe COVID-19 outcomes. It not only helps improve lung function and the immune system but also reduces the overall risk of respiratory infections. For individuals who are concerned about their susceptibility to COVID-19 and its potential consequences, quitting tobacco should be a priority. Keeping in mind the above facts regarding lockdown and tobacco consumption, the aim of present study to assess the effect of covid-19 related lockdown over quit rate of tobacco consumption. Whereas, objectives of the current study to assess the understanding about the association with covid-19 and tobacco consumption and to analyze the effect of covid-19 related lockdown on tobacco consumption rate of current tobacco users of Government Medical College, Gujarat.

Methodology

The current study was the longitudinal follow-up study type which was carried out in medical college of

Gujarat on Class 3 and Class 4 (total 307) employees working there. Using the universal sampling technique and after taking their interview it was found that out of all the employees, 178 were consuming tobacco in one or the other form. 5 employees were not willing to participate in the study. Hence, 173 was the final sample size, considered for the study. Study duration was January 2020 to November 2020 with 5 follow-ups. Each time questions related with their current status of tobacco consumption, their perception for covid and tobacco, their reason for decreasing/ quitting were asked. Participants in the study provided verbal informed consent, and they were assured of the confidentiality of their data. The study commenced after receiving Institutional Ethical Clearance from the Ethics Committee, with the Ethical Clearance Certificate Reference Number IEC/CERTI/66/02/2020. The current article is a component of a comprehensive study conducted on tobacco users in the designated area. The study employed a pre-tested, semi-structured questionnaire for data collection. Initial data was gathered through individual interviews, and subsequently, five focused group discussions were conducted, involving a total of 15 groups with seven members in each group. During the Focused Group Discussions (FGD), we evaluated information pertaining to the reduction or cessation of tobacco consumption, along with the associated reasons. Additionally, we assessed the quitting rate among current tobacco users and its correlation with awareness of COVID-19 and tobacco.

Definition/Criteria used in the study [11]

1) Current tobacco user – An employee who was using tobacco in any form like bidi, cigarette, pan masala or any other chewable form in last 12 months.
2) Former tobacco user – An employee who used to have tobacco in any form in any time during his life but stopped from the past 12 months.
3) Non-user – An employee who had never used tobacco in any form during his life.

Results

Among 307 employees of the institute who were interviewed, 56.35% participants were current tobacco user, 7.81% were former tobacco user while 35.83% were not using tobacco. Out of those current tobacco user Class 3 employees were 24.43% while 75.57% belonged to the Class 4. According to Table 1, the socio-demographic distribution of current tobacco users in the study sample reveals several key insights. Firstly, in terms of age, the majority of participants fall within the age brackets of 28-37 and 38-47, comprising 31.79% and 28.32% of the sample, respectively. This suggests that tobacco use is more prevalent among individuals in their late twenties to mid-forties. Interestingly, participants aged 18-27 and those aged 48-57 also constitute significant proportions, though slightly lower. However, individuals over 58 represent a minimal portion of the sample, indicating a decline in tobacco use among older age groups. Secondly, regarding gender, males significantly outnumber females, with 75.14% of participants being male. This gender disproportionality aligns with broader trends indicating higher tobacco consumption rates among men. Thirdly, marital status analysis reveals that the vast majority of participants are married (87.28%), potentially implying that marital

status might be associated with tobacco use behavior. Lastly, in terms of family type, nuclear families constitute the majority, followed by joint and third-generation families, suggesting that family structure may play a role in influencing tobacco use habits. Overall, this data underscores the importance of considering socio-demographic factors when studying tobacco use patterns and designing targeted interventions for prevention and cessation.

According to Table 2, the association between socio-demographic details and tobacco consumption patterns among study participants reveals several significant findings. Firstly, the prevalence of family history of tobacco consumption and friends/ colleagues' history of tobacco consumption is high, with 80.92% and 85.55% respectively. This suggests a strong influence of social networks and familial factors on tobacco use behavior among individuals. Secondly, smokeless tobacco consumption (chewing) is notably more prevalent (90.75%) compared to smoking, indicating a preference for this form of tobacco among the study participants. Additionally, the majority of participants report daily tobacco use (92.48%), with a significant proportion using tobacco 3-5 times per day (48.55%). This suggests a pattern of regular and frequent tobacco consumption among the sample. Furthermore, a relatively small percentage of participants report using other substances (12.13%), implying that tobacco is the primary substance of choice for the majority of individuals in this study. Overall, these findings highlight the interconnectedness of socio-demographic factors and tobacco consumption behaviors, emphasizing the need for targeted interventions that address social influences and patterns of tobacco use among specific demographic groups.

Table 1. Socio-demographic Distribution of study participants (Current Tobacco Users)

Variable	**No. of Participants (%)**
A] Age	
18-27	29 (16.76%)
28-37	55 (31.79%)
38-47	49 (28.32%)
48-57	36 (20.81%)
>58	4 (2.31%)
B] Gender	
Male	130 (75.14%)
Female	43 (24.85%)
C] Marital Status	
Married	151 (87.28%)
Unmarried	22 (12.72%)
D] Family Type	
Nuclear	112 (64.73%)
Joint	41 (23.69%)
3rd Generation	20 (11.56%)

Table 2. Association between socio-demographic details and tobacco consumption pattern in study participants

A] Family History of Tobacco Consumption	
Yes	140 (80.92%)
No	33 (19.08%)
B] Friends/ Colleagues History of Tobacco Consumption	
Yes	148 (85.55%)
No	25 (14.45%)
C] Tobacco Form	
Smokeless (chewing)	157 (90.75%)
Smoke	16 (9.25%)
D] Tobacco Use	
Daily	160 (92.48%)
Occasional	13 (7.52%)
E] Frequency of Tobacco Use (per day)	
0-2	25 (14.45%)
3-5	84 (48.55%)
6-8	57 (32.94%)
>9	7 (4.04%)
F] Use of other substances	
Yes	21 (12.13%)
No	152 (87.87%)

After Covid-19 lockdown on follow up after 10 months it was found that 49 participants had quit tobacco consumption completely. For the sake of convenience abstinence of tobacco intake for at least 1 month was considered as quit. As per Figure 1, people who quit tobacco, majority of them gave reason for quitting and decreasing use was increased price or financial crisis and unavailability of tobacco. Least common reason given by users was that of opportunity to quit. (Figure 2). As per Figure 3, nearly two-thirds of the participants were unaware of the link between tobacco consumption and COVID-19. Out of the total 173 participants, only 118 (68.2%) were uninformed about the connection between harmful tobacco use and COVID-19 outcomes, while 55 (31.79%) were aware of the association [$\chi 2=11.53$, p-value=0.00069]. Among participants with awareness of the association between tobacco consumption and COVID-19 outcomes, 43.64% quit tobacco during the study period. The quit rate among those aware of the COVID-19 and tobacco connection was twice that of those who were unaware, indicating a significant difference and a higher likelihood of quitting tobacco when individuals were informed about the association [$\chi 2=12.057$, p-value=0.00051]. The prevalence of current tobacco users exhibited a decreasing trend before and after the lockdown, as illustrated in Figure 4.

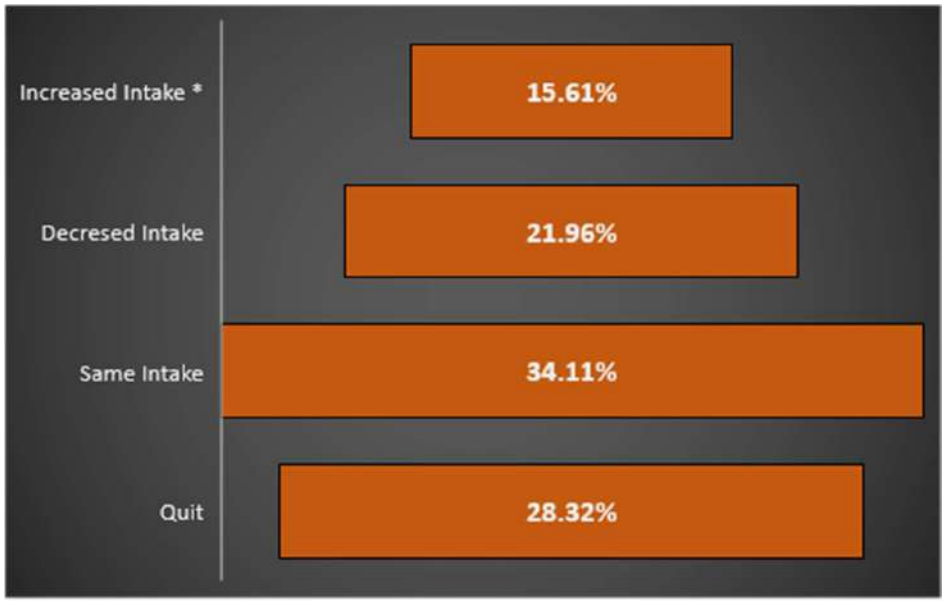


Figure 1. Outcome of COVID-19 Lockdown among Current Tobacco Users (%)
*Increased use due to increased stress

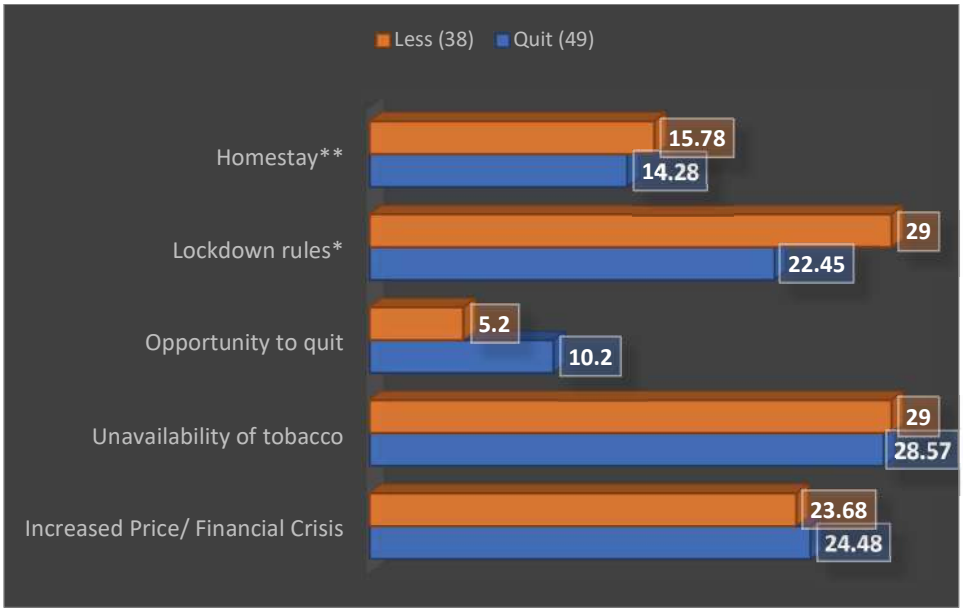


Figure 2. Reasons for Decreasing / Quitting Tobacco Use (%)

**Decreased due to family
*Can't go outside

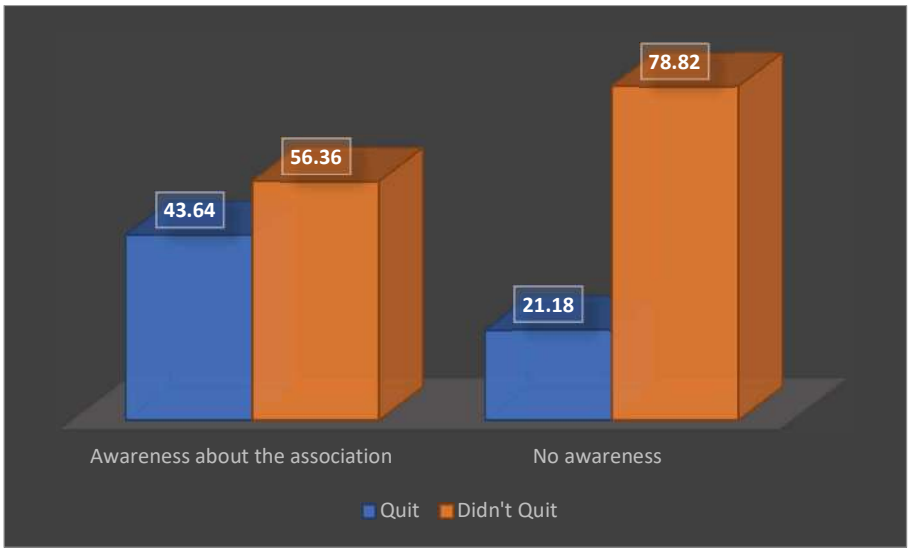


Figure 3. Association between Awareness and Quit Rate (%)

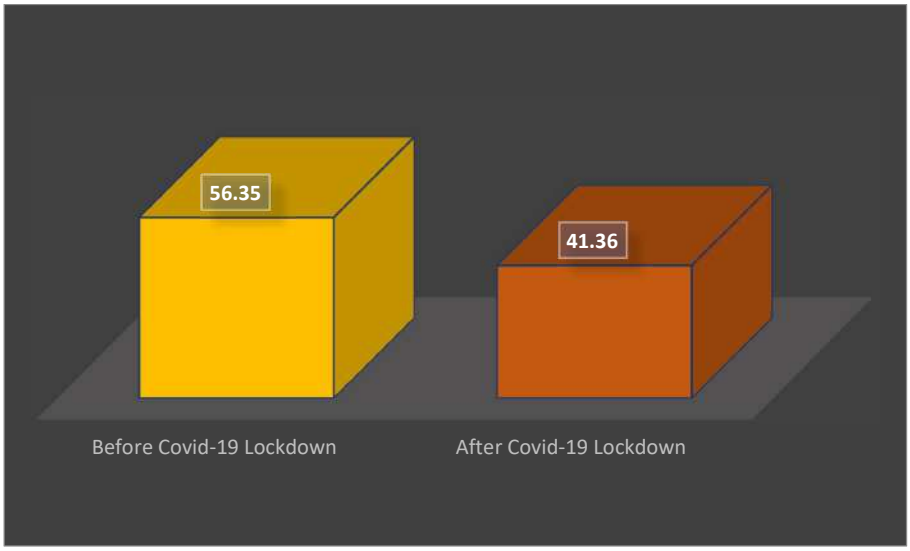


Figure 4. Prevalence (%) of Current Tobacco Users Before and After Lockdown showing a decreasing trend

Discussion

Using a series of monthly follow up, we observed changes in tobacco intake, reduction, attempts to quit from January 2020 till November 2020 when covid-19 lockdown was implemented by government. In the current study, 56.35% were current tobacco user, almost 90.75% participants were using smokeless form like chewing pan masala, gutkha and mawa masala also tobacco consumption was highly common in males (75.14%) as compared to females (24.85%); while as per Himanshu A. Gupte et al. [12] 46% were smokers, 45% smokeless tobacco users. The majority of participants, comprising 96%, were males, with an average age of 40 years. In alignment with S. Veeraiah et al.

[13], the mean age was 42.5 years (SD=14; range: 15–76), and the majority were males (n = 243, 97%). Out of the total participants, 101 (40%) were current tobacco users, with 61% being smokers, 35% using smokeless tobacco, and 4% employing both forms. Notably, almost two-thirds of the participants in the current study were unaware of the association between tobacco consumption and COVID-19. The quitting rate among individuals aware of the association between COVID-19 and tobacco was twice that of those who were unaware. This significant difference suggests a higher likelihood of quitting tobacco when a person is informed about the connection between tobacco consumption and COVID outcomes [p-value<0.05]. The reasons for quitting or reducing tobacco use in our study included the heightened prices or financial constraints and the unavailability of tobacco. This aligns with findings by Himanshu A. Gupte et al. [12], where 67% were unaware of the tobacco and COVID-19 association. The most common impacts reported were non-availability of tobacco products (45%) and increased prices (27%). Some users saw this as an opportunity to quit (24%), while a small proportion (4%) reported an increase in tobacco use due to heightened stress in the current context.

In the current study during follow up of 10 months, 49 participants had quit tobacco consumption completely but 3 participants started tobacco consumption for the first time; while as per Himanshu A. Gupte et al. [12] out of the contacted tobacco users, a total of 219 individuals (38%) claimed to have refrained from tobacco use since the onset of the lockdown. Notably, among those aware of the association between COVID-19 and tobacco use, the proportion of users who abstained was twice as high (51%) compared to those who were unaware (25%). According to Romain Guignard et al. [14], among current smokers, 26.7% reported an increase in tobacco consumption since the beginning of the lockdown (i.e., during the 2 weeks before the survey), 18.6% reported a decrease, while it remained stable for 54.7%. According to S. Veeraiah et al. [13], 64% of tobacco users reported a reduction in tobacco use during the lockdown, while usage remained unchanged for 20%, and it increased for 16%. A significant portion, nearly two-thirds (63%), expressed an intention to quit during the lockdown. Out of those with intentions to quit, 6% sought help or consultation, and 38% made an actual quit attempt during the lockdown. Interestingly, only 15% had the urge to increase tobacco use during this period. In our study, reduced tobacco use during the lockdown was associated with both the intention to quit (P = 0.02) and actual quit attempts (P = 0.01). Notably, over 50% of participants cited increased tobacco prices or financial constraints and unavailability of tobacco as reasons, with the least common reason being the 'opportunity to quit.' In contrast, Himanshu A. Gupte et al. [12] found that the main reason for stopping tobacco use was related to lockdown or concerns about the coronavirus, accounting for 51%. Additionally, as per S. Veeraiah et al. [13], more than half (56%) reported easy availability of tobacco products. During the lockdown, almost two-thirds (66%) of tobacco users bought tobacco products daily from shops, 27% had existing stocks, and the remaining 6% obtained tobacco from peers. The majority of tobacco users reported easy access to tobacco products, with a significant proportion being able to purchase them daily from shops during the

lockdown. The data indicates blatant breaches of lockdown regulations, particularly in the context of a strict ban on tobacco product sales in the city. Encouragingly, nearly two-thirds of tobacco users reported a reduction in tobacco use, with an equal number expressing an intention to quit during the lockdown. A recent study by Elling et al. [15,16] highlighted that smokers were more motivated to quit due to the heightened risk of contracting COVID-19 as a smoker and increased social support for tobacco cessation.

Conclusion

The COVID-19 pandemic and the ensuing lockdown have acted as substantial catalysts for various mental health challenges, such as anxiety and depression. Additionally, there has been a notable increase in unhealthy behaviors, including heightened tobacco consumption, as individuals seek coping mechanisms for negative emotions. However, within our study, a subgroup of participants saw the lockdown as a chance to decrease or quit tobacco use, and notably, some of them successfully initiated quit attempts. In our research, approximately 28.32% of participants managed to quit tobacco entirely, while 21.96% reduced their tobacco intake. To further increase the rate of successful quitting, it is imperative to implement effective measures aimed at motivating and supporting tobacco users in their cessation efforts. Another critical aspect of tobacco use that demands attention within the context of COVID-19 is the behavioral component. Smoking often involves repeated hand-to-mouth contact, which could elevate the risk of virus transmission from contaminated surfaces to the mouth. This behavior might inadvertently expose smokers to the virus, particularly in public settings or shared smoking areas. Addressing this concern necessitates comprehensive education and awareness initiatives regarding COVID-19 and tobacco. Remarkably, individuals who were aware of the link between COVID-19 and tobacco were more inclined to quit compared to those without awareness. Consequently, increasing awareness about the harmful effects of tobacco and fostering an environment with restricted access to tobacco products can play a role in partially reducing tobacco consumption. To sum up, the relationship between COVID-19 and tobacco usage is complex and worrisome. Tobacco use can undermine lung health, suppress the immune system, and instigate inflammation, collectively heightening the risk of severe outcomes in the context of COVID-19. Ceasing tobacco use not only contributes to long-term health but also plays a crucial role in alleviating immediate risks linked to the pandemic. It's vital for tobacco users to seek support and resources for quitting, alongside adhering to public health guidelines to minimize the risk of COVID-19 transmission. Combining these efforts can yield improved individual and public health outcomes in the fight against COVID-19.

Recommendation

Based on the research findings concerning COVID-19 and tobacco use, several recommendations can be put forth to mitigate the potential risks linked to tobacco consumption during the pandemic. It's important to recognize that tobacco is detrimental in any circumstance. Therefore, based on multiple follow-up assessments, in-depth interviews, and focus group discussions, a strong emphasis should be placed on deaddiction as the preferred

approach to address this issue. Primary care physicians and mental health specialists should take special care to consider this possibility. Healthcare professionals should conduct thorough assessments of their patients, ensuring a comprehensive examination that includes evaluating for signs of substance abuse. Additionally, sustaining ongoing research efforts to delve into the complex interplay between tobacco use and COVID-19 outcomes is crucial. This involves studying the impact of various tobacco products and shifts in smoking behavior during the pandemic. Such research forms the foundation for evidence-based policies and interventions aimed at diminishing the health risks linked to tobacco use, both in the context of COVID-19 and beyond.

Limitations of the study

This study has its share of limitations that merit acknowledgment. Firstly, the reliance on self-reported data introduces the possibility of recall bias, potentially leading to less than completely accurate information about participants' tobacco habits. Second, establishing causation is intricate due to confounding factors such as age, comorbidities, and socioeconomic status, which are interconnected with both tobacco use and COVID-19 outcomes. Furthermore, the dynamic nature of the COVID-19 pandemic and the emergence of new variants pose challenges in generalizing our findings across diverse time periods and regions. While our study provides valuable insights into potential associations, these limitations emphasize the need for cautious interpretation. It is advisable to consider multiple sources of evidence for a more comprehensive understanding of the impact of tobacco use on COVID-19.

Author Contributions

The manuscript has been read and approved by us and we believe that the manuscript represents honest work.

Conflict of Interest

The authors declares that they do not have conflict of interest.

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Ethical Approval

Ethical Clearance Certificate Reference Number IEC/CERTI/66/02/2020)

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ORIGINAL ARTICLE

Comparative Evaluation of Imaging Techniques for Paraspinal Muscle Fat Quantification

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Abstract

Introduction: Low back pain (LBP) is a prevalent health issue associated with morphological changes in paravertebral muscles. Magnetic resonance imaging (MRI) is effective in identifying muscle steatosis, with MR spectroscopy (MRS) considered the gold standard. However, MRS is limited by technical challenges, prompting interest in Dixon sequences for fat quantification. **Materials and Methods:** We conducted a study comparing Multi Echo VIBE Dixon with single-voxel MR spectroscopy in quantifying fat fractions in lumbar multifidus muscles of chronic LBP patients. Ninety-eight measurements from 49 patients were analysed. Qualitative and quantitative image analyses were performed, and statistical analysis was conducted using SPSS 27. **Results:** Significant positive correlation (correlation coefficient: 0.992, $p < 0.001$) was found between Dixon and MRS fat fraction measurements. Intra-class correlation coefficient was 0.991 ($p < 0.001$), indicating strong agreement. No proportion bias was observed. Factors such as age, sex, and spinal degeneration correlated positively with multifidus fat atrophy. **Conclusion:** T2*-corrected Dixon imaging aligns well with spectroscopic measurements, offering an accurate alternative for estimating paraspinal muscle fat content in chronic LBP patients. Further studies are needed to establish threshold values for Dixon imaging. Chronic LBP is associated with multifidus muscle atrophy and fat infiltration, highlighting the need for effective management strategies.

Keywords: Low back pain, multifidus muscle, MRI, Dixon imaging, MR spectroscopy.

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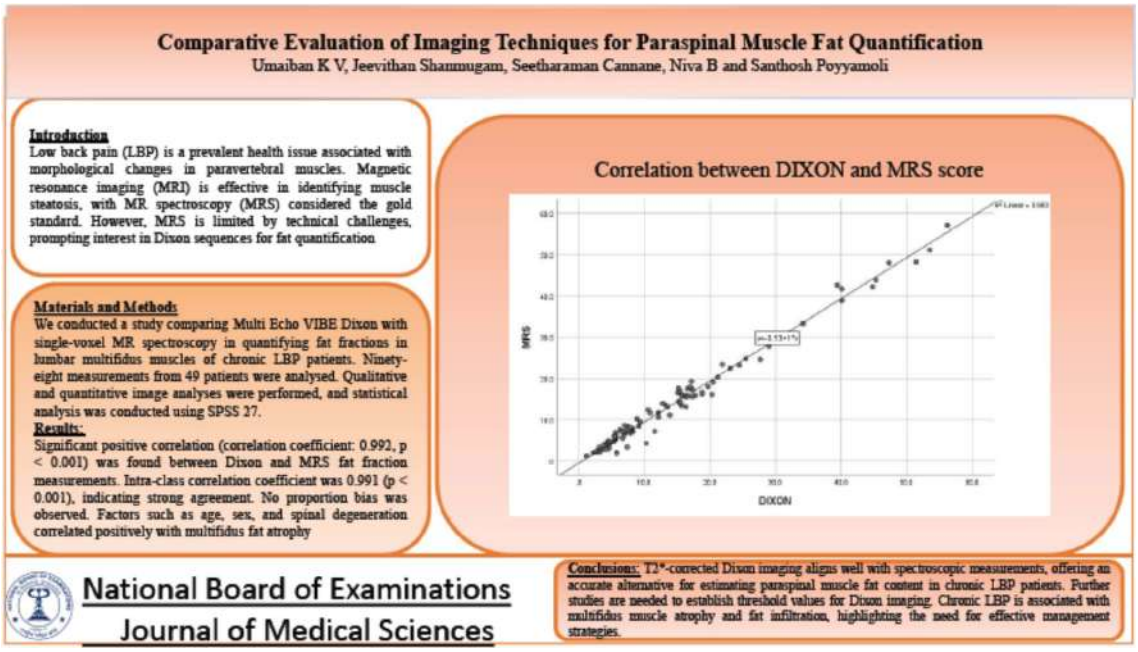
Graphical Abstract



Introduction

Low back pain (LBP) poses a significant health concern and is a primary cause of disability among working-age individuals. Over the past decade, the prevalence of low back pain in adults has doubled, with a particular rise noted in the aging population [1]. Scholars have long acknowledged the link between chronic low back pain and morphological alterations in the paravertebral muscles. Substantial research efforts have been dedicated to investigating fatty infiltrations and reductions in paravertebral muscle volume as potential clinical indicators for post-operative outcomes, spinal stability, and certain chronic conditions like age-related sarcopenia [2]. Histologically, the decline in muscle endurance often correlates with changes in muscle structure, such as atrophy of muscles and infiltration of fat, which can be identified through cross-sectional imaging techniques [3].

Among various imaging modalities such as ultrasonography, computed tomography, and magnetic resonance imaging (MRI), MRI stands out as the most objective and sensitive method for detecting and quantifying muscle steatosis. MR imaging offers superior accuracy in identifying and quantifying fat infiltration within the muscles of the lumbar spine, particularly in patients experiencing low back pain. MR spectroscopy, a technique within MRI, accurately displays increased fat signal fractions in lumbar paraspinal muscles and is considered the "gold standard" for fat quantification in MR imaging. This spectroscopic method has found widespread use in measuring fat deposition not only in the liver, heart, pancreas, and skeletal muscle but also in bone marrow [3-5]. Although MR spectroscopy is lauded for its ability to detect even minute amounts of fat, it is not commonly utilized in routine clinical settings due to several drawbacks. Firstly, the technique is time-consuming, which limits its feasibility for widespread use. Secondly, it requires specialized technical

expertise, making it challenging to perform reliably in routine practice. Additionally, MR spectroscopy is susceptible to sampling errors stemming from the arbitrary placement of the region of interest and the relatively low spatial resolution compared to other imaging modalities. These factors collectively contribute to its limited adoption in everyday clinical practice.[5] Quantitative Dixon sequences have emerged as a promising and dependable tool for both fat suppression and fat quantification [6]. When compared to MR spectroscopy (MRS), the Dixon method offers several notable advantages, including rapid and volumetric data acquisition, the visualization of anatomical structures, and the ability to determine fat content within a defined region of interest (ROI) [7]. Multi-echo variants that has been developed recently enhances the separation of fat and water signals consistently, correcting for confounders that may introduce systematic errors in fat-signal fractions.

The primary objective of our study is to compare Multi Echo VIBE Dixon with single-voxel MR spectroscopy in quantifying fat signal fractions within the lumbar paraspinal muscles. Specifically, we aim to estimate the degree of fat infiltration in the multifidus muscle among patients experiencing chronic low back pain. Additionally, we seek to explore whether factors such as age, sex, duration of pain, degenerative disc disease, nerve compression, and endplate changes exert any influence on the fat content of paraspinal muscles.

Materials and Methods

This study was conducted at the Radiology department of a tertiary care hospital in South India, with approval from the Institute's ethical and scientific committee and obtaining written informed consent from all research participants. The study included adult patients aged >18 years experiencing chronic low back pain (defined as “disabling pain in the lower spine persisting for more than 3 months”) who underwent MRI examination of the lumbosacral spine at the hospital between August 2019 and July 2021. Patients with general MRI contraindications, a history of prior spine surgery, or patient motion during acquisition were excluded, along with cases of inflammation that could interfere with total water fraction measurements. Those who were eligible for the study were contacted by the principal investigator and were explained about the background for the study, need for the study, its objectives and other ethical considerations. The Patient Information sheet was given to them, and adequate time was given to understand the contents. Those who were willing to participate were requested to sign the written informed consent form.

MRI sequences were supplemented by multi-echo Dixon and MR spectroscopy to quantify fatty degeneration of bilateral lumbar multifidus muscles at the L4-L5 intervertebral level.

A) MRI Technique

All MRI procedures were conducted using a 3.0 Tesla MRI system (Siemens) with dedicated spine coils. Standard clinical MR imaging protocols for low back pain assessment were performed, including whole spine T2 sagittal, lumbar spine T1 sagittal, IR sagittal, IR and T1 coronal SI joint, and T2 axial sequences. Additionally, a T2-weighted multi-echo VIBE Dixon sequence with 6 echoes was added to the protocol, providing water-

only, fat-only, fat fraction, and R2* mapping image series with corrections for multiple resonance lines in the fat spectrum. Single-voxel point-resolved MR spectroscopy was also acquired as a standard reference.

B) Qualitative Image Analysis

Standard MR imaging sequences were assessed for spinal degenerative features such as disc desiccation, facet arthropathy, endplate signal changes, nerve root compression, and spondylolisthesis, with findings recorded for each patient.

C) Quantitative Image Analysis

MR Spectroscopy (MRS)

Single voxel point-resolved MR spectra were obtained by placing spectroscopy voxels in bilateral multifidus muscles on axial T2-weighted MR images at the L4-L5 intervertebral level. Fat fraction (FF) was automatically calculated based on signals from fat and water at each echo time, with spectroscopy voxel positioning documented for reference in Dixon fat fraction mapping images.

Dixon

Regions of interest (ROIs) were drawn on automatically generated axial fat fraction mapping images from the T2*-corrected six-echo VIBE Dixon sequence, corresponding to the location of spectroscopic voxels. Two independent observers recorded FF values for Dixon and MRS, blinded to each other's measurements except for the voxel position. The diameter of the circular ROI was determined based on the voxel size of MR spectroscopy. Imaging parameters for Dixon were as follows:

- Echo Time: 1.05 ms
- Repetition Time: 9.00 ms
- Field of View (FOV): 450 mm
- Matrix: 111 x 160
- Bandwidth: 1080 Hz/Pixel
- Acquisition Time: 13 sec
- Slice Thickness: 3.5 mm

Data were inputted into an Excel spreadsheet and analyzed utilizing SPSS version 27. Categorical variables were depicted as proportions or percentages, while numerical variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR). To compare the Multi Echo VIBE Dixon with single-voxel MR spectroscopy in measuring fat signal fraction within the lumbar multifidus muscles of patients experiencing chronic low back pain, Spearman's rank correlation was utilized. The difference in mean fat fraction concerning study variables was evaluated using either the Mann-Whitney U test or Kruskal-Wallis test. Additionally, intra-class correlation was computed to assess the relationship between both methods. A Bland-Altman plot was generated to elucidate the agreement between the two techniques. Statistical significance was defined as a p-value below 0.05.

Results

A total of 98 measurements of spectroscopic fat fraction were obtained from 49 patients, evenly split between males and females. All patients underwent bilateral examinations, and those with incomplete assessments were excluded. Spectroscopic values served as the reference standard.

Age of the study participants ranged from 22 to 77 years, while the mean age was 50.56±14.01 years. The duration of back pain Ranged from 3 months to 6 years,

with a mean duration of 25.95±26.35 months. Most patients (67.3%) couldn't localize their pain, while 17.3% reported left-sided pain and 15.3% reported right-sided pain. Conditions observed included nerve compression (68.4%), facet arthropathy (48%), spondylolisthesis or spondylolysis at L4/L5 (12.2%), modic end plate changes (37.8%), and ligamentous flavum atrophy (26.5%). Additionally, 42.9% had mild disc desiccation, 25.5% had moderate desiccation, and 18.4% had severe desiccation (Table 1).

Table 1. Socio demographics and clinical parameters of study population

Parameter	Sub classification	FREQUENCY	PERCENTAGE
AGE	Below 30 years	9	9.1
	31 - 40 years	18	18.4
	41 - 50 years	20	20.5
	51 - 60 years	26	26.6
	Above 60 years	25	25.4
SEX	Male	48	49.0
	Female	50	51.0
SIDE OF PAIN	Indifferent	66	67.3
	Left	17	17.3
	Right	15	15.4
NERVE COMPRESSION	Present	67	68.4
	Absent	31	31.6
FACET ARTHROPATHY	Present	47	48
	Absent	51	52
SPONDYLOLISTHESIS/ SPONDYLOLYSIS AT L4/L5	Present	12	12.2
	Absent	86	87.8
ASSOCIATED MODIC END PLATE CHANGES	Present	37	37.8
	Absent	61	62.2
DISC DESSICATION	No	13	13.3
	Mild	42	42.9
	Moderate	25	25.5
	Severe	18	18.4

LIGAMENTUM FLAVUM ATROPHY	Present	26	26.5
	Absent	72	73.5

Table 2. ICC values for Fat measurement between DIXON and MRS

ICC	95% Confidence Interval		Significance	
	Lower limit	Upper limit	F Value	P Value
0.991	0.984	0.994	235.97	<0.001

Regarding fat content measurements, the mean percentage fat content of the multifidus muscle was 14.87±12.89 using the MRS method and 15.46±12.84 using the DIXON method. (Table 2) There was a strong positive correlation (correlation coefficient: 0.992, $p < 0.001$) between fat fractions derived from DIXON and MRS methods. The intra-class correlation coefficient between MRS and DIXON was 0.991 indicating strong agreement between the two methods (Fig. 1) Analysis of agreement limits showed no proportion bias between fat fraction values from MRS and DIXON (Fig. 2).

Statistical analysis revealed a positive correlation between multifidus fat atrophy, spinal degenerative factors, increasing age, and female sex. The association between disc desiccation grades and paraspinal muscle fat percentage also indicated higher fat fraction values with increasing severity of desiccation.

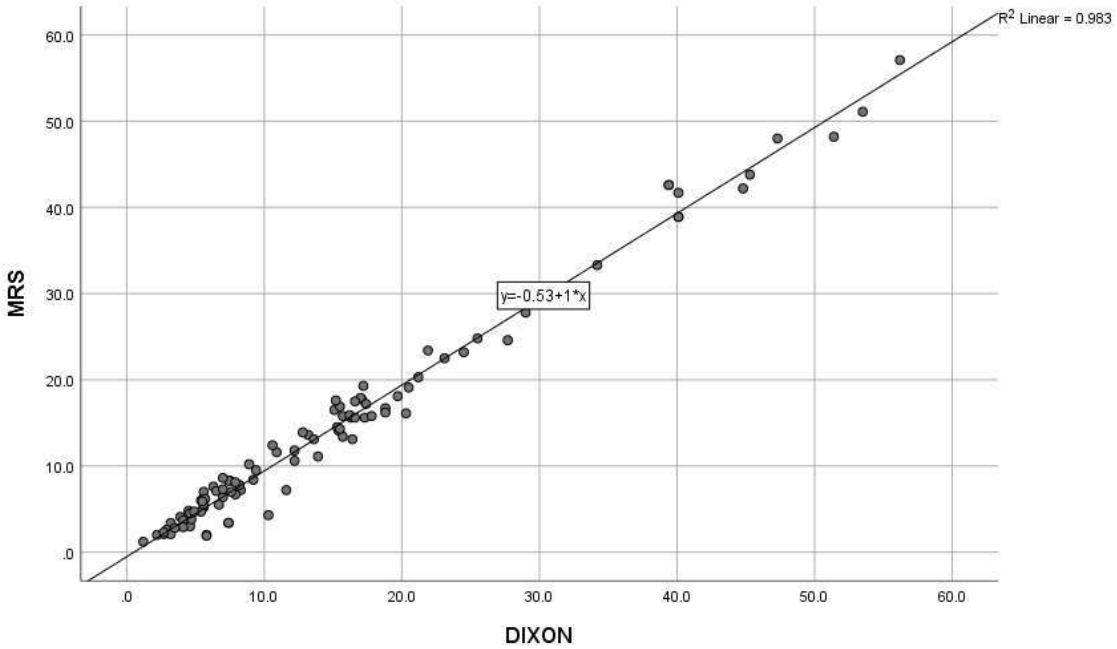


Figure 1. Correlation between DIXON and MRS score

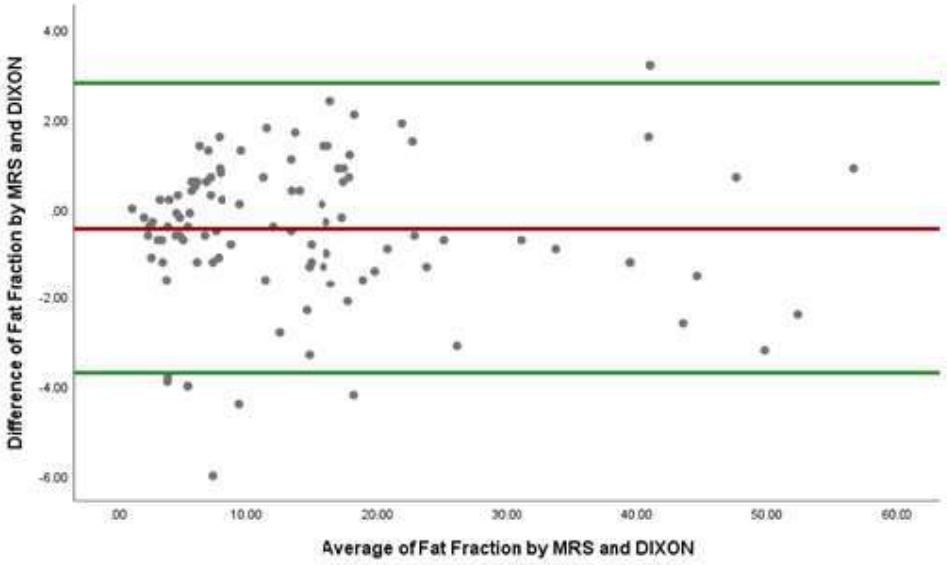


Figure 2. Bland Altman Plot

Discussion

MRI is widely acknowledged as a reliable and effective method for investigating muscles due to its excellent soft-tissue contrast. Continuous advancements in technology, along with the introduction of new sequences and tools, have led to improving accuracy in assessing pathological changes in tissues [8]. Many studies have emphasized the importance of quantitatively evaluating muscle fat content for precise detection and grading of diseases, even when muscles are minimally affected [9]. Advanced MR imaging techniques, such as MR spectroscopy, have been utilized to evaluate and quantify fatty atrophy in muscles such as the supraspinatus and paraspinal muscles. There has been considerable research focused on quantifying local fat levels in skeletal muscle, liver, and bone marrow lesions using various techniques. Among these, single-voxel MRS imaging is commonly considered the gold standard for accurate local fat analysis in vivo [4]. However, MRS poses technical challenges and is prone to sampling errors due to its low spatial resolution [5]. Conversely, Dixon sequences enable precise analysis of muscle fat and its distribution in large volumes with superior spatial resolution and minimal sampling errors in clinical settings [7].

In this study, we aimed to validate whether chemical shift imaging with Dixon sequences could accurately calculate the fat percentage of paraspinal skeletal muscles, comparable to MRS.

Our study yielded consistent findings, demonstrating a significant positive correlation between fat fraction measurements obtained from T2-corrected multi-echo Dixon and MR spectroscopy. Several researchers have investigated the quantification of skeletal muscle fat using MR imaging in various anatomical regions, such as thigh muscles, rotator cuff, and paraspinal muscles, employing the Dixon technique with or without T2 correction.

Yoo et al., in their study, highlighted that fat fraction derived from T2-corrected six-echo VIBE Dixon sequences displayed superior agreement with MR spectroscopic fat fraction data, in

contrast to non-T2 corrected two-echo and T2-corrected three-echo VIBE Dixon data. This finding is consistent with previous research in liver fat fraction analysis, which has demonstrated that T2 correction enhances the precision of fat fraction calculation in multi-echo VIBE Dixon sequences [10].

Contrary to the findings by Yoo et al., Fisher et al. observed that T2 correction did not result in a stronger correlation compared to non-T2 corrected multi-echo sequences when compared with spectroscopic fat fraction data. They proposed that this inconsistency might be due to the decrease in signal-to-noise ratio (SNR) that occurs following T2 correction [9]. Another study by Gaeta et al. reported that T2 correction did not offer greater benefits than the non-T2 corrected method in skeletal muscle fat quantification [11].

Although the necessity of T2 correction for estimating skeletal muscle fat remains uncertain, we opted to incorporate T2 correction into the six-echo VIBE Dixon sequence. This decision was based on the consideration of potential factors that could induce T2 decay in skeletal muscle. Multiple investigations have underscored the association between chronic low back pain and the reduced strength and endurance of paraspinal muscles [12,13]. However, whether these changes are causative factors or consequences of back pain remains a subject of debate. Researchers have specifically noted that among paraspinal muscles, fatty degeneration in chronic low back pain is particularly prominent in the multifidus muscle, which plays a crucial role in lumbar segmental stability [14].

Kjaer et al. presented compelling evidence from a sizable population sample, demonstrating a robust association between fat infiltration in the lumbar multifidus muscle and low back pain in adults [15]. Likewise, Mengiardi et al. discovered significantly elevated fat content in the multifidus muscles of individuals experiencing low back pain compared to asymptomatic volunteers, with no notable difference observed in the fat content of the longissimus muscle. In our investigation, we observed that the percentage of multifidus fat content in patients with chronic low back pain was around 15%, which is notably lower than the 23.6% reported by Mengiardi et al. [5] This discrepancy may be attributed to differences in patient selection criteria and the average duration of symptoms in our patients was shorter compared to those in prior studies, although the age of patients was comparable.

Our study revealed a significant correlation between age and gender with multifidus fat fraction, suggesting that differences in body composition may contribute to variations in multifidus muscle fat content between males and females. This raises questions regarding whether grading scales and cutoff points for fat percentage should be unique for each gender. Additionally, we observed a higher prevalence of fat infiltration in paraspinal muscles among the elderly, irrespective of the duration of back pain [16].

However, further longitudinal studies are needed to elucidate the extent to which age and duration of low back pain contribute to the development of fat atrophy in the lumbar multifidus muscle. Numerous authors have reported declines in cross-sectional area (CSA) and density of back muscles with age, underscoring the importance of considering age as a confounding factor in studies evaluating the association between paraspinal muscle fat

content, spinal degeneration, and low back pain. Additionally, personal factors such as activity level, smoking, type II diabetes mellitus, and cardiovascular diseases may influence fatty infiltration of paraspinal muscles, necessitating further investigation into these influences.

Although body mass index (BMI) was not recorded in our study subjects, previous research has failed to establish a significant association between BMI and muscle fat concentration. Similarly, the thickness of subcutaneous fat has not been found to correlate significantly with the quantity of fat accumulated in muscles [17].

We observed a positive correlation between spinal degeneration features such as disc desiccation, facet arthropathy, modic endplate changes, nerve compression, ligamentum flavum hypertrophy, and spondylolisthesis with multifidus fat content. Disc desiccation and modic endplate changes were found to be independently associated with increased fat percentage of the multifidus muscle.

While lumbar disc herniation with compression of nerve roots can lead to muscle dysfunction [18], we did not observe a statistically significant correlation between the side of pain and muscle fat atrophy in our study. However, severe fatty infiltration of the lumbar multifidus muscle was observed in a patient with unilateral disc protrusion and severe nerve compression on the same side, indicating a potential link between nerve compression and muscle fat atrophy [19].

Numerous studies have reported associations between spinal degeneration, spinal muscular fat, and low back pain. However, it remains unclear whether fat infiltration of the lumbar multifidus muscle serves as a prognostic indicator or if patients with both low back pain and multifidus fat atrophy require special treatment [20,21].

Our study has limitations, including its single institutional nature with a limited number of subjects. Additionally, we used MR spectroscopy as the standard of reference rather than conventional histopathology confirmation via muscle biopsy, which is invasive and may not always be feasible due to ethical concerns. Moreover, clinical data such as pain intensity, functional ability, BMI, and level of physical activity were not evaluated in our study, and there was no control group.

Conclusion

Our study demonstrates that T2-corrected multi-echo VIBE Dixon measurements align well with T2-corrected spectroscopic measurements of fat fraction estimates in the lumbar multifidus muscles of patients with chronic low back pain. Therefore, T2*-corrected Dixon imaging can be favoured over MR spectroscopy in routine clinical practice as it offers an accurate alternative for estimating paraspinal skeletal muscle fat content. However, further large-scale studies are warranted to establish threshold values for chemical shift Dixon imaging that indicate fatty degeneration within the muscle.

Chronic low back pain is associated with atrophy and fat infiltration of the multifidus muscle. Our findings also reveal a significant association between various spinal degenerative factors and multifidus fat infiltration. It is crucial to conduct further research to determine the effectiveness of specific approaches for managing low back pain and preventing progressive fat infiltration of the lumbar paraspinal muscles and spinal degeneration.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

Ethics approval

Ethical approval obtained from all patients.

Human and animal rights

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

For this type of study formal consent is not required.

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ORIGINAL ARTICLE

Assessment of PSR as a Novel Parameter in Perfusion Imaging for CNS Tumor Characterization: An Observational Study

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Abstract

Introduction: Magnetic resonance imaging (MRI) has emerged as the primary modality for diagnosing and evaluating central nervous system (CNS) tumors, transitioning from structural to functional assessment. Advanced MRI techniques, including MR spectroscopy and perfusion imaging, offer insights into functional, metabolic, and hemodynamic changes in addition to structural abnormalities. The study aims to assess the role of PSR (Post-Contrast Signal Recovery) alongside rCBV (Relative Cerebral Blood Volume) and rPSR (Relative Percentage of Signal Recovery) in differentiating grade IV glioma, solitary brain metastasis, and primary CNS lymphoma. **Materials and Methods:** An observational study was conducted on 38 patients with lymphoma, metastases, and grade IV glioma, utilizing DSC (Dynamic Susceptibility-Weighted Contrast-Enhanced) perfusion imaging and histopathology reports. Sociodemographic, clinical, and MRI parameters were collected. PSR measurements were obtained from perfusion maps using dedicated software. Statistical analysis was performed using SPSS version 27.0. **Results:** Among the study population, the mean age was 54.16±12.47, with male predominance (63.2%). Conventional imaging characteristics revealed significant differences, including T2 hypo intensity in lymphoma and FLAIR hyperintensity in all gliomas. Perfusion parameters showed higher rCBV in metastases and grade IV glioma compared to lymphoma, whereas PSR and rPSR were higher in lymphoma. PSR and rPSR effectively differentiated among the tumor types ($p<0.001$). **Conclusion:** Our study underscores the critical role of advanced MRI techniques, particularly DSC perfusion imaging, in differentiating between grade IV gliomas, solitary brain metastases, and primary CNS lymphomas. PSR emerges as a valuable parameter alongside rCBV and rPSR, demonstrating potential for accurate tumor characterization.

Keywords: Magnetic resonance imaging, CNS tumors, PSR, rCBV, rPSR

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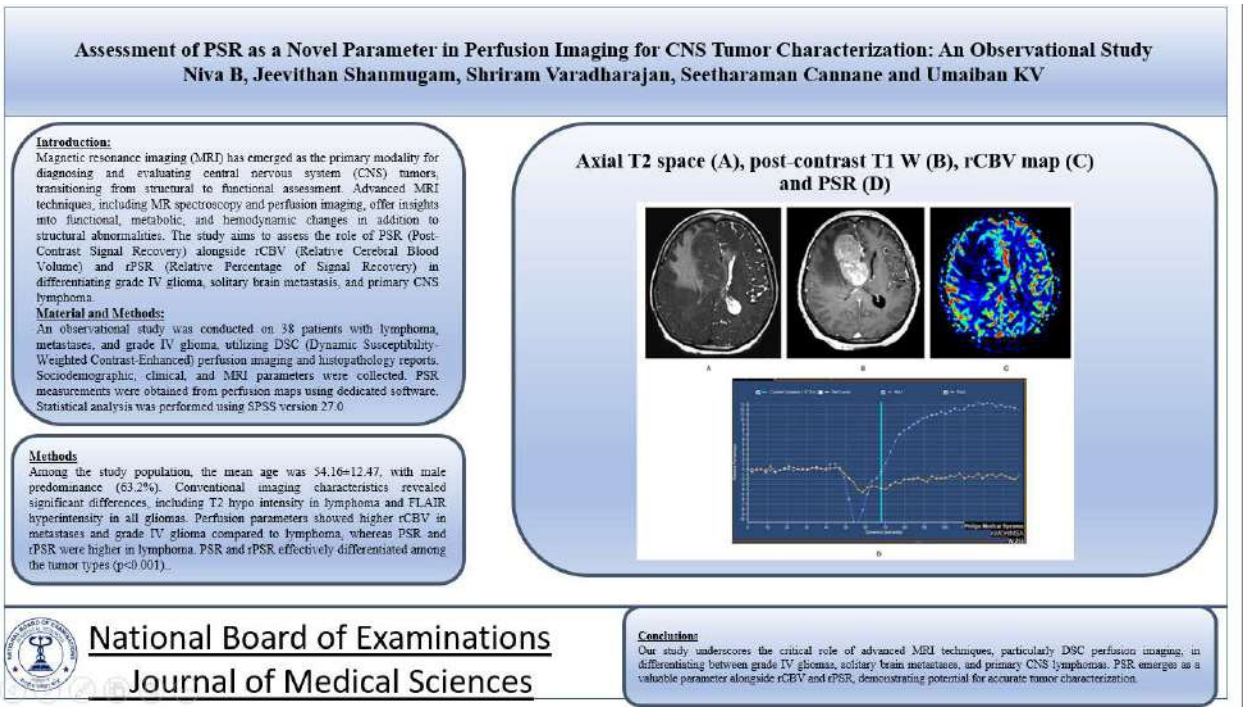
Graphical Abstract



Introduction

Magnetic resonance imaging (MRI) after its widespread availability has evolved as the imaging modality of choice in the diagnosis and evaluation of CNS tumors. The role of neuroimaging in brain tumors has advanced from purely structural to functional imaging. Apart from assessing structural abnormality and tumor-related complications, MRI is also used to identify functional, metabolic, hemodynamic, cellular, and cytoarchitectural changes. Advanced MRI techniques are now commonly used in the evaluation of brain tumors. These include MR spectroscopy for metabolite assessment and perfusion imaging for microvascular characterization. Often these advanced imaging techniques are useful in predicting the grade of the neoplasm and its biological behavior, especially given the recent modifications in the WHO classification. These may in the future be incorporated into radiogenomic signatures. In 2016, the World Health Organization revised its basic classification of primary brain tumors to incorporate genetic information and molecular status superseding histological grade.

There is considerable intersect in the conventional MRI appearances of common intracranial malignant lesions, such as gliomas, metastases, and lymphoma. Early Prompt diagnosis is important as management differs in these three groups. Although the histopathological examination is the gold standard for the diagnosis of brain tumors, it carries an inherent risk of sampling bias. Molecular status and advanced imaging can therefore supplement routine work up such as conventional imaging for more accurate diagnosis and prognostication. Therefore, newer techniques in MRI should

be utilized to differentiate between these various brain tumors.

Dynamic susceptibility-weighted contrast-enhanced (DSC) MRI is a perfusion imaging that is used to assess the capillaries and microvascular characteristics of these tumors. Relative cerebral blood volume (rCBV) is a commonly used perfusion parameter that is a marker of vascularity and neo-angiogenesis in brain tumors. It is considered as one of the most important hemodynamic variables used in the characterization of tumors. In lymphomas, rCBV is lower than in gliomas and metastases owing to the lack of neo-angiogenesis. However, rCBV values often overlap in gliomas and metastases. Percentage of signal recovery (PSR), which is a lesser utilized DSC derived parametric, plays an important role in such cases.

PSR, or Post-Contrast Signal Recovery, denotes the proportion of signal intensity regained following the initial administration of contrast relative to the baseline signal intensity (before contrast administration). Initially, there is a decline in signal intensity after the contrast agent is administered, which gradually reverts towards the baseline due to the first pass circulatory effect. The extent of this recovery determines the PSR value and is influenced by various factors such as contrast agent leakage, extravascular space size, and blood flow rate [1-6].

There are reports of low values of PSR in metastatic lesions, intermediate in glioblastoma (GBM), and high (overshooting) in primary central nervous system lymphomas (PCNSL). The relative percentage of signal recovery (rPSR) is a related parameter whose role is still under evaluation. Hence in this study, we wanted to evaluate the role of PSR as compared to rCBV and rPSR in differentiating grade IV glioma, solitary brain metastasis, and primary CNS lymphoma.

Materials and Methods

We conducted an observational study in the Department of Radiology, Kovai Medical Centre and Hospital, Coimbatore. In our study, 38 patients with lymphoma, metastases, and grade IV glioma with optimum DSC perfusion imaging and histopathology report during the period of August 2019 to July 2021 were included after discussing with the participants about the need for the study, objectives and other ethical issues concerned. Patient information was given to the participant. Ample time was given to the study participant for understanding the study. Once they agreed to participate, written informed consent was obtained. A structure clinical proforma was designed for the study. Sociodemographic variables, clinical history/ findings and MRI parameters were elicited. None of the lymphoma patients had signs of immunosuppression and no patient had signs of systemic involvement. Only patients with solitary metastasis were included in this study.

Exclusion criteria included general contraindications for MRI, incomplete studies due to various reasons like an uncooperative patient, poor image quality, and extensive artifacts. Those who had contraindication for MRI contrast were also excluded.

Imaging was performed with either a 1.5 T [Ingenia; Philips Medical Systems] or 3T [MAGNETOM Skyra; Siemens Healthcare]. Our tumor protocol included T1 in three orthogonal planes, coronal T2, axial T2 FLAIR, SWI, DWI axial, ADC, MR spectroscopy, and post-contrast T1 images in all 3 planes. Using a gradient recalled T2*weighted echo-planar imaging sequence (ep2d_perf), DSC imaging was performed.

Parameters used in 1.5 T were as follows:

- TR/TE of 2341/40 ms,
- FOV of 220 mm,
- Voxel size of 2.4 x 2.4 x 5 mm,
- Slice thickness of 5 mm.
- A total of 30 image volumes each with 40 image sets were acquired (a total of 1200 images), in which the first 5 image volumes were acquired before starting the contrast agent injection to establish a pre-contrast baseline. At the end of the 5th image volume, 0.1-0.2mmol/kg gadolinium contrast was injected using a power injector at a rate of 2.5-3 ml/s through an 18 or 20 G intravenous catheter. This was immediately followed by a bolus injection of saline (a total of 20 ml at the same flow rate).

Parameters used in 3 T were as follows:

- TR/TE of 2340/30 ms,
- FOV of 220 mm,
- Voxel size = 1.7 x 1.7 x 4 mm,
- Slice thickness= 4 mm.
- A total of 30 image volumes each with 60 image sets were acquired (a total of 1800 images), in which the first 5 image volumes were acquired before starting the contrast agent injection to establish a pre-contrast baseline. At the end of the 5th image volume, 0.1-0.2mmol/kg gadolinium contrast was injected using a power injector at a rate of 2.5-3 ml/s through an 18 or 20 G intravenous catheter. This was immediately followed by a bolus injection of saline (a total of 20 ml at the same flow rate).

PSR measurement

All perfusion data were transferred to a stand-alone workstation for post-processing using dedicated advanced software packages [Neuro Perfusion Evaluation, Syngo multimodality workplace (MMWP) VE61B, Siemens Healthcare Gmbh, Germany or T2* MR Neuro Perfusion, IntelliSpace Portal (ISP) Version 9.0, Philips Medical Systems Netherlands B.V.]. From the processed perfusion images color-coded CBV maps were obtained. For PSR measurement, an ROI (Region of Interest) of 25-40 mm^2 was drawn on the perfusion maps carefully excluding areas of necrosis or hemorrhage. The signal intensity curves were thus obtained and the PSR value was calculated as follows:

$$PSR = 100\% \times (S_1 - S_{min})/ (S_0 - S_{min})(1,2),$$

Where,

S_0: baseline pre-contrast T2*W signal intensity.

S_1: recovered post-contrast T2*W signal intensity.

S_{min}: minimum T2*W signal intensity

Another ROI was simultaneously placed in the contralateral normal-appearing brain and rPSR was calculated as follows:

rPSR= PSR (lesion)/PSR (contralateral normal brain)(3).

Statistical analysis

The data were entered into MS Excel and analyzed using Statistical Package for Social Sciences (IBM SPSS) version 27.0. Sociodemographic variables were analyzed as proportions or percentages for categorical variables, either mean ± SD or Median (IQR) were analyzed for numerical variables. The difference in mean between the different types of tumors was analyzed using the Kruskal Wallis test. A Chi-square test was used to analyze the relationship between various study variables and different types of tumors. The p-value <0.05 was considered statistically significant.

Results

A total of 38 patients including 24 high-grade IV gliomas, 7 primary CNS lymphomas (PCNSLs), and 7 brain metastases were included in the study. In our study, the mean age of the participants was 54.16±12.47. Out of 38 patients, 24 (63.2%) were male and 14 (36.8%) were female. The most common location of the tumors included in our study was frontal parenchyma (47.4%). Baseline signal characteristics on conventional imaging were analyzed. Lymphoma was the only tumor to show frank T2 hypointensity more commonly while all gliomas showed FLAIR hyperintensity (Table 1). Thus, these signal characteristics on the T2 weighted image and FLAIR were found to be statistically significant. Among the various other p

arameters studied, SWI blooming and cystic necrosis were also found to be statistically significant. Blooming on SWI was found in 45.8% of patients in the grade IV glioma group and 85.7% in the metastases group. Cystic necrosis was present in 45.8% of patients in the grade IV glioma group and 85.7% in the metastases group (Table 1). Figures 1, 2 and 3 show the representative conventional images of a case of CNS lymphoma, solitary brain metastasis, and grade IV glioma.

Among perfusion parametrics, the mean rCBV value was higher in metastases (3.23±0.51) and grade IV glioma (3.08±0.67), whereas low in lymphoma (1.14±0.25) with a p-value of <0.001. The mean PSR value was lower in metastases (56.03±7.87) and grade IV glioma (80.69±6.48), whereas higher in lymphoma (146.13±40.97) with a p-value of <0.001. The mean rPSR value was lower in metastases (0.69±0.03) and grade IV glioma (0.92±0.05), whereas higher in lymphoma (1.84±0.68) with a p-value of <0.001, which is statistically significant. In our study, we found that PSR and rPSR values can differentiate lymphoma, metastases, and grade IV glioma lesions (Table 2).

Chi-square test was done for various categorical variables measured to find out if any association is present with the HPE diagnosis. There was no significant difference between the HPE diagnosis and sex, Laterality, Location of tumor, supra/ infratentorial region, Predominant signal on T1, Diffusion restriction of solid component and Lipid Lactate Peak.

Table 1. Distribution of study population according to Socio demographic and clinical variables

Variables	HPE						χ^2 Value	p Value
	Lymphoma		Grade IV glioma		Metastases			
	n=7	%	n=24	%	n=7	%		
Age								
≤60	3	42.9	18	75	6	85.7	3.620	0.164
>60	4	57.1	6	25	1	14.3		
Sex								
Male	6	85.7	14	58.3	4	57.1	1.880	0.391
Female	1	14.3	10	41.7	3	42.9		
Predominant signal on T1 weighted image								
Hypointense	4	57.1	15	62.5	2	28.6	2.536	0.281
Isointense	3	42.9	9	37.5	5	71.4		
Predominant signal on T2 weighted image								
Hypointense	1	14.3	0	0	0	0	11.283	0.024
Isointense	1	14.3	0	0	2	28.6		
Hyperintense	5	71.4	24	100	5	71.4		
Signal on Flair								
Hyperintense	5	71.4	24	100	5	71.4	7.664	0.022
Isointense	2	28.6	0	0	2	28.6		
Perilesional edema								
Mild	1	14.3	13	54.2	0	0	12.722	0.013
Moderate	5	71.4	10	41.7	4	57.1		
Marked	1	14.3	1	4.2	3	42.9		
SWI blooming	0	0	11	45.8	6	85.7	10.433	0.005
Cystic necrosis	0	0	11	45.8	6	85.7	10.433	0.005
Diffusion restriction of solid component	7	100	22	91.7	6	85.7	1.000	0.607
Lipid lactate peak	4	57.1	6	30	4	80	4.717	0.095
Enhancement of solid component	5	71.4	21	87.5	7	100	2.252	0.283

Table 2. Comparison of Mean rCBV, PSR, rPSR with HPE diagnosis

HPE	**Maximum rCBV**			**PSR**			**rPSR**		
	Mean	**SD**	**Median (IQR)**	**Mean**	**SD**	**Median (IQR)**	**Mean**	**SD**	**Median (IQR)**
Lymphoma	1.14	0.25	1.03 (0.96-1.46)	146.13	40.97	150 (106.1-186.7)	1.84	0.68	2.05 (1.04-2.42)
Grade IV glioma	3.08	0.67	3.06 (2.52-3.70)	80.69	6.48	81.65 (75.53-86.83)	0.92	0.05	0.92 (0.91-0.96)
Metastases	3.23	0.51	3.04 (2.88-3.72)	56.03	7.87	53.4 (51.6-62.8)	0.69	0.03	0.70 (0.67-0.71)
Kruskal Wallis Value	17.077			26.742			20.401		
p Value	<0.001			<0.001			<0.001		

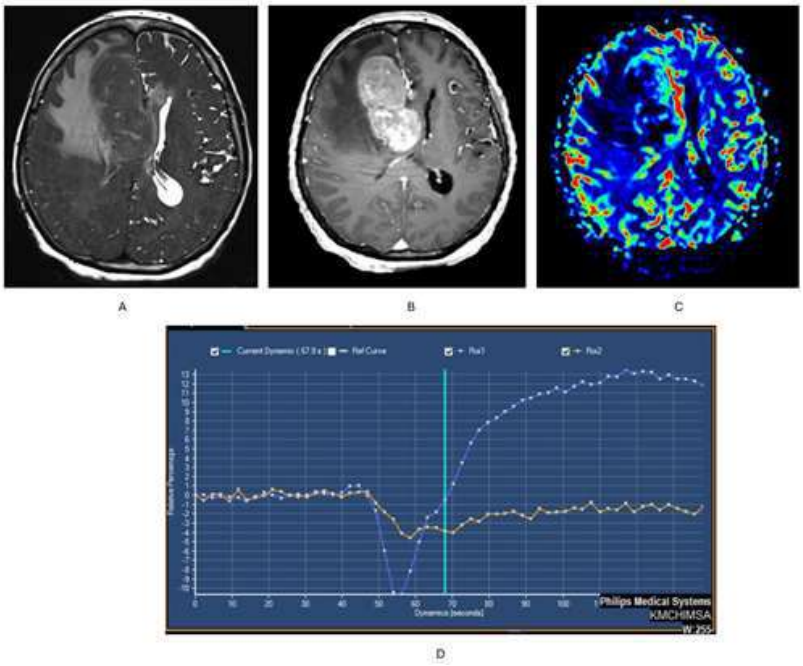


Figure 1: Axial T2 space (**A**), post-contrast T1 W (**B**), rCBV map (**C**) and PSR (**D**) images in a case of lymphoma show a well-defined solid intra-axial mass lesion involving the right parasagittal frontal parenchyma which appears relatively hypointense on T2, shows heterogeneous enhancement, relative hypoperfusion with few eccentric areas of raised rCBV and high PSR with overshooting.

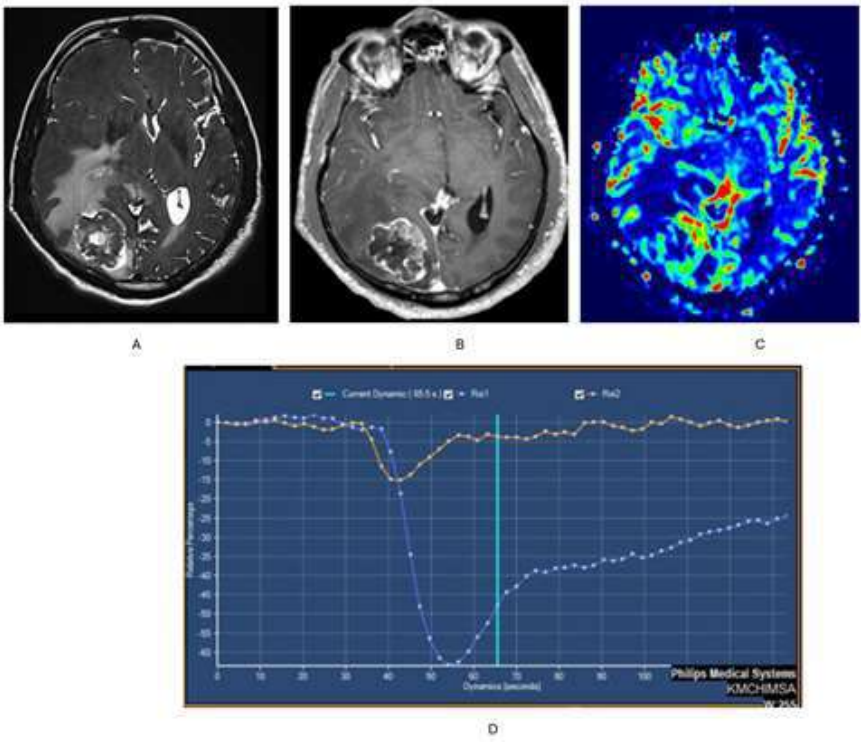


Figure 2. Axial T2 space (**A**), post-contrast T1 W (**B**), rCBV map (**C**) and PSR (**D**) images in a case of solitary brain metastasis show an irregular solid intra-axial lesion in the right occipital lobe. It appears heterointense on T2 with central cystic area, enhancement of solid component on post-contrast images, increased perfusion in enhancing component and low PSR

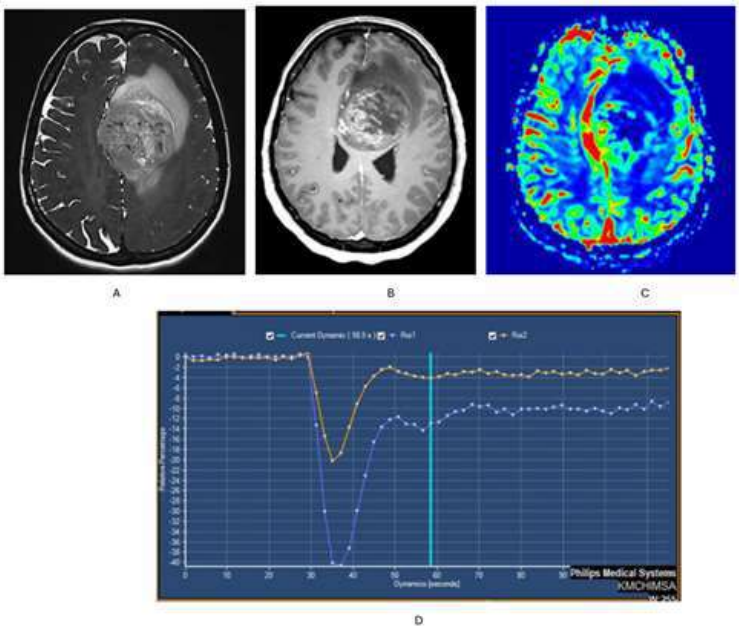


Figure 3. Axial T2 space (**A**), post-contrast T1 W (**B**), rCBV map (**C**) and PSR (**D**) images in a case of glioblastoma show an ill-defined infiltrative intra-axial left parasagittal lesion involving superior frontal and cingulate parenchyma which appears heterointense on T2, shows heterogenous post-contrast enhancement with internal necrosis and anterior non-enhancing areas, increased perfusion in enhancing component and intermediate PSR.

All those who were diagnosed with Glioma had hyperintensity on T2 and FLAIR compared to 71.4% in lymphoma and metastasis. SWI blooming and cystic necrosis was not present in Lymphoma, it was present in 45.8% of Glioma and 85.7% in Metastasis.

Discussion

In this study, we looked at the role of T2* MRI perfusion imaging, focusing on the lesser utilized parametric namely the percentage signal recovery (PSR) in the differentiation of the various malignant brain tumors, and compared its diagnostic accuracy with the more commonly used perfusion parameter, relative cerebral blood volume. This study included high-grade gliomas (Grade IV gliomas/GBMs), CNS lymphomas, and solitary metastases. Accurate diagnosis of these tumors is crucial for preoperative treatment planning and prognostication. There is a substantial difference in management strategies for these brain tumors. Although histopathology is the gold standard, surgical methods are invasive and even within certain tumors have sampling bias. Pre-operative diagnosis can help the surgeon decide on the optimal treatment strategy. Although conventional MRI helps narrow down the differential diagnosis of a brain tumor, its diagnostic accuracy in their differentiation is low and can be increased using advanced imaging methods such as perfusion and spectroscopy. Considerable overlap exists in the signal characteristics on conventional sequences among these tumors. Advanced imaging adds as an adjunct in further narrowing the differential and excluding certain tumors on many occasions. Among the various perfusion methods, T2* is the most used technique, and relative cerebral blood volume is the most common parameter studied. Although percentage signal recovery has been additionally studied as a parameter in various previous studies, it has not been routinely incorporated into the imaging guidelines and practice protocols. In our study, we have included advanced perfusion parameters of the common brain tumors namely grade IV glioma, PCNSL, and solitary brain metastases. We aimed to evaluate their role in the accurate diagnosis of these brain lesions. We have also tried to compare the diagnostic accuracy of the perfusion parameters like rCBV, PSR, and rPSR using histopathology as the gold standard.

In our study, almost all the grade IV glioma and lymphoma cases were supratentorial in location. This correlates well with other studies in the past which have also shown that nearly all GBMs were localized to the supratentorial parenchyma [7].

With respect to signal characteristics, T2 and FLAIR signals were found to be discriminatory. It also varies according to the immune status. Prior literature has shown that the T2 hypointensity usually seen in lymphomas may be attributed to the high nuclear-cytoplasmic ratio [8]. All grade IV gliomas in this study showed hyperintense signal on FLAIR as compared to 70% of the other two groups, which was statistically significant. This is similar to a prior study done by Elghany et al. [9], where the majority of GBM (98.1%) were hyperintense.

It is important to differentiate PCNSL from other tumors as the first line of treatment for lymphoma is chemotherapy and not surgical resection [10]. We have found that PCNSL has low rCBV as well as higher PSR and rPSR values. Possibly here, the T1 effect is dominant over the T2* effect leading to the overshoot above baseline. Other factors like cellularity, blood volume, and vascular permeability may also have a role in this [11-13]. Even though the signal intensity curve of PCNSL showed characteristic overshoot, the diagnostic performance of rCBV was found to be better than PSR. Nonetheless, both the parameters were significant with varying thresholds.

Due to the significant overlap of the perfusion values in gliomas and metastases, rCBV was not sensitive enough to differentiate between grade IV glioma and metastases with similar higher values. However, the mean PSR was statistically significant among these groups. We reckon that metastases produce more pronounced T2* effects due to prominent capillary fenestration and the lack of BBB integrity, whereas high-grade gliomas demonstrate moderate T2* effects due to lesser capillary fenestration and partial disruption of BBB components [14-16].

Conclusion

Our study underscores the critical role of advanced MRI techniques, particularly DSC perfusion imaging, in differentiating between grade IV gliomas, solitary brain metastases, and primary CNS lymphomas. PSR emerges as a valuable parameter alongside rCBV and rPSR, demonstrating potential for accurate tumor characterization. These findings emphasize the significance of incorporating advanced imaging modalities into routine clinical practice, aiding in early and precise diagnosis, thereby facilitating tailored therapeutic interventions for improved patient outcomes.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

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Ethics approval

Ethical approval obtained from all patients.

Human and animal rights

This article does not contain any studies with human participants or animals performed by any of the authors.

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REVIEW ARTICLE

Review of National Suicide Prevention Strategy and Other Suicide Prevention Initiatives in India

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Abstract
India's launch of the National Suicide Prevention Strategy in 2022 underscores the gravity of suicides as a pressing public health issue. Globally, suicides rank as the fourth leading cause of death among individuals aged 15 to 29, with low and middle-income countries bearing the brunt. Within India, suicides increased by 7.2% from 2020 to 2021, with Maharashtra and Tamil Nadu reporting the highest numbers. Despite decades of initiatives, including the National Mental Health Program (NMHP) since 1982, challenges persist in policy implementation, skilled manpower, and political hurdles, impeding desired outcomes. While commendable, the recent National Suicide Prevention Strategy faces limitations in execution. A critical review of government efforts reveals gaps in resource allocation and execution, hindering the impact of mental health programs. Addressing these challenges demands enhanced policy implementation, mental health infrastructure, and resource allocation. Additionally, public awareness and destigmatization are crucial components. In conclusion, India's efforts in suicide prevention reflect progress, yet significant gaps remain. Sustained commitment and innovative strategies are needed to mitigate the escalating burden of suicides. This review underscores the urgency for comprehensive measures to combat rising suicide rates effectively.

Keywords: Suicide, National Suicide Prevention Strategy, India

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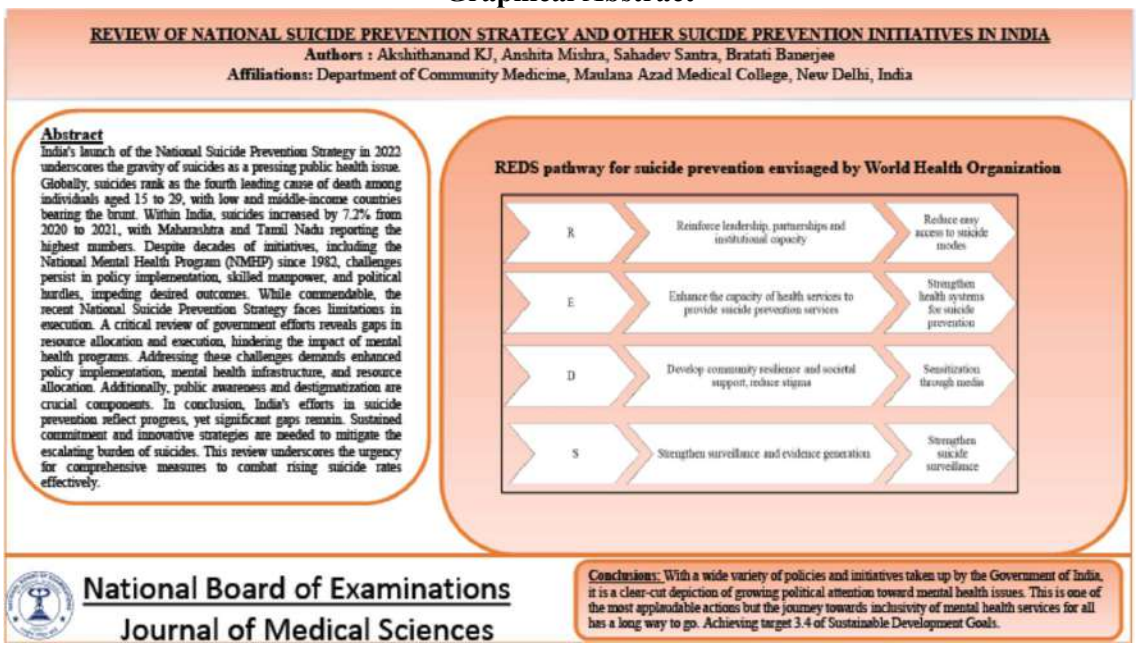
Graphical Abstract



Background

Mental health, as defined by the World Health Organization (WHO), is integral to overall well-being and is affected by disorders present worldwide, affecting approximately 1 in 10 individuals, with depression and anxiety being the most common [1]. Severe cases of mental health disorders can escalate to suicide, a critical public health concern across all age groups. The Sustainable Development Goals (SDGs), particularly Goal 3, aim to ensure healthy living and promote well-being, with Target 3.4 specifically addressing mental health promotion. The Suicide mortality rate serves as an indicator for measuring progress toward reducing suicide [2].

Suicide surpasses malaria, HIV/AIDS, breast cancer, war, and homicide in causing mortality globally. While the global age-standardized suicide rate decreased by 36% from 2000 to 2019, over 700,000 deaths were attributed to suicide in 2019, making it the fourth leading cause of death among individuals aged 15-29 worldwide [3]. Men are 2.3 times more likely to die by suicide than women, though the Southeast Asia region exhibits a higher female age-standardized suicide rate than the global average, warranting attention to factors influencing young women's high suicide rates [4].

Over half of all suicides occur before age 50, emphasizing its significance as a leading cause of death among young people [5]. Pesticide self-poisoning is a prevalent method, particularly in rural agricultural regions of low- and middle-income countries, with hanging and firearms also commonly employed. Low and Middle-Income Countries account for 77% of total suicide deaths, with most adolescent suicides occurring in these regions. India, ranking 38th globally, reported a suicide rate of 12.7 per lakh population in 2019, marking a gradual decline over two decades [6,7,8].

In 2021, India experienced a 7.2% increase in reported suicides compared to 2020, with Maharashtra and Tamil Nadu recording the highest numbers [9]. Mental health disorders like depression and alcohol

use disorders often precede suicide, but impulsive acts during crises, financial difficulties, relationship strains, and chronic illness also contribute [10]. Previous suicide attempts pose a significant risk, yet suicide is preventable, with interventions possible at population, sub-population, and individual levels.

The article aims to critically review India's efforts to address rising mental health concerns, including the recently launched National Suicide Prevention Strategy, recognizing the multifaceted approach required to combat suicide trends effectively.

Indian Mental Health Programs

In 1974, the WHO expert committee recognized that there is a heavy burden and huge treatment gaps concerning mental health disorders and that mental health has become a severe public health problem without any fundamental guidelines or infrastructure to meet the population's mental health needs, and asserted mental health care of the developing countries as its priority [11]. Following this, in 1979, the WHO Mental Health Advisory Group advised all member nations to prepare their own National Mental Health Programme (NMHP) to meet the mental health needs of the population, making use of the existing healthcare facilities and in 1982, per the WHO directives, India became one of the first nations to launch its own NMHP [12]. In 1982, it was through dedicated and relentless efforts that the senior psychiatrists of India drafted the NMHP after multiple reviews and workshops before it was tabled in the Central Council of Health and Family Welfare, where the NMHP was adopted [13].

The NMHP was adopted with the objectives of increasing accessibility and availability of mental health care for all, encouraging the application of mental health knowledge in general health care, and promoting community participation in mental health services. However, the program faced many challenges from its inception due to various ambiguities like the absence of proper budgetary allocation, lack of clarity funding for the program, and the lack of support from psychiatrists. Later, in 1996, as the government tried to set the district as the basic unit for implementing and monitoring the program to cover for the shortcomings of NMHP, the District Mental Health Program (DMHP) was launched. This was done based on the Bellary model shown by the National Institute of Mental Health and Neuro-Sciences (NIMHANS). NMHP was re-strategized in 2003 with increased budgetary allocations for the program, and later, in 2009, along with the development of the Center of Excellence in Mental Health, manpower development became important. Over the years, there has been an increasing need to focus on community mental health using Information Education and Communication (IEC) activities. Further along, the NMHP was gradually inculcated into the National Health Mission (NHM) to meet the needs of both rural and urban areas [14].

Various other acts, policies, and programs have come into place over time to support the mental health framework of the country like the National Mental Health Policy (NMHP), The Mental Health Care Act (MHCA) 2017, the National Tele Mental Health Program, the National Suicide Prevention Strategy.

In 2014, the National Mental Health Policy (MHP) was launched with the vision

to promote mental health, prevent mental illness, enable recovery from mental illness, promote de-stigmatization, and ensure socio-economic inclusion of persons affected by mental illness by providing accessible, affordable, quality health and social care. The National Mental Health Policy, with its 3 goals and 10 objectives, aims to bridge the treatment gap, thereby reducing mortality and morbidity along with an enhanced understanding of the issue and strengthening the leadership at all levels in the mental health sector [15].

The Mental Health Care Act 2017 was passed on 7 April 2017 and came into existence on 29 May 2018, it superseded the previous Mental Health Act 1987. The major highlight of the act was that it decriminalized suicide attempts. Also, it focused on promoting and fulfilling the rights of people during the delivery of mental healthcare and services for matters connected therewith or incidental thereto and created provisions for the registration of mental health-related institutions and their regulations [16].

The launch of the National Tele Mental Health Programme in 2022, known as Tele Mental Health Assistance and Networking Across States (Tele MANAS), underscores the government's commitment to providing universal, accessible, and quality mental health care through tele-mental health counseling services across all states and union territories. [17].

Despite these various programs and acts in action, the government has consistently failed to meet the manpower needs that form its backbone. From the data depicted in Table 1, India faces a significant shortfall of mental health professionals, including psychiatrists and clinical psychologists, compared to the growing demand for mental healthcare services. Addressing this shortage is crucial to improving our country's mental health support and services [18,19,20].

Table 1. Current scenario of mental health professionals in India [18,19,20]

Manpower	**Requirement (per lakh population)**	**Availability (2012)**	**Availability (per lakh population)**
Psychiatrist	36,000 (>3)	3,800	Approx 9000 (0.75)
Clinical psychologist	17,250 (1.5)	898	0.05
Psychiatric social worker	23,000 (2.0)	850	0.07
Psychiatric nurse	3000 (1.0 per 10 psychiatric beds)	1,500	N/A
Total	**79,250**	**7,048**	-

National Suicide Prevention Strategy

In line with WHO's Strategy on suicide prevention, the National Suicide Prevention Strategy (NSPS) was launched in November 2022, with the aim to reduce suicide mortality by 10% in the country by 2030 in comparison to the prevalence in the year 2020. It is the first of its kind in India, making suicide prevention a public health priority. The NSPS intends to reach this objective by implementing efficient surveillance systems by 2025, ensuring the availability of suicide prevention services and incorporating a mental well-being curriculum into all educational institutions by 2030 [21].The NSPS has mapped out the 'REDS' pathway for suicide prevention as shown in Figure 1.

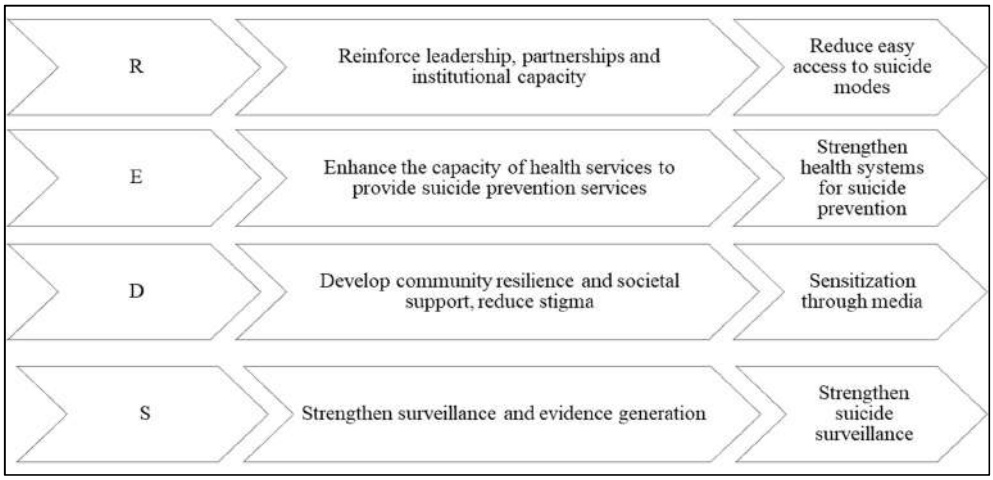


Figure 1. REDS pathway for suicide prevention envisaged by World Health Organization [21]

The Action plan formulated to realize these crucial objectives has five key themes: recognizing strategies, delineating actions to be taken, specifying the indicators that will help us plot our progress, identifying key stakeholders, and defining the timelines to achieve our objectives [21]. NSPS has taken a multi-sectoral approach to suicide prevention involving international, national, and regional agencies and NGOs, as shown in Figure 2.

Figure 2. A multi sectoral approach under National Suicide Prevention Strategy [21]

Swoc Analysis

Even with extreme efforts put in by various agencies, there is always a scope for improvement. Hence, NSPS has been identified with its shortcomings, its strengths, and the opportunities it has to prevent the coming mental health pandemic along with certain challenges that are to be kept in mind. Figure 3 highlights some of the points of Strength, Weakness, Opportunities, and Challenges (SWOC) analysis that can be further utilized to improve the policy-making process and more importantly its implementation.

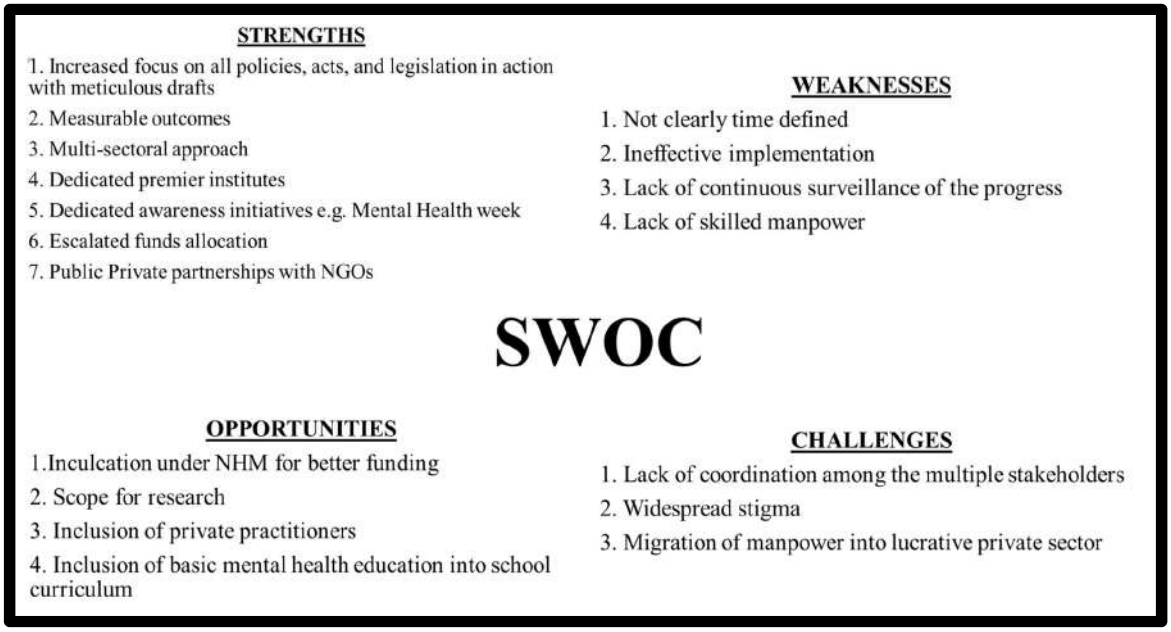


Figure 3: SWOC analysis of Mental health initiatives in India

Conclusion

With a wide variety of policies and initiatives taken up by the Government of India, it is a clear-cut depiction of growing political attention toward mental health issues. This is one of the most applaudable actions but the journey towards inclusivity of mental health services for all has a long way to go. Achieving target 3.4 of Sustainable Development Goals i.e.: Reducing mortality from non-communicable diseases and promoting mental health is just witnessing a start from these initiatives but full-fledged implementation with appropriate man-power both in terms of quantity and quality needs to be urgently deployed to achieve better results. We advocate for better funding, improving mental diseases surveillance, increasing research activities and political will for a mentally healthier nation.

Conflicts of interest

The authors declares that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

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LETTER TO THE EDITOR

Paraquat Toxicity on Substantia Nigra: Pioneering Insights from an Autopsy Based Pilot Study

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Paraquat (N,N′-dimethyl-4,4′-bipyridinium dichloride) is one of the widely used herbicides in Indian agriculture. This compound is at the centre of polemics, involving debates on its effects on sustainable agriculture, potential health risks, and unintended applications. Paraquat (PQ) also gained ill repute globally due to the controversy surrounding its association with Parkinson's disease [1]. Furthermore, our country witnessed a rise in paraquat-related deaths attributed to its misuse for suicide, prompting a consistent call for proper regulation and a potential ban [2]. Paraquat exerts its toxicity through corrosion and the generation of Reactive Oxygen Species (ROS) causing cytotoxic effects that contribute to multiorgan failure. There is no specific antidote for paraquat (PQ) poisoning, and the lethal toxicity of this substance is responsible for a poor prognosis, even with minimal consumption.

Paraquat neurotoxicity studies in Wistar rats indicated changes, including the loss of dopaminergic neurons and astrocyte proliferation, with the degree of changes escalating proportionally with increased dosage [3]. However, human autopsy-based studies on this subject are limited. A thorough review of literature (light microscopy and electron microscopy) in cases of paraquat and diquat poisoning indicated a few neuropathological changes, encompassing findings such as brain oedema, haemorrhagic leukoencephalopathy, anoxic neuronal depletion, myelin destruction, astrocytic fibrous gliosis, and hypoxic purpuric staining in the basal ganglia etc. [4].

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In the context of limited availability of human studies on histopathological changes in the substantia nigra related to paraquat poisoning, a pilot project was initiated. A thorough case selection process was conducted, excluding deceased individuals with pre-existing neurodegenerative disorders or any neuropathology. This pilot study was conducted collaboratively between the Department of Forensic Medicine and the Department of Pathology at Andhra Medical College, Visakhapatnam, spanning a 6-month period from August 2023 to January 2024. We utilized formalin (immersion)-fixed brain samples obtained during forensic autopsies conducted at our institute. These specimens were immersed and fixed in 10 percent formalin for a duration of 3-6 weeks. It is crucial to note that all samples were derived from cadavers promptly preserved in cold storage at 4 degrees Celsius as early as possible following death, ensuring the preservation of the brains under standardized conditions to the extent possible.

The substantia nigra of fixed brains in paraquat poisoning cases (n=9, 5 Males, 4 Females) was subjected to histopathology, stained with Hematoxylin and Eosin, and compared with a control group (n=6, 5 Males, 1 Female) comprising autopsy cases with causes of death unrelated to paraquat poisoning. The details of the cases and controls are presented in Table 1. The diagnosis of poisoning was confirmed through postmortem chemical analysis of viscera in all the cases.

The examination of the substantia nigra in post-mortem brain specimens in the cases revealed distinctive neuropathological changes compared to controls. Specifically, the substantia nigra in paraquat-exposed brains exhibited a considerable reduction in neuronal density, accompanied by oedema and a decrease in neuromelanin pigment content. The neuropathological features were accentuated in long-term survivors, characterized by astrocytosis, rarefaction and inflammatory markers (Figures 1-7). Contrastingly, the substantia nigra of the control brains demonstrated a superior staining affinity, indicating a dense congregation of neurons without discernible rarefaction and normal neuromelanin pigment levels (Figures 7-11). These observations highlight a notable disparity between the substantia nigra of cases and controls, implicating the neurotoxicity of paraquat.

The current pilot study is a pioneering attempt in the domain of paraquat neurotoxicity. Nevertheless, our results are concordant with an MRI-based imaging study in acute paraquat poisoned patients which revealed CNS toxicity and lesions in multiple areas of brain, including the basal ganglia [5]. Indeed, studies that integrate clinical examination of patients with MRI imaging will yield fruitful results in understanding the acute toxicity of PQ on humans. By the same token, conducting serial follow-ups with PQ poisoning survivors will help us comprehend the subacute and chronic toxicity of this substance on the basal ganglia, shedding light on its potential association with Parkinson's disease.

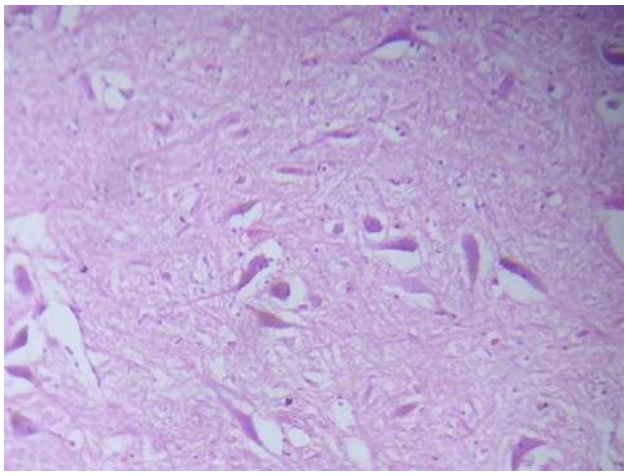
In conclusion, the present study indicates that paraquat crosses blood brain barrier and exerts its toxicity on brain in general and substantia nigra in particular. However, the limitations of the present study include its reliance on a limited sample size, and the absence of exact age-matched controls. Similarly, special stains were not employed for the examination of brain tissue. Future studies are needed to further validate the results of our study preferably with a larger sample size and more standardized sampling and processing

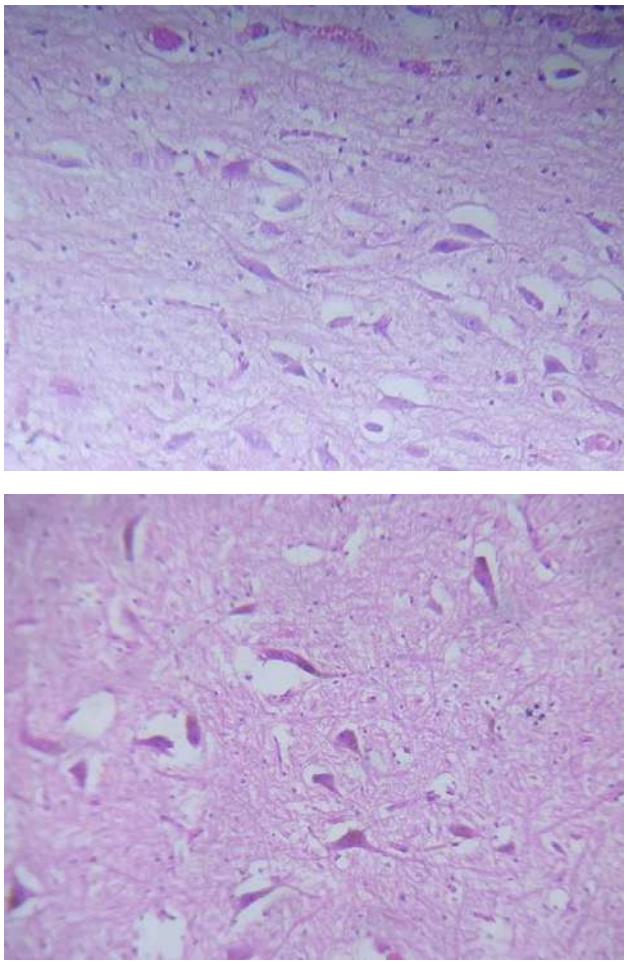
conditions to minimize the impact of postmortem artifacts. The significance of traditional autopsy and virtopsy in investigating toxicopathology is poised to become a pivotal subspecialty within the field of toxicology in the near future.

Table 1. Details of Cases and Controls in the Pilot Study

S.No	Case/Control (Age (in years) & Sex)	Time Since Death(in hours)	Time Since Consumption of Paraquat (in hours)	Cause of death
1	Case 1(22, F)	15	72	PARAQUAT POISONING
2	Case 2(31,F)	16	48	
3	Case 3(58,M)	15	29	
4	Case 4(20,F)	19	52	
5	Case 5(21,M)	10	168	
6	Case 6(20,M)	23	42	
7	Case 7(21,F)	18	264	
8	Case 8(29,M)	12	54	
9	Case 9(22,M)	16	25	
10	Control 1(32,M)	26	NOT APPLICABLE	Cut Throat Injury
11	Control 2(59,M)	24		Blunt Injury to the Chest
12	Control 3(29,M)	25		Olanzapine Poisoning
13	Control 4(53,M)	98		Coronary Artery Disease
14	Control 5(38,M)	24		Hanging
15	Control 6(6,F)	15		Thermal Burns

M: Male, F: Female





Figures 1-3. Photomicrograph H & E, High Power.
Cases 1-3, Substantia Nigra Showing a Decrease in Neuromelanin Pigmentation, Paraquat Poisoning.

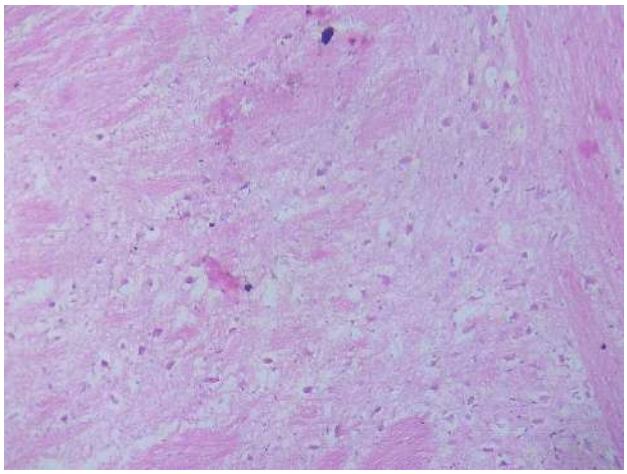


Figure 4. Photomicrograph H & E, Scanner View
Case 5, Substantia Nigra Showing A Decrease In Neuronal Density, Paraquat Poisoning.

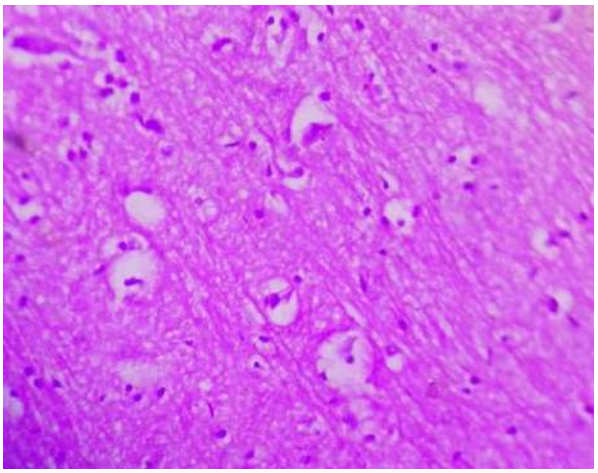


Figure 5. Photomicrograph H & E, Low Power.
Case 5, Substantia Nigra Showing A Decrease In Neuronal Density, Paraquat Poisoning.

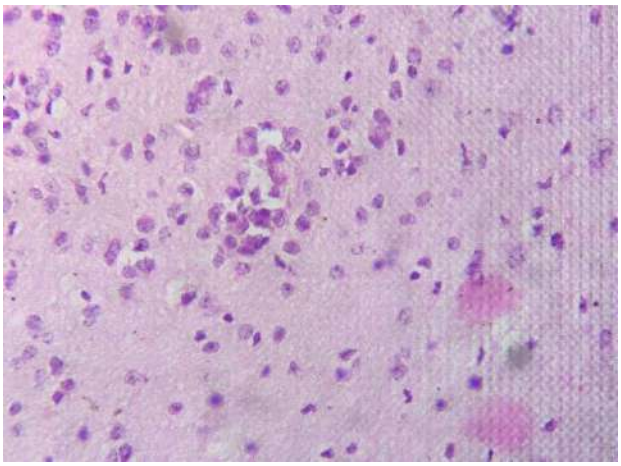


Figure 6. Photomicrograph H & E, High Power
Case 7, Substantia Nigra Showing Astrocytosis, Paraquat Poisoning.

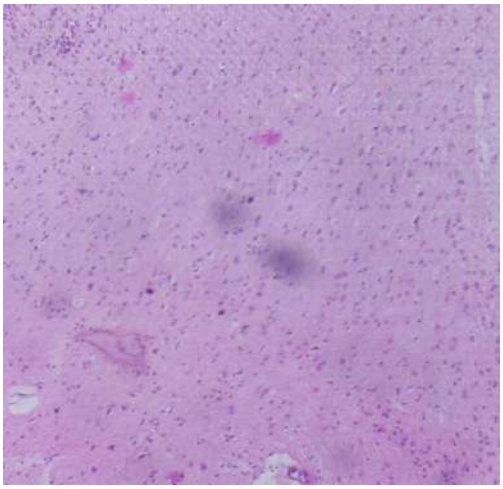
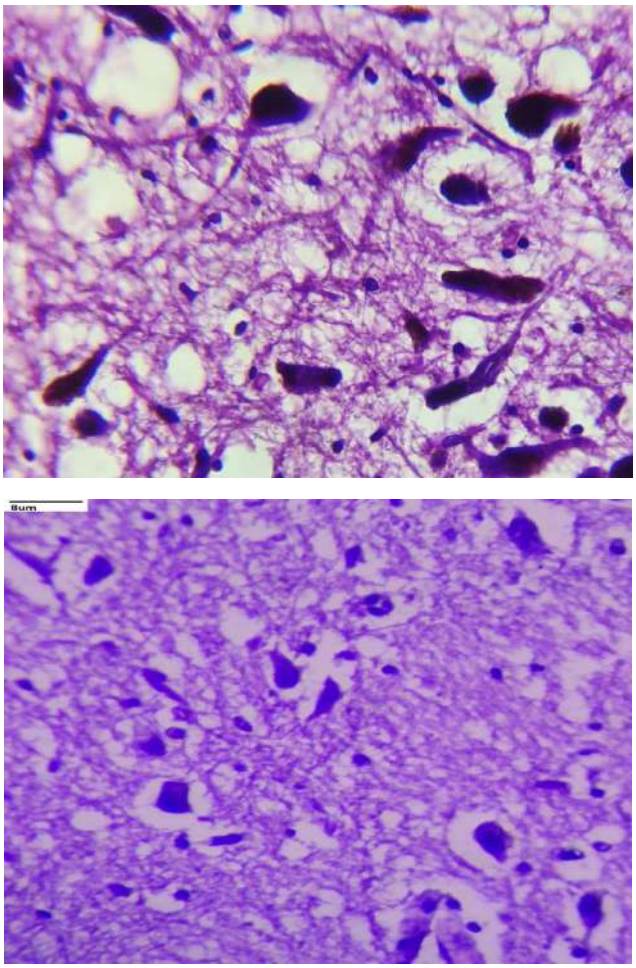


Figure 7. Photomicrograph H & E, Low Power
Case 7, Substantia Nigra Showing Astrocytosis, Paraquat Poisoning.



Figures 8-9. Photomicrograph H & E, High Power

Control 3, Showing Neuromelanin In Substantia Nigra (Normal Histology)

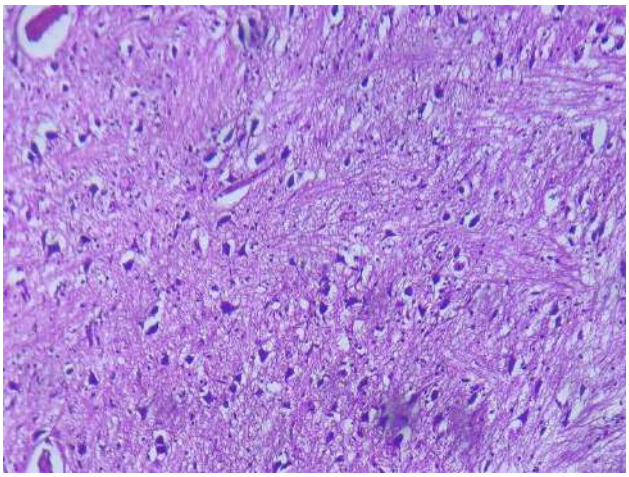


Figure 10. Photomicrograph H & E, Low Power

Control 5, Showing Normal Histology of Substantia Nigra

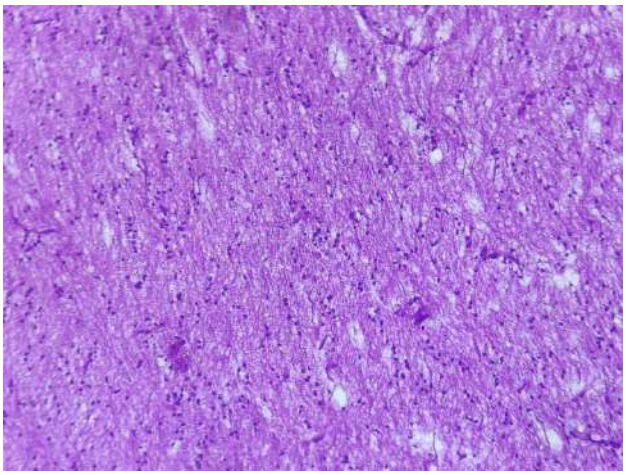


Figure 11. Photomicrograph H & E, Scanner View.

Control 2, Substantia Nigra Showing Normal Histology

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Ethical Issues

All ethical issue to be addressed by the authors

Conflicts of interest

The authors declares that they do not have conflict of interest.

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PERSPECTIVE

Toilet Scrolling: A Predisposing Factor for Haemorrhoids?

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Abstract

Scrolling smartphones while sitting on the toilet is believed to be one of the reasons predisposing to haemorrhoidal disease. Not much is written about the problem of the use of smartphones and the development of haemorrhoidal disease in the literature, but the rising incidence of haemorrhoids globally does require guidelines to be set for toilet hygiene, especially in the young generation to prevent this issue from becoming an epidemic in future. It may be time to designate the washroom as a smartphone-free zone.

Keywords: Toilet scrolling, Haemorrhoidal disease, Smartphone Free Zone, Smartphone addiction

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While the incidence of haemorrhoids is on the rise in countries like Australia, Israel, and Korea, India is also contributing significantly to the case list with 50% of the population predicted to have had symptoms of haemorrhoids at some point in their life at 50 years of age, and approximately 5% of the population suffer from haemorrhoids at any given point of time [1]. Apart from a sedentary lifestyle leading to chronic constipation, the role of sitting for a prolonged period in the washroom with a smartphone performing 'toilet scrolling' needs to be investigated and highlighted in the etiopathogenesis of haemorrhoids.

Toilet scrolling is a global issue with studies revealing that 79.8% of respondents from Spain take their smartphone to the loo followed by Poland, the USA, Lithuania, and Canada [2]. This survey also revealed that while Canadians like to play games with their smartphones while sitting in the washroom, Americans prefer to chat or call people while in the toilet. The French divide the bathroom phone time between social media scrolling, gaming, and reading the news. A recent study found that 90% of residents of Hong Kong take their smartphones to the toilet and 61.1% toilet -scrolling of social media [3]. Social media platforms like Facebook, Twitter, and Instagram were the primary focus of scrolling for 61.6% of respondents during their toilet time.

The two important health concerns of toilet scrolling are the development of haemorrhoids due to prolonged sitting in the washroom and the touchscreen becoming a potential source of contamination for bacterial infection. Smartphones are regarded as "mosquitoes of the digital age" as they carry ten times more germs than toilet seats [4]. A study conducted by the London School of Hygiene & Tropical Medicine and Queen Mary, University of London concluded that 1 in 6 smartphones was contaminated with faecal matter [5]. But another surgical problem that is lurking behind is the formation of haemorrhoids because of prolonged sitting in the washroom due to toilet scrolling.

A recent study did find a linear association between the time spent on the toilet and the degree of haemorrhoids [6], but not much literature has predicted the dark side of toilet scrolling associated with the grades of haemorrhoids. Toilet reading habits were evaluated in the general population from Israel and it was found to involve 52.7% of the population and these people had an increased incidence of haemorrhoids, though it was not statistically significant [7]. Though chronic constipation and straining at defecation are important etiological factors, the use of cell phones during defecation diverts one's attention from the so-called "Nature's call" and thus affects the normal anal synergia of the defecatory reflex. It may be graded as a part of attention disorder. A psychological angle of "cell phone addiction" may also be contributory.

It is well established that haemorrhoids develop when the supporting tissues of the anal cushions disintegrate or deteriorate resulting in an abnormal downward displacement of the anal cushions resulting in dilatation of the veins. Though the amount of toilet time and pressure required to initiate this pathology is still not established, the incidence of haemorrhoidal disease was found to be higher in the patients using a bidet (Western) toilet compared to those using a squat (Indian) toilet, which could be attributed to the longer toilet sitting periods

in the bidet toilet and scrolling on the mobiles [8]. 10 minutes has been the maximum recommended time to be spent in the toilet according to various non-peer-reviewed data available as there are no hard-core evidence-based retrospective or prospective studies in this matter [9]. Smartphone addiction has been associated with teenage anxiety, depression, stress, and loneliness which might indirectly lead to spending more time sitting in the toilet for scrolling in solitude.

With the prevalence of haemorrhoidal disease estimated to be around 20.8 to 38.2% by colonoscopy findings [10], it is extremely important to declare the washroom as a 'Smartphone Free Zone' and all types of mobile scrolling to be discouraged right from the school days. Toilet training and toilet hygiene should make it mandatory for all to avoid mobiles inside the washroom. To prevent the future generation from developing various grades of haemorrhoids, a timer or alarm has to be set for spending a maximum of 10 minutes inside the washroom. Until and unless strict guidelines and health regulations on the use of smartphones in the washroom are made with lifestyle modifications, we may be encountering an epidemic of bleeding per rectum in the future.

Conflicts of interest

The authors declares that they do not have conflict of interest.

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CASE SERIES

Rhomboid Flap Reconstruction for the Treatment of Pilonidal Sinus: A Case Series

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Abstract
Pilonidal sinus disease (PSD) is a chronic inflammatory disease affecting the soft tissue of the sacrococcygeal region and remains a challenging disease for surgeons to treat. With controversies in management to prevent recurrence leading to economic burden to the patient, these cases require special care by expert surgeons. From Jan 2023 to Nov 2023, 10 patients with pilonidal sinus were treated with complete excision of the tract and reconstruction using a rhomboid flap. The factors evaluated included the duration of surgery, postoperative pain, length of hospital stay, and postoperative complications. The patients were followed up on an outpatient basis, monthly for the first three months. The majority of the patients were young males with a mean age of 28 years. The surgery time was 40 to 75 minutes, and the mean operation time was 55 minutes. The stitches were removed after 2 weeks. Among complications, two patients developed mild discharge with infection. In one patient, necrosis at the tip of the flap was noted. We recommend the Rhomboid flap as a method of choice for surgical management of Pilonidal sinus in a postgraduate medical college as it is easy to teach, learn, and perform and gives complete recovery of the patient with negligible recurrence rate.

Keywords: Pilonidal sinus, Bascom procedure, Limberg procedure

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Introduction

The incidence of pilonidal infections and chronic pilonidal sinuses are usually found in the midline of the sacrococcygeal region of young hirsute men with the incidence of disease approximately being 26 per 100,000 population. The hall mark in the pathogenesis of the disease is the presence of hair in the gluteal cleft [1]. The disease rarely occurs in those with less body hair. Other risk factors include obesity, local trauma, sedentary lifestyle, deep natal cleft, and family history. Diagnosis is generally a clinical one; patients usually present with chronic inflammation or a sinus with persistent drainage. They may also present acutely with an abscess or multiple complex subcutaneous tracks. Several surgical procedures have been described to treat pilonidal sinus, each claiming to be the best. But without prospective trials, such claims are just not scientific evidence. Usually, the surgeon decides the treatment plan according to his preference, his perceived recurrence rates, and the patients' ability to be off work and afford treatment. Marsupialisation, Wide excision with laying open of all tracks, the excision of all tracks with primary or secondary closure, and excision with cover by a flap to offset a midline closure through a Limberg procedure, Z-plasty or a Karydakis procedure are the common treatment options [2]. An ideal surgical treatment option for pilonidal disease is still elusive, the most essential factor being tension-free healing with a negligible recurrence rate. The rationale behind selecting a Rhomboid flap in pilonidal sinus is because it maintains continuity of texture, colour, and vascularity with the surrounding tissue, eliciting the most successful aesthetic outcome.

Materials and Methods

This study was conducted from Jan 2023 to Dec 2023 in the Department of Surgery of Mata Gujri Memorial Medical College and LSK Hospital, Kishanganj, Bihar. 10 patients were taken for the study who underwent surgery for pilonidal sinus disease by wide sinus excision followed by rhomboid flap reconstruction procedure. The inclusion criteria were each patient who had undergone operation because of pilonidal sinus and exclusion criteria was patients with acute pilonidal sinus diseases and highly complicated sinuses, past history of pilonidal sinus surgery and history of systemic diseases (DM, malignancy, etc.)

Three patients had a history of perianal abscess drainage in the past. Patients were placed in a jack-knife position with strapping of the buttocks for maximum pull for giving a wide exposure. Preoperative incision and planning were done, and flap lines marked with a sterile marker pen (Figure 1). The marked rhomboid encompassed the pilonidal sinus. The skin incisions (with each side equal in length) were made up to the pre-sacral fascia centrally and to the gluteal fascia laterally (Figure 2), the pilonidal sinus tract was excised in toto until the sacrum or coccygeal bone was exposed. All the hair follicles seen during the excision were removed. A hydrogen peroxide wash was given before flap cover. The flap was raised without undermining the skin up to the presacral fascia (Figure 3). The flap was then mobilised into the defect with minimal tension and primary skin closure was done over a suction drain (Figure 4). The skin

was approximated with 2-0 Nylon, and the excised specimen was sent for histopathology (Figure 5).

Intravenous Metronidazole was given for 2 days, and the drain removed after 72 hours. Skin sutures were removed after the 10th postoperative day. Postoperative sitz bath twice a day was advised, and all postoperative patients were followed up in the outpatient department monthly for 6 months. All the records of the patient were maintained throughout hospitalization including the postoperative course till the date of discharge.

Figure 1. Marking of the rhomboid flap with pilonidal sinus tract

Figure 2. Deepening until presacral fascia

Figure 3. Preparation of the flap

Figure 4. Closure of the flap

Figure 5. Excised tract with hairs

Results

Our case series consisted of 8 males (80%) and 2 females (20%), with a mean age of 28 years (range 16–50 years) with an average operative time of an hour. Three patients developed mild infection with pus discharge which was treated with Metronidazole for a week. All patients recovered completely except one patient who developed flap necrosis in the tip which healed with conservative management. Most of the patients underwent stitch removal on the 10th day and were advised rest and to avoid sitting for a long duration for the first 2 weeks. All the patients were advised to have a soft cotton pad under the undergarment to prevent soiling of the dress during office work or outside activities. The postoperative course was uneventful and all the patients were completely cured at the time of discharge (Table 1).

Table 1. Postoperative complications

Complications	Number
infection	1
necrosis	1
gaping	0
recurrence	0

Discussion

Though the incidence of pilonidal sinus is 26 per 100,000 population, there is a significant increase of this disease incidence after the Covid-19 pandemic probably due to long hours in sitting posture for online activities, especially among the young generation [2]. According to the latest report, the prevalence of pilonidal sinus is estimated at 6.6% in India with the peak age of incidence at 16 years to 25 years. Males are generally more commonly affected than females and common risk factors are poor hygiene, stiff body hair, obesity, a less bathing habits, and a sedentary lifestyle, especially in those who sit for more than six hours a day [3]. Management requires not only operative management of the pilonidal sinus but also preventing recurrence and complications.

The recurrence rates range from 0.3% for Limberg/Dufourmentel flaps to 6.3% for incision and drainage at 1-year follow-up [4]. A recent study found postoperative wound healing in a case of pilonidal sinus being influenced by the presence of Seborrheic dermatitis, obesity, and psychiatric illness [5].

Given the surgery is being conducted in a postgraduate teaching hospital, it was preferred to perform a rhomboid flap as compared to other choices.

The rhomboid flap is a type of transposition local flap commonly used in the treatment of hidradenitis suppurativa. It is an easy and reproducible surgery, has less

postoperative pain, infection rates, and early return to work with a negligible recurrence rate. The disadvantage of rhomboid flap is in patients with a lower body mass index and with less available skin.

Historically, rhomboid flap design was first described in 1928 by Professor Alexander Alexandrovich Limberg of Leningrad and the first description in English language was a chapter in Modern Trends in Plastic Surgery, edited by Thomas Gibson in the year 1963. It is only after this description, the flap became popular globally [6].

One of the earliest evidence highlighting a randomised controlled trial meta-analysis comparing the rhomboid flap versus primary closure for the defect left behind after excision of sacrococcygeal pilonidal disease on 641 patients found rhomboid flaps significantly cause lower wound infection and dehiscence. The study concluded that the rhomboid flap was superior to primary closure [7].

Finally, the first original research on pilonidal sinus disease was started by Dr AW Anderson in the year 1847, who removed tufts of hair from the sacrococcygeal region of a young man. Currently, Turkey leads globally in the research on pilonidal sinus and literature publications [8].

Conclusion

Given the easy technique with a negligible learning curve, we recommend rhomboid flaps for the surgical management of pilonidal sinus in post-graduate medical institutions where there are no plastic surgeons or colorectal surgeons available. Rhomboid flaps give excellent postoperative recovery with hardly any recurrence.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

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Author Contribution

All authors are equally contributed.

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CASE REPORT

Gangrene and Partial Auto-Amputation of the Penis in a Case of Priapism

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Abstract

Background: Penile Gangrene is rare, usually associated with extensive pelvic trauma, mechanical constriction, infection due to urinary extravasation and uncontrollable systemic infection. The objective of this case report is to stress upon the need for early detumescence by means of aspiration of accumulated blood, injection of phenylephrine, proper shunting of blood and adequate compression dressing with necessary antibiotic cover. **Case Presentation:** We present a case of 33-year-old married man who was hospitalized under general surgery department for left AK amputation because of lower limb gangrene. On 3rd postop day, patient was noted to have a turgid penis and unable to urinate. Urology consultation was sought after 3 days for suspected priapism. We immediately shifted the patient to OT and the detumescence of penis was achieved by means of aspiration and injection of phenylephrine followed by Winter's shunting. The penis was noted to be flaccid with normal hue and patient was discharged. After 1 month, he returned to the hospital with extensive gangrene of the entire distal half of the penis with features of auto amputation of distal portion of penis. **Conclusions:** This report is aimed to prevent ischaemic complications of priapism like penile gangrene. Various factors like time of intervention, urethral catheter, tight pressure bandage dressing around the penis and local infection alone or in combination, have been implicated in causing penile gangrene in cases of priapism. Penile detumescence should be achieved on an emergency basis to prevent its ischaemic complications.

Keywords: Penile gangrene, detumescence of penis, Winter's shunt

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List of Abbreviations

AK: Above Knee

DVT: Deep Vein Thrombosis

Background

Penile Gangrene is not very common, usually associated with extensive pelvic trauma, mechanical constriction, infection due to urinary extravasation and uncontrollable systemic infection [1]. In our case, penile gangrene occurred despite treatment for priapism (idiopathic/Ischaemic). The objective of this case report is to emphasize the need for early detumescence by means of aspiration of accumulated blood, injection of phenylephrine, proper shunting of blood and adequate compression dressing with necessary antibiotic cover.

Case Details

A 33-year-old married man was hospitalized under general surgery department for left AK amputation because of gangrene. Doppler showed left lower limb DVT and absent arterial flow in posterior tibial and dorsalis pedis arteries. Post operatively patient developed right lower limb edema with persistent left thigh edema, and after Doppler confirmation, he was started on heparin infusion in view of B/L lower limb DVT. On 3rd postop day, patient was noted to have a turgid penis and unable to urinate. He was catheterised. Urology consultation was sought after 3 days for suspected priapism. Complete physical examination revealed no abnormalities except an erect, tender and oedematous penis with bluish discolouration. Routine laboratory analyses were normal. Iliac vessel Doppler was done in which internal iliac vein couldn't be commented upon, but rest of the vessels were normal. We immediately shifted the patient to OT and the detumescence of penis was achieved by means of aspiration and injection of phenylephrine followed by Winter's shunting. Gentle compression dressing was done and adequate antibiotic cover was given. The patient was shifted back to general surgery department, after brief observation, with only minimal erection. Two days postoperatively, the compression dressing was removed, penis was noted to be flaccid with normal hue and patient was discharged. After 1 month, he returned to the hospital with extensive gangrene of the entire distal half of the penis with features of auto amputation of distal portion of penis. Debridement was done under local anaesthesia and we could insert 14FR Foleys catheter through the proximal part of penile stump. The postoperative recovery was uneventful and he was discharged next day. As the patient is improving with spontaneous epithelisation by nature, he is being followed up at regular intervals.

Figure 1. Penile gangrene with partial amputation (dorsal view)

Figure 2. Penile gangrene (ventral view)

Figure 3. Gangrenous part debrided.

Figure 4. Post debridement

Discussion

Priapism is an infrequently encountered disease with most cases being idiopathic in origin. Priapism is described as involuntary, painful, and prolonged erection of penis persisting for more than four hours not related to sexual stimulation and unrelieved by ejaculation. Ischemic priapism accounts for >95% of cases of priapism [2]. Our patient had neither tight compressive dressing nor local infection as a causative factor for the gangrene. However, the occurrence of peripheral limb gangrene led to further investigations and Doppler study showed arterial and venous thrombosis at multiple levels of bilateral lower limbs. The treatment involves resuscitation of the patient and decompression of the cavernosal bodies to achieve penile detumescence. Various

factors like time of intervention, urethral catheter, tight pressure bandage dressing around the penis and local infection alone or in combination, have been implicated in causing penile gangrene in cases of priapism [3].

Conclusions

This report is aimed to prevent ischaemic complications of priapism like penile gangrene. Penile detumescence should be achieved on an emergency basis to prevent its ischaemic complications [4].

Conflicts of interest

The authors declares that they do not have conflict of interest.

Funding

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CASE REPORT

Laparoscopic Spleen-Preserving Decapsulation of the Splenic Cyst: A Case Report

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Abstract

Worldwide the Incidence of Primary nonparasitic splenic cysts are rare. They were incidentally diagnosed while evaluating other diseases by imaging. We here by present our experience of a case of 23-year-old woman, with a primary nonparasitic splenic cyst. The patient underwent laparoscopic spleen-preserving decapsulation of the splenic cyst. The patient recovered well and had no postoperative complications.

Keywords: primary splenic cyst, laparoscopic decapsulation, spleen-preserving surgery

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Introduction

Splenic cysts are rare and are discovered incidentally during workup for other diseases. According to Martin's classification [1], a primary or true splenic cyst lined by the epithelial lining, whereas a secondary or pseudocyst lacks the epithelial lining. Primary cysts may be parasitic (75%) or nonparasitic (25%). Secondary cysts are mainly due to trauma.

Most patients are asymptomatic unless the cyst enlarges to the point of compressing surrounding structures. Splenic cysts are diagnosed by imaging, primarily abdominal ultrasonography and computed tomography (CT), with CT playing an important role in diagnosis. Splenectomy was once considered the treatment of choice but was associated with post-splenectomy complications, with OPSI (overwhelming post-splenectomy infection) being the most feared. In recent years, spleen-preserving surgery has emerged as a viable treatment modality that avoids post-splenectomy complications. With the advent of laparoscopy and increasing experience in laparoscopic surgery, laparoscopic spleen-preserving surgery is increasing worldwide.

Case Report

A 23-year-old young woman with hypothyroidism presented with complaints of generalized weakness and back pain for one year. The pain was intermittent, dull, and worsened with physical activity. History revealed early satiety and weight loss. The patient gave no history of fever, altered bowel habits, or trauma.

On examination, the patient was pale. Abdominal fullness was visible in the left hypochondric region. A palpable intra-abdominal mass with four-finger widths below the left costal margin, which is well defined and was not painful. On further investigation with contrast-enhanced computed tomography (CECT) of the abdomen (Figure 1), the spleen was enlarged and measured 17.4 cm with a large, well-defined cyst measuring 14x15x12 cm (anterior-posterior x cephalo-caudal x medio-lateral), displacing on the adjacent fundus and proximal body of the stomach to the right. Inferiorly, the lesion was closely abutting and exerted a mass effect on the superior border of the distal body and tail of the pancreas, preserving the intervening fat plane. Carcinoembryonic antigen (CEA) and cancer antigen (CA) 19.9 levels were within the normal range, and serologic testing for hydatid was negative.

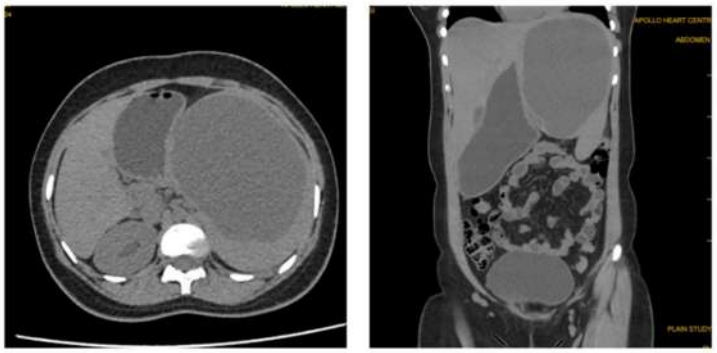

Figure 1. CT SCAN -axial and coronal plane showing splenic cyst

Because of the size of the cyst, a detailed discussion was held with the patient about the risks and possible complications after splenectomy. We proceeded with the spleen-preserving surgery.

Under general anesthesia, the patient was positioned in the modified recumbent right lateral position. After standard preoperative maneuverers, inserting a Veress needle at the level of the umbilicus and created a pneumoperitoneum. A 10-mm camera port was inserted at the level of the umbilicus. A 5-mm working port for the left hand was inserted into the epigastrium, a 12-mm port for the right hand at the midclavicular line, and a 5-mm port for retraction were placed in the left anterior axillary line, as shown in (Figure 2). On entering the abdomen, a large solitary splenic cyst, about 15x12 cm in size, arising from the superior pole of the spleen and pushing the stomach to the right side (Figure 3). 1200 ml of hemorrhagic fluid was aspirated. Using a harmonic shear (Ethicon) most of the cyst wall is excised by decapsulation (Figure 4); preserving the remaining part of the spleen, and hemostasis is achieved. Placing the omentum into the residual cyst cavity (Figure 4) performed omentopexy. A size 16 Fr Romovac suction drain was placed in the cyst cavity. On postoperative day 1 the abdominal drain were removed, and on the same day patient was discharged. The patient recovered well postoperatively and was asymptomatic at later follow-up visits.

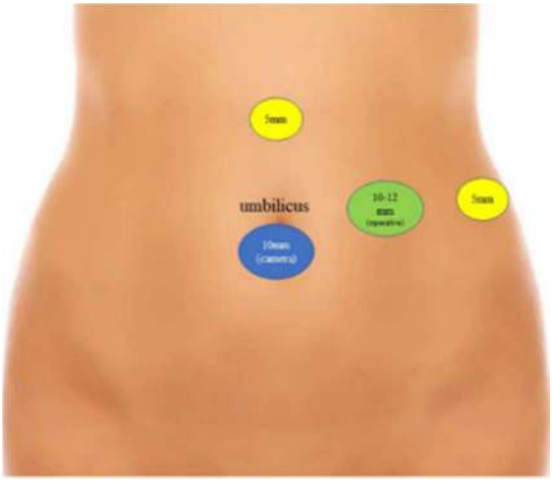

Figure 2. Port positions

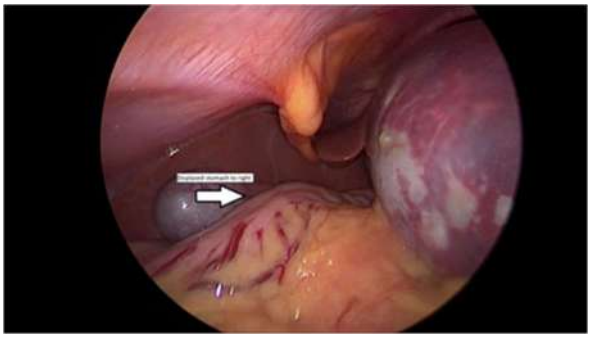

Figure 3. Splenic cyst pushing the stomach to the right

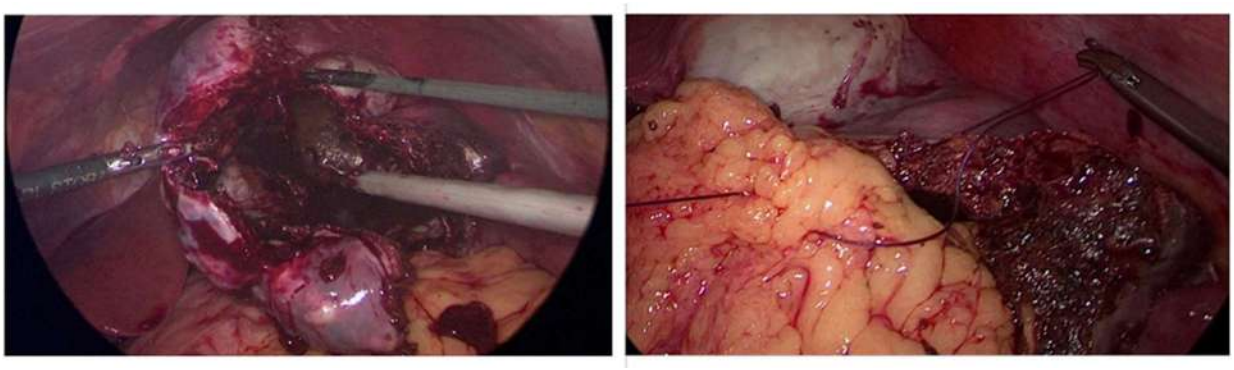

Figure 4. Laparoscopic splenic cyst deroofing and Omentopexy

Histopathologic examination revealed a densely fibrotic cyst wall with fibro collagenous stromal tissue and dystrophic calcification (Figure 5). The final impression was a hemorrhagic cyst wall with focal calcification and nonspecific chronic inflammation.

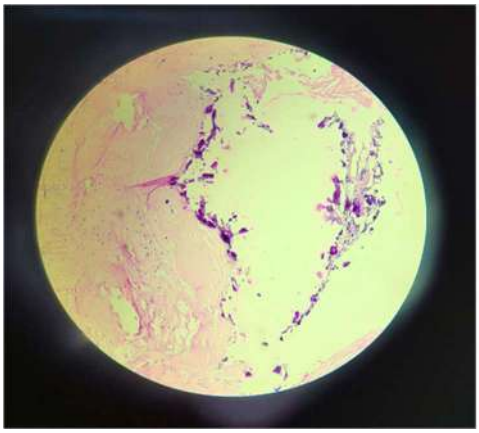

Figure 5. Histopathology showing fibro collagenous stromal tissue

Discussion

The true incidence of splenic cysts is unknown. Splenic cysts are more common in the younger age groups of the second and third decades. The first case of splenic cyst was reported by Andral in 1929 [2]. After studying the patterns and findings of more than 400 cases, Fowler was the first to classify splenic cysts.

In 1958, Martin et al. [1] on the basis of the histopathological findings classified splenic cysts: (a) True/type 1 cysts are primary cysts characterized by the presence of inner epithelial lining of the stratified squamous epithelium. They account for 20% of all cysts, which are sub-classified into congenital and neoplastic cysts. Congenital cyst is thought due to the entrapment of peritoneal mesothelial cells into the splenic parenchyma during embryogenesis [3]. Neoplastic cysts of the spleen consist of hemangiomas and lymphangiomas. The other is parasitic and is most commonly caused by the tapeworm Echinococcosis granulosus infestation. (b) False splenic cysts/type 2 are secondary cysts; they lack epithelium lining and are called pseudocysts. False splenic cysts are more common than the true cysts, account for 80% of all splenic cysts. These false cysts are secondary to trauma, disorganized hematoma, splenic infarction, and splenic abscess.

Although most patients are asymptomatic, symptoms result from the compressive effect of the enlarging cyst on surrounding structures. In our case, the patient suffers from early satiety due to the compressive effect on the stomach. In the primary splenic cysts levels of CEA and CA 19-9 may be elevated [4]. In our case, CEA and CA 19-9 are in the normal range. The splenic cysts are mainly diagnosed by imaging modality, which include ultrasonography, computed tomography, and magnetic resonance imaging (MRI). CT and MRI can provide detailed information about the size, morphological features of the splenic cyst and its relationship to the adjacent organs [5].

Because of the rare incidence of primary splenic cysts, there is no standardized protocol for the management cysts and its controversial. Aim of the Surgical treatment is to remove the cyst and prevent a recurrence. Surgical options include both open and laparoscopic techniques. These includes open or laparoscopic total splenectomy, partial splenectomy (preserving more than 25% of the spleen), deroofing, and marsupialization [6].

Asymptomatic cysts, which is less than 5 cm is managed by regular follow-up. Surgical treatment is mainly for the Cysts more than 5 cm and are symptomatic. Spleen preserving surgery is mainly preferred for the upper pole and lateral cysts. For the cysts which are located in the lower pole or at the hilum, Splenectomy is recommended [7]. Indications for splenectomy include multiple cysts, very large cysts, cysts in the hilum of the spleen, intrasplenic cysts completely covered by splenic parenchyma, and intraoperative uncontrollable hemorrhage [8]. Other non-surgical options include image-guided drainage / aspiration of the cysts. But the recurrence rate following the drainage / aspiration has been reported to be as high as 100%. For this reason, surgery is considered the treatment of choice [9].

In this era of laparoscopic surgery, laparoscopic deroofing of splenic cysts was performed with shorter stay in hospital, less complications, and better outcomes [6]. It also prevents the potential post operative complications of the splenectomy by preserving the splenic parenchyma. To reduce the recurrence risk, most of the cyst wall should be excised while preserving the parenchyma, as done in our case. An omentopexy helps to prevent the risk of cyst recurrence [10].

Conclusion

In conclusion, treatment options for primary splenic cysts focus mainly on the laparoscopic approaches with spleen presevation. Because of the important immunologic functions of the spleen in inducing peripheral tolerance through its various immune components, phagocytosis of the capsulated microorganism and the risk of overwhelming infection after splenectomy, the trend has shifted toward the conservative spleen preserving surgery with minimal invasive approaches.

Statements and Declarations

Conflicts of interest

The authors declares that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

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CASE REPORT

A Late presentation of Gossypiboma presenting as a cutaneous fistula with purulent discharge in an operated case of Lower segment caesarean section

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Abstract
Gossypiboma, a retained surgical sponge, is a rare complication following any surgical procedure and is primarily a result of human error. Such patients often have vague clinical presentations and the diagnosis often comes as a surprise and has serious medicolegal implications. We present a case of a 28-year-old female with a long-standing duration of 9 months with purulent discharge from the operated scar site of Lower segment caesarean section done 2 years back and then diagnosed to have a gossypiboma in the ureterovesical space causing structuring of the ipsilateral ureter which was successfully managed by Exploratory laparotomy with removal of the retained gossypiboma and right sided ureteric reimplantation.

Keywords: Gossypiboma, cutaneous fistula, lower segment caesarean section.

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Introduction

The literal definition of gossypiboma means finding Surgical sponges and gauze retained in the body after a surgical procedure. This term is derived from the Latin word, Gossypium (cotton) and the Kiswahili word, boma (a place of concealment) [1]. It is often a rare clinical entity. Patients often experience symptoms for years before a definitive diagnosis is made. In most such cases, the diagnosis is unexpected and comes as a surprise [2]. Although it is an iatrogenic and preventable entity; it can be a source of significant morbidity for the patient. Another important aspect of such an inadvertent occurrence is the medicolegal implications behind it. Several such cases have been reported in the literature up until now. However, physicians seldom consider it in their differential diagnoses. We present a case of a 28-year-old female with a long-standing duration of 9 months with purulent discharge from the operated scar site of Lower segment caesarean section done 2 years back and then diagnosed to have a gossypiboma in the ureterovesical space causing structuring of the ipsilateral ureter which was successfully managed by Exploratory laparotomy with removal of the retained gossypiboma and right sided ureteric reimplantation.

Case report

A 28-year-old female presented to the outpatient department of a tertiary care centre with complaints of purulent discharge from abdominal wound since last 9 months. Patient reports history of 3 lower segment caesarean section in the past. The last lower segment caesarean section was done 2 years back. There was no history of wound related complications in the immediate postoperative period. After around 15 months post-surgery, patient developed a small pustule in the centre of the scar of the operated site which burst leading to purulent discharge which continued over a period of 9 months for which she visited the treating gynaecologist (Figure 1).

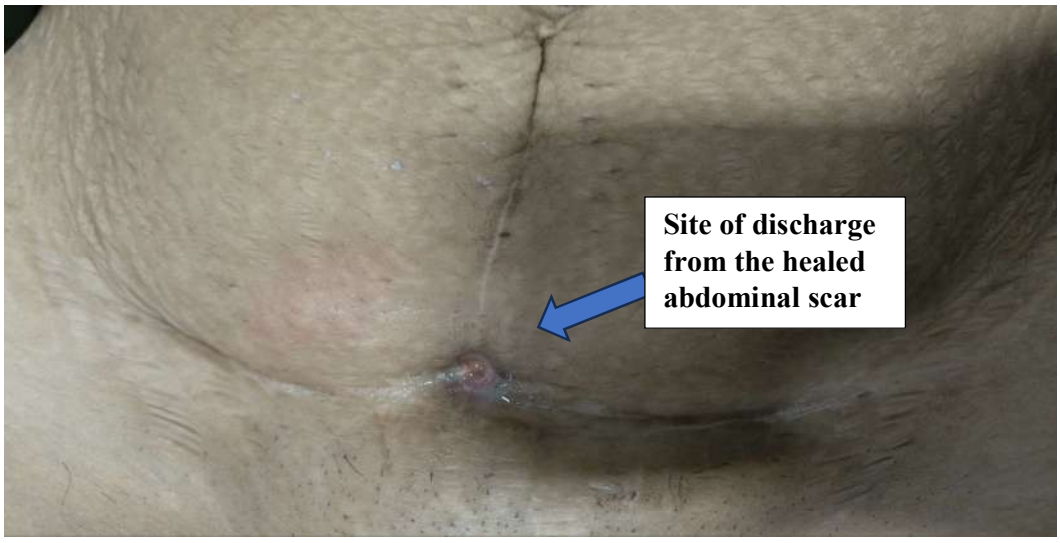

Figure 1. Clinical picture showing the healed abdominal scar with the site from where the purulent discharge was seen.

Patient was evaluated using ultrasound followed by Contrast enhanced Computerised Tomography of Abdomen and pelvis which revealed heterogenous mass with collection in the vesicouterine space with Right ureter seen involved by the mass and causing upstream right sided hydrouretero-nephrosis. The imaging findings were suggestive of a retained gauze piece with pus collection in the vesico-uterine space with resultant involvement of the right sided ureter causing right sided upstream hydro-ureteronephrosis.with a fistula formation (Figure 2).

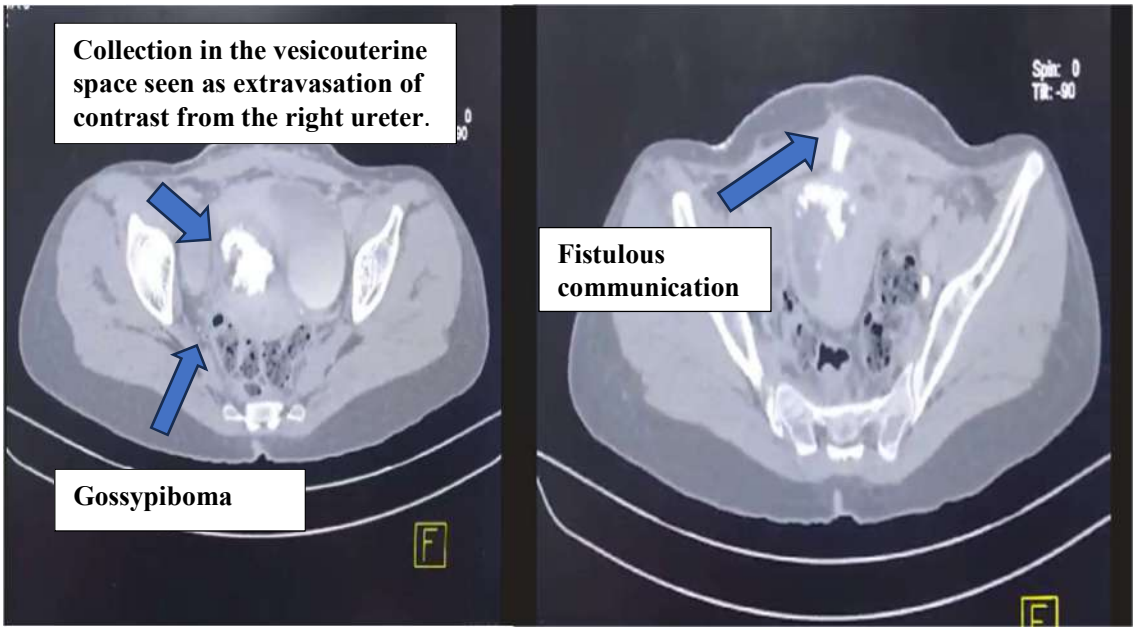

Figure 2. Contrast Enhanced Computerised scan images of the patient.

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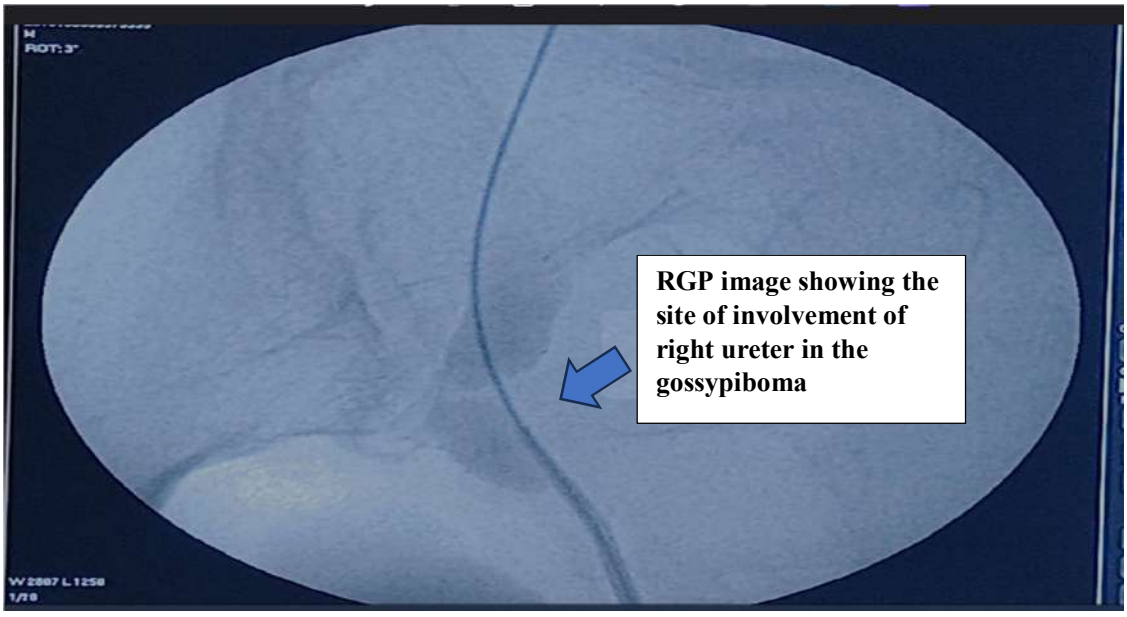

Figure 3. Retrograde pyelography image showing the site of involvement of the right ureter segment in the gossypiboma.

Patient underwent exploratory laparotomy through a lower midline vertical incision. Intraoperative, in the lower midline part the bowel was adherent to the lower abdominal wall and the bladder and the uterus. On careful dissection and separation of the bowel, the vesicouterine space was created and it was found to contain pus and retained gauze piece (gossypiboma). The right ureter was seen to be involved in this retained gossypiboma along with pus containing cavity and was seen to be dilated proximally. The pus was drained and the retained gauze piece was removed followed by right sided ureteric reimplantation by Lisch-Gregoir technique followed by omental transposition in the uterovesical space with placement of pelvic drain. (Figures 4 to 6)

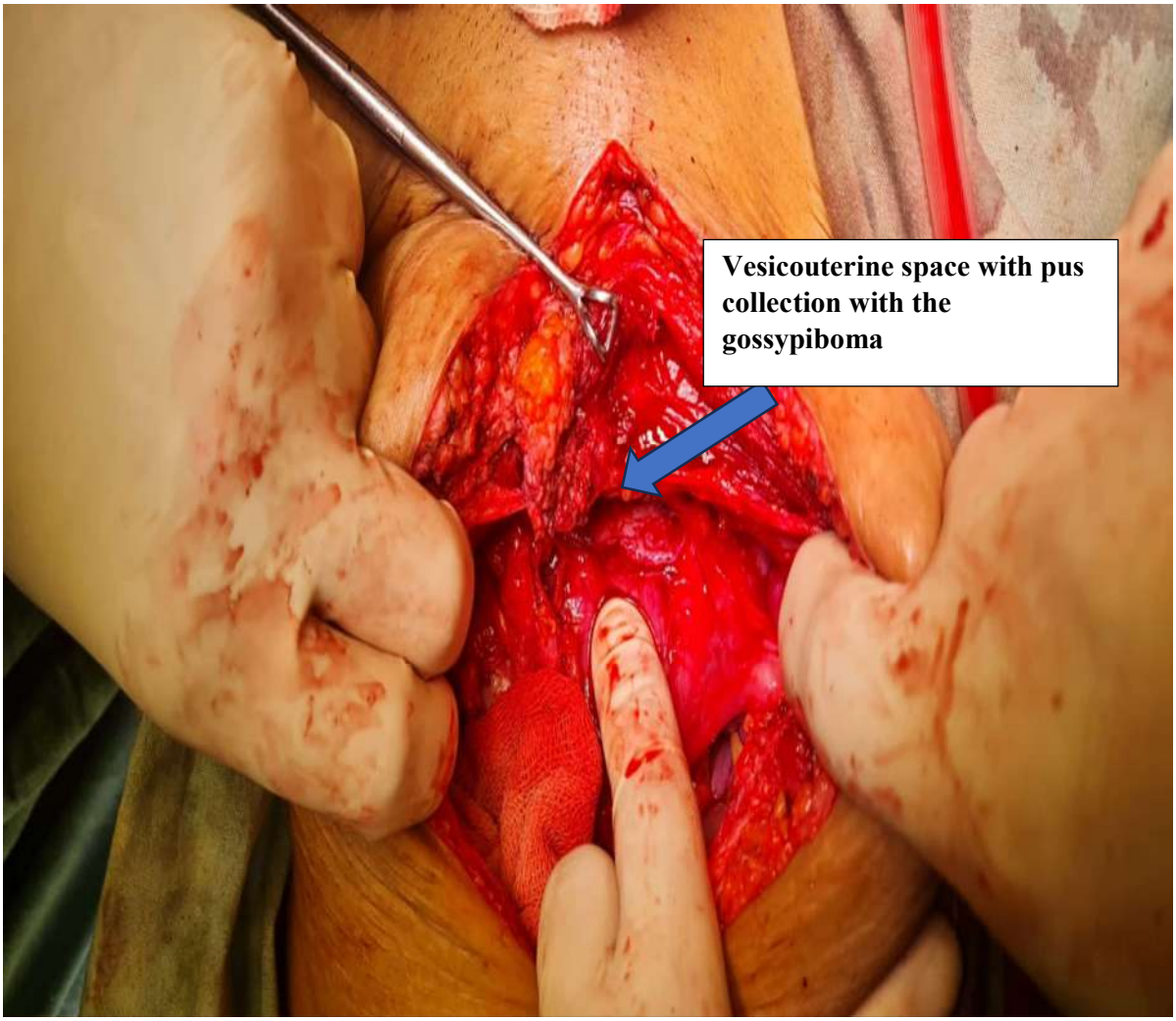

Figure 4. Intraoperative picture showing Vesicouterine space with pus collection with the gossypiboma.

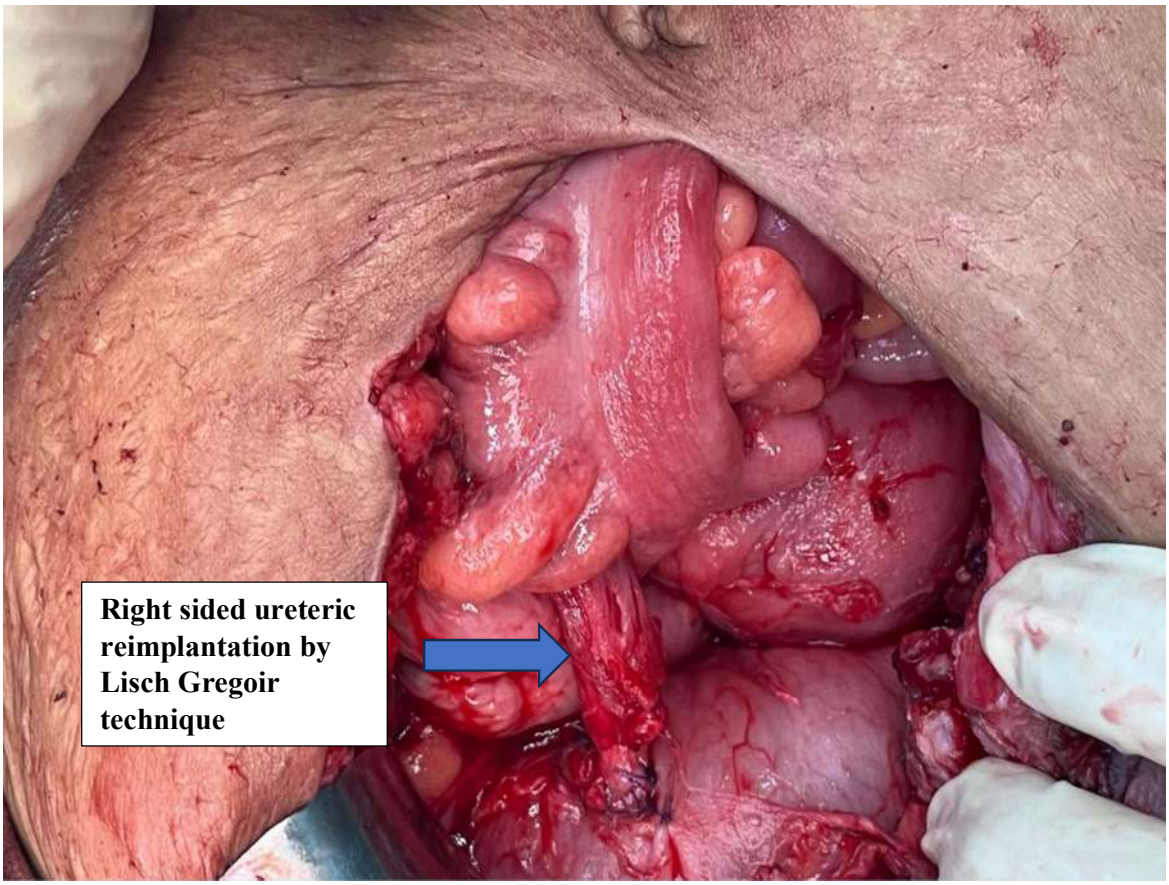

Figure 5. Intraoperative image showing Right sided ureteric reimplantation by Lisch Gregoir technique.

Figure 6. Clinical picture of the bits of the removed gossypiboma.

Patient tolerated the procedure well and was discharged after 7 days of admission. Patient underwent right sided DJ stent removal after 6 weeks and has been on regular follow up for a period of 6 months with 3 monthly ultrasound which has shown normal findings.

Discussion

Gossypiboma is a condition in which every reported case in literature is a unique presentation and hence, provides a lot of valuable information and insights about what erev the circumstances in which it occurred, how the patient presented with different symptoms, how it was diagnosed and finally, how it was effectively managed. Therefore, a high clinical suspicion is necessary and essential to diagnose it. Since gossypiboma is a preventable iatrogenic complication that can have detrimental effects on both patients and operating surgeon, careful measures should be made to prevent and minimize the morbidity-related complications [3].

Conclusion

Gossypiboma is a rare iatrogenic disorder with substantial morbidity and significant medicolegal implications. Such incidents are wholly avoidable and prevention is far better than cure. Emergency nature of surgery and poor communication among members of the healthcare team are strongly associated with the possibility of a retained surgical sponge. Most patients with this disorder present with vague clinical features. Therefore, a high clinical suspicion is required on part of the treating physician is required in diagnosing and managing this condition.

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Conflict of Interest

The authors declares that they do not have conflict of interest.

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Ethical approval

Patient consent was obtained for publication of the case report.

Data availability

It is a case report and data was obtained from the hospital records.

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