

MANUSCRIPT

# TITLE- EFFICACY OF FINE NEEDLE ASPIRATION CYTOLOGY IN TRIBAL AREA- GUJARAT

RUNNING TITLE—EFFICACY OF FINE NEEDLE ASPIRATION CYTOLOGY IN CERVICAL REGION.

DR GAURAV S PAWAR<sup>1</sup> DR CHARU TRIPATHI<sup>2</sup> DR RAM KUMAR<sup>3</sup>

<sup>1</sup> ASSISTANT PROFESSOR, ZYDUS MEDICAL COLLEGE AND HOSPITAL DEPARTMENT OF PATHOLOGY, DAHOD, GUJARAT, EMAIL- [drdsp11@gmail.com](mailto:drdsp11@gmail.com), [gauravpawar@aol.com](mailto:gauravpawar@aol.com)

<sup>2</sup> ASSISTANT PROFESSOR, DEPARTMENT OF PATHOLOGY, ZYDUS MEDICAL COLLEGE AND HOSPITAL, DAHOD, GUJARAT, INDIA

<sup>3</sup> HEAD OF DEPARTMENT, DEPARTMENT OF PATHOLOGY ZYDUS MEDICAL COLLEGE AND HOSPITAL, DAHOD, GUJARAT, INDIA

## INTRODUCTION-

NECK LESIONS ARE FREQUENTLY ENCOUNTERED IN CLINICAL PRACTICE AND FOUND RESPONSIBLE FOR SIGNIFICANT MORBIDITY AND MORTALITY IN INDIA. SOME OF THE LESIONS OF THE NECK REGION INCLUDE TUBERCULOSIS & OTHER CHRONIC INFLAMMATORY LESIONS, PLEOMORPHIC ADENOMA & CYSTS. MALIGNANT LESIONS-PRIMARY AS WELL AS METASTATIC, COMMON TO THE CERVICAL GROUP OF LYMPH NODES, ARE ALSO FREQUENTLY NOTED.

FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) IS A SIMPLE, ECONOMICAL, HIGHLY ACCURATE TOOL IN THE DIAGNOSIS OF CERVICAL LESIONS. IT IS ALSO IDEAL FOR SAMPLE COLLECTION FOR ANCILLARY STUDIES SUCH AS CBNAAT. FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) SAMPLES FROM THE NECK REGION OF PATIENTS CAN BE REVIEWED IN ORDER TO EVALUATE THE EFFICACY OF THIS METHOD IN THE DIAGNOSIS OF CERVICAL LESIONS. THE MAIN EMPHASIS OF THIS STUDY IS TO DETERMINE DIFFERENT CYTOMORPHOLOGICAL ENTITIES AND PROVIDE THE DETAILS OF BURDEN OF TUBERCULOSIS IN THE TRIBAL AREA. TUBERCULOSIS IS THE MOST COMMON CAUSE OF LYMPHADENOPATHY IN DEVELOPING COUNTRIES SUCH AS INDIA AND SHOULD BE CONSIDERED IN EVERY CASE OF GRANULOMATOUS LYMPHADENOPATHY UNLESS PROVED OTHERWISE.[1]

## METHOD AND MATERIAL-

THIS STUDY WAS CONDUCTED FROM 1 JUNE 2019 TILL NOVEMBER 2020 IN ZYDUS MEDICAL COLLEGE AND HOSPITAL, DAHOD. FNAC WAS DONE IN THE OUTPATIENT PATHOLOGY BLOCK OF THE HOSPITAL. ASPIRATION WAS DONE USING A 5 ML SYRINGE WITH 22-24 GAUGE NEEDLE. SLIDES WERE PREPARED AND STAINED WITH H&E, GIEMSA AND PAPANICOLAOU STAIN, ZN STAIN, USED AS AND WHERE REQUIRED. THE DETAILED HISTORY, CLINICAL EXAMINATION AND INVESTIGATIONS DONE WERE RECORDED. REPORTING WAS DONE BY CYTOLOGISTS. REPEAT SAMPLING WAS DONE IN FEW CASES DUE TO INADEQUATE SAMPLING REPORTED.

## Statistical Analysis Methods

Predictive analysis relied on logistic regression to obtain a probability for everyone to belong to the group SEX = M. We then drew a ROC curve to present the different decision thresholds.

## Predictor variables

We selected the candidate predictor variables from the set of collected variables in such a way that there were less than 20% of patients with missing data or variables with less than 5% missing values. The predictor variable AGE was defined a priori based on data from the literature. The candidate predictor variables were included in a Least Absolute Shrinkage and Selection Operation (LASSO) penalized regression model. The penalty coefficient (lambda) was chosen to provide an estimation error lower than one standard deviation of the minimum error obtained by 10-fold cross-validation, while being as parsimonious as possible. No variable had a coefficient different from 0 with this lambda coefficient.

## Validation

Model performance (AUC) was calculated from a bootstrap resampling (100 iterations). using the same procedures for variable selection and calculation of logistic regression coefficients. We then carried out the procedure for correcting over-optimism in performance measurement and performed coefficient shrinkage to improve prediction on external data.

## RESULT

THIS STUDY WAS CONDUCTED IN ZMCH, DAHOD BETWEEN 1 JUNE 2019 TO 30 NOVEMBER 2020. FNAC OF 178 CASES WAS DONE FOR CERVICAL LESIONS OTHER THAN THYROID. CASES WERE DEVIDED IN THREE GROUPS AS <18 YRS, 18-45 YRS AND >45 YRS. IN WHICH 99(55.6%) WERE MALE AND 79(44.4%) WERE FEMALES. THE RATIO OF MALE AND FEMALE WAS 1.25:1. MAXIMUM NUMBER OF CASES WERE OF AGE GROUP 18-45 YRS (83/178) 46.6%. IN MALES, MAXIMUM CASES WERE OF <18 YRS AGE GROUP (41/99), 41.4%. IN FEMALES MOST OF CASES WERE OF 18-45 YRS AGE GROUP (44/79) 55.6% (TABLE/FIG 1/2).

IN 4 CASES (2.2%) SMEARS WERE UNSTISFACTORY. MOST COMMON LESION WAS CHRONIC NON SPECIFIC LYMPHADENITIS/REACTIVE LYMPHADENITIS (68/178) 38.2%, FOLLOWED BY CHRONIC GRANULOMATOUS LYMPHADENITIS (54/178) 30.34% IN OUR STUDY (TABLE/FIG 3/4). IN MALES MOST COMMON LESION WAS CHRONIC NON

SPECIFIC LYMPHADENITIS/REACTIVE LYMPHADENITIS(40/99) 40.4% AND IN FEMALES PREDOMINANT LESION WAS CHRONIC GRANULOMATOUS LYMPHADENITIS (30/78)38.5%(TABLE FIG 3/4).IN MALES <18YRS,MOST COMMON LESION IS CHRONIC NON SPECIFIC LYMPHADENITIS/REACTIVE LYMPHADENITIS(27/41)65.85%, BETWEEN 18-45 YRS , MOST COMMON LESION WAS CHRONIC GRANULOMATOUS LYMPHADENITIS (17/35)48.57% ,>45YRS , MOST COMMON LESION WAS MALIGNANT LESION(12/19) 63.1%(TABLE/FIG 5/6/8).IN FEMALES, <18 YRS, CHRONICNON-SPECIFIC LYMPHADENITIS/REACTIVE LYMPHADENITIS AND CHRONIC GRANULOMATOUS LYMPHADENITIS WERE EQUALLY COMMON LESIONS (12/24),50%.BETWEEN 18-45 YRS MOST PREVALENT LESION WAS CHRONIC GRANULOMATOUS LYMPHADENITIS (17/44)38.6% AND >45YRS MOST PREVALENT LESION WAS MALIGNANT LESION (5/11)45.45%(TABLE/FIG5/7/8)16(8.98%) CASES OF ABSCESS AND 2 (1.1%) CASES OF PLEOMORPHIC ADENOMA WERE FOUND. LIPOMA AND EPIDERMOID CYST WERE FOUND IN 3(1.69%) CASES EACH.

#### DISCUSSION-

THIS STUDY WAS CARRIED OUT TO FIND THE RELATIVE INCIDENCE OF NECK LESIONS IN DAHOD DISTRICT OF GUJARAT.FINE NEEDLE ASPIRATION CYTOLOGY IS A RESOURCEFUL TOOL WITH HIGH RATE OF SPECIFICITY GIVING AN APPROPRIATE AND SYSTEMIC TREATMENT LINE WITH EARLY PREVENTIVE OF SURGICAL INTERVENTION. THE CONCLUSIVE RESULT AND OUTCOME IN DAHOD SHOWS A SIGNIFICANT RISE OF CASES OF REACTIVE LYMPHADENITIS. OVERALL, 97.8% CASES WERE FOUND SATISFACTORY WHICH WERE SIMILAR TO STUDY RAHUL *ET AL* 98.15% CASES ALSO CORRELATED WITH HEMALATHA *ET AL* WITH 98% OF CASES [1,2] . THE CERVICAL LESIONS WHICH WERE MORE DOMINANT AMONG MALES THAN FEMALES WITH RATIO OF 1.25:1, WHICH CORRELATE TO THE OTHER STUDIES RAHUL *ET AL* 1.5:1 ALSO THERE WAS CLOSE PROXIMITY WITH R. RANI *ET AL* 1.31:1 [1,4].

THE MAXIMUM NUMBER OF CASES IN OUR STUDY WITH CERVICAL PATHOLOGY ON SMEAR SHOWED CHRONIC NONSPECIFIC LYMPHADENITIS/ REACTIVE LYMPHADENITIS WITH 68/178(38.1 %) CASES WHICH ARE SIMILAR TO 43.4% CASES RAHUL *ET AL*, 56 % DHINGRA V *ET AL*, 64 % TRIPATHI *ET AL* [1, 6,7] TABLE/FIG3,4. VARIABLE NUMBER OF CASES OF LYMPHADENOPATHY WERE FOUND IN DIFFERENT AGE GROUPS. MOST RELEVANT FINDING IN OUR STUDY THE CHRONIC NONSPECIFIC LYMPHADENITIS /REACTIVE LYMPHADENITIS WAS THE MOST STRIKING CYTOLOGICAL FEATURE WITH < 18YEARS AGE GROUP 39/65(60% ) CASES, FOLLOWED BY TUBERCULAR LYMPHADENITIS 19/65 (29 %) CASES WHICH WERE FOUND IN SIMILAR STUDY RAHUL *ET AL* 55.74 % AND 30.4 % , DHINGRA V *ET AL* 56 % AND 28.1 % , R KHAJURIA *ET AL* 74.5 % [ 1,6,5].

AGE GROUP 18- 45YEARS SHOWED TYPICAL FEATURE OF CYTOLOGICAL FINDINGS WITH PREDOMINANCE OF CHRONIC GRANULOMATOUS LYMPHADENITIS WITH 34/83 (40.9 %) FOLLOWED BY CHRONIC NONSPECIFIC /REACTIVE LYMPHADENITIS 25/83 (30.1 %) WHICH CORRESPOND WITH OTHER STUDIES 58.9 % R KHAJURIA *ET AL*, SHRIVASTAVA *ET AL* WITH TUBERCULAR LYMPHADENITIS 46.28 % AND REACTIVE LYMPHADENITIS 28.08 %, Badge SA *ET AL* (32.90 % )[5,8,9].

AND ABOVE 45 YEARS AGE GROUP OUR STUDY SHOWED 17/30 CASES (56.6%) WHICH WERE SIMILAR TO FINDINGS OF MALIGNANT LYMPHADENOPATHY CASES CONFRONTED TO RAHUL *ET AL* 68.54 % , 56.33 % SHRIVASTAVA *ET AL* [1,8].

#### CONCLUSION-

IN THE PRESENT STUDY THE CYTOMORPHOLOGICAL FINDING PREDOMINANTLY IS CHRONIC NONSPECIFIC LYMPHADENITIS/ REACTIVE LYMPHADENITIS WITH OTHER STUDIES SHOWING SIMILAR FEATURES AND INCIDENCE IN DIFFERENT DEMOGRAPHIC REGIONS OF RURAL INDIA. FINE NEEDLE ASPIRATION CYTOLOGY IS AN EFFECTIVE AND COST BENEFICIAL METHOD WITH MINIMAL INVASIVE AND INVOLVES LESSER TRAUMA TO PATIENT AND THE FURTHER TREATMENT LINE CAN BE EASILY APPROACHABLE WITH PROPER PALLIATIVE CARE AND AVOIDANCE OF SURGICAL INTERVENTION. MANY PATIENTS WERE ALSO SUBJECTED TO NAA AND CBNAAT.

#### Conflicts of interest

There are no conflicts of interest.

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#### REFERENCE-

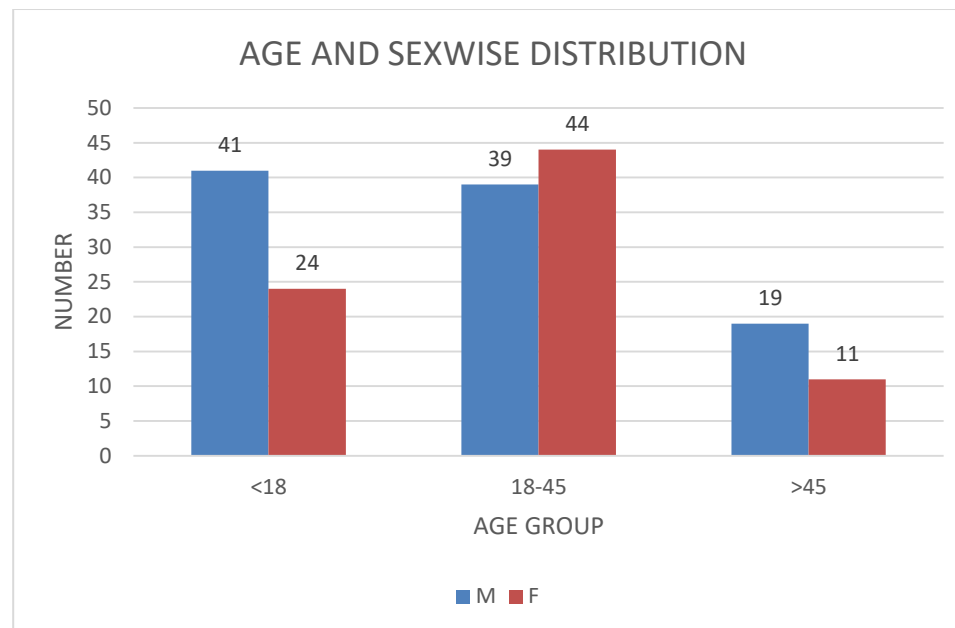
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• TABLES AND CHART –

AGE	M	F	TOTAL
<18	41	24	65
18-45	39	44	83
>45	19	11	30
TOTAL	99	79	178

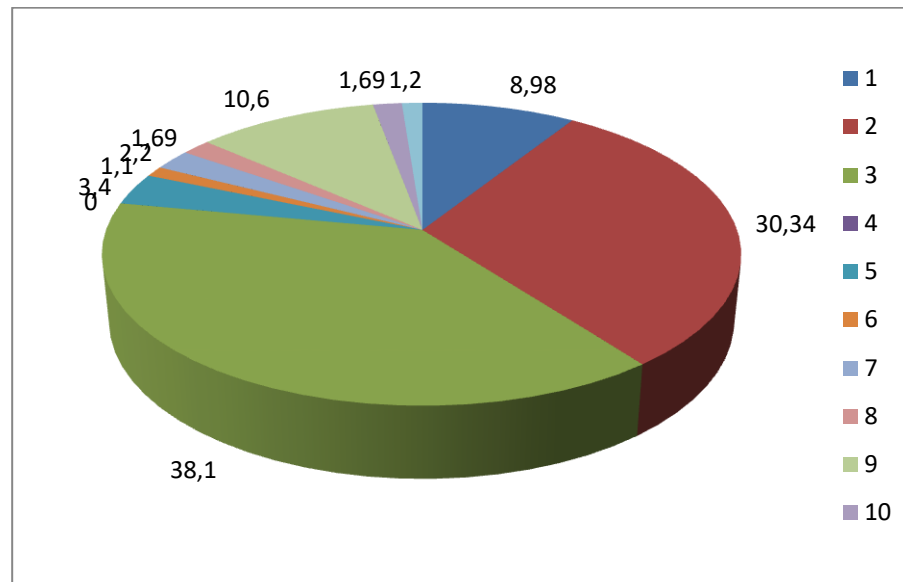
TABLE/ FIG 1 . AGE AND SEX WISE DISTRIBUTION OF CASES



TABLE/ FIG 2 AGE AND SEX DISTRIBUTION SHOWING NUMBER OF LESIONS AMONG THE 178 CASES.

MICROSCOPY	MALE S	FEMAL E	TOTAL	%
1) ABSCESS	9	7	16	8.98
2)CHRONIC GRANULOMATOUS LYMPHADENITIS	24	30	54	30.34
3) CHRONIC NON SPECIFIC LYMPHADENITIS/REACTIVE LYMPHADENITIS	40	28	68	38.1
4)NECROTIZING LYMPHADENITIS	2	4	6	3.4
5)PLEOMORPHIC ADENOMA	1	1	2	1.1
6) UNSATISFACTORY	4		4	2.2
7)LIPOMA	2	1	3	1.69
8)MALIGNANT LESION	14	5	19	10.6
9)EPIDERMOID CYST	2	1	3	1.69
10)CASEOUS NECROSIS(? T.B.)		2	2	1.2
TOTAL	99	79	178	100

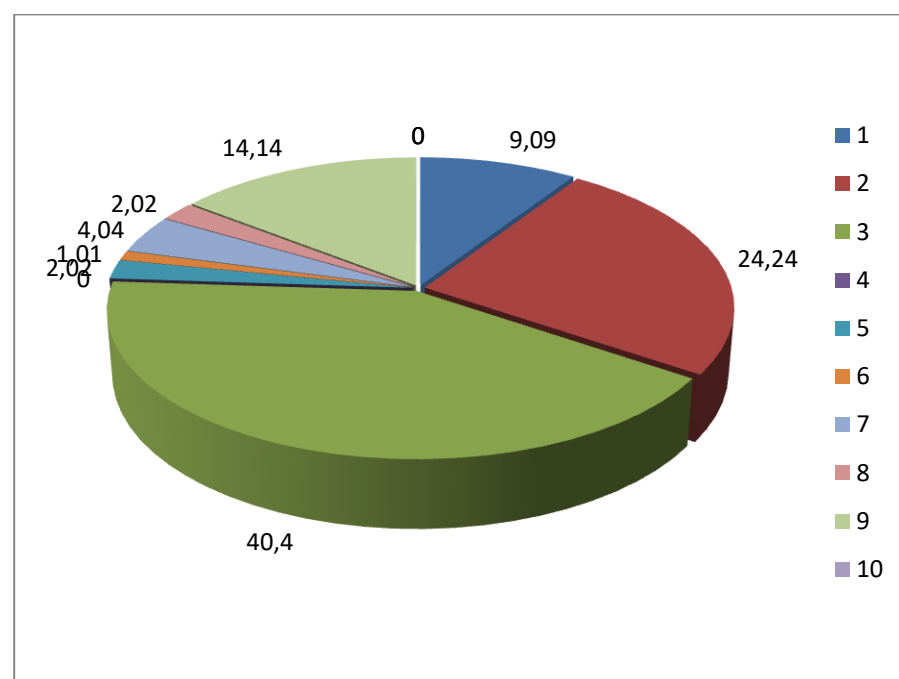
TABLE/FIG 3, SEX WISE DISTRIBUTION OF CYTOMORPHOLOGICAL FINDINGS



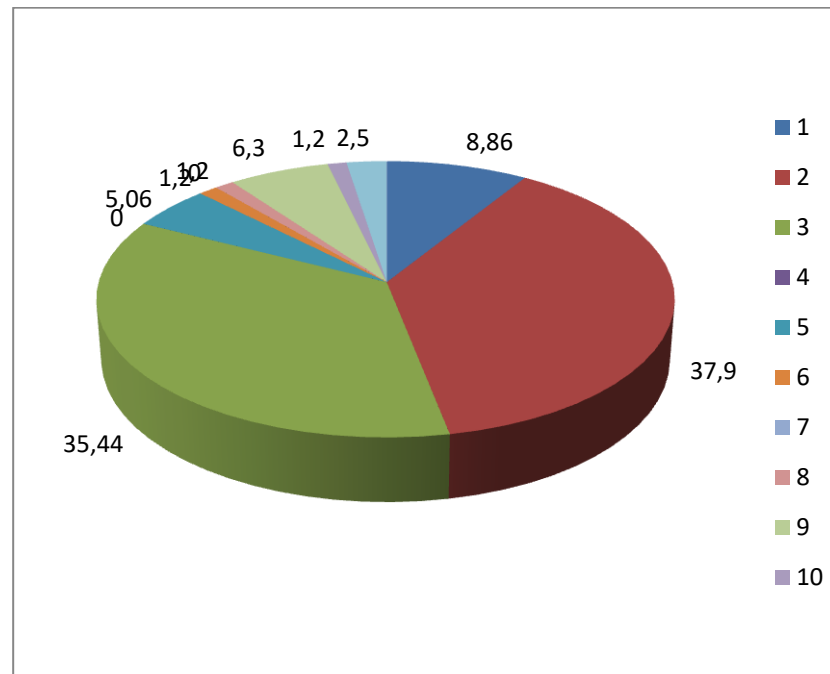
TABLE/FIG.-4, DISTRIBUTION OF DIFFERENT LESIONS

MICROSCOPY	MALES					FEMALE				
	<18	18-45	>45	TOTAL	%	<18	18-45	>45	TOTAL	%
1) ABSCESS	2	5	2	9	9.09	4	3	7	7	8.86
2)CHRONIC GRANULOMATOUS LYMPHADENITIS	7	17		24	24.24	12	17	1	30	37.9
3) CHRONIC NON SPECIFIC LYMPHADENITIS/REACTIVE LYMPHADENITIS	27	11	2	40	40.4	12	14	2	28	35.4
4)NECROTIZING LYMPHADENITIS	1	1	1	2	2.02	4			4	5.06
5)PLEOMORPHIC ADENOMA	1			1	1.01	1			1	1.2
6) UNSATISFACTORY	3		1	4	9.09					0
7)LIPOMA		2		2	2.02	1			1	1.2
8)MALIGNANT LESION		2	12	14	14.14			5	5	6.3
9)EPIDERMOID CYST		1	1	2		1			1	1.2
10)CASEOUS NECROSIS(? T.B.)					0	2			2	2.5
TOTAL	41	39	19	99	100	24	44	11	79	100

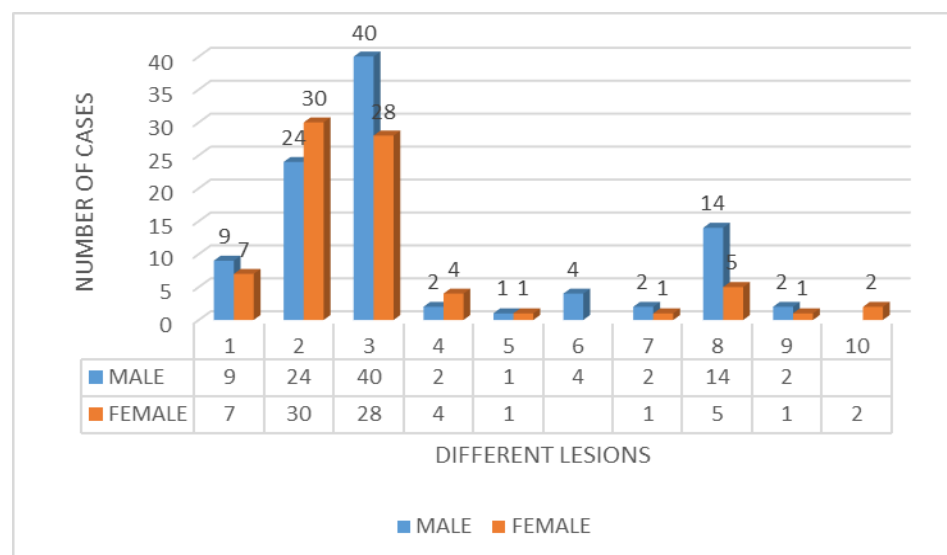
TABLE/FIG- 5DISTRIBUTION OF CYTOLOGICAL LESION DIAGNOSED ON FNAC WITH RESPECT TO AGE DISTRIBUTION AND SEX



TABLE/FIG. -6, AGEWISE DISTRIBUTION OF LESIONS IN MALES



TABLE/FIG.-7 AGEWISE DISTRIBUTION OF LESIONS IN FEMALES



TABLE/ FIG.-8 SEX WISE DISTRIBUTION OF LYMPHADENOPATHY.

**Tables**

**Descriptive analysis**

**Quantitative variables**

	mean (SD)	median [Q25-75]	min	max	n
AGE	27.1 (17.8)	22.5 [14.0; 35.0]	2.00	95.0	178

**Qualitative variables**

		n (%)
SEX	M	99 (56%)
	F	79 (44%)

**Univariate analysis**

**By AGE**

		mean (SD)	median [Q25-75]	min	max	n	p	test
SEX	M	26.2 (±18.4)	22.0 [10.0 - 37.5]	2.00	70.0	99	0.49	Welch
	F	28.1 (±17.0)	24.0 [18.0 - 35.0]	2.00	95.0	79	-	-

**Logistic regression model**

	Odds-Ratio	p	Coefficients
Intercept	1.47 [0.856; 2.54]	0.17	0.307
AGE	0.994 [0.978; 1.01]	0.49	-0.00299

**Predictive Analysis**

The probability of an individual belonging to the group SEX = M depends on the coefficients of the underlying logistic regression model:

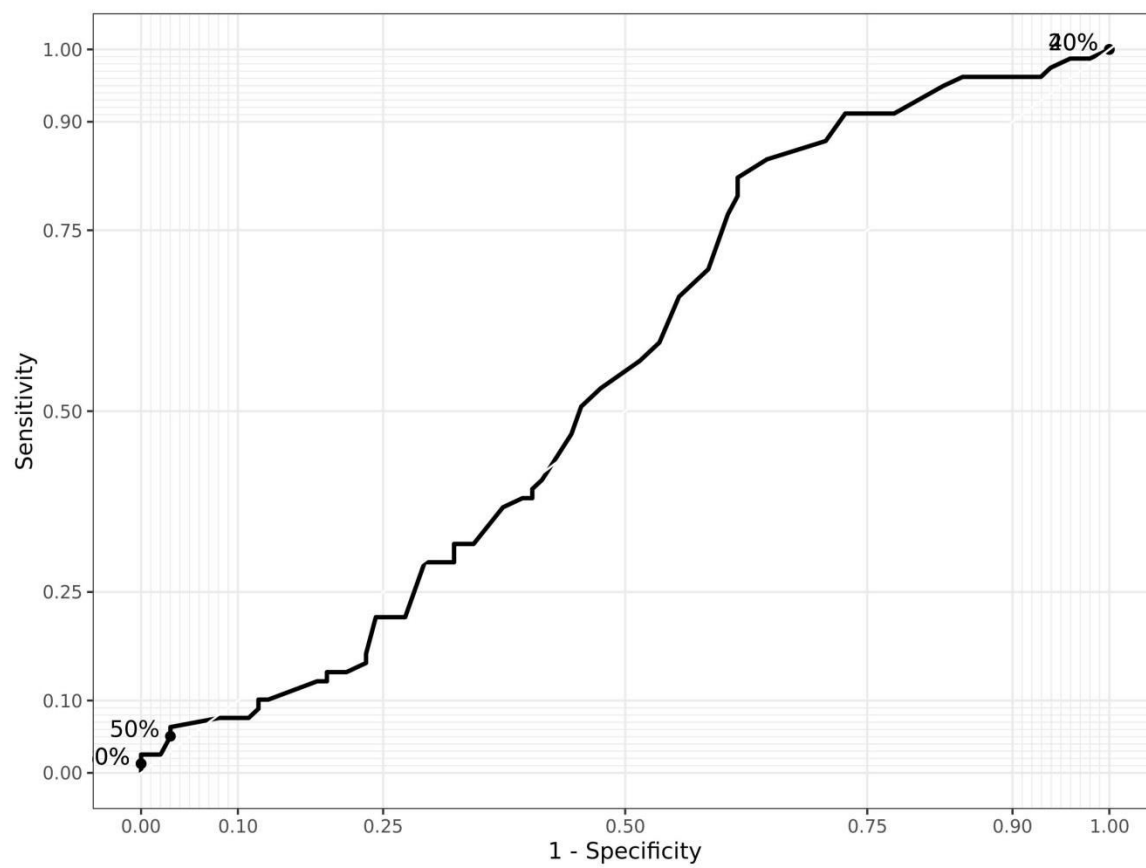
$$\frac{e^{0.307-0.00299xAGE}}{1 + e^{0.307-0.00299xAGE}}$$

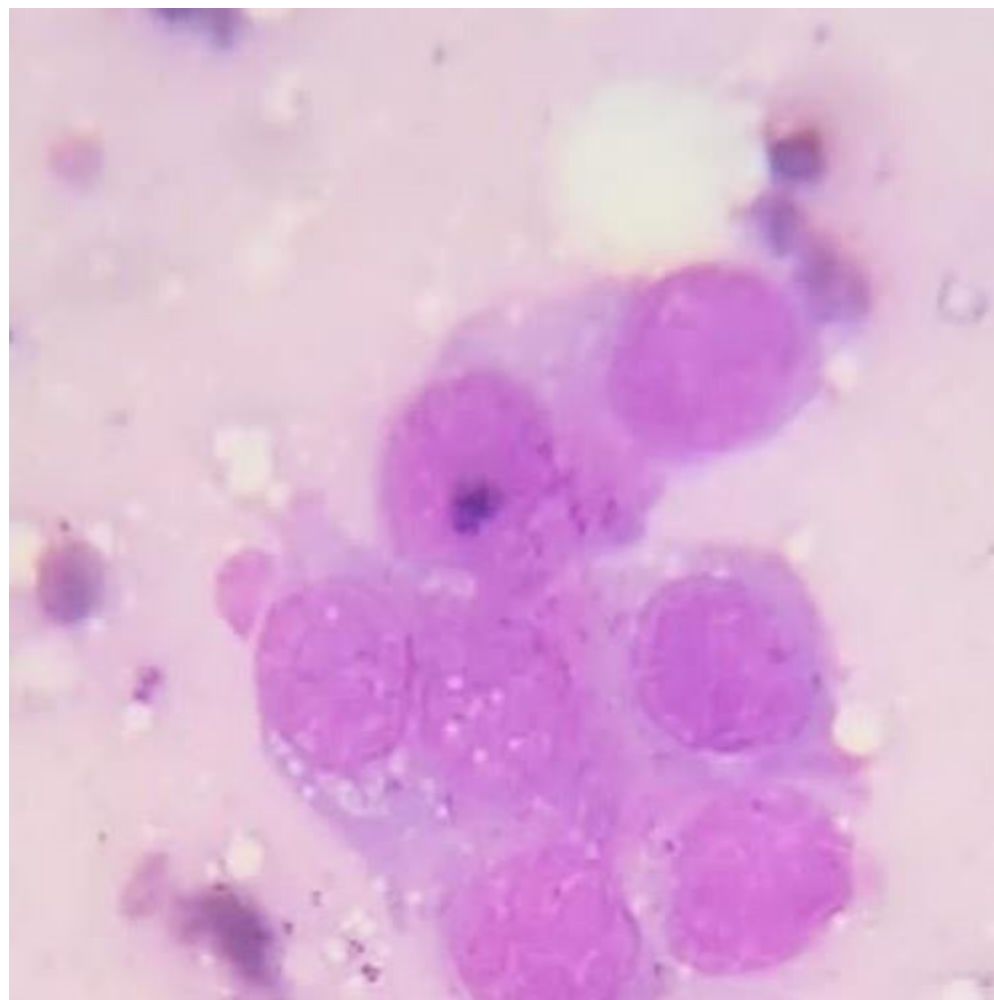
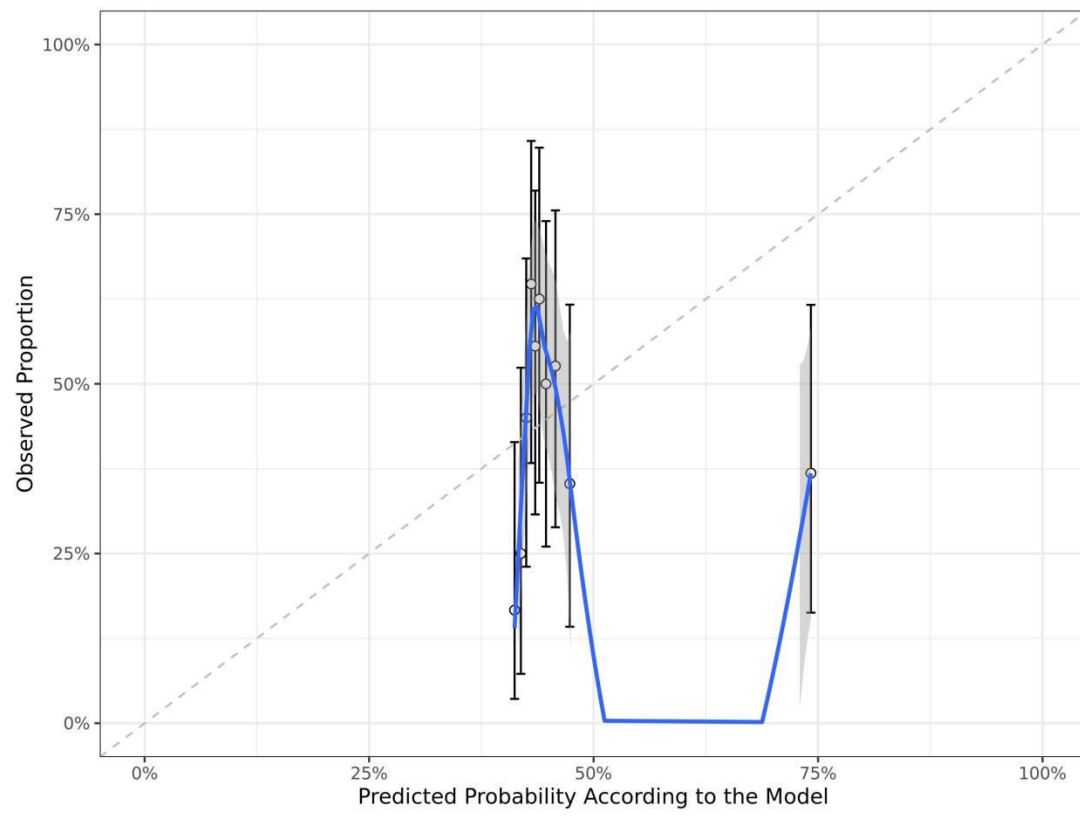
**Performance**

Area Under the Curve: 0.527 [0.441 - 0.615].

**Sensitivity and specificity according to probability thresholds**

Threshold	Sensitivity	Specificity
0.1	100% [95% - 100%]	0% [0% - 3.7%]
0.2	100% [95% - 100%]	0% [0% - 3.7%]
0.3	100% [95% - 100%]	0% [0% - 3.7%]
0.4	100% [95% - 100%]	0% [0% - 3.7%]
0.5	2.5% [0.31% - 8.8%]	98% [93% - 100%]
0.6	0% [0% - 4.6%]	100% [96% - 100%]
0.7	0% [0% - 4.6%]	100% [96% - 100%]
0.8	0% [0% - 4.6%]	100% [96% - 100%]
0.9	0% [0% - 4.6%]	100% [96% - 100%]
1.0	0% [0% - 4.6%]	100% [96% - 100%]





METASTATIC LYMPH NODE