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Associative Study of Fine Needle Aspiration Cytology of Thyroid with Histopathological Study – A Prospective Study

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Abstract:-
Introduction:-
Thyroid diseases are frequently encountered endocrine disorders in clinical practice. Majority of these are benign, of which goitre is the commonest. Only a few are malignant. Clinical evaluation helps in diagnosis but it has limitations. Nevertheless, it is difficult to distinguish the early malignant lesions from the more prevalent benign goitres
Material & Methods:-
This study was conducted including patients who visited SVS Medical College and Hospital, Mahabubnagar, during the period from October 2015 to September 2017 with palpable thyroid swellings and were subjected to needle aspiration. Data was summarized by mean+- SD for continous data and percentages for categorical data. Chi-square test was done to compare variable and p value less than 0.005 is taken as statistically significant
Results:-
Patients who presented with palpable thyroid swellings during the study period from October 2014 to September 2016 were subjected to fine needle aspiration cytology. Of these 54 turned out to be unsatisfactory, as aspirate consisted non specific material. Of the remaining 332 cases, 150 patients underwent surgery in this hospital. The histopathological diagnosis was compared with
Cytological diagnosis in these patients. The majority of the patients were in their 3rd, 4th, and 5th decades of life. 138 were females and 12 were males, the female to male ratio being 11.5:1
Conclusion:-
Multinodular goitres and colloid goitres were easily diagnosed by FNAC, but confusion prevailed in cases of follicular adenomas. Difficulty was experienced in distinguishing Hashimoto's thyroiditis from hyperplastic nodular goitre. FNAC is simpler, safer, quicker and more informative, compared to other sophisticated investigations in the diagnosis of thyroid lesions. It should be exploited to its maximum benefit on all thyroid swellings.

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I. Introduction

Thyroid diseases are frequently encountered endocrine disorders in clinical practice. Majority of these are benign, of which goitre is the commonest. Only a few are malignant. The magnitude of the problem in South East Asia is evident by the recent estimates that 172 million people are affected by goitre in this region, and another 600 million are at risk for developing iodine deficiency disorders.[1]

Clinical evaluation helps in diagnosis but it has limitations. Nevertheless, it is difficult to distinguish the early malignant lesions from the more prevalent benign goitres. A radionuclide scan with radioactive Iodine or Technetium delineates the functional status of nodules, but fails to establish its accurate histological nature of the currently available diagnostic armamentarium.

Ultrasonography can only differentiate solid from cystic enlargement. Thus, the distinction between benign and malignant nodule of the thyroid remains relatively unclear, despite the sophisticated tools with which the clinician is equipped today. Surgical excision has been the only means by which a precise diagnosis of the swelling could be made based on histopathological examination, until recently. Since, most of the swelling being benign and some due to cysts and inflammatory lesions, indiscriminate surgery is obviously unjustified. Hence, an alternative approach other than operative is called for.

Fine needle aspiration cytology (FNAC) is a simple and safer procedure, devoid of any serious complications. It can be carried out in the outpatient department or in the laboratory with minimum equipment. It

does not require any anaesthesia, has a good patient compliance and results can be known quickly within one hour.

This study aims correlating the cytological diagnosis with the final histopathological diagnosis to evaluate the sensitivity, specificity and predictive values of positive smears. Thereby its role in preoperative diagnosis of thyroid swellings is assessed in planning proper management.

II. Materials And Methods

This study was conducted including patients who visited SVS Medical College and Hospital, Mahabubnagar, during the period from October 2015 to September 2017 with palpable thyroid swellings and were subjected to needle aspiration.

The cytological diagnosis was correlated with histopathological diagnosis in those patients who underwent surgery in SVS Hospital, Mahabubnagar. Those patients presenting with thyroid swellings to the SVS Hospital during the study period and underwent surgery for the same were included in the study. Patients in euthyroid state only were included in this study. Those patients who either refused to get admitted at the SVS Hospital or those who refused to undergo surgery at this hospital were excluded. All the patients with severe cardiac risk for surgery were excluded. Those patients whose clinical findings and lab investigations affected the cytological criteria were excluded from the study to avoid bias.

Complete data of the patient from the time of admission till discharge was obtained informed consent. Analysis of age, gender, etiology, duration, treatment and histopathological studies was done in our study. Data was analysed by Microsoft excel software. Data was summarized by mean+- SD for continous data and percentages for categorical data. Chi-square test was done to compare variable and p value less than 0.005 is taken as statistically significant.

III. Results

386 Patients who presented with palpable thyroid swellings during the study period from October 2014 to September 2016 were subjected to fine needle aspiration cytology. Of these 54 turned out to be unsatisfactory, as aspirate consisted non specific material. Of the remaining 332 cases, 150 patients underwent surgery in this hospital. The histopathological diagnosis was compared with

Cytological diagnosis in these patients. The majority of the patients were in their 3rd, 4th, and 5th decades of life. 138 were females and 12 were males, the female to male ratio being 11.5:1.

FNAC was done on 386 patients with thyroid swellings. Of all these aspirations, 54 were unsatisfactory as aspirate consisted of non-specific material.

Of the remaining 332 patients only 150 patients underwent surgery. Thus, 150 cases were selected for correlative study of FNAC and Biopsy.

1. Overall incidence

Total number of aspirations (FNAC)	**386**
Number of satisfactory smears	**332**
Number of unsatisfactory smears	**54**
Total number of patients for surgery	**150**

Table 1: Overall incidence

2. Age Distribution

Age (in years)	**No. of patients**	**Percentage (%)**
17 to 23	18	12.00
24 to 31	25	16.67
32 to 39	34	22.67
40 to 47	30	20.00
48 to 55	29	19.33
56 to 63	9	6.00
64 to 70	5	3.33
Total	150	100.00

Table 2: Age distribution

The study group of 150 cases ranged from 17 years to 70 years with mean age of 32 years. Majority of the thyroid lesions (52.66%) seen in 3rd and 4th decades of life (31-50 years).

3. SEX

Sex	No. of patients	%
Male	12	8.00
Female	138	92.00
Total	150	100.00

Table: 3 Sex Distributions

The study group of 150 patients consisted of 138 females constituting 92% and 12 males comprising 8%. Female to male ratio was 11.5:1.

4. Duration of swelling at the time of presentation

Duration (in months)	No. of patients	%
3 to 21	67	44.67
22 to 40	56	37.33
41 to 59	11	7.33
60 to 78	7	4.67
79 to 97	5	3.33
98 to 116	0	0.00
117 to 132	4	2.67
Total	150	100.00

Table 4: Distribution based on the duration of the swelling

Most of the patients have approached within a period of 3-4 years of the manifestation of the swelling and most of them were benign, Patients who presented lately showed evidence of malignancy in most of them, signifying the chances of conversion to malignancy on long standing.

5. clinical diagnosis

Clinical Diagnosis	No. of patients	%
DG	15	10.00
MNG	65	43.33
SNT(L)	28	18.67
SNT(R)	42	28.00
Total	150	100.00

Table 5. Clinical diagnosis

Among 150 patients, 65(43.3%) of them have presented with a multinodular goitre, 42(28%) of them had right solitary swelling and 28(18.7%) had left solitary swelling.

6. Cytological diagnosis

FNAC	No. of patients	%
CG	52	34.67
MNG	41	27.33
HT	7	4.67
CN	13	8.67
FN	3	2.00
FLT	3	2.00
PC	14	9.33

NG	15	10.00
AC	1	0.67
LT	1	0.67
Total	150	100

Table 6: cytological diagnosis

Among 150 thyroid swellings present in the study, cytologically 136 cases were found to be benign and 15 cases malignant. No cases were toxic.
Of the 150 excised specimens, on HPE 127 were benign, 21 were malignant, 11 were Hashimoto's thyroiditis.
2 case of florid lymphocytic thyroiditis on FNAC which were suspicious of malignancy, turned out to be malignant lymphoma.
Among the 127 benign cases diagnosed by biopsy, 52 were multinodular goitres, 21 were follicular adenomas, 23 were colloid goitres, 11 turned out be microfollicular adenomas, 7 turned out be Hurthle cell adenomas.
Among the 23 malignant cases diagnosed by HPE, 14 were papillary carcinomas, 5 was follicular carcinoma, 2 turned out to be lymphoma and 1 turned out to be anaplastic carcinoma.
Of the 12 male cases, 3 were Hashimoto's thyroiditis, 4 were multinodular
goitres, 1 colloid goitre, 1 was follicular adenoma, 1 was papillary carcinoma, 1 follicular carcinoma and 1 turned out to be lymphoma.

7. Type of surgery underwent by patients

Surgery	No. of patients	%
RHT	36	24.00
LHT	24	16.00
STT	66	44.00
TT	24	16.00
Total	150	100.00

Table 7. Type of surgery underwent by patients

8. Diagnosis based on Biopsy
On biopsy of the thyroid swellings 52(34.7%) of them were diagnosed to have multinodular goitre, 23 colloid goitre, 22 Follicular adenoma, 14 papillary carcinoma, 11 Hashimoto's thyroiditis and 11 Microfollicular adenoma.

Biopsy/HPE	No. of patients	%
MNG	52	34.67
CG	23	15.33
FA	22	14.67
PC	14	9.33
HT	11	7.33
MFA	11	7.33
HCA	7	4.67
FC	6	4.00
LYM	3	2.00
AC	1	0.67
Total	150	100.00

Table 8: Diagnosis based on biopsy

9.Incidence of Malignancy
23 cases were diagnosed to have malignancy on histopathological examination among 150 cases. On FNAC only 14 cases were found to be malignant and on biopsy 9 other cases were which were benign on FNAC were found to be malignant on biopsy, of which 3 nodular goitre and 3 follicular neoplasms were Follicular carcinoma and one colloid goitre was Papillary carcinoma and 2 Lymphomas.

Parameters	No. of patients	%
Malignancy	23	15.33
Benign	127	84.67
Total	150	100.00

Table 9: Incidence of malignancies

10.Age wise distribution of disease pattern

		Biopsy/HPE										
	Age(yrs)	***MNG***	***CG***	***HT***	***MFA***	***FA***	***HCA***	***FC***	***PC***	***LYM***	***AC***	***Total***
	17 to 23	0	15	0	3	0	0	0	0	0	0	18
	24 to 31	2	3	0	6	12	2	0	0	0	0	25
	32 to 39	9	3	1	2	9	4	0	6	0	0	34
	40 to 47	24	0	3	0	0	0	0	2	1	0	30
	48 to 55	17	1	6	0	1	1	2	1	0	0	29
	56 to 63	0	1	1	0	0	0	3	3	1	0	9
	64 to 70	0	0	0	0	0	0	1	2	1	1	5
	Total	52	23	11	11	22	7	6	14	3	1	150

Table 10: Age wise distribution of disease pattern

11.Comparison of diagnosis on FNAC & Biopsy

On comparing FNAC and biopsy 79 cases had similar cytological diagnosis. Most of them were MNG

		Biopsy/HPE										
		MNG	***CG***	***HT***	***MFA***	***FA***	***HCA***	***FC***	***PC***	***LYM***	***AC***	***Total***
FNAC	***MNG***	39	0	2	0	0	0	0	0	0	0	41
	CG	2	19	0	9	17	4	0	1	0	0	52
	HT	0	0	7	0	0	0	0	0	0	0	7
	CN	0	4	0	2	5	2	0	0	0	0	13
	FN	0	0	0	0	0	0	3	0	0	0	3
	NG	9	0	2	0	0	1	3	0	0	0	15
	LT	1	0	0	0	0	0	0	0	0	0	1
	PC	1	0	0	0	0	0	0	13	0	0	14
	AC	0	0	0	0	0	0	0	0	0	1	1
	FLT	0	0	0	0	0	0	0	0	3	0	3
	Total	52	23	11	11	22	7	6	14	3	1	150

Table 11: Comparison of diagnosis on FNAC and Biopsy

IV. Discussion

Aspiration Biopsy Cytology (ABC) includes coarse and large needle biopsy (CNB and CND), the term Fine Needle Aspiration Biopsy (FNAB) was preferable. Vim-Silvermann needle biopsy is also included by some workers. The fine needle has a gauge of 22-27. In the present study 23 gauge and one and half inch long disposable needle was used. Most pathologists agree that there is nothing to choose in the gauge from 22-27. But most of them use 22-25 gauge.

Braun and Silver (1984)[52] used 18 and 19 gauge needles for cystic lesions. But many have aspirated fluid with fine needle also. Large needles injure blood vessels and the aspirate is mixed with blood.

The length of the needle favoured was one and half inches and in the present study the same was used. It was of sufficient length and reached all the areas in a thyroid swellings. Longer needle bends when it is manipulated within the swelling. All the workers used disposable needles including in the present study as they are least traumatic, less painful and perfectly sterile.10 ml or 20 ml syringes were used in this study.

Thomas A Colacchio et al. (1980)[53] used 5 ml syringe. 1 ml tuberculin syringe with a 1.5 cm long 25 gauge needle mounted on it was employed by Norton LW et al. (1982)[54]. A 10 ml disposable syringe was used for all the cases in this study. Majority used special syringe holder Cameco. Special syringe holder helps to apply suction and release with one hand only while tile other hand fixes the swelling. We could not obtain a syringe holder, but still managed to obtain samples.

A local anaesthetic was infiltrated into the skin to avoid pain to the patient.None of the patients complained of significant pain in the present study. There is noneed of local anaesthesia if the patient is cooperative, when a fine and disposal needle (22-24) is used.

There were 62 (7.5%) inadequate aspirations out of 820. They contained only blood. The procedure could not be repeated. These patients did not undergo surgery.Block MA et al.[66] (1983) have advocated rebiopsy after 6-12 months which ensures greater assurance for patients who refuse surgery for indeterminate lesions. Block MA et al.[66] (1983) are of the view that adequate biopsy must show atleast eight clusters of epithelial cells on at least two slides. Table 6 shows success rate of aspiration biopsy by different authors. If the technique is correct, the most important causes of inadequate material are cystic and benign lesions.

However, our quantum of work is comparable to the standard laid down by Van Henle et al.[55] (1982). They advocate examination of at least 10 smears per week or 500 smears per year. But others like Asp AA et al. [56] (1987) have questioned the feasibility of strictly adhering to these criteria and they feel that reasonably good results can be obtained, if the pathologist is keen and well trained.

Age Distribution

The age of the patients varied from 16 to 70 years with the mean age of 32 years. The mean age of the group studied by Gershengorn et al (1977) was 39 years. Colacchio et al (1980) reported the age of their patients ranging between 30 to 60 years. The age of the patients of Klemi PJ et al.[67] (1990) ranged from 21 to 86 years with the mean age of 50 years. In the present series, patients in the 3rd and 4th decades of life comprised 66%. In the same age group, Pandit AA and Kinare[57] (l986) have reported 62%. For the age group of 20 to 60 years Starvic GD et al (1980) and Colacchio et al. (1980) showed 72% and 60% respectively. The majority of the patients in the study conducted by Tabaqchali et al.[58] (2000) and Sclabas GM et al.[59] (2003) were between 30 and 50 years.

Sex Incidence

The sex ratio (female:male) in the present study group was 11.5:1 with 138 women and 12 men. In the series of Gershengom et al (1977) female to male ratio was 28:5, Harsoulis et al (1986) series it was 993:107 (9:1) and the male proportion in the Colacchio et al (1980) series was 16%. In Pandit and Kinare (1986) series F:M = 58:26, Klemi PJ et al. series (1990), F:M = 8:1. High frequency of women were observed on the present series.

Incidence of Malignancy

21 out of the 150 cases (14%) we have studied were malignancies. The other figures are Chu et al (1979) 26%, Lowhagen et al (1979) 20%, Colacchio et a1 (1980)16%, Silver et al (1981) 22%, Ramaciotti et al (1984) 20%, Braun and Silver
(1984) 18%, Harsoulis et a1 (1986) 19%, Klemi PJ et al[67] (1990) 11.8%., Godinho L et al(1992) 21%, Pommata M et al.[60] (1997) 35.3% and Sclabas GM et al.[59] (2003)

ACCURACY RATE

The overall accuracy was more than 75% in the 10 series on the subject reported by various authors and more than 90% in 6 series.

FALSE NEGATIVE: The false negatives ranged from nil to 23% from the 20 series (Table 11). But majority of the false negatives were below 5% and in the present study it was 2.3%. The false negatives were due to misdiagnosis of follicular carcinoma as follicular adenoma and misdiagnosis of papillary carcinomas as goitrouslesion and follicular adenoma. The difficulty in distinguishing follicular carcinoma from its benign counterpart was experienced even in histological sections since capsular and vascular invasion were essential for the diagnosis of malignancy, which cannot be demonstrated on cytology. It is difficult to differentiate Lymphoma from Hashimoto's thyroiditis.[61] The possibility of Papillary carcinoma with cystic degeneration must b e kept in mind in cystic lesions though most of them are benign[62] and wall must be aspirated after evacuating the cyst completely.[62] False negative results are uncommon, supporting the practice of observation in most of the patients.[59]

FALSE POSITIVE: There were 1 false positive smears in the present series. False positives ranged from 0-19% in the following series of various workers (Table 12). False positives were less frequent than false negatives. They are due to a typical appearances of follicular ceils with moderate variation in size. Such a change can be observed in benign lesions also as hyperplastic reaction of thyroid cells. In our study,the false positive was just one percent. The high rate of 23.5% of false positives in the series of Ramaciotti et al (1984) was due to inclusion of smears suggestive of malignancy in the malignant category. Suen KC, Quenville NF (1983)54 concluded the common false positives as

1. Cellular colloid goitre mistaken for neoplasm,
2. Thyroiditis mistaken for lymphoma and
3. Cellular atypia due to hyperplastic reaction in adenoma

PREDICTIVE VALUE

The predictive values of FNAC in the present series are as follows

- SENSITIVITY : 75%
- SPECIFICITY : 88%
- OVERALL ACCURACY : 77%
- PREDICTIVE VALUE OF A POSITIVE RESULT : 91%

SENSITIVITY AND SPECIFICITY

According to Frable MA (1980) for an acceptable screening test FNAC should have sensitivity and specificity more than 83%. Sensitivity and specificity in the 8 series ranged from 70% to 100%. More false negatives decrease the specificity and sensitivity. More false positives decrease the predictive value of a positive result and also the value of the study.

In a large cyst over 4 cms that reaccumulates haemorrhagic fluid after complete evacuation,malignancy should be suspected. Cytological diagnosis is less accurate for cystic than solid lesions .

After studying the results of both FNAC and CNB (169) Miller M. et al. (1979) and Colacchio et al. concluded that the accuracy is similar but the superiority of FNAC lies in its simplicity and absence of complications. The accuracy has not exceeded 90% with Vim-Silvermann needle in the works of Crile and Vickery (65%), Hamlin and Vickery (74%), Ferrita and Verace (67%), and Wang Chu et al (90%). The procedure is painful and traumatic and the specimen obtained is less representative. Complications like haemorrhage and haematoma, tumour implantation in the needle tract and puncture of trachea are reported. The technique is useless for swellings less than 1.5 cm size and cystic lesions. The procedure cannot be repeated.

Among the large number of benign thyroid nodules occurring in the general population, the detection of a malignant tumour is difficult and unreliable. Sophisticated investigations like thyroid scintigraphy, ultrasonography and biochemical tests are of little avail in resolving this diagnostic enigma. In Sweden FNAC has been employed in the preoperative diagnosis of thyroid lesions for morethan 40 years and over the last two decades the method has gained popularity the world over. It has been favoured as the first choice for the examination of a solitary nodule of thyroid. The method is cost effective. It eliminates the need for diagnosticsurgery. FNAC can also recognise the underlying thyroiditis in hypo or hyperthyroidism (Klemi PJ et al., 1990; Godinho L et al.,1992).

According to Godinho L et al. (1992) FNAC had essential role in the diagnosis and management of 23% of their patients (144), a confirmatory role in 61% of patients, a non-contributory inconclusive role in 13% when the specimens were inadequate and was misleading in 3% where the results were false negative. The detection of neoplasia and thyroiditis is a justification for subjecting the patient to FNAC. Since the regular use of FNAC, unnecessary operations on thyroid have decreased, cancer yield has increased and medical expenses and bed occupancy have reduced (Hamberger B et al., 1982). Diagnosis on FNAC is very closely approximate to that on surgical biopsy (Miller M et al., 1979). Operation should be accorded high priority for indeterminate or suspicious lesions, as emphasized by Block MA et al.[66] (1983).

In the study conducted by Pomata M et al. (1997),[60] malignant lesions were detected in 30 cases (35.3%). True positive cases were 14, true negative 48, false positive and false negative cases were 2 and 3 respectively. Due to high number of false negatives, the sensitivity of FNAC was only 51.8%, specificity was 96% and accuracy, 80.5%. They concluded that FNAC was certainly the main diagnostic tool in thyroid pathology. Its employment should undergo to a centralised diagnostic evaluation in such a way that cytology is analysed together with clinical and other instrumental data.

Sclabas GM et al. (2003)[59] conducted a study for 240 patients. FNAC results were 32% positive for malignancy, 22% negative for malignancy, 42% were indeterminate for malignancy and 5% were non-diagnostic. Among those with indeterminate biopsy results, high-risk subgroups included patients with FNAC results suspicious for papillary carcinoma and follicular neoplasms > 2 cms.

In the study conducted by Boeving, Anke, Cubas, Santos et al. (2005),[63] the cytological analysis found 50.9% of the cases negative and 14.5% positive for malignancy. 29.3% presented follicular lesion and 5.15% obtained an inconclusive cytology. The histological analysis demonstrated a malignancy rate of 21.2%. The study concluded that FNAC was accurate in the diagnosis of nodular thyroid disease, presenting a high correlation rate with histology. It had a higher incidence of falsepositive and false-negative results, compared to literature. However the rate of inconclusive results by cytology was lower.

Difficulty in distinguishing between multinodular goitre from follicular neoplasm. It reiterates the fact that a negative FNAC report should not modify the clinical diagnosis and proposed line of management.

V. Conclusion

- The majority of our patients were in the third to fourth decade of life, females being predominant.
- The majority of the cases were benign, of which multinodular goitre was the most common pathology (34.67%).
- Among the malignancies, the majority of the cases were papillary carcinomas (76%).The sensitivity, specificity and predictive value of positive smears were 77%, 88% and 91% respectively.
- FNAC was of greater help in the preoperative diagnosis of thyroid swellings.

Multinodular goitres and colloid goitres were easily diagnosed by FNAC, but confusion prevailed in cases of follicular adenomas. Difficulty was experienced in distinguishing Hashimoto's thyroiditis from hyperplastic nodular goitre.

- Majority of the patients who cannot be followed up regularly and for long time, hence clinical suspicion of malignancy should be one of the indications of surgery, inspite of FNAC report being negative.
- FNAC is simpler, safer, quicker and more informative, compared to other sophisticated investigations in the diagnosis of thyroid lesions. It should be exploited to its maximum benefit on all thyroid swellings.

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