International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 08, Issue 10, October 2023,
https://doi.org/10.23958/ijirms/vol08-i10/1758

Original article

Intraoperative Consultation of Sino-Nasal Lesions: A Decade Experience at Tertiary Care Hospital

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Received 07 September 2023; Accepted 05 October 2023; Published 12 October 2023

Abstract

Background: Sino-nasal lesions present similar to each other ranging from congenital, infectious, inflammatory, and traumatic to neoplastic causes, which need histopathological confirmation. Lesions like fungal sinusitis represent a fulminant, potentially fatal, disease process in immunocompromised patients. The diagnosis rests on high index of clinical suspicion with diagnostic and therapeutic implications of intraoperative consultation. Present study aimed at evaluation of sensitivity, specificity and diagnostic accuracy of intraoperative consultation in Sino-nasal lesions. ***Design:*** Present study is 10year observational cross-sectional study (October 2011 to October 2021). A total of 203 Sino-nasal lesions that were received for intraoperative consultation at histopathology laboratory were included. Frozen slides and confirmed histopathology slides of these cases were reviewed and statistical analysis done. ***Results:*** Total 203 cases were reviewed. The cases were categorised into non neoplastic, benign and malignant lesions. Fungal sinusitis (mucormycosis> aspergillosis > candidiasis) was commonest in non-neoplastic, inverted papilloma was commonest in benign lesions and adenocarcinoma was commonest in malignant lesions. Male predominance was seen in all 3 categories. Predominant age group affected was 41-60 years. The sensitivity, specificity, positive predictive value, and negative predictive value of non-neoplastic, benign and malignant lesions of frozen section were 93%, 75%, 98.80%, and 64.86%; 100%, 100%,100%, and 100%; and 100%, 98.90%, 100% and 85.70%, respectively. ***Conclusion:*** Present study emphasises that frozen studies are highly sensitive in the diagnosis of Sino-nasal lesions. Intra-operative diagnosis of fungal infections thereby facilitates immediate targeted treatment strategies for optimal outcomes.

Keywords: ***Intraoperative consultation, sino-nasal lesions, mucormycosis, papilloma, adenocarcinoma.***

Introduction

Frozen section (FS) technique was first introduced by the William H. Welch, from John Hopkins Hospital in 1891 [1,20]. By the early and mid-1920s, the technique became popular and was used for intraoperative consultation practice. The preparation of frozen section was made easier in the 1950s and 1960s by the development of the modern cryostat, a cabinet cooled to -20 to -30 degree Celsius and enclosing a microtome blade [1,2]. The main purpose of frozen section is to provide rapid diagnosis to guide intra or perioperative patient management [1]. The practice of frozen section in surgical pathology is an art form that has been passed on from one generation of pathologists to the other by traditional "at the scope" teaching [3].

The nasal cavity and paranasal sinuses-including the maxillary, ethmoid, sphenoid, and frontal sinuses are collectively referred to as the sinonasal tract [3,21]. The sinonasal tract is anatomically and embryologically distinct from the nasopharynx. Although the sinonasal tract and nasopharynx have identical-appearing ciliated respiratory epithelium, the epithelium of the sinonasal tract is ectodermally derived, while that of nasopharynx is endodermally derived. This embryologic difference may be a factor in the development of certain epithelial lesions unique to this surface. Of all the malignant neoplasms, carcinomas account for 0.2-0.8% of nasal cavity and paranasal sinuses [3]. Varied lesions from inflammatory to neoplasm are encountered in sinonasal tract. Acute invasive fungal rhinosinusitis (AIFRS) is a life-threatening infection that typically occurs in patients with a quantitative or functional immunodeficiency. An immunocompromised state places these patients at risk for infection by causative organisms, such as mucormycosis and aspergillus [4]. Aspergillus or Mucor in immunologically compromised patients, a feature heavily influenced by neutrophil dysfunction in the form of either frank neutropenia or diabetes mellitus [5]. The extensive tissue necrosis commonly encountered in this condition may be related to the prominent vascular and perineural invasion by the organism [6]. It is quite impossible to distinguish clinically between simple nasal polyps, polypoidal lesions and polypoidal neoplasms, hence it becomes important that all polyps and polypoidal lesions of nose should be submitted for histopathological examination [7,13,22].

The indications for intraoperative consultation in Sinonasal lesions include [7,19]:

1. Render histologic assessment of the adequacy of resection for the presence of dysplasia and/or carcinoma when definitive therapeutic intervention/ decision is planned immediately.

2. Preliminary assessment of the nature of a planned procedure based on the extent and distribution of the neoplasm.
3. Adequacy for diagnostic purposes.
4. Render early treatment for fungal infections.

The present study was taken to know about intra-operative consultation efficacy in sinonasal lesions.

Materials and Methods

Present study is 10-year cross sectional study (October 2011 to October 2021). Institutional ethical clearance was obtained numbered as SDMIEC/2021/104. Patients were clinically evaluated by history, examination, haematological and radiological investigations. The material for cytology examination (squash) and frozen sections were taken pre operatively. Tissue for frozen section is received fresh or in normal saline. Bar code is generated and biopsy number is assigned. Adequate tissue is sampled and excess water content is removed from tissue by using blotting paper. Tissue is freezed at -210 C in a cryostat using tissue freezing medium which contains Polyvinyl alcohol, potassium formate and polyethylene glycol. Tissue is sectioned at 5micron thickness. Frozen sections were subjected to rapid hematoxylin and eosin stain. Remaining tissue was taken for routine processing. Paraffin-embedded sections were stained with hematoxylin and eosin stain. A rapid opinion regarding the presence of fungus, neoplastic or non-neoplastic lesion was given. The findings were compared with the paraffin-embedded sections for histopathological final diagnosis and statistical analysis done using SPSS version 20.2 software. The cases were categorised into non neoplastic lesions, benign lesions and malignant lesions.

Sensitivity, specificity, positive predictive value and negative predictive value of frozen section was calculated taking histology as gold standard.

Results

A total of 203 cases were studied, which were categorised into non-neoplastic, benign and malignant lesions. 181 cases were classified under non-neoplastic lesions, 14 cases under malignant, 8 under benign. Out of 203, 64 were female and 139 were male with male preponderance (Pie chart).

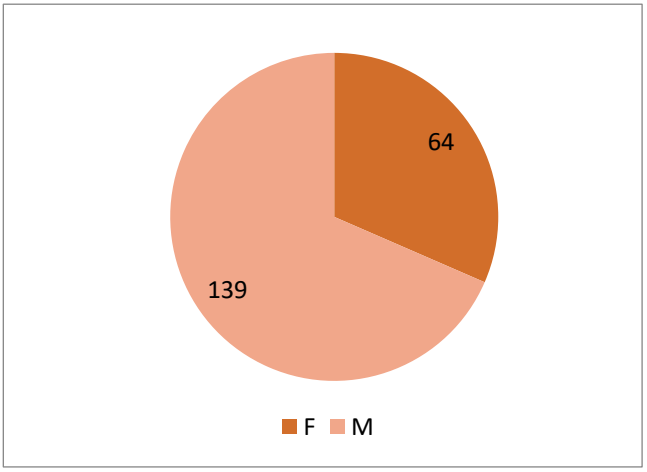

Chart: 1: Age ranged between 18 to 93 years. Among both males and females 41-50 years was most commonly involved (**Table 1**) and mean age was 50.24 years.

Table 1: Age distribution

Age (in years)	No. of patients
0-10	0
11-20	3
21-30	15
31-40	31
41-50	55
51-60	51
61-70	38
71-80	9
81-90	0
91-100	1
Total	203

Most common site of involvement was sinus cavity followed by nasal cavity. Most common non-neoplastic lesion encountered was Mucormycosis (**Fig 1**) followed by Inflammatory Polyp (**Fig 2**). Coming to most common benign lesion encountered in the study was inverted papilloma and most common malignant lesion found was adenocarcinoma.

Non neoplastic lesions.

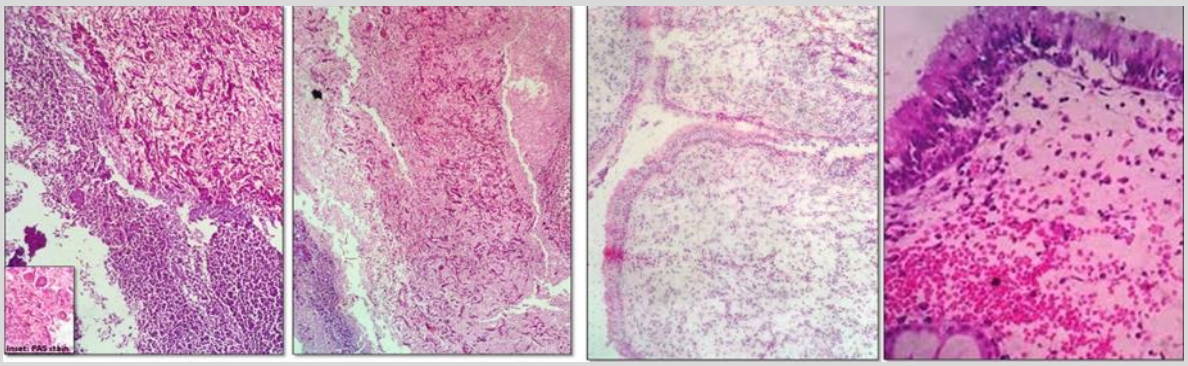

Figure 1: Case of Mucormycosis

Figure 2: Case of Inflammatory Polyp

Fig 1: Leftside: Frozen image 400X H&E stain shows pseudo hyphae and spores of fungus
Fig 1: Rightside: FFPE sections 400X H&E stain confirming Mucormycosis infection.

Fig 2: Leftside: Frozen image 400x H&E stain shows Polyp lined by respiratory epithelium and stroma edematous and congested, given as inflammatory polyp.
Fig 2: Rightside: FFPE sections 400x H&E stain confirming Inflammatory polyp.

Out of 203 cases, 181 cases were diagnosed as non-neoplastic on frozen. 155 cases out of 181 were concordant with final histopathology report (**Table 2**) and rest 26 cases were discordant (**Table 3**).

Table 2: List of concordant cases of frozen report and final histopathological diagnosis.

Lesions category on frozen study	No of cases	Histopathology diagnosis
Positive for fungal elements	67	53cases of mucormycosis 7cases of aspergillosis 1case of candidiasis 6cases of mixed fungal infection
Negative for fungal elements	68	52cases normal mucosa 12 cases inflammatory lesion 4cases inflammatory polyps
Inflammatory lesion	6	1case of tuberculosis 2 cases of allergic polyp 3 cases of chronic rhinosinusitis
Inflammatory polyps	10	7cases of inflammatory polyps 2cases of antra choanal polyp 1case of ethmoidal polyp
Others Non representative biopsy No e/o inverted papilloma Mucinous glands hyperplasia	4	 2cases were non representative 1case of infarction and thrombosis- vascular lesion 1case of Respiratory epithelial adenomatoid hamartoma
Total non-neoplastic cases	155 cases	

Table 3: list of discordant cases.

Intraoperative diagnosis	Number of cases	Histopathology diagnosis
Negative for fungal elements	10	7 were mucormycosis 1 candidiasis 1 aspergillosis 1 angioleiomyoma
Suspicious for fungal elements	3	3 Mucormycosis
Positive for fungal elements	7	Negative for fungal elements Chronic inflammatory lesion
Inflammatory lesion	6	3 aspergilloses 1 mucormycosis 1sinonasal type hemangiopericytoma 1hematoma
Total cases	26 cases	

Benign lesions

Out of 203 cases, 8 cases were found to be benign lesions and all were concordant with final histopathology report. 6 cases were reported as inverted papilloma, [**Fig 3 (in that 1case was with dysplasia)**], 1 case of capillary haemangioma and 1 case of fibrous dysplasia of frontal bone (**fig 4**) was given on frozen and confirmed on histopathology.

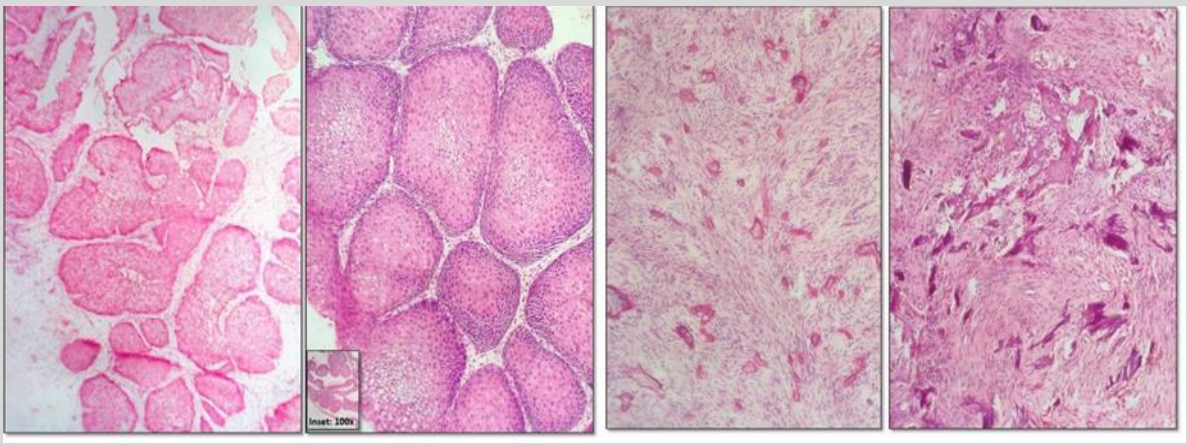

Figure 3: Case of Sino-nasal Inverted Papilloma **Figure 4: Case of Fibrous Dysplasia**

Fig 3: Leftside-Frozen image 400x H&E stain shows endophytic growth of epithelial cells with smooth outer contour given as inverted papilloma.
Fig 3: Rightside: FFPE sections 400x H&E stain confirming Sinonasal Inverted Papilloma

Fig 4: Leftside: Frozen image 400x H&E stain shows branching and anastomosing irregular trabeculae of woven bone and fibrous stroma suggested as fibrous dysplasia.
Fig 4: Rightside: FFPE sections 400x H&E stain confirming Sino-nasal fibrous dysplasia.

Malignant lesions

Out of 203 cases, 14 cases were found to be malignant lesions and 12 cases were concordant with histopathology diagnosis which included Squamous cell carcinoma (**3 cases, fig 5**), Embryonal Rhabdomyosarcoma (**Fig 6**), Ewing's' Sarcoma (**Fig 7**), Malignant Melanoma (**Fig 8**) Monophasic Synovial Sarcoma (**Fig 9**), Sino-nasal Undifferentiated Carcinoma, Nasopharyngeal Carcinoma, Nasopharyngeal Papillary Adenocarcinoma, Neuroendocrine tumour, Adenoid cystic carcinoma: 1 each case respectively.

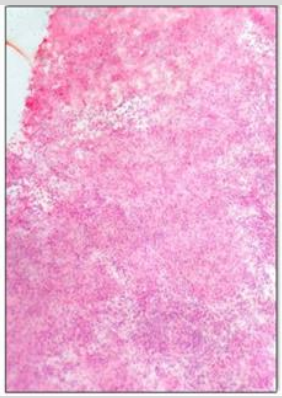

Figure 5: Case of Squamous cell carcinoma

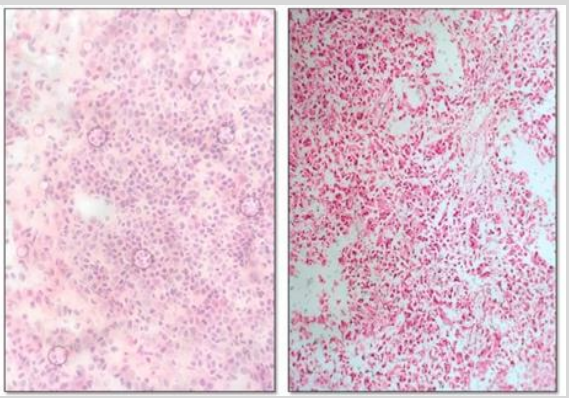

Figure 6: Case of Embryonal Rhabdomyosarcoma

Fig 5: Leftside: Frozen image 400x H&E stain shows atypical squamous cells arranged in nest and sheet suggesting malignancy Squamous cell carcinoma.
Fig 5: Rightside: FFPE sections 400x H&E stain confirming Squamous cell carcinoma of maxillary sinus

Fig 6: Leftside: Frozen image 400x H&E stain shows atypical round cells with high N:C ratio arranged in lobules and nests suggesting blue round cell tumour.
Fig 6: Rightside: FFPE sections 400x H&E stain confirming Embryonal Rhabdomyosarcoma.

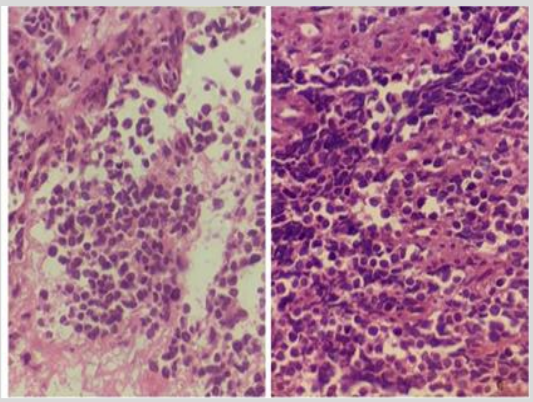

Figure 7: Case of Ewing's' Sarcoma

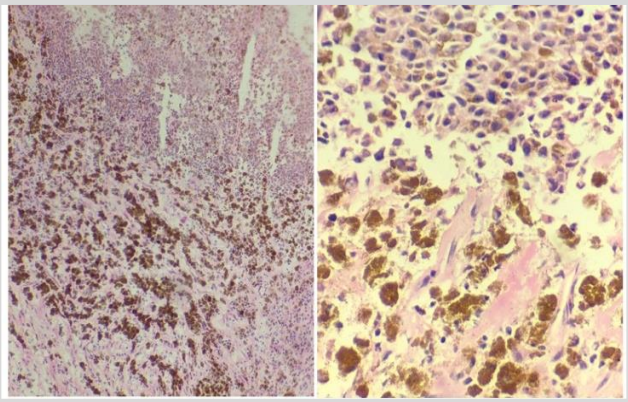

Figure 8: Case of Malignant Melanoma

Fig 7: Leftside: Frozen image 400x H&E stain shows atypical round cells with high N:C ratio arranged in rosettes and nest pattern suggesting Blue Round Cell Tumour.
Fig 7: Rightside: FFPE sections 400x H&E stain confirming Ewing's' sarcoma

Fig 8: Leftside: Frozen image 400x H&E stain shows atypical cells with vesicular nucleus prominent nucleoli and moderate cytoplasm with evident intracellular melanin pigment given as Malignant Melanoma.
Fig 8: Rightside: FFPE sections 200x H&E stain confirming Malignant Melanoma.

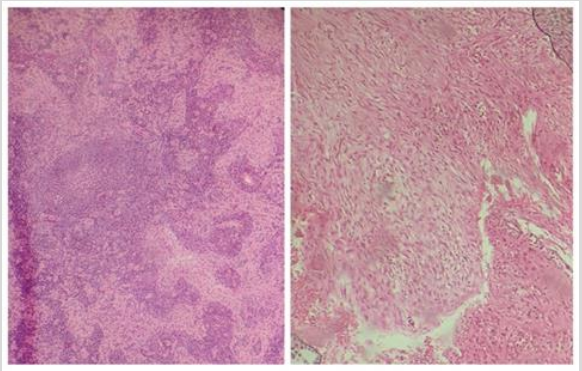

Figure 9: Case of Monophasic Synovial Sarcoma.

Fig 9: Left side: Frozen image 400x H&E stain shows spindle cells arranged in fascicles and sheets with pleomorphic features having hyperchromatic nucleus and scant cytoplasm, suggested spindle cell tumour.
Fig 9: Right side: FFPE sections H&E stain confirming Monophasic Synovial Sarcoma

Two cases were discordant which was given as plasmacytoma on frozen which turned out as ectopic pituitary adenoma of sphenoid sinus and other case was given as giant cell reparative granuloma which was diagnosed as hypertrophied mucosa on histopathology.

Sensitivity, specificity, positive predictive value and negative predictive value of non-neoplastic, benign and malignant lesions of frozen section were calculated taking histopathology as gold standard.

The sensitivity, specificity, positive predictive value, and negative predictive value of non-neoplastic, benign and malignant lesions of frozen section were 93%, 75%, 98.80%, and 64.9%; 100%, 100%,100%, and 100%; and 100%, 98.9%, 100% and 85.70%, respectively (Bar Diagram).

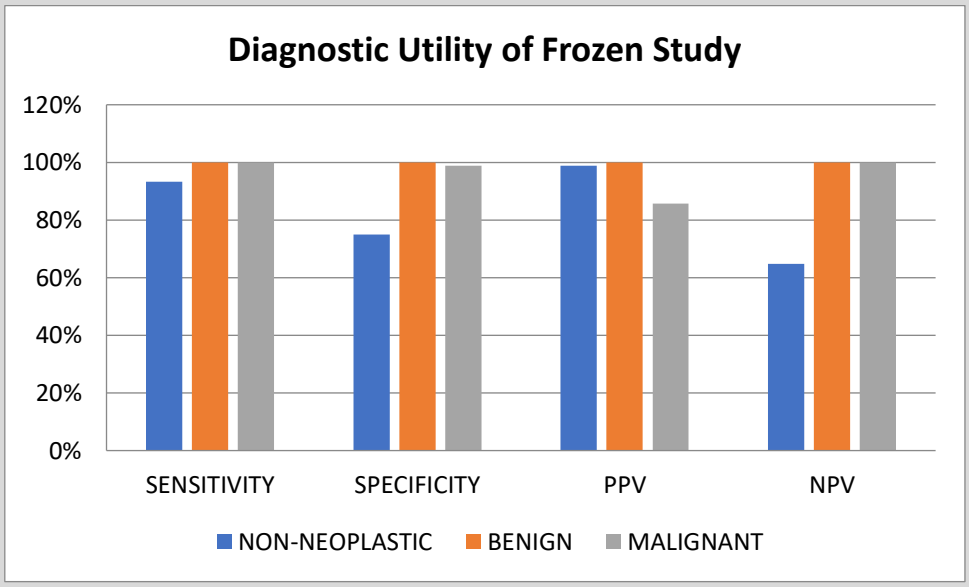

Chart 2: Bar diagram showing Ss, Sp, PPV and NPV

Discussion

Frozen section has gained importance due to rapid evaluation. There are 3 principal reasons for operating room consultations. These are to provide rapid gross or microscopic diagnosis for intra- or peri-operative patient management, to optimally process tissue for special studies to be used for diagnosis, treatment, or research, and to confirm lesion affected tissue is present for diagnosis. Combinations of frozen sections and squash preparation are often used in intra-operative diagnosis. The nasal cavity and paranasal sinuses are exposed to a variety of infections, chemically irritating and antigenically stimulating, mechanical, and traumatic influences [3,22]. As a consequence of these exposures, there are formations of tumour-like and truly neoplastic conditions. The nose and paranasal sinuses accounts for less than1% of all malignant tumours in the general and not more than 3% of the head and neck region malignancies [3]. Table 4 shows comparison of studies in literature with present study.

Table 4: Comparison of present study with other study.

	Present study	Nigam et al STUDY[3]	Papagiannopoulos et al STUDY[4]
Cases	203	30	18
Study duration (Years)	10	-	10
Mean Age	50.24752	30.5	48.8
Gender	Male	Male	Male
Common site	Sinus cavity	Left nasal cavity	-
Acute invasive fungal rhinosinusitis	68	-	18
Non neoplastic lesions	181	20	-
Benign	8	6	-
Malignant	14	4	-

Chandra Mouleeshwari et.al concluded that frozen section diagnosis is very useful and highly accurate procedure. Methodical macroscopic examination and accurate sampling by pathologist, avoiding technical errors in sectioning and staining, a correct combination of knowledge about the clinical presentation, radiological, biochemical findings and good rapport with the operating surgeon can reduce the limitations and provide rapid, reliable and cost-effective details necessary for rapid diagnosis and on table patient management [2].

Nigam et.al concluded that intra-operative cytology and frozen section examinations of lesions of nose and paranasal sinuses are useful, quick, and reliable diagnostic technique for rapid and early diagnosis in the operation theatre and can be used as an adjunct to histopathology for better management of patients [3].

In the present study statistical analysis included sensitivity, specificity, positive predictive value, and negative predictive value of non-neoplastic, benign and malignant lesions of frozen section were 93%, 75%, 98.8%, and 64.7%; 100%, 100%,100%, and 100%; and 100%, 98.9%,100% and 85.70%, respectively, which was comparable to study done by Nigam3 et al which was 100%, 96.15%, 80 % 100 % respectively and diagnostic accuracy was 96.7%. This was also observed by study done by Papagiannopoulos et al who had sensitivity 72.7%, specificity 100%, PPV 100% and NPV 64.7% [4].

Author Taxy JB studied 60 cases of para-nasal fungal sinusitis and concluded that frozen section is a collaborative effort among the physicians with the best interests of the patient in mind. Nevertheless, the responsibility for handling the tissue belongs to pathologists. A frozen section is not a trivial procedure. Tissue analysis under these circumstances may be difficult and the stakes are high, so requests for frozen section should be judiciously initiated and answered. Close attention to the quality and size of the sample, the morphologic features of the disease, and the possible organisms and insistence on appropriate clinical information are needed. The combined use of rapid Romanowsky and H&E stains may be diagnostically helpful. The experience with the present cases indicates that frozen section has a meaningful role in the care of patients with this serious infection [5].

Author Selva Kumar AS and co-authors in their study titled "Intraoperative frozen section consultation- an audit in a tertiary care hospital" observed that Oro-pharyngo-laryngeal region (48.84%) was the main site sampled for frozen study. The main indication was margin status assessment (52.27%). Accuracy rate was 98.65% with an error rate of 1.35% was observed. The discordant cases had misinterpretation error in 5 cases and sampling errors in the remaining 2 cases. Three cases (0.58%) were deferred. Sensitivity (90.91%) and specificity (96.59%) was obtained. They concluded that frozen section plays a critical role in the surgical management by avoiding second surgeries and can be of great value to the surgeon when carried out keeping in mind all its limitations [8]. Chiu et.al and Silveira et.al concluded that intraoperative frozen margins for Sino-nasal tumours are reliable for most histologic subtypes and a fast and reliable exam to confirm the diagnosis of fungal invasion, present study agrees on the same [9,12].

Guarner Jand Mary EB discussed elaborately in their paper titled "Histopathologic Diagnosis of Fungal Infections in the 21st Century" about significance of histopathologic examination of tissues to detect fungal invasion of tissues and vessels. Therefore, histopathologic diagnosis should be primarily descriptive of the fungus and should include the presence or absence of tissue invasion and the host reaction to the infection. Present study had observed huge raise in fungal infection (approximately 81cases) especially mucormycosis in the pandemic era of SARS CoV2 infection. The pathology report should include a comment stating the most frequent fungi associated with particular morphology as well as other possible fungi and parasites that should be considered in the differential diagnosis. Alternate techniques are available to determine the specific agent present in the histopathologic specimen, including immunohistochemistry, in situ hybridization, and PCR [11].

Mane et.al concluded that Sino-nasal masses or polyps can be non-neoplastic or neoplastic lesions and histopathological examination remains mainstay in differentiating these lesions [13].

Annam et.al, Bist et.al and Gillespie et.al studied role of radiological images in sino-nasal lesions and said that use of CT scan, MRI and rigid nasal endoscopy with frozen section biopsy and histopathological evaluation of suspicious nasal lesions allows tumour free resection, correct and timely diagnosis, intervention improves survival [10,14,16].

Zachary MS and Rodney JS had a literature review of role of fungus in diseases of sinonasal lesions and concluded that each form of fungal rhinosinusitis has a characteristic presentation, clinical course and outcome with the immune status of the host playing a critical pathophysiological role. Accurate diagnosis and targeted treatment strategies are necessary to achieve optimal outcomes [15].

Ismaiel et.al observed that incidence of acute invasive fungal rhinosinusitis is markedly more prominent in post-COVID-19 patients than in non-COVID-19 especially in immuno-compromised patients, diabetic, renal and liver dysfunction patients and patients with risk factors for rhinosinusitis which was observed in present study as well and thus cautioning to be careful while reporting frozen in immune compromised cases [17].

DiNardo et.al evaluated frozen section results and are highly specific (98.9%) but only moderately sensitive (88.8%) compared with final margins from the resection specimen [18].

Conclusion

Frozen section showed good diagnostic accuracy and specificity. Thus, intra-operative consultation proved to be useful, quick, and reliable diagnostic technique for rapid diagnosis in the operation theatre and can be used as an adjunct to histopathology for better management of patients.

Ethics approval and consent to participate.

Institutional ethical clearance (IEC) was obtained numbered as SDMIEC/2021/104. IEC is recognised and this is registration details Reg No. ECR/950/Inst/KA/2017/RR-21(DCGI); EC/NEW/INST/2021/1761(DHR); IORG- 0007404 (HHS, USA)

Conflicts of Interest

"The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper."

Funding Statement

NA

Authors' contributions

SR involved in research proposal preparation, data collection, getting all formation from medical records, filling the proforma and analysis of results.

APJ involved in concept development, research proposal preparation for IEC, proforma and data collection sheet, analysis of data, interpretation of slides. manuscript preparation. APJ is major contributor for research.

VSA involved in manuscript editing.

Acknowledgments

Authors thank the technical staff and Medical Record Department for assisting in retrieval of archival slides and clinical details.

Supplementary Materials

NA

Acknowledgment

Authors thank the technical staff and Medical Record Department for assisting in retrieval of archival slides and clinical details.

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