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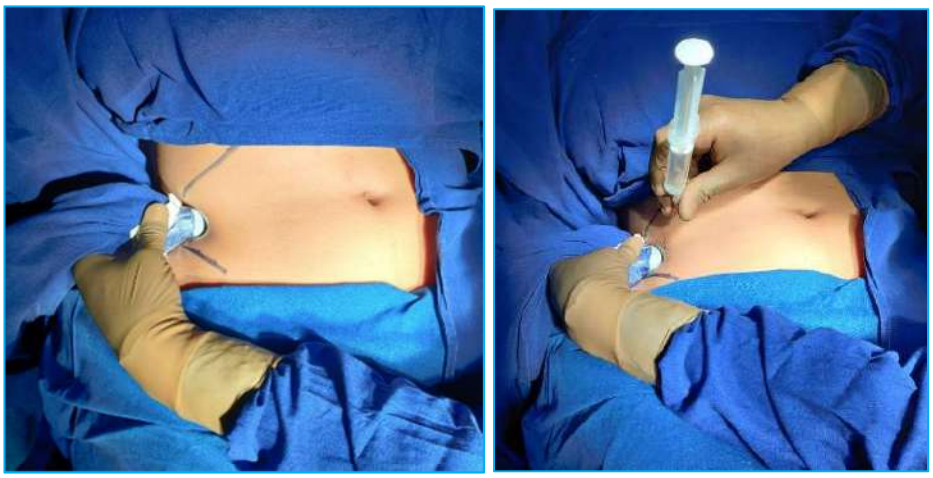

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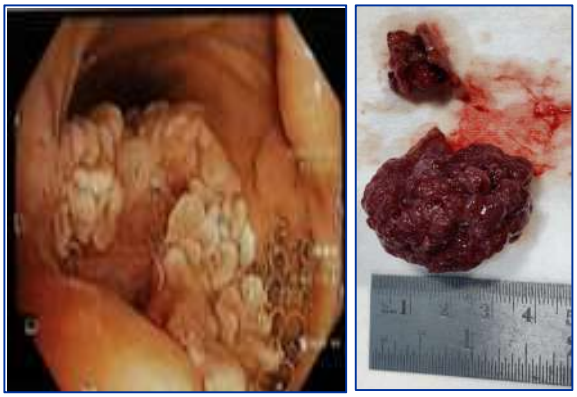

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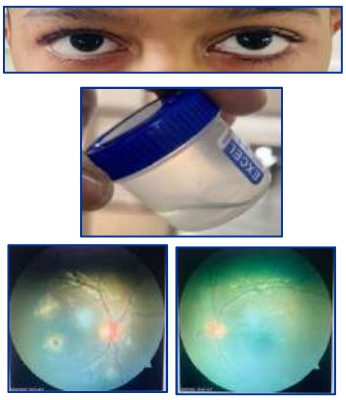

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EDITORIAL

'Educationist' in Medical Training: The 'Missing Link'

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The shelf life of medical knowledge is becoming increasingly shorter. The digital platforms provide a constant flow of material, but, from a trainee's perspective this knowledge is not always regulated. Training needs to be step wise, structured & navigated with utmost focus, which it deserves. That is where comes the role of a medical educationist.

In 2014, the one-year program of Advance Course in Medical Education (ACME) was introduced as a part of a multi-tier approach to strengthen the quality of medical education in India. However, the initiative has not been very successful, and only a few institutions such as JIPMER, Pondicherry, and KEM, Mumbai have set up the Department of Medical Education.

One of the reasons for the lack of demand for medical educationalists in India may be the limited employment opportunities available. The private sector and the government may not be able to provide enough employment opportunities for those who complete the ACME course.

Another challenge is the disparity in the methods adopted to impart education. Some institutions may not be equipped with the latest technologies and teaching methods, which may result in subpar education.

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To overcome these challenges, it is necessary to invest in healthcare education and training. This can be done by increasing the number of institutions that provide quality healthcare education, promoting research and innovation in healthcare education, and incentivizing healthcare professionals to continue learning and updating their skills. Additionally, the government and private sector should work together to bridge the demand-supply gap of healthcare resources by providing more funding and resources for healthcare education.

Unfortunately, there are no limits to the difficulties encountered in medical education. Whether it's overcoming opposition to the launch of a new educational program, gaining faculty support for a teaching initiative or obtaining resources (e.g., time, space, personnel) to support the development of a new curriculum, change is hard. As a medical educator, it is all about leading change and guiding others through it and becoming someone with a title but rather anyone trying to make a difference by advancing the status quo.

The educator must use their vision, strategy and influence to make an impact by communicating the goal of the change with the use of data (e.g. needs assessment), testimonials and appeals to authority (e.g., accreditation requirement) whenever possible. Providing the necessary training and resources to ensure their success (i.e., faculty development). Track and demonstrate progress with metrics and awards. Finally, involving others in the design and implementation of the initiative helps get buy-in. Allow people to provide feedback and customize based on their specific requirements. These are the keys to motivating others to join in the efforts to create change in medical education.

It is also frequently necessary to obtain the necessary resources or institutional support to facilitate the educational goal. The educator must demonstrate how their educational initiative is a priority by aligning it with the organization's strategic goals, also to be practical, bringing solutions to anticipated implementation problems. This allows others to see the project's feasibility and the due diligence you have already performed. In addition, a stakeholder analysis helps to address political dynamics that may play a role in the change initiative.

Practical difficulties in implementation of course

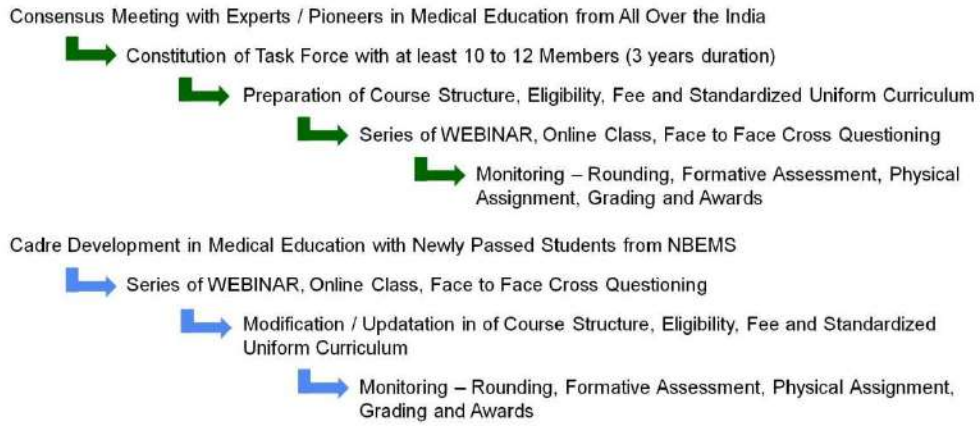
The government and private hospital establishments in India follow Article 21 of the Constitution of India, that is, Right to Health with a very few and necessary disciplines of medical sciences such as Medicine, Surgery, Orthopaedics, ENT, Dermatology etc. The comparative assessment between Medical Colleges and Govt. and Private Hospitals is given below:

Medical College	Govt. /Pvt. Hospital
• Equipped with Pre & Para Medical Faculties	• No Pre & Para Medical Faculties
• Established to provide Medical Education	• Basically Patients Centric, Not to Provide Medical Education
• Attached with a Hospital to Provide Clinical Education	• Very few or not associated with Medical College
• Equipped with Data facility (Library, Internet, Books)	• Limited Data Facility
• Equipped with Laboratories survices	• Limited Laboratories Services
• Equipped with Teaching Environment e.g. Centralized Monitoring, Formative Assessment, Assignment, Tracking and Grading, Virtual and Face to Face Cross Questioning with Health Educators	• Limited Teaching Environment as very few Hospitals Providing Accreditation or Medical Degrees

Solution

- Making a provision for the post of Medical Educator in every Medical College or Govt./Pvt. Hospital who are running NBENS courses.
- In hospitals, where no scientist position is available, a scientist with degree in Medical Education could be hired. He/she would play the role of, not only of medical educator, but, teaching basic science, as well.
- In contrast to the pure clinician who (if) does not have teaching responsibilities, the clinician-teacher or clinical educator typically adds this dimension to his or her professional portfolio after receiving a course in medical education.
- An estimated 69 thousand public and private hospitals were recorded across India in 2019. Of these, 43 thousand were private sector hospitals, outnumbering the public sector. The state of Uttar Pradesh had the highest number of hospitals that year. (© Statista 2022). If a percentage of these hospitals hire at least one Health Educator, the positions of medical educator could be generated which would be scalable as the engagement rises.

The NBEMS Roadmap



Setting the goals for future health care should be process enabled & should encompass-

Strategic planning, Complex problems, Change management, Learning by doing, Appropriate clinical exposure in different phases of training, Role modelling, Designing the hidden curriculum, Educational tools & Quality care.

The essential elements of the module would be- *General principles of Education, Instructional methodology, Assessment & evaluation, Curriculum Development & such others.*

In conclusion, with the Government's effort to ramp up the healthcare man power, particularly, the UG & PG courses, it is the need of the hour to give due attention to the process of change and to the way educational science could be brought in to where it is needed. Effective change management is essential to maintain enthusiasm to invest in the health care of the future. Educationalist science provides several important insights that help us find the optimal shape of the program.

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ORIGINAL ARTICLE

F-18 FDG PET/CT characterization and predictive efficacy for driver mutation positive and negative pulmonary adenocarcinoma in correlation with clinico-pathologic data

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Abstract:

Background: Fluorine-18 (isotope)-Fluoro-deoxyglucose positron emission tomography computed tomography (F-18-FDG PET/CT) as a non-invasive method could predict driver mutation status in pulmonary adenocarcinoma.

Aim: To assess whether F-18 FDG PET/CT can differentiate between positive and negative driver mutation status of pulmonary adenocarcinoma.

Settings and Design: Hundred biopsy proven, untreated pulmonary adenocarcinoma patients tested for EGFR and ALK gene mutations underwent staging F-18 FDG PET/CT scan at our institute.

Methods and Material: Metabolic parameters like SUV_{max} of the primary ($pSUV_{max}$), SUL_{peak}, SUV_{mean}, Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) of primary lesion, SUV_{max} of the most avid metastatic regional lymph node ($nSUV_{max}$) and extra thoracic metastasis ($mSUV_{max}$) and average SUV_{max} of the primary lesion, regional nodal metastasis and extra thoracic metastasis were calculated.

Statistical Analysis Used: The independent sample 'T' test and Mann-Whitney U test were used for analysis. Receiver operating characteristic (ROC) curves were used to determine the cut-off value of $pSUV_{max}$ for predicting ALK mutation status.

Results: Fourty one patients showed EGFR mutations, 14 showed ALK rearrangements and 45 were wild-type. Patients with ALK rearrangements showed a lower $pSUV_{max}$, SUL_{peak}, SUV_{mean} and TLG compared to wild type patients. ROC curve analysis showed a $pSUV_{max}$ cutoff of $\leq$11.0 yielding an area under the curve (AUC) of 0.709. Patients with EGFR mutations showed a lower $mSUV_{max}$, MTV, and TLG compared to wild type.

Conclusions: FDG- PET/CT can be a useful non- invasive tool if tumor tissue is not available, although genetic testing continues to be the gold standard.

Keywords: FDG/PET CT, driver mutation, pulmonary adenocarcinoma, metabolic parameters, EGFR, ALK.

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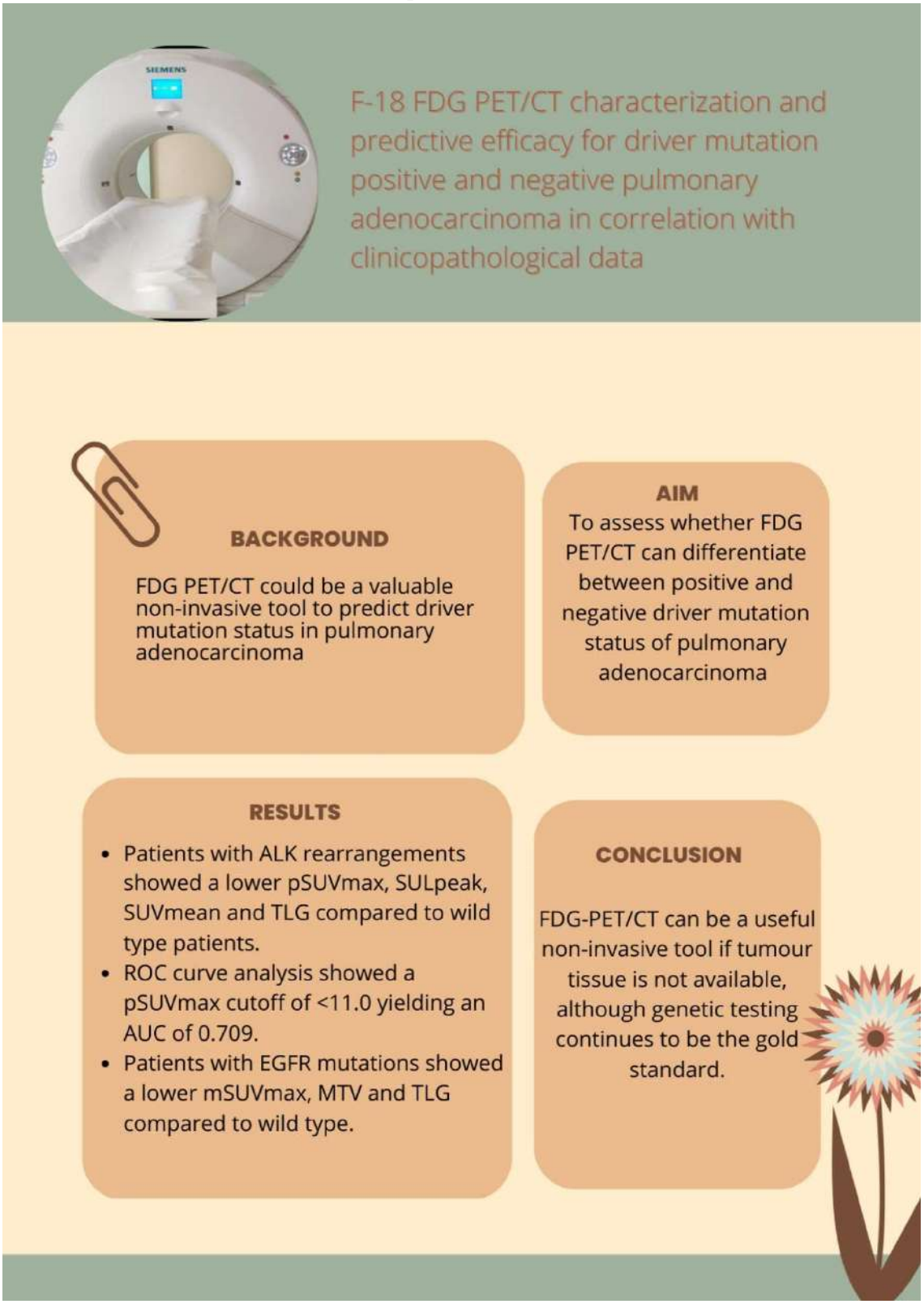
Graphical Abstract



Introduction

The discovery of mutations in lung cancer has resulted in the creation of targeted therapies which help in improving the survival of patients with metastatic cancer. Specific mutations in genes encoding components of the epidermal growth factor receptor (EGFR) and downstream mitogen-activated protein kinases (MAPK) and phosphatidylinositol 3-kinases (PI3K) signaling pathways can now be used to designate subsets of adenocarcinoma. This can be exploited by targeted therapies. Targeted EGFR treatments, for example, have enhanced response rates in patients with EGFR mutations when compared to standard chemotherapies. Tyrosine kinase inhibitors (TKIs), including gefitinib and erlotinib, were developed and have demonstrated to be an excellent treatment for individuals with EGFR gene mutations [1]. Fusion of ALK with EML4 genes forms translocation products that are responsive to pharmacological inhibition of ALK by agents such as crizotinib. Therefore, it is essential to identify EGFR and ALK mutation status before attempts at targeted therapy.

Fluorine-18(isotope)–Fluoro-deoxygl-ucose positron emission tomography computed tomography (F-18-FDG PET/CT) is a valuable modality which combines the metabolic and anatomic information in assessing the lesion. Tumor biopsies for the detection of oncogenic driver mutations have limitations. The site of tumor biopsy may have a significant impact on the detection and outcome, and the patients' overall health may limit the use of biopsies in clinical practice. Therefore, the use of medical imaging as a non-invasive method to obtain information about the tumor phenotype could provide clues to predict mutation status of the EGFR and ALK gene. This has been investigated in several studies wherein F-18-FDG PET/CT has been used to predict the mutation status of EGFR and ALK in patients with lung adenocarcinoma. However, the results remain controversial [2].

The goals of this study were to see if metabolic parameters from F-18-FDG PET/CT and clinicopathological data could predict EGFR and ALK expression and mutation status in patients with lung adenocarcinoma, and to create a prognostic template based on changes in EGFR/ALK mutation status, which can be used to guide individualized molecular targeted therapy.

Methods

This prospective observational study was conducted from December 2020 to February 2022 in our institute after approval from the Institutional Ethics Committee. It consisted of hundred patients with inclusion criteria being patients with biopsy proven pulmonary adenocarcinoma in whom EGFR and ALK mutation analysis was performed and the patient not started on any treatment before the scan. The exclusion criteria included patients who underwent previous treatment with chemotherapy/radiotherapy or surgery before scan, and patients with pulmonary adenocarcinoma in whom driver mutation analysis was not done.

Patients were subjected to the F-18 FDG PET/CT scan after obtaining prior informed consent. Patients were instructed to come fasting for atleast 6 hours. Blood sugar levels, height, weight, blood urea, and creatinine of the patient were recorded. A single injection of 5-10 mCi of F-18 FDG was injected intravenously through a secured I.V line as per standard protocol, based on the patient's weight. Whole-body F-18 FDG-PET/CT scan was performed at 60 minutes post-injection on Siemens Biograph mCT PET/CT scanner with 40 slice CT (diagnostic contrast-enhanced CT)(CECT).

The matrix used was 128 x128 for PET & 512 x512 for CT. Image reconstruction was done with OSEM (ordered subset expectation maximization), iterative reconstruction method. CT scan was then fused with PET images and transferred to the processing system for analysis.

PET/CT images were analyzed on a dedicated workstation that was provided with commercial software called Syngo. via. A large region of interest (ROI) involving the entire

primary tumor was drawn for the calculation of the metabolic parameters which were calculated by the syngo.via software (Figure 1). The maximum standardized uptake value (SUV_{max}) was calculated as the activity in the hottest voxel of the tumor. Maximum standardized uptake value corrected for lean body mass (SUL_{peak}) algorithm automatically identified the mean value of the voxels within a fixed sphere of $1cm^3$, centered on the hottest area of the tumor.The global semiquantitative parameters like mean standardized uptake value (SUV_{mean}), metabolic tumor volume (MTV) and tumor lesion glycolysis (TLG) were automatically calculated by the software based on the fixed relative threshold method with threshold fixed to 40 %, i.e., the lesion limits were determined by selecting all voxels within 40% of the SUV_{max} inside the master voxel of interest (VOI) drawn around the lesion.

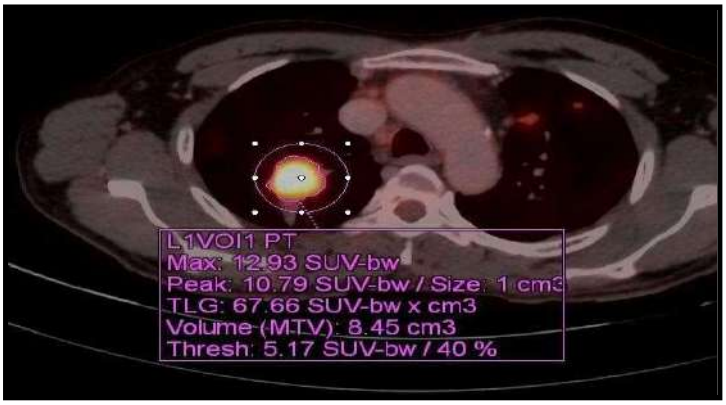


Figure 1. Selection of ROI for analysis of FDG-PET parameters

SUV_{max} of the most avid metastatic regional node ($nSUV_{max}$) if present was calculated. SUV_{max} of the most avid extrathoracic metastasis ($mSUV_{max}$) if present was calculated. Average SUV_{max} of the primary lesion ($pSUV_{max}$), regional nodal metastasis ($nSUV_{max}$) and extrathoracic metastasis ($mSUV_{max}$) was calculated using the formula

$$\text{Average } SUV_{max} = \frac{pSUV_{max}+nSUV_{max}+ mSUV_{max}}{3}$$

Statistical Analysis

All continuous variables were represented by mean ± standard deviation. Percentages were used to represent all categorical variables. The independent sample' T' test was used to compare continuous variables that were normally distributed. The Mann-Whitney U test was used to compare continuous variables that were not regularly distributed. Receiver operating characteristic (ROC) curves were used to determine the cut-off value of the primary tumor SUV_{max} ($pSUV_{max}$) for predicting ALK mutation status. Data was entered into a Microsoft Excel spreadsheet. SPSS (Statistical Package for Social Sciences) version 26.0 was used to analyze the data. P values less than 0.05 were deemed statistically significant.

Results

This study included 100 patients, 29 of whom were female (29 percent) and 71 of them were male (71 percent). Patients ranged in age from 28 to 85 years old. The bulk of the participants were between the ages of 51 and 70, with the median age being 57 years.

Ten patients were histopathologically well differentiated, i.e. Grade I (10%), 64 were moderately differentiated, i.e. Grade II (64%), and 26 were poorly differentiated, i.e. Grade III (26%).

Patients were staged according to AJCC 8th edition of TNM in lung cancer which is the standard of NSCLC staging since January 1st, 2017 [3]. Five patients belonged to stage I (5%), 1 belonged to stage II (1%), 18 belonged to stage III (18%), and 76 belonged to stage IV (76%).

Among the 100 patients who were tested for EGFR and ALK mutations, 41 were positive for EGFR mutation (41%). 14 showed ALK rearrangement (14%) and remaining 45 were wild type (45%).

Amongst the 41 patients who showed EGFR mutation, 8 were female (19.5 %) and 33 female (80.5%). 34 patients were well to moderately differentiated (82.9 %) whereas 7 patients were poorly differentiated (17.1 %). 3 patients belonged to stage I- II (7.3 %) while 38 patients were of stage III-IV (92.7 %).

Out of the 14 patients who showed ALK rearrangement, 7 were female (50 %) and 7 were male (50 %). 6 patients were well to moderately differentiated (42.9%) whereas 8 patients were poorly differentiated (57.1%). 1 patient belonged to stage I-II (7.1 %) while 13 patients were of stage III-IV (92.9 %).

Amongst the 45 patients who were EGFR and ALK wild type, 14 were female (31.1%) and 31 were male (68.9%). 34 patients were well to moderately differentiated (75.6%) whereas 11 patients were poorly differentiated (24.4%). 2 patients belonged to stage I-II (4.4%) while 43 patients were of stage III-IV (95.6%).

Metabolic Parameters

pSUVmax was lower in ALK positive patients (7.3 ± 4.2) compared to EGFR positive (11.1 ± 5.6) (p = 0.024) and wild type patients (11.8 ± 5.5) (p =0.007), both of which were statistically significant. pSUVmax was lower in EGFR positive patients (11.1 ± 5.6) compared to wild type patients (11.8 ± 5.5). However, the difference was not found to be statistically significant (p = 0.589).

To determine the cut-off value of the pSUVmax for predicting ALK mutation status, receiver operating characteristic (ROC) curves were plotted. The ROC curve revealed a cut-off point for pSUVmax of 11.0 with area under the curve (AUC) of 0.709 (95 % CI, 0.55- 0.96) with p = 0.026

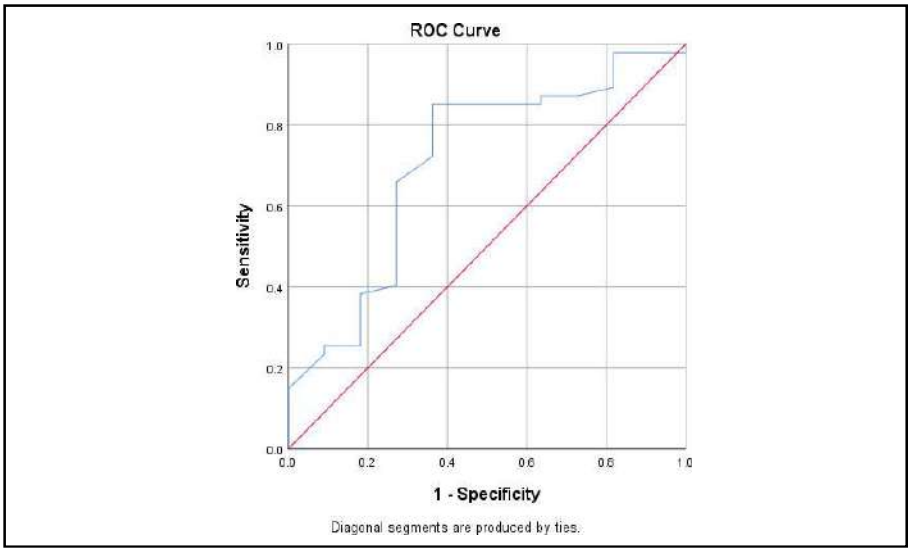


Figure 2. ROC curve plotted to obtain cut-off for pSUVmax to predict ALK mutation status

SUL_{peak} was lower in ALK positive patients (5.8 ± 3.1) compared to EGFR positive (9.1 ± 5.6) (p = 0.017) and wild type patients (9.7 ± 4.3) (p = 0.003), both of which were statistically significant. SUV_{mean} was also lower in ALK positive patients (4.4 ± 2.4) compared to EGFR positive (6.7 ± 3.6) (p = 0.024) and wild type patients (7.1 ± 3.4) (p = 0.006), both of which were statistically significant.

The data for $nSUV_{max}$ was obtained in patients who had regional nodal metastasis, i.e., in 78 out of 100 individuals (78 %), out of which 33 were EGFR positive (80.4 %), 11 were ALK positive (78.5 %) and 34 were wild type (75.6 %). $nSUV_{max}$ was lower in EGFR positive patients (7.7 ± 4.2) compared to ALK positive (9.5 ± 6.0) and wild type patients (8.3 ± 4.4), neither of which were statistically significant (p = 0.284 and p = 0.604 respectively).

The data for $mSUV_{max}$ was obtained in patients who had distant extra thoracic metastasis, i.e. in 63 out of 100 individuals (63 %), out of which 30 were EGFR positive (73.2%), 9 were ALK positive (64.2 %) and 24 were wild type (53.6 %). $mSUV_{max}$ was lower in EGFR positive patients (9.3 ± 5.2) compared to wild type patients (12.16 ± 4.2) which was statistically significant (p = 0.033).

Average SUV_{max} was calculated as average of $pSUV_{max}$, $nSUV_{max}$ and $mSUV_{max}$ in patients with nodal and distant metastases. Average SUV_{max} was lower in ALK positive patients (8.4 ± 5.1) compared to EGFR positive patients (9.3 ± 4.3) and wild type patients (10.5 ± 4.4) neither of which was statistically significant (p = 0.546 and 0.15 respectively).

Mann- Whitney U test was used to compare continuous variables with non-normal distributions, such as MTV and TLG. MTV and TLG were lower in patients with EGFR mutation compared to wild type patients which were statistically significant with p= 0.009 and p=0.013 respectively. TLG was lower in ALK positive compared to wild type patients, which was also statistically significant (p = 0.024).

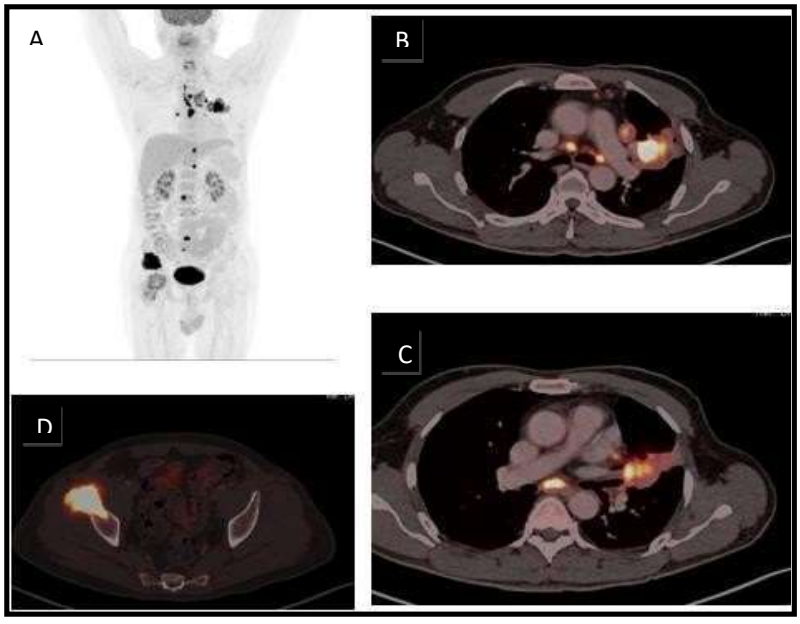


Figure 3. **A**- MIP image, **B**- Fusion image of F-18- FDG PET/CT in a 57 year old male with poorly differentiated lung adenocarcinoma of upper lobe of left lung, measuring 2.9 x 2.7 cms. SUVmax- 20.7, SULpeak- 13.7, SUVmean- 11, MTV- 6.3,TLG- 71 with nodal and distant metastases (Stage IVB). **C**- Metabolically most active regional subcarinal node and **D**- Distant skeletal metastasis in the right ilium. The patient tested positive for EGFR mutation.

Discussion

Since TKIs targeting EGFR and ALK have substantially improved survival in patients with NSCLC, genomic profiling has become the standard of practice for advanced NSCLC patients. For NSCLC, next-generation sequencing (NGS) is recommended to detect gene mutations or rearrangements [4]. However, tumor inaccessibility, insufficient sample tissue for identification, and patients' unwillingness to undergo invasive diagnostic techniques are all factors that can limit it. PET/CT has the added advantage of being a non- invasive method which can predict the status of EGFR and ALK mutations.

Reduced $pSUV_{max}$ was associated with EGFR positive status, according to Zhilei Lv et al. [5], and could be used with other clinical criteria to predict EGFR mutation status in some NSCLC patients who did not have access to genetic testing. Low $nSUV_{max}$ and $mSUV_{max}$ were likewise linked to the presence of an EGFR mutation. In our study, $mSUV_{max}$ was lower in EGFR positive patients (9.3 + 5.2) compared to wild type patients (12.16 + 4.2) which was statistically significant ($p = 0.033$), consistent with the above study. $pSUV_{max}$ was shown to be unrelated to ALK status in the above study. However, the study included all subtypes of NSCLCs like adenocarcinoma, squamous cell carcinoma and large cell carcinoma whereas our study included only adenocarcinomas. This might explain the discrepancy in these findings.

Hongyoon Choi et al. [6] found that ALK-positive lung cancer had higher glucose metabolism and faster nodal or distant metastases than EGFR-mutated and wild-type lung adenocarcinoma, implying that ALK rearrangement is more aggressive. The ALK positive group had a higher SUV_{max} of primary lesion than the EGFR positive and wild type groups (12 ± 7.86, 4.42 ± 3.61, and 5.96 ± 5.07, respectively). However, the study had a heterogeneous population with respect to stage, with 125 out of 156 (80.1%) from EGFR group belonging to stage I and II, 105 of 157 (66.9%) from wild type group belonging to stage I and II, but only 4 out of 18 patients (22.2%) from ALK positive group belonged to stage I and II. Also, the prevalence of ALK rearrangement in the patient population was not big enough to have statistical significance. Our study being prospective had no selection bias. Moreover, the patient sample was homogeneous with respect to the stage, with 92.7 % of EGFR group, 92.9 % of ALK group and 95.6 % of wild- type group belonging to stage III-IV. Also, 14% of the population was ALK positive which was considerably higher to assume statistical significance.

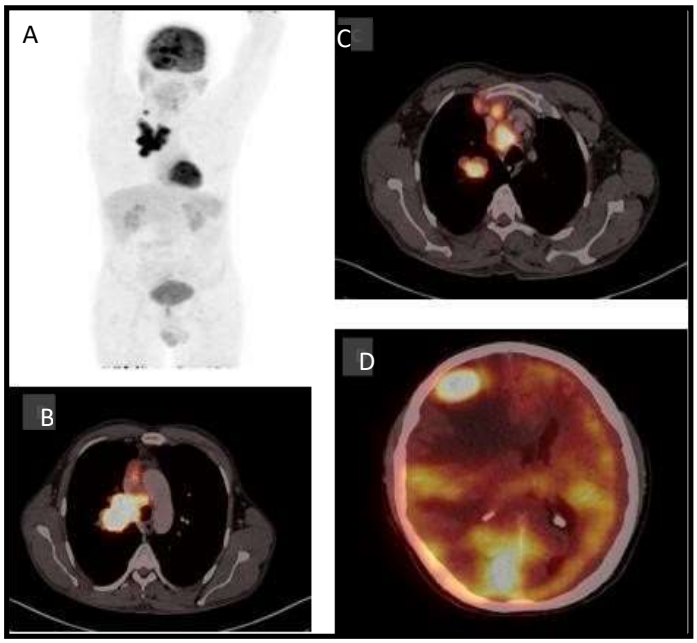


Figure 4. **A**- MIP image, **B**- Fusion image of 18F-FDG PET/CT in a 45 year old male with moderately differentiated lung adenocarcinoma of upper lobe of right lung, measuring 9.8 x 5.0 cms. SUV_{max}- 15.7, SUL_{peak}- 14.2, SUV_{mean}- 10.4, MTV- 51.3, TLG-534.8, with nodal and brain metastases (Stage IVB). **C**- Metabolically most active regional right upper paratracheal node and **D**- Distant brain metastasis in the right frontal lobe. The patient tested negative for both ALK and EGFR mutation.

According to Ao Liu et al [7], NSCLC patients with EGFR mutationsexhibited lower MTV than wild type patients ($p = 0.001$), which is similar to our findings. Patients with EGFR mutations had significantly lower SUV_{mean} values ($p = 0.031$) than those with wild-type EGFR. No statistically significant link was established between EGFR mutation positive and wild type patients in terms of SUV_{max}, similar to our study.

Bin et al. [8] conducted a retrospective study and found that 18F-FDG PET/CT metabolic characteristics combined with clinicopathological information had moderate diagnostic efficacy in predicting EGFR mutation status and were associated with prognosis in EGFR mutation positive and negative NSCLC, providing a pointer for personalized targeted therapy. It showed that EGFR positive patients had decreasedMTV and TLG, which matched our findings. EGFR positive patients had a lower SUV_{max} than wild type patients in this study.

Raymond et al [9] found increased FDG avidity in the EGFR wild type group with greater normalized SUV_{max} in a retrospective study. The normalized SUV_{max} was computed by dividing the lesion's SUV_{max} by the SUV of blood in the pulmonary artery. To discriminate between wild-type and EGFR mutation positive tumors, ROC curve analysis produced an area under the curve of 0.62, with a threshold > 5.0.

Lei et al. [10] found that measurements in FDG-PET/CT have limited predictive potential for the existence of EGFR mutation in lung adenocarcinoma. SUV_{max}, SUV_{mean}, SUV_{peak}, and SUVratio (the ratio of the primary tumor to the mediastinal blood pool) were all lower in EGFR-mutated tumors than in wild-type cancers. It hypothesized that EGFR positive pulmonary adenocarcinomas maybe physiologically more indolent than the EGFR-wild type ones, with reduced glucose metabolism.

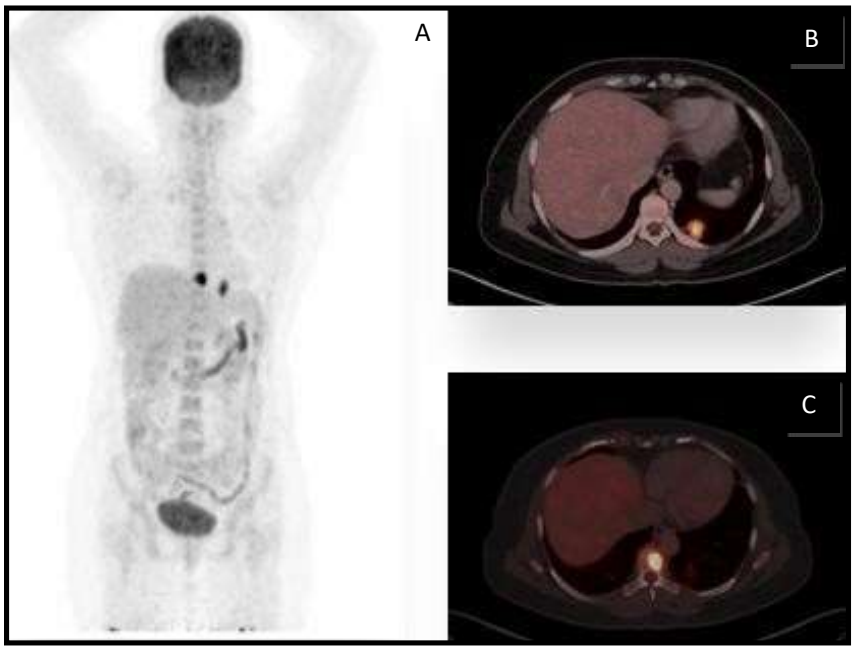


Figure 5. **A**- MIP image, **B**- Fusion image of 18F-FDG PET/CT in a 51 year old female with poorly differentiated lung adenocarcinoma of lower lobe of left lung, measuring 1.9x 1.8 cms. SUV_{max}- 9.8, SUL_{peak}- 6.9, SUV_{mean}- 5.9, MTV- 3.1, TLG- 18, with solitary skeletal metastasis (Stage IVA). **C**- Metabolically most active skeletal metastasis in **D**8 vertebra. The patient tested positive for ALK mutation.

According to a study by Kazuya Takamochi et al. [11], EGFR positive adenocarcinomas were physiologically indolent, with likely lower glucose metabolism than wild-type tumors. EGFR mutations were more common in tumors with lower SUV_{max}, while KRAS mutation status had no correlation with SUV_{max}.

SUV_{max} may be a predictive factor for EGFR mutation status, and MTV and TLG of primary tumors are promising prognostic indicators, according to a retrospective study by Il Ki Hong et al [12]. When EGFR positive tumors were compared to EGFR wild type tumors, the mean SUV_{max} was lower. Low SUV_{max} was found to be substantially linked to the presence of an EGFR mutation.

A possible explanation to these variances in the above studies can be that SUV_{max} can vary with different PET scanners, fasting time, plasma glucose level, and other factors, whereas MTV gives a more comprehensive overview of the overall metabolic activity of the tumor.

In our study, we found that various metabolic parameters were found to be reduced in both EGFR and ALK positive patients, when compared to wild- type patients. While ALK positive patients had a lower $pSUV_{max}$, SUL_{peak}, SUV_{mean} and TLG, EGFR positive patients had a lower $mSUV_{max}$, MTV, and TLG compared to wild type population. The $pSUV_{max}$ cutoff of ≤11 was found to be a predictor for ALK rearrangement. The mean pSUVmax for EGFR positive patients was 11.1 ± 5.6 and that of wild type patients was 11.8 ± 5.5 in comparison.

However, $pSUV_{max}$, SUL_{peak}, SUV_{mean} did not correlate with the presence of EGFR mutation. Considering the limitation of SUV_{max}, an alternative variable like metabolic tumor volume (MTV) and tumor lesion glycolysis (TLG) can be explored to assess the relationship between EGFR mutation status and PET/CT metabolic parameters, as our study demonstrated a lower MTV and TLG in EGFR mutated patients and lower TLG in ALK positive compared to wild type patients.

Conclusion

Based on this study, it was concluded that FDG- PET/CT can be used as a surrogate non-invasive tool that may provide important information in patients in whom tumor tissue is not available, although genetic testing continues to be the gold standard. PET/CT can help the clinician in assessing the disease prognosis, provide the appropriate treatment without delay, and better patient counseling for further management, as a surrogate marker which needs further support from trials. However, a multi-institutional trial on a larger population for a longer duration would further is needed for further modification of findings of the study.

Conflicts of interest

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

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ORIGINAL ARTICLE

A prospective observational study of the impact of the quadratus lumborum block (QLl1B) on post operative pain after laparoscopic ventral hernia repair

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Abstract

Aims & Objectives: To evaluate the outcome of addition of a pre operative quadratus lumborum type 1 nerve block (QL1B) in an elective laparoscopic ventral hernia repair.

Material and Methods: Prospective, observational, single-center study with patients scheduled for elective laparoscopic ventral hernia repair. After taking informed consent, patients underwent Laparoscopic IPOM (Intra Peritoneal Onlay Mesh) Repair of the hernia with mesh fixed using tackers. Preoperative QL1 Block was given to all patients after induction of anaesthesia. Pain scores at 2-, 6-, 12-, and 24-hours post-surgery were noted using a visual analogue scale (VAS). The need for rescue analgesics and total requirement of analgesics postoperatively was noted.

Results: A total of 35 patients were enrolled for the study. The mean VAS score at 2-, 6-, 12- and 24-hours post-surgery was found to be 5.11, 4.14, 3.14, 2.31 respectively. Twenty nine patients (82.86 %) were managed with routine post operative analgesia (Total 4 gm. intravenous paracetamol) while six patients (17.14%) required an additional rescue analgesic. [Inj. Tramadol Hydrochloride (Total dose 100 mg.) in 5 patients and Inj. Diclofenac Sodium (Total dose 150 mg.) in 1 patient].The average time taken till the requirement of rescue analgesic was 3.83 hours.

Conclusions: The QL1 Block appears to provide adequate analgesia that may last for up to 24 hours post laparoscopic IPOM repair. It should be considered as part of a multimodal postoperative pain management regimen to reduce post-operative pain and enhance recovery in patients undergoing a laparoscopic IPOM repair.

Keywords: Laparoscopic ventral hernia (IPOM), Quadratus lumborum block (QLB), VAS score, post-operative pain

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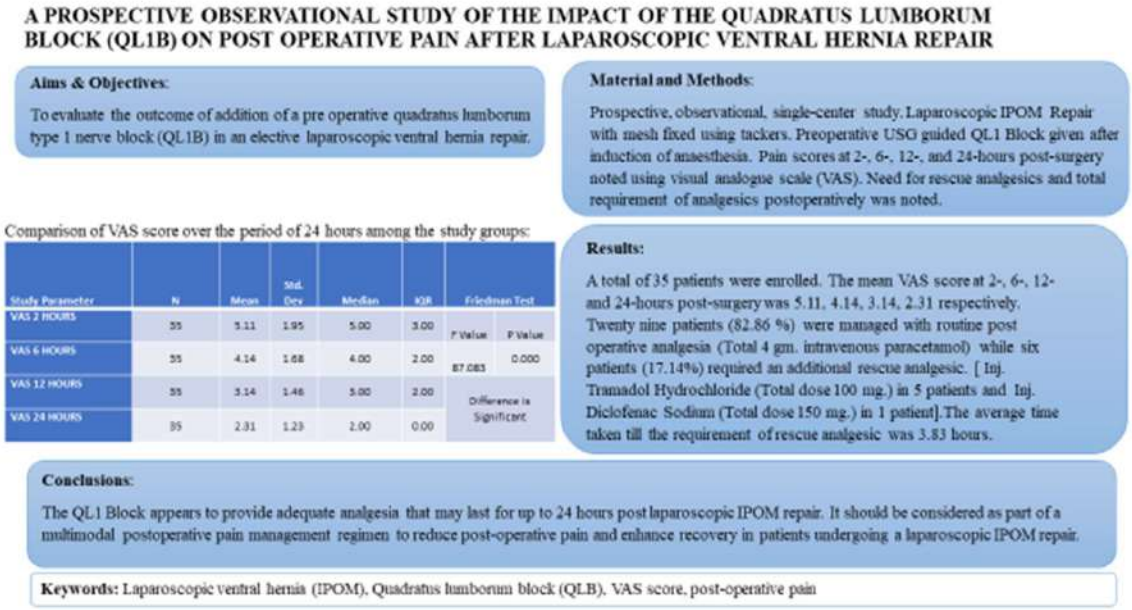
Graphical Abstract



Introduction

A hernia is an abnormal protrusion, bulge, or projection of an organ or part of an organ through the body wall that normally contains it [1].

Ventral hernias occur anteriorly including primary ventral hernias (epigastric, umbilical, Spigelian), parastomal hernias, and most of the incisional hernias (ventral incisional hernias). They may be repaired with sutures, mesh, or advanced techniques such as component separation. Simple sutured repair is performed using an open approach while mesh repair and component separation may use open, laparoscopic or robotic techniques [2].

Mesh may be placed above the fascia (onlay), between the rectus muscles and peritoneum/posterior rectus sheath (sublay), below the peritoneum (underlay or intraperitoneal onlay [IPOM]), or in between fascial edges (inlay). The onlay and sublay techniques use an open surgical approach, whereas underlay (IPOM) technique may be open or laparoscopic. The inlay technique bridges the fascial defect with mesh and is used only when the fascial defect is too large to primarily close with any other techniques [3,4,5].

Laparoscopic ventral hernia repair involves placement of a mesh in an underlay/IPOM position which is fixed to the anterior abdominal wall with transfascial sutures, tacks, or a combination of the two.

This is a commonly performed procedure associated with significant postoperative pain. This leads to increased morbidity and a delayed postoperative recovery with prolonged hospital stay, thus negating the benefits of short hospital stay and early return to normal activities offered by laparoscopy [6,7,8]. Persistent unrelieved postoperative pain is associated with complications like hypoxemia, pulmonary atelectasis, deep vein thrombosis, and delayed ambulation [9,10,11,12].

Postoperative pain is managed with intravenous (IV) and oral analgesics, however, these have their own risks, such as nausea, sedation, respiratory depression, constipation, increased bleeding, kidney or liver dysfunction.

Peripheral nerve blocks may help reduce this post-operative pain and facilitate an early return to daily activity. If these blocks are

given pre operatively, the intraoperative anaesthetic and analgesic requirements, especially of opioid analgesics may be reduced leading to early recovery and reduced opioid side effects. The use of regional anaesthetic blocks like the transversus abdominis plane (TAP) block has been shown to reduce post-operative pain and facilitate an early recovery [13].

The quadratus lumborum (QL) block involves injection of local anaesthetic (LA) in a fascial plane formed partly by the posterior surface of the QL muscle under ultrasound guidance. It has been shown to produce anaesthesia of the anterior abdominal wall in the T7 to L1 dermatome distribution. Compared with ultrasound-guided TAP blocks, QL blocks can cover more extensive dermatomes with better cephalad and posterior spread. QL blocks may provide both visceral and somatic analgesia, likely due to paravertebral and possibly epidural spread[14,15].

There is insufficient data available for the correlation of quadratus lumborum blocks and their effects in laparoscopic ventral hernia repair surgeries. There is also a lack of Indian studies available on the impact of these regional anaesthetic blocks on post-operative recovery following laparoscopic ventral hernia (IPOM) repair.

This study aims to evaluate if the addition of the quadratus lumborum peripheral nerve block (QL1 block) pre operatively can decrease post-operative pain scores up to 24 hours and decrease the overall need of post-operative analgesics.

Patient and Methods in Clinical Studies

A prospective, observational, single center study was conducted at Kokilaben Dhirubhai Ambani Hospital and Medical Research Institute from 31st August 2020 to 31st May 2021.

Inclusion Criteria:

Patients of either sex, 18 years and above, ASA class 1-3, scheduled for elective laparoscopic ventral hernia repair who voluntarily agreed to sign informed consent form.

Exclusion Criteria:

Patients known or believed to be pregnant; with significant renal, hepatic disease; ASA class 4-5; known hypersensitivity and/or allergies to local anaesthetics or emergency/complicated surgery in view of obstruction/perforation of bowel.

Procedure followed:

Patients were admitted one day prior to surgery and pre-operative evaluation done. After taking written informed consent for surgery and pre-operative QL1 block, patients underwent Laparoscopic Ventral Hernia Repair (IPOM) under general anaesthesia. Standard ASA monitoring of heart rate, electrocardiogram, noninvasive blood pressure, pulse oximeter and end tidal carbon dioxide with anaesthesia gas analyzer used.

Inj. Propofol 2-3 mg/kg and Inj. Fentanyl1- 2 mcg/kg used for induction of anaesthesia. Muscle relaxation achieved by Inj. Atracurium or Inj. Cisatracurium. Sevoflurane or Desflurane with oxygen and air was used for maintenance. Inj. Paracetamol 1g. was administered intravenously to all patients.

Under all aseptic precautions, a pre-operative quadratus lumborum 1 block under ultrasound guidance was given, after induction of anaesthesia, with patient in supine position. A linear ultrasound transducer (6 to 18 Hz) (Sonosite™ Turbo probe, Bothell, WA, USA) was placed in axial plane at midpoint between costal margin and iliac crest, in the mid axillary line.

The external oblique, internal oblique (IO), transversus abdominis (TA) muscles, and the peritoneal cavity were visualized, muscles traced laterally until a tail was seen where the TA merges with the IO, becoming the transversalis fascia. The QL muscle was identified deep to the transversalis fascia.

At the point where the transversus abdominis muscle ends and the quadratus lumborum (QL) muscle begins, a 22-gauge, 100- to 150-mm echogenic needle was inserted in-plane in medial to lateral direction until the needle tip penetrates the posterior aponeurosis

of the transversus abdominis muscle. Position was confirmed by injecting normal saline between the aponeurosis and TLF at the lateral margin of the QL muscle.

After negative aspiration, 20 mL of 0.2% Ropivacaine was injected in 5-mL increments, with gentle aspiration between injections. Expansion of the fascial space visualized as LA was injected and quadratus muscle displaced downward. Similar procedure repeated on the opposite side. Totally 40 ml of 0.2% ropivacaine (20 ml. on either side) was used for the block. Maximum toxic dose of 2mg/kg of body weight was not exceeded.

All patients received Inj. Cefuroxime 1.5 gm. intravenous single dose perioperatively. Standard 3 trocar placement with 2 working ports (5 mm and 10 mm), one camera port (5 mm 30-degree standard laparoscope) and pneumoperitoneum created. Hernia sac was identified, adhesiolysis done, contents of hernia reduced.

A dual mesh of appropriate size as per size of defect was selected and fixed using double layer of permanent titanium tacks (double crown technique) delivered by ProTack™ 5mm (Autosuture, Tyco Healthcare, USA) device. Haemostasis checked, pneumoperitoneum evacuated, 10 mm camera port site sheath closed using synthetic absorbable surgical suture polyglactin No. 1, and skin incisions sutured using absorbable sutures.

All patients were given intravenous paracetamol 1 gm. 6 hourly as routine post-operative analgesia. NSAIDs were the primary rescue analgesics used, opioid analgesics being the next option if NSAIDs were contraindicated or pain relief was inadequate after the first dose of NSAIDs.

Measurement of outcome of interest:

1. Visual Analogue Scale for assessment of pain at 2, 6, 12 and 24 hours post-surgery.

2. In case of requirement of rescue analgesic, time till use of rescue analgesic (in hours).

3. Total requirement of analgesics in the post-operative period.

Results and Analysis

On analyzing the results using standard statistical analysis tools, the mean VAS score at 2-, 6-, 12- and 24-hours post-surgery was 5.11, 4.14, 3.14, 2.31 respectively which is lower than that observed in available historical data.

Out of 35 patients, 29 patients (82.86 %) required only routine post-operative intravenous analgesics; 6 patients (17.14%) required additional intravenous rescue analgesic (NSAIDs or opiates) for adequate pain relief.

Thus, within the first 24 hours of surgery, 29 of 35 patients (82.86%) received 4 gm. intravenous paracetamol; 1 of 35 patients (2.86%) received 4 gm. intravenous paracetamol and 150 mg. diclofenac sodium; and 5 patients (14.29%) received 4 gm. intravenous paracetamol and 100 mg. tramadol hydrochloride.

The average time taken till the requirement of rescue analgesic was 3.83 hours.

Table 1. Comparison of VAS score over the period of 24 hours among the study groups

Study Parameter	N	Mean	Std. Dev	Median	IQR	Friedman Test	
VAS 2 HOURS	35	5.11	1.95	5.00	3.00	F Value	P Value
VAS 6 HOURS	35	4.14	1.68	4.00	2.00	87.083	0.000
VAS 12 HOURS	35	3.14	1.46	3.00	2.00	Difference is Significant	
VAS 24 HOURS	35	2.31	1.23	2.00	0.00		

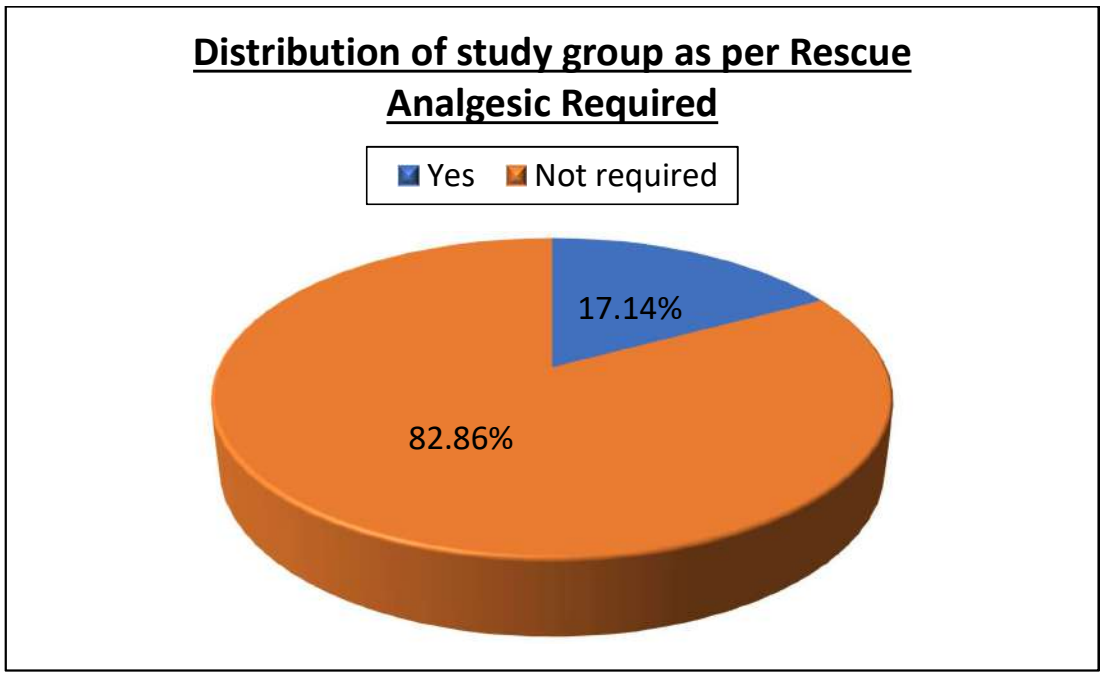


Figure 1. Distribution of study group as per requirement of rescue analgesic

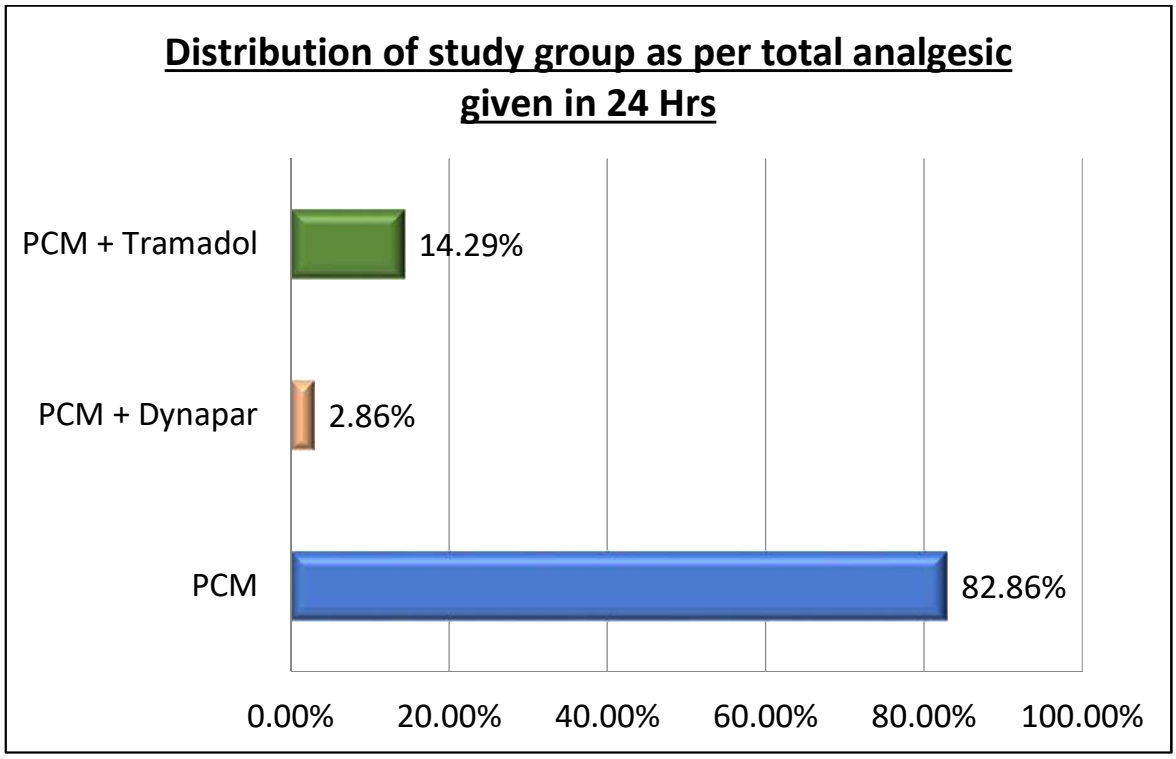


Figure 2. Total analgesic given in first 24 hours

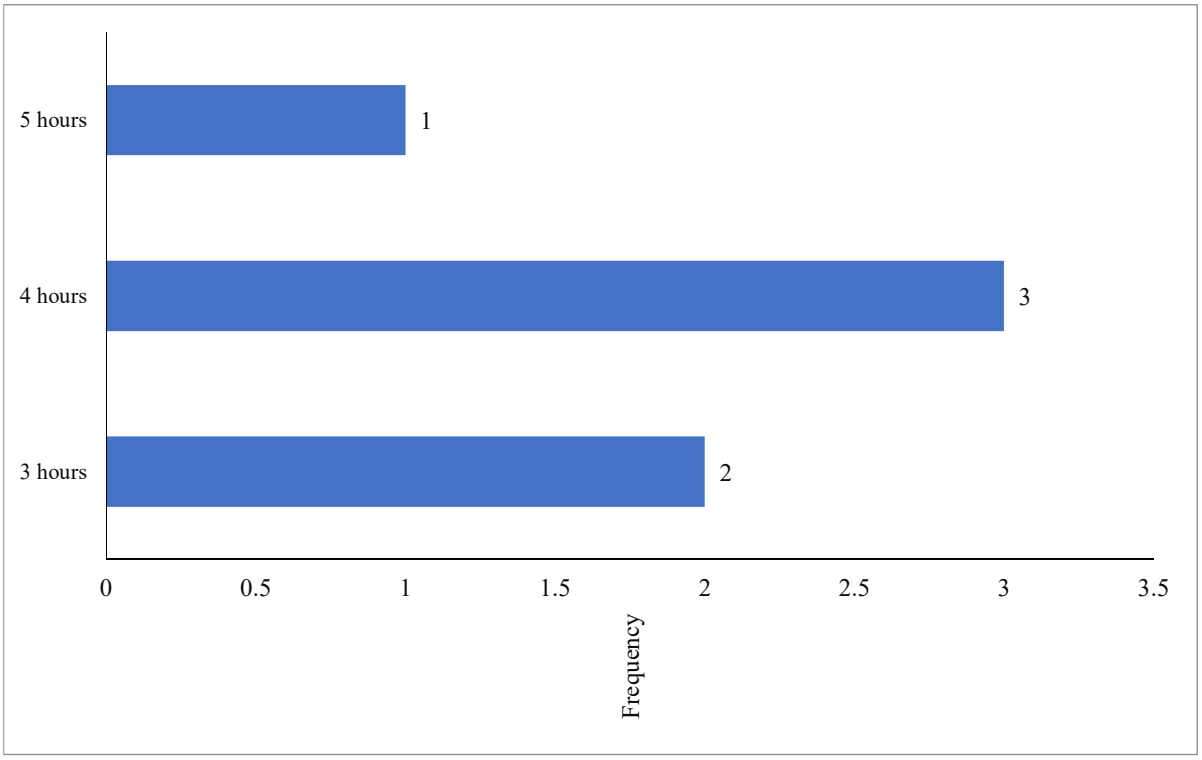


Figure 3. Time till rescue analgesic was required

Table 2. VAS score over 24 hours when classified according to patients who required rescue analgesics

	Required					Not required					Mann-Whitney U	P Value
	No	Mean	Std Dev	Median	IQR	No	Mean	Std Dev	Median	IQR		
VAS 2 HOURS	6	7.50	1.38	7.00	1.00	29.00	4.62	1.68	4.00	2.00	-3.196	0.001
VAS 6 HOURS	6	6.00	2.10	5.50	4.00	29.00	3.76	1.33	4.00	1.00	-2.466	0.014
VAS 12 HOURS	6	4.67	1.21	4.00	1.00	29.00	2.83	1.31	2.00	2.00	-2.866	0.004
VAS 24 HOURS	6	4.00	1.67	4.00	1.00	29.00	1.97	0.78	2.00	0.00	-3.442	0.001

Clinical Images (Figures 4-7):

Figure 4. Probe position for QB type 1 block

Figure 5. Needle position for Ultrasound guided QL type 1 block

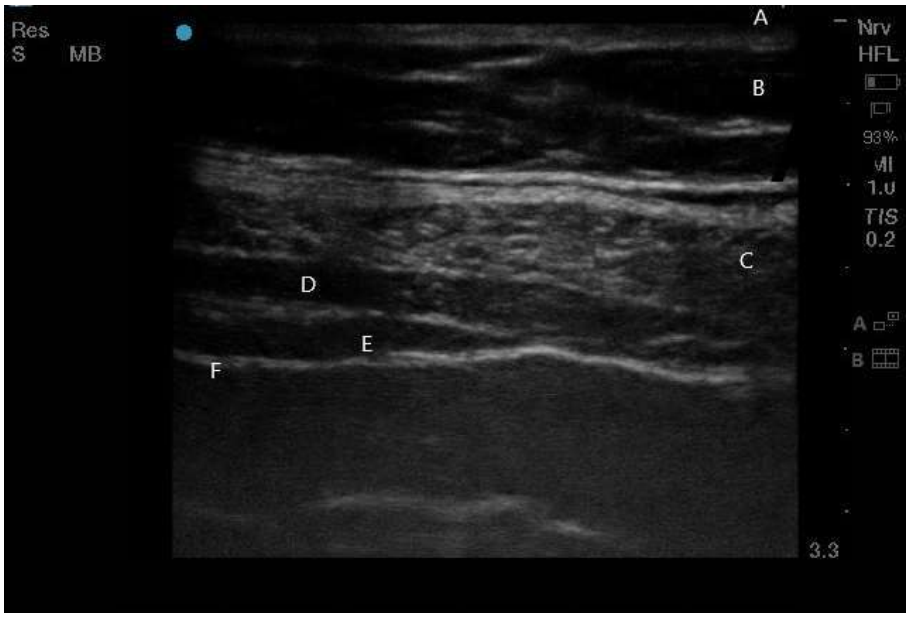


Figure 6. Normal anatomy visualized during QL type1 Block

A – Skin, B – Subcutaneous tissues, C – External Oblique, D – Internal Oblique, E – Quadratus Lumborum, F – Transversalis Fascia

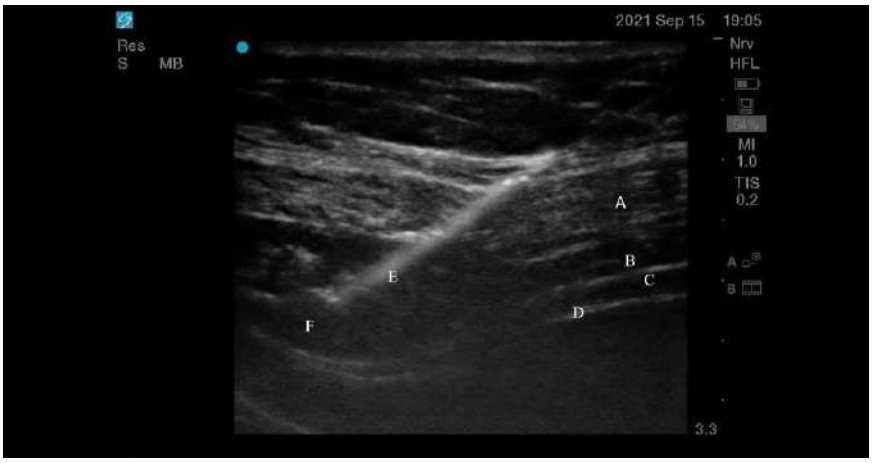


Figure 7. QLB1 block in progress

A – External Oblique, B – Internal Oblique, C – Quadratus Lumborum, D - Transversalis Fascia, E – Needle tip, F – Local Anaesthetic spread

Discussion

This was a hospital based, prospective, observational, single center study to evaluate the efficacy of an ultrasound guided Quadratus Lumborum type 1 Block in providing postoperative analgesia in patients who underwent an elective laparoscopic ventral hernia repair.

Current literature on the QL block describes 4 different types/approaches. The lateral, anterior, posterior and the trans muscular variants [16,17]. In our study we used the type 1 i.e., lateral QLB.

A total of 35 patients presenting with ventral hernias were enrolled in the study. Of these, 23 patients (65.71%) were females while 12 patients (34.29%) were males, indicating a female preponderance. This is similar to previous studies which suggest that ventral hernias occur more frequently in females than in males with a ratio of 3:1 [18].

The mean age of presentation of patients was 55 years. 24 out of 35 patients (68.57%) belonged to ASA II category, 9 patients (25.71%) were ASA I whereas only 2 (5.71%) was ASA III. 32 patients (91.43%) had no history of allergies to any medications. No patient had a history of allergy to any local anaesthetic.

The mean VAS score in our study at 2, 6-, 12- and 24-hours post-surgery was found to be 5.11, 4.14, 3.14, 2.31 respectively. When the VAS scores at 2-, 6-, 12- and 24-hours post-surgery were examined within the study group, a statistically significant difference was identified between scores at 2 hours and those at 6 hours, 12 hours and 24 hours.

The pain seen after a laparoscopic ventral hernia repair is largely related to mesh fixation techniques. Early post-operative pain is thought to be secondary to dissection in the area of mesh application. A large number of studies have been done comparing various mesh fixation techniques and their outcomes including early and chronic post-operative pain [19,20,21,22,23].

A randomized control study conducted by Bansal et al. compared the long-term outcome and quality of life after laparoscopic repair of incisional and ventral hernias with suture fixation with and without tacks [22]. In this study, mean VAS score at 1, 6 and 24 hours was observed to be 6.1 ± 1.7 (2–10), 5.6 ± 1.8 (1–10) and 3.9 ± 1.5 (1–8) in the group using transfascial sutures and tacker (double crown method). Persistently higher pain scores were seen in the patients who had undergone tacker mesh fixation as compared to those with only suture fixation.

A study conducted by Muysoms et al. [23] compared mesh fixation using the ‘double crown’ technique with fixation using sutures

and tacker. It showed a significant lower mean VAS score 4 hours post-operatively at rest and during coughing in the double crown group as compared to the group where both sutures and tacker were used (3.1 and 5.2 versus 4.4 and 6.8 respectively).

A randomized clinical trial by Eriksen et al. [20] comparing fibrin sealant and titanium tacks for mesh fixation in laparoscopic ventral hernia repair reported significantly lower pain scores during post-operative day (POD) zero to POD 10 when fibrin sealant was used.

A trial by Chawla et al. [24]studying the impact of mesh soakage with bupivacaine solution versus normal saline solution on post-operative pain found a statistically significant difference in mean VAS at 6 hours post surgery where bupivacaine solution was used (5.05 ± 1.2) compared to where normal saline was used (5.54 ± 1.1). However, mean VAS at 24 hours post operatively was not significantly different (3.16 ± 1.2 and 3.58 ± 1.4 respectively).

A simple way to prevent pain caused by fixation materials would be to use no fixation at all. A few studies have compared tacks versus no fixation, both in TEP repairs for inguinal hernias. There was a tendency towards less pain in the no fixation group[25,26].

VAS scores of the patients over 24 hours were compared among the study population when classified according to gender, ASA grade, reducibility and duration of hernia, whether the hernia was recurrent or a primary ventral hernia and as per requirement of rescue analgesic. There was no significant difference found in VAS score when patients were classified as per gender. The mean VAS score at 2, 6, 12 and 24 hours was 5, 4, 3.25 and 2.25 respectively in males and 5.17, 4.22, 3.09 and 2.35 respectively in females.

Mean VAS score at 2, 6, 12 and 24 hours was 5.27, 4.18, 3.09 and 2.27 respectively where duration of hernia was up to six months and 2.05, 1.70, 1.40 and 1.01 respectively when more than 6 months. The mean VAS score was observed to be lower in those with long standing hernias however the difference was not found to be statistically significant (p value > 0.05).

There was no statistically significant difference seen when VAS score was compared amongst patients with recurrent and primary ventral hernias. The mean VAS score at 2, 6, 12 and 24 hours was 4.68, 3.95, 2.86 and 2.14 respectively in patients with a reducible hernia and 1.63, 1.71, 1.56 and 1.61 respectively in those with irreducible hernias.

Although the mean VAS score was observed to be lower in those patients who had an irreducible hernia; the difference was not found to be statistically significant (p value >0.05). There was no statistically significant difference seen in VAS score when patients were classified as per ASA grade, however it was observed that ASA III patients appeared to have a higher pain score at all time intervals when compared to ASA 1 and ASA II patients.

The VAS score was significantly higher (p value < 0.05) in patients who required a rescue analgesic when compared to those who did not require one. The mean VAS score at 2, 6, 12 and 24 hours was 7.50, 6, 4.67 and 4 respectively in those who required a rescue analgesic and 4.62, 3.76, 2.83 and 1.97 respectively in those who did not.

Alleviation of postoperative pain after laparoscopic ventral hernia repair in patients given a preoperative QLB may be effective as majority of the patients remained comfortable. Analgesia lasted for 24 hours in most patients. Ishio and colleagues conducted a study [27] on the efficacy of ultrasound-guided posterior QLB in treating postoperative pain following laparoscopic gynaecologic surgeries and concluded that posterior QLB significantly reduces postoperative pain in movement and at rest.

A study conducted by Kadam et al.[28] used QL block under ultrasound guidance as the postoperative analgesia technique in a laparotomy case and recommended QL block for major abdominal surgeries. A study conducted by Hesham Elsharkwy et al., using anterior QL block with liposomal bupivacaine

showed analgesia lasting up to 48 hours and a sensory level from T7 to L1 [29].

Various studies have proven that duration of analgesia achieved with single shot technique exceeds expectations and lasts for more than 24 hours especially when a long acting local anaesthetic agent is used [30,29].

Although QLB seems similar to Transversus Abdominis Plane (TAP) block, the point of injection, the spread of drug, the levels of analgesia achieved and the duration of action vary widely from that of TAP block [28,31].

Studies show the main advantage of QLB is the wider spread of the local anaesthetic agent which produces an extensive analgesia and prolonged duration of action. QL blocks cover more extensive dermatomes and may also provide somatic and visceral analgesia likely due to paravertebral and possible epidural spread [14,15].

Ultrasound guided TAP blocks might not consistently produce a sensory level above the umbilicus unless a subcostal injection is added. The localized effects of the TAP block have minor contributions to pain control in comparison with analgesia achieved by extension into paravertebral space [29]. Studies have shown a reduction in 24-hour postoperative opiate consumption after administration of the quadratus lumborum block [32,31].

As QLB involves manipulation of the fascia where blood vessels exit from the paravertebral space, it should be used with caution in people receiving anticoagulant therapy due to risk of hematoma formation. Lower-extremity muscle weakness after QL block has been reported as a complication by Hironobu Ueshima et al. after a posterior and an anterior QL block. However, no such incidents have been reported with respect to lateral QLB [33].

Needle trauma like unintentional puncture of the peritoneum, intestine, liver, kidney, large blood vessels associated with blind methods could be overcome by performing the block under ultrasound guidance, with mandatory monitoring of the needle tip prior to injection of the drug. We did not come across any complications due to the QLB technique in our study.

Epidural anaesthesia used to be considered the standard for perioperative analgesia, however a shift from open to laparoscopic surgery has diminished its advantages. Analgesia employing epidural techniques is often not clinically superior to its alternatives; is associated with a small but relevant number of serious complications; and has a relatively high failure rate[34].

Studies have shown less post-operative nausea and vomiting, decreased post-operative sedation, decreased length of hospital stay and earlier urinary catheter removal when abdominal trunk blocks are used [35]. Improved early oral intake and early mobilization are easily achieved with good pain control. Quadratus Lumborum Block has a great potential in this area of Enhanced Recovery After Surgery (ERAS) protocol.

Conclusion

This study showed that the quadratus lumborum type I block appears to provide adequate analgesia that may last for at least up to 24 hours post-surgery. In the majority of patients enrolled in the study, only the routine non opioid post-operative analgesic medications were required for adequate pain relief. In the setting of availability of adequate infrastructure and clinical expertise for giving safe and efficient regional anaesthetic blocks such as the quadratus lumborum block; and in absence of contraindications for the same, the practice of peri operative blocks may be included in routine practice to enhance the postoperative recovery of patients undergoing laparoscopic ventral hernia (IPOM) repair.

Conflicts of interest

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

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ORIGINAL ARTICLE

Study of Electrocardiographic Changes in Patients of Chronic Kidney Disease

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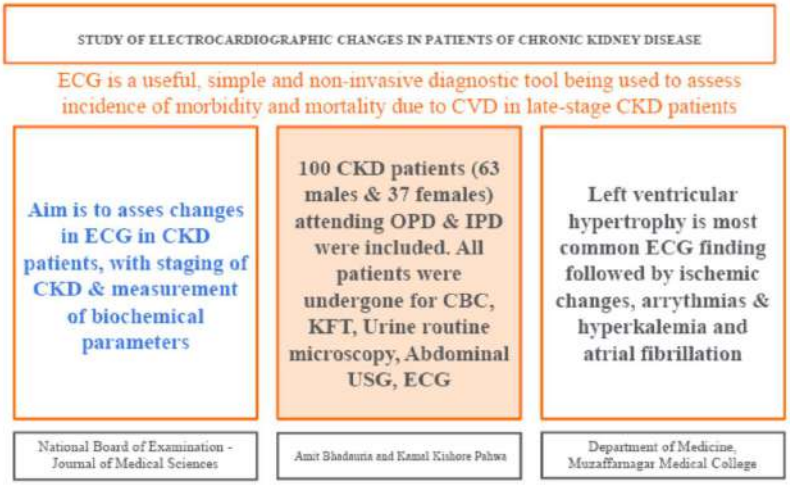
Abstract

CKD and its associated risk factors cause a rise in tendency to develop the cardiovascular (CV) diseases. The spectrum of CVD consists of left ventricular hypertrophy, congestive heart failure, ischemic heart disease, peripheral vascular disease and arrhythmias. The objective of the current investigation is to recognise electrocardiographic alterations in people with chronic diseases. A total of 100 CKD patients (63 males & 37 females) attending OPD & IPD were included. All patients were undergone for CBC, KFT, Urine routine microscopy, Abdominal USG, ECG. The present study shows subjects with electrocardiographic changes in chronic kidney disease. Maximum 36% cases were with LVH, followed by 22% cases being normal, 10% eachwere with ischemia and conduction abnormalities, Hyperkalemia 3%, Atrial fibrillation seen in 2% cases. To detect any early indication of CVD, regular ECG monitoring is necessary.

Keywords: CKD, CVD, ECG, LVH

Graphical Abstract



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Introduction

Chronic Kidney Disease (CKD) consists of various pathophysiologic processes that are linked with abnormal function of kidney, leading to decrease in the glomerular filtration rate [1]. CKD is being explained as abnormality in the different stages of kidney, affecting its function and structure, lasting for more than 3 monthsof time and having different health implications.[2] CKD is being categorised into five different stages. Stage 1 shows a slight disturbance in kidney function; having a normal or relatively high GFR (≥90 ml/min/1.73m^2) with constant albuminuria. In Stage 2 CKD, mild reduction in GFR (60–89 ml/min/1.73m^2) is observed with damage to kidney. Stage 3 shows a moderate level of reduction in GFR (30–59 ml/min/1.73m^2). In stage 4 CKD, there is severe reduction in GFR (15–29 ml/min/1.73m^2), and in Stage 5, an established failure of kidney (GFR <15 ml/min/1.73m^2) is observed, that require a permanent renal replacement therapy [1].

The mortality rate among CKD patients has increased due to increased vulnerability to CVD more commonlyand even before time. In patients with CKD and ESRD, the spectrum of CVD consists of congestive heart failure, ischemic heart disease, peripheral vascular disease and arrhythmias. The incidence of CVD was found to be 20- 30times more in patients with ESRD, but now CVD risk is being observed in all CKD stages [2].

To detect any early indication of CVD, regular ECG monitoring is necessary [3] ECG also helps indetecting the signs of myocardial ischemia, disturbances in heart rhythm, abnormalities in chambers and cardiac conduction [4]. Thus, the current study has been conducted to analyze the electrocardiographic changes in CKD patients in Muzaffarnagar medical college and their significance with Stages of CKD.

Materials and Methods

Study design: Descriptive cross-sectional study

Study place: Department of General Medicine, Muzaffarnagar Medical College & Hospital,Muzaffarnagar, U.P.

Study Duration: One year (From 1st April 2021 to 31st March 2022)

Sample Size: 100 patients

Sample Technique: Outdoor and indoor patients of chronic kidney disease (undergoing dialysis also) attending department of General Medicine, Muzaffarnagar Medical College & Hospital, Muzaffarnagar, U.P. willbe evaluated before being taken up for the study.

Inclusion Criteria:

a) Selection of cases with CKD without considering the etiology.

b) Patients with chronic kidney disease on dialysis.

Exclusion Criteria:

a) Documented ischemic heart disease.

b) Congenital heart disease.

c) Valvular heart disease.

d) Age less than 18 years.

Study Method: The study was conducted in Muzaffarnagar Medical College and Hospital, Muzaffarnagar, U.P. on both indoor and outdoor patients of General Medicine department by following inclusion and exclusion criteria, history taking, general physical examination and relevant clinical examinations and interpretation of electrocardiograph by taking 12 lead ECG.

Data Collection Method: The data of the patients was collected in Case Record Form. The collecteddata was entered into Microsoft Excel spreadsheet.

Results

Table 1. Distribution of Study Subjects According to Gender

Gender	Number of patients (n)	Percentage (%)
Female	37	37.0
Male	63	63.0
Total	100	100.0

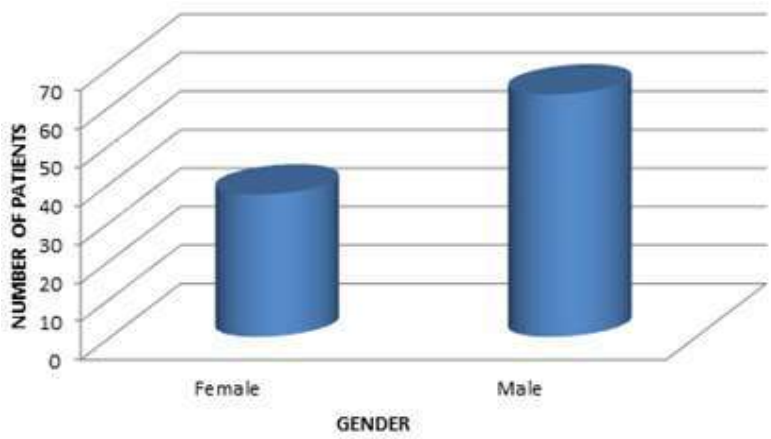

Figure 1. Distribution of study subjects accordingto gender

Table 1 and Figure 1 shows the gender distribution amongst the study subjects. Out of 100 patients included in the study 63 were males and 37 females.

Table 2. Distribution of Study Subjects According to Stage of CKD

Stage	Number of patients (n)	Percentage (%)
Stage 3.00	9	9.0
Stage 4.00	27	27.0
Stage 5.00	64	64.0
Total	100	100.0

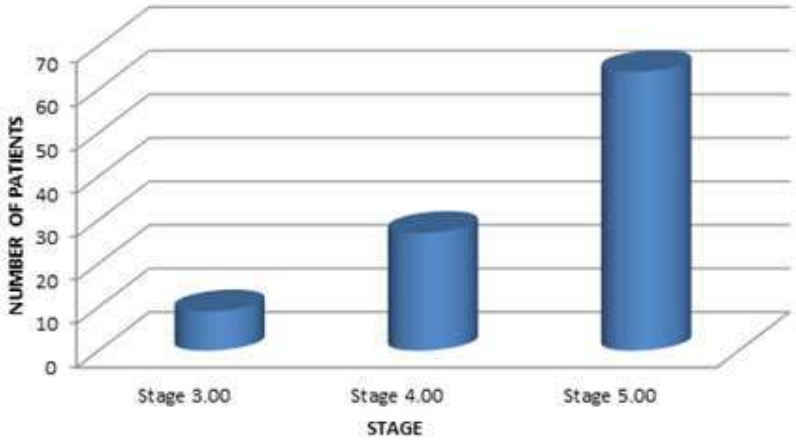

Figure 2. Distribution of Study Objects According to stage of CKD

Table 2 and Figure 2 displays the distribution of study subjects according to stage. Maximum 64% cases werehaving stage 5, followed by 27% subjects with stage 4 and 9% with stage 3.

Table 3. Mean Biochemical Parameters

	Minimum	Maximum	Mean	Std. Deviation
Blood urea	46.00	467.00	159.8400	72.14320
Serum creatinine	1.20	20.70	6.8280	3.99657
Na+	116.00	142.00	130.35	28.491
K+	2.90	8.00	4.8910	.92301
Cl-	98.00	108.00	101.5800	1.74182
Ca+2	5.50	9.80	7.9770	.99512
Bicarbonate	8.00	23.00	17.04	3.123

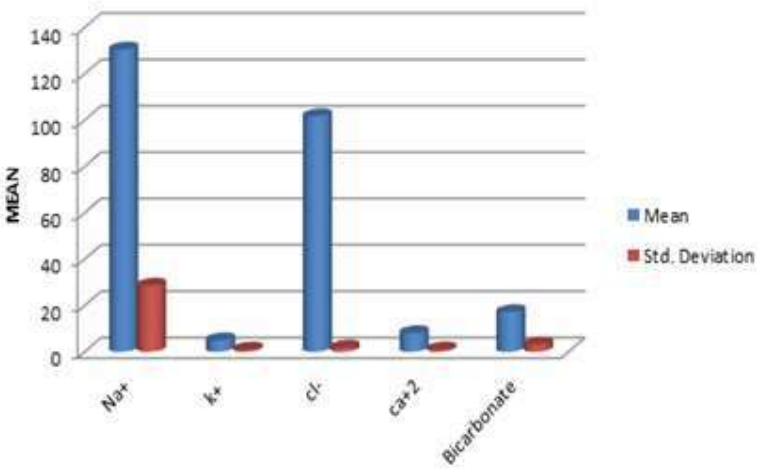

Figure 3. Mean biochemical parameters

Table 3 and Figure 3 shows mean of various biochemical parameters. Mean Blood urea was 159.84±72.14,mean Serum creatinine was 6.82±3.99, mean Na+ levels was 130.35±28.4, mean K+ was 4.89±0.92, mean Chloride was 101.58±1.74, mean calcium was 7.97±0.99 and mean Bicarbonate levels was 17.04±3.12.

Table 4. Study of Electrocardiographic Changes in CKD

ECG CHANGES	FREQUENCY	PERCENTAGE (%)
ISCHEMIA	15	15
ATRIAL FIBRILLATION	2	2
CONDUCTION ABNORMALITIES	10	10
HYPERKALEMIA	3	3
LEFT AXIS DEVIATION	2	2
LEFT ATRIAL ENLARGEMENT	2	2
LEFT VENTRICULAR HYPERTROPHY	36	36
SINUS TACHYCARDIA	8	8
NORMAL	22	22
TOTAL (N)	100	100

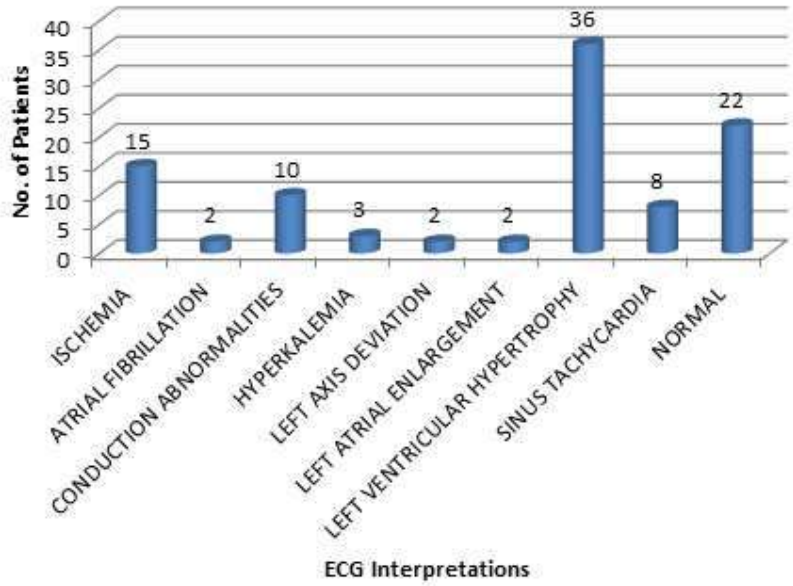

Figure 4. ECG changes in study subjects

Table 4 and Figure 4 shows study subjects with electrocardiographic changes in chronic kidney disease. Maximum 36% cases were with LVH, followed by 22% cases being normal, 15% each were with ischemia and 10% conduction abnormalities.

Discussion

Mean Blood urea was 159.84±72.14, mean Serum creatinine was 6.82±3.99, mean Na+ levels was 130.35±28.4, mean K+ was 4.89±0.92, mean Chlorine was 101.58±1.74, mean calcium was 7.97±0.99 and mean Bicarbonate levels was 17.04±3.12. In accordance with our study, Singh et al. [5] found showed the average urea level in blood was 114.18±42.95 mg/dl which is comparable with the study of Singh et al [6] (121.2 ± 30.6), Foley et al. [7] (117 ± 15.3). The mean blood urea level in Chafekar et al. [8] was 77.0725.39 mg/dl, which is inconsistent with the results of the current study. Similar to our study, Singh et al. [5] found that mean serum creatinine level was 6.63±3.59 mg/dl. With respect to other studies, the mean serum creatinine level, for instance, varies Singh et al. [6] (3.5 ± 1.0) and Chafekar et al. [8] (5.75 ± 1.32). According to research studies, hyperkalemia is the most prevalent electrolyte imbalance in people with chronic renal disease. In Singh et al. [5] study 32% of patient had K+ level >5 meq/l, with the mean K+ level was 4.73±1.13 mEq/dl it is similar to the research on Singh et al. [6]

Similar to our study, Soren et al. [9] found that in 14.76% and 8.3% of patients, respectively, left ventricular hypertrophy (LVH) and left atrial enlargement (LAE) were observed. 4.3% of the patients had atrial fibrillation. Other ECG changes included atrial ectopics (2.6%), tall T waves (7.3%), left axis deviation (7%) and right axis deviation (RAD) (6%).

Singh et al. [5] cardiovascular problems that were identified by electrocardiogram in 72% of individuals. Thirty percent of patients had LVH, sixteen percent had ischemia, sixteen percent had intraventricular conduction disturbances, ten percent had p mitrale, and six percent had arrhythmia. 28 individuals (28%) had normal ECGs. The aforementioned finding is comparable to that of a study by Krivoshiev et al. [10], which found that the majority of patients had LVH in their ECG results, whereas studies by Soman et al. [11] and Menon et al. [12] found that the majority of patients had ischemia in their ECG results.

It was noted that stage 4 and stage 5 of CKD accounted for the majority of the aberrant ECG readings. Therefore, It is essential to regularly check on CKD patients to see if their ECG has changed. The likelihood of aberrant ECG readings rises with CKD stage progression, especially in the latter stages.

Conclusion

CKD has become a major public health concern, with a prevalence rate of 11–13% globally, and mainly stage 3 being most common. The main causes of increased prevalence are rise in cases suffering with diabetes and hypertension. The mortality rate among CKD patients has increased due to increased vulnerability to CVD more commonly and even before time. Although CVD is the main cause of mortality in CKD patients, but it has been observed that mortality rate is even higher in patients who are not undergoing dialysis.

When evaluating the incidence of morbidity and mortality from CVD in patients with late-stage CKD, an electrocardiogram (ECG) is a helpful, straightforward, and non-invasive diagnostic tool. The abnormalities noticed in ECG can be the predictor for diagnosing CVD independently ECG also helps in detecting the signs of myocardial ischemia, disturbances in heart rhythm, abnormalities in chambers and cardiac conduction.

Statements and Declarations

Conflicts of interest

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

Funding

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POINT OF VIEW

Is there a need for a Uniform Cadaveric Oath for Medical Graduates?

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Abstract:

Cadavers have been used for dissection to learn the basics of anatomy since the 3rd century BC. Even today freshly admitted medical students are first taken to the Anatomy dissection hall to learn from cadavers and get an understanding of the enormity of the profession they chose. Most institutes have teachers explaining to the freshers what their reaction should be on seeing a cadaver and how it is to be treated. Some institutes make students take a cadaveric Oath. Today, the cadaver is not just an anatomy learning tool, but has far more uses in surgical basic and advanced training and enhancing our knowledge of medicine. And cadaver transplantation is a common practice now. With many places finding it difficult to access cadavers now, due to human rights issues, it is very important for the medical community to not only adopt but showcase to the world that they respect and acknowledge the role of a cadaver in both diagnostic and therapeutic modality. And frame a strong, uniform Cadaveric Oath to be taken by all medical students to emphasize that.

Keywords: Cadaver, Cadaveric Oath, Organ Transplantation, Surgery Trainees, Anatomy

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Introduction

A Cadaveric Oath is a pledge that a medical student takes before touching the cadaver in the anatomy dissection hall that emphasizes on proper handling of the cadaver without any insult or disrespect to the body while paying tribute to the soul. This also instils the idea of empathy and sacrifice in the young medical entrants. Since there is no uniformity or protocol followed in this oath, it is now felt necessary to make this cadaveric oath uniform. In view of the role of cadavers in surgical training and teaching, a proposal to revise the Cadaveric oath is being suggested.

Cadaveric Oath

Unlike the Hippocratic Oath, there is no uniformity in Cadaveric Oath, and neither is there any compulsion in the medical college on an oath-taking ceremony before touching a cadaver. However, the usual Oath is...

"*I do solemnly pledge that-*

• *I will always treat you with respect and dignity of the highest order, as you are my first Anatomy teacher*

• *I will always respect your privacy and confidentiality*

• *I will use this knowledge for the service of the society*

• *In all my deeds from now onwards, I will do justice to your great sacrifice*

• *My heart fills with gratitude, as I realize your kind & courageous act of donating your body for the purpose of our learning*

• *I will be grateful to you and your family for this act of 'Living After Death*"

Why the Cadaveric Oath is useful?

Dissections of humans started as far back as the 3rd century BC, when Herophilus of Chalcedon and Erasistratus of Chios performed the first cadaveric dissection to understand the whole body from the viewpoint of anatomy and physiology. Then why did this oath come into play now? The essence of the Cadaveric oath is to make the fresh medical students get 'acclimatized ' to the environment of a human dissection hall and understand as well as uphold the dignity of the body, prevent any emotional or violent reaction at the scene of touching a cadaver, develop and inculcate interest in surgery and other surgical disciplines for the future, understand the sacrifice of the dead man or his family who donated the body for anatomy dissection in a medical college knowing fully well that the body will undergo dissection at various places for learning purposes. Finally, every student should understand that in the age of digital learning with 3-D computer-aided simulation images, cadaver dissection remains the best mode of learning human anatomy by understanding the three-dimensional relationship of different anatomical structures and appreciating anatomical variations [1]. A survey conducted on Venezuelan surgeons concluded that 88% of surgeons felt that cadaveric dissection was the most effective way to teach anatomy [2].

Is there a need for a Cadaveric Oath for surgeons?

Given the development of a cadaver laboratory that uses frozen cadavers for hands-on training, education, and development of new surgical techniques, the oath needs to percolate from the four walls of the anatomy dissection hall to the cadaveric operation theatre. Cadaveric dissection improves the learning curve of fresh surgical graduates. Cadavers are also used in research when designing and developing medical devices. The cadaveric oath needs to also highlight the importance of cadaveric organ donation in brain-dead individuals inspite of the various legal, cultural, and religious sanctions in various countries [**3**]. Cadaveric implants like fat grafts, bone implants, or dental implants are used regularly in medical science.

Role of Cadavers in Minimally invasive surgery learning

With laparoscopy and robotic surgery becoming more popular worldwide, learning anatomy is also becoming virtual without any feel of the tactile sensation of the organ. Cadaveric courses and workshops are devised for the surgeons to improve and familiarize themselves with the surgical outcomes by identifying the proper anatomical landmarks, practicing new surgical skills more comfortably on cadavers without any stress of the operation room, and learning, redefining or devising a new modification of a minimally invasive surgical technique on cadavers with confidence.

Role of Cadavers in Plastic Surgery

Plastic surgeons extensively use cadaver dissections to practise various well-established and newer flap procedures. They have also developed a cadaveric model for a new and innovative methodology of implanting very small electrodes more efficiently within a nerve by dissecting fascicles and assessing their action. They have advocated that the microsurgery technique could be practiced on cadaver models to establish protocols before beginning with a first patient [4]. It was seen that cadaveric-based studies and simulation in the curriculum during postgraduation increased a resident's operative skills and the teachers observed an increase in knowledge of anatomy and confidence in technique among all resident trainees. Another benefit of surgical simulation on cadavers was that teachers can identify and individually supervise struggling residents for skill enhancement [5]. A proposal to establish high-fidelity cadaveric simulation through the development of a perfused cadaveric model whereby simulation is further able to approach life-like surgery and teach one of the more technically demanding skills of plastic surgery- 'microsurgery' was also reported [6]. Cadaver skin grafting to tide over major burn victims is not just a learning exercise but an instance in that cadavers are used for treatment!

Role of Cadavers in Cardiothoracic Surgery

Simulation through cadavers has a vital role to play in Cardiothoracic resident training [7]. It was concluded that the repetition of procedures allows the young cardiac surgery trainee to acquire dexterity. A partnership between the University of Rochester and LSI SOLUTIONS® created an interactive translational research model utilizing cadaveric simulation that has been successfully applied to accelerate bringing minimally invasive cardiac surgical techniques and innovative devices to patients [8].

Role of Cadavers in other surgical specialties

The role of cadaver hands-on dissections for training novice surgeons for basic and advanced oculoplastic surgeries has been reported where surgical efficiency was improved and lethal complications prevented with improvement in their augmented operative autonomy, confidence level, and surgical skills [9]. The role of a cadaver for neurosurgeons in skull-based surgery learning and endoscopic neurosurgery training is also well established [10]. Cadaver studies played a central role in the discovery and definition of the Anterolateral ligament of the Knee, its anatomical features, biomechanical role, and reconstruction techniques. Thus, a cadaver is a powerful tool to develop, experiment with and test new devices which could be useful in clinical and surgical practice [11].

A new and revised Cadaveric Oath:

3D simulations, 3D printing, and working with silicone models have not been able to replace the importance or usefulness of a cadaver in basic medical and advanced surgical training. Many countries are also finding it difficult to provide cadaver training due to the non-availability of cadavers or human rights issues that develop with unclaimed bodies. In this scenario, it is of

paramount importance that we cherish the learning that a cadaver can offer trainees and popularise a strong Oath to be taken by all medical graduates so that it is not felt that cadavers are being misused or even abused disrespectfully. We need to frame an oath that incorporates these sentences too:

1. ***I acknowledge that you are essential for advancing medical knowledge.***

2. ***I will remain thankful for all your organs that have made people live.***

3. ***I realise that is a huge privilege bestowed upon me for being able to learn from you and will always remain grateful for that.***

4. ***I vow to treat the cadaver with the utmost dignity and respect and will always maintain a professional demeanour during dissection. I will refrain from any disrespectful behaviour, such as making inappropriate comments or taking photographs or videos for non-educational purposes.***

5. ***I will always remember the generous donation made by the individual whose body I am dissecting, and I will honour their memory by learning as much as I can from this invaluable opportunity. I pledge to use this knowledge to benefit the patients under my care and to always strive to provide the highest quality of medical care.***

Conclusion:

Even in these times of 3D simulations, cadaver dissections are an essential tool not only for fresh medical students to learn anatomy, but for all surgical trainees throughout their careers to hone and advance surgical skills. Cadavers find increasing use in organ donation too. It is vital that just like the Hippocratic oath which is compulsorily taken by medical graduates to heal the living, a cadaveric oath too should be mandated to respect the dead.

Author Contribution

1. Conception or design of the work… Kaushik, Neela
2. Data collection…Kaushik Neela
3. Data analysis and interpretation…. Neela
4. Drafting the article…Kaushik Neela
5. Critical revision of the article… Neela
6. Final approval of the version to be published… Neela Kaushik

Conflicts of interest

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

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CASE REPORT

A Case of Duodenoduodenal Intussusception Secondary to Duodenal Polyp

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Abstract

Adult intestinal intussusception accounts for 1 to 5 percent of mechanical bowel obstructions and is relatively rare. Its presentation, aetiology and treatment varies greatly from childhood intussesception. Duodenoduodenal intussusception (DDI) is unusual due to fixed position of the duodenum within the retroperitoneum with only a few cases of adult DDI reported in literature. In adults, a pathologic lead point within the bowel typically leads to intussusception, and this may be malignant in up to 77 percent of cases. DDI is a challenging condition due to its rarity and nonspecific presentation. Here, we present a case of DDI secondary to a duodenal polyp.

Keywords: Adult intestinal intussusception, Duodenoduodenal intussusception, duodenal polyp, adult small bowel obstruction

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Case Report

A 49 year old gentleman, premorbidly healthy, no prior surgical history, presented with complaints of umbilical and epigastric pain since 25 days. Pain was mild to moderate in intensity, colicky in nature and associated with nausea. History of increased pain since 2 days, abdominal bloating and vomiting which was non bilious and occurred within 1-2 hours of food intake.

On examination, patient was afebrile, haemodynamically stable, abdomen soft, non-tender, no guarding, rigidity or organomegaly. Systemic examination unremarkable. Biochemical and haematological investigations within normal limits. Ultrasound (USG) abdomen and pelvis showed bowel within bowel appearance in the supraumbilical region. Contrast enhanced computed tomography (CECT) of abdomen suggestive of DDI involving third part of duodenum (D3) for approximate length 5.5 cm with dilatation of stomach. Further investigation with oesophagoduodenoscopy (OGDscopy) showed large duodenal polyp (about 4 to 5 cm.) almost occluding entire lumen in second part of duodenum (D2). Biopsy showed tubular adenoma with low grade dysplasia, negative for malignancy. In view of these findings and persistence of symptoms, patient was taken up for exploratory laparotomy.

During surgery large D2 polyp was seen extending into D3 segment causing intussusception. Intussusception was reduced, duodenum opened and polyp delivered out. Wide excision of polyp at its base was done using 55mm blue linear stapler. Duodenum closed transversely with 2-0 Vicryl® and No. 10 flat drain kept in abdomen. Contrast gastrography (CONRAY) done on post operative day (POD) 1 showed no leak or extravasation from anastomotic site. Following this, nasogastric tube was removed and patient gradually started on oral diet. Abdominal drain was removed on POD 4. Post operative recovery of the patient was uneventful with stay of 6 days. Histopathological examination of resected polyp showed tubular adenoma with low grade dysplasia, negative for malignancy. At one year follow up, patient was symptom free..

Figure 1. Endoscopy showing large polyp in D2

Figure 2. Wide excision of D2 polyp at base

Discussion

Intussusception refers to the invagination (telescoping) of a part of the intestine into itself. Adult intestinal intussusception accounts for 1 to 5 percent of mechanical bowel obstructions and is relatively rare [1]. In adults, a pathologic lead point within the bowel typically leads to intussusception, and this may be malignant in up to 77 percent of cases [2]. In case of adult intestinal intussusception, 90% occur in small or large bowel and 10% involve either stomach or surgically created stoma [3]. DDI is extremely rare as duodenum is a fixed retroperitoneal structure. While exact mechanism of DDI is not fully understood, any lesion in the duodenal wall or irritant within the lumen that can alter normal peristaltic activity may initiate an invagination. The lead points for intussusception may be benign, malignant, or idiopathic [4].

Clinical manifestations of DDI are usually nonspecific; it presents with obstructive features which may be acute, chronic, or intermittent and also with weight loss, fever, and a palpable abdominal mass. Involvement of the ampullary region and obstruction of common bile duct and pancreatic duct may occur with features of obstructive jaundice or acute/chronic pancreatitis [5].

Due to its non-specific presentations and relative rarity, clinical diagnosis may be challenging and is often delayed..

Various modalities such as USG, upper gastrointestinal series (UGI), CECT, and endoscopy have been used to establish diagnosis; however, this is frequently confirmed only during surgical intervention.

Sonography may show a “target sign or doughnut sign” while CECT is reliable for preoperative diagnosis showing characteristic “bowel within bowel appearance” and “target sign” consisting of outer intussuscipiens, inner intussuceptum, and central fat density formed by intussuscepted mesenteric fat and vessels[6,7].

Endoscopy can give a tissue diagnosis to help plan definitive treatment.

Surgical procedure is determined by the size and site of lesion and presence of complications. Adult intussusception is usually treated surgically or endoscopically and not by fluoroscopic reduction as done in paediatric population.

Diagnosis of intussusception is important due to high risk of complications such as bowel ischemia, obstruction, and intraluminal bleeding.

In conclusion, DDI is a challenging diagnosis and surgeons should maintain a differential diagnosis of intussusception in patients with nonspecific abdominal pain, gastric outlet obstruction, duodenal stricture, pancreatitis, upper gastrointestinal bleed or obstructive jaundice. A high index of suspicion with appropriate imaging can help in pre operative diagnosis and better management of these patients.

Conflicts of interest

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

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CASE REPORT

An Interesting case of Supernumerary Kidney with PUJ obstruction in the native kidneys

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Abstract:

Congenital anomalies of Kidney and Urinary Tract (CAKUT) present with interesting challenges to a urologist in his practice. The incidence of CAKUT is 4.2 per 10,000 births. CAKUT are one of the major risk factors in adults requiring renal replacement therapy. Although children with CAKUT are often asymptomatic, CAKUT are estimated to be implicated in 30% to 60% of cases of childhood-onset chronic kidney disease (CKD) in different populations. We hereby present a rare case of a patient with Supernumerary Kidneys in which both bilateral native kidneys showed evidence of Pelvi-ureteric junction obstruction and ectopic pelvic kidney with normal function.

Keywords: Supernumerary kidney, CAKUT, PUJ obstruction, ectopic.

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Case report

A 20-year-old male patient presented with history of difficulty in passing urine per urethraly for a period of 1 month which was insidious in onset and gradually progressed and patient developed pain in bilateral flank region which was continuous, dull aching in nature and non-radiating in nature and associated fever. He was admitted and evaluated with complete blood count, renal function test and urine was sent for culture and sensitivity. He underwent ultrasound which revealed bilateral hydronephrosis with left sided renal parenchyma thinned out and right sided kidney with decreased thickness of the renal parenchyma and the findings were suggestive of bilateral Pelvis-ureteric junction (PUJ) obstruction of the two orthotopic kidneys with pyonephrosis. Hence, patient underwent bilateral percutaneous nephrostomy insertion under ultrasound guidance. Patient was managed with nephrostomy for the next 3 weeks. Daily nephrostomy output on the right side was 800 ml and on the left side it was 400 ml. After 3 weeks, left side percutaneous nephrostomy stopped draining. Patient was then evaluated using Computerised tomography Intravenous Pyelography (CT IVP). This showed evidence of two orthotopic kidneys and an ectopic right kidney located in right iliac fossa along with fusion of right orthotopic and ectopic kidney. The right sided orthotopic kidney showed gross hydronephrosis and caliectasis with thinning of right renal parenchyma with non-visualisation Left kidney showed enlarged kidney with gross hydronephrosis and thinning of renal parenchyma with transient delayed visualisation till the level of mid-ureter. The right sided ectopic kidney was located in the right iliac fossa.

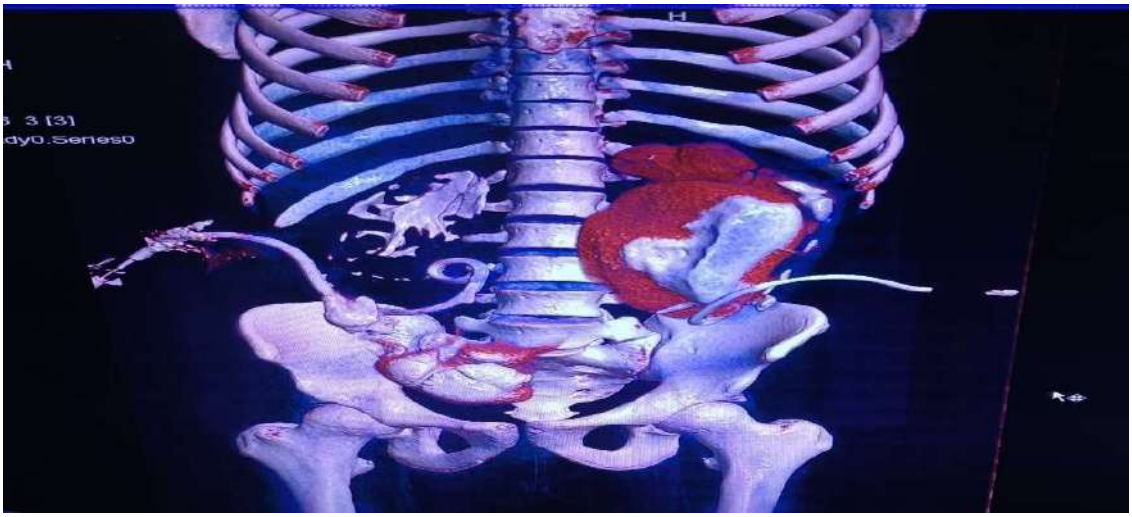

Figure 1. Reconstructed CT image shows evidence of two orthotopic kidneys with grossly dilated bilateral hydronephrosis with bilateral nephrostomy tubes in situ. Also seen is ectopic right sided kidney in the right iliac fossa.

Decision was made to internalize the drainage and to do bilateral DJ stenting of the two orthotopic kidneys. Patient then underwent Cystoscopy proceed Retrograde Pyelography (RGP) with Bilateral DJ stenting. RGP findings revealed evidence of gross hydronephrosis of right sided kidney with delayed drainage; the right sided orthotopic kidney fused with the ureter from the right sided ectopic kidney at the level of L4 level and then draining into the bladder. Left sided RGP showed evidence of gross hydronephrosis more than the right side with tapering at the level of PUJ suggestive of Left sided PUJ obstruction.

Figure 2a. Right sided RGP shows evidence of gross hydronephrosis of right orthotopic kidney with delayed drainage showing evidence of right sided PUJ obstruction.

Figure 2b. Right sided RGP shows evidence of ectopic right sided kidney in the right iliac fossa with normal excretion.

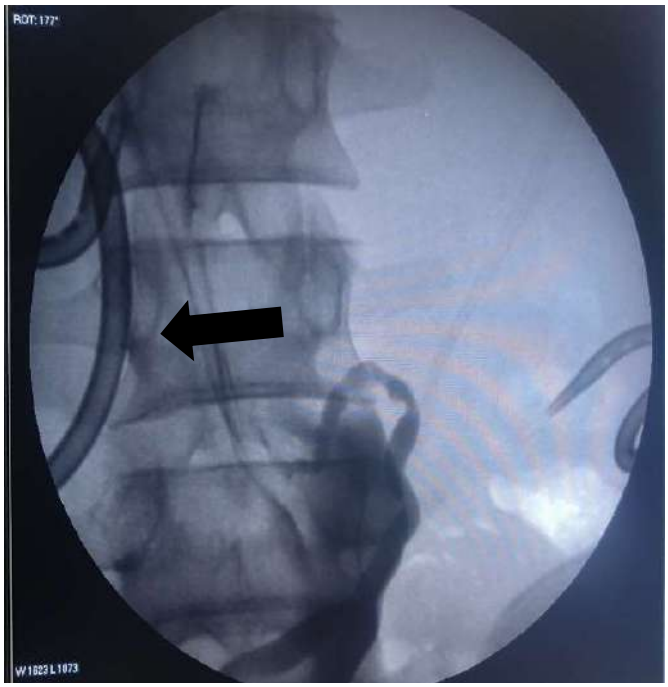

Figure 3. Left sided RGP shows evidence of kink and narrowing at the level of left sided RGP and a grossly dilated left sided renal pelvis; on account of the gross dilatation of the pelvis; contrast is not visualised in the left renal pelvis in the static images as it got diluted in the system; however, a jet going into the left sided renal pelvis was seen during the dynamic images.

Then the patient underwent DTPA scan to know the functional status of the orthotopic and the ectopic kidneys. It revealed that the orthotopic Left kidney showed adequate cortical function with obstructed excretion at PUJ level. The orthotopic and the ectopic right kidneys showed severe cortical dysfunction (<5 % combined function).

Management

The patient underwent left sided open pyeloplasty followed by open right sided nephrectomy of the native and the orthotopic right kidneys after 4 weeks. He then underwent Left sided DJ stent removal with retrograde pyelography for the left kidney 8 weeks after the pyeloplasty and it revealed prompt drainage of the left sided pelvis-collecting system with a good dependent funnel-shaped PUJ.

Discussion

Congenital anomalies of kidneys (CAKUT) presentation in patients can vary from being an incidental finding detected on imaging to a patient with renal failure or anomaly incompetent with life and stillbirth. Management of these anomalies presents a challenging task to the concerned urologist. Supernumerary Kidney may arise from irregular and abnormal division of the nephrogenic cord, which gets divided into two metanephric blastemas, which ultimately develop into two kidneys with incomplete or double ureteral bud [1-3]. Around the fifth to seventh week of gestation, when urogenital system development occurs, embryologically this anomaly used to develop. The rarity of this anomaly, its varying appearance, and the paucity of literature evidence make diagnosis and treatment difficult [4,5].

SK is an unusual urinary system congenital anomaly, with just around a hundred cases recorded in past research. It might be completely separated from the usual kidney or attached by a loose areolar tissue and it is normally smaller and less functioning as compared to normal kidneys [6]. SK is a rare congenital anomaly of the urogenital system in

which an accessory/extra or third present along with two normally located kidneys.

In our case, it was a supernumerary kidney in the right iliac fossa which was fused with the orthotopic kidney on the right side; the pelvicalyceal system of the right sided kidney showed evidence of PUJ obstruction and its ureter fused with the ureter arising from the ectopic kidney and both then draining into the bladder. The left sided orthotopic kidney also showed evidence of PUJ obstruction.

Conflicts of interest

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

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CASE REPORT

Choroidal Tuberculoma as a Presenting Sign of Tuberculosis

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Abstract:

The unusual ocular type of tuberculosis (TB), known as choroidal tuberculoma, poses diagnostic and treatment challenges, particularly when it occurs in the absence of other disease signs. Patients with ocular tuberculosis have choroidal tuberculomas. They rarely present as the first sign of tuberculosis without any prior systemic symptoms, and they typically occur in patients who have had the disease in the past. We present a 13 year old Boy with unilateral choroidal tuberculoma with meningitis as the primary sign of presumptive ocular tuberculosis allowed for early therapy to be started.

Keywords: Mycobacterium tuberculosis, tuberculoma, choroid, choroidal mass, OCT, QuantiFERON-TB

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Introduction

Large solitary lesions called choroidal tuberculomas typically develop in people with a history of tuberculosis (TB) [1]. Young patients with chronic illnesses frequently experience them. They are typically more clearly defined than their counterpart choroidal tubercles because there is less surrounding retinal edoema. Typically, they are found in the posterior pole, especially in the parafoveal region [2]. When a patient has ocular TB without a systemic presentation, it is uncommon for choroidal tuberculoma to make its initial appearance. Tuberculosis of the eye is uncommon. Just 1% of tuberculosis cases worldwide are caused by it [3,4]. Either systemic tuberculosis is present or absent when ocular tuberculosis develops. It typically manifests as posterior uveitis, particularly as many choroidal tubercles. A massive choroidal tuberculoma caused by ocular tuberculosis is extremely uncommon [3].

Within a tuberculoma, the tubercle bacilli proliferate, causing exudative retinal detachment and tissue damage through liquefactive necrosis [3]. Clinical evaluation of the system, therapy effectiveness, and diagnosis are done. Investigative techniques like Fundus fluorescein angiography (FFA) and USG B-scan can rule out other diagnoses like amelanotic choroidal melanoma and choroidal metastases [4,5,6]. Correct diagnosis and treatment results in choroidal tuberculoma clearing up and visual acuity improving. A 6- to 12-month anti-tubercular regimen is regarded as conventional therapy. Although if inflammation is reduced in advanced disease, symptoms may not completely go away [4-7].

In their reviews of intraocular TB, El-Asrar et al. and Gupta et al. provided the following definitions for assumed intraocular TB: Strongly positive tuberculin skin test results ((≥15 mm area of induration/necrosis), radiological proof of a healed or active tubercular lesion in the chest, or proof of an active extrapulmonary TB infection, as determined by microscopic examination or by culture from affected tissue; positive response to antituberculosis treatment with no relapse; ocular findings consistent with possible intraocular TB; and ancillary testing [8,9]. According to reports, the most typical intraocular symptom of tubercular posterior uveitis is several choroidal tubercles. Less frequently, intraocular TB may manifest as a massive tuberculoma, or a single, big yellow or grey lesion, typically in the posterior pole [10]. A tuberculoma's rapid bacilli multiplication can lead to tissue loss by liquefactive necrosis, which can result in an exudative retinal detachment around the tumour [11].

Only a sizable isolated choroidal tubeculoma was present in this case; there was no exudative retinal detachment. 20% of patients with extrapulmonary involvement and 50% of those with extrapulmonary involvement may have negative PPD skin test results (12). Interferon gamma measurement by QuantiFERON-TB® or enzyme-linked immunosorbent spot has emerged as a new method to identify tuberculosis infection in recent years. Since it is unaffected by prior BCG vaccinations, QuantiFERON-TB®, an indirect test for Mycobacterium tuberculosis infection, has higher specificity than PPD (13). A conclusive diagnosis would be made by intraocular fluid study or tissue biopsy, but these procedures are not usually available.

Nucleic acid amplification can be used to diagnose using either transcription-mediated 16S RNA amplification or PCR amplification of mycobacteria DNA sequences. Furthermore utilised for diagnosis, chorioretinal biopsy is compatible with nucleic acid amplification methods. The FFA demonstrates late leaking and early hyperfluorescence of active choroidal lesions. Early blocked hyperfluorescence with late staining is seen in cicatricial lesions. Large tuberculomas exhibit moderate to low internal reflectivity, which allows ultrasonography to identify them from intraocular cancer.

Here, we report In this case, choroidal tuberculoma with meningitis was the only presenting symptom; ocular TB was assumed to be the cause. We received permission to use the

patient's name and the mentioned image in this case report.

Case Report

A 13 year old previously healthy boy initially presented to our Outpatient Department with complains of fever ,vomiting & headache and photophobia for 20 ,15,and 5 days duration respectively with significant weight loss.He had not received BCG and there was no history of seizures.He had received several course of antibiotics without any response.

There was no substantial medical history, and there have never been any comorbid conditions. Physical examination revealed a sick looking, moderately anemic, febrile child. His pulse rate, respiratory rate and blood pressure were 112/min, 17 breaths/min, 112/74 mm Hg respectively.Auscultation of chest revealed normal finding .Signs of meningeal irritation were present. Alternate convergence Present [Fig 1], pupils were equal and reactive, skin sensations, muscle tone and cranial nerves were intact.Deep tendon reflexes were normal and Babinski reflex was absent

Among laboratory investigations hemogram showed Hb -11.2 g/dl, TLC -8600/cumm, DLC -P83L14M01E02 and ESR-40 mm in 1st hour. Mountoux test and sputum for AFB were negative.Skiagram of the chest showed normal findings. Widal test positive with TO Titre 1:320.Lumbar puncture was done and cerebrospinal fluid was clear [Fig 2] with total nucleated cell count 500 cells /cumm, polymorphs 90%, lymphocytes and mononuclear cells 10%, and protein content was 6.6 gm with a low grade glucose level equal to 14 gm/dl.

Microbiologic direct exam was negative and revealed absence of bacilli .culture was negative & True Nat shows mycobacterium tuberculosis complex -MTB rifampicin sensitive complex .Renal and Liver functions tests were normal .PPD skin testing was negative .

CECT Brain shows mild prominence of bilateral lateral ventricles and 3rd ventricle with normal study for brain parenchyma.MRI brain scan was not done.

Ocular examination shows normal pupillary reflexes. Fundus examination of both eyes revealed hypopigmented and hyperpigmented lesions in the foveal area and temporal to the optic disc [Fig 3] suggestive of tuberculous choroiditis .Optic disc of both eyes were hyperaemic and blurring of margin was seen suggestive of papilloedema .On Indirect ophthalmoscopy right eye showed hyperpigmented well defined lesions in the foveal area and few hypopigmented lesions inferior to optic disc, left eye- hypopigmented lesions temporal to the optic disc.

We investigated this patient thoroughly for his immune status.

He had been diagnosed with tubercular choroiditis and suspected tuberculous meningitis. Papilloedema was established. She was started on anti-tubercular therapy for a total duration of 12 months as 2(HRZE) in intensive phase and 10(HR) and steroids to which child responded and there was significant improvement in vision.Patient was advised regular follow ups.

Result

After receiving treatment, the patient had made great progress. Upon review choroid tubercles was found to be healed and resolved in both eyes [Fig 4].

Discussion

The lungs are the main organs affected by the deadly infectious disease tuberculosis. The Mycobacterium tuberculosis complex contains acid-fast bacteria that cause tuberculosis (TB) [4]. Aside than the lungs, any other body tissue can be affected. One kind of TB that poses a hazard to vision is ocular TB [3,4]. The involvement of the lid and adnexa, as well as orbital cellulitis, are some of the different ocular symptoms of tuberculosis.

Conclusion

Choroid tubercles considered highly specific for miliary tuberculosis,may occur in isolated tuberculous meningitis. As the ocular lesion completely heals, prompt care of choroidal inflammation helps avoid vision loss. Early TBM diagnosis is essential for preventing death and impairment symptoms in youngsters. CSF investigation and neuroimaging is important to establish the diagnosis but despite advances in diagnosis with Xpert MTB/RIF, most children with TBM are not bacteriologically confirmed.

This case highlights the facts that a seemingly innocuous eye movement could be associated associated with significant Systemic tuberculosis & thus requires thorough investigation and timely prompt treatment.

Figure 1 (eyes). Alternate Convergence

Figure 2. (CSF). Clear CSF

Figure 3. Fundus: Hypopigmented & Hyperpigmented Lesions in the Foveal Area and Temporal to Optic Disc

Figure 4. Fundus: Resolution of Lesions after ATT.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the forms, the parents have given their consent

Conflicts of interest

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

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