

ORIGINAL RESEARCH

Histo frozen correlation-A periodic performance analysis at a tertiary care hospital

¹Gundimeda V.R.N.K.Kanth, ²Madhuri Shreesh Kate, ³Sharathchandra.Keshapaga, ⁴Tejomayi Regulavalasa

¹Professor & HOD, ³Assistant Professor, Department of Pathology, ESIC Medical College, Sanathnagar, Hyderabad, India

²Dir.Professor & Dean, ⁴Senior Resident, ESIC Medical College, Sanathnagar, Hyderabad, India

Corresponding author

Gundimeda V.R.N.K.Kanth

Professor & HOD, Department of Pathology, ESIC Medical College, Sanathnagar, Hyderabad, India

Received: 18 November, 2023

Accepted: 22 December, 2023

ABSTRACT

Introduction: Frozen section otherwise called as intra operative consultation helps the operating surgeon in making on table decision for patient management. These results are further supplemented by findings on permanent sections. The present study is a periodic performance analysis taken up at a tertiary care centre. **Objective/Aim:** The primary objective of the study is to compare the degree of concordance between frozen section and permanent sections. The secondary objective is to study the cause for discrepancies. **Materials and methods:** The present study was a prospective study of 75 cases received for frozen section and the diagnosis delivered on frozen is compared with that found on permanent sections. Accuracy, sensitivity, specificity, positive predictive value and negative predictive value are calculated. **Results:** 73 cases out of 75 had concordance with permanent sections. Sampling errors and inherent deficiencies in frozen section are responsible for the discordance. Accuracy(97%), sensitivity(95%), Specificity(100%), Positive predictive value(100%), Negative predictive value(94.5%) are comparable to other studies in the literature. **Conclusion:** Our study has reiterated the role of frozen section and also studied its usefulness in special situations like diagnosis of Mucor in Post covid scenario. The discordances gave an opportunity to learn the sources of error and paved the way for corrective future action.

Key words: Frozen section, Mucor, concordance

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

INTRODUCTION

Frozen section is a rapid intra-operative diagnostic procedure which helps the operating surgeon for further decision making in the patient management. This rapid frozen section method was first introduced by Welch in 1891 and developed as a diagnostic tool by Cullen, Wilson, Mac Carty. This Frozen section method is mostly used for purposes like determining the nature of the lesion, differentiating between benign and malignant lesions, knowing the surgical margin status, adequacy of a surgical resection, identification of metastatic deposits in lymph nodes etc.

This method aids in intra operative decision making by the surgeon but it is not a replacement for the formalin fixed paraffin embedded (FFPE) tissue technique, the confirmatory diagnosis is always rendered on the permanent sections. Relatively this frozen section method is inferior to the paraffin tissue section method due to its own limitations like technical difficulties in getting good quality sections and thus interpretation by the pathologists. This necessitates the importance of periodical analysis of frozen section diagnosis and its correlation with the

histopathological diagnosis to know the potential causes of errors and the measures that need to be taken to help prevent such discrepancies.

The present study aims to evaluate the diagnostic accuracy of the frozen section examination of various specimens in comparison with the routine FFPE tissue sections.

MATERIALS AND METHODS

The present study was a prospective type of descriptive study carried out at Histopathology department of ESIC Medical college & hospital, Hyderabad for a period of one year from January 2021 to December 2021. During the study period a total of 75 patients underwent surgery with intra operative pathologic consultation for various malignant and non-malignant conditions.

Inclusion criteria: All the cases that were referred to the department of pathology for frozen section examination were included in the study.

Exclusion criteria: Cases with sampling errors/poor sampling showing only necrotic or hemorrhagic tissue are excluded.

Fresh tissues in normal saline were sent from the operation theater for frozen section examination. The gross specimens were inspected, dissected and the sections were taken from areas of interest. Sections were snap frozen in the cryostat using an Optimal Cooling Temperature (OCT) embedding medium. The blocks were then cut and sections were subjected to rapid Hematoxylin- Eosin (H&E) staining.

The tissue sections were examined by the pathologists and surgeons were informed of the frozen section diagnosis immediately. The frozen remnant tissue and the further non-frozen tissue sent were fixed in 10% Formalin (NBF) solution and processed according to the standard protocols. The tissue sections were then stained by Conventional H&E staining and submitted for further reporting.

The initial frozen section impression was compared to the final histopathological diagnosis and the results were categorized into either Concordant or

Discordant. The data was further analysed using SPSS software and accuracy, sensitivity, specificity, positive predictive & negative predictive values were calculated.

RESULTS & DISCUSSION

The present study was conducted during one year duration of January 2021 to December 2021 in a tertiary care referral institute in Telangana state. A total number of 75 cases were received and included in the present study. The age group of the patients was between 19-77 yrs. The most common indication for frozen section in our center was to establish the diagnosis of malignancy followed by cases sent for confirmation of Mucor. The minor group of cases were sentinel lymph nodes sent for the presence of any tumor metastasis and cases sent for margin assessment in a known case of malignancy.(Table 1)

Table 1(Distribution of cases based on Indication)

S.No	Indication for Frozen	No of cases
1	Definitive diagnosis (to rule out malignancy)	37
2	To rule out presence of Mucor	22
3	For margin status in known case of malignancy	11
4	Sentinel lymph node for metastasis	05

Out of the cases received for frozen section the major tissue was Breast followed by Head and neck for Mucor mycosis. Oral cavity lesions and FGT were the next frequent sites .Also received for frozen are the tissues from Thyroid, Parathyroid, Gall bladder ,Lymph nodes, foot and Bone.(Table 2)

Table 2 (organ wise distribution of cases)

S.No	Organ distribution	No of cases
1	Breast	23
2	Head and Neck (for mucor)	22
3	Oral cavity	08
4	Female genital tract	07
5	Lymph node	05
6	Thyroid	04
7	Gall bladder,CBD	03
8	Others(Parathyroid,Bone,Foot)	03

All the cases subjected to frozen section were later compared with permanent sections and both the diagnosis were compared.

Discrepant results were seen in 2 cases of FGT. One case was reported as smooth muscle tumor but later turned out to be endometrial stromal sarcoma with co existent smooth muscle neoplasm. Another case was reported as mucinous cystadenoma but finally turned out to be Atypical proliferative mucinous tumor.

Based on the concordance and discordant results, Sensitivity was calculated using the formula True positives/True positives+ False negatives and was found to be

Specificity was 95% calculated by the formula True negatives/True negatives+ false positives.

Accuracy was 97% calculated using the formula True positive+ True negative/True positive+ True Negative+ False positive+ False negative.

Positive predictive value was 100% calculated using the formula True positive/True positive + False positive

Negative predictive value was 94.5% calculated using the formula True negative/True negative+ False negative

The most important indication for frozen section in our study was to determine the nature of lesion and to differentiate whether the lesion is malignant or not [1-2].

But in contrast to other studies the second most common indication in our study was for confirmation of Mucor which is an unique feature of the study and not seen in earlier studies. The other indications like margin status and sentinel lymph node metastasis assessment are similar to that in other studies.

In our study, Breast was the commonest organ received for frozen which is comparable to other

studies in the literature [3]. Among the 23 cases received for frozen section, three cases were having a proven malignancy and planned for breast conservation surgery in young patients and were sent

for assessment of margins. Out of the 20 cases, in 15 cases there was unambiguous evidence of malignancy which was found to be concordant on permanent sections. [Figure 1]

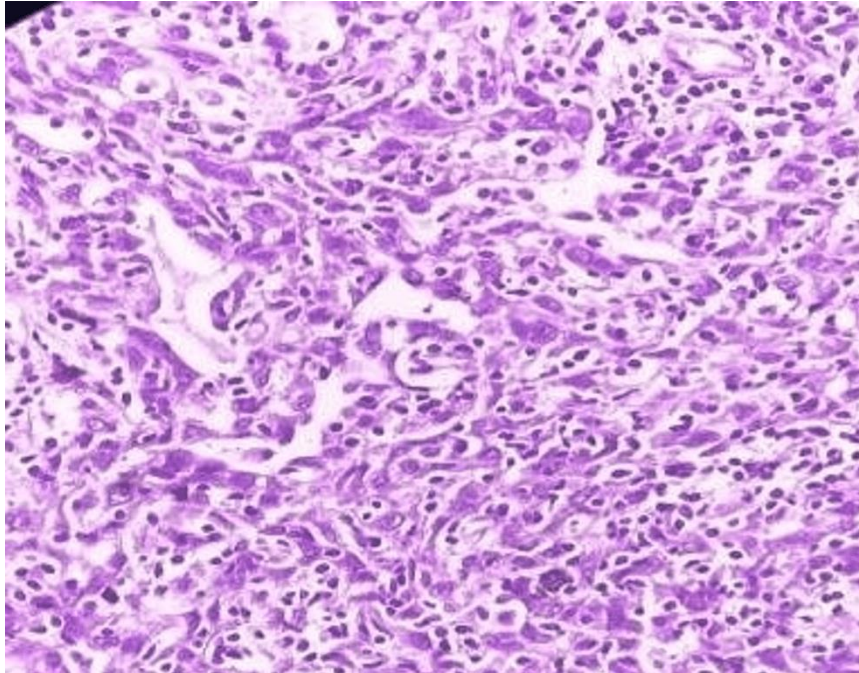


Figure 1: Appearance of Invasive ductal carcinoma of breast on Frozen

The diagnosis of malignancy was thus delivered on 75% of cases which is comparable to that of 76.3% in the study done by Altaf et al [4] and 64% in the study of Nju Yun et al [5]. There was no residual tumor in one case where resection was planned after NACT. Another case was given as sclerosing adenosis which

was later confirmed on permanent sections. One case was reported as suspicious for malignancy and finally turned out to be Solid papillary carcinoma. One case was diagnosed as Mastitis [Figure 2] and no tumor was detected even on permanent sections

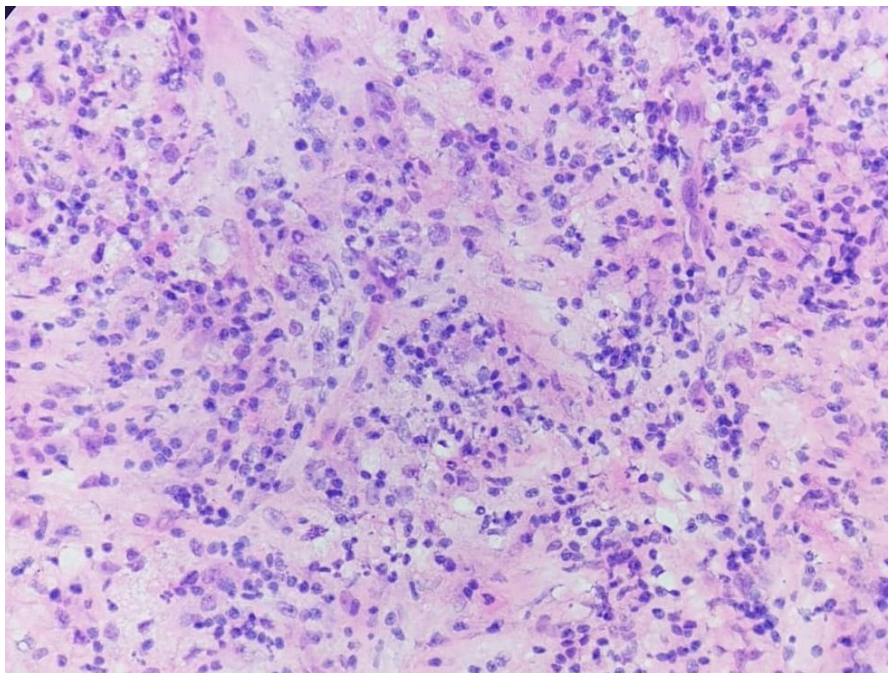


Figure 2: Appearance of mastitis on frozen in a case sent with suspicion of malignancy

3 cases of proven breast carcinoma were sent for assessment of margins, in all the 3 cases, margins were negative which was later confirmed on permanent sections. Thus the overall concordance in breast lesions was 100% while in the other studies in the literature the concordance varied between 98.3 % in Mahadevappa et al [6] and 99.5% in studies by Karve et al [7]

The second commonest site was Head and neck for the confirmation of Mucor. The 22 cases sent included those from Rhino orbital region, Maxillary sinus, Hard palate, Sphenoid sinus and left middle meatus. 9 cases were found to be positive for mucor [figure 3] and 13 cases were negative for Mucor

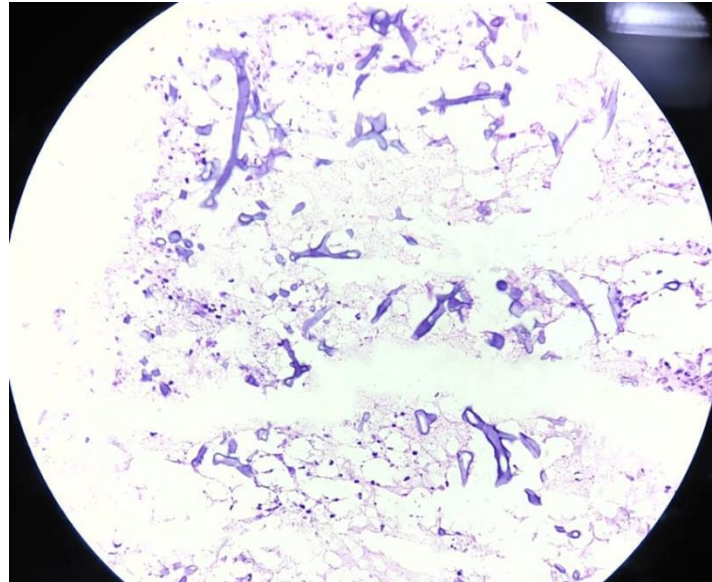


Figure 3: Appearance of Mucor on frozen

In the post COVID era there is an unexpected surge in Mucor infections and delivering appropriate diagnosis on frozen was the need of the hour as it would help the surgeon to take intra operative call on surgical debridement and early surgical debridement is most important given the deadly aggressive and destructive nature of Mucor. All the cases submitted for Mucor involvement were further analyzed on Permanent sections with H&E and special stains like GMS and PAS and it was found that all the diagnosis made with respect to Mucor were proven on H& E and Giemsa

as well. There are very few studies in the literature regarding the role of frozen in Mucor but one of the study by Rahaf Alkhateb et al [8] showed a concordance of 88.5%

There were 8 cases of oral cavity lesions from buccal mucosa and tongue that have come for Frozen section. Out of these 5 cases were for the margin status and the rest were for confirmative diagnosis. All the 3 cases were diagnosed as squamous cell carcinoma and the margins were free in all the 5 cases. (Figure 4)

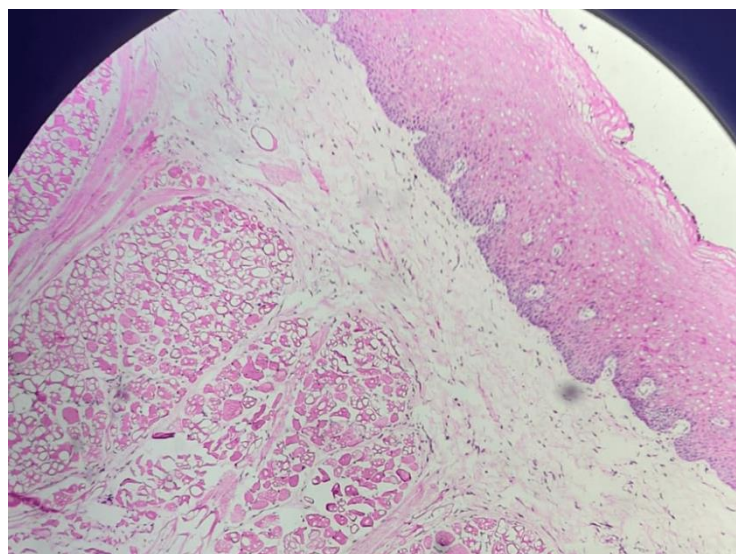


Figure 4: Negative surgical margin on Frozen

The overall concordance in oral cavity lesions was comparable to other studies in the literature like sayeed etal (90%) [9] and sallie etal (96%) [10].

There were 7 cases of FGT lesions that came for frozen out of which there was concordance in 5 cases but in two cases there were discrepant results.

One case was diagnosed as smooth muscle tumor but was later found out in Permanent sections to have a co

existent endometrial stromal sarcoma. The reason for this discrepancy has been analyzed and is due to sampling error. Only the sections from the fibroid area were given and thinking the tumor to be homogenous other areas were ignored but actually there was a soft lesion adjacent to the fibroid which finally turned out to be sarcoma.[Figure 5]

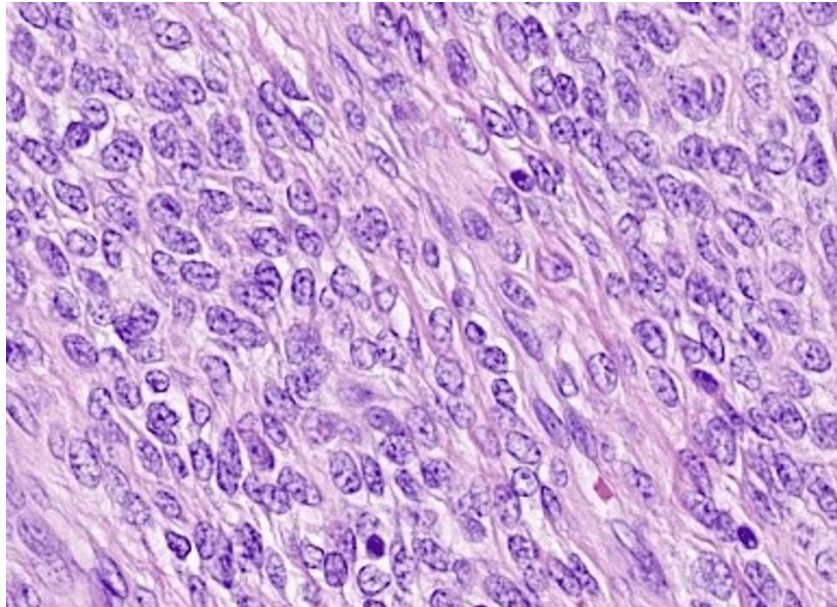


Figure 5: Endometrial stromal sarcoma missed on Frozen

This was an eye opener emphasizing the need to look into the entire tissue and sample the heterogenous areas but given the short time available in frozen such errors are not totally unavoidable. Another case was diagnosed as mucinous neoplasm probably benign but later turned out to be a borderline tumor, this was because there were few foci of less than 5 mm stromal invasion on thorough sampling on permanent sections which again reflects a limitation of frozen section where thorough sampling cannot be done given the limitation of time. This too carried a message of caution for all the reporting pathologists that lesions with heterogenous nature cannot be deciphered on Frozen section. The concordance of frozen section was thus only 75% in our present study in contrast to 85% in studies by sathish etal [11] and 93% in studies by palakkan etal [12]

The other lesions from gall bladder, Thyroid, Parathyroid were concordant with the final histopathological diagnosis

The sensitivity and specificity of frozen section was comparable to that in other studies(Table 3)

CONCLUSION

Frozen section is an important tool for the decision making of the surgeon on the table. Preparing to report a frozen section would require prior information of the case including FNAC, Core biopsy findings, clinical and radiological findings and

interaction with clinician. With proper ground work done, avoiding sampling and interpretative errors, Frozen section is really an indispensable tool for the surgeon and pathologist.

Our study in addition to adding to the existing knowledge on frozen section accuracy has helped to explore its role in post covid mucor diagnosis intraoperatively.

ACKNOWLEDGEMENTS

We acknowledge the efforts of all the faculty involved in diagnostic work at our institute as well as the efforts of our histopathology technicians.

REFERENCES

1. Hossein Hatami et al .The Diagnostic Accuracy of Frozen Section Compared to Permanent Section: A Single Center Study in Iran. *Iran J Pathology*. 2015; 10: 295-299. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4539748>
2. Dr. Pragati Prabhakar Rao, Dr. Sarita Devrao Dakhure. The Diagnostic Accuracy of Frozen Section Compared to Routine Histopathological Technique – A Comparative Study. *International journal of science and health care research*. July-Sept. 2018; 3:88-92, DOI: <https://doi.org/10.52403/ijshr>
3. Dr. K. Chandramouleeswari¹, Dr. M. Yogambal², Dr. P. Arunalatha³, Dr. Jagadeesh Chandra Bose⁴, Dr. A. Rajendran Frozen and paraffin sections - Comparative study highlighting the concordance and discordance

- rates in a tertiary care centre IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861. Volume 12, Issue 5 (Nov.-Dec. 2013), PP 26-30
<https://www.iosrjournals.org/iosr-jdms.html>
4. Fadwa J Altaf Audit of breast frozen sections *Ann Saudi Med*. 2004 Mar-Apr; 24(2): 141–144. doi: [10.5144/0256-4947.2004.141](https://doi.org/10.5144/0256-4947.2004.141)
 5. NIU Yun, FU Xi—lin, YU Yong, Peizhong Peter Wang and CAO Xu—chen Intra-operative frozen section diagnosis of breast lesions : a retrospective analysis of 13243 chinese patients *Chinese Medical Journal* 2007 : 120(81 : 630—635
<https://pubmed.ncbi.nlm.nih.gov/17517175/>
 6. Mahadevappa A., Nisha T. G., Manjunath G. V. Intra-operative diagnosis of breast lesions by imprint cytology and frozen section with histopathological correlation. *Journal of Clinical and Diagnostic Research*. 2017;11(3):p. EC01–EC06. doi: [10.7860/JCDR/2017/24454.9323](https://doi.org/10.7860/JCDR/2017/24454.9323).
 7. Karve P. V., Jambhekar N. A., Desai S. S., Chinoy R. F. Role of frozen section evaluation in patient with breast lumps: a study of 251 cases. *The Indian Journal of Surgery*. 2005;67:241–245 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9152418/>
 8. Rahaf Alkhateb, Preethi Dileep Menon, Hamza Tariq, Sarah Hackman, Alia Nazarullah, Daniel D Mais, Accuracy of Intraoperative Frozen Section in Detection of Acute Invasive Fungal Rhinosinusitis *Arch Pathol Lab Med* (2021) 145 (6): 736–743
<https://pubmed.ncbi.nlm.nih.gov/33091928/>
 9. Sayed Akbar Abbas¹, Mubasher Ikram², Muhammad Usman Tariq³, Ahmed Raheem⁴, Javeria Saeed⁵ Accuracy of frozen sections in oral cancer resections, an experience of a tertiary care hospital *J Pak Med Assoc* 2017 May;67(5):806-809
<https://pubmed.ncbi.nlm.nih.gov/28507379/>
 10. Sallie M. Long, MD^{1,2}; Timothy Mclean, MBBS¹; Cristina Valero Mayor, MD, PhD¹; et al Use of Intraoperative Frozen Section to Assess Final Tumor Margin Status in Patients Undergoing Surgery for Oral Cavity Squamous Cell Carcinoma *JAMA Otolaryngol Head Neck Surg*. 2022;148(10):911-917. doi: [10.1001/jamaoto.2022.2131](https://doi.org/10.1001/jamaoto.2022.2131)
 11. Sathish Selvakumar, **Role of Frozen Sections in Diagnosing Female Genital Tract Lesions: A Tertiary Centre Study in Chennai, India National Journal of Laboratory medicine. 2023 Volume 12 issue 2 page 5-10**
<https://pubmed.ncbi.nlm.nih.gov/32090007/>
 12. Saphina Palakkan¹, Tony Augustine^{1,*}, M. K. Valsan¹, K. P. Abdul Vahab¹ and Lekha K. Nair Role of Frozen Section in Surgical Management of Ovarian Neoplasm *Gynecol Minim Invasive Ther*. 2020 Jan-Mar; 9(1): 13–17. DOI: [10.4103/GMIT.GMIT_2_19](https://doi.org/10.4103/GMIT.GMIT_2_19)
 13. Farah-Klibi F, Neji O, Ferjaoui M, Sfar R et. al. Accuracy of frozen section diagnosis: An analysis of 1695 consecutive cases. *Tunis Med*. 2008; 86: 693-7
<https://pubmed.ncbi.nlm.nih.gov/19472734/>
 14. Sudha Ayyagari¹, Anusha Potnurul², Sk Aamer Saleem¹, Pavani Marapakal Analysis of frozen section compared to permanent section: a 2 years study in a single tertiary care hospital *Journal of Pathology of Nepal* (2021) Vol. 11, 1854-1858.
<https://www.nepjol.info/index.php/JPN/article/view/37681/32615>