JMGV005N04

October-December 2018 Volume 5 Number 4

ISSN 2347-7946
eISSN 2347-7962

MGM Journal of MEDICAL SCIENCES

MGMJMS

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The Official Publication of
Mahatma Gandhi Mission Institute of Health Sciences
(Deemed to be University u/s 3 of UGC Act 1956)
Kamothe, Navi Mumbai, Maharashtra, India

JAYPEE

October-December 2018 Volume 5 Number 4 ISSN 2347-7946

MGM Journal of Medical Sciences

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MGM Journal of Medical Sciences

1. Aims and Scope

MGM Institute of Health Sciences (Deemed to be University u/s 3 of UGC Act 1956) is committed to promote excellence in medical education and research, and finding better, safer and affordable ways of diagnosing, treating and preventing diseases. With this view in mind, the university has launched a quarterly peer-reviewed scientific journal "MGM Journal of Medical Sciences" in 2014. It publishes original research papers, review articles, interesting case reports, pictorial reviews, letters to editor, book reviews and notices of important professional meetings and conferences. All submitted articles are scrutinized by peer-reviewers and the editorial team, before being published. From time to time, this journal may bring out special issues focusing on specific themes. A section may also be devoted exclusively to young researchers and students to stimulate their innovative and creative ideas.

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The Journal is printed on acid-free paper.

MGMJMS

October-December 2018 Vol. 5 No. 4

MGM Journal of Medical Sciences

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From the Editor's Desk

Telemedicine (or Telehealth as World Health Organization calls it) is defined as use of modern, advanced information and telecommunication technologies to provide healthcare services to remotely located patients, both in urgent and non-urgent situations. Healthcare systems of most countries, especially the developing ones, lack adequate human and capital resources, to provide service on demand. First telemedicine clinic is reported to have been established by Massachusetts General Hospital, Boston, USA in 1967. It provided emergency health services to travellers and employees of Boston International Airport, located 3 miles away from the hospital. Ever since, telemedicine has been growing rapidly, triggered by phenomenal advances in information and communication technologies. Robots in hospitals, controlled by remotely located surgeons are carrying out complex surgeries successfully.

Telecardiology is one of the important disciplines of telemedicine. Electrocardiography (ECG) is a basic diagnostic modality of heart disease, especially life-threatening arrhythmias. It can be transmitted wirelessly to any remote center for instant interpretation by an experienced doctor, who can order immediate lifesaving therapeutic measures to the healthcare personnel at site. Thus, lives can be saved. In fact, Willem Einthoven, the inventor of ECG, was the first to transmit ECG data from hospital room to his laboratory in 1907 over telephone wire, because the hospital did not allow him to move patients from the hospital room to his laboratory to test his ECG machine. A review article in the current issue of MGM Journal of Medical Sciences (MGMJMS) discusses newer, portable second generation devices developed in India, that can transmit 12-lead ECG simultaneously from the patient's bedside to any remote center over mobile telephone network.

Friends, we have pleasure in bringing new issue of MGMJMS to you with a variety of articles on various disciplines of medical sciences. We, in the Editorial Board, convey our deep gratitude to all the learned contributors as well as to our esteemed readers.

Shibban K Kaul MS, MCh, FIACS
Editor-in-Chief
MGM Journal of Medical Sciences
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Navi Mumbai, India

MGM Journal of Medical Sciences

October-December 2018 Volume 5 Number 4

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CASE REPORTS

10.5005/jp-journals-10036-1207

GUEST EDITORIAL

Roadmap to Leadership in Humanities, Science, and Medicine

Virinder K Moudgil

Keywords: Humanities, Leadership, Roadmap.

How to cite this article: Moudgil VK. Roadmap to Leadership in Humanities, Science, and Medicine. MGM J Med Sci 2018;5(4):149.

Source of support: Nil

Conflict of interest: None

There has been a significant and amplified worldwide interest in Science, Technology, Engineering, and Math or STEAM, the latter with the inclusion of Arts in the equation, for the past several years. The insurgence of interest is a valid proposition given sustained efforts invested in finding the relevance of education to the economic and entrepreneurial needs of academic communities and business corporations. Without a firm foundation in the humanities, from classical literature, history, writing skills, and interpersonal communication there is something left desired from an educated person. Without such even, the foremost expert in the STEAM disciplines are limited in reaching his or her potential. This may come as a shock to some, coming from the president of an institution like Lawrence Technological University (LTU), a broad-based education is a key to differentiate between just securing a job and evolving into a leader.

One might be among the world's most brilliant clinicians, scientists, engineers, architects or accountants. But if people can not communicate their work and discoveries effectively to relevant recipients; if they can not convincingly persuade others that their innovations and discoveries make a difference; if their business invention or idea is not relayed in understandable language; and if they can not work effectively with those around them, succeeding and reaching their full potential in the long run could be elusive.

That is why college students in technological and clinical disciplines need to study not only calculus and chemistry, but also attend classes focused on philosophy, political theory, science, and religion that contributed to the development of society, along with others exploring the great works of literature and art in their historical context and the basics of expository composition.

Just as an opera singer should be able to balance a checkbook and calculate percentages, I believe a competent physician, engineer or designer should have the ability to write a coherent essay and be able to quote from Tagore, Gandhi, Shakespeare, and Einstein.

It strikes me that the current division between science and art, and the scorn to which humanities subjects are occasionally subjected, is a relatively recent phenomenon. After all, there was a little division between science and art for great figures of the past like Leonardo da Vinci–or, more recently Steve Jobs, whose business acumen ad products combined trail-blazing function with exquisite design. And who cannot sense the mathematical precision behind the music of Bach or Mozart? Similarly, students in audio engineering technology and clinical simulation laboratories who learn how solid-state electronics work and become familiar with the intricacies of the science of acoustics, can at the same time develop an ear for what makes a great guitar solo. Thus, a broad educational experience is the key to leadership.

LTU was established in 1932 as an engineering school, and soon thereafter added programs in business, architecture, and design. LTU has always been a leader in what most educational authorities view as the most important parts of higher education in today's economy—STEM, for science, technology, engineering, and mathematics, which has lately been expanded to STEAM, adding art and architecture. However, the university is also home to a healthy humanities program that is crucial to our students' success. For only those with an appreciation for all of the world's incredible body of knowledge, can our full potential be realized?

President and CEO

Lawrence Technological University, Southfield, Michigan, USA

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10.5005/jp-journals-10036-1208

ORIGINAL ARTICLE

Does Computed Tomography Scan of the Brain in Pediatric Non-head Injury Patients Influence their Management in the Acute Setting?

[1]Nevine Anandan, [2]Alexander Johnson, [3]Soraya Hachemi, [4]Nikhil Bhuskute, [5]Shalini Nandish

ABSTRACT

Brain imaging with computed tomography (CT) is commonly performed in those with suspected intracranial abnormalities. The indications are many, among which trauma is the commonest followed by meningoencephalitis.

We present a retrospective review of 663 pediatric CT scans performed in our secondary care center in the United Kingdom for over three years. The aim of the study was to review (a) Indications for CT scan other than trauma, (b) Evaluate the distribution of scan requests during and outside office hours, (c) Correlation of scan findings with ancillary investigations such as lumbar puncture and clinical recordings such as Glasgow coma scale (CGS), and (d) Positive predictive value (PPV) of CT scan with respect to clinical outcomes in diagnosis of meningoencephalitis

In this study, they found no direct correlation of CT findings with signs of raised intracranial pressure and there was a poor positive predictive value of CT findings in the diagnosis of meningoencephalitis and raised intracranial pressure.

We conclude that in our center, there is a low clinical referral threshold for CT brain imaging in children with suspected meningoencephalitis. The study shows that CT brain scan is valuable in the diagnosis of complications of meningitis but has a poor predictive value for the diagnosis of meningitis/encephalitis and raised intracranial pressure. We recommend that brain imaging with CT should be performed in the appropriate clinical setting and the risk of radiation in children should not be ignored. Magnetic resonance imaging (MRI) may be a more sensitive modality in clinically stable patients when imaging is required.

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Keywords: Computed tomography brain, Encephalitis, Brain;Intracranial pressure, Meningitis.

How to cite this article: Anandan N, Johnson A, Hachemi S, Bhuskute N, Nandish S. Does Computed Tomography Scan of the Brain in Pediatric Non-head Injury Patients Influence their Management in the Acute Setting? MGM J Med Sci 2018;5(4):150-153.

Source of support: Nil

Conflict of interest: None

BACKGROUND

Computed tomography (CT) is a quick and noninvasive test in the investigation of cranial abnormalities although it does come at the expense of ionizing radiation. This is more relevant in the pediatric population where ionizing radiation effects can be significant.

We present findings of a retrospective audit study undertaken in the secondary care District General Hospital, where CT brain was performed for nontraumatic clinical indications in children under the age of 16.

AIM

To assess the appropriateness of acute CT head scans in the setting of non-trauma in children aged 16 and less. We looked at the indications for the acute CT, patient's GCS at the time of arrival, highlighted any differences in scans requested in and out of hours (after 5 pm) and level of senior review before requesting the scan.

We also looked at ancillary investigations [lumbar puncture (LP), electroencephalogram (EEG), MRI brain] performed, assessed any radiological differences in patients who had both CT and MRI brain and the PPV of CT scans in patients who presented clinically with meningitis/encephalopathic symptoms.

MATERIALS AND METHODS

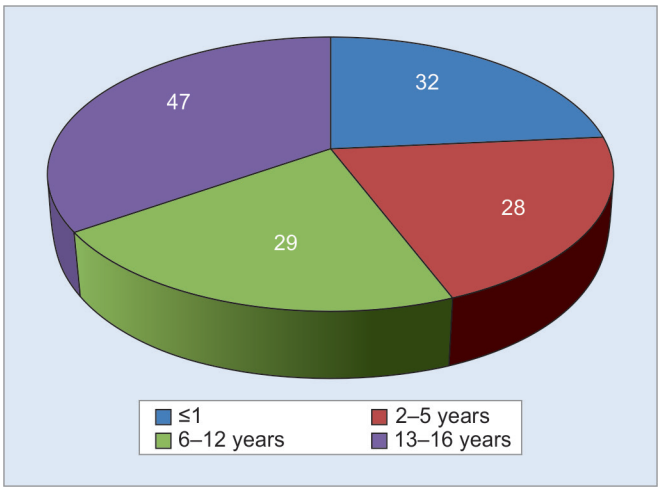
Six hundred sixty-three pediatric CT scans (0–16 years) performed over three years between January 2015 to December 2017 were assessed. Data collection was mainly from the hospital radiology information systems (RIS), picture archiving and communications system (PACS) and emergency department records.

Exclusion criteria were scans performed for suspected head trauma, craniosynostosis, those querying an intracranial bleed, orbital cellulitis and children with possible complications of ventricular drainage shunts.

After applying exclusion criteria, 136 scans were analyzed where the clinical indication was mainly symptoms under the broad term of encephalopathy and included features such as confusion, seizures, drowsiness, and vomiting.

RESULT

The number of children scanned among different age groups were similar although there was a slightly higher number in the age group of 13–16 (Graph 1).



Graph 1: Graph showing the distribution of various age groups

Scan findings in patients presenting with meningitis/encephalopathic symptoms were mostly normal in 81% (110) of the cases and abnormal in 19% (26). This shows a very low PPV of CT in this subset of patients. Abnormal findings were broadly due to ventricular system abnormalities, intracranial hemorrhage, sinus disease, empyema, tumor, lesion of infective origin, thrombosis, etc (Graph 2).

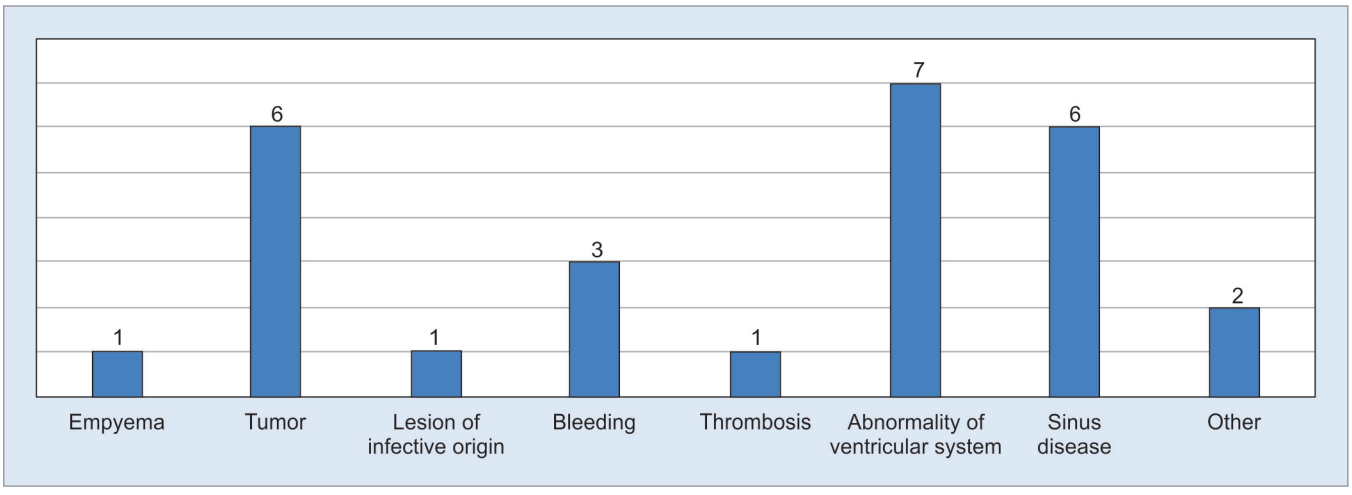
Of the 26 patients who had abnormal CT findings, 15 (58%) patients had an MRI scan. Of these 14 had abnormal findings. Total 6 patients (23%) had a LP of which one patient had an abnormal result, five being normal. Four patients (15%) had an EEG in which one was abnormal.

Of the 110 patients who had a normal CT scan, 36 patients (33%) had an MRI scan. Thirty-two of these were normal. Abnormal findings seen in four patients were distributed as non-specific white matter changes in two patients, mild cerebral atrophy in one patient and suspicion of a small infarct in one patient. Three patients had coexistent sinusitis. A total of 45 patients (41%) with a normal CT had a concomitant lumbar puncture of which two patients had a failed attempt. Sixty-five patients (59%) did not have a lumbar puncture as they had blood culture positive meningococcemia. Twenty-eight patients (25%) had an EEG of which 10 (36%) had abnormal results.

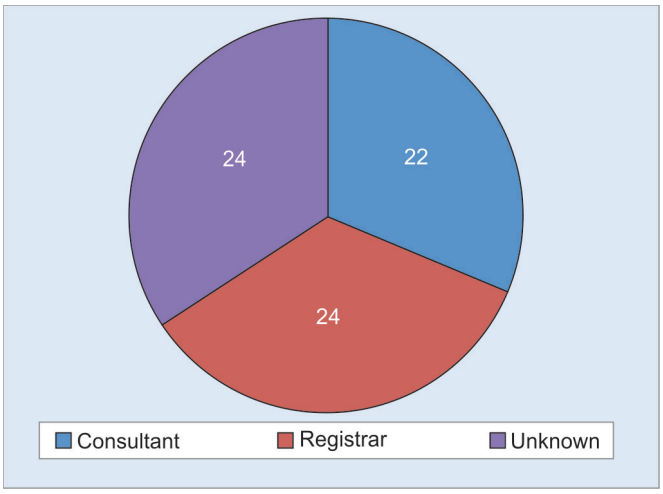
Twenty (15%) out of the 136 patients had a scan requested specifically for meningitis and queried raised intracranial pressure (ICP) before performing a LP. When the CT scan was reported normal, 11/15 patients had an LP. Four patients did not require LP as they had positive blood cultures for meningococcemia. When CT was abnormal, 2 out of 5 patients only had LP (both of which were normal).

Of the 15 normal scans, no significant MR findings were demonstrated. Of the five abnormal scans, three patients had an MRI scan that demonstrated abnormal findings. Two patients did not have an MRI.

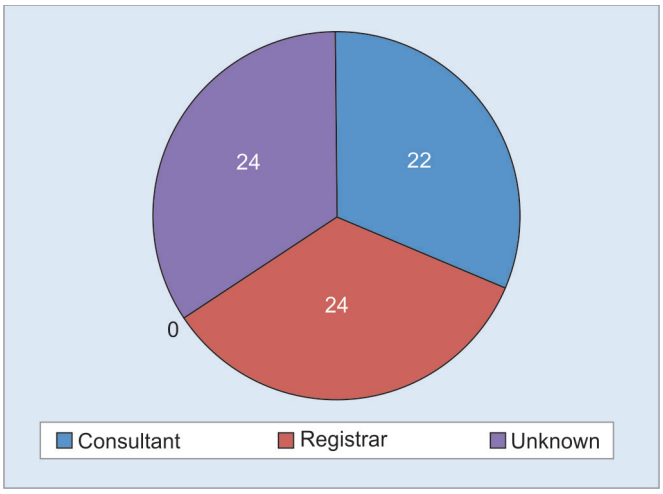
There was no significant difference while comparing CT scan results performed in an out-of-hours, although the scans performed out-of-hours had a slightly higher number of abnormal findings. The level of senior clinical review before the scan was similar both in and out-of-hours (Graphs 3 and 4).



Graph 2: Graph depicting the causes of abnormal scans in 19% of patients



Graph 3: Graph showing the level of senior clinical review before CT in hospital working hours



Graph 4: Level of senior clinical review before CT out-of-hours

Glasgow coma scale documentation was relatively poor, and 72 (53%) (57 normal and 15 abnormal scan results) of the 136 patients had no documentation. The GCS was 15 in 34 patients (27 normal and seven abnormal scans), less than 15 in 25 patients (22 normal and three abnormal scans) and a fluctuating GCS in 5 patients (4 normal and one abnormal scan) (Graph 5).

CONCLUSION

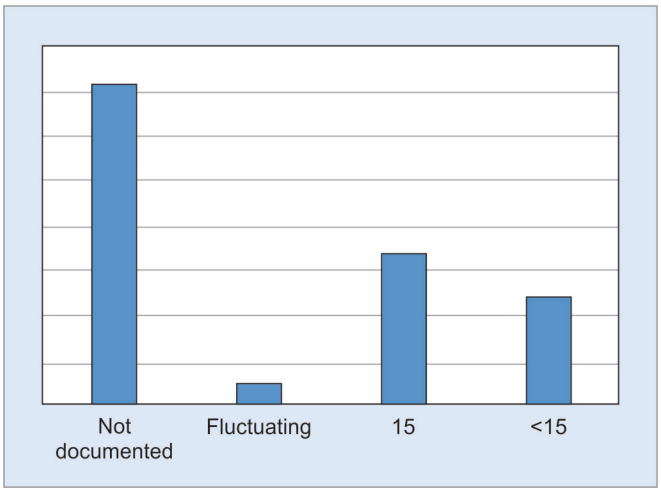
Our 3-year audit has proved that there is no significant benefit in performing an acute CT brain in pediatric patients presenting with meningitis/encephalopathic symptoms.

Brain imaging is of no value in the immediate diagnosis of meningitis and is an insensitive method for the detection of raised intracranial pressure.[1-3] This should be guided by clinical signs of raised ICP [(pupillary dilatation (unilateral or bilateral), pupillary reaction to light (impaired or lost), bradycardia (heart rate <60)], hypertension (mean blood pressure above the 95th centile for age), abnormal breathing pattern, abnormal posture or an initial Glasgow coma scale (GCS)<= 12.[4]

The role of imaging is to identify complications of meningitis or to exclude focal brain pathology simulating meningitis encephalitis.

For scan requests to exclude raised ICP before LP, it has been shown that coning can occur after LP in children with meningitis even when neuroimaging has been normal. So, the decision to perform LP in children with clinically diagnosed meningitis should be guided solely by clinical signs and should be avoided if consciousness is impaired or there are clinical signs of raised intracranial pressure.[5]

Close clinical evaluation including GCS assessment is mandatory as it may help determine clinical deterioration or lack of clinical response to treatment that may require further investigation with imaging.



Graph 5: Graph depicting patient GCS at the time of arrival to the emergency department

The PPV of CT in meningoencephalitis is also proven to be poor. The sensitivity is better in those that have clinically raised ICP and in those with focal neurological signs as seen in our study.

CLINICAL SIGNIFICANCE

This project has highlighted the lack of any significant benefit in performing premature CT brain in the non-traumatic pediatric patient. Although CT is quick and easily available, the radiation risks should not be ignored, and careful use of this modality is required, particularly in children. It also helps in avoiding unnecessary investigations and associated costs that do not add value to the immediate management of an unwell patient.

Positive indications for CT or MRI are progressive focal neurological signs, prolonged decreased level of consciousness, prolonged or focal seizures, increasing head circumference, evidence of continuing infection or recurrence of symptoms.[4] It is useful to consider brain MRI in clinically stable patients when imaging is required.

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10.5005/jp-journals-10036-1209

ORIGINAL ARTICLE

In Vitro Antifungal Drug Susceptibility Testing of *Aspergillus* Isolates from Clinical and Environmental Samples

[1]Raksha, [2]Gurjeet Singh, [3]Anant D Urhekar

ABSTRACT

Background: Antifungal drug susceptibility testing (ADST) is still not done routinely for detection of drug resistance pattern of *Aspergillus* species. Physicians prescribe treatment to patients empirically which has led to the emergence of drug resistance in *Aspergillus* species.

Aim: The study aims to standardize the facility for antifungal drug susceptibility testing of *Aspergillus* species**.**

Materials and methods: *In vitro* drug sensitivity testing was done using the method as per Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: Drug sensitivity by phenotypic method revealed resistance to fluconazole for all *Aspergillus* species whereas miconazole, nystatin, and clotrimazole showed 100% sensitivity to all *Aspergillus* species. However, itraconazole and amphotericin - B showed 33.33–66.67% sensitivity, and ketoconazole showed 44.44–100% sensitivity.

Conclusion: Drug resistance testing by phenotypic method revealed that *Aspergillus* isolates from patient samples were resistant to fluconazole for all *Aspergillus* species whereas miconazole, nystatin, and clotrimazole show 100% sensitivity to all *Aspergillus* species. Itraconazole shows 66.67–33.33% sensitivity. Amphotericin B shows 66.67–33.33% sensitivity. Ketoconazole shows 100–44.44% sensitivity to various *Aspergillus* species.

Keywords: Antifungal drugs, *Aspergillus*, Drug resistance, Disk diffusion method, E-test.

How to cite this article: Raksha, Singh G, Urhekar AD. *In Vitro* Antifungal Drug Susceptibility Testing of *Aspergillus* Isolates from Clinical and Environmental Samples. MGM J Med Sci 2018;5(4):154-158.

Source of support: Nil

Conflict of interest: None

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INTRODUCTION

Fungal infection is a growing problem in the developed world. Fungi readily infect immunocompromised patients, and systemic infections typically cause high morbidity.[1,2] Reports of fungal infections in healthy populations are also rising for example, because of the increased virulence of pathogens such as *Aspergillus fumigatus*. Fungi are now as a serious threat to human health as bacteria, viruses, and parasites.[1-4] *Aspergillus* species cause a wide range of diseases including chronic, acute and sub-acute diseases. Invasive aspergillosis (IA) causes approximately 30% of fungal infections in patients dying with cancer. The crude mortality from IA is approximately 85% and falls to approximately 50% if treated. The most common isolates from clinical samples are *Aspergillus fumigatus*; other species like *A. flavus*, *A. niger*, and *A. terreus* may also cause infections.[5]

The gold standard antifungal drug is amphotericin B, while fluconazole and itraconazole are also used. Voriconazole may be useful against yeasts and filamentous fungi.[6] The CLSI has developed broth microdilution method for of antifungal drug sensitivity pattern of molds. Also, an agar diffusion method has been developed for yeasts by disk diffusion (CLSI M44-A). Still, no guidelines are available for antifungal drug susceptibility (ADS) of the mold by the disk diffusion method.[7] The aim of the present study aims to standardize a cheap and easy to perform a method to test the ADS of *Aspergillus* species.

MATERIALS AND METHODS

This prospective study was conducted at Mycology Laboratory, Department of Microbiology, Mahatma Gandhi Mission Medical College and Hospital, Kamothe, Navi Mumbai, India, over a period of one year from January 2015 to December 2015. *In vitro* drug sensitivity testing was done using the method as per CLSI guidelines. For Disk diffusion testing of antifungal drugs, i.e., amphotericin-B, fluconazole, clotrimazole, itraconazole, ketoconazole, miconazole and nystatin (Fig. 1) and for E-test strip amphotericin- B, fluconazole, voriconazole, itraconazole and ketoconazole (Fig. 2) were purchased from HiMedia Company.

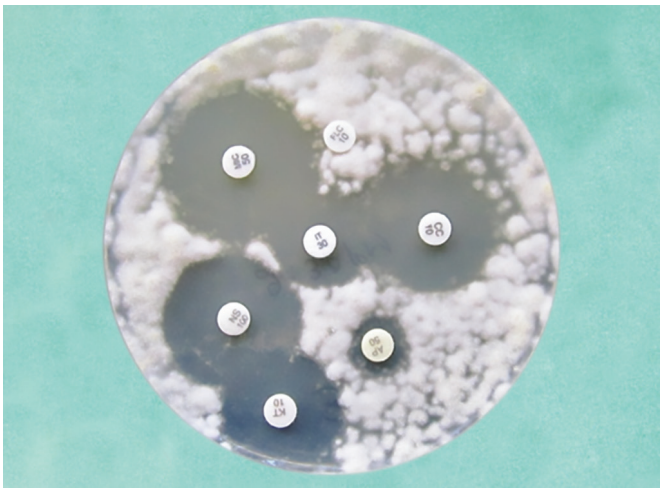

Fig. 1: Showing antifungal sensitivity testing by disk diffusion method

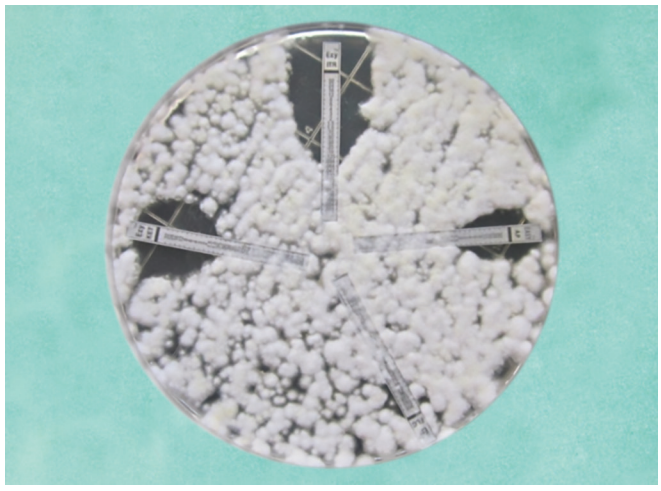

Fig. 2: Showing antifungal sensitivity testing by disk E-test method

Disk Diffusion Method

Preparation of Inoculum

Test inoculum was prepared by adding mold (hyphae and spores) overnight old culture which was grown on Sabouraud's dextrose agar after incubation at 37°C. Fungal growth was mixed with sterile saline in a test tube.

Tubes were vortex on a vortex mixture and turbidity was adjusted equal to the 0.5 McFarland standard.

Test Procedure

Muller Hinton agar containing 2% glucose and 0.5 mg/mL methylene blue dye was prepared in Petri dish for antifungal drug susceptibility test.

A sterile cotton swab was moistened with prepared inoculums and dipped swab rotated on upper inside wall of the inoculums tube to avoid excess quantity of the inoculums. Inoculated onto Muller Hinton agar prepared plate by lawn culture method with the moistened swab three times. Inoculated plate cover with a lid and allowed to dry for 5–10 minutes.

Antifungal Disks were applied with the help of sterile pointed forceps under strict aseptic condition.

Plates were incubated at 37°C in bacteriological incubator and 25°C in biological oxygen demand (BOD) incubator for 24 hours. After the incubation period of 24 hours, each plate was examined.

E-test Method

Preparation of Inoculum

Test inoculum was prepared by adding mold (hyphae and spores) overnight old culture which was grown on Sabouraud dextrose agar after incubation at 37°C. Fungal growth was mixed with sterile saline in a test tube.

Tubes were vortex on a vortex mixture, and turbidity was adjusted equal to the 0.5 McFarland standard.

Test Procedure

Muller Hinton agar containing 2% glucose and 0.5 mg/mL Methylene blue dye was prepared in Petri dish for E-test.

A sterile cotton swab was moistened with the and dipped swab rotated on upper inside wall of the tube to avoid excess quantity of the inoculums. Inoculated onto Muller Hinton agar prepared plate by lawn culture method with the moistened swab three times. Inoculated plate cover with a lid and allowed to dry for 5–10 minutes.

Kept Ezy MIC™ strip at room temperature for 15–20 minutes before applying.

Ezy MIC™ strip was placed over the inoculated plate and within 1 minute Ezy MIC™ strip was absorbed and adhere with the inoculated plate surface. Plates were incubated at 37°C in bacteriological incubator and 25°C in BOD incubator for 24 hours. After the incubation period of 24 hours, each plate was examined.

Minimum Inhibitory Concentrations Reading

Plates were read-only when sufficient growth was seen.

Minimum inhibitory concentrations (MIC) was read where the zone of inhibition may interfere with the MIC scale on the strip.

After an overnight incubation period each plate was examined.

RESULTS

Aspergillus isolates from patient samples showed following drug susceptibilities: Fluconazole showed resistance for all *Aspergillus* species, miconazole, nystatin, and clotrimazole showed 100% sensitivity for all *Aspergillus*

species, itraconazole showed 66.67–3.33% sensitivity, amphotericin-B showed 66.67–33.33% sensitivity, and ketoconazole showed 100–44.44% sensitivity (Table 1).

Aspergillus isolates from environment showed following drug susceptibilities: Fluconazole showed resistance for all *Aspergillus* species, miconazole, nystatin, and clotrimazole showed 100% sensitivity to for *Aspergillus* species, itraconazole showed 100–40% sensitivity, amphotericin-B showed 100–40% sensitivity, and ketoconazole showed 55.56–33.33% sensitivity (Table 1).

Antifungal drug sensitivity was performed for amphotericin-B, fluconazole, itraconazole, ketoconazole, miconazole, nystatin, clotrimazole by disk diffusion method and also antifungal drug sensitivity was performed by E-test for amphotericin-B, fluconazole, Itraconazole, ketoconazole, and voriconazole. Fluconazole showed resistance to all *Aspergillus* species from patient and environment (Table 2).

Disk diffusion test for antifungal drugs showed that sensitivity in patient samples was less than from environment. It means that aspergilli have developed resistance upon entry in patient's tissues.

DISCUSSION

In vitro drug sensitivity was performed as per standard procedures mentioned in materials and methods. Drug sensitivity of aspergilli isolated from patient samples and the environment was studied and compared. *Aspergillus* isolates from patient samples showed the following findings: Fluconazole showed resistance for all *Aspergillus* species, miconazole, nystatin, and clotrimazole showed 100% sensitivity for all *Aspergillus* species, itraconazole showed 66.67–33.33% sensitivity, amphotericin-B showed 66.67–33.33% sensitivity, and ketoconazole showed 100–44.44% sensitivity. *Aspergillus* isolates from the environment showed the following findings: Fluconazole showed resistance for all *Aspergillus* species, miconazole, nystatin, and clotrimazole showed 100% sensitivity to for *Aspergillus* species, Itraconazole showed 100–40% sensitivity, amphotericin-B showed 100–40% sensitivity, and Ketoconazole showed 55.56–33.33% sensitivity (Tables 1 and 2).

Gupta et al.[8] studied 44 isolates. Their results showed by disk diffusion method amphotericin B showed 87.5%, voriconazole (93.8%) and caspofungin (100%) and E-test amphotericin B 93.8%, voriconazole (93.8%) and caspofungin (100%). Espinel–Ingroff et al.[6] studied on 555 isolates. Amphotericin B and itraconazole, voriconazole, caspofungin posaconazole. Disk diffusion test showed a satisfactory zone of inhibition in comparison of MICs, i.e., 91–100% versus 82–100% for 4 out of 5. Arikan, et al.[7] studied on 78 isolates caspofungin. Caspofungin drug showed effective against *Aspergillus* species.

Serrano et al.[4] studied 77 isolates. Disk diffusion method was found equally good as the results showed by E-test. Kazemi et al.[9] studied on 50 isolates using Voriconazole, itraconazole and amphotericin B. Voriconazole was more sensitive than itraconazole with MICs between 0.5–1 µg/mL. It appears that all *Aspergillus* species from patient's samples and environment have developed

Table 1: Antifungal drug resistance pattern of *Aspergillus* species isolated from patient and environmental samples by disk diffusion test

	Antifungal drugs sensitivity testing in patient samples by disk diffusion						
Patient samples	*FLC*	*IT*	*AP*	*KT*	*MIC*	*NS*	*CC*
A. niger (n = 18)	0 (0%)	9 (50%)	10 (55.56%)	8 (44.44%)	18 (100%)	18 (100%)	18 (100%)
A. fumigatus (n = 9)	0 (0%)	4 (66.67%)	4 (66.67%)	2 (33.33%)	9 (100%)	9 (100%)	9 (100%)
A. flavus (n = 7)	0 (0%)	4 (57.14%)	3 (42.86%)	3 (42.86%)	7 (100%)	7 (100%)	7 (100%)
A. brasiliensis (n = 3)	0 (0%)	1 (33.33%)	1 (33.33%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)
A. terrus (n = 2)	0 (0%)	1 (50%)	1 (50%)	2 (100%)	2 (100%)	2 (100%)	2 (100%)
Environmental Samples							
A. niger (n = 20)	0 (0%)	14 (70%)	14 (70%)	10 (50%)	20 (100%)	20 (100%)	20 (100%)
A. fumigatus (n = 9)	0 (0%)	9 (100%)	8 (88.89%)	5 (55.56%)	9 (100%)	9 (100%)	9 (100%)
A. flavus (n = 5)	0 (0%)	2 (40%)	2 (40%)	2 (40%)	5 (100%)	5 (100%)	5 (100%)
A. brasiliensis (n = 3)	0 (0%)	3 (100%)	3 (100%)	1 (33.33%)	3 (100%)	3 (100%)	3 (100%)
A. terrus (n = 2)	0 (0%)	2 (100%)	2 (100%)	1 (50%)	2 (100%)	2 (100%)	2 (100%)

Abbreviations: FLC = Fluconazole, IT = Itraconazole, AP = Amphoterecin-B, KT = Ketoconazole, MIC = Miconazole, NS = Nystatin, CC = Clotrimazole

Table 2: Antifungal drug resistance pattern of *Aspergillus* species isolated from patient and environmental samples by E-test

		Fluconazole 0.016–256 µg/mL	*Itraconazole 0.002–32 µg/mL*	*Voriconazole 0.002–32 µg/mL*	*Ketoconazole 0.002–32 µg/mL*	*Amphoterecin-B 0.002–32 µg/mL*
Patient samples	*A. niger* (n = 18)	6–64	0.125–1.125	0.02–0.50	0.32–0.5	0.5–2
	A. fumigatus (n = 9)	3–7	0.125–1.50	0.05–0.5	0.32–0.5	0.5–2
	A. flavus (n = 7)	6–256	0.047–0.94	0.03–0.4	0.32–0.75	0.5–1.5
	A. brasiliensis (n = 3)	16–157	0.5–4.0	0.03–0.6	0.64–2	2–12
	A. terrus (n = 2)	12–250	0.032–0.5	0.03–0.3	0.5–3	0.125–3
Environmental samples	*A. niger* (n = 20)	6–64	0.125–1.125	0.02–0.50	0.32–0.5	0.5–2
	A. fumigatus (n = 9)	3–7	0.125–1.50	0.05–0.5	0.32–0.5	0.5–2
	A. flavus (n = 5)	6–256	0.047–0.94	0.03–0.4	0.32–0.75	0.5–1.5
	A. brasiliensis (n = 3)	16–157	0.5–4.0	0.03–0.6	0.64–2	2–12
	A. terrus (n = 2)	12–250	0.032–0.5	0.03–0.3	0.5–3	0.125–3

resistance to fluconazole. Aspergilli from both groups show sensitivity to miconazole, nystatin, and clotrimazole. However, patient samples show less sensitivity to itraconazole, amphotericin-B, ketoconazole than the environment, suggesting the development of resistance because of certain conditions in patients.

In E-test, however, the sensitivity of *Aspergillus* isolates from patient and environment is similar in E-test measuring MIC. However, it is different in disk diffusion test. E-test measures the minimum inhibitory concentrations values of the organism, while the disk diffusion method measures the sensitivity to fixed, clinically required optimal concentration of the drug.

It is possible that the disk diffusion test is showing resistance at a particular concentration (e.g., 1 µg/mL) but E-test may show sensitivity at 1.5 µg/mL or 2 µg/mL. In this situation, if the patient needs a particular drug, it can be given in higher concentration but considering the side effects.

Antifungal drug sensitivity was performed for amphotericin-B, fluconazole, itraconazole, ketoconazole, miconazole, nystatin, clotrimazole by disk diffusion method and against amphotericin-B, fluconazole, itraconazole, ketoconazole, and voriconazole. Fluconazole showed resistance to all *Aspergillus* species from patient and environment.

Disk diffusion test for antifungal drugs showed that sensitivity in patient samples was less than from environment. It means that aspergilli have developed resistance upon entry in patient's tissues. This resistance can be developed by organisms to counteract the antimicrobial agents used by patients.

Cost-effectiveness of any test is important to make it available to a greater number of suspect cases. At the same time, it is necessary to maintain quality control in relation to control strains, i.e., American type culture collection (ATCC) strains.

CONCLUSION

Comparison of sensitivity of *Aspergillus* species to antifungal drugs showed less sensitivity in patient isolates as compared to those isolated from the environment. It means that aspergilli in the environment have good sensitivity, but upon entry in patients, the aspergilli acquire greater resistance possibly because of struggle to survive in conditions which are directed to the elimination of aspergilli from patient tissues. The differences in sensitivity are observed in disk diffusion test where optimal drug concentration is used. However, there is no difference in sensitivity by E-test method which measures MIC. Minimum inhibitory concentration is a predetermined level in aspergilli which possibly cannot be modified in adverse conditions. Disk diffusion test is clearly cheaper than E-test. Disk diffusion test can be routinely performed while E-test can be performed whenever needed.

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10.5005/jp-journals-10036-1210

ORIGINAL ARTICLE

Study of Cyclophilin-A, High Sensitivity C-reactive Protein, and Malondialdehyde in Obese and Nonobese Type 2 Diabetes Mellitus Patients

[1]Jasmin Kumar, [2]ZG Badade, [3]Sandeep Rai

ABSTRACT

Aim and objectives: To study cyclophilin-A, high sensitivity C-reactive protein (hsCRP) and malondialdehyde in obese and nonobese type 2 diabetes mellitus (DM) patients.

Material and methods: A total of 120 subjects aged 35–65 years were enrolled and grouped as:

- Obese subjects with diabetes,
- Nonobese subjects with diabetes,
- Obese subjects without diabetes,
- Nonobese subjects without diabetes.

Their serum was tested for estimation of 4 biochemical parameters, namely cyclophilin-A, hsCRP, malondialdehyde, and lipid profile.

Observation and results: The mean cholesterol, triglycerides (TG), VLDL, LDL levels were significantly higher in obese diabetics as compared to obese nondiabetics, normal body mass index (BMI) diabetics, and control group. The mean HDL was higher in nondiabetic obese as compared to obese diabetic patients, normal BMI diabetics and control group and this difference was statistically insignificant. Cyclophilin-A and hsCRP were significantly higher in obese diabetics as compared to non-diabetic obese patients, Normal BMI diabetics and control group. The mean lipid peroxide (malondialdehyde) was significantly higher in nondiabetic obese patients, as compared to obese diabetics, normal BMI diabetics, and control group.

Conclusion: Cyclophillin-A (CypA) and hsCRP were significantly elevated in obese type 2 diabetics while malondialdehyde was significantly higher in nondiabetic Obese patients. Lipid profile parameters were also significantly elevated in obese type 2 diabetics. These inflammatory cardiometabolic risk biomarkers can be used for diagnostic, therapeutic and prognostic decision-making, especially in the context of inadequate quantitative risk assessments available to clinicians.

Keywords: Cyclophilin-A, High sensitivity C-reactive protein, Malondialdehyde, Obese, Type-2 diabetes mellitus patients.

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How to cite this article: Kumar J, Badade ZG, Rai S. Study of Cyclophilin-A, High Sensitivity C-reactive Protein, and Malondialdehyde in Obese and Nonobese Type 2 Diabetes Mellitus Patients. MGM J Med Sci 2018;5(4):159-163.

Source of support: MGMIHS

Conflict of interest: None

INTRODUCTION

According to the latest 2016 World Health Organization (WHO) data, an estimated 422 million adults are living with diabetes mellitus globally.[1] Diabetes is growing alarmingly in India. India had 69.2 million people living with diabetes (8.7%) as per the 2015 data. Calling India, the diabetes capital of the world, the International Journal of Diabetes in Developing Countries say that there is an alarming rise in incidence in India.[2] WHO project that diabetes will be the 7th leading cause of death in 2030.[3] Obesity is a major independent and modifiable risk factor for type 2 diabetes mellitus (T2DM) and many epidemiological studies have suggested a progressive increase in the prevalence of T2DM with obesity.[4,5]

The etiology of obesity-related type 2 diabetes is multifactorial. Factors, such as insulin resistance, β-cell dysfunction, physical inactivity and body fat distribution are all inter-related and play a causal role in its development. Chronic hyperglycemia in diabetes is linked to long-term damage, dysfunction and failure of different organs, especially kidneys, nerves, eyes, heart and blood vessels.[6]

Type 2 diabetes mellitus (T2DM) is associated with the development of premature arteriosclerosis, adding further to cardiovascular morbidity and mortality. The most common lipid abnormality noted in diabetics is Hypertriglyceridemia. In obese diabetics, the hepatic clearance of lipids and insulin are decreased as evident by studies showing increased levels of portal free fatty acids (FFA).

Cyclophilins are proteins belonging to the superfamily of immunophilins. The CypA is normally an intracellular protein. In diabetes, high glucose levels and reactive oxygen species activate monocytes to secrete CypA via vesicles. Secreted CypA acts as a proinflammatory cytokine that activates endothelial cells and leukocytes,

increasing inflammation in vessels and promoting atherogenesis. Diabetes and atherosclerosis can affect one another, with CypA being one of the factors connecting diabetes and atherosclerosis. Therefore, we conducted a present study to evaluate CypA, hs-CRP, malondialdehyde and lipid profile in diagnosed cases of Obesity and T2DM and compare with healthy control.

AIMS AND OBJECTIVES

- To estimate levels of cyclophilin-A, high sensitivity C-reactive protein, malondialdehyde and lipid profile in diabetes and obese patients.
- To compare and correlate CypA, high sensitivity C-reactive protein (CRP), malondialdehyde and Lipid profile in study groups.

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Biochemistry and the Department of General Medicine at MGM Hospital, Kamothe, Navi Mumbai from February 2017 to March 2018. The study was approved by the Institutional Ethics Review Committee. Patients from groups 1, 2 and 3 were enrolled from medicine ward. Group 4 was from the general population as well as the medicine ward. Total of 120 subjects was enrolled and grouped as mentioned below aged 35–65 years.

- *Group 1*: Obese subjects with diabetes
- *Group 2*: Nonobese subjects with diabetes
- *Group 3*: Obese subjects without diabetes
- *Group 4*: Nonobese subjects without diabetes

Inclusion Criteria

- *Group 1 (Obese subjects with diabetes):* Proven diabetics as per WHO criteria, BMI >25 kg/m^2.
- *Group 2 (nonobese subjects with diabetes):* Proven Diabetics as per WHO criteria and BMI <25 kg/m^2.
- *Group 3 (obese subjects without diabetes):* BMI >25kg/ m^2
- *Group 4 (nonobese subjects without diabetes):* Patients without any cardiovascular event and BM1 <25 kg/ m^2.

Exclusion Criteria

Age less than 35 years and more than 65 years, with chronic liver disease, chronic renal disease, HIV patient, tuberculosis, asthma, malignancy,pPregnant women, any chronic inflammatory disease.

Sample Collection

Venous blood was collected under strict aseptic conditions in the plain bulb for serum for estimation of biochemical parameters—cyclophilin-A, CRP, malondialdehyde, lipid profile. All estimations were analyzed in the central clinical laboratory of MGM Hospital, Navi Mumbai. Plasma glucose, serum cholesterol, serum triglyceride, and serum HDL cholesterol were analyzed on AU480 autoanalyzer. Serum CypA) was analyzed by Allianz-bio human CypA ELISA kit. Serum hsCRP was analyzed by turbidimetric immunoassay.

Statistical Analysis

All the collected data were entered in the Microsoft Excel sheet and then transferred to Statistical Package for the Social Sciences (SPSS) software ver. 17 for analysis. Qualitative data were presented as frequency and percentages and analyzed using the Chi-square test. Quantitative data were presented as mean and standard deviation (SD) and compared by analysis of variance ANOVA test. A p value <0.05 was taken as a level of significance.

OBSERVATION AND RESULTS

In our study, there were no significant differences in the mean age and sex distribution among the groups.

ANOVA Test

As seen in the Table 1, the mean cholesterol, TG, VLDL, LDL was significantly higher in obese diabetics as compared to obese patients, normal BMI diabetics and control group. The mean HDL was higher in obese as compared to obese diabetics patients, normal BMI diabetics and control group and this difference was statistically insignificant, depicted in Graph 1.

As seen in Table 2, the mean hsCRP and cyclophillin-A were significantly higher in obese diabetics as compared to obese patients, normal BMI diabetics and control group. The mean lipid peroxide (malondialdehyde) was significantly higher in obese as compared to obese diabetics patients (2.86 ± 0.65), normal BMI diabetics and control group, depicted in Graph 2.

DISCUSSION

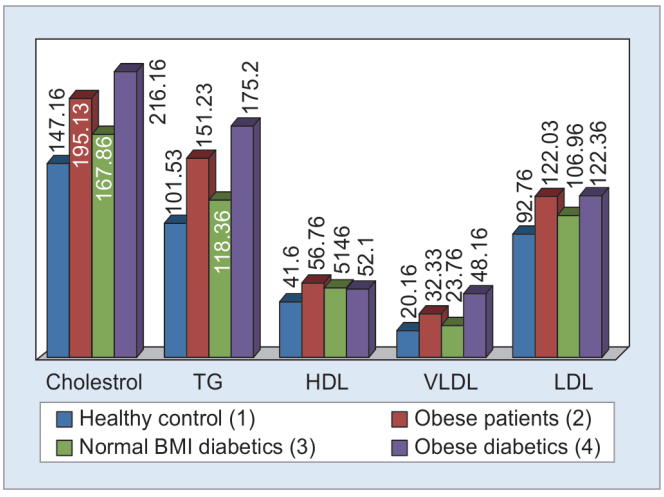
Obesity is associated with a chronic low-grade inflammation, as evidenced by an increase in circulating inflammatory markers, such as CRP.[7-12] The presence of systemic inflammation in visceral obesity has been linked to an increased risk of developing CVD and type 2 diabetes.[13-15] Obesity results when there is an imbalance between energy ingested and energy expended.[16] A relative excess of energy (either genetic or diet-induced) results in two major cellular features; adipocyte expansion and infiltration of inflammatory cells into adipose tissue in both mice and humans.[17-19]

Table 1: Lipid profile parameters amongst different study population

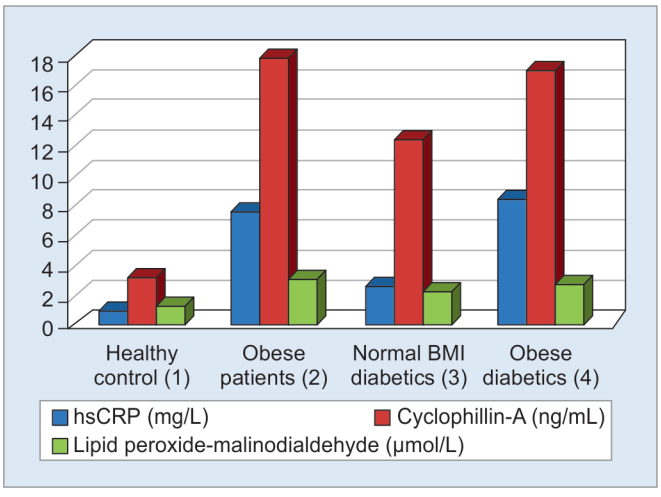
mg/dL	*Healthy control Mean ± SD*	*Obese patients Mean ± SD*	*Normal BMI diabetics Mean ± SD*	*Obese diabetics Mean ± SD*	*p value*
Cholesterol	147.16 ± 31.65	195.13 ± 21.27	167.86 ± 39.10	216.16 ± 27.44	0.0001
TG	101.53 ± 21.47	151.23 ± 59.04	118.36 ± 52.88	175.2 ± 92.16	0.0001
HDL	41.6 ± 11.41	56.76 ± 63.52	51.46 ± 16.93	52.1 ± 63.52	0.633
VLDL	20.16 ± 4.29	32.33 ± 17.18	23.76 ± 10.53	48.16 ± 41.43	0.0001
LDL	92.76 ± 9.96	122.03 ± 33.85	106.96 ± 89.22	122.36 ± 42.23	0.0001

Table 2: Mean hsCRP, cyclophillin-A, and malondialdehyde amongst different study population

	Healthy Control mean ± SD	*Obese patients Mean ± SD*	*Normal BMI diabetics mean ± SD*	*Obese diabetics Mean ± SD*	*p value*
hsCRP (mg/L)	1.06 ± 0.52	7.8 ± 1.91	2.73 ± 0.73	8.5 ± 2.11	0.0001
Cyclophillin-A (ng/mL)	3.33 ± 2.13	17.9 ± 9.42	12.44 ± 3.96	17.13 ± 5.07	0.0001
Malondialdehyde (µmol/L)	1.39 ± 0.16	3.20 ± 0.35	2.38 ± 0.24	2.86 ± 0.65	0.0001



Graph 1: Lipid profile parameters amongst different study population



Graph 2: Mean hsCRP, cyclophillin-A, and Malondialdehyde amongst different study population

Adipocytes and macrophages both generate inflammatory molecules, which lead to insulin resistance and systemic inflammation.

In this study, there were no significant differences in the mean age and sex distribution among the groups. These findings are in agreement with the study conducted by Lamiaa et al.[20]

In the present study, lipid profile parameters like cholesterol, TG, VLDL, LDL was significantly higher in obese diabetics as compared to obese patients, normal BMI diabetics and control group. While the mean HDL was higher in obese as compared to obese diabetics patients, normal BMI diabetics and control group and this difference was statistically insignificant ($p < 0.001$). This finding is consistent with the Lamiaa et al. study, which showed a significant increase in total cholesterol, LDL-C, non-HDL-C and triglycerides in obese subjects with and without diabetes, while HDL-C was significantly reduced.[20]

The mean cholesterol, TG and LDL was higher in obese diabetics as compared to obese patients and control group. The significant differences in lipid profile markers between healthy and obese non- diabetic groups were consistent with the study of Khan and Khaleel et al., whereas the study of Songa et al. did not show significant differences in lipid profile markers between healthy and obese nondiabetic groups.[21,22] This did not match our results. Both studies and many other similar studies, Yadav et al however, agrees with our findings regarding the significant difference in the lipid profile of diabetic patients and controls.[23] Lipid profile parameters differ significantly in obese diabetic and nondiabetic subjects, due to the fact that the insensitivity of adipose cells and other target tissues to insulin (insulin resistance), clearly seen in obesity and T2DM, leads to dysregulation of enzymes such as lipoprotein lipase, leading to increased and extended lipemia and failure to clear plasma triglycerides rapidly.[24]

Dyslipidemia in the two diabetic groups is supported by the following facts and theories. Insulin is known to have major regulatory influence on lipid metabolism, and

the effects of primary abnormalities in lipid metabolism on insulin resistance contribute to pathogenesis of diabetes. Dyslipidemia in type 2 diabetes is characterized by an increased level of triglyceride and decreased high- density lipoprotein cholesterol (HDL-C), which is known to be present for many years before diabetic hyperglycemia begins.

The mechanism by which hypertriglyceridemia occurs in diabetes is fairly well understood. Levels of non-esterified fatty acids (NEFAs) are increased because, in many patients, the adipose tissue mass from which these are released, particularly the more metabolically active and centrally distributed adipose, is increased. Hormone-sensitive lipase, the intracellular lipase present in adipose tissue is activated by the insulin deficiency or resistance present in diabetes. This increases the release of NEFAs from triglyceride stored in adipose tissue. High circulating levels of NEFAs increase hepatic triglyceride production.[25]

In the present study, biomarkers like hsCRP and CypA was significantly raised in obese diabetics as compared to obese patients, normal BMI diabetics and control group while the mean malondialdehyde was significantly higher in obese as compared to obese diabetics patients, normal BMI diabetics and control group. These findings are consistent with the study conducted by Lamiaa et al., in which the inflammatory markers (hsCRP) in the obese group increased compared to the controls.[20] Similarly, Ramachandran et al. in their report showed that CypA which is secreted by monocytes and plays vital role in proinflammatory stimulus for vascular inflammation and diabetes.[26] Satoh et al., also reported higher level of CypA in diabetic patients with coronary artery disease as compared to healthy volunteers, signifying its role in increasing vascular disease in type 2 diabetes.[27]

The hsCRP appears strongly associated with diabetes mellitus and resistance to insulin. These findings are consistent with the study conducted by Safiullah Amanullah et al., the hsCRP levels in diabetic subjects were increased in comparison with nondiabetic subjects.[28] Several studies have shown that hsCRP predicts diabetes in western populations earlier.[29,30] Goodarzi et al. support the correlation between the degree of hyperglycemia and oxidative stress.[31] Gillery et al., explains that hyperglycemia generates an increase of the intensity of the reactions of nonenzymatic glycation proteins that are associated with oxidative stress, well described in patients with diabetes.[32] Abdul-Ghani et al., in their study reported that type 2 diabetic participants had an increased rate of mitochondrial ROS production compared with age-and BMI-matched nondiabetic participants.[33]

CONCLUSION

C-reactive protein (CRP), CypA were significantly elevated in obese type-2 diabetics while malondialdehyde was significantly higher in obese patients. Lipid profile parameters were also significantly elevated in obese type-2 diabetics. These cardiometabolic risk inflammatory biomarkers play a critical role in diagnostic, therapeutic and prognostic decision making, especially in the context of insufficient quantitative risk assessments available to clinicians. In order to reduce modifiable risk factors, this could significantly reduce the burden of complications on patients and the healthcare system.

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10.5005/jp-journals-10036-1211

ORIGINAL ARTICLE

Knowledge and Awareness Survey about Universal Safety Precautions among Undergraduate Medical and Dental Students

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ABSTRACT

Aim: Although crucial in prevention and transmission of blood-borne infections (BBI), the concept of universal safety precautions (USP) is disregarded by the medical professionals in their early career years, mainly due to the lack of knowledge and awareness regarding the same. This study, through a questionnaire survey, aimed to assess the awareness of the 1st year medical and dental students about USP and its application in daily practice.

Materials and methods: A questionnaire-based survey consisting of 12 questions on USP was given to the students to fill. An interventional lecture with interactive sessions was conducted for the students to educate them about USP. The same set of questions was again provided to the students one week after the lecture.

Results: Out of the 210 participants that were included, 63% were unaware of USP. Eighty-three percent of the students did not adhere to proper barrier protections like gloves, gowns, and goggles and 56% did not handle sharps such as needles and blades correctly. These results showed a significant improvement when assessed after the interventional lecture.

Conclusion: The knowledge of students regarding USP is inadequate. The interventional lecture and interactive sessions helped increase their awareness of USP.

Clinical significance: The importance of teaching USP to medical and dental students in their early years of professional career for preventing transmission of BBI is highlighted in this study.

Keywords: Bloodborne infection, Interventional session, Questionnaire survey, Universal safety precaution.

How to cite this article: Padhye MM, Padhye NM, Kattimani YR, Inamdar RS. Knowledge and Awareness Survey about Universal Safety Precautions among Undergraduate Medical and Dental Students. MGM J Med Sci 2018;5(4):164-167.

Source of support: MGMIHS

Conflict of interest: None

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INTRODUCTION

Risk of contracting infection is an important problem among healthcare workers (HCW) worldwide. It is a significant cause for morbidity and mortality among HCW associated with clinical, diagnostic and therapeutic procedures in patients.[1] Blood and certain body fluids are considered potentially infectious for human immunodeficiency virus (HIV), hepatitis B virus (HBV) and other blood-borne infections. Worldwide, it is estimated that about 40% of HBV infections and 2.5% of HIV infections in HCWs are due to occupational hazards of sharp exposures.[2,3]

Universal safety precautions (USP) are a set of evidence-based clinical work practices published by the Centers for Disease Control and Prevention in 1996 and updated in 2007. These were specifically designed to prevent transmission of HIV, HBV, and other blood-borne pathogens when providing health care. The USP apply to blood, cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids. They usually do not apply to feces, nasal secretions, sputum, sweat, tears, urine, and vomitus unless they contain visible blood.[4,5] Protective measures such as washing hands, use of protective barriers like gloves, gowns, aprons, masks or protective eyewear form the basis of USP. Adoption of safe practices for usage and disposal of needle sticks and other sharp objects is equally important. Hand hygiene, being the most important, has been known to reduce healthcare-associated infections as well.[6,7]

Despite the huge number of cases of BBI as an occupational hazard, a lack of awareness and training has resulted in an inadequate knowledge and understanding of USP among HCW.[8] The problem is magnified in early academic years of medical and dental course, when students start attending hematology experiments, where blood collection is involved, as a part of their curriculum. They constitute a particularly high-risk group since they are inexperienced and are hurried for time and often tempted to ignore USP to complete the work assigned to them. They are also likely to be less informed about the dangers of percutaneous exposure to body fluids and the steps to be taken in case of such events and are thus at a greater risk of occupational exposure

to all kinds of blood-borne pathogens. Not even a single case of seroconversion in medical students, because of lack of knowledge and awareness about USP, should be acceptable. Thus, the aim of the present survey was to assess the knowledge and awareness of USP among undergraduate medical and dental students. Furthermore, an intervention in the form of a lecture and interactive sessions were conducted. The outcomes of the information were compared before and after the session.

MATERIALS AND METHODS

The longitudinal study was conducted in March and April 2018 in the Department of Physiology at the Mahatma Gandhi Medical College and Hospital, Navi Mumbai, India. Ethical approval was sought from the institutional ethical committee. The study population included 1st-year Bachelor of Medicine, Bachelor of Surgery (MBBS) and Bachelor of Dental Surgery (BDS) students. All students willing to participate in the study were included and written informed consent was taken from all participants. A predesigned validated questionnaire of 12 questions about USP was prepared for the study (Table 1). After explaining the purpose of the study the questionnaire was given to the participants to fill. Students whose questionnaires were incompletely filled were excluded from the study. An informative session about USP of 1-hour duration was conducted for the participants. In the lecture, the participants were informed about various BBI, their routes of transmission and various effective measures to prevent these. Their queries regarding the same were discussed in an interactive session which followed the lecture.

A 7 days post-session, the same questionnaire about USP was given to the same batch of students. A comparative study of the pre- and post-session response to assess the awareness and retention of knowledge were done. Data analysis was done using Windows PC based software "MedCalc Statistical Software" version 13.3.1.

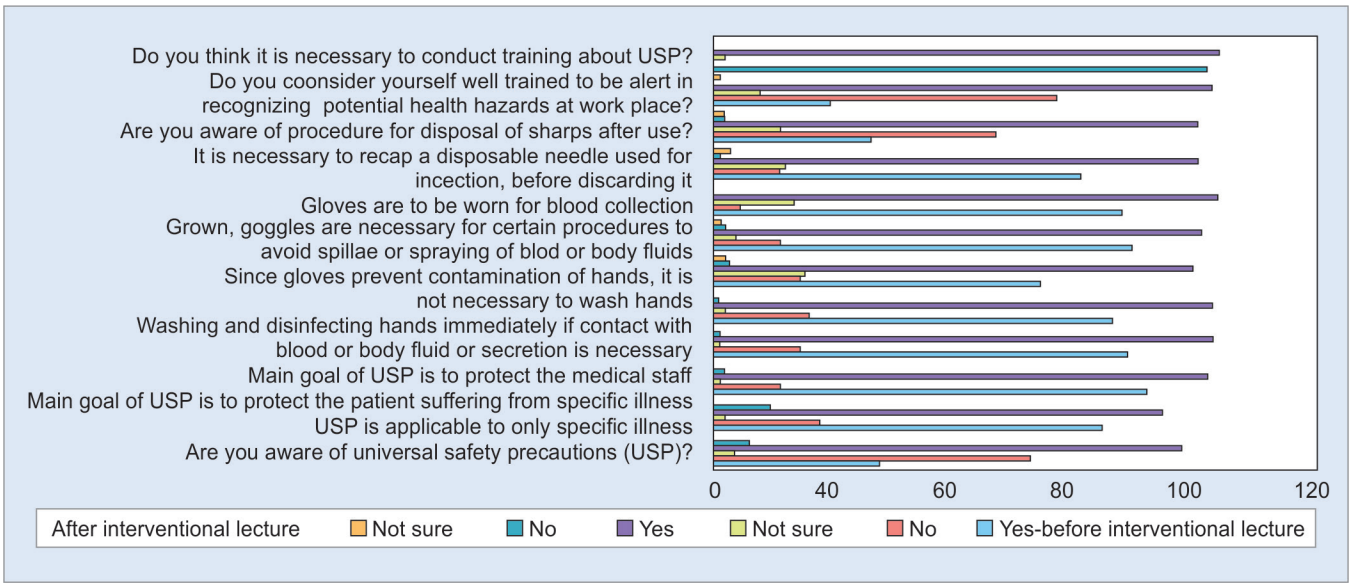
Distribution of responses was examined using frequencies and percentages, and descriptive statistics were presented for the scores of questionnaires. Statistical analysis of the obtained data were done using the Chi-square test.

RESULTS

A total of 220 students participated in the survey from which 10 students were excluded. Out of the remaining 210, 112 (53.33%) were females and 98 (46.66%) males. A total of 132 (63%) participants stated that they were unaware of USP, whereas 162 (77%) participants thought that USP applies only to specific illnesses. One hundred seventy-two (82%) students considered the main goal of USP was to protect the medical staff which increased to 208 (99%) after the lecture. Forty participants (19%)

Table 1: Distribution of responses of the participants to various questions

Question no.	*Question*	*Response*	*Before interventional lecture (%)*	*After interventional lecture (%)*
1.	Are you aware what Universal Safety Precautions (USP) means?	Yes	69 (33%)	195 (93%)
		No	132 (63%)	15 (7%)
		Not sure	8 (4%)	0
2.	USP is applicable to only specific illness	Yes	162 (77%)	187 (89%)
		No	44 (21%)	23 (11%)
		Not sure	4 (2%)	0
3.	Main goal of USP is to protect the patient suffering from specific illness	Yes	181 (86%)	206 (98%)
		No	27 (13%)	4 (2%)
		Not sure	2 (1%)	0
4.	Main goal of USP is to protect the medical staff	Yes	172 (82%)	208 (99%)
		No	36 (17%)	2 (1%)
		Not sure	2 (1%)	0
5.	Washing and disinfecting hands immediately if contact with blood or body fluid or secretions is necessary	Yes	166 (79%)	208 (99%)
		No	40 (19%)	2 (1%)
		Not sure	4 (2%)	0
6.	Since gloves prevent contamination of hands, it is not necessary to wash hands	Yes	137 (65%)	200 (95%)
		No	36 (17%)	6 (3%)
		Not sure	38 (18%)	4 (2%)
7.	Gown, goggles are necessary for certain procedures to avoid spillage or spraying of blood or body fluids	Yes	174 (83%)	204 (97%)
		No	27 (13%)	4 (2%)
		Not sure	8 (4%)	2 (1%)
8.	Gloves are to be worn for blood collection	Yes	170 (81%)	210 (100%)
		No	11 (5%)	0
		Not sure	34 (16%)	0
9.	It is necessary to recap a disposable needle used for injection, before discarding it	Yes	153 (73%)	202 (96%)
		No	27 (13%)	2 (1%)
		Not sure	29 (14%)	6 (3%)
10.	Are you aware of procedure for disposal of sharps after use?	Yes	65 (31%)	202 (96%)
		No	118 (56%)	4 (2%)
		Not sure	27 (13%)	4 (2%)
11.	Do you consider yourself well trained to be alert in recognizing potential health hazards at work place?	Yes	48 (23%)	208 (99%)
		No	143 (68%)	0
		Not sure	19 (9%)	2 (1%)
12.	Do you think it is necessary to conduct training about USP?	Yes	206 (98%)	210 (100%)
		No	0	0
		Not sure	4 (2%)	0



Graph 1: Percentage distribution of participant responses to the questions before and after interventional lecture

reported that washing hands immediately after contact with blood or body fluids was not necessary which reduced to 2 (1%) participants, and 36 (17%) participants did not feel the necessity to wash hands if wearing gloves which reduced to 6 (3%) participants after the lecture. A total of 174 (83%) and 170 (81%) were of the opinion that barrier protection was necessary for certain procedures and gloves were necessary for blood collection respectively. About 56% of the students were unaware about the procedure for disposal of sharps (needles, blades and others) which decreased to 2%, whereas only 23% considered themselves well trained to recognize potential health hazards which increased exponentially to 99% after the interventional lecture (Graph 1). All of the responses showed a statistically significant improvement after the interventional session.

DISCUSSION

This questionnaire survey showed that the knowledge and awareness of USP among undergraduate students was variable. The majority of them (63%) were not aware of USP which is higher than in the study carried out by Vaz et al. in 2010[9] amongst health care workers. 77% of the students were of the opinion that USP is applicable only to specific illnesses such as HIV and HBV. The fact that 69% of the students were unaware of the correct disposal of sharp instruments is alarming. Since the risk of seroconversion after percutaneous exposure is about 0.3%,[10] it is absolutely essential to train the students in this aspect.

Protective barriers, such as gowns, goggles, masks or gloves are known to reduce the risk of exposure of the skin or mucous membranes to potentially infectious materials. However, about 13% of the students were of the opinion that such protective barriers were not necessary to carry out certain examinations and procedures. This needs to be addressed to reduce the risk of exposure to blood and other body fluids to which USP apply.

Awareness level about USP improved from 33–93% after intervention. The fact that USP is applicable to all patients for the protection of medical staff was realized by 99% against 82% previously. Awareness level about cleaning hands, use of protective barriers such as gowns, goggles, and gloves increased by 20%, 14%, and 19% respectively. The concept of handling and disposing of sharps did show improvement by 23% and 65%, respectively.

This study showed that there was inadequate knowledge among undergraduate medical and dental students about USP. This may be attributed to noninclusion of such information during introductory training lectures and orientation program. Since the undergraduate students are exposed to the hematology related experiments in the first year of training, it is important that they have a good understanding about the risk of blood-borne pathogens at the workplace and the preventive measures for reducing the risk. Overall importance and awareness level regarding blood-borne infection and USP increased from 23–99% with the intervention, namely, informative and interactive session. The improvement in knowledge and awareness noted after the interventional session on the guidelines and principles of USP highlights the need and importance of such repeated sessions even before the students are exposed to the clinical environment. These findings suggest that the training on USP should be undertaken at the beginning of their clinical career to prevent any occupational hazards. Reinforcement of the information is required from time to time, even before actual contact with patients. Also, knowledge about post-exposure prophylaxis should be given to the students before they enter the clinics.

Despite meticulously designing the study, it does have its share of limitations. A larger sample size along with a longer gap between the intervention and post-session evaluation can be considered for future studies. Multiple interactive sessions to reinforce the guidelines of USP for better retention of the knowledge can be undertaken.

CONCLUSION

Within the limitation of this study, it can be inferred that the knowledge and awareness of the students about blood-borne infections and USP improved after an informative and interactive session about the same. This may empower them with adequate knowledge and skills to protect themselves from occupational hazards such as transmission of BBI.

CLINICAL SIGNIFICANCE

This study is clinically significant as it will help us reduce the transmission of blood-borne infections among the HCW namely, medical and dental students. The study also stresses the importance of including the guidelines of USP in the early academic learning years of the students.

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10.5005/jp-journals-10036-1212

ORIGINAL ARTICLE

Correlation of Microalbuminuria and Estimated Glomerular Filtration Rate in Hypertensive Patients

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ABSTRACT

Microalbuminuria has been shown to be an intermediate end point and a powerful predictor of morbidity and mortality in patients with diabetes. This study aims to analyze the correlation between microalbuminuria and estimated glomerular filtration rate (eGFR) in hypertensive nondiabetic patients, to understand the role of microalbuminuria as a disease marker in hypertensive renal disease. Data of 100 patients meeting the inclusion and exclusion criteria were collected. Early screening of patients with hypertension, for microalbuminuria, by carrying out simple, inexpensive tests like urinary dipstick and spot urinary albumin/creatinine ratio, can help prompt the physician to initiate antihypertensive therapy in positive cases. Prevalence of microalbuminuria, which is an indicator of early chronic kidney disease (CKD), is about 49% among patients with hypertension.

Keywords: Estimated glomerular filtration rate, Hypertensive renal disease, Microalbuminuria, Urinary albumin/creatinine ratio.

How to cite this article: Nagpal RR, Bawikar P, Ghanekar J. Correlation of Microalbuminuria and Estimated Glomerular Filtration Rate in Hypertensive Patients. MGM J Med Sci 2018;5(4):168-172

Source of support: MGMIHS

Conflict of interest: None

INTRODUCTION

Microalbuminuria (MA) is typically defined as a 24 hours urinary albumin excretion rate of 30–300 mg (>20 to < 200 µg/min) or Urinary albumin/creatinine ratio (UACR) of 2.5–30 mg/mmoL in men, 3.5–30 mg/mmoL in women[1] (Table 1).

For several years, the gold standard for measurement of MA was protein quantification of a 24-hour urine collection. Collection errors and inconvenience have eliminated this approach for screening purposes.[2] The use of an early morning "spot" urine albumin-creatinine measurement (expressed as mg of albumin per gram creatinine) performed three times within a few weeks has been validated as an appropriate way to assess whether MA is present or not.[3,4] The National Kidney Foundation Disease Outcomes Quality Initiative (DOQI) guidelines recommend an untimed spot urine sample, with a preference for first morning samples.[5] A variety of antibody-based methods are available to measure urinary albumin. These include radioimmunoassay (RIA), nephelometry, immunoturbidimetry, and enzyme-linked Immuno-absorbent assay (ELISA). A more accurate high-performance liquid chromatography (HPLC) method that is more sensitive to detect microalbuminuria has been developed recently.[6]

Microalbuminuria (MA) can be reduced, and progression to overt proteinuria prevented, by aggressive blood pressure reduction, especially with a regimen based on medications that block the renin-angiotensin-aldosterone system, and control of diabetes.

The National Kidney Foundation recommends that blood pressure levels be maintained at or below 130/80 mm Hg in anyone with diabetes or kidney disease. Clinical studies have shown that small increases in micro-albuminuria indicate worsening cardiovascular disease, involving endothelial dysfunction and accelerated atherosclerosis, and are associated with significant increases in the risk of end-organ damage, major CV events and death.[7,8]

Microalbuminuria is an independent predictor of hypertension, metabolic syndrome, type 2 diabetes and coronary artery disease.[9]

Microalbuminuria develops from progressive, subclinical, structural and functional changes within the kidney and represents a sensitive marker of early renal disease.[10,11] Microalbuminuria is reported to be present in approximately 30–40% of patients with hypertension and appears to correlate both with severity and duration of hypertension.[12,13]

The Losartan Intervention for endpoint reduction in hypertension (LIFE) study[14] confirmed the predictive power of microalbuminuria and its changes over time[15] in a large cohort of carefully monitored patients during a 5-year follow-up; however, the renal predictive value of albuminuria is thus far limited to high-risk patients with or without diabetes.[16,17]

Table 1: Proteinuria *vs.* microalbuminuria[9]

	24-hour albumin (mg/24-hour)	*Albumin/Creatinine ratio (mg/g)*	*Dipstick proteinuria*	*24-hour urine protein (mg/24-hour)*
Normal	8–10	<30	Absent	<150
Microalbuminuria	30–300	30–300	Absent / Trace/1+	
Proteinuria	>300	>300	Trace–3+	> 150

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Microalbuminuria

A Genova investigation on complications (MAGIC) study,[18] comprised a total of 1230 patients with primary hypertension who were recruited between 1993 and 1997and were followed-up for a median of 11.8 years (range 1.6–14.2 years). The study cohort was composed of 917 patients who did not have diabetes and had hypertension and was aged 49 ± 10 years (median 51 years) without previous cardio-renal events or known renal disease.

At baseline, microalbuminuria was present in 36% of those who developed chronic renal insufficiency (CRI) compared with only 7% of control subjects. Patients who had hypertension and developed chronic renal insufficiency were older and showed higher BP levels and worse renal function than those who remained free from renal endpoints. Patients with microalbuminuria were more likely to be males and showed higher BP and higher serum uric acid levels as compared with patients without microalbuminuria, despite similar renal function and lipid profile.

Microalbuminuria has been shown to be an intermediate endpoint and a powerful predictor of morbidity and mortality in patients with diabetes. In particular, the degree of albuminuria is strongly related both to the progression of diabetic renal disease and to the risk for cardiovascular events.[19]

The overall prevalence of MA in another study conducted in Kottayam Medical College, in patients with essential hyper-tension was 26.67%.[20] which was slightly higher than the prevalence of MA observed (23%) in the LIFE study.[21]

MATERIAL AND METHODS

A cross-sectional cohort study was conducted in hypertensive patients, either visiting outpatient department (OPD) or getting admitted to MGM Hospital, Kamothe, Navi Mumbai, Maharashtra, India, between November 2015 to November 2017 after the approval from the institutional ethics committee. Written informed consent was taken from patients or their respective relatives, satisfying the study criteria. Inclusion and exclusion criteria are shown below:

Inclusion criteria	*Exclusion criteria*
Age group of 25–60 years Male and female Newly detected hypertensive patients Known cases of hypertension since 5 years with/without treatment	Overt proteinuria Congestive cardiac failure Chronic renal failure Urinary tract infections. Diabetes mellitus Pregnant women Obstructive uropathy and nephrolithiasis Renovascular hypertension Drugs causing hypertension: Steroids, amphetamines NSAIDS

A detailed history was taken from all patients about the duration of hypertension, previous therapies, responses, and side effects, family history of hypertension and cardiovascular disease, dietary and psychosocial history, other risk factors: weight change, dyslipidemia, smoking, diabetes, physical inactivity. Patients were evaluated for evidence of secondary hypertension: history of renal disease; obstructive sleep apnea , hypo- or hyperthyroidism; use of agents that may increase blood pressure like high-dose estrogens, steroids, decongestants, appetite suppressants, cyclosporine, tricyclic antidepressants, monoamine oxidase inhibitors, erythropoietin, nonsteroidal anti-inflammatory agents, cocaine; evidence of target organ damage: history of transient ischemic attack (TIA), stroke, transient blindness; angina, myocardial infarction, congestive heart failure; Sexual dysfunction; Other comorbidities. Patients were categorized on the basis of grades of hypertension according to the Joint National Committee (JNC) for hypertension (Table 2).

Based on the duration of hypertension, the study population was divided into four groups:

1. Newly detected hypertensives
2. Duration 1 month to 1-year
3. Duration 1–2 years.
4. Duration above 2 years but below 5 years.

All patients underwent following basic investigations for initial evaluation: fundoscopy, blood for CBC, lipid profile, renal function tests (RFT), electrolytes, blood sugar levels, TSH levels, urine for routine microscopy, dipstick, spot urine albumin/creatinine ratio, standard urinary dipstick and ultrasonography of abdomen and pelvis.

Operational Definitions

- *Newly diagnosed hypertensive*: History of hypertension less than 1 month.
- *Recently diagnosed hypertensive*: History of hypertension from 1 month to 1 year.
- Cockroft Gault formula for eGFR (mL/min):
  (140–age) × Weight
  72 × Creatinine
  For females, multiply result by 0.85
- MDRD-IV Formula for eGFR (mL/min):
  $186.3 \times Cr^{-1.154} \times age^{-0.203} \times GN_F \times ET_F$
  GN_F–Gender factor (male = 1; female = 0.742)
  ET_F–Ethnicity factor (white, non black = 1; black race = 1.212)

Table 2: JNC-7 classification of BP for adults aged 25 years or older

BP classification	*Systolic, mm Hg*	*Diastolic, mm Hg*
Normal	< 120	And < 80
Prehypertension	120–139	Or 80–89
Stage 1 Hypertension	140–159	Or 90–99
Stage 2 Hypertension	>160	Or ≥ 100

- *Microalbuminuria:* Positive UACR: Value more than 30–300 mg of albumin per 24 hours (30–300 mg/mg creatinine). *Negative UACR:* Values less than <30 mg of albumin per 24 hours or <30 mg/g creatinine.

Study Design

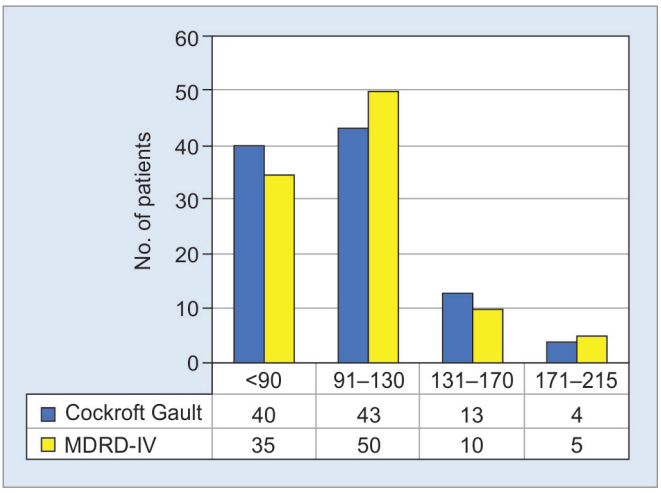
The study comprised of 100 patients. Patients fulfilling the study criteria were examined clinically and underwent routine investigations for initial evaluation. Patients were categorized on the basis of JNC-7 classification, severity (blood pressure on admission) and duration of hypertension. Three urine samples on three separate occasions were sent for spot UACR. The mean of 3 values of UACR was calculated quantitatively and categorized as UACR positive (≥30 mg/g) or UACR negative (<30 mg/g). The qualitative result of UACR was then correlated with other parameters. Patients with UACR ≥30 mg/g were screened for further end-organ damage.

RESULTS

Data were entered and analyzed by Microsoft Excel 2016 and Statistical Package for the Social Sciences (SPSS) 20.0. Univariate analysis (Chi-square test) was used to determine the relationship between Microalbuminuria and eGFR. Results of the study were expressed as *p* values.

Graph 1, compare the number of patients belonging to 4 categories of eGFR when calculated by Cockroft Gault and MDRD-IV method. The values of eGFR have been divided into four categories:

<90 mL/min; 91–130 mL/min; 131–170 mL/min and 171–215 mL/min. Microalbuminuria was evident in patients with an eGFR of <90 mL/min or between 91 mL/min and 130 mL/min calculated either by Cockroft Gault or MDRD-IV formulae. It indicates that patients with hyper-filtration have a protective mechanism and microalbuminuria does not manifest in these patients.



Graph 1: Hypertension and eGFR (Cockcoft Gault) vs. (MDRD–IV)

Chi-square Test

Graph 2 and Table 3 Interpretation: Since *p* value for the Chi-square test is greater than that of 0.05, and it indicates no significance of the association between eGFR and UACR.

Chi-square Test

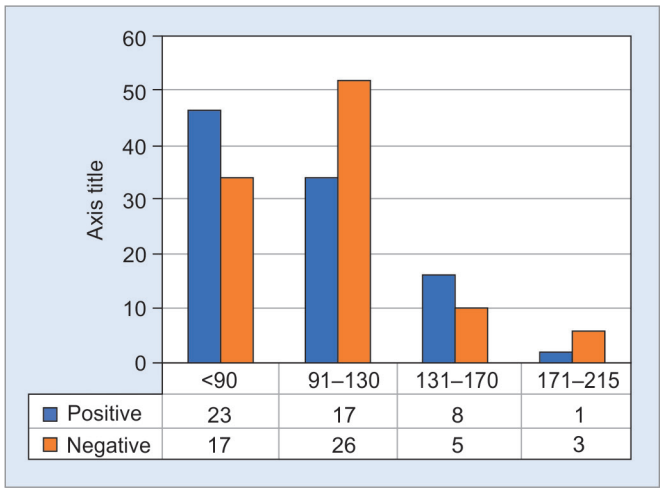
Graph 3 and Table 4 interpretation: Since *p* value for the Chi-square test is greater than that of 0.05, it indicates no significance of the association between eGFR and UACR.

Graph 4 shows that most of the patients in the study belonged to the G1 stage of KDIGO for chronic kidney damage.

Graph 5 depicts the distribution of patients with microalbuminuria according to GFR (KDIGO Staging of Chronic Kidney Damage, Table 5). Out of the 49 patients with microalbuminuria, 32 patients were in G1 stage, 15 in G2 and one each in G3b and G4.

Chi-Square Test Result

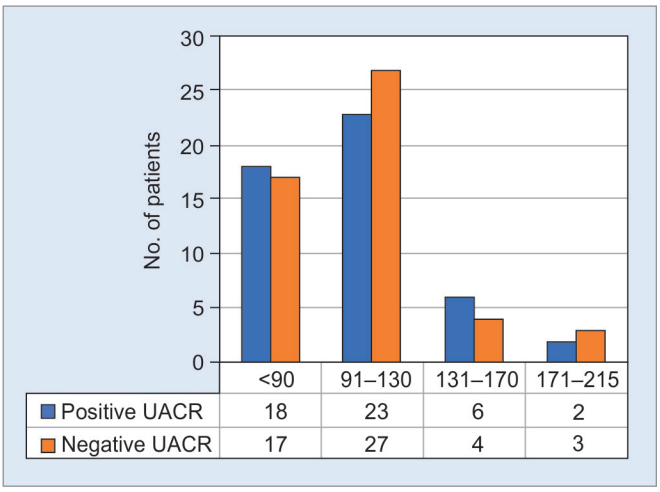
Graph 5, Table 6 interpretation: Since *p* value for the chi-square test is less than that of 0.05, it indicates that the proportion of the positive cases is not equal in all the classes. It can be observed from the residual table that the proportion of positive cases is significantly more in G1 and less in G3b and G4.



Graph 2: Effect of eGFR calculated by Cockroft Gault method on UACR

Table 3: Chi-square tests

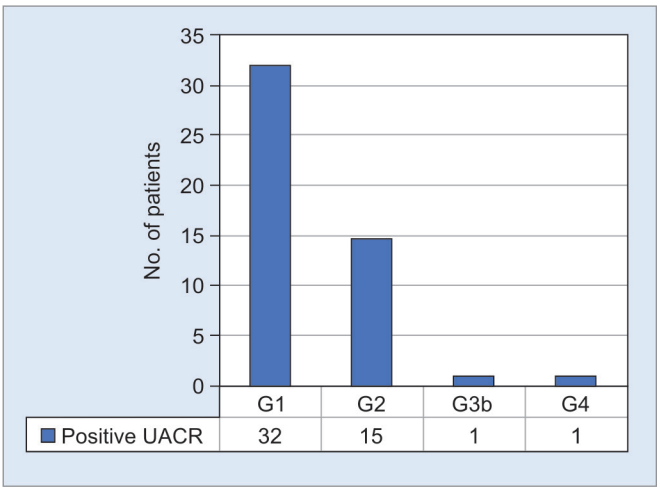
	Value	*df*	*Asymp. Sig. (2-sided)*
Pearson Chi-square	4.438[a]	3	0.218
Likelihood ratio	4.506	3	0.212
Linear-by-linear association	0.825	1	0.364
No. of valid cases	100		



Graph 3: Effect of eGFR (MDRD-IV) and UACR

Table 4: Chi-square tests

	Value	*df*	*Asymp. Sig. (2-sided)*
Pearson Chi-square	0.909a	3	0.823
Likelihood ratio	0.913	3	0.822
Linear-by-linear association	0.027	1	0.870
N of valid cases	100		



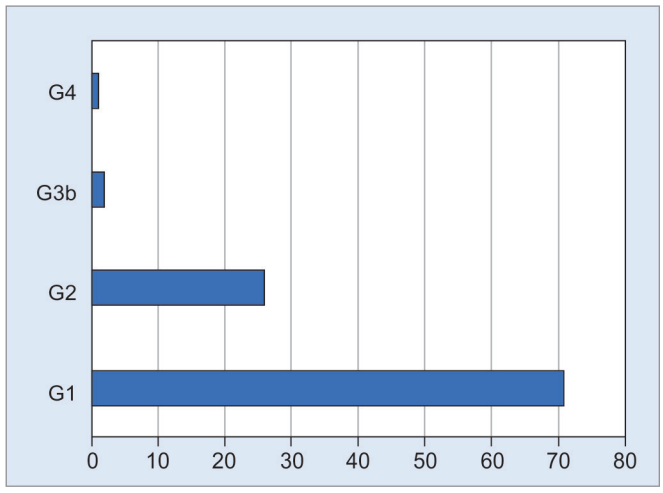
Graph 5: Distribution of study population with microalbuminuria according to KDIGO staging of CKD (chronic kidney damage)

Table 6: Test statistics

	VAR00007
Chi-square	53.122[a]
Df	3
Asymp. sig.	0.000

DISCUSSION

Glomerular filtration rate (GFR) >120 mL/min indicates glomerular hyperfiltration in pre-hypertension, stages 1 and 2 of hypertension. Glomerular hyperfiltration precedes microalbuminuria. Hyperfiltration induces preglomerular arterial vasospasm creating glomerular ischemia, which initially protects and later is



Graph 4: Hypertension and GFR (KDIGO staging of chronic kidney damage)

Table 5: Hypertension and GFR (KDIGO* staging of chronic kidney damage)

KDIGO Stage		*GFR (mL/min/1.73 m²)*	*Patients*	*Positive UACR*
G1	Normal or Increased GFR	≥ 90	71	32
G2	Mild or Decrease in GFR	60–89	26	15
G3a	Mild to moderate decrease in GFR	45–59	0	0
G3b	Moderate to Severe Decrease in GFR	30–44	2	1
G4	Severe decrease in GFR	15–29	1	1
G5	Kidney Injury	< 15 or dialysis	0	0

*Kidney disease: Improving global outcomes

compensated by efferent arteriolar constriction to maintain GFR. The GFR then starts dropping with progressive glomerular hypertension, arteriosclerosis, afferent arteriolar dilatation in some glomeruli, and glomerulosclerosis in others respectively, till ESRD develops. Hyperfiltration → Glomerular afferent arteriolar constriction → Ischemia → Efferent arteriolar constriction → Glomerular hypertension → Microalbuminuria.

Saha and Bhattarai et al. in their study, established a positive correlation between eGFR (Cockroft Gault and MDRD-IV) and UACR in cases with diabetes type-2 and primary hypertension. In our study eGFR was calculated by Cockroft Gault and MDRD-IV and these values of eGFR have been divided into four categories as, <90 mL/min, 91–130 mL/min, 131–170 mL/min and 171–215 mL/min, for statistical analysis. Microalbuminuria was evident in patients with a GFR of <90 mL/min or between 91–130 mL/min calculated either by Cockroft Gault or MDRD-IV formulae. But these were statistically insignificant hence association between GFR (Cockroft Gault and MDRD-IV) and UACR could not be established. When GFR was categorized on the basis of KDIGO staging for

CKD, microalbuminuria was most commonly found in G2 stage (57.7% = 15 out of 26), followed by G1 stage (45.07% = 32 out of 71), although the proportion of positive cases was significantly more in G1 stage. Prevalence of microalbuminuria, an indicator of early CKD burden in the community, was 49% among the patients with hypertension. Early screening of patients with hypertension, for microalbuminuria, by doing simple, inexpensive tests like urinary dipstick and spot urinary albumin/creatinine ratio, can help prompt the physician to initiate antihypertensive therapy in positive cases. Early diagnosis and prevention of microalbuminuria might reduce the progression of hypertensive end-organ damage such as stroke, CKD and cardiovascular events in the community. Although eGFR by Cockroft Gault and MDRD-IV methods can give a good estimate of GFR, newer formulas like GFR by EPI cystatin-C and EPI creatinine–cystatin may be better predictors of actual GFR. Nevertheless, in a developing country like India, eGFR by Cockroft Gault and MDRD-IV methods come in handy, for the screening of patients with microalbuminuria, to predict renal and cardiovascular events.

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10.5005/jp-journals-10036-1213

ORIGINAL ARTICLE

Evaluation of the VITEK Mass Spectrometry System for Rapid Identification of Medically Important Yeasts and Molds

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ABSTRACT

Background: Rapid identification of fungi and molds reduce turnaround time and cost for diagnosis of infections with these organisms in a clinical microbiology laboratory. We report here the clinical evaluation of the VITEK mass spectrometry system for rapid fungal identification in comparison to the internal transcribed spacer (ITS) DNA polymorphism method.

Methods: Total 136 archived isolates comprising 126 yeast and 10 molds were analyzed by mass spectrometry (VITEK system) and ITS sequencing for identification of fungi.

Results: Majority of the yeast isolates belonged to genus *Candida* (N = 123), followed by one isolate each of *Trichosporon, Cryptococcus*, and *Rhodotorula*. Amongst molds, *Aspergillus* (N = 4), *Trichophyton* (N = 3), *Fusarium* (N = 2) and *Rhizopus* (N = 1) were identified. Overall, correct species-level identification was obtained in 135/136 (99.26%) isolates with a single isolate of *Candida auris* misidentified as *Candida haemulonii* by VITEK MS.

Conclusion: The VITEK MS system, a matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) system, is a reliable and rapid method for the identification of most of the fungi. Further expansion of the database of the VITEK MS for emerging pathogens is needed to enhance its performance.

Keywords: *Candida auris, Candida haemulonii*, Internal transcribed spacer, Matrix-assisted laser desorption ionization time-of-flight mass spectrometry.

How to cite this article: Shetye S, Chheda P, Amberkar S, Madhu G, Mukundan U. Evaluation of the VITEK Mass Spectrometry System for Rapid Identification of Medically Important Yeasts and Molds. MGM J Med Sci 2018; 5(4):173-177.

Source of support: Nil

Conflict of interest: None

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INTRODUCTION

There has been an increase in the incidence of invasive fungal infections (IFIs), specifically *C. albicans* and invasive molds such as *Aspergillus* species.[1] The high rate of morbidity and mortality due to fungal infections is seen in immunosuppressed patients with solid-organ and hematopoietic stem cell transplants.[2]

Rapid identification of fungal species helps in early successful therapy by choosing appropriate therapeutic options and avoiding the use of potentially toxic antifungal agents.[3] This approach benefits the patient in terms of improved clinical outcome at reduced costs.[3,4] There has been a significant development in laboratory diagnosis of fungal agents due to automated biochemical methods as well as molecular methods. Though these methods have enhanced the ability to identify different pathogenic species, there exist concerns related to cost, turnaround time and expertise.[2,5] In rare situations the phenotypic method may not successfully identify less common fungal species. Molecular techniques such as deoxyribonucleic acid (DNA) sequencing are highly accurate but costlier and time consuming.[6]

Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) has recently been introduced for rapid and accurate identification of bacteria, mycobacteria, and yeasts and is now routinely used in the clinical microbiology laboratory.[4,7-12] MALDI-TOF MS-based microbial identification relies on the generation of the unique organism-specific mass spectrum or "protein fingerprint" that is examined against a reference database to provide organism identification. The VITEK MS system (bioMérieux, Marcy l'Etoile, France) and Microflex LT Biotyper (Bruker Daltonics, Bremen, Germany) are commercially available systems that have been studied extensively.[13,14]

The protocol for MALDI-TOF MS-based identification is quite different for different groups of organisms such as gram-positive or gram-negative bacteria, mycobacteria, or fungi. The sample preparation methods vary between yeasts and, and certain mold genera are even more challenging. Though extensively used for bacterial identification, there are limited studies on MALDI-TOF MS-based identification of fungal isolates. The objective of this study was therefore to evaluate the performance of the VITEK MS MALDI-TOF mass spectrometer (bioMéri-

eux) in conjunction with the VITEK MS v 2.0 database in comparison with ITS DNA polymorphism for the identification of yeasts and molds isolated in the diagnostic clinical microbiology laboratory.

MATERIALS AND METHODS

A total of 136 archived isolates (126 yeasts and 10 molds) were subjected to MALDI-TOF MS analysis and ITS sequencing. These isolates were previously identified using standard phenotypic methods including VITEK 2 identification system (bioMérieux) and archived in sterile distilled water over a period of one year. The isolates were cultured on Sabouraud dextrose agar for 48–96 hours at 30°C before MALDI-TOF MS analysis. The study was carried out at Metropolis Healthcare Ltd. from Jan '2017 to June '2017.

Identification by VITEK MS

The yeast isolates were prepared for mass spectrometric analysis on target slide (bioMérieux) composed of a polypropylene carrier using the protocol described earlier.[4] A small portion of a single fungal colony was picked up using a 1 µL loop and layered on to the slide, followed by application of 0.5 µL formic acid (bioMérieux). It was allowed to dry for about 2–3 minutes at room temperature. This was followed by application of 1 µL of cyano-4-hydroxycinnamic acid (CHCA) matrix solution (bioMérieux). Sixteen samples were prepared on different slots of the same slide. After drying, the slide was processed for mass spectrometric analysis on VITEK MS acquisition station using Myla v 2.4 middleware software.

For molds, a wet swab was used to take a small piece (1 cm^2) from Sabouraud dextrose agar plate, suspended in a 1.5 mL microcentrifuge tube containing 500 µL 70% ethanol and vortexed.[5] The tube was centrifuged at 3000 g for 2 minutes. The supernatant was discarded and 40 µL of 70% formic acid was added to the pellet and vortexed. This was followed by addition of 40 µL of 100% acetonitrile. The tube was vortexed and centrifuged at 3000 g for 2 minutes. One µL of the supernatant was added to the target slide and was allowed to dry at room temperature. This was followed by application of 1 µL CHCA matrix on the sample spot and dried at room temperature. The slide was analyzed using Myla v2.4 middleware software on VITEK MS platform.

Molecular Identification by Inferior Temporal Sulcus Sequencing

The molecular identification of all isolates in the test collection was carried out by sequencing of ITS. Briefly, DNA was extracted and purified directly from single fungal colonies with the DNA Min Kit (Qiagen). PCR was set up using primers ITS1 (5′-TCC GTA GGT GAA CCT TGC GG-3′) and ITS4 (5′-TCC TCC GCT TAT TGA TAT GC-3′) as described earlier[15] amplification of the ITS region was carried out using the following conditions: denaturation at 94°C for 5 minutes, followed by 35 cycles of denaturation at 94°C for 30 s, annealing at 58°C for 45 s, and elongation at 72°C for 60 s, with a final extension step of 10 min at 72°C. The resultant PCR product (300 bp to 880 bp) (Fig.1) was sequenced and the obtained sequences were compared to ITS sequences that are found in public database: NCBI (https://blast.ncbi.nlm.nih.gov/). The identity of each isolate was determined by sequence similarity of the ITS regions, specifically using those results with 97% similarity and 99% coverage and the species showing maximum score was considered.

Ethics

This study was conducted as part of clinical laboratory test validation on archived fungal isolates and not on patients or patient material. Hence, ethical committee approval was not required.

RESULTS

We analyzed 136 fungal isolates comprising of 126 yeast and 10 molds by VITEK MS and DNA sequencing of ITS region. 8 genera and 21 different species were identified (Table 1). Majority of the yeast isolates belonged to genus *Candida* (N = 123), followed by one isolate each of *Trichosporon, Cryptococcus, and Rhodotorula*. Out of 126 yeast isolates, ITS region sequencing revealed identical results in 125 (99.20%). One isolate identified as *C. haemulonii*, turned out to be *C. auris* on molecular typing. This isolate was further evaluated on VITEK 2 system for confirmation and it was identified as *C. auris* confirming the findings by DNA sequencing. Thus VITEK MS failed to correctly identify this medically important species.

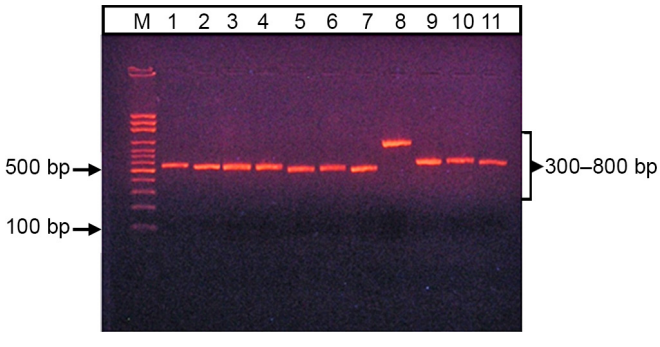

Fig. 1: Gel image for ITS PCR (300–800 bp), M-100 bp ladder, 1: *C. albicans*, 2: *C. krusei*, 3: *C. tropicalis*, 4: *C. parapsilosis*, 5: *C guilliermondii*, 6: *R. mucilaginosa*, 7: *A. niger*, 8: *C. neoformans*, 9: *C. glabrata*, 10: *C. keyfr*, 11: *A. flavus*

Table 1: Correlation between MALDI-TOF MS (VITEK MS) and Molecular (ITS Sequencing) identification of yeasts and molds

Identification by VITEK MS	*Identification by ITS sequencing*	*Correct Identification No. (%)*	*Misidentification Isolate No. (%)*
Candida albicans	*Candida albicans*	73 (100%)	-
Candida tropicalis	*Candida tropicalis*	14 (100%)	-
Candida glabrata	*Candida glabrata*	12 (100%)	-
Candida kefyr	*Candida kefyr*	7 (100%)	-
Candida krusei	*Candida krusei*	7 (100%)	-
Candida guilliermondii	*Candida guilliermondii*	4 (100%)	-
Candida parapsilosis	*Candida parapsilosis*	2 (100%)	-
Candida zeylanoides	*Candida zeylanoides*	1 (100%)	-
Candida inconspicua	*Candida inconspicua*	1 (100%)	-
Candida lusitaniae	*Candida lusitaniae*	1 (100%)	-
Candida haemulonii	*Candida auris*	0 (0%)	1 (100%)*
Trichosporon asahii	*Trichosporon asahii*	1 (100%)	-
Rhodotorula mucilaginosa	*Rhodotorula mucilaginosa*	1 (100%)	-
Cryptococcus neoformans	*Cryptococcus neoformans*	1 (100%)	-
Aspergillus niger	*Aspergillus niger*	1 (100%)	-
Aspergillus sydowii	*Aspergillus sydowii*	1 (100%)	-
Aspergillus flavus	*Aspergillus flavus*	1 (100%)	-
Aspergillus versicolor	*Aspergillus versicolor*	1 (100%)	-
Trichophyton mentagrophytes	*Trichophyton mentagrophytes*	3 (100%)	-
Fusarium solani	*Fusarium solani*	2 (100%)	-
Rhizopus homothallicus	*Rhizopus homothallicus*	1 (100%)	-

*Isolate misidentified as *Candida haemulonii*

C. albicans (N = 73) was the most common pathogen detected, followed by *C. tropicalis* (N = 14) and *C. glabrata* (N = 12).

Successful mass spectra were generated for all the 10 mold isolates and there was a 100% correlation with DNA sequencing data. *Aspergillus* (N = 4), *Trichophyton* (N = 3), *Fusarium* (N = 2) and *Rhizopus* (N = 1) were different molds that were identified. Overall, VITEK MS could correctly identify, up to species level, 135 out of 136 (99.26%) fungal isolates that were archived in the laboratory.

DISCUSSION

The main objective of a diagnostic laboratory is to deliver accurate and clinically useful results in the shortest possible time. For fungal identification, though microscopy offers quick presumptive diagnosis, growth on culture media, followed by biochemical or morphological identification is necessary for confirmatory diagnosis. Molecular methods, like DNA sequencing, though gold standard for the identification of fungi at the species level, are expensive and require specialized equipment and expertise and are not commonly available in clinical laboratories. When species belonging to the same genus have different antifungal susceptibility profiles, a reliable species-level identification of the isolate is crucial for therapeutic decision-making. MALDI-TOF MS offers a balance between speed, cost, and accuracy for fungal identification in clinical settings.[16] The procedures for preanalytic processing of organisms and analysis by MALDI-TOF MS are technically simple and reproducible and commercial databases, and interpretive algorithms are available for the identification of a wide spectrum of clinically significant organisms. The platform has been successfully employed in clinical microbiology laboratories to identify bacterial pathogens and yeasts, but not for identification of molds. Recent progress in extraction protocols and composition of comparative libraries, support potential application of MALDI-TOF MS for mold identification in clinical microbiology laboratories. MALDI-TOF technology patented by VITEK® examines the patterns of proteins detected directly from intact bacteria or lysed yeast and mold preparations. The sample to be analyzed is mixed with another compound, called a matrix, applied to a metal plate and irradiated with a laser. The matrix absorbs the laser light and vaporizes, along with the sample, in the process gaining an electrical charge (ionization). Electric fields then guide the ions into the time of flight mass spectrometer, which separates them according to their mass to charge (m/z) ratio, and ultimately the quantity of each ion is measured. Detection is achieved at the end of the flight tube. VITEK® MS contains a comprehensive IVD-CE marked database for bacteria and fungi, including mycobacteria, *Nocardia* and molds.

For molecular identification of fungal species, we chose to sequence Internal Transcribed Spacers 1 and 2 (ITS 1 and ITS 2 regions) since it has been successfully used for identification of medically important yeast and *Aspergillus* species in previous studies.[17,18] The ITS region

has been more reliable in comparison to the large-subunit RNA gene (D1-D2 region) for the identification of closely related *Aspergillus* species.[18]

In this study on 136 fungal isolates (126 yeast and 10 molds) showed 99.26% concordance of results between mass spectrometry and molecular-based identification. All the medically important *Candida* species, such as *C. albicans*, *C. parapsilosis*, *C. tropicalis*, *C. guilliermondii*, *C. krusei*, *C. glabrata*, and *C. kefyr* were all successfully and accurately identified by VITEK MS. However, *C. auris*, a multidrug-resistant yeast was mistyped as *C. haemulonii* on MALDI-TOF MS (IVD) analysis. The same isolate was identified as *C. auris* on ITS sequencing as well as on VITEK 2 v.8.01 system. Several studies published recently report that *C. auris* in routine microbiology laboratories remains under-reported, as 90% of the isolates characterized by commercial biochemical identification systems are misidentified primarily because of a lack of the yeast in their databases.[19-25] A comprehensive study from India investigated 102 clinical isolates previously identified as *C. haemulonii* or *C. famata* by VITEK 2 system and found that 88.2% of the isolates were *C. auris* on ITS sequencing.[22] There is another study from India where a total of 125 clinical fungal culture isolates (yeasts and filamentous fungi) were studied and all 88 yeast isolates were correctly identified by MALDI-TOF/MS. *C. auris* was however, not amongst the study isolates.[26] Previous database of VITEK 2 lacked *C. auris* strain; hence all the strains were misidentified as *C. haemulonii*, but *C. auris* was identified by Bruker's MALDI Biotyper Microbial Identification system.[22]

In a multicentric study, out of 852 yeast isolates, 24 (2.8%) were not identified and 5 (0.6%) were misidentified in comparison to molecular typing of D2 region of the 26S rRNA gene.[4] Since the majority of the yeast isolates were identified up to species level (96.1%), authors conclude that MS is superior to the phenotypic identification systems.[4] A study by Iriart et al. reported that none of the *Aspergillus* species absent from the database were misidentified, showing the good specificity of the method.[2] Incorrect species identification on VITEK MS was observed for an isolate of *Candida palmioleophila* which was misidentified as *Candida haemulonii*.[2] It is to be noted that it is possible to use an updated research-use-only (RUO) library or database, which can also be updated in-house. Also, the profile for identification of *C. auris* is built into the upcoming IVD database of VITEK MS, as confirmed by the manufacturer (bioMérieux, Marcy l'Etoile, France).

Regarding molecular analysis, the phylogenetically closely-related species sometimes cannot be identified correctly by sequence analysis ITS.[18] However, we did not come across any such problem, probably due to limited sample size.

CONCLUSION

This study highlights the usefulness of MALDI-TOF MS (VITEK system) as a good alternative to conventional methods for rapid identification of yeasts and molds in clinical settings so that appropriate therapy can be instituted at the earliest. It is also cost-effective. However, a larger number of general encompassing several species of fungi by MALDI TOF-MS and molecular typing should be added to their database.

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10.5005/jp-journals-10036-1214

ORIGINAL ARTICLE

Magnesium Sulfate for Control of Eclampsia: Do Indian Women Need Lower Doses?

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ABSTRACT

Background: Pritchard regime is considered the benchmark for control of convulsions in patients with eclampsia. Indian patients with smaller body mass may require smaller doses of Magnesium sulfate.

Aims: To compare the efficacy of low dose magnesium sulfate ($MgSO_4$) regimen in eclampsia with standard Pritchard's regimen.

Materials and methods: A total of 60 patients presenting with eclampsia were recruited and randomly divided into two groups: Group A: 30 patients who received standard Pritchard's regime and Group B: 30 patients who were given low dose $MgSO_4$. The outcome was measured in terms of effectiveness in control of convulsions and magnesium related toxicity.

Results: Overall success rate was 100% with a low dose regimen as compared to 93.3% with Pritchard's regimen. Failure to control convulsions was noted in two patients on Pritchard's regimen group as compared to none on a low dose regimen (p <0.01). No difference was observed among study groups with respect to the type of delivery (p <0.59). Maternal complications were higher in cases receiving Pritchard's regimen: loss of knee jerk (30% vs. 16.7%), oliguria (16.7% *vs.* 10%) and postpartum hemorrhage (PPH) (23.3% *vs.* 16.7%). However, the difference was not statistically significant.

Conclusion: A lower dose of magnesium sulfate is equally efficient with fewer complications as compared to the standard dose regimen in the management of eclampsia.

Keywords: Eclampsia, Low dose $MgSO_4$ for Indian women, $MgSO_4$ toxicity, Pritchard's regimen for eclampsia.

How to cite this article: Bhojwani D, Kumar S. Magnesium Sulfate for Control of Eclampsia: Do Indian Women Need Lower Doses? MGM J Med Sci 2018;5(4):178-182.

Source of support: MGMIHS

Conflict of interest: None

INTRODUCTION

Eclampsia is a serious complication of pregnancy that affects the safety of the mother as well as the fetus. Until recently the treatment of eclampsia was diverse throughout the world. Various drugs and regimens have been advocated for the management of eclampsia. In 1950, Menon introduced the famous 'lytic cocktail' in India.[1] The lytic cocktail was a combination of drugs like pethidine, promethazine, and chlorpromazine. This lytic cocktail was only partially effective. Dr Prichard in 1984 used $MgSO_4$ for control of convulsions in eclamptic patients. This regimen was found to be very effective and became standard treatment for eclampsia. Indian women have lower body mass as compared to their western counterparts. Therefore, appropriate doses of magnesium sulfate and the therapeutic serum magnesium levels among the Indian patients have been a matter of debate.[2] This study was carried out to find out whether lower doses of $MgSO_4$ are as effective as standard doses for treatment of eclampsia in Indian patients.

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AIM AND OBJECTIVES

To compare the effectiveness of low dose magnesium sulfate regimen in eclampsia and severe preeclampsia with standard Pritchard's regimen in terms of:

- Effectiveness in control of convulsions,
- Maternal outcome
- Magnesium related toxicity

MATERIALS AND METHODS

Study Area

Department of Obstetrics and Gynecology at the MGM Hospital, Kalamboli, Mumbai, Maharashtra, India.

Study Population

Pregnant patients above 20 weeks presenting with eclampsia at our hospital.

Study Design

A randomized comparative study

Sample Size Calculation

A total of 60 cases presenting with eclampsia at our hospital were randomly divided into two groups (30 each) using computer-generated random numbers:
Group A: Standard Pritchard's regime.

Group B: Low dose $MgSO_4$ regime.
Study Duration: July 2016–Feb 2018

Inclusion Criteria

- Pregnant patients presenting after the 20th week of pregnancy with BP>140/90 mm Hg and history of convulsions with or without proteinuria.
- Patients who have not received any anticonvulsant treatment before admission.

Exclusion Criteria

- Cases presenting with serious complications of eclampsia, namely:
  - Renal failure
  - Cerebrovascular accident
  - HELLP syndrome
- Patients not consenting to participate in the study.

Methodology

Informed consent was taken from all the patients or their relatives (in case the patient was not in a condition to give consent). A detailed history was taken with special emphasis on the history of epilepsy or renal failure. Clinical assessment was carried out. Prepregnancy BMI was obtained from her old records. Following investigations were carried out: blood group, complete blood count (CBC), platelet count, serum creatinine, liver function tests, prothrombin time and urine analysis. Additional investigations were performed on the case to case basis.

Drug ($MgSO_4$) Regimen for Group A

- 4 g $MgSO_4$ 20% IV stat.
- 3 g IM in each buttock stat.
- 2 g IM on alternate buttock four hourly for 24 hours after delivery or last convulsion whichever was later.

Drug ($MgSO_4$) Regimen for Group B

- 4 g $MgSO_4$ 20% IV stat.
- 5 g on each buttock.
- 5 g IM 4 hourly on the alternate buttock. Medication was continued for 24 hours after the delivery or last seizure.

Respiratory rate, patellar reflexes and urinary output were monitored hourly for impending magnesium toxicity. Next scheduled dose of $MgSO_4$ was not given if there was any sign of magnesium toxicity (absence of patellar reflex, urinary output less than 30 mL/hour or respiratory rate less than 16/min). If convulsions recurred after the initial dose, the patient was given additional of 2 g of $MgSO_4$ by IV route. This additional dose of $MgSO_4$ was given to the patients in both groups. In case the patient had convulsions even after an additional dose of $MgSO_4$, IV diazepam was given. Intravenous Labetalol in incremental doses of 20–80 mg was used if BP was more than 160/110. Lower segment cesserian section (LSCS)/induction of labor was done to terminate the pregnancy within 48 hours of an initial dose of $MgSO_4$.

Statistical Analysis

The quantitative data are represented as their mean ± SD. Categorical and nominal data is expressed in percentage. The t-test is used for analyzing quantitative data, or else nonparametric data are analyzed by Mann–Whitney test and categorical data are analyzed by using Chi-square test. The significance threshold of p value is set at <0.05. All analyses were carried out by using Statistical Package for Social Sciences (SPSS) software version 21.

RESULTS

Mean age of patients in the study was 27.3 years with the majority of them (73.3%) between 21–30 years of age. No difference was observed among study groups with respect to age distribution (p 1.0). Out of the total 60 cases, 58.3% were primipara while the remaining 41.7% were multipara. No difference was observed among study groups with respect to parity (p 1.0). No difference was observed among study groups with respect to mean BMI and gestation age ($p > 0.05$), (Table 1).

Out of the total 60 cases, 25% had more than five episodes of convulsions. No difference was observed among study groups with respect to a number of convulsion episodes (p 1.0). Overall success rate observed was 100% with a low dose regimen as compared to 93.3% with Pritchard's regimen. Additional doses were required in 2 cases of each group. Failure to control convulsions was

Table 1: Baseline distribution of patients in two groups

	Regimen		
Age group	*Low dose*	*Pritchard's*	*Total*
<20	1	2	3
	3.3%	6.7%	5.0%
21–25	16	15	31
	53.3%	50.0%	51.7%
26–30	12	11	23
	40.0%	36.7%	38.3%
>0	1	2	3
	3.3%	6.7%	5.0%
Total	30	30	60
	100.0%	100.0%	100.0%
Parity			
Primi	17	18	35
	56.7%	60.0%	58.3%
Multi	13	12	25
	43.3%	40.0%	41.7%
Total	30	30	60
	100.0%	100.0%	100.0%

Table 2: Comparison of no. of convulsions in both the groups and the outcome related to the control of convulsions in both the groups

Number of convulsions	*Regimen low dose*	*Regimen Pritchard's*	*Total*	*p value*
	22	23	45	
</=5	73.3%	76.7%	75.0%	
	8	7	15	
>5	26.7%	23.3%	25.0%	1.0
	30	30	60	
Total	100.0%	100.0%	100.0%	
Convulsions controlled	30	28	58	
	100.0%	93.3%	96.7%	0.49
Additional dose required	2	2	4	
	6.7%	6.7%	6.7%	1.00
Failure rate	0	2	2	
	0.0%	6.7%	3.3%	0.49

noted in 2 cases of Pritchard's regimen group and none in the low dose regimen group (Table 2).

The higher mean dose of $MgSO_4$ was associated with Pritchard's regimen (33.8 g) as compared to the low dose Low dose regimen (21.7 g) (p <0.01) (Table 3).

Higher prevalence of cesarean section was observed in both groups (overall 61.7%). No difference was observed among study groups with respect to the type of delivery (p 0.59). Complications associated with magnesium, i.e., loss of knee jerk (30% *vs.* 6.7%) and oliguria (16.7% *vs.* 10%) were higher in cases with Pritchard's regimen (Table 4).

DISCUSSION

Eclampsia is a major cause of maternal and fetal morbidity and mortality around the world, especially so in a developing country like India. Magnesium sulfate is the drug of choice for the treatment of eclampsia. The effectiveness of magnesium sulfate has been proven in a variety of randomized controlled trials. There has been a constant debate concerning the dose of magnesium sulfate .[2] Pritchard's regime has been tailored at different hospitals offering different regimes. Long-term statistical data has not been reported, and the protocol has not been

Table 4: Comparison of study groups based on mode of delivery and maternal complications

Mode of delivery	*Low dose regimen*	*Pritchard's regimen*	*Total*	*p value*
LSCS	17	20	37	
	56.7%	66.7%	61.7%	
Vaginal	13	10	23	0.59
	43.3%	33.3%	38.3%	
Total	30	30	60	
	100.0%	100.0%	100.0%	
Maternal complications				
Loss of knee jerks	5	9	14	
	16.7%	30%	23.3%	0.36
Oliguria	3	5	8	
	10.0%	16.7%	13.3%	0.70

Table 3: Comparison of mean dose of $MgSO_4$ used in both group

Variables	*Group*	*N*	*Mean*	*SD*	*p value*
Total $MgSO_4$ dose (G)	Low dose	30	21.70	2.27	<0.01
	Pritchard's	30	33.80	7.64	

standardized. Pritchard himself in 1984 suggested that the dose of magnesium sulfate should be limited in women who appear to be small built.[2] The present study was thus planned to compare the effectiveness of low dose magnesium sulfate regime with Pritchard's regime in controlling convulsions during eclampsia in Indian women.

Baseline Characteristics

Mean age of the females in the study was 27.2 years and 27.4 years in a low dose regimen group and Pritchard's regimen group respectively (p 0.93). Mean BMI was 21.34 and 20.96 kg/m^2 in low doses and Pritchard's regimen group respectively (p 0.71). Parity, gestation age and a number of convulsions (Table 1) were also comparable in this study.

The similar demographic pattern was also observed in other studies.[3-9] Ranjana et al.[10] reported that the mean age of the patients was 25.8 ± 3.43 years with low dose regimen and 25.7 ± 3.53 years with Pritchard's regimen. Most women were of small built with a body mass index of 20.31 ± 1.34 kg/m^2 and 19.99 ± 2.15 kg/m^2 in groups A and group B, respectively. Nautiyal et al.[11] in their study observed the mean age of the patients of eclampsia/preeclampsia as 25.5 years while Sharma et al.[12] recorded a mean age of 25.9 years in their study. Kumar et al.[13] reported a mean age of 25.07 (range 19–40) years in their study of 123 cases. The majority were in the age group of 21–25 years (51.21%), followed by 26–30 years (35.78%). Jana et al.[14] reported that measured most women were of small stature, with a mean body mass index of 19.3 ± 2.1. Bangal et al.[15] observed that 70% of women had a body weight less than 50 kilograms at the time of admission.

Eclampsia occurs mostly in primigravida as seen in the study (59 %). Others have observed similar incidence: Ranjana et al.[10] 70 %, Bangal et al.[15] 15 75% and Sardesai et al.[16] 79%.

CONTROL OF CONVULSIONS

A number of seizures occurring after the initial dose of $MgSO_4$ was the parameter used to measure the effectiveness of the drug. Recurrence of convulsions occurred in two patients in each group after the initial dose. These patients were given an additional dose of $MgSO_4$. In group A, both the patients responded while in group B, in spite of giving 2 g i.v dose of $MgSO_4$, further convulsions occurred in both the patients. The failure rate was 6.7% in Pritchard's regimen as compared to 0% in the low dose regimen (Table 2).

Pritchard et al.[2] the pioneer of $MgSO_4$ regimen reported a 12.1% recurrence rate in 83 patients. By using the Pritchard regimen in his patients, Sibai et al.[4] reported 14.2% recurrence with Pritchard's regime. Jana et al.[14] reported a 5.7% recurrence rate with the same regimen. Recurrence rate with Pritchard's regimen as noted by Ranjana et al.,[10] Sharma et al.[12] and Mohanapu et al.[17] was 2.5%, 6.7%, and 4%, respectively. The recurrence rate of 7.89% by Sardesai et al.[16] and 1.5% by Begum et al.[18] was reported. Ranjana et al.,[10] Kumar et al.,[13] Nautiyal et al.[11] and Mohanapu et al.[17] reported recurrence rate of 5%, 0.81%, 6.6%, and 10%, respectively with low dose regimen. All these results indicate that a low dose regime is as effective as the standard regime in controlling eclamptic seizures in Indian patients are in conformity to our study also.

Higher prevalence of cesarean section was observed in both groups (overall 61.7%). No difference was observed among study groups with respect to the type of delivery (*p* 0.59). Most cesarean sections were carried out for fetal distress and nonprogress of labor (Table 4). Cesarean section rate noted by Ranjana et al.[10] was 57.5% in Low Dose regimen and 67.5% in Pritchard's regimen. Nautiyal et al.[11] reported a cesarean section rate of 63% and Ali et al.[19] 57.5 %. The high rate of LSCS in eclamptic mothers as seen in most studies shows that obstetricians prefer elective LSCS to avoid complications likely to occur in mother and fetus while awaiting delivery. Institutional policies and protocols also have an influence on decision-making, whether to go for LSCS or vaginal delivery in patients with eclampsia.

MATERNAL COMPLICATIONS

A higher dose of $MgSO_4$ was used in Pritchard's regimen (mean 33.8 g) as compared to the low dose regimen (mean 21.7 g) (Table 3). Higher doses used in Pritchard regimen may be responsible for higher complication rates due to magnesium toxicity in this group, namely, loss of knee jerk (30% *vs.* 16.7%) and oliguria (16.7% *vs.* 10%) (Table 4).

Ranjana et al.[10] reported a loss of deep tendon reflexes in 25% of patients receiving Pritchard's regimen and 15% patients of low dose regimen. Oliguria occurred in 15% of patients of the Pritchard regime group and 10% of patients receiving Dhaka regime. Shilva et al[20] reported absent deep tendon reflexes(DTR) in low dose group as 8% while 32% of patients in the standard group had loss of DTR (p = 0.03). Similarly in the study by Nautiyal et al.[11] 4 (13%) patients in group B (Pritchard's) compared to three patients (10%) in group A (low dose) experienced loss of deep tendon reflexes. Six (20%) patients developed oliguria in standard dose group compared to two (6.6%) patients on a low dose regimen of $MgSO_4$.

Maternal mortality in cases of eclampsia ranges from 0.4% to 14%. Greater the organ damage and longer the delay in seeking treatment, higher is the mortality. In the present study, no mortality was observed because patients with serious complications of eclampsia were excluded.

A study conducted by Ranjana et al.,[10] one mortality was reported in a low dose group and two in Pritchard's regimen (combined mortality rate of 3.75%). Sardesai et al.[16] reported a maternal mortality of 2.63%. The maternal mortality was 3% with a Pritchard regime group in the Collaborative eclampsia trial.[2] and study by Nautiyal et al.[11] reported a maternal mortality rate of 3.3%.

CONCLUSION

With this study, we came to a conclusion that a lower dose of magnesium sulfate is effective in controlling convulsions in eclampsia and has lesser complications compared to standard Pritchard's regimen in Indian patients, probably because of their less body mass. Further studies need to be conducted to re-evaluate the correct dosage of magnesium sulfate for the treatment of Indian patients with eclampsia. After all, why should we use higher doses of drugs if lesser doses are as effective and less toxic?

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10.5005/jp-journals-10036-1215

ORIGINAL ARTICLE

Functional Outcome of Postburn Flexion Contractures of Hand after Treatment

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ABSTRACT

Contractures of hand produce considerable morbidity. Despite improvements in the overall management of acute thermal injuries, contractures still occur and are the most common cause of skin contracture in hand. These are largely preventable by good initial care. We studied 24 consecutive patients of postburn contractures of hand treated at MGM Medical College, Aurangabad, Maharashtra, India, with the aim to evaluate the functional outcome. Age of patients ranged from 2 to 60 years. The right hand was affected in 10, left in 7 and both hands in 7. Average total body surface area burned was 10.15%. The flame burn was a major cause of deformity in 16 patients. Mean QuickDASH Score was 19.6 and it improved to 5.1 at 1 year. All patients underwent contracture release, full thickness skin grafting, and K wire fixation. Post-treatment, the majority of the patients had good to excellent Total Active Motion (TAM) rating. To conclude, appropriate and timely reconstructive procedures can greatly improve the function of hands afflicted with post-burn contractures. Time of presentation, age and gender do not significantly affect the degree of improvement in the functional outcome.

Keywords: Contracture release, Hand burns, Postburn hand deformity.

How to cite this article: Patil AJ, Vichare A, Yelikar A, Kulkarni J, Tolat T. Functional Outcome of Postburn Flexion Contractures of Hand after Treatment. MGM J Med Sci 2018;5(4):183-188.

Source of support: MGMIHS

Conflict of interest: None

INTRODUCTION

Hand burns predominantly affect children and young people and have serious social and financial implications. Though hands constitute only 2% of total body surface area (TBSA), they represent 60% function of upper limbs. Tredget[1] stated that 54% of hand burns occur in patients with less than 15% TBSA burned. Hands are third most frequent sites of burn scar contracture deformity.[2] Despite increasing sophistication in the overall management of acute thermal injuries, contractures still occur and are the most common cause of contracture in the hands,[3] leading to functional and aesthetic morbidity. In major burns survivors, quality of life is, to a large extent, proportional to the functionality of the hands.

Contractures in hand occur in fingers, dorsum, palms and interdigital clefts either singly or in more than one of these sites. Most of the literature on long-term outcome after hand burns focuses on techniques for correction of scar contractures. Published studies on functional outcomes are not too many. Keeping that in mind, we conducted a prospective study at MGM Medical College, Aurangabad in the Department of Plastic Surgery. Our aim was to assess:

- Functional score before and after surgical correction of the deformity.
- Whether time since burn injury affected the change in functional assessment score.

Due to thinner skin and slower withdrawal response in children, deep burns occur in them at lower temperatures.[4,5] However thicker adipose layer protects deeper tissue and makes excision of full-thickness burns easier in children than in the adults.[5] We used McCauley et al.[6] classification of burn scar contractures, which is as follows:

- Symptomatic tightness but no limitation in range of motion; normal architecture.
- Mild decrease in range of motion without significant impact on activities of daily living; no distortion of normal architecture.
- Functional deficit present, with early changes in the normal architecture of hand.
  - Flexion contractures.
  - Extension contractures.
  - Combination of flexion and extension contractures.
- Loss of hand function with the significant distraction of normal architecture of the hand.
  - Flexion contractures.
  - Extension contractures.
  - Combination of flexion and extension contractures.

MATERIALS AND METHODS

A prospective study was conducted at MGM Medical College, Aurangabad, Maharashtra, between 1st July

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2015 and 30th August 2017. A detailed history was taken and clinical examination of the patients was carried out at the time of admission with special references to demographic characteristics, disease chronology, type of burn and severity of contracture (Figs 1 and 2). We included all patients of postburn thermal flexion contractures of the fingers in the age group 2–60 years who underwent a surgical correction and had minimum follow-up of 6 months. Patients less than 1 year age, electrical/chemical burns and those who could not be followed up not for minimum 6 months were excluded. After admission type of surgery along with any complications were recorded. The goniometer was used for a range of motion and total active motion (TAM) was calculated for each finger as per the method recommended by American Society of Surgery of the Hand (ASSH).[7] Sensory assessment was done but not used for the outcome. A scoring system called quick disability of arm, shoulder and hand (DASH) was used to assess the outcome. Preoperatively the burns contractures were assessed by recording range of motion, web space angle, sensory loss if any, Kapandji score (for apposition and counter-apposition of thumb)[8] and quick DASH Questionnaire. Various deformities were managed as per the guidelines are given by Raja Sabapathy et al.[9] The QuickDASH consists of 11 items from the original DASH. Each item has five response scores and the scores for all items are used to calculate a scale score ranging from 0 (no disability) to 100 (most severe disability). Data were analyzed statistically. Patients were followed up for one year to see the overall outcome.

RESULTS

Twenty-four patients underwent a surgical correction and functional assessment. Patients were followed up postoperatively at 6 months, and 1-year interval. Minimum age of the patient was 2 years and a maximum of 60 years (average 18.8, SD +/– 11.09). Nine patients (37.5%) were 12 years and above and 15 patients (62.5) below12 years in age. Thirteen patients were male and 11 female (Table 1). The study group was divided into two groups for calculating quick DASH: Group 1–those below 12 years and group 2–12 years and above.

The right hand was involved in 10 patients, left hands in 7 and both hands in remaining 7. Average total body surface area (TBSA) burned was 10.15% (range 1–50%). Sixteen patients had sustained flame burns. Rest were caused by contact thermal injury, scalds and cracker blasts. The average time of presentation after the injury was 4.57 years (range 2 weeks–26 years). Thirteen patients (54.2%) presented within 1 year (Table 2). Further groups were made for patients as early group who presented within 1 year of burns and the late group who presented after 1 year or later.

QuickDASH scoring was done for 15 group 2 patients (12 years and above). Mean preoperative QuickDASH score in this group was 19.60 (SD+/–18.19). Scoring was repeated postoperatively at 6months and at the end of one year (Table 3). QuickDASH score at 1 year had significantly improved to 5.14.

Outcome assessment was compared between patients in the Early presentation group (<1year) to the late presentation group (>1 year) (Table 4). The degree of improvement in the QuickDASH score of the affected hands did not show any statistically significant difference between the two groups (p value – 0.034).

All patients underwent contracture release and full thickness skin grafting, with K wire fixation. The majority had good to excellent TAM as per the Johnson et al[10] classification (Fig. 3). TAM was assessed in all patients in all digits. Mean and standard deviation of TAM was calculated preoperatively and postoperatively at 3 months, 6 months and end of one year (Table 5). Preoperative Mean TAM was 125 and it improved

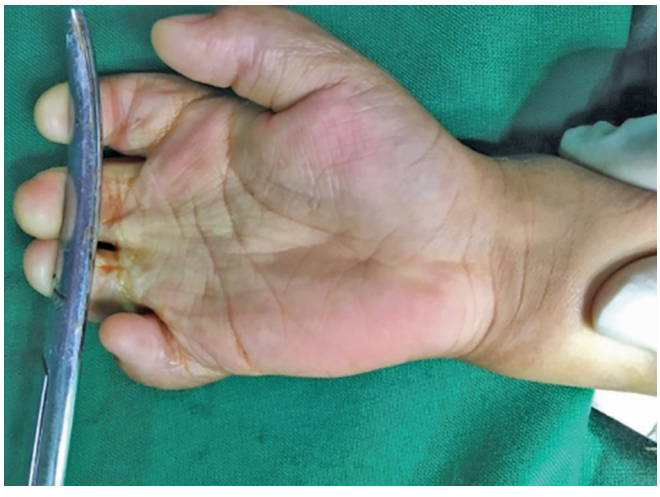

Fig. 1: Preoperative 1

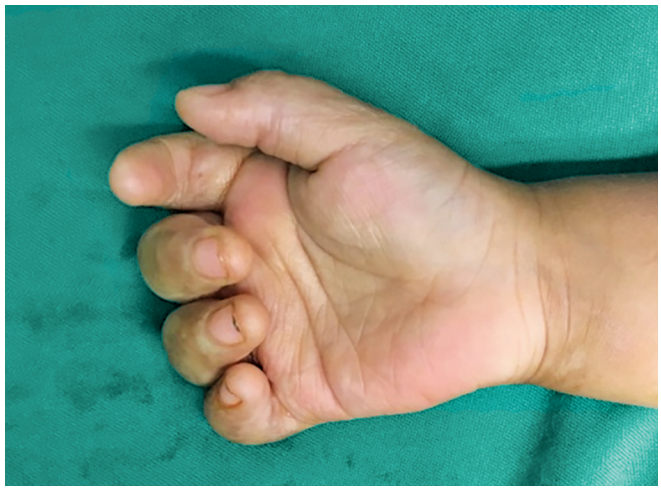

Fig. 2: Preoperative 2

to 225, which represents an excellent outcome (Figs 4 to 7).

The degree of improvement of mean TAM was compared between patients of early presentation (<1 year) and those of late presentation group (>1 year) (Table 6). The difference in the improvement of mean TAM between the two groups was not statistically significant (p >0.05).

In all patients, K wire was used for maintaining the functional position of the hand. The first web space angle and Kapandji score[8] improved in all patients, both early presentation and late presentation groups. Complications observed in this study included partial skin graft loss (4 patients), which was treated successfully with regrafting. Other minor complications were pin tract infections (managed with oral antibiotics) and hypertrophic scar (managed with scar massage and silicone based ointments) (Table 7).

Table 1: Demographic profile of patients

	Age-group (n = 24)	*No. of patients*	*Percentage (%)*
Age group	≤12 years	09	37.5
	>12 years	15	62.5
	Mean ± SD	18.79 ± 11.09 years	
Gender	Male	13	54.2
	Female	11	45.8

Table 3: Comparison of mean difference of DASH score between pre- and post-6 months and 1 year

	Mean ± SD	*p value*
Pre-	19.60 ± 18.19	p <0.0001 S
Post-treatment 6 months	10.20 ± 10.39	
Post-treatment 1 year	5.14 ± 8.24	

DISCUSSION

This study was specifically designed to assess the functional outcome of postburn deformities of fingers and to find out the change in functional score over a period of postoperative follow up. The burns of the upper extremity need to be considered in the context of the whole patient.[11] It is evident that hand burns and hand function cannot be evaluated in isolation. The shoulder, axilla, elbow, and wrist play a significant role in determining hand function.

Table 2: Injury in patient

Particular		*No. of patients* (n = 24)	Percentage (%)
Cause of burn injury	Flame	16	66.7
	Contact	02	08.3
	scald	04	16.7
	cracker	02	8.3
Time since injury (2 weeks–26 years)	<1 year	13	54.2
	2–5 years	02	8.3
	5–10 years	07	29.2
	>10 years	02	8.3
Hands affected	Right	10	41.6
	Left	07	29.2
	Bilateral	07	29.2

Table 4: Comparison of mean difference of DASH scores between pre- and post-6 months and 1 year in early and late

		Mean ± SD	*p value*
Pre-	Early	15.11 ± 11.42	p <0.0001
	Late	29.89 ± 14.32	S
Post-treatment 6 months	Early	9.28±7.44	p <0.0001 S
	Late	15.73 ± 10.02	S
Post-treatment 1 year	Early	3.23 ± 2.14	p = 0.034
	Late	5.01 ± 2.87	S

Table 5: Comparison of mean difference of TAM between pre- post-6 months and 1 year

Digits	*Preoperative*	*Postoperative 6 months*	*Postoperative 1 year*	*p value*
Thumb	110.62 ± 35.91	128.71 ± 33.87@	138.12 ± 29.55#	p <0.001
Index	199.37 ± 47.30	224.58 ± 45.34@	224.58 ± 45.34#	p <0.001
Middle	167.50 ± 53.77	212.37 ± 40.98@	295.20 ± 70.34#	p <0.001
Ring	170.41 ± 69.79	219.58 ± 48.76@	242.50 ± 42.52#	p <0.001
Little	134.58 ± 88.21	189.17 ± 66.36@	226.45 ± 61.84#	p <0.001

@: Significant difference between preoperative and postoperative 6 months , #: Significant difference between pre-op and postoperative 1 year

Table 6: Comparison of mean difference of TAM between preoperative and post-6 months and 1 year

Digits		*Preoperative*	*Postoperative 6 months*	*Postoperative 1 year*
Thumb	Early	116.92 ± 29.75	135.92 ± 28.82	141.15 ± 17.69
	Late	103.92 ± 43.32	120.18 ± 42.53	134.54 ± 40.09
Index	Early	164.62 ± 54.10	189.61 ± 42.49	221.92 ± 41.66
	Late	175.90 ± 77.13	210.90 ± 52.05	227.72 ± 51.25
Middle	Early	148.07 ± 47.36	206.92 ± 31.98	237.69 ± 30.59
	Late	190.45 ± 53.73	218.81 ± 50.52	363.18 ± 65.59
Ring	Early	160.76 ± 75.96	213.84 ± 43.92	240.76 ± 30.52
	Late	182.72 ± 61.33	226.36 ± 55.32	244.54 ± 54.92
Little	Early	129.23 ± 80.56	190.00 ± 50.90	236.53 ± 39.70
	Late	147.27 ± 93.20	188.18 ± 83.76	214.54 ± 81.34

Table 7: Complications

Complications	*No. of patients*
Partial SSG loss	3
Hypertrophy scars/ keloids	3
Pin tract infection	2
Recontracture	1

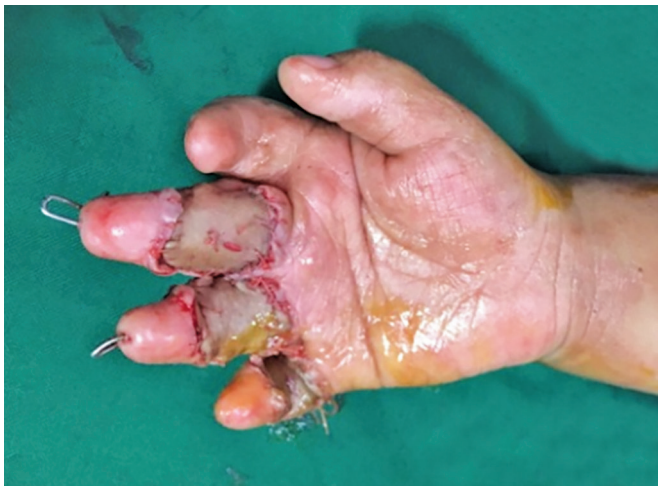

Fig. 3: Intraoperative

Subjects in this study had a mean age of 18.8 years. 37.5% of the patients were under 12 years old. This high susceptibility of pediatric age group patients to thermal injuries is consistent with other published studies, where the incidence of burns was high in children aged 11 years or less (77.9% and 50%, respectively).[12,13]

Majority of patients (66.7%) in our study had sustained domestic flame burns. Similar observations about domestic accidents as a cause of burns have been made by others.[13]

Nearly 54.2% of patients presented within one year and rest after one year. All underwent reconstructive surgery. Our results showed that functional outcomes were good to excellent (as assessed by TAM and Quick DASH scores) in all patients and there was statistically no difference in the degree of improvement achieved, irrespective of whether the patient had come within one year or after one year after sustaining burns. Gokalan et al.[12] however reported that early reconstruction gives better results in the form of greater improvement in range of motion. Zuijlen et al.[14] got results similar to our study. They analyzed hand function by using the seven objective

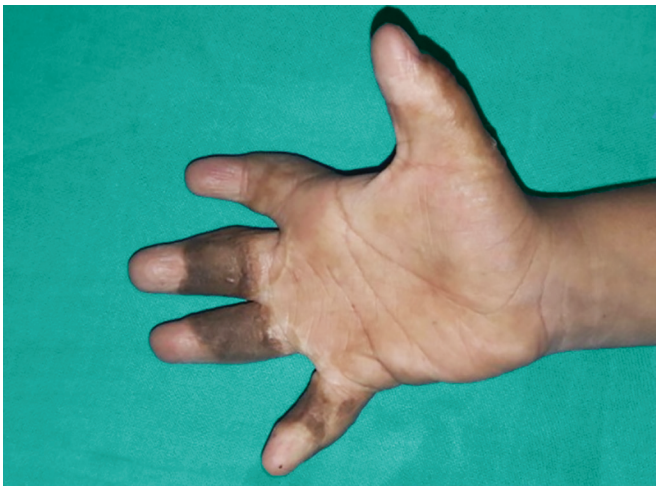

Fig. 4: Postoperative 1

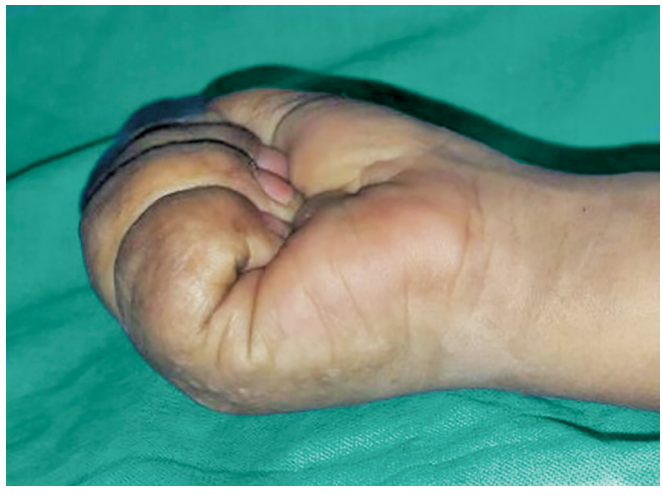

Fig. 5: Postoperative 2

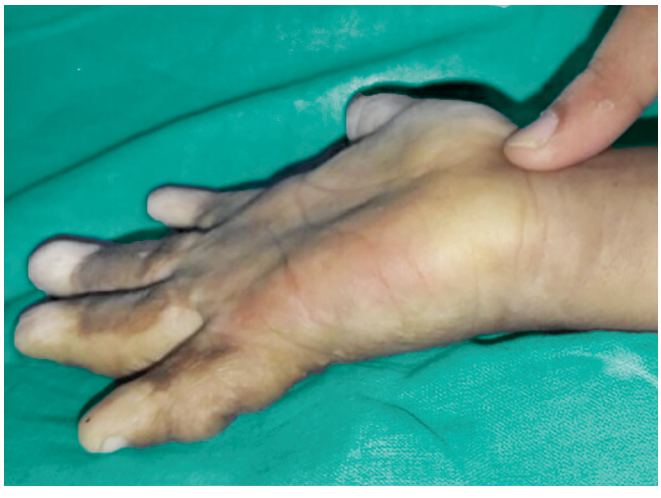

Fig. 6: Postoperative 3

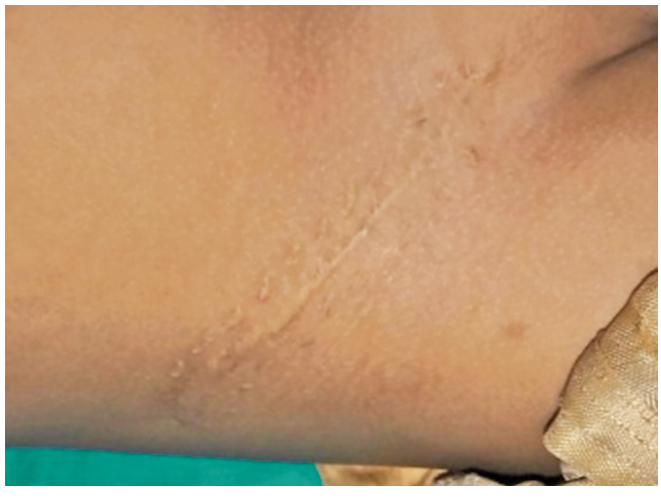

Fig. 7: Donor

test criteria (7–OTC) as described by Jebsen.[15]Also Mohammadi et al.[16] reported in their paper that there is no statistically significant difference in functional outcome between the two groups of early and late grafting in terms of deformity severity, scar formation, sensation, major activities, and overall satisfaction. They used the DASH score to assess the hand function.

In our study, though Kapandji score[8] and measurement of 1st web space angle (to assess apposition and counter-apposition of thumb) were recorded in most patients, it was not used in scoring. Grip strength and key pinch could not be done because of technical problems.

The factors that did not influence the result of the surgery or improvement in the degree of improvement of score included age, sex (in QuickDASH) and most important, time elapsed since the burn injury. Karemer et al.[17] made similar observations in their paper, but they had used a different grading system for assessing hand function (Normal, Functional and Unsatisfactory for describing a range of motion and functional activity).

Many studies have used TAM, Grip, Key and Pinch Strength measurements for assessment of long-term outcome after burn injuries. QuickDASH score has been used less frequently. Authors believe that the QuickDASH scoring system is quite reliable and sensitive to assess, monitor and rehabilitate the upper limb after burn injury. The reliability and validity of the QuickDASH was tested in the patients with upper limb burn injury by Wu et al.[18], in a recent study and they found it a consistent, reliable and sensitive tool. QuickDASH also gives information for planning surgical treatment and rehabilitation to achieve normal or near normal hand function.

The study is limited by its small sample size. Measuring each joint in 2 planes of motion produces an enormous amount of data on a small number of subjects, which reduces the power of the study. We simplified the data by using the TAM which was introduced by the American Society for Surgery of the Hand (ASSH). But it is open for the criticism as to whether a digit of 90° of flexion and –45° extensions can be considered the same as a digit with 45° of flexion and zero extension. As per the study done by Johnson et al.,[10] rating scale established for tendon injuries in fingers[19] is applicable to burned hands as well. In this study the mean TAM for all fingers of the hand was <180° at preoperative assessment. Lower scores were observed in the thumb (110.62) and little finger (134.5). Mean preoperative TAM for all the digits in 24 hands operated was 156.4°. This is clearly a significant functional loss, and surgical reconstruction had a significant impact on the improvement in the score to 225.3° after 1 year, which is a good outcome.[20] Barillo et al.[21] in 83 hand burns found an average TAM of 230° three months after injury. Cartotto.[22] reported mean TAM of 225° for patients with deep partial or full-thickness hand burns that were grafted.

CONCLUSION

This prospective study of 24 patients with hand burns, who underwent treatment in our center and were followed up for one year, has shown that:

- Domestic accidents of flame burns are a major cause of hand burns.
- Children are more prone to suffer hand burns than other age groups.
- The average time of presentation for treatment was 4.57 years after sustaining burns, which is rather too long.
- QuickDASH and TAM are good assessment tools to rate the function of hand preoperatively, to plan surgical reconstruction, to follow the progress of the patients postoperatively and for rehabilitation.
- Both QuickDASH and Mean TAM scores improved significantly after treatment in all patients.
- The degree of functional improvement of hands was more or less similar between those who presented early and those who presented late.
- Age and gender of the patients also did not influence the degree of functional outcome.

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REVIEW ARTICLE

Mobile Network-based Tele-electrocardiography: A Review

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ABSTRACT

Easy accessibility and affordability of the mobile phone network have made a mobile network-based tele-electrocardiography (ECG) a reality during the last 15 years. The instrument required for this purpose is very small compared to conventional ECG machines. It is lightweight, easy to carry and several folds lower in cost. Thus, it can be used in rural areas where there are no facilities available for managing cardiac emergencies. Many products are commercially available from domestic as well as international manufacturers. The technology has moved on from sequential 12 lead configurations to simultaneous 12 lead configurations; yet maintaining the overall size limited to credit card dimensions. Some of these have built-in interpretation algorithms (like Glasgow interpretation algorithm ECG), some offer cloud computing, whereas othersare developing their algorithms for incorporating diagnostic features. All these technologies are reviewed in this paper for comparison.

Keywords: Android, Cloud computing, Rural healthcare, Tele-ECG, Wireless communication.

How to cite this article: Lakhe AS, Anathakrishnan TS, Athavale PP, Jindal GD. Mobile Network-based Tele-electrocardiography: A Review. MGM J Med Sci 2018;5(4):189-194.

Source of support: Board of Research in Nuclear Sciences, Department of Atomic Energy, Government of India

Conflict of interest: None

INTRODUCTION

India has vast and varied topography with a dense population with more than 70% residing in rural areas, many of which are very remote. Commuting infrastructure is far from satisfactory in these areas. Reaching medical help within a crucial time becomes a challenge. Low doctor-to-patient ratio[1] and lack of uninterrupted power supply in remote villages are formidable challenges. Therefore, telemedicine can have a big role in improving healthcare services in these places.

Rapid advances in telecommunication technology havemade telemedicine feasible for diagnosis and treatment of patients who do not have access to advanced medical facilities. Initially, when satellite communication was not available conventional telephone lines were used for electrodiagnostic signal transmission. It was possible to transfer images and data only after the advent of satellite communication. This resulted in the development of several centers in the country for the healthcare of patients.[2] Seoncheol et al. reported that "Satellite communication link was 10–30 times faster than conventional terrestrial link."[3] However infrastructure required for satellite-based telemedicine is limited mostly to metrocities in our country and therefore not feasible for remote rural areas.

Worldwide communication has become easier and much faster with the introduction of mobile cellular networks like global system for mobile (GSM) or third/fourth/fifth generation network (3G/4G/5G). Availability of mobile network in Indian villages, the familiarity of rural masses with mobile phonesand the availability of mobile phones at an affordable cost has helped the development of telemedicine. Routine checkup, monitoring of patients at home, during traveling or at work has become possible via mobile phone.

Electrocardiogram (ECG) is an essential emergency diagnostic tool. Immediate diagnosis of acute myocardial Infarction by ECG can be lifesaving because once diagnosis is confirmed; treatment can be commenced within the golden hour. In ECG surface electrodes are used to sense electrical activity of the heart and graphically record the same.It was first introduced by Willem Einthoven in 1896 (his experiment shown in Fig. 1).[4] ECG is recorded by placing 10 surface electrodes on the body from various spatial perspectives; commonly known as leads.

Rashid et al.[5] conducted feasibility studies of transmission of biomedical signals through Bluetooth communication to mobile phone and subsequently to the cellular network. That is when the concept of tele-ECG was born. Since then many research and development organizations and several manufacturers of medical instruments have been developing battery-operated, portable and low-cost mobile network-based ECG machines. Their functions and capabilities are reviewed in this paper.

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Figs 1A and B: Original arrangement used by Einthoven are shown in A to record ECG signal. The electrodes, show in B in form of saline tanks; (B) ECG recording by string galvanometer (*courtesy:* W. Einthoven)[5]

FIRST GENERATION TELE-ECG (SEQUENTIAL LEADS)

Bhabha Atomic Research Center (BARC) was probably the first to develop a low cost, battery operated handheld tele-ECG unit (shown in step 2 in Figure 2) which has a bluetooth interface with a cellular phone.[6,7] It comprises a hand-held tele-ECG unit which is connected via bluetooth to a mobile phone. The unit is capable of sequentially acquiring ECG data from all the 12 leads connected to a patient. The data, in turn, is transferred to a mobile phone or a laptop using a Bluetooth interface. The tele-ECG unit can be activated, operated and controlled by either of them. Using a mobile phone or laptop the operator can acquire and view signals from different leads. The data can be saved in the mobile phone in files. It can be transferredto other mobiles. The data can be transferred from a laptop over the internet. The file format used for storing acquired data is png/bmp. To get an expert opinion, the ECG data can be sent to an expert of choice through the GPRS network. The six steps followed for tele-ECG with the help of this unit are illustrated in Figure 2, for the purpose of administering emergency treatment to the patient in the golden hour.It has been providing cardiac care to the rural population. The report generated can also be shared through local area network (LAN) for integration with the hospital management system (HMS). This paperless procedurehas proved advantageous over the hardcopy, which gets faded with time and also is at risk of being lost.This product has been clinically validated by Medical Institutes of national importance and has been commercialized. It has been successfully used for testing the heart condition of defense personnel,who are deployed at high altitude and other uncongenial locations.

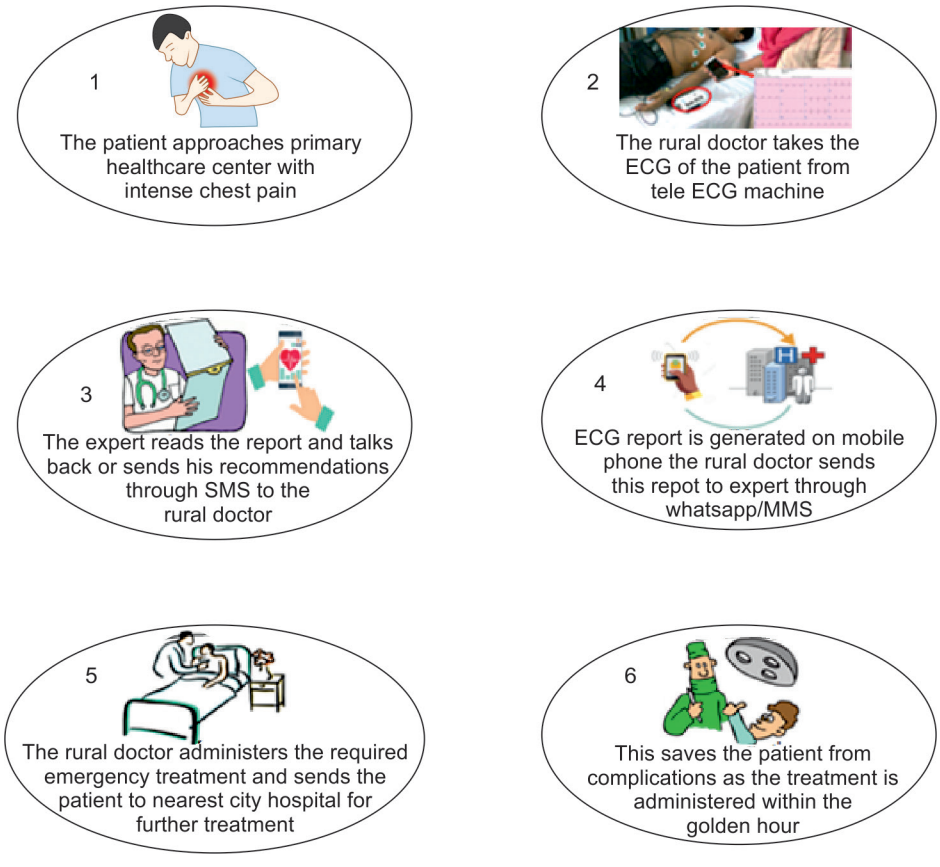


Fig. 2: Model of mobile network-based tele ECG

SanketLife, a match-box size ECG machine, was next among the domestic developments. It is very economical, portable and one which does not use patient cable. It is bluetooth enabled 12-lead ECG monitor which not only monitors heart but also gives alert for heart attack. It provides cloud storage along with heart rate variability to monitor daily, weekly or monthly trends. It has been clinically validated, and accuracy is claimed to be 98%.[8,9] The leads are captured sequentially by placing the metallic exposed part of the device at a specific position as guided in the user manual. The industry has a panel of cardiologists to review not only ECG reports generated by SanketLife but alsoany other ECG report through SanketLife application. SanketLife has many models to suit the user's choice.

Brucal et al.[10] have also described a portable ECG device, which can be interfaced with smartphones. The device has 9V CMOS batteries and leads ports to connect lead cables. The signal acquired from electrodes is processed through the instrumentation amplifier, bandpass filter, non-inverting amplifier, and pulse amplitude modulator. The signal is transferred to smartphone through the audio jack. Further processing is done in the android application in the smartphone. The processed signal could be sent to the doctors through the internet. The signal can be saved to Google drive (cloud) and in "0.3 gp" format. On similar lines, Jadhav et al.[11] have developed a smartphone-based ECG monitoring system. There is no external power supply needed as a power requirement is taken care from a mobile phone via the audio jack. They have interfaced the signal with PC as well as a mobile phone through the audio jack. The waveform is displayed using windows sound-card oscilloscope application on PC and using the android application on mobile phone. ECG was successfully displayed on PC application whereas it was corrupted with noise on mobile.

Walker and Muhlestein[12] have reviewed some of the globally manufactured products (USA, Italy and Singapore) using mobile network based Tele-ECG technology (Kardia, ECG Check, D-Heart, QardioCore, EPI Mini and iHealth Rhythm). They are more or less similar to the BARC and Sanket models in hardware but possess enhanced software compatibility with i-phone, Blackberry, etc. Bansal and Joshi have reviewed the performance of some of these models with respect to their diagnostic accuracy and utility stating their pros and cons.[13]

Over a period of time, an up-gradation for simultaneous recording of 12 leads has become necessary, which necessitated higher power consumption and an increase in size. Having 12 identical channels (preamplifier and main amplifier) using conventional electronic devices and crossover noise as a consequence of limited size has resulted in a paradigm shift from analog instrumentation to digital instrumentation. This has given rise to the second generation of tele-ECG.

SECOND GENERATION (SIMULTANEOUS 12 LEADS)

The Tele-ECG technology developed by BARC has been upgraded to 12 channel simultaneous ECG recording. A VLSI (very large scale integration) chip of Texas Instrument USA ADS 1298 was used for the technology up-gradation. It provides 8 channels of identical differential amplifiers for amplification of bio-electric signals such as ECG, EMG (electromyograph), EEG (electroencephalograph), etc. The inherent noise in the linear design could be eliminated by the use of VLSI technology since most of the signal processingis done in the digital domain. Also, the use of ADS 1298 results in compact design reducing hardware requirement. The 12 lead tele-ECG unit, developed by BARC, uses microcontroller MSP430FG4618 which consumes less power. The Bluetooth module used is RN42.

ECG potentials sensed from the body using the 10 surface electrodes (RL, LL, RA, LA, V1, V2, V3, V4, V5, V6) are connected to the VLSI ADS 1298 through protectioncircuit. While leads I, II and V1 to V6 are directly amplified by ADS1298, leads III, aVR, aVL, and aVF are derived from leads I and II. For example, Lead III is (Lead II–Lead I); aVR is –(Lead I + Lead II)/2 and so on. In addition, ADS1298 derives lead-fail detection internally. Wilson center terminal is derived internally by three integrated amplifiers. The right leg drive is derived from the combination of input channels. Also, the problem of electrode potential, an inherent limitation of electrodiagnostic instruments, is taken care of in the digital domain with the help of 24-bit sigma-delta analog to digital converter.

The output of ADS1298 is read by the microcontroller through a serial peripheral interface (SPI). From mobile or PC, data and commands are transferred through a Bluetooth module, interfaced with the microcontroller as shown in Figure 3, with the help of embedded firmware described below. ECG recording is initiated and guided through laptop/desktop or mobile phone. All the required operations like display of ECG data, saving and transmitting data, saving of patient's information can be done from laptop/desktop or mobile. After start command, ADC data is read and transferred repeatedly through bluetooth module to laptop/desktop or mobile. The sampling interval is 2 milliseconds. The unit checksfor start/stop which may come from mobile phone or desktop via bluetooth. The initial data is acquired in the calibration mode. The on-screen indication is provided

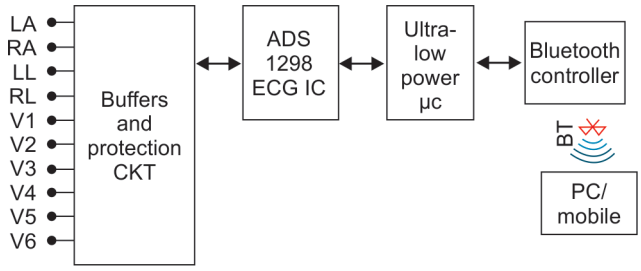
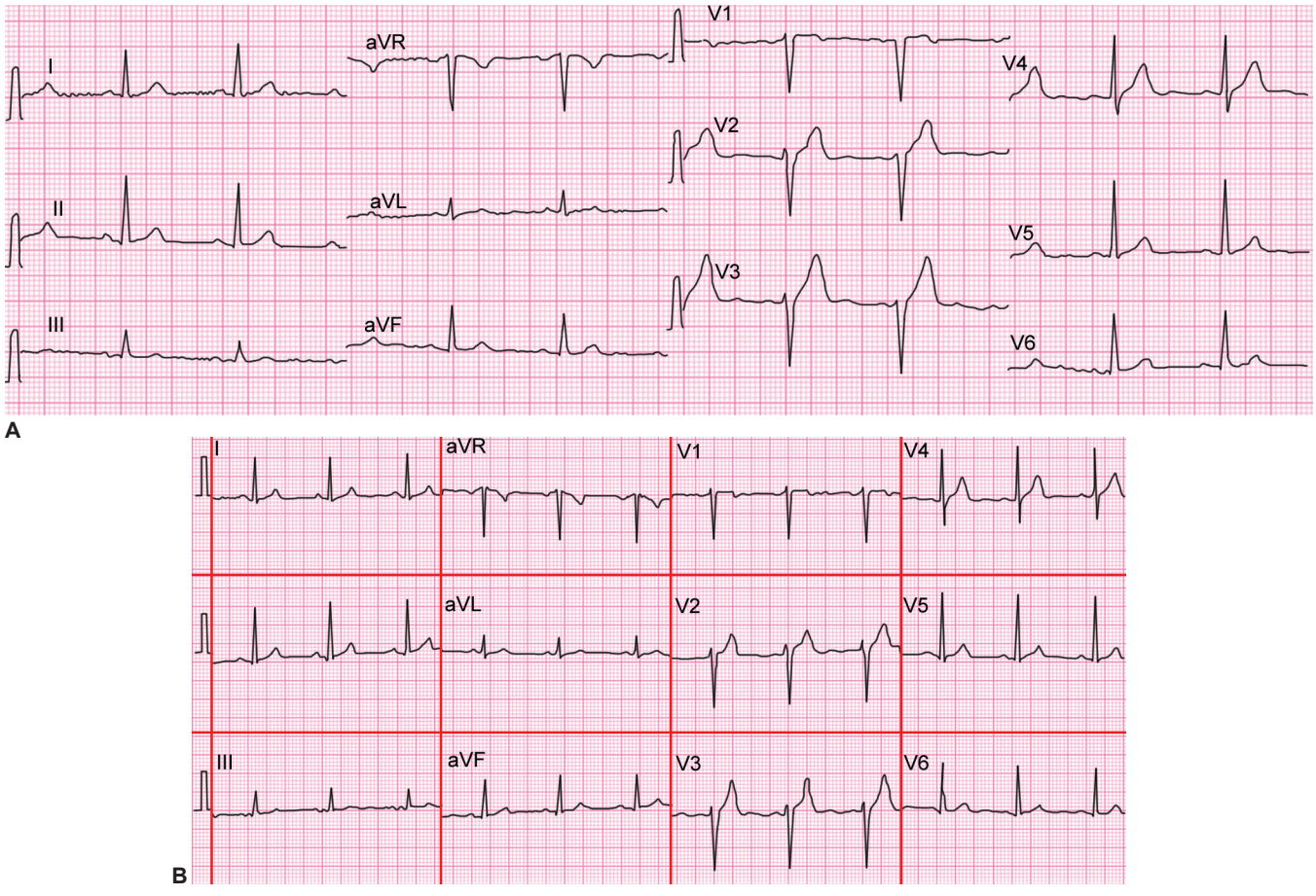


Fig. 3: Schematic chart of BARC's simultaneous 12 channel tele-ECG system

for battery charge level. Bluetooth devices in the vicinity are checked by the application software on mobile. After discovering and selecting "ECG12CH", Bluetooth link is established between mobile and ECG device. After successful connectivity, the user interface screen appears. Menu option provides facility to enter information like name, age, gender, etc. This can be saved for generating a report. Click on start button initiates acquisition in auto mode. The signal from various leads is displayed on the screen. It can display all 12 leads simultaneously. Different menu options like test and ECG mode, filtering, etc. are also available. An option to generate an ECG report in .png format is provided. It contains patient information like name, age, sex along with the date. The report is stored in the internal memory of mobile which can be used for sending MMS, or it can be sent through email. The report can be sent to expert through WhatsApp or any other file sharing application.[14]Automatic shutdown after 5–10 minutes (adjustable) of non-usage limits battery consumption.This unit can also be used to study Heart Rate Variability (HRV) and performs statistical analysis for the purpose of stress monitoring. Postgraduate Institute of Medical Education and Research, Chandigarh;[15] Medical Division, BARC and Father Muller Medical College Mangalore have tested and validated this instrument.

Graph 1 shows ECG obtained from the conventional machine and that by tele-ECG unit at medical division BARC. Leads I, II, III, aVR, aVL, aVF, and V1 to V6 are shown in the figure in familiar conventional format. It has been confirmed through a comparative study that the ECG machine from BARC is at par with that of the commercial ECG machine. There is no significant loss of information. The conventional ECG and digital tele-ECG have the same morphology in all the 12 leads as is evident from the figure. No qualitative loss in ECG received at the experts' end has been reported. The technology has been transferred to more than 10 entrepreneurs for commercial production. Many models are available in the market.[16,17]



Graphs 4A and B: 12 Channel ECG recorded from a conventional ECG machine (top) and BARC's tele-ECG machine (bottom). As seen the bio-potentials recorded by tele-ECG have the same morphology as that of conventional ECG in all the 12 leads. Amplitudes recorded with tele-ECG appear to be little higher than the conventional ECG and may call for fine tuning in the device gain

Similar technology is also available from two other well-known brands in healthcare, namely BPL (BPL Cardioline Touch ECG) and Phillips (Efficia ECG100).[18,19] Table 1 compares the features of these units with BARC developed tele-ECG.

CLOUD COMPUTING IN TELE-ECG

Mobile cloud computing is the next level of advancement in tele-ECG. There is huge storage and computations requirement in the processing of ECG data. Adaptation of the mobile cloud computing approach resolves the difficulties mentioned above. The cloud computing model as described by Venkatesana et al.[20] is shown in Figure 4.

ECG sensors and mobile devices are wirelessly connected to the cloud. The cloud storage space is used to store a large volume of data. Complex mathematical computations are carried out in a virtual machine for cloud computing. Hseih and Hsu[21] have described cloud computing based 12 lead tele-ECG. According to them, "The cloud computing-based ECG teleconsultation service expands the traditional 12 lead ECG application onto the collaboration of clinician at different locations or among hospitals."

Cloud Computing is the Method of Choice for the Following Reasons

It reduces the burden of heavy storage in individual devices like ECG machine, mobile phone, laptops or desktops. The patient data is securely preserved on the cloud even if there is a problem in the device.

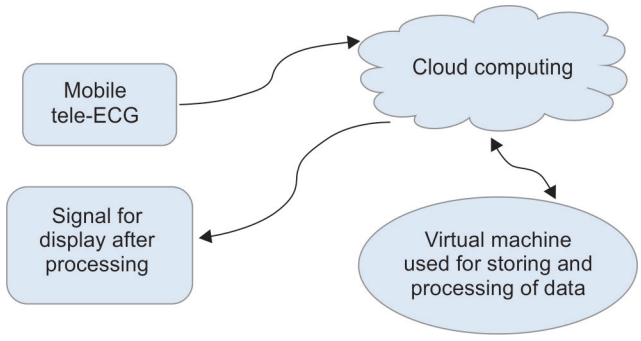


Fig. 4: Cloud computing model

Upgradation of software application can be achieved without much hassle through cloud computing; upgrading on device basis is a tedious process as the vendor has to call back the machines from the users and upgrade them.

If the application is cloud-based, it can be used by other manufacturers through mutual agreement. Any user can view analyzed ECG reports irrespective of the specific model of the machine used.

Cloud computing has been very helpful in huge data analytics as healthcare industries can share data to build a more comprehensive database which can be used for medical research.

CONCLUSION

Recent developments of the mobile-based tele-ECG system are reviewed. These technologies aim at easy,

Table 1: Features of BARC, BPL and Philips technologies

Feature	*BARC Technology*	*BPL*	*Philips*
Size/weight	Credit card size, Small (3.5"x2.5"x1.0") and light weight (100 grams)	Extremely small, light-weight (<90 grams)	Palm size, small (< 300 grams)
Battery life	Li-ion rechargeable battery, records >100 ECG's on single recharge	Not Specified	Li-ion rechargeable battery, 4 hours of non-stop usage
Simultaneous no. of Leads	12	12	12
Storage	ECG report stored for future reference in .TXT, .DAT and PDF	The data can be stored in PDF and SCP formats	Stores ECG in PDF format. Large storage capacity (1000 ECGs per 1GB) on the device.
Interfaced with/ display on	PC (Windows) Smartphone (Android)	PC (Windows) Smartphone (Android)	Smartphone (Android)
Connectivity	Unit-Mobile/PC→Bluetooth	Unit-Mobile/PC→Bluetooth	Unit-Mobile→Wi-Fi
	Mobile-Mobile→MMS/ Apps/ internet/ Bluetooth	Mobile-Mobile→ MMS/ Apps/ internet/ Bluetooth	Mobile-Mobile→MMS/ Apps/ Wi-Fi/ internet
	Mobile-PC→Internet/Bluetooth	Mobile-PC→Internet/Bluetooth	
Report printing	A4 paper to print in grayscale or color	Not Specified	A4 paper to print in grayscale or color
Reference past ECGs	Yes	Not specified	Yes
Indications	Low Battery, lead fail	Not specified	Lead map, lead fail, and noise level indicators.
ECG interpretation and analysis	Not specified	Glasgow ECG interpretation algorithm built in the unit	Not specified
Cost	Rs. 25,000 – Rs. 40,000	Not specified	Rs. 25,000–Rs 60,000.

affordable and faster consultations available to the remote rural population as well as to people living in towns and cities for diagnosing life-threatening cardiac emergencies within the golden hour. Though first generation technology does not record all the 12 leads simultaneously, it still has relevance due to its low cost and cloud computing-based ECG analysis. Advancement to second generation simultaneous 12 leadrecording gives an edge to this technology in terms of greater diagnostic accuracy. All the machines can be integrated with Hospital Management Systems. Another new dimension to this technology is cloud computing which resolves the problem of storage and processing of massive amounts of data generated.

ACKNOWLEDGMENTS

Authors gratefully acknowledge Bhabha Atomic Research Centre and Board of Research in Nuclear Sciences (BRNS), Department of Atomic Energy, Government of India for supporting tele-ECG work. The authors thank Dr SK Narayankhedkar, Principal, MGM's College of Engineering and Technology (MGMCET), Smt. Anita Behere, Head, Electronics Division, BARC and Prof UR Bagal, Head, Bio-Medical Engineering Department, MGMCET for their continuous support. Technical expertisefrom Shri RK Jain, Shri Vineet Sinha, and Smt Sushma N Bhat is gratefully acknowledged.

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10.5005/jp-journals-10036-1217

SHORT COMMUNICATION

Novel School Health Initiative

[1]Shridhar Dwivedi, [2]Om P Yadava, [3]Deepa Chugh

ABSTRACT

India is currently facing an epidemic of noncommunicable diseases. This epidemic can possibly be halted by creating awareness about these diseases and inculcating a healthy lifestyle among adolescent children. Keeping this in mind, National Heart Institute has started a 'Novel School Health Initiative' in which senior faculty gives illustrative lectures on a healthy lifestyle like 'you and your heart', 'menstrual hygiene' (exclusively for girls) and 'personal hygiene' giving power point presentations to class VIII/IX students. There were no financial implications for the schools.

Twenty Delhi schools including public, private and central schools were included in this program to make it more objective. Lectures were preceded and followed by an objective questionnaire. Though a large number of students knew about healthy lifestyle and heart disease in general, the awareness level increased considerably following the lecture. The fact that the students received these lectures with enthusiasm and their level of awareness increased in the post-test evaluation, indicates that these students will be an awakened lot and will try to follow a healthy lifestyle.

The long-term effect of such lectures needs periodical evaluation. This model can be replicated in other schools by neighborhood medical college/ hospitals in the entire country.

Keywords: Healthy lifestyle, Menstrual hygiene, Personal hygiene, School, Tobacco.

How to cite this article: Dwivedi S, Yadava OP, Chugh D. Novel School Health Initiative. MGM J Med Sci 2018;5(4):195-196.

Source of support: Nil

Conflict of interest: None

DESCRIPTION AND FINDING OF PROJECT

Quite realizing the rapidly surging pandemic of noncommunicable diseases (NCDs) like hypertension, diabetes mellitus (T2DM), obesity, coronary artery disease (CAD), stroke and cancer in urban as well as in rural India, National Heart Institute (NHI) New Delhi took upon itself voluntarily and consciously an initiative to educate and sensitize young school children belonging to class VIII and class IX about the above problems and steps to prevent these by observing simple lifestyle measures.[1] The project started in April 2016. We would like to mention that similar efforts were made by Hamdard Institute of Medical Sciences and Research (HIMSR), Jamia Hamdard, New Delhi, which started in 2013.[2] A series of lectures on six subjects viz 'lifestyle, you and your heart', 'adolescent obesity/diabetes mellitus, 'tuberculosis' and personal hygiene' were delivered by us. A special topic on 'menstrual hygiene' was chosen exclusively for girl students. Senior faculty from NHI and HIMSR offered themselves for this initiative.

In order to provide an academic framework for such lectures NHI has published a 'School Health Book' containing relevant lessons pertaining to healthy lifestyle, prevention of hypertension, diabetes, and tuberculosis, ideal posture, personal hygiene, menstrual hygiene, etc.[3] Education Department of National Capital Government of Delhi lent support for these lectures in some 12 schools on pilot basis. So far we have conducted twenty lectures in different schools of national capital. These schools represent a mix of all socioeconomic segments of society, public schools, central schools, and Delhi government boys and girls schools. The lectures are given both in English and Hindi using power point presentations with a lot of pictures and graphics. Each lecture is about thirty minutes in duration with 10 minutes for interaction. Continuing this journey, we also organized a lecture on 'healthy lifestyle' in government blind school, New Delhi. This time we took help of' a 'documentary ' prepared by World Health Oganization-South-East Asia Regional Office (WHO-SEARO) in which NHI had given its academic and professional inputs. Its main emphasis was on prevention of tobacco use.[4] We were very pleased when the Principal of the blind school personally thanked us for giving a talk against tobacco use because gutkha consumption was very high in their hostel. Very often on a surprise check-up, gutkha-surti pouches used to be found with inmates. The principal added that our lecture and docudrama will go a long way in controlling this menace among hostel students.

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Table 1: Pre- and post-lecture assessment in girl's school

Girl's school (n = 96)		
	Awareness pre-lecture	*Awareness post-lecture*
Menstrual hygiene	71.6%	77.6%
Healthy lifestyle	74.4%	74.4%

Table 2: Pre- and post-lecture assessment in Co-ed Public School

Public School (n = 110)		
	Awareness pre-lecture	*Awareness post-lecture*
Healthy lifestyle	89.8%	92.4%
You and your heart	88%	92.6%

To assess the impact of this initiative objectively, we designed a pre-test and post-test evaluation questionnaire containing five core questions drawn from the two lectures given on that day. So, far this exercise has been done in three schools out of which two were exclusively girls and one co-ed public school. The preliminary results have been interesting (Tables 1 and 2).

The results are important on several counts. A large number of classes VIII, IX students knew what a healthy lifestyle means. Our lecture increased this awareness in another 5–10% of students, taking the awareness level to above 90%. However, what matters most is how many of them actually follow healthy lifestyle practices, like doing physical exercise, participating in sports, consuming healthy food, etc., in their day-to-day routine.[5] One can only hope for the best; at least those who have not already started tobacco chewing or smoking, will not fall prey to this habit in future after attending these lectures and those who are using tobacco products, may seriously think of quitting tobacco.

We wish to take this initiative more aggressively by covering all government schools in national capital region (NCR) and involving many more faculties from different medical schools/health institutions of the capital city of Delhi and neighborhood.[6] It has to be a movement to create 100% awareness among school children about healthy lifestyle, personal hygiene, and civility so that the rapidly spreading epidemic of NCDs can be halted effectively.

ACKNOWLEDGMENT

Help provided by Miss Harshita Mangla, BCLT Scholar, Divya Tomar, M Sc Nursing and Nisha Vohra, Ph.D. Scholar in organizing these lectures/questionnaire is gratefully acknowledged.

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10.5005/jp-journals-10036-1218

CASE REPORT

Surgical Management of Secondary Hyperparathyroidism in End-stage Kidney Disease: A Case Report

[1]Leszek Sulkowski, [2]Maciej Matyja, [3]Artur Pasternak

ABSTRACT

A 56-year-old male patient with end-stage kidney disease (ESKD) on hemodialysis, presented with features of severe secondary hyperparathyroidism (SHPT). He failed to respond to conservative management. So he was evaluated for surgical treatment (parathyroidectomy). Radionuclide scintigraphy revealed hypertrophied and adenomatous parathyroid glands. He underwent parathyroidectomy, in which all parathyroid glands were excised. Postoperatively patient felt significant relief in bone pain. Parathyroidectomy can be offered to a patient of secondary hyperparathyroidism due to chronic renal failure if conservative measures fail.

Keywords: Secondary hyperparathyroidism, Technetium 99m Methoxy-Isobutyl-Isonitrile scintigraphy, Parathyroid gland, Parathormone, Parathyroidectomy, End-stage renal disease; Hemodialysis.

How to cite this article: Sulkowski L, Matyja M, Pasternak A. Surgical Management of Secondary Hyperparathyroidism in End-stage Kidney Disease: A Case Report. MGM J Med Sci 2018;5(4):197-199.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Renal failure is the most common cause of secondary hyperparathyroidism (SHPT). Due to the nonactivation of vitamin D by failed kidneys, calcium absorption from the gut is reduced, leading to hypocalcemia. Phosphate excretion by kidneys is also reduced, leading to hyperphosphatemia.[1]

In response to hypocalcemia, parathyroid glands start overproducing parathormone. Over some time, parathyroid glands undergo hypertrophy and adenomas may also develop. Due to high levels of parathormone in blood, bones undergo demineralization, as a result of which the patient gets persistent pains in bones and joints. In the early stages, most of these patients can be managed successfully with drugs viz. phosphate binders, vitamin D_3 supplements, vitamin D, and cinacalcet. Some patients, especially in later stages fail to respond. They are the ones who may benefit from surgery, in the form of parathyroidectomy.[1,2]

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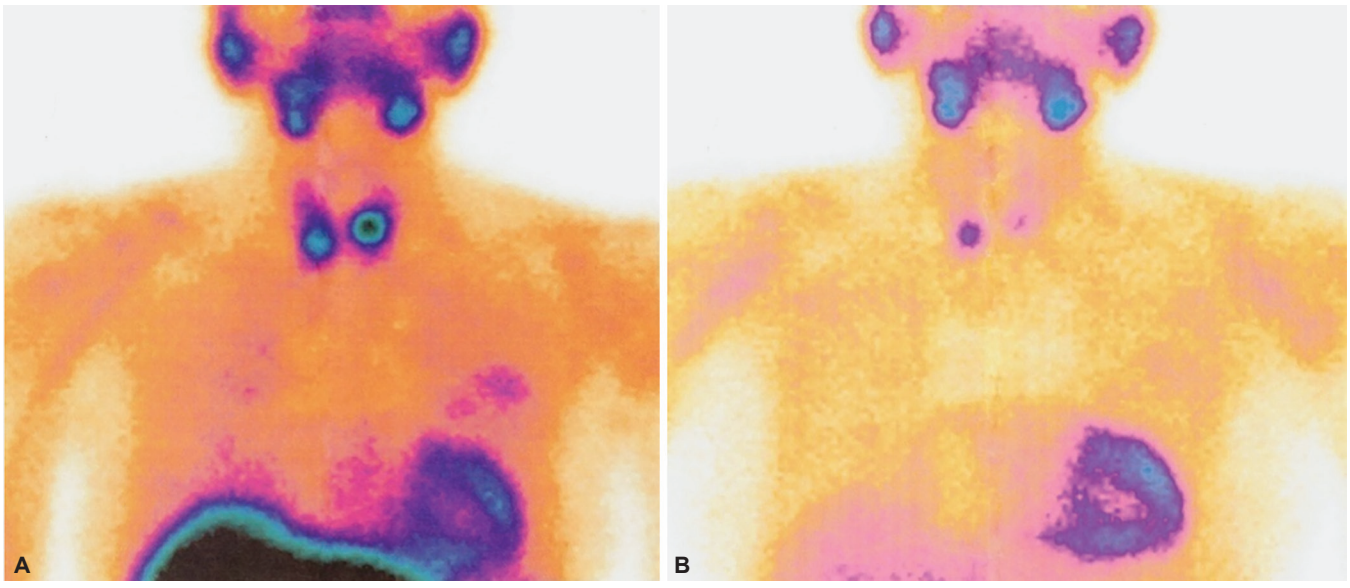
CASE REPORT

A 56-year-old male patient was undergoing hemodialysis thrice a week for end-stage kidney disease (ESKD) for 5 years. He started feeling increasing pain in his bones and joints. The pain became very troublesome and failed to respond to conservative management with low phosphate diet and drugs (phosphate binders, vitamin D_3, active vitamin D_3, and cinacalcet). So he was referred to our department by his treating nephrologist for evaluation for parathyroidectomy.

To evaluate the location and size of parathyroid glands, the patient underwent Technitium 99 m methoxy-isobutyl-isonitrile (Tc99m MIBI) scintigraphy. Two scans were taken, one 10 minutes and another 2 hours after radionuclide injection (Fig. 1). All four parathyroids were located in their usual anatomical positions behind thyroid gland, and all were enlarged. So he was taken up for parathyroidectomy under general anesthesia through a transverse skin incision over the neck. All four parathyroids were easily located (Fig. 2). They were enlarged and excised (Fig. 3). The patient made an uneventful recovery. He was put on calcium carbonate and alfacalcidol postoperatively. He was discharged on the 4th postoperative day. Histopathological examination of the parathyroid glands showed hypertrophy. The patient is currently on follow-up and admits significant relief in his symptoms (bone and joint pains).

DISCUSSION

Parathyroidectomy should be considered in a severely symptomatic patient of SHPT, who fails to respond to conservative management.[1-3] Elevated parathormone levels come down and excessive bone demineralization stops. This leads to significant clinical improvement in



Figs 1A and B: 99mTc-MIBI scintigraphy. The scans took 10 minutes (A) and 2 hours; (B) after radionuclide injection

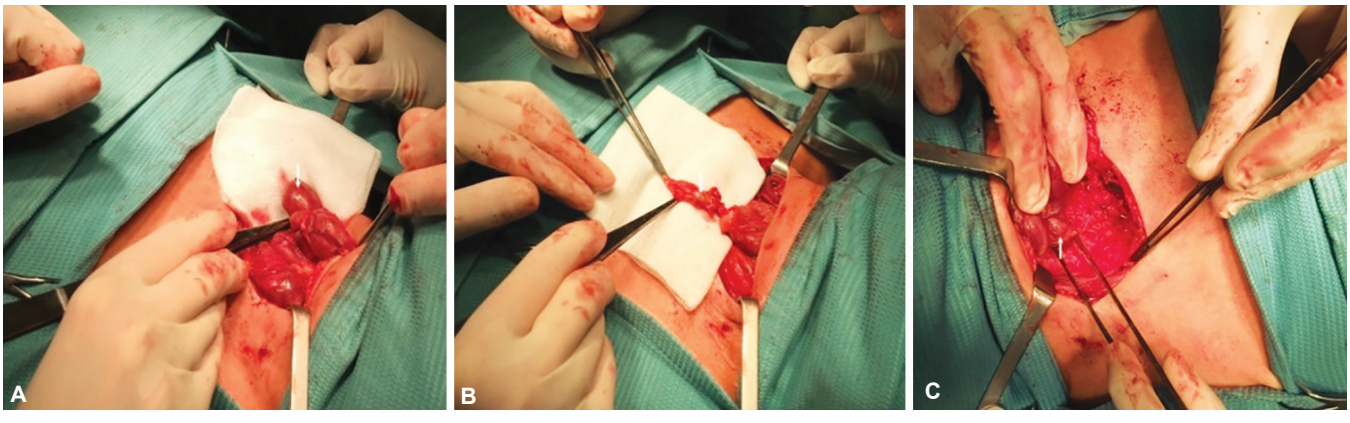
symptoms, as we saw in this patient. Before surgery, it is essential to locate parathyroid glands accurately. A 99mTc-MIBI scintigraphy is quite useful in finding the exact location of parathyroids and in evaluating their size. Some patients may have ectopic parathyroids also, located in the mediastinum or elsewhere. Radionuclide scintigraphy will reveal their presence, as well as that of normally positioned parathyroids. If a supernumerary or ectopic parathyroid is missed at surgery, surgery will be incomplete and so ineffective. Therefore, we believe, 99m Tc-MIBI scintigraphy is an essential imaging investigation before carrying out parathyroidectomy.[1,4]

Other surgical procedures described are subtotal parathyroidectomy (in which 3 out of 4 parathyroids are totally excised, and most of the 4th parathyroid is also excised except a tiny part) and total parathyroidectomy with autotransplantation of one gland into the forearm. Both these procedures are aimed at retaining some parathormone secretion from the gland. Recurrence of SHPT is, however, possible if some part of the gland is retained. Autotransplantation in forearm has the advantage that it is easily accessible, should need for re-exploration arise.[1,5]

Quality of life of a patient of ESKD on hemodialysis is not quite satisfactory. If SHPT comes on top of it, causing severe pain in bones and joints, quality of life further worsens. So parathyroidectomy has a role to improve a patient's quality of life a little, if conservative management fails, by relieving his symptoms.[6,7]

CONCLUSION

A case of SHPT in a patient of ESKD on hemodialysis, who failed to respond to conservative treatment with drugs, was subjected to parathyroidectomy. Before surgery, 99m Tc-MIBI scintigraphy was carried out to locate the glands and evaluate their size. He made an uneventful recovery, and his symptoms of severe bone and joint pains showed marked improvement. Parathyroidectomy has a definite role in the management of SHPT in ESKD patients, in whom conservative management fails.



Figs 2A to C: Intraoperative neck exploration: (A) Right inferior parathyroid gland; (B) Left inferior parathyroid gland; (C) Right superior parathyroid gland

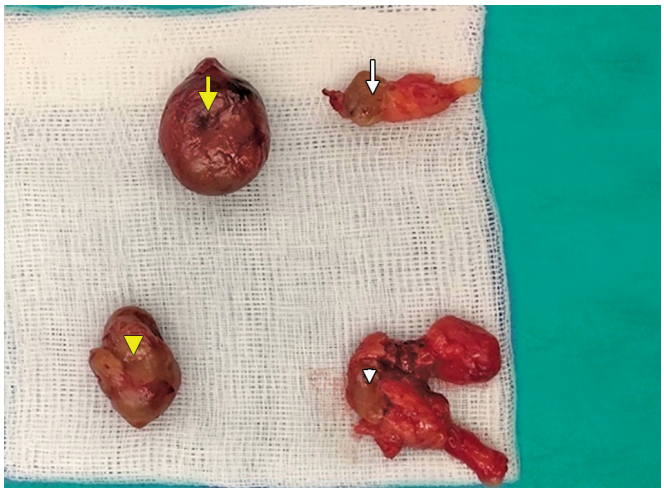


Fig. 3: Parathyroid glands postoperatively (yellow arrow head–right inferior PG; white arrowhead–left inferior PG; yellow arrow–right superior PG; white arrow–left superior PG)

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10.5005/jp-journals-10036-1219

CASE REPORT

Facade of Behavioral Problems in Chronic Medically Sick Children and Adolescents with Underlying Depression: A Report of Three Cases from India

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ABSTRACT

Depression in children and adolescents with chronic medical conditions is an important area of clinical interest and research. There is sparse literature from developing countries such as India on the interface areas of pediatric mood disorders and chronic medical conditions. Clinical manifestations of depression in children and adolescents with chronic medical conditions can be different as compared to adult depression. Behavioral overlays can be present in child and adolescent depression which can add on to the complexities of diagnosis and treatment. We present three sick children with behavioral problems, who were suffering from α-thalassemia, systemic lupus erythematosus (SLE), and xeroderma pigmentosum. Relevant literature on clinical manifestations, atypical behavioral presentations, challenges faced in clinical assessments, diagnosis, and management of depression in chronic medically sick children and adolescents are discussed.

Keywords: Behavioral problems, Chronic medically sick children and adolescents, Depression α-thalassemia, Systemic lupus erythematosus, xeroderma pigmentosum.

How to cite this article: Kaur D, Landge AP, Dere S, Ghildiyal R. Facade of Behavioral Problems in Chronic Medically Sick Children and Adolescents with Underlying Depression: A Report of Three Cases from India. MGM J Med Sci 2018;5(4):200-202.

Source of support: MGMIHS

Conflict of interest: None

INTRODUCTION

Chronic illnesses in children are significantly associated with early-onset depressive symptoms, impairment in social functioning, learning problems, and challenging behaviors.[1,2] We describe three cases of depression presenting as behavioral problems in medically sick children and adolescents referred for consultation-liaison psychiatric evaluation and the challenges in assessment, diagnosis, and management of depression.

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CASE REPORTS

Case 1

Master ABC, a 14-year-old boy, a known case of α-thalassemia was referred for withdrawn behavior, not eating food, agitated and getting angry easily. History elicited from parents revealed that since the past 6 months, the boy had been looking sad and was not going to school regularly. He was also crying excessively and expressing ideas of hopelessness. The child stated that he was very depressed and did not like to interact with others and felt very low all the time throughout the day. He felt that with his kind of illness and frequent hospitalizations, there was no future for him. His mental status examination (MSE) showed psychomotor retardation, the cognitive triad of hopelessness, helplessness, and worthlessness. His primary mental functions were intact and there were no delusions nor hallucinations.

Case 2

Miss PQR, the 11-year-old girl, diagnosed with SLE, was referred in view of behavioral problems of irritability, getting angry, refusing to eat food and quarreling with siblings. The referring team had requested for behavior therapy in their reference notes. Clinical evaluation and MSE showed that the patient was having symptoms of depression for past 1 year with low mood, crying spells, anhedonia (not getting pleasure in normally pleasurable activities), negative thoughts about self, others and future, hopelessness and helplessness, loss of appetite and weight gain. Her treatment history revealed treatment with immune modulators and steroids for SLE. There was no history of any substance use, psychosis, mania, obsessive–compulsive disorder (OCD) or anxiety disorder. MSE revealed depressive mood subjectively, and the effect was depressed with reduced range and reactivity of mood. She also had depressive cognitions and schemata of loneliness and helplessness.

Case 3

Miss XYZ, 8-year-old girl, a case of xeroderma pigmentosum was referred for behavioral disturbances in the ward like pushing other children, throwing things and temper tantrums. Reason for referral was behavioral issues in the

child. We found, after clinically interviewing the child and her parents, that the child had features of depression. She was not going to school nor going to play with other children. She preferred to be at home and would not talk much with her parents for the past 1 year. She appeared sad and would cry frequently. She would get angry, start shouting if her demands were not fulfilled and would be very irritable. On the clinical interview, the child reported that she was very sad about her skin condition and other children bullied her, and she did not like to have friends. She mentioned that she felt sad all the time during the day and parents also reported that her sadness appeared pervasive. She felt very hopeless and felt that there was no future for her due to her skin problems. On mental status examination, she was depressed with psychomotor retardation with depressive cognitions of hopelessness and helplessness.

All three cases when evaluated had certain common factors. They were admitted in the pediatric ward for inpatient management of their medical conditions. They were referred to the psychiatry department for consultation-liaison psychiatry, and the reason for reference as documented was behavioral problems and therefore were referred for behavior therapy. Some of the behavioral problems mentioned were: throwing temper tantrums, irritability, not fully cooperating to medical treatment, refusing to eat food, throwing things, hitting other children, withdrawn, etc. All three cases had pervasive low mood present throughout the day affecting their areas of educational and social functioning significantly. There was no history of substance abuse, psychosis, mania, OCD or anxiety disorder. There was no significant history of premorbid developmental delays nor any family history or past history of psychiatric disorders. They were not fully cooperative for a formal mental status examination initially. During the initial part of the clinical interview, they were appearing withdrawn. The poverty of speech and psychomotor retardation was present. Subjectively mood was depressed as well as Affect was depressed with reduced range and reactivity. However, towards the end of the clinical interview, they did open up and reported feeling low and depressed, perceived themselves as a burden on their families, felt guilty and hopeless of the situation. They also reported that they missed their school and were not going regularly to school because of their illness and they missed their friends and outdoor play activities tremendously. All three had not shared their feelings with anyone since their admission and were very sad and angry internally at why the almighty had chosen them for such an illness. They were diagnosed as severe depression without psychotic symptoms, comorbid with their respective medical sickness. They were started on serotonin selective reuptake inhibitor (SSRI) medication (Tablet fluoxetine 5 mg daily titrated upward gradually to 10 mg, based on response). Psychotherapy techniques combining cognitive, behavioral, play and supportive therapy were done in a holistic manner focused on individual needs and developmental age of the child, on a regular basis. Child apperception test revealed features of depression in all three of them with themes depicting helplessness, hopelessness, guilt, anger, low , and inferiority complex. Centre for epidemiological studies depression scale for children (CES-DC) score was used to assess all three children. These scores were over 15, which is suggestive of significant depression. All of them showed considerable improvement in mood symptoms and behavioral problems throughout 2–4 weeks. They continue to be on regular monthly outpatient follow-up and improvement is maintained.

DISCUSSION

Depression in children suffering from chronic medical conditions can be explained by various factors, such as social and physical restrictions, lifestyle changes due to illness and treatment protocols involving painful and distressing procedures. Besides, biopathological changes that occur in most chronic medical conditions that can also mitigate the development of childhood depression. Children with Thalassemia major can have depression and behavioral problems more frequently than healthy subjects and complicated and burdensome medical regimen in Thalassemia can potentially impact the emotional functioning of patients.[3,4] Depression and anxiety were found to be high and undertreated in children with SLE and mixed connective tissue disorders.[5] Cutaneous and ocular photosensitivity and an increased risk of developing cutaneous neoplasms with associated features of microcephaly, hypogonadism, neurological disorders, mental and growth retardation exist in De Sanctis–Cacchione syndrome, a rare form of Xeroderma pigmentosum. Sparse literature is available on neuropsychiatric co-morbidities in xeroderma pigmentosum.[6] Despite advancements in medical care for chronic illnesses, these children experience significant psychosocial morbidities, such as depression and anxiety.[7] Management of childhood depression in chronic medical conditions should be comprehensive and needs a multidisciplinary approach. Evidence and expert clinical consensus support the use of selected antidepressants in the treatment of depression in youths. The use of the recommended antidepressant medications requires appropriate monitoring of potential adverse effects. Other evidence-based treatment modalities include cognitive behavioral therapies.[8] Attention to psychiatric co-morbidities will not only result in enhanced quality of life but will also promote better adherence to medical recommendations.[1] Depression can

exist in children with chronic medical conditions and has the potential to impact developmental and mental health outcomes. Primary care physicians should be attentive to depressive symptoms in this special patient population.[2]

CONCLUSION

Symptoms of depression in children may differ from those of adults in terms of its nature and intensity.[9] Pediatricians should be attentive to depressive symptoms which can have behavioral overlays. Chronic medically sick children should be screened for depression and provided appropriate consultation-liaison psychopharmacological and psychotherapeutic treatment. A multidisciplinary approach that takes into account the individual variability of the chronic medical condition and its clinical manifestations helps to improve early detection of depression.[10]

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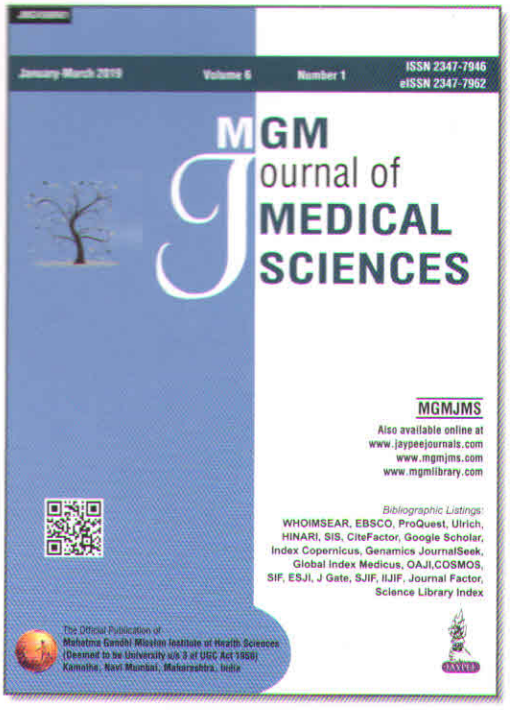

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