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Contents

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A Case Report of Rare Disease: Adenocarcinoma Esophagus in 12-years-Old Boy in Children's Hospital, Lahore

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ABSTRACT

Introduction: *Squamous cell carcinoma of esophagus is more common than adenocarcinoma. It is most common in Asian countries and more prevalent in black population as compared to white population. Its incidence has a decreasing trend, recent years. This disease is very rarely seen in children and adolescents.*

Case Report: *A 12-years-old boy with moderately differentiated adenocarcinoma of lower esophagus is reported because it is a very rare disease in children. Patient presented with vomiting and dysphagia. Surgery was not possible due to wide spread disease. Chemotherapy followed by radiotherapy was given. Patient started taking semisolids after two courses of chemotherapy.*

Discussion: *Esophageal carcinoma is disease of old age and most prevalent in Asian countries. Most patients with this disease are male and have age more than 50 years. This disease is very rarely found in children, the youngest patient presented with the disease was eight years old. It frequently metastasizes to lungs, liver and mediastinal lymph nodes.*

Key Words: Esophagus, Dysphagia, Adenocarcinoma, Asia, Squamous cell carcinoma, Mediastinal lymph nodes

INTRODUCTION

Patients with esophageal carcinoma present after 5th or 6th decade of life. It is more common in males than in females. Squamous cell carcinoma is more common than adenocarcinoma of esophagus. This disease is more common in Asian countries and more prevalent in black population as compared to white population. Its incidence has a decreasing trend in recent years. This disease is very rarely seen in children and adolescents. Cases reported in younger age group mostly presented with squamous cell carcinoma of esophagus. We present a case of very rare childhood adenocarcinoma of esophagus in a 12-years-old boy.

CASE REPORT

A 12-years-old boy presented with progressive dysphagia for last 6 months and vomiting after every meal for two months. Vomiting was initially with solid food, then progressively with semisolid food, and for two weeks he was unable to take even liquids. His dysphagia was not associated with any chest or throat pain. He had no history of any corrosive intake. His birth history was insignificant, he achieved

all his milestones on time and was vaccinated on time as per Government policy. There was no history of esophageal and gastrointestinal malignancies in 1st or 2nd degree relatives. He lost around 5 kg weight in last 3 months.

Except for low hemoglobin levels (7.8 gm/dl),other lab in vestigations and chest X-ray were normal. Upper GI endos copy showed normal hypopharynx, a friable mass seen from 6 to 30 cm from incisors completely obstructing the lumen. Scope could not be negotiated to stomach. Biopsy showed moderately differentiated adenocarcinoma. CT abdomen and chest showed large lobulated circumferential wall thickening involving mid and distal part of esophagus with metastatic pulmonary nodules and calcified hepatic deposits as well as calcified abdominal lymphadenopathy.Figure 1 and 2 shows pulmonary nodules and hepatic involvement.

At time of initial hospital admission, he was unable to take anything orally and it was not possible to pass NG tube due to complete obstruction. Surgical opinion was obtained and it was decided that surgery is not possible due to extensive local disease and presence of lung and hepatic metastasis. Feeding jejunostomy was planned but refused by family. It was decided in review board to give systemic chemotherapy followed by radiation. Systemic chemotherapy including pa clitaxel and 5-FU given. After two courses of chemotherapy, patient started semisolid diet. Six cycles of chemotherapy completed and radiotherapy was given.

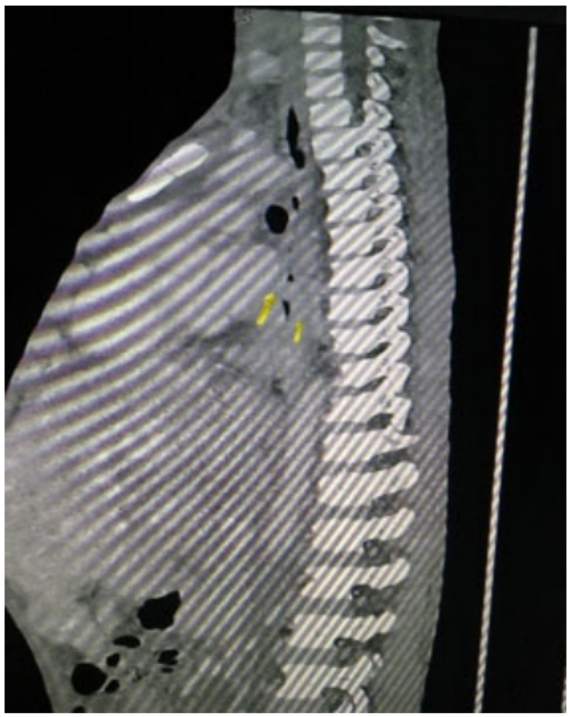

Figure 1: Axial slice of CT scan showed multiple nodules in the pulmonary parenchyma.

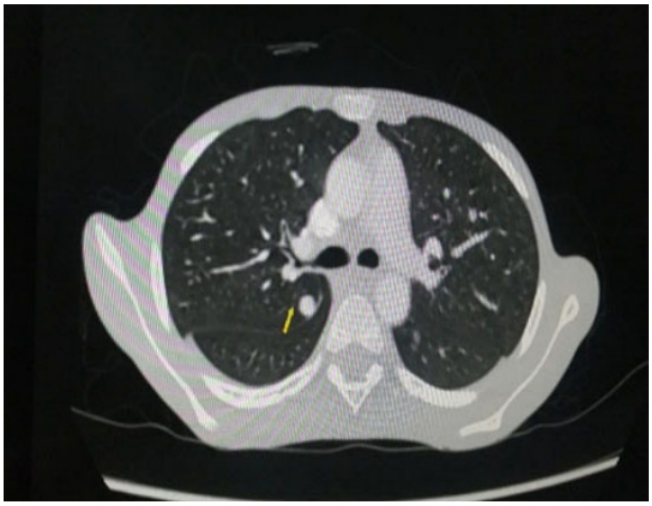

Figure 2: Axial slice of CT scan showed multiple nodules in the lung.

DISCUSSION

Esophageal carcinoma is disease of old age. Among the two types of this cancer, squamous cell carcinomaesopha gus (SCCE) is more prevalent than adeno carcinoma esophagus(ACE). A large study analyzed the data of 40 years and concluded that most of the patients with this disease are male and have age more than 50 years. They also stated that although SCC is more prevalent, incidence of ACE is on the rise compared to SCC. 1Another study stated that esophageal carcinoma is most prevalent in Asian countries and overall incidence is decreasing but cases with ACE are on the rise.2The risk factors for esophageal carcinoma include obesity, gastroesophageal reflux disease, Barrett's esophagus (BE), tobacco use, alcohol and a diet low in vegetables and fruits.3These patients are old age and mostly men. This disease is very rarely found in children.4,5 Only few case reports are found in literature and mostly from south Asia.6,7 The youngest patient presented with the disease was eight years old. Almost all of these children presented with squamous cell carcinoma of esophagus. A study conducted in US analyzing the data from 1950 to 2015 found only 3 cases of esophageal cancer below 1 years and only one child has ACE.8 Among younger patients risk factors identified for ACE are infre quent teeth cleaning, passive tobacco smoke exposure, and pest infestation of grains.9 Our patient was 12 years old boywith ACE, very rarely seen in children. He belonged to sub-urban area and we did not find any risk factor in his history which could be associated to esophageal carcinoma.The clinical presentation of ACE is similar to adults such as weight loss, dysphagia, regurgi tation, hematemesis, chest pain and palpable mass whereas our patient presented with weight loss and dysphagia.10 This cancer frequently metastasizes to lungs, liver and mediastinal lymph nodes and in our patient, it involved lungs, liver and abdominal lymphnodes.11

The management in this situation involves passing jejunostomy or gastrostomy tube to provide nutrition but our patients' family refused so we had to go for total parenteral nutrition. Surgery could not be done due to metastatic disease so he was treated with chemotherapy and radiotherapy. After two courses of chemotherapy, he was able to take semisolid food.

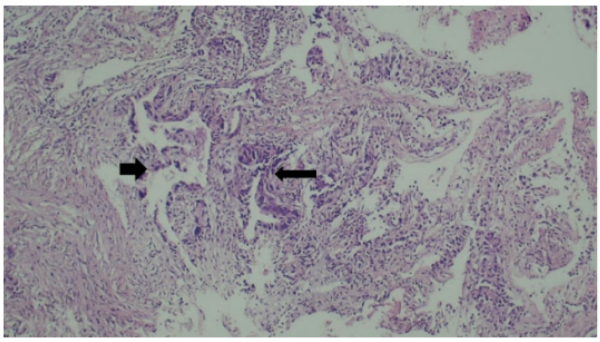

Figure 3: Photomicrograph shows neoplastic cells arranged tubules present in esophageal wall, Moderately Differentiated Adenocarcinoma, pT2 (Arrows) X 20.

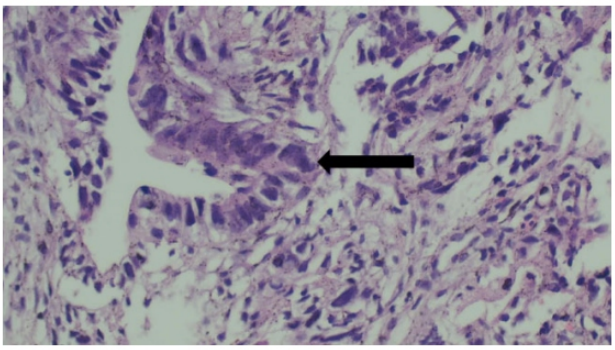

Figure 4: Photomicrograph shows atypical cells with increased N:C ratio lining the glands, Moderately Differentiated Adenocarcinoma, pT2 (Arrows) X40.

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Authors' Contribution:

Dr. Alia Ahmad; Concept of study

Dr. Fariha Sahrish; Planning & Manuscript drafting

Dr. Ayesha Bibi; Study conduction

Dr. Zainab Ehsan; Analysis & interpretation of discussion

Dr. Mahvish Hussain; Facilitation of study and revision for intellectual content

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Rescue Balloon Aortic Valvuloplasty for Malignant Ventricular Arrhythmias and Cardiogenic Shock

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ABSTRACT

Introduction: *Severe Calcific Aortic Stenosis (AS) remains a major cause of morbidity and mortality in aged population. Asymp tomatic with reduced LVEF has high risk of sudden death.Aim: To study the complexity of clinical course of Severe Calcific AS with LV Dysfunction.*

Case Report: *A Seventy-Six-year-old male was admitted with ACS, NSTEMI, LVEF 35% and Severe Calcific AS. With plan of AVR, CAG was done and showed Mild CAD. Post procedure he had sequence of catastrophic clinical events that includes, A systolic Cardiac Arrest (reverted after CPR) and Protracted Pulmonary edema (Connected to Mechanical Ventilation). Later had Malignant Ventricular Arrhythmias, treated with 34 times DC Shocks. He was not suitable for Surgical AVR or TAVI. After high-risk consent, he successfully underwent emergency Aortic Balloon Valvuloplasty (ABV) with significant drop in AV gradients. Post ABV, also had Paroxysmal AF. Arrhythmias were also treated with Beta blocker, Antiarrhythmics, Digoxin and Potassium supplementation. Gradually stabilized, discharged and followed up.*

Discussion: *Aortic stenosis, a disease of elderly age group. Symptomatology varies widely. It has limited management options. In our case, Post CAG critical illness was probably due to "Pre -CAG" LV dysfunction with sub clinical symptoms. ABV used as bail out procedure in high-risk patients.*

Conclusion: *ABV is considered as a viable palliative option, with introduction of smaller profile balloons, rapid pacing and vascular closure devices. ABV can safely used as bridging procedure before Surgical AVR or TAVI in high-risk patients.*

Key Words: Aortic Balloon Valvuloplasty, Surgical Aortic Valve Replacement, Trans Aortic Valvular Implantation, Malignant Ventricular Arrhythmias

INTRODUCTION

Severe Calcific aortic stenosis remains a major cause of mortality and morbidity in the aging population.1 Surgical replacement remains the treatment of choice. Balloon aortic valvuloplasty was introduced as a palliative procedure.1

We report an unusual clinical course of Severe Calcific Aortic Stenosis in a Seventy-Six-year-old male. He had fairly healthy active life till now and daily walks about 6 to 8 kms. He came with history of retrosternal chest pain for one day with one episode of vomiting. His clinical examination was unremarkable except Grade 3/6 Ejection Systolic murmur in Aortic Area and radiates to Carotids. Preliminary investigations include ECG and 2D Echo. ECG shows Sinus Rhythm with ST depression and T Wave inversion in Inferior leads. 2D Echo confirms presence of RWMA, Moderate LV Systolic Dysfunction with LVEF of 35% and Severe Calcific Aortic Stenosis (PPG / MPG = 74/48 mm of Hg)(Fig 1 –Complete 2D Echo stills) and (Fig 2 –Complete Doppler Echo stills). In view of these observations, he was advised AVR after coronary evaluation.Next day he underwent conventional Coronary Angiogram, reported as Mild CAD for Medical Management (Fig 5 A - CAG). Immediately

following Coronary Angiogram, he had Asystolic Cardiac Arrest. Cardiac activity returned after brief period of CPR done as per ACLS protocol, followed by Flash Pulmonary Edema. As he did not respond to anti failure measures (Oxygen, Lasix and Nebulizations), he was then electively intubated for Mechanical Ventilation support. IV Noradrenaline infusion started in view of persistent hypotension. CXR showed Pulmonary edema and ABG readings suggestive of Hypoxia. Mechanical Ventilation was continued under IV Sedation (IV Vecuronium + IV Fantaline + IV Medazolam) (Fig 3-ECGs, CXR and ABG). After 24 hours of Mechanical Ventilation support - while we are planning for extubation, he had Recurrent VT (Ventricular Tachycardia), which continued for next two more days. He had recurrent VT about 34 times (Fig 4A- Recurrent VT) and reverted to Normal Sinus Rhythm after receiving DC shocks(150 Joules) each time. Initially DC shocks were given manually and then by Automatic Electronic Defibrillator (AED) paddles used externally. Also received IVAmiodarone, IV Lignocaine, IV Metoprololand oral Potassium supplementation. To rule out electrolyte and hormonal imbalances - S.Ca+, S. Mg+,S. K+ and thyroid functions were checked, monitored and none found abnormal.

Meanwhile in view of his critical condition, had detailed discussion with patient's relatives. Counselled for Emergency high risk Surgical AVR, TAVI and ABV. CTVS opinion was taken and they ruled out possibility of undergoing Surgical AVR (Aortic Valve Replacement), because of his elderly age and current critical illness. Immediate TAVI (Trans Aortic Valvular Implantation) was also not possible, because of lack of Pre TAVI assessment like CT Aorta. So the only bail out option was ABV (Aortic Balloon Valvuloplasty), which can be done as bridging therapy for future Surgical AVR or TAVI if symptom recurs. After detailed discussion with relatives, agreed for high risk ABV. With help of Cardiac Anesthetist, both CVP and Arterial lines were placed. Strict Intake / Output were monitored with the help of CVP line, Arterial line, NG tube and Foleys Catheterization.

Intervention

On 3rd day of admission and after high-risk consent, underwent successful ABV. Procedural detailsas follows. Procedure was done via Left Femoral approach using 2 sheaths - 12F sheath via Left Femoral Artery for actual procedure and 6F sheath via Left Femoral vein for TPI (Temporary Pacing Implantation). TPI tip was positioned at RV apex. Prior to Balloon inflation, AV gradients by 2D Echo and decreased waist (Internal stenotic AV area) by Aortogram done in Cathlab. Then via 12F sheath and by Seldinger technique over the guide wire, 20 x 40 mm of Mammoth OTW Balloon was placed across the stenotic Aortic Valve. Balloon was inflated with simultaneous rapid RV pacing at 250 beats by TPI. Balloon was inflated using 16 cc of fluid (1:5 dilution of Contrast and Normal Saline). The procedure was repeated until waist at Aortic Valve disappeared. Post Balloon inflation, AV gradients were again noted by 2D Echo in Cathlab. Immediate fall in Aortic gradients were noted from Pre to Post procedure (from 80 mm of Hg to 40 mm of Hg). Complete details of Pre and Post procedural AV gradients of both 2D Echo and Cathlab readings were mentioned in Table 1. (Fig 2-Complete 2D Echo AV gradients) (Fig 5-CAG and Pre & Post ABV Cath Cine Stills). Procedure ended successfully without any further complications.

Post Intervention

IV Noradrenaline infusion, gradually tapered and stopped. All supports were continued. Post Procedure frequency of VT has come downdrastically and gradually. Later he developed Paroxysmal AF(Fig 4 B - Paroxysmal AF). He was again treated with IVAmiodarone, IV Digoxin, IV Meto prololand Oral Potassium supplementation.His arrhythmias were gradually controlled from Recurrent VT to Ill-Sustained VT AF with Fast Ventricular Rate Paroxysmal AF Normal Sinus Rhythm. Arrhythmias drastically improved after oral Potassium supplementationand we frequently monitored Serum

Potassium level too. On 4th day of Post ABV procedure, he was gradually weaned from Me chanical Ventilation and then extubated. Post extubation, no recurrence of arrhythmias was noted. Both bedside mobili zation and increased food intake were done gradually. Also treated with Antiplatelets, Statins, Diuretics, Antibiotics, Ipravent & Budecort Nebulizations, N-Acetyl Cysteine and IV Fluids.In view of Mechanical Ventilation support and rise in RFT, cross consultations weredone with both Pulmonologist and Nephrologist - managed conservatively. At discharge, relatives were again counselled for TAVI or Surgical AVR, if he became symptomatic again.

DISCUSSION

Aortic stenosis, a disease of elderly age group.1It has wide spectrum of clinical presentations with limited management options, includes Medical Therapy, Surgical Replacement and Catheter Interventions.2 (Catherine M. Otto, 2020)Aortic Balloon Valvuloplasty (ABV) was once considered as palliative option, but now trend changing with introduction of smaller profile balloons, rapid pacing and closure devices.2Complete clinical spectrum of Asymptomatic severe AS mentioned in Table 2 (Clinical Spectrum of Asymptomatic Severe AS).2 It summarizes that irrespective of symptoms and LV function, AVR has better survival rate.2 In our case the probable reasons for Cardiac Arrest and followed by Acute LV failure was Vasovagal, Critical engagement of coronary ostia during CAG, Preexisted LV dysfunction, Decreased Myocardial tissue perfusion and elderly age. Recurrent arrhythmias were probably due to Decreased Myocardial tissue perfusion (because of Mild CAD), IV No radrenaline (causes Vasospasm and +ve ionotropic effect) and Stress (due to restlessness). Initially all Antiarrhythmics were failed. One should remember that all Anti arrhythmics are Pro arrhythmics. We used Potassium supplementation as Anti arrhythmics, because of its good negative ionotropic effect. It was given orally and then serial serum level was monitored. K+ supplementation should never be given as direct IV, as heart may stops suddenly in Diastole due to its good negative ionotropic effect. He also developed Acute Kidney Injury (AKI) as suggested by rise in RFT. This is probably due to Elderly age, Mechanical Ventilation, Car diogenic Shock, IV Noradrenaline infusion, Diuretics and Myolysis probably due to repeated DC Shocks. He survived after ABV, a bridging therapy for future Surgical AVR or TAVI advised, if symptoms recur. Currently on regular clinical follow up.

CONCLUSION

Severe AS with LV dysfunction represents a unique en tity that poses clinical dilemmas to physicians worldwide very frequently in clinical practice.3 (V Tsampasian, 2022) In elderly patients with severe but asymptomatic AS, mild symptoms may be difficult to detect, particularly when their mobility is impaired and severe symptom onset is common.4 (Robert Z, 2017) The meta-analysis by Tsampasian V et al. shows that the data from the two recent large randomized controlled trials and previous observational studies demon strate a favorable outcome in the group of patients treated with early intervention rather than conservative manage ment.3 Less symptom or Low AV gradient across Aortic Valve associated LV dysfunction and so one should intervene Aortic Stenosis management as early as possible with care.1

Learning Points

- Unexpected clinical course to be expected inAortic Stenosis with LV dysfunction
- Remember all Anti Arrhythmics are Pro Arrhythmics
- Must monitor Thyroid Function Tests, Serum Electrolytes, Calcium and Magnesium
- With intractable arrhythmias, we can use Potassium supplementation with caution and serum potassium monitoredfrequently.

Limitations- because of his critical illness, unable to undergo:

- Speckle Tracking Test / Cardiac MRI perfusion scan
- Cardiac CT
- Electro Physiologic (EP) study

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Source of Funding: None

Authors contributions:

Chandra Shekara Reddy as First Author prepares, edit and submit complete manuscript, Arun Srinivas as Corresponding Author provides complete proof correction of manuscript, Siddarth Kumar Chawath guides complete journal search and publication guidelines. Nithin Bharadwaj pro vides 2D Echocardiographic Clips and Raju provides CAG and ABV Cath Cine Clips.

Note:

- This is neither Human nor Animal study and hence Ethical clearance letter not provided
- Informed consent taken although this is retrospective clinical analysis
- References prepared as per IJCRR guidelines

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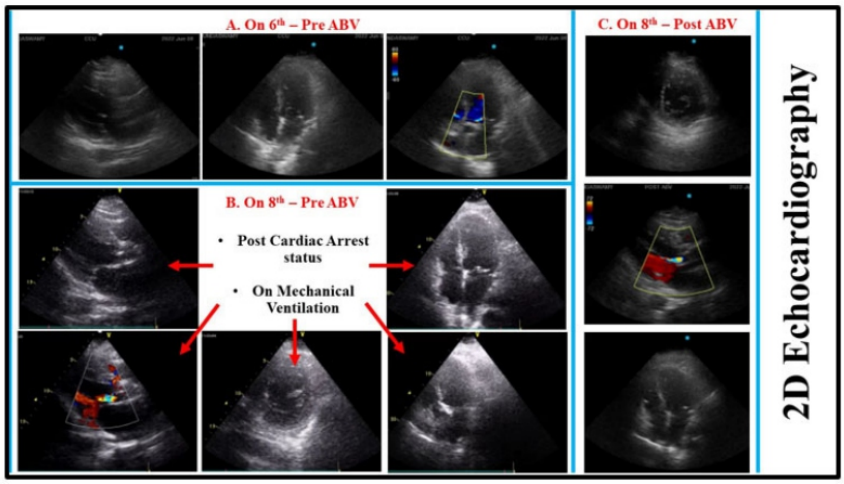


Figure 1: Complete 2D Echocardiographic stills.

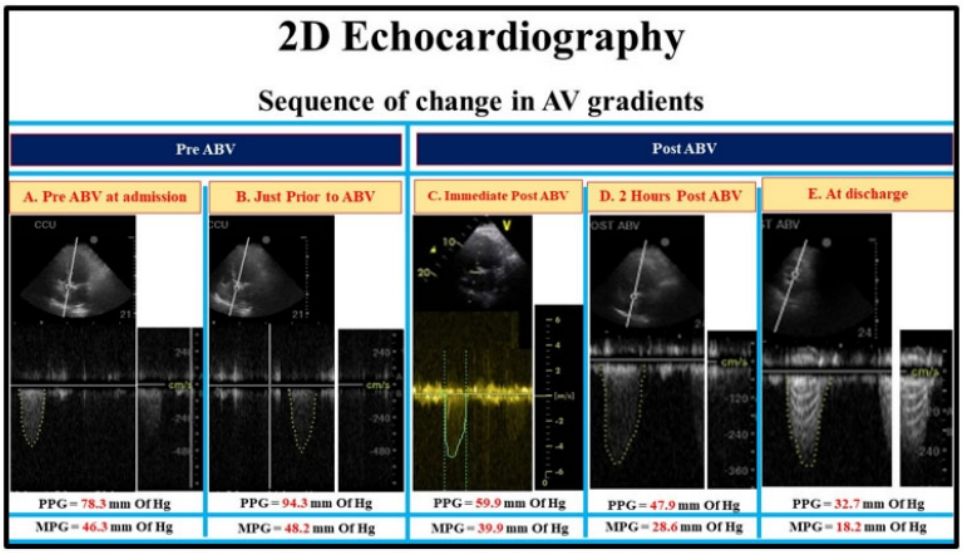


Figure 2: Complete sequence of change in AV gradients.ABV = Aortic Balloon Valvuloplasty, PPG = Peak Gradient, MPG = Mean Gradient.

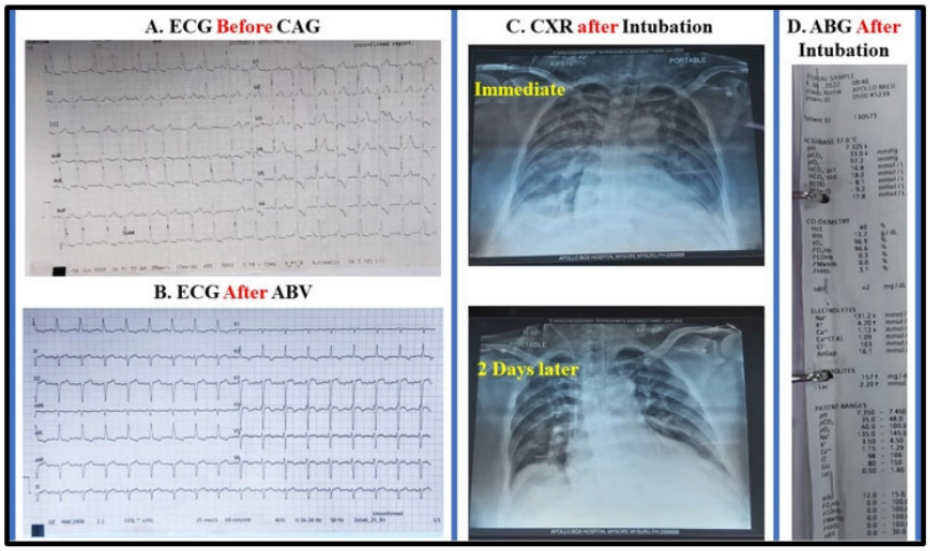


Figure 3: ECGs, CXR and ABG.
ECG = Electrocardiogram, CXR = Chest X Ray, ABG = Arterial Blood Gas Analysis, CAG = Coronary Angiogram, ABV = Aortic Balloon Vavuloplasty.

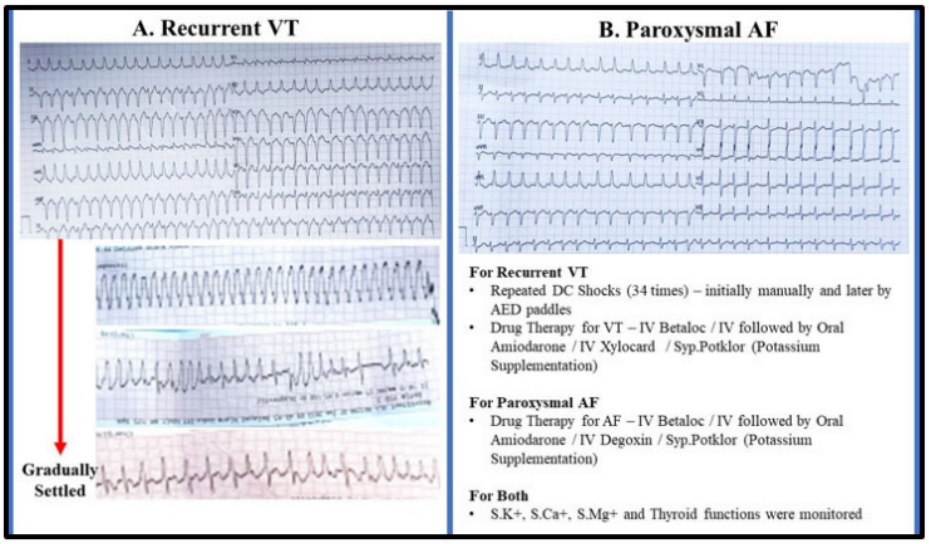
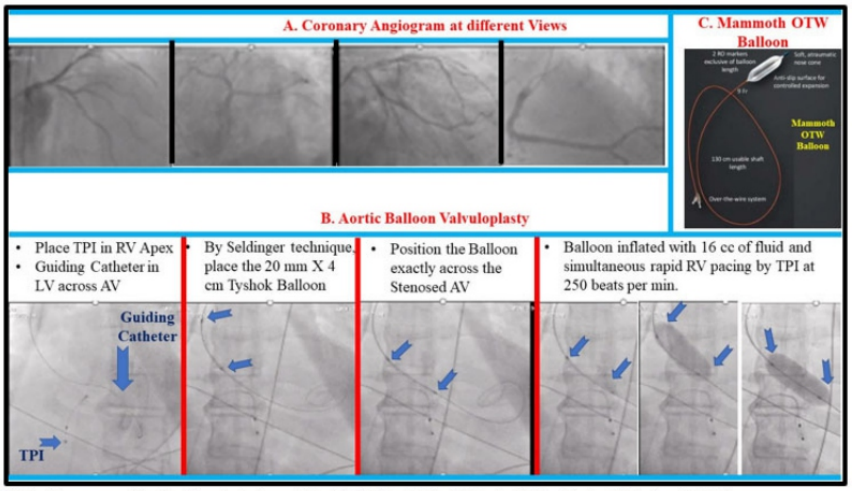


Figure 4: Complete Arrhythmias.



TPI = Temporary Pacing Implantation: RV =Right Ventricle: LV =Left Ventricle: AV =Aortic Valve

Figure 5: Coronary Angiogram and Aortic Balloon Valvuloplasty.
TPI = Temporary Pacing Implantation, RV =Right Ventricle, LV = Left Ventricle, AV = Aortic Valve

Table 1: Complete AV Gradients

Cath gradients		
Pre ABV	80 mm of Hg	
Post ABV	40 mm of Hg	
2D Echo gradients (mm of Hg)		
	PPG	**MPG**
Pre ABV		
A. At admission	78	46
B. Prior to ABV	94	48
Post ABV		
C. Immediately Post ABV	60	40
D. 2 Hours after ABV	48	29
E. At Discharge	33	18

PPG = Peak Gradient: MPG = Mean Gradient: ABV = Aortic Balloon Valvuloplasty

Table 2: Clinical Spectrum of Asymptomatic Aortic Stenosis2

Definition / Type	**Valve Anatomy**	**Valve Hemodynamics**	**Hemodynamic Consequences**	**Symptoms**
Asymptomatic Severe Aortic Stenosis	Severe leaflet calcification/fibrosis or congenital stenosis with severely reduced leaflet opening	Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg AVA typically is ≤1.0 cm² (or AVAi 0.6 cm²/m²) but not required to define severe AS Very severe AS is an aortic V_{max} ≥5 m/s or mean P ≥60 mm Hg	LV diastolic dysfunction Mild LV hypertrophy Normal LVEF	None Exercise testing is reasonable to confirm symptom status
Asymptomatic Severe Aortic Stenosis with LV systolic dysfunction	Severe leaflet calcification/fibrosis or congenital stenosis with severely reduced leaflet opening	Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg AVA typically ≤1.0 cm² (or AVAi 0.6 cm²/m²) but not required to define severe AS	LVEF <50%	None

V_{max} = Maximum Velocity m/s = meters per second, ΔP = Pressure Gradient, AVA = Aortic Valve Area, cm² = Square Centimeters, AVAi = Aortic Valve Area Index

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In Vitro Detection of Virulence Factors of Candida albicans & non-albicans Candida species Isolated from the Samples in ICU Patients

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ABSTRACT

Aim: *To isolate and identify Candida albicans and non-albicans Candida from various clinical specimen of Intensive care Unit and to investigate some virulence factors and perform their Anti- fungal susceptibility.*

Materials and Methods: *Overall 32 isolates (12 Candida albicans and 20 non- albicans Candida spp.) were included in this study. Virulence factors were studied. In isolates, egg yolk agar was used for determining phospholipase activity, while sheep and human plasma used to determine coagulase activity, Sabouraud dextrose agar with sheep blood for hemolysin activity. Biofilm formation was detected by the tube adherence method.*

Results: *In both Candida spp., it was found that hemolytic activity were higher next to phospholipases activity. It was also found that Coagulase activity were detected in Candida species found to be higher with sheep plasma compared to human plasma. Biofilm production was found to be less and mostly were from blood culture isolates.*

Conclusion: *Knowledge of these virulence factors is an important tool to understand pathogenesis of candidiasis and in addition will help to explore new antifungal drug targets for improved therapeutic regimens.*

Key Words: Candida spp., Virulence factors, Non-albicans Candida spp.

INTRODUCTION

Infections caused by opportunistic pathogens, such as yeasts, have become important reasons of morbidity and mortality because of alterations in the immune system and invasive hospital procedures 1 . AIDS, organ transplantation, chemo therapy, invasive procedures and radiotherapy increased the prevalence of immunocompromised individuals and also diabetes mellitus, and the over use of extended spectrum antibiotics made an increment in these infections 2,3.

Infections due to yeast like fungi have increased in intensive care units too4. In the last two decades, nosocomial fungal infections increased all around the world. Yeast like fungi are the fourth most common agent in the blood stream infections. C. albicans, C. tropicalis and C. parapsilosis are the three most common yeast like fungi causing blood stream infection5.

Unnecessary use of broad spectrum antibiotics, catheterization, and mucosal colonization in patients with risk factors are important predisposing factors6. Initiation of azole group antifungal drugs for prophylaxis and treatment led to increased isolation of resistant non-albicans Candida strains7.

Candida spp. have some virulence factors that facilitate proliferation, may result in adhesion to the epithelium and invasion of the host tissue8 .

It seems that extracellular hydrolytic enzymes play an important role in candidal overgrowth9. The extracellular hydrolytic enzymes including secreted aspar tyl proteinase and phospholipases degrade immunoglobulins and proteins of the extracellular matrix; they also inhibit the phagocytosis of polymorphonuclear neutrophils and induce inflammatory reactions10. Furthermore, the survival and abil ity of Candida albicans to establish infections within hu mans are mainly related to its ability to procure elemental iron through hemolysin production11.

Among Candida spp., expression of virulence factors may vary depending on the infecting species, geographical ori gin, type of infection, the site and stage of infection, and host reaction. Knowledge of these virulence factors is an important tool to understand pathogenesis of candidiasis and in addition will help explore new antifungal drug targets for improved therapeutic regimens.

OBJECTIVES

With this background, we did this study to isolate and iden tify Candida albicans and non- albicans Candida from vari ous clinical specimen of Intensive care Unit and to study the virulence factors and perform the antifungal susceptibility profile of isolated Candida albicans and non-albicans Candida.

MATERIAL AND METHOD

A cross-sectional study was carried out in the Department of Microbiology, MGIMS, Sevagram, during the period of April-August 2018 after approval from the Institutional Ethi cal Committee. Study was carried out in the Microbiology department, MGIMS, Sewagram. All the samples requested for aerobic culture and sensitivity from Intensive Care Units were processed in our laboratory and those found to be culture positive for Candida albicans and non-albicans Candida spp. were included in the study.

Candida albicans and non-albicans Candida spp. isolated from various clinical samples like blood, sputum, urine, wound swabs, pus, CSF, oral swabs, etc. The organisms were identified by germ tube test, morphology on cornmeal agar (HiMedia), chromagar media (HiMedia) and growth at 45°C, which were done as per standard microbiological protocols12. VITEK 2 YST identification card (bioMerieux, France) was used for yeast identification as per manufacturer's instruc tions and the antifungal susceptibility testing of Candida spp. was performed using VITEK2 AST- YS08 cards. The virulence factors studied were exo enzymatic activities like phospholipase , coagulase, hemoly sin production & biofilm formation.

1. Phospholipase Production: The phospholipase activity of Candida spp was detected by the method of Samaranayake et al(13). Approximately 5 L of stand ard inoculum of test strain containing 108 Candida cells/mL was aseptically inoculated onto egg yolk agar. The plates were dried at room temperature and then incubated at 37◦ C for 48 h. The plates were ex amined for the presence of precipitation zone around the colony. The presence of precipitation zone indi cated expression of phospholipase enzyme. C. albicans ATCC 10231 was used as positive control. The phospholipase index (Pz) is defined as the ratio of the diameter of the colony to the total diameter of the colony plus the precipitation zone. A Pz value of 1 denoted no phospholipase activity; Pz < 1 indicated phospholipase production by the isolate. The lower the Pz value, the higher the phospholipase activity. To minimize experimental error, the assay was conducted in duplicate conditions on three separate occasions for each isolate.

2. Coagulase Activity: Coagulase production by Can dida spp. was detected bythe method of Yigit et al.(14). Approximately 0.1 mL of an overnight culture of Candida spp. was aseptically inoculated into a tube containing 500 L of sheep plasma and human plasma separately. The tubes were incubated at 35◦ C

and observed for clot formation after 2, 4, 6, and 24 h. The presence of a clot that could not be resuspended by gentle shaking indicated positive coagulase test.
Staphylococcus aureus ATCC 25923 and S. epider midis ATCC 14990 were used as positive and negative controls, respectively.

3. Hemolysin Production: Haemolytic activity of Can dida spp was screened on sheep blood Sabouraud dex trose agar plate by the method described by Manns et al.11. Approximately 10 L of standard inoculum (108Candida cells/mL) were aseptically inoculated onto the medium. The culture plates were incubated at 37◦C for 48 h. C. albicans ATCC 90028 was used as the control strain. Streptococcus pyogenes and Strepto coccus pneumoniae were used as positive controls for beta andalpha haemolysis, respectively. The presence of a zone of haemolysis around the colony indicated haemolysin production. Haemolytic activity (Hz) was calculated in terms of the ratio of diameter of the colony to that of the translucent zone of haemolysis (in mm)

4. Biofilm Formation: The ability of Candida spp iso lates to form biofilms was assessed by the tube method described by Yigit et al.15. Colonies of Candida spp from Sabouraud dextrose agar was inoculated in saline and incubated overnight at 37◦ C. 0.5 mL of this saline suspension was added into screw capped conical poly styrene tubes containing 5 mL of Sabouraud dextrose broth supplemented with glucose (final concentration of 8%). The tubes were incubated at 35◦ C for 48 h without agitation. After incubation the broth from the tubes were aspirated gently using Pasteur pipette. The tubes were washed twice with distilled water and stained with 2% safranin. The stain was decanted after 10 min. The tubes were rinsed with distilled water to remove excess stain. Presence of visible adherent film on the wall and at the bottom of the tube indicated biofilm formation. Ring formation at the liquid interface was not considered as an indication of biofilm produc tion. Staphylococcus epidermidis ATCC 35984 and C. albicans ATCC 10231 were used as positive and negative controls, respectively

RESULTS

During the study period, a total of 32 non repeat Candida spe cies were isolated from similar number of samples; which included 16 (50%) blood, 7 (21.9%) urine, 5 (10.6%) sputum, 2 (6.2%) pus and 1 (3.1%) each of oral swab and CSF. All the Candida isolates were processed for species identification, detection of virulence factors and antifungal susceptibility testing. These Candida so isolated were 16 (50%) from NICU, 13 (40.6%) from MICU, 2 (6.2%) from SICU, and 1(3.1%) from PICU. (Table-1).
Out of 32 candida isolates, 12(37.5%) were C. albicans, 7(21.9%) were C. utilis, 4 (12.5%) C. krusei, 3(9.4%) C. tropicalis, 2(6.2%) were C. pelliculosa and 1(3.1%) was C. dubliniensis. Rest 3(9.4%) remained unidentified and grouped under Candida species (Table-2). In the present study, amongst 32 Candida isolates, phospholipase activity was seenin 16(50%) and Hemolysin activity was seen in 32(100%). (Table-3 & Figure1-4). All the 32 isolates are susceptible to caspofungin and voriconazole. 91.7% of C. albicans were susceptible to fluconazole,flucytosine and amphotericine B. Furtheramong C. utilis, 85.7% were susceptible to flucytosine. Rest 11 isolates of Candida species and 2 isolates of C. pelliculosa were susceptible to all the antifungals tested.(Table-4)

Table 1: Distribution of Candida isolated from the ICUs, collected from different samples

Samples	NICU	MICU	SICU	PICU	Total
Blood	16	0	0	0	16
Sputum	0	5	0	0	5
Urine	0	6	0	1	7
Pus & Wound swab	0	0	2	0	2
Others(CSF, Oralswab)	0	2	0	0	2
Total	16	13	2	1	32

Table 2: Distribution of isolated Candida species (n=32)

Isolates		Number	%
Candida albicans		12	37.5%
Non-albicans Candida species	*Candida utilis*	7	21.9%
	Candida krusei	4	12.5%
	Candida tropicalis	3	9.4%
	Candida dubliniensis	1	3.1%
	Candida pelliculosa	2	6.2%
	Not identified	3	9.4%

Table 3: Comparison of virulence factor producers in isolates from different samples

Samples	Phospholipase activity	Coagulase test	Hemolysin activity	Biofilm formation
Blood (n=16)	8	4	16	6
Sputum(n=5)	2	0	5	0
Urine(n=7)	6	3	7	2
Pus & Wound swab (n=2)	0	0	2	0
Others(CSF,Oral swab) (n=2)	0	0	2	0
Total	16	7	32	8

Table 4: Antifungal sensitivity on Candida isolates

Species	Fluconazole	Voriconazole	Caspofungin	Amphotericin B	Flucytosin
Candida albicans	91.7%	100%	100%	91.7%	91.7%
Non- albicans Candida	100%	100%	100%	100%	85.7%

DISCUSSION

Candida is an asexual, dimorphic fungi present as normal flora in humans. A small number of candida species are pathogenic for humans. Its infections may be primary or secondary. These organisms are capable of causing superficial and deep seated infections such as cutaneous, mucocutaneous, subcutaneous and systemic candidiasis. They are commensals and act as pathogens when host defenses are interrupted.

Risk factors include prolonged stay in ICU's, diabetes mel- litus, prolonged usage of antibiotics, immunosuppression, defects in CMI etc. In the present study, the phospholipase, hemolysin, Coagulase and Biofilm production of Candida species in the Intensive Care Units of a tertiary care hospital were studied. In our study, a total of 32 Candida were isolated out of which 12(37.5%) were C.albicans and 20(62.5%) were non- albicans Candida. These results are in agreement with those of Ruchika et al whose study also showed the same results.16. In the recent studies, observation of a shift towards non-albicans Candida species from Candida albicans is seen17. Some studies have reported increasing trend ofincidences of infections caused by non-albicans Candida, thus gradually changing the cause of

candidemia to be non-albicans Candida and not Candida albicans in some regions18. Contribution of factors like increased use of antifungal drugs and broad spectrum antibiotics, long term use of catheters and increase in the number of immune-compromised patients has led to the emergence of non-albicans Candida species in increasing numbers19,20,21. Non-albicans Candida species cannot be overlooked as mere contaminants or non-pathogenic commensals as mostof them show reduced susceptibility to commonly used antifungal drugs (22).

In Candida, the transition from commensalism to pathogenicity, is attributed to the selective expression of different virulence factors that act synergistically under favourable conditions. The type, stage and infection site in addition to the immune response, determine which virulence factors are expressed. Among these virulence factors, phospholytic, coagulase, hemolytic activity and biofilm formation seems to play a major role in the pathogenicity of these microorganisms. Not only the absence or presence of a virulence factor but when present the amount of its activity is also an important factor contributing to pathogenicity. Research on prevalent Candida species along with their virulence factors in a givenset up would be an important tool to prove the relation between the infective species of Candida and infection.

Phospholipase activity in our study was demonstrated in 16 out of 32(50%) Candida isolates. These results correlate closely with those of Faris et al.23 who reported phospholipase activity in 44% of Candida isolates. Our study also agrees with Deepthi et al.24 who reported 53.4% of Candida isolates showing phospholipase activity. Candida albicans is a stronger hemolysin producer compared to non albicans Candida species. In our study 32 out of 32 isolates were observed to be hemolysinproducers, i.e. 100% of the Candida isolates were positive for hemolysin production. 100% hemolysin producers have also been reported in other studies25.Coagulase tests are routinely used to detect the presence of S. aureus. The coagulasetube test is the most frequently used method for Staphylococci because of greater accuracy and its ability to detect both bound and free coagulase. In the present study, sheep and human plasma showed different sensitivities when used to test the coagulase activities of Candida isolates. Sheep plasma showed more sensitivity with 21.87 % of all Candida isolates being positive for Coagulase activity whereas human plasma expressed no activity for any Candida spp. tested. This study agrees well with Yigit et al.14which showed no sensitivity to human plasma and in sheep plasma 20.8% Candida showed Coagulase activity. Biofilm formation was carried out by tube adherence.

In our study, 8 out of 32(25%) Candida isolates showed biofilm formation in which 75% were from blood samples. In the study by Tortorano et al.26 showed 39% of Candida isolates showing biofilm formation. Also Faris et al.23 reported 40% of Candida isolates positive for biofilm production. In this study we also conducted antifungal susceptibility tests. The study showed that all Candida isolates are susceptible to Voriconazole and Caspofungin. Susceptibility of C. albicans to Amphotericin B was 91.7% and to Fluconazole was 91.7%. Shivanand(27), Araj28 got similar results for voriconazole but differed in the results where they got 100%susceptibilty to AMP-B. Also, Amina29 got a susceptibility of 78.3% only for AMP-B and against Voriconazole too Amina found only 30.4% susceptibility, alongwith only 30.4% susceptibility to fluconazole whichis very less than other studies. However, our study agrees with the study by Deepthi et al.24 which showed 100% susceptibility to voriconazole and 92.3% to fluconazole.

CONCLUSION

Infections due to yeast like fungi have increased in Intensive Care Units. In this study, most of the Candida were isolated from neonatal intensive care units(50%) and from blood samples(50%). This may be due to invasive procedures, prolonged hospitalization, chronic antibiotic uses and low birth weight. It is necessary to understand the pathogenic mechanism of Candida spp. for implementation of

new antifungal therapy. Hence our study on virulence factors of Candida spp. highlighted the way for better patient management and prognosis of patients.

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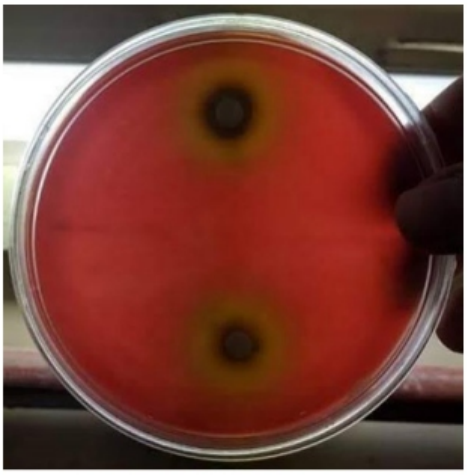
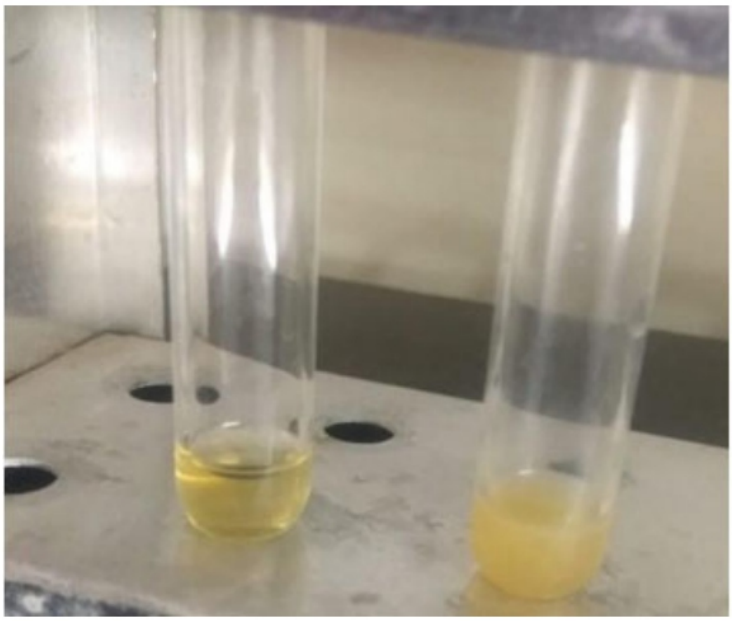


Figure 1: Hemolysin activity on Sabouraud s Dextrose Agar with 3% blood.

Figure 2: Phospholipase activity on Sabouraud's Dextrose Agar with egg yolk.



Fiure 3: Coagulase activity by Tube Method

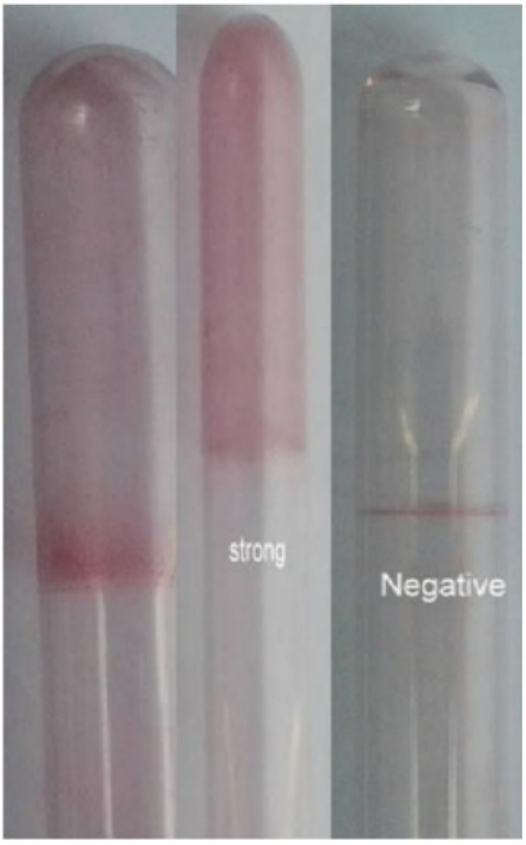


Figure 4: Biofilm production by Tube method.

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Effectiveness of Electromyographic (EMG) Biofeedback in Osteoarthritis of the Knee joint: A Brief Narrative Review

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ABSTRACT

Introduction: *After knee osteoarthritis (OA), the patient will have a varying degree of quadriceps weakness, affecting the joint range of motion and physical function. Therefore, effective physical therapy is a common therapy for clinicians. Recently, there has been increased interest in the use of biofeedback approaches in rehabilitation interventions, and it is progressively being regarded as a helpful strategy to reduce pain and boost the effectiveness of major therapies.*

Methodology: *Studies on the topic of the effect of using EMG biofeedback (EMGBF) in osteoarthritis of the knee joint were reviewed so the findings of those articles were used to explore the additive effect of EMG biofeedback training that would affect quadriceps pain and Vastus medialis Oblique (VMO) thickness in patients with osteoarthritis of the knee joint.*

Results: *In terms of the results of this approach in patients with knee OA, some studies have discovered that it has a favorable impact on pain alleviation, function, and muscular strength in patients treated with exercise with Electromyographic (EMG) biofeedback, while others have found that it has no extra effects on patients.*

Conclusion: *Employing EMGBF has certain benefits, and the decision to utilize it or not is based on its ease of access, costeffectiveness, and physician-patient desire.*

Key Words: Knee Osteoarthritis, Biofeedback, EMG biofeedback, Quadriceps strength, VMO strength, Knee extensor

INTRODUCTION

The western population is susceptible to osteoarthritis (OA), a degenerative joint condition. The knee is the peripheral joint that is most frequently damaged, leading to a gradual loss of function, pain, and stiffness.1 Roughly one in ten people over the age of 50 are anticipated to be affected.2 Pain and muscle wasting are the two most prevalent signs and symptoms of knee osteoarthritis.3 Weakness in the quadri ceps muscles is assumed to be brought on by disuse atrophy, which is brought on by joint pain.4 One of the earliest clinical findings in individuals with knee OA, occurring before symptoms and impairment are observed, is reduced quadriceps strength, and it may be crucial to the course of the disease.5,6 Research shows that thigh muscle strength may offer protection against joint injury and the progression of pre-existing OA. Quadriceps weakness has been connected to the development of pre-existing knee OA. 7-11

Feedback is described as sensory information resulting from numerous movements.12 This input might be sensory (intrinsic) or enhanced (extrinsic).13,14 Extrinsic feedback is biological information delivered in a treatment situation when the patient is given supplemental information beyond what is normally accessible to them.13-17 Biofeedback ena bles the patient to consciously regulate these physiological processes, which are considered automatic reactions of the autonomic nervous system.18 The technique of using equip ment to reveal to humans some of their internal physiologic events, both normal and abnormal, in the form of visual and audible signals in order to teach them how to control these otherwise involuntary or unfelt events by manipulating the displayed signals is defined as EMG-

biofeedback.19 Exercise regimens with EMG biofeedback are recommended because they boost patient motivation and compliance.20 Electromyo graphic biofeedback (EMGBFB) is a method that allows a person to detect and magnify electrical activity in the mus cles. The patient is provided visual and audio feedback on the increased muscular tension.21 EMG biofeedback is often used in situations of muscular weakness to offer muscle re education and to recover muscle strength.22 The use of EMG biofeedback in rehabilitation regimens can improve patient adherence to exercise. 23 The EMGBF has been postulated to enhance the muscular strength and neuromuscular control of the quadriceps muscle group; 24,25,26 as a result, clinicians may find it important to understand the real effect EMGBF has on quadriceps muscle strength in order to correctly treat quadriceps weakness. EMG-biofeedback has been shown to be effective in the rehabilitation of patients with vastus medi alis atrophy caused by knee osteoarthritis. There is minimal evidence that it works in knee OA. The goal of this research is to investigate the additive effect of EMG biofeedback in the rehabilitation of knee osteoarthritis.

METHODOLOGY

MATERIAL AND METHODOLOGY

DATABASE:

A computer-based literature search was done using the PUB MED, PUBMED CENTRAL, and GOOGLE SCHOLAR

INCLUSION CRITERIA:

Relevant articles with a full text published in English between the years 2010 to 2021 were screened and included.

• To be included, a study needed to meet the following criteria:
(a) Design: Only randomized controlled trials were included.
(b) Interventions: The EMGBF and a comparative exer cise-only and/or placebo intervention used to increase quadriceps strength were included.
(c) Study population: Participants having OA of knee joint
(d) Outcome measure: The study needed to investigate isometric quadriceps strength in response to the previously stated interventions.

EXCLUSION CRITERIA:

• Editorials, Commentaries, Discussion papers, Confer ence abstracts, Reviews, and Duplicates were excluded.
Figure 1 shows the search strategy for this review. The char acteristic of the reviewed article is summarized in table 1.
All studies have examined the association between real-time EMGBF & OA of the knee. Out of 4 studies, 1 study demon strated that EMGBF may be a useful rehabilitative tool for patients with OA knee. One study demonstrated that EMGBF was not better than exercise without biofeedback in any vari ables. And other three studies demonstrated improvement in OA knee treated with real EMGBF accompanied by isomet ric exercises and significant improvement in knee pain, joint stiffness, and function of patients with knee OA treated with isometric exercise accompanied by EMGBF. The effect of this method did not significantly exceed those of exercise without biofeedback, and also the patient with exercise and motivation increased when EMGBF was accompanied by exercises, and it is very

important to keep them motivated to their exercise program

SUMMARY OF REVIEWED ARTICLES

Seyed Ahmad Raeissadat et al. (2018)27

The goal of this research was to see how integrating elec tromyographic biofeedback (EMGBF) to isometric training altered pain, function, thickness, and maximal electrical ac tivity in the vastus medialis oblique (VMO) muscle during isometric contraction in patients with knee osteoarthritis (OA). The case group included 23 patients who engaged in EMGBF-associated exercise, whereas the control group included just 23 patients who engaged in isometric exercise. Variables in each group and between the two groups were compared before and after the exercise program. Isometric exercises with EMGBF and the same activities without bio feedback both resulted in substantial improvements in pain and function in individuals with knee OA after two months. Except for the VAS score, real EMGBF was not better than exercise without biofeedback in any of the assessed variables.

Yun lak choi et al. (2015)28

The goal of this research was to see whether EMGBF and USBF training will improve quadriceps MVIC, pain, and VMO thickness in individuals with knee OA. The EMGBF and USBF training groups got the relevant physical train ing exercise program targeting the Vastus medialis oblique, whilst the control group received standard physical therapy such as ultrasound, hot pack and transcutaneous electrical nerve stimulation. The MVIC in the EMGBF and USBF training groups was considerably higher than in the control group, whereas the VAS score (for measuring pain) in the EMGBF and USBF training groups was significantly lower than in the control group. Only the EMGBF training group has substantially increased VMO thickness compared to the control group. While EMGBF and USBF training dramati cally enhanced the MVIC of the VMO and decreased pain on the afflicted side, conventional physical therapy had no effect on the MVIC of the quadriceps. Surprisingly, only the EMGBF training group exhibited a substantial increase in VMO thickness, whilst the other two groups showed no change.

Shahnawaz Anwer, S. et al. (2011)29

The goal of this randomized controlled experiment was to assess the efficacy of electromyographic biofeedback as an adjunct treatment to isometric exercise on quadriceps strengthening in patients with knee osteoarthritis. Thirty-three individuals with knee osteoarthritis, ten men and 23 women, took part in the research. For 5 weeks, the biofeedback group got an electromyographic biofeedback-guided isometric exercise program, while the control group received merely an exercise program. In between-group comparisons, the maximal isometric quadriceps strength in the biofeedback group was substantially larger than that of the control group at the end of the fifth week (p 0.004). When compared to the exercise pro gram alone, the addition of electromyographic biofeedback to a 5-week isometric training program showed to enhance quadriceps muscle strength in adults with knee osteoarthritis.

Ozlen O. et al. (2010) 30

The authors conducted a study on “The efficiency of EMG biofeedback in knee OA” In knee OA, the authors com pared an EMG-biofeedback-assisted strengthening exer cise program to a regular strengthening exercise program. As a consequence, both groups saw statistically significant improvements in pain ratings and WOMAC pain, disabil ity, and functional status scores. In addition, both groups showed considerable improvement in isometric and isokinetic muscular strength following therapy. However, no statistically significant difference between groups was seen in these evaluations.

In terms of quality of life aspects, the strengthening exercise group improved physical mobility and pain. However, there was an improvement in the measures of physical activity, pain, sleep, and energy in the EMG biofeedback strengthening aided exercise group. Finally, it should be highlighted that the incorporation of biofeedback during strengthening activities increased the quality of life even more. However, no statistically significant difference was found in terms of the other assessed parameters. These findings might be attributed to the short sample size.

CONCLUSION

In conclusion, our study found no significant superiority of an EMGBF-assisted strengthening exercise regime over a strengthening exercise program without EMG biofeedback. When exercise treatment is carried out correctly and on a regular basis, it is an effective therapeutic strategy that improves pain, function, and muscular strength.

This research emphasizes the usefulness of quadriceps strengthening activities in reducing pain and enhancing function in individuals with knee OA. When EMGBF was followed with exercises, patients' compliance and motivation rose, and as we know in older patients, it is critical to keep them motivated to stick to their exercise regimen. One of the primary goals of rehabilitation in patients with knee OA is pain reduction, as as previously stated, patients experience less pain when EMGBF is used. To summarise, employing EMGBF has certain benefits, and the decision to utilize it or not is based on its ease of access, cost-effectiveness, and physician-patient desire.

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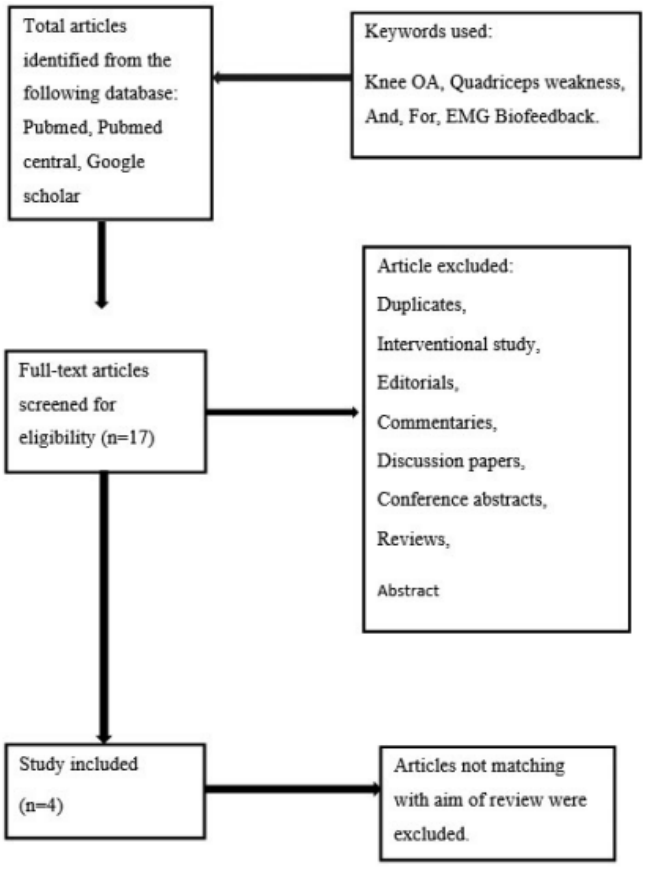

Figure 1: Searching strategy: A total of 45 articles were identified from the computer-based literature search. After excluding the duplicates, interventional studies, editorials, commentaries, discussion papers, conference abstracts, reviews, and abstracts 17 full-text articles were screened. Out of that, only 4 articles were included as matched with the aim.

Table 1: Summary of reviewed articles

No.	Author (Year)	Research Design	Aim	Key Finding
1.	Seyed Ahmad Raeissadat et al. (2018)	Randomized Controlled trial	The purpose of this study was to see how introducing electromyographic biofeedback (EMGBF) into isometric exercise affected pain, function, thickness, and maximal electrical activity in the vastus medialis oblique (VMO) muscle in patients suffering from knee osteoarthritis (OA).	Despite considerable improvements in knee pain, joint stiffness, and function in individuals with knee OA treated with isometric exercises accompanied with EMGBF, the results of this technique did not outperform those of exercise alone.
2.	Yun lak choi et al. (2015)	Randomized Controlled trial	The purpose of this study was to look at how isometric exercises with electromyographic biofeedback (EMGBF) & ultrasound biofeedback (USBF) affected maximum voluntary isometric contraction (MVIC), pain as evaluated by the Visual Analogue Scale (VAS), as well as vastus medialis oblique (VMO) thickness in knee osteoarthritis patients (OA).	USBF training is useful in treating patients with knee OA and is similar to EMGBF training in terms of efficacy. Only the EMGBF training group had substantially greater VMO thickness than before training.
3.	Shahnawaz Anwer, S. et al. (2011)	Randomized Controlled trial	To determine the efficacy of EMG biofeedback as an addition to quadriceps muscle strength training in individuals with knee OA.	The study's findings revealed that combining EMG biofeedback with isometric training resulted in better improvements in isometric quadriceps strength.
4.	Ozlen O. et al. (2010)	Randomized Controlled trial	To investigate the additive effect of biofeedback in OA of knee rehabilitation.	There was no significant difference between the EMG biofeedback-assisted strengthening exercise program and the strengthening exercise program without EMG biofeedback. When exercise treatment is conducted correctly and on a regular basis, it is an effective therapeutic strategy that improves pain, function, and muscular strength.

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Radiographical and Anatomical Assessment of Mandibular Mental Foramen Variations for a Sample of Yemeni Patients Undergoing Dental Implant Placement

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ABSTRACT

Aim: *To assess the prevalence, the diameter and location of mental foramen MF, and Accessory mental foramen AMF, by conebeam computed tomography (CBCT) for a Sample of Yemeni Patients.*

Methodology: *The study was an analytical retrospective cross-sectional study conducted on 420 CBCT images of mandibles referred from general practitioners, surgery departments and surgeons for implant demands. The data collection took from April 2018 to July 2018. The sample size was divided according to gender, age, side, and dental condition. The images were analyzed and the measurements were done using the tools given in the software (Ez3D plus with Ez3D-I software).*

Results: *MF was found in all patients (51.4% males and 48.6% females). The means of the MF diameter, MF-H, MF-V, MF-M1, MF-M2, AMF-HMD and AMF-VMD were 2.60 mm, 3.74 mm, 3.08 mm, 7.61 mm, 10.99 mm, 1.88 mm and 1.63 mm, respectively. Most of the cases were located under the apex of the 2nd premolar was found in only 4 (1%) of all cases.*

Conclusion: *The most prevalent location of the MF was under the long axis of the 2nd premolar. The round shape of the MF was more prevalent than the oval shape.*

Key Words: Radiographical Assessment, MF, AL, IC, CBCT, Yemeni Patients

INTRODUCTION

Mental foramen (MF) is a single foramen, found in the buccal bone plate, but any multiple or any duplication in number of mental foramen in the same side is considered accessory mental foramen (AMF).1 So, AMF defined as “a nutrient foramen formed in a prenatal stage”. Moreover, the sub mental, lower lip, buccal arteries and direct branches of the facial artery distribute from the buccal foramen into the mandibular cancellous bone.2 Precise knowledge on the variation in the position, number, size, and shape of the MF and the presence of the AMF would be great to surgeons because it leads to disruption into the Inferior Alveolar Nerve block.3

Currently, high resolution CBCT is the most promising and accurate technology available for quantitatively determining the position and size of MF and the presence of AMF.

It represents high resolution cross-sectional images,5 and makes a multiple continuous sectional view in different di mensions (Sagittal, Axial, and Transverse) to give the best view for each soft and hard tissue.6

Good pre-surgical knowledge of the exacted location and size of the MF is crucial for preventing any surgical com plications in the inter-foraminal area during the local men tal nerve block, periapical surgery, orthographic surgery or placement of endoosseous implant.7 Furthermore, because no

pervious study – up to the researchers knowledge – has been conducted to study the prevalence, size, and location of the MF and AMF on the Yemeni population, the outcomes of this study can be used as a primary guideline for surgeons and dentists who are interested to do any surgical procedures of dental implant installations in the anterior mandibular regions for Yemeni patients.

MATERIALS AND METHODS

Study sample:

An analytical retrospective cross-sectional study. It included 1000 mandibular arch CBCT images of patients who were referred from maxillofacial surgery departments and surgeons or periodontologist for implant demands to a private radiology center at Sana'a city during the period from January 2016 to December 2018. The data were collected using a data collection sheet.

By using the G*Power 3, the study sample size calculated was 400 CBCT images of mandibles that were selected randomly. The final sample size became 210 CBCT images. Each mandible was considered two cases according to a study conducted by.5 Consequently, the cases became 420. The sample size was divided according to gender (male – female), age (>40 year-old – ≤40 year-old) , side (right – left), and dental condition (edentulous – non-edentulous).

Inclusion & Exclusion criteria

Inclusion criteria include dentate or edentulous patients; ages between 18 and 70 years; and CBCT images from the distal of 1st molar in the right side to the distal of 1st molar in the other side. Whereas exclusion criteria include images with any syndromic or congenital disorders; images with history of trauma, pathology to the mandible or surgical intervention in the inter-foraminal region; any radiographic signs of mandibular pathology or pervious surgery in the study region of mandible; inadequate quality of CBCT images (i.e.: patient movement, operation errors, etc.); any impacted teeth in the in interforaminal area; fracture of the lower jaw in the midline of mandible or in the mental foramina area; and ongoing orthodontic treatment .

Ethical approval

Prior to the study, ethical approval to carry out this study was granted from the ethical committee of the Faculty of Medicine and Health Sciences, University of Science & Technology (MECA No.: EAC/UST165).

Technique and reconstruction parameters

All images were taken by a CBCT system unit (PaX-Flex3D P2, Vatech, Korea) using the following exposure parameters:

kVP = 77 - 90, mA = 4.7–5.7, t =15–24 seconds, field of view = (12×8.5) cm and with a voxel size of 0.160–0.20 mm for full views and 0.06–0.02 mm for other field of views (FOVs). Moreover, the images were analyzed and the measurements were done using the tools given in the software (Ez3D plus with Ez3D-I software). A single operator worked with all the files from a personal laptop (Dell – Core(TM) i7-3520M CPU @ 2.90GHz with a Ram of 16 GB with a serial No.: 115570-0000045).

The images of each case were managed and analyzed through three steps: First step in which the axial sections were generated in a way to exhibit the right and left MF together at the same time and in the same level; Second step in which the panoramic curve was drawn from the right MF to the left MF on the axial section; Third step in which multiple serial cross-sections from the panoramic view were obtained.

Study variables:

The current study investigated the location of mental fora men MF by CBCT method to attain the location, shape, and size of MF in a group of Yemeni population. The horizontal and vertical lines were determined in the panoramic recon structing view by a straight ruler of the Ez3D software so as to determine the Location of MF which was assessed accord ing to the line drawn as a long axis passing through the apex of the tooth based on the classification "proposed by8 which is as follows: position I is in line with the long axis of the 1st premolar ; position II is between the 1st and 2nd premolars ; position III in line with the long axis of the 2nd premolar ; Position IV Between the 2nd premolar and the 1st molar ; and Position V Distal to the 1st molar. Because the MF in some cases was located distal to the canine due to the extraction to the 1st premolar, and was located distal to the 1st premolar in some others due to the extraction of 2nd premolar, it was also assessed in two additional positions which are: Position VI distal to canine with extraction to 1st premolar and Position VII distal to 1st premolar with extraction of 2nd premolar.

The shape of MF was assessed according to the classification "proposed by Zhang et al. (2015) depending on the ratio of two diameters (H: V), since H represented as a horizontal diameter of MF and V represented as a vertical diameter of MF, into one of three Types (Fig. I):Type I (Oval horizontal form, H: V > 1.24); Type II (Oval vertical form, H: V< 0.76) ; and Type III (Round form, 0.76 ≤ H: V ≤ 1.24).

Measurements of MF: CBCT images were measured according to the following:9 The vertical distance from the superior margin of MF to the alveolar ridge was represented in this study as (M1) ; The vertical distance from the inferior margin of MF to the inferior border of the mandibular was represented in this study as (M2) ; The horizontal diameter of MF (HMD) was the inner horizontal distance mesial to the distal side of the foramen ; and The vertical diameter of MF (VMD) was the inner vertical distance superior to the inferior side of the foramen (Fig. I and II).

Accessory Mental Foramen (AMF) was measured by the panoramic reconstructing view as single or double in one side or in both sides of the mandible. Besides, the shape of AMF was simultaneously determined with those of MF (Oval horizontal form, Oval vertical form, and Round form) (Figure III, IV, and V)

Statistical analysis

Data were analyzed by the Statistical Package for Social Sciences (SPSS) version 24. Descriptive statistics (mean, variance, standard deviation, and minimum and maximum values) were used in the data analysis. The mean differences in the measurements of MF, AL, and IC were analyzed by T-test in which p-value less than 0.05 was considered statisti cally significant. The data were represented using tables and figures.

Study reliability

Thirty cases were examined as a pilot study. The measurements were evaluated twice by the researcher himself as an intra-observer. The two measurement results were analyzed using the Cohen's Kappa statistic. Findings showed 'substantial' agreement between the two measurements'. After that, the same pilot study cases were measured by two interobservers: (AA) assistant Professor of Oral and Maxillofa cial Surgery and (LA) assistant Prof. of Oral Diagnosis and Radiology. Findings also showed mean 'substantial' agreement between the measurements' was 86.8.

RESULTS

A total of 420 cases from CBCT images of 210 patients (51.4% males and 48.6% females) were analyzed according to gender, age, side and dental condition (Table I). The 1stgroup was ≤40 years

consisting of 98 (23.3%) the 2nd group was the non-edentulous consisting of 314 (74.8%). The data shows that there are significant of the mean diameters of the MF regarding the gender and dental condition, males 2.71 mm and 2.63 mm in the non-edentulous compared to others.

The mean of the MF-H and MF-V was 3.74 mm and 3.08 mm respectively. Moreover, the maximum width of the MF-H and MF-V was 8.30 mm and 8.20 mm, respectively (Table II).the mean and SD of the MF diameter were 2.60 mm. The mean of M1 was 7.61 and M2 10.99 mm.

Table III showed significant differences of MF-H and MF-V according to gender males were 3.94 mm and females were 3.52 mm ($p = 0.000$), the mean in males/females were 3.18 mm and 2.96 mm ($p = 0.005$), respectively. Also there is significant differences of MF-V according dental condition edentulous/non-edentulous 2.92 and 3.13, respectively.

Regarding the mental foramen length, there was a significant difference in only the mean lengths of MF-M2 regarding gender ($p = 0.000$), the mean lengths of both MF-M1 ($p = 0.000$) and MF-M2 ($p = 0.023$) (Table IV).

Table V showed the location of MF, 124 (39.5%) representing the majority of cases showed MF under the apex of the 2nd premolar (male = 43.13%, female = 35.71%), In the ≤40 year-old group, 30 (33.7%) cases showed MF under the apex

DISCUSSION

Preventing any postoperative complications in the inter foraminal area during any dental implant surgery depends mainly on dentists' good pre-surgical knowledge of the exacted location and size of the MF and AMF that can be accurately identified by several methods; including manual palpation, cadaveric dissection, peri-apical radiographs, panoramic radiographs, MDCT, CBCT or MRI.

There are many previous studies aimed to study the prevalence, size, and location of the MF AMF by using different conventional methods including panoramic radiography,human dry mandible technique,3,9-12 and spiral CT imaging method .

On the other hand, CBCT imaging method, as the most promising and accurate method available for determining the position and size of MF and AMF, and the presence of Al4was used in many other previous studies.1,8,13-15

The current study was conducted to determine the prevalence of the MF and AMF, the position and diameter of the MF and AMF by using CBCT imaging among a group of Yemeni adults. Moreover, the study results cannot be generalized among Yemeni population because the study sample was taken from one city, Sana'a, due to the lack of CBCT radiological centers in other cities.

Nevertheless, this study is considered, according to the researchers' knowledge, the first study investigating all the measurements of the three variables; MF altogether in literature and also the first study identifying the shape and location of AMF in literature. Besides, it is also considered, based on the National Information Center, Yemen, the first study determining and measuring the MF, AL and IC in Yemen.

Additionally, the results of this study are compared to the results of the previous studies that used CBCT imaging method for detecting and measuring the MF and AMF. MF was found in all patients on both sides representing 100%, representing 51.4%, and in 204 females representing 48.6%, while in the right and left sides the MF was equally found representing 50%.

The mean of the MF horizontal width (MF-H) was 3.74 mm which is relatively similar to that of13 (3.7 mm), less than those of Zhang et al., 2015, and16 (5.14 mm, 6.8 mm, and 5.325 mm, respectively), and more than those of17,18 (3.5 mm, 3.2 mm, and 2.97 mm,, respectively).

Furthermore, the mean of the MF vertical height (MF-V) was 3.08 mm which is relatively equal to that of Von Arx et al., 2013 (3.0 mm), less than those of 2,13,16 (3.92 mm, 3.4 mm, and 5.9 mm,

respectively), and more than those of 15-19(2.6 mm, 2.11 mm, and 1.9 mm, respectively).

The study demonstrated that the horizontal and vertical sizes of the MF on CBCT were significantly greater in males than in females ($p = 0.000$ horizontally and $p = 0.005$ vertically). This result is similar to that of13 in which p-value < 0.005. Moreover, the study also showed that the vertical sizes of the MF on CBCT were significantly greater in the non-edentulous cases than in the edentulous ($p = 0.020$).

The mean diameter of the MF was 2.60 mm which is less than that of Sheikhi and Kheir, 2016 (3.59 mm), and more than that of 20 (2.26 mm among Americans and 2.13 mm among Taiwanese). Besides, the study indicated that the diameter of the MF on CBCT was significantly greater in males than in females and in the non-edentulous cases than in the edentulous ($p = 0.000$).

The mean distance from the MF to the teeth apex or to the crest of alveolar ridge (MF-M1) was 7.61 mm which is less than those reported by,20 (12.6 mm, 11.88 mm and 14.3 mm, respectively) and more than that reported by 13 (4.0 mm). However, the mean distance from the MF to the inferior bor der of the mandibular bone (MF-M2) was 10.99 mm which is less than those reported by 13(13.8 mm, 13.56 mm, 13.2 mm and 12.6 mm, respectively).

Furthermore, the study showed that MF-M1 on CBCT was significantly greater in the non-edentulous cases than in the edentulous ($p = 0.000$). In addition, MF-M2 on CBCT was significantly greater in males than in females ($p = 0.000$).

Regarding the shape of the MF, most of the cases were round, followed by oval horizontal, then oval vertical (52.9%, 45.2%, 1.9%, respectively). However, most of the cases reported by10 were round, followed by oval vertical, then oval horizontal (61.60%, 27.30%, 11.15%, respectively), those reported by15 (were mostly oval horizontal, followed by round, then oval vertical (56.3%, 39.03%, and 4.675%, respectively), and those reported by Zhang et al, 2015, were mostly oval horizontal (67%), followed by round (33%), and no oval vertical cases were found (0%).

The MF location in the current study depended on the apex of the adjacent teeth of only the non-edentulous cases of which 39.5% were located under the apex of the 2nd premolar, 14.3% distal to the 1st premolar with the extraction of 2nd premolar, 18.8% between the 1st and 2nd premolar, 8.0% distal to the canine and extraction to the 1st premolar, 7.3% between the 2nd premolar and the 1st molar, 6.4% under the apex of the 1st premolar, and only 1.0% were located under the 1st molar.

In the research literature, the most common location of the mental foramen is the region of the second premolar in the completely developed mandible,1 but individual variations may occur occasionally.2

In the current study, most of the cases were located under the apex of the 2nd premolar. This result agrees with those reported by,5 but it does not agree with those of ,22 and 10 who reported that most of the cases were located between the 1stand 2nd premolars.

The MF prevalence rates according to its location varies from a study to another because some studies assessed the MF location according to the classification proposed by,3some assessed it only in two locations,17 and,18 and some oth ers assessed it only in three locations.10 However, the current study assessed it in seven locations.

AMF is “a rare anatomical variation with particular impor tance in local anesthesia and surgical procedures, especially the placement of dental implants,23

Most of the AMFs were found in the 1st permanent molars area.11,12,14

In the current study, the AMF was found in only 4 (1%) of all cases as a duplication of the AMF in 2 CBCT images. These 4 AMFs were found in the non-edentulous males aged >40 years. Besides, 1 (25%) of these AMFs was found in the right side and was round in shape. However, the remaining 3 AMFs were in the left side; 2 (50%) of which were oval horizontal and 1 (25%) was round.

The AMF prevalence rate was 1% which is less than those of,13,8,5 who reported that AMF was found in 11.33%, 6.5%, 7.54%, and 2.53%, respectively.

The mean of the AMF horizontal width (AMF-HMD) was 1.88 mm which is more than those reported by 13 (1.6 mm, 1.6 mm, and 1.49 mm, respectively). While, the mean of the AMF vertical height (AMF-VMD) was 1.63 mm which is more than those reported by 13 (1.2 mm and 1.4 mm), and less that reported 8 (1.83 mm).

"In patients who had accessory innervation due to the presence of AMF, anesthetic failure is expected to occur in 10-20% of cases if only the inferior alveolar nerve is blocked,24during surgical placement of dental implant, reports of neu rosensory disturbances were not rare.23 If the inferior alveolar nerve, mental nerve or its accessory branches are damaged, the sensory dysfunction due to the nerve damage can occur.25

In addition, an AMF and its potential variations may give way to important neurovascular anatomic structures, and their detection is fundamental to safe and successful surgical installation of dental implant".23

New information about MF and AMF present in this study can help the surgeons to decrease of the nerve damage during any dental implant surgery. Because this study is the first study conducted on a group of Yemeni population by using the CBCT images.

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Table I: Descriptive results of sample according to demographic variables and the mean diameter of MF according to the study variables

Variables		Frequency	Percent	Mean diameter of MF	SD	P-value
Gender	Male	216	51.4	2.71	0.50	0.000
	Female	204	48.6	2.49	0.50	
	Total	420	100.0			
Age	≤40 years	98	23.3	2.60	0.41	0.832
	>40 years	322	76.7	2.61	0.54	
	Total	420	100.0			
Sides	Right	210	50.0	2.59	0.50	0.362
	Left	210	50.0	2.62	0.53	
	Total	420	100.0			
Dental dentation	Edentulous	106	25.2	2.53	0.44	0.000
	Non-edentulous	314	74.8	2.63	0.54	

Table II: Descriptive results of the measurements of horizontal height MF-H, vertical width MF-V, and diameter of mental foramen

MF measurement	N	Mean	SD	Maximum	Minimum
MF-H	420	3.74	0.93	8.30	1.50
MF-V		3.08	0.82	8.20	1.30
MF Diameter		2.60	0.52	1.30	5.00
MF-M1		7.61	4.37	0.10	19.40
MF-M2		10.99	2.18	3.80	21.70

MF-H: MF horizontal height, MF-V: MF vertical width.
MF-M1: distance from MF to teeth apex or to crest of alveolar ridge.
MF-M2: distance from MF to inferior border of mandibular bone.

Table III: Measurements of the MF-H and MF-V according to independent variables

MF Measurements	Male (n=216)	Female (n=204)	Total (n=420)	P-value
MF-H	3.94±0.90	3.52±0.92	3.74	0.000
MF-V	3.18±0.81	2.96±0.81	3.08±0.82	0.005
	≤40 years (n=98)	>40 years (n=322)		
MF-H	3.63±0.67	3.77±1.00	3.74±0.93	0.191
MF-V	3.17±0.74	3.05±0.84	3.08±0.82	0.212
	Right (n=210)	Left (n=210)		
MF-H	3.70±0.90	3.77±0.97	3.74±0.93	0.462
MF-V	3.07±0.80	3.09±0.84	3.08±0.82	0.802
	Edentulous (n=106)	Non-Edentulous (n=314)		
MF-H	3.69±0.93	3.75±0.94	3.74±0.93	0.532
MF-V	2.92±0.60	3.13±0.87	3.08±0.82	0.020

MF-H: MF horizontal height, MF-V: MF vertical width.

Table IV: MF length measurements according to other demographic variables

Variable			N	Mean	SD	P-value
Gender	MF-M1	Male	216	7.57	4.37	0.848
		Female	204	7.66	4.39	
	MF-M2	Male	216	11.87	1.99	0.000
		Female	204	10.06	1.97	
Age group	MF-M1	≤40 years	98	7.87	4.51	0.506
		>40 years	322	7.54	4.33	
	MF-M2	≤40 years	98	10.65	2.38	0.075
		>40 years	322	11.10	2.10	
Side	MF-M1	Right	210	7.49	4.34	0.562
		Left	210	7.74	4.41	
	MF-M2	Right	210	10.91	2.23	0.460
		Left	210	11.07	2.13	
Dental condition	MF-M1	Edentulous	106	5.76	3.89	0.000
		Non-Edentulous	314	8.24	4.35	
	MF-M2	Edentulous	106	10.58	2.08	0.023
		Non-Edentulous	314	11.13	2.19	

MF-M1: distance from MF to teeth apex or to crest of alveolar ridge.
MF-M2: distance from MF to inferior border of mandibular bone.

Table V: MF location according to gender, age, and side with respect to adjacent teeth

MF Location	Gender						Age						Side					
	Male		Female		Total		≤40 years		>40 years		Total		Right		Left		Total	
	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%	Freq.	%
Under Apex of 1st Premolar	11	6.9%	9	5.8%	20	6.4%	6	6.7%	14	6.2%	20	6.4%	12	7.5%	8	5.2%	20	6.4%
Under Apex of 2nd Premolar	69	43.1%	55	35.7%	124	39.5%	30	33.7%	94	41.8%	124	39.5%	67	42.1%	57	36.8%	124	39.5%
Between 1st & 2nd Premolar	36	22.5%	23	14.9%	59	18.8%	28	31.5%	31	13.8%	59	18.8%	26	16.4%	33	21.3%	59	18.8%
Between 2nd Premolar & 1st Molar	10	6.3%	13	8.4%	23	7.3%	5	5.6%	18	8.0%	23	7.3%	14	8.8%	9	5.8%	23	7.3%
Under 1st Molar	2	1.3%	1	0.6%	3	1.0%	2	2.2%	1	0.4%	3	1.0%	1	0.6%	2	1.3%	3	1.0%
Distal to Canine with extraction to 1st Premolar	10	6.3%	15	9.7%	25	8.0%	4	4.5%	21	9.3%	25	8.0%	11	6.9%	14	9.0%	25	8.0%
Distal to 1st Premolar with extraction of 2nd Premolar	22	13.8%	38	24.7%	60	19.1%	14	15.7%	46	20.4%	60	19.1%	28	17.6%	32	20.6%	60	19.1%
Total	160	100%	154	100%	314	100%	89	100%	225	100%	314	100%	159	100%	155	100%	314	100%

Table VI: description of Prevalence and shape of Accessory Mental Foramen

MF	Accessory MF				Total	
	No Accessory MF		Accessory MF			
	N	%	N	%	N	%
MF-Found	416	99.0%	4	1.0%	420	100%
AMF Shape	Right		Left			
Oval horizontal shape of MF	0	0.0%	2	50.0%	2	50.0%
Oval vertical shape of MF	0	0.0%	0	0.0%	0	0.0%
Round Shape of MF	1	25.0%	1	25.0%	2	50.0%
Total	1	25.0%	3	75.0%	4	100%
AMF measurements	N	Mean	Minimum	Maximum		
AMF-HMD	4	1.88	1.20	2.80		
AMF-VMD	4	1.63	1.10	2.20		
AMF-M1	4	9.95	6.50	14.20		
AMF-M2	4	11.03	10.10	12.50		
Total	416	99.0%	4	1.0%	420	100%

AMF-HMD: AMF horizontal width.
AMF-VMD: AMF vertical height.
AMF-M1: distance from AMF to teeth apex or to crest of alveolar ridge.
AMF-M2: distance from AMF to inferior border of mandibular bone.

Table VII: Frequency of AMFs according to gender, Age, side, and dental condition

	Accessory MF				Total	
	No Accessory MF		Accessory MF			
	N	%	N	%	N	%
Male	212	50.5%	4	1.0%	216	51.4%
Female	204	48.6%	0	0%	204	48.6%
≤40 years	98	23.3%	0	0.0%	98	23.3%
>40 years	318	75.7%	4	1.0%	322	76.7%
Right	209	49.8%	1	0.25%	210	50%
Left	207	49.3%	3	0.75%	210	50%
Edentulous	106	25.2%	0	0%	106	25.2%
Non-edentulous	310	73.8%	4	1.0%	314	74.8%
Total	416	99.0%	4	1.0%	420	100%

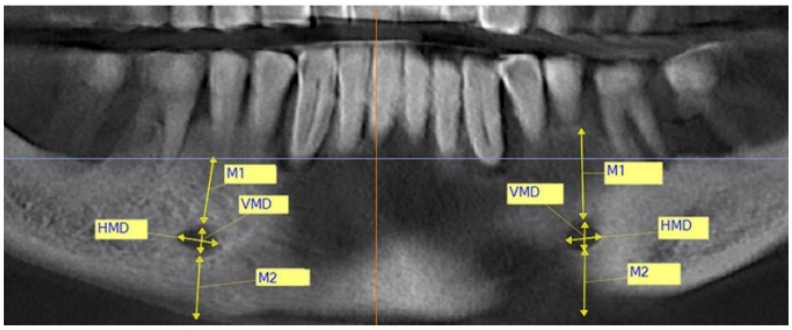

Figure I: Panoramic sectional image showing VMD and HMD of MF shapes in non-edentulous patients.

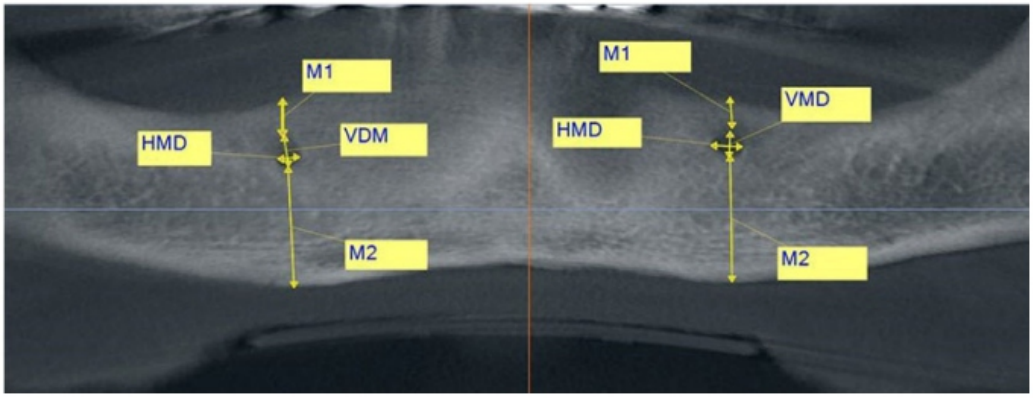

Figure II: Panoramic sectional image showing VMD and HMD of MF shapes in edentulous patients.

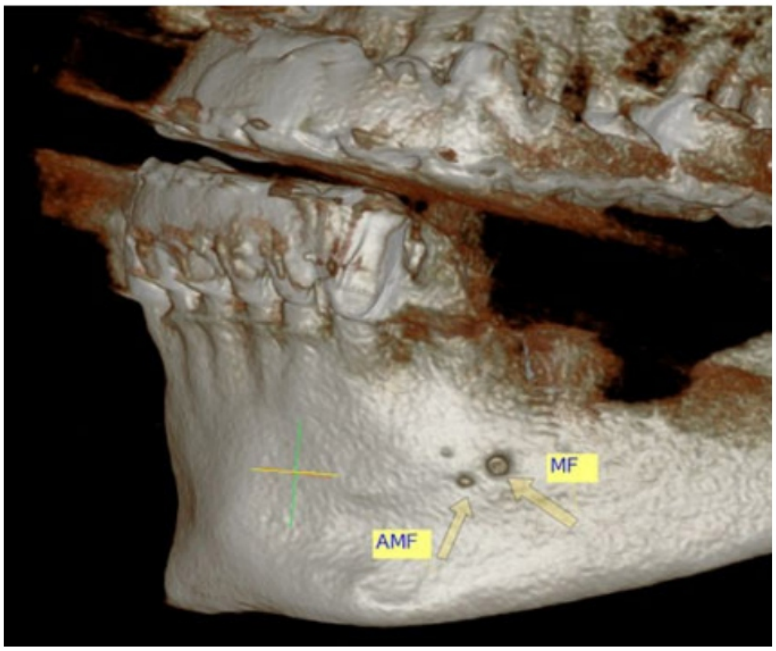

Figure III: 3D view showing MF and AMF on the left side

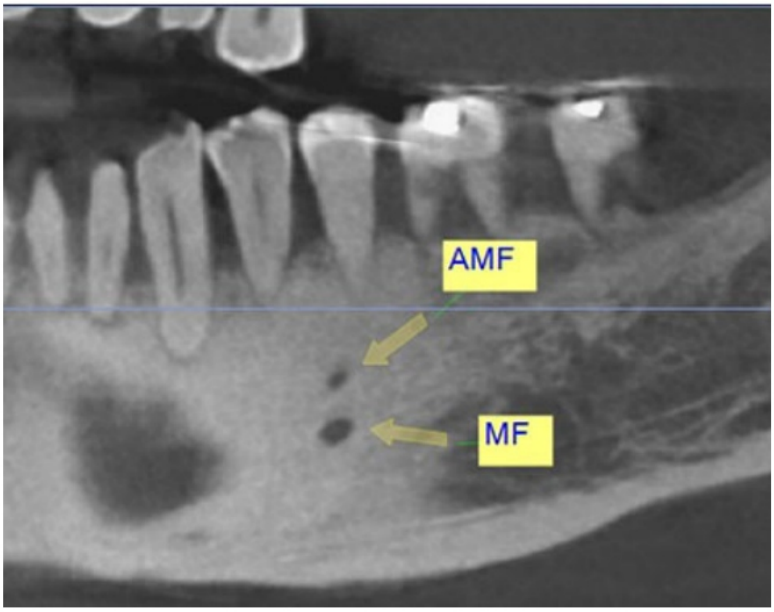

Figure IV: panoramic view showing MF and AMF on the left side.

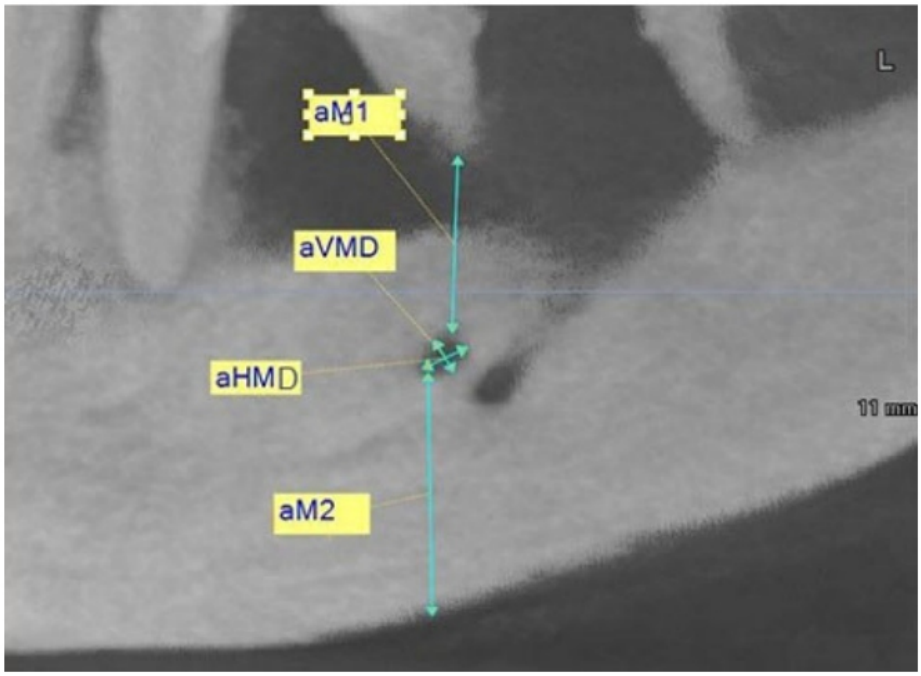

Figure V: Panoramic sectional image showing VMD and HMD of AMF shapes

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