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A Clinico-Pathological Study of Carcinoma in Multinodular Goitre Vs Solitary Thyroid Nodule

Dr.Vijayalakshmi Manubolu [1], Dr.Venkata Narayana Badipatla[2]
1. CORRESPONDING AUTHOR:Assistant Professor, General Surgery,Anil Neerukonda Hospital, Visakhapatnam
2. First Author: Assitant Professor,General SurgeryAnil Neerukonda Hospital ,Visakhapatnam

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INTRODUCTION

Thyroidnodulespresentachallengeintheirdiagnosis,evaluation,andmanagement. Often these abnormal growths/lumpsarelarge in size and developatthe edge of the thyroid gland, sothatthey are felt or seen as a lumpin front of theneck.The prevalenceofthesenodules ina given population dependsona numberoffactorslikeage,sex,diet,iodinedeficiency,and eventherapeuticandenvironmental radiation exposure. Prevalence increases with age, with spontaneousnodules occurring at a rate of 0 - 0.8% per year, beginning early in life and extendingintotheeighthdecade[1,2].

True solitary thyroidnodules (STN)occur in4 - 7%of the adult population.Theyarepresentin5%ofpersonsatanaverage of60years.Theyaremorecommoninfemales(6.4%) as comparedto males(1.5%) and thispredispositionexiststhroughoutallagegroups.Many palpablethyroidnodules,thoughttobesolitary, are actually part of a multinodular thyroid gland. In general, a nodule mustreach a size of 1 cm in diameter to be detectable by palpation. Thyroid nodules couldbe adenomas or malignancies. Most thyroid nodules are benign hyperplastic lesions,but 5 -20% of these nodulesare true malignanciesin nature. Childhoodthyroidnodulesneedspecialattentionduetohigherincidenceofmalignancy,i.e.,15-25%as compared to adults. Further, thyroid cancer runs a more aggressive course inchildren and is associated with early metastasis locally to regional lymph nodes anddistant sites including lungs and bones[3,4]. Currently, many investigations includingdiagnosticimagingstudies,serologicandcytogeneticstestsaswellashistopathologicaltechniquesareavailabletoevaluateSTN.Outofalltheseinvestigations,fine needleaspiration cytology (FNAC)hasbecome thediagnostictool ofchoicefortheinitial evaluationofSTN[3-12]

Multinodulargoiterdescribesanenlarged,diffuselyheterogeneousthyroidgland. Initialfindingsmay include diffuse enlargement,but asymmetricnodularity ofthe mass often develops. The cause of this mass is usually iodine deficiency. Initiallythe mass is euthyroid, but with increasing size, elevations in T_3 and T_4 can occur andgraduallyprogresstoclinicalhyperthyroidism.Workupanddiagnosisinvolveevaluationofthyroidfunctiontests.Ultrasoundandradioisotopicscanningdemonstrateheterogeneousthyroidsubstance.Noduleswithpooruptake canappear aslesions suggestive of malignancy .MNG hadbeen traditionally thought tobeat alow risk for malignancy ascompared to a solitarynodule thyroid [13,14,15].However, various studies have reported a 7 to 17% incidence of malignancy in MNG[14,16,17].Therefore,FNACfordiagnosisandresectionforsuspiciouslesionsisconsidered.[18]

Theultimateaimintheevaluationofsolitarythyroidnodule(STN)andmultinodulargoitre(MNG)istodifferentiate benignhyperplasiafromtrueneoplasm.

AIMS AND OBJECTIVES

1. **ToevaluatetheSTNandMNGcasesclinicallyandpathologically**
2. **TostudytheincidenceofcarcinomainbothSTNandMNG**
3. **ToStudytheclinicalpresentationofcarcinomainbothSTNandMNG**
4. **CorrelationofFNACwithHPE**
5. **Toknowwhichpathologicalvariantofcarcinomamostcommonlyoccursinbothcases.**

PATIENTS & METHODS

Studydesign: Prospectivestudy.
Placeofstudy:

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DepartmentofSurgery,KingGeorgeHospital, Andhra Medicalcollege,Visakhapatnam

Periodofstudy:

AperiodoftwoyearsfromJuly2012toJune2014

Samplesize:

Totalof258caseswereenrolledinthestudyamong which158wereSolitaryThyroidNoduleand100wereMultinodulargoitre

.**InclusionCriteria**

- OnlythosepatientswithclinicalevidenceofSolitaryThyroidNodule&MultinodularGoiter,attendingGeneral surgeryOPDoverstudyperiod
- Allpatientsareeuthyroidstate

.**ExclusionCriteria**

- PatientsclinicallydiagnosedasSTNturnedtobeDominantNoduleThyroidOnUltrasonography
- Patientswhohavenotgivenconsentforstudyorhavenotonfollowup

Methodofstudy.

The present study of "Clinicopathological Study of Carcinoma in MultinodularGoitrevsSolitaryThyroidNodulehasbeen conductedbyutilizingthecasesdiagnosed clinically as STN & MNG and managed both as inpatient and outpatientbasisinthedepartmentofGeneralSurgeryatKingGeorgeHospital,Visakhapatnam..

The patients were selected according to the inclusion and exclusion criteria asmentionedabove.Allthesecaseswerestudiedindetail, clinicallyandrecordedasper the proforma that was prepared. The relevant investigations whenever indicatedwereperformed.

The investigations included Hemoglobin percentage, blood sugar estimation,blood urea estimation, blood grouping and Rh typing, serum cholesterol, x-ray of theneck-AP and lateral views and chest X-ray and ENT examination. All patients wereinvestigated for Thyroid profileand submitted for FNAC of the thyroid swelling andultrasoundneck.

EVALUATION AND MANAGEMENT:

Nodules diagnosed as benign radiologicaly and on FNAC are managedconservativelywithfollowup.Benign pathologieswereoperatedonwhen:

Nodulesizeisincreasing,Patientinsistenceofcosmoses, Patientswhoarelesscompliantforregularfollowup,Patientswhoareunderhighriskcategory.

The main indications of surgery in MNG are cosmetic problem, pressure effectsymptoms,secondarythyrotoxicosisandsuspicion ofmalignancy.Subtotalthyroidectomyisthesurgeryofchoiceforthe MNG.Butatrendtowardstotalthyroidectomy isreplacing subtotal thyroidectomy inthemanagementofMNGasrecurrence of goiter is avoided and second thyroid surgery is difficult and associatedwithhighriskofcomplications.Toxicnodules arenotsubjectedtoscintigraphyduetounavailabilityofNuclearscaninourhospitalanddistrict

4.1KingGeorgeHospitalSurgeryOPDStatistics2012-2014

CASES	No	PERCENTAGE
TotalsurgeryOP	120000	-
Thyroidpatients	1200	1%ofsurgeryOP
Solitarynodule thyroid	250	20.83%ofthyroidpts.
Multinodulargoiter	600	50%ofthyroidpts

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DISORDER	No	PERCENTAGE
MNG	600	50
Diffuse goitre	350	29.1
STN	250	20.83
TOTAL	1200	

RESULTS OF THE STUDY

1. AGEANDSEXDISTRIBUTION

5.1 Age&SexDistributionInSTN&MNGCases

AGE(yrs)	STN			MALIGNANCIES	MNG			MALIGNANCIES
	FEMALE	MALE	TOTAL		FEMALE	MALE	TOTAL	
0-10	0	0	0	0	0	0	0	0
11-20	13	1	14	3	4	0	4	0
21-30	61	4	65	6	10	2	12	3
31-40	31	5	36	5	36	2	38	3
41-50	26	3	29	5	29	3	32	2
50&above	13	1	14	2	9	5	14	2
TOTAL	144	14	158	21	88	12	100	10

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There were 14 male and 144 femalepatientsin STN group , resulting in afemaletomaleratioof 10.28:1andthere are12malesand88femalesin MNGgroup , resulting in a female : male ratio of 7.33:1. This ratio varied throughout thevariousagegroups.MeanageforSTNis34.61,Meana geforMNGis41.7.Malignant cases were 21 in STN out of which 4 aremales and 17 arefemales. InMNGmalignantcasesare10outofwhich2aremalesand 8arefemales

2. SYMPTOMS:

Allpatientspresentedwiththyroidswelling,eithernotice dthemselvesorincidentallynoticedbyothersincaseofST Nabouttheppresenceofnodule.Only4patientsofSTNpres ented with other symptoms. 3 (1.89%) had pain during deglutition and 1(0.63%) had voice change. Out of 100 patientsof MNG 16% presented with painduringdeglutition,6%camewithdysopnea.

5.2 ClinicalPresentationof158STNcasesand100MNGcases

Symptom/sign	STN		MNG	
	Number	percentage	Number	Percentage
Swellinginfrontoftheneck	158	100	100	100
Painfuldeglutition	3	1.89	16	16
Hoarsenessofvoice	1	0.63	1	1
Palpablecervicallymphnodes	4	2.53	6	6
Dysopnea	0	0	6	6%

Figure5.1CommonClinicalPresentation-Swelling

Multinodulargoitre **Solitarythyroidnoduleright**

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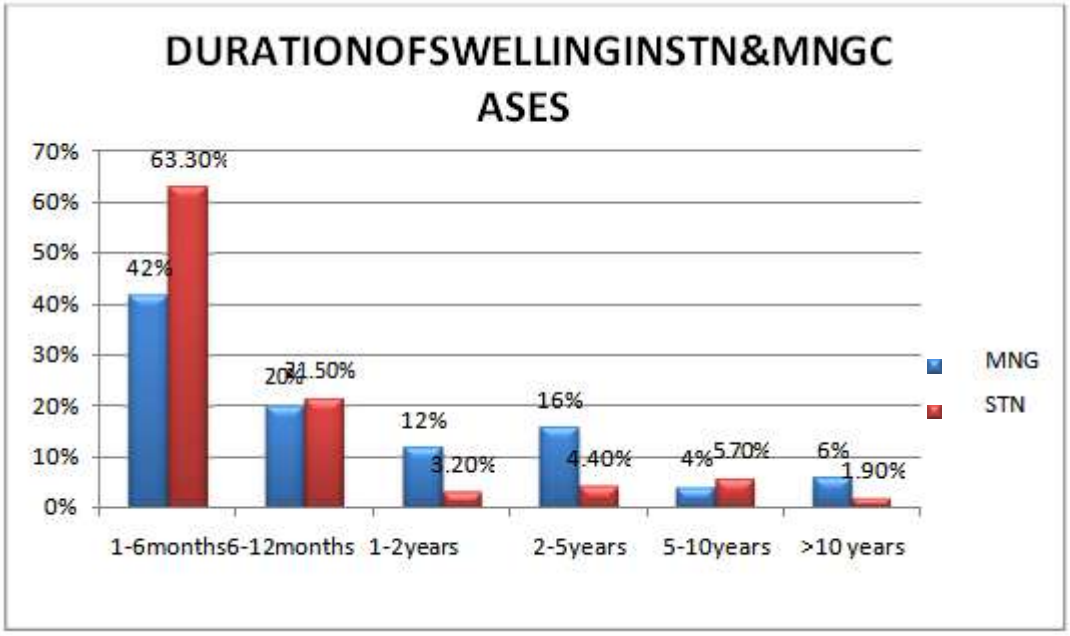
3. DURATION:

5.3 DurationofSwellingofSTN&MNGcases

Durationofswelling	MNG		STN	
	TotalNo.of cases	Percentage	Totalnoofcases	Percentage
1–6months	42	42%	100	63.30%
6–12 months	20	20%	34	21.50%
1–2years	12	12%	5	3.20%
2–5years	16	16%	7	4.40%
5–10years	4	4%	9	5.70%
>10years	6	6%	3	1.90%
Total	100	100%	158	100%

Figure5.2Barchartrepresentationofdurationofswelling



Thedurationofcomplaintsrangedfrom1weekto10years beforetheycametoourhospital.Eightpatientspresented withhistoryofrecentonsetofpain,3areSTNand 5areMNG,MajorityofthepatientsI.e.100(63.3%)ofST Nand42(42%),presentedbetween1weekto6months.

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4. PASTHISTORY:

a) H/O.Similarcomplaint:
1patientofSTNhadaH/OSimilarcomplaint8yragoandunderwenthemithyroidectomyforfollicularneoplasm,thepostoperativebiopsycameasfollicularadenoma.

b) H/O.Irradiationinchildhood:
NoneofthepatientsinourstudyhadH/O.irradiationintheirchildhood.

5. FAMILYHISTORY:
2outof158STNpatientsand4outof100MNGpatientshadpositivefamilyhistory

5.4 FamilyHistoryinSTN&MNGcases

	STN		MNG	
	NO OFCASES	PERCENTAGE	NOOFCASES	PERCENTAGE
WITH AFAMILYH/O	2	1.2%	4	4%
NOFAMILYH/O	156	97.8%	96	96%

6. PERSONALHISTORY:

a. ExcessiveeatingofBrassicafamilyvegetables:
12%ofourpatientshadH/O.excessiveeatingofBrassicavegetables.

b. Typeofsaltused:
45%ofthepatientsinourstudywereusingrocksalt,30%wereusingiodizedsaltand25%wereusingacombinationofboth.

c. Residentofhillyarea:
32%ofourpatientswereresidentsofhillyareasaroundVisakhapatnamsuchasAraku,Paderu,Seleru

7. LOCALEXAMINATIONOFNECK:

a.Presentationoftheswelling:
Outof158STNcasesstudied,
89(58.1%)caseshadnoduleinrightside69(41.9%)caseshadnoduleonleftside

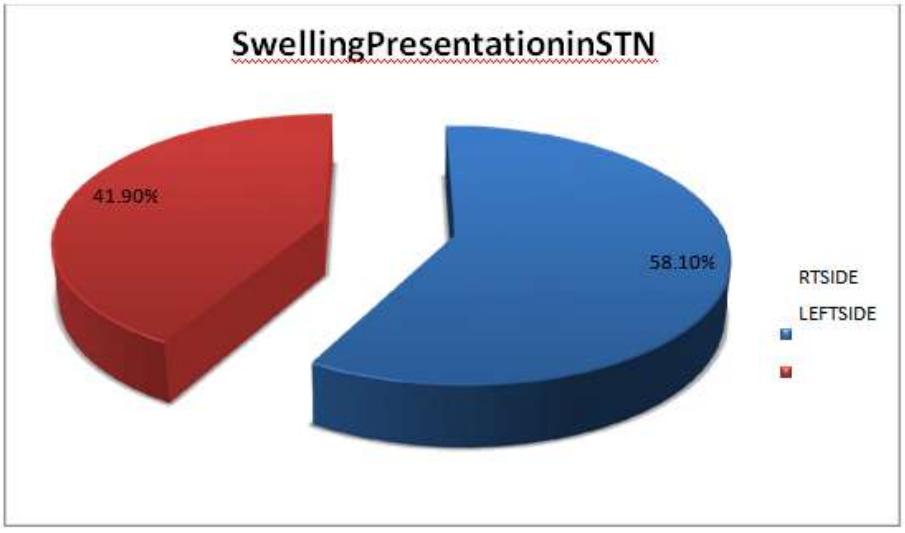

Figure5.3PieDiagrammaticRepresentationOfSwellinginSTN

InMNGbothlobeswereinvolvedin66 caseswithpredominantly involvingrightlobeandremaining34casesinvolvingpredominantlyleftlobe.

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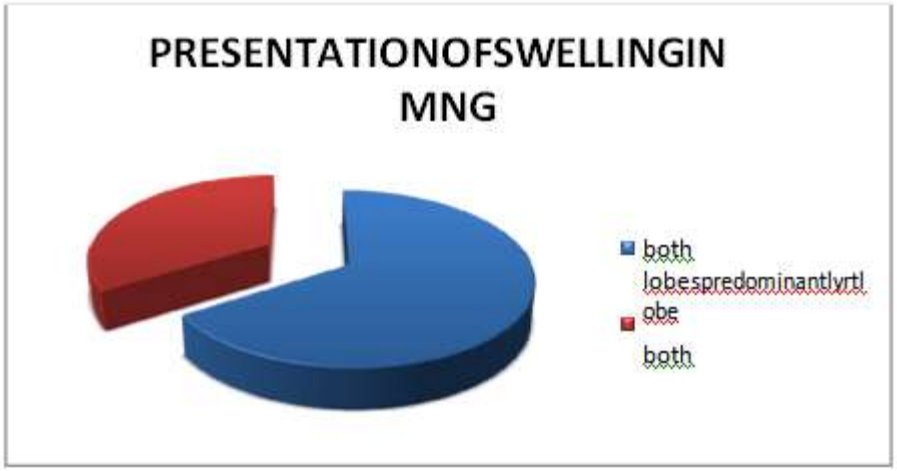

Figure5.4PieDiagrammaticRepresentationOfSwellinginMNG

8. SYSTEMICEXAMINATION:

MUSCULOSKELETAL:

One (0.63%) of the 158 STN patients had skull secondaries One patient outof100MNGpatientshadbonesecondariesintheform ofswellingoverthesternum

9. FNAC:

FNACreportsarebroadlyclassifiedas:

a) Insignificant
b) Benign
c) Suspiciousofmalignancy
d) Malignancy

5.5 FNACofSwellingofSTN&MNGCases

FNACofswelling	STN		MNG	
	No	Percentage	No	Percentage
Benign	93	58.86%	86	86%
Insignificant	54	34.17%	6	6%
Suspicious	3	1.89%	4	4%
Malignancy	8	5.06	4	4%
	158		100	

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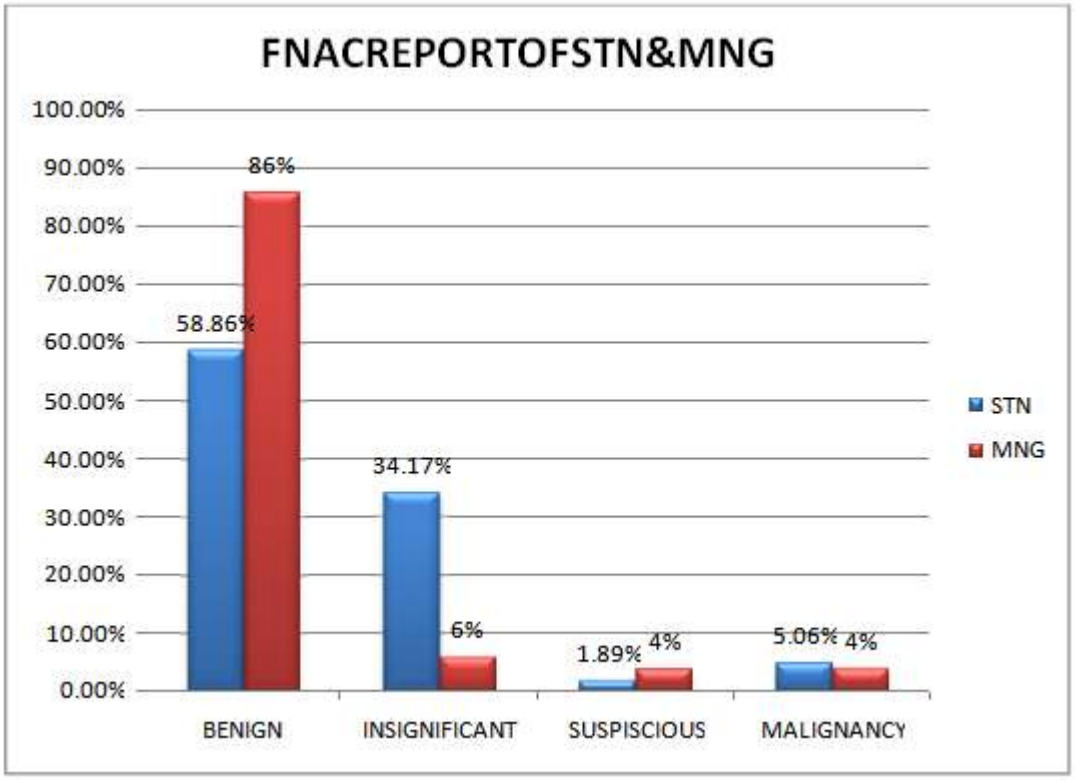
Figure5.5BarchartrepresentationFNACreportofSTN&MNG



CERVICALLYMPHNODES:

5.6 CervicalLymphNodesinSTN&MNGCases

	Palpablelymph nodes	Bilaterallypalpable nodes	FNACprovenmetastatic deposits
STN	4	1	2
MNG	6	2	5

SURGICALPROCEDURE:

Out of 158 cases, 89 were operated with a preoperative diagnosis of benignnodule in 24 cases ,follicular neoplasm in54 , suspicious of malignancy in 3 andformalignancyin8cases.

Total thyroidectomy was done in 11 cases with neck dissection in 3 cases .77cases underwent hemithyroidectomy of which 11cases again underwent completionthyroidectomyformalignantconfirmationonHPE.1casewhounderwenthemithyroidectomy8yrsagopresentedwithSTNhasunderwentleftcompletionthyroidectomy in upfront which is also malignant on HPE. Though FNAC suggestedbenigncytologyintraoperativelyduetosuspiciousmalignancy,totalthyroidectomywasdonein1case.1casewastoxicnodulewhichunderwenthemithyroidectomy.

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5.7 SurgeriesinSTNcases

SURGERY	No.	Percentage	CompletionThyroidectomy
Righthemithyroidectomy	43	48.31	6
Lefthemithyroidectomy	34	38.2	5
Totalthyroidectomy	8	8.9	
Totalthyroidectomy+ND	3	3.7	-
Completionthyroidectomy	1	1.12	-
Total	89	100	-

In MNG main indication for surgery in our serieswas cosmetic problem. Thenextcommonindicationwasforpressureeffectsofthe goiterlikedysphagiaanddyspnoeaand secondary thyrotoxicosis. Thesix casesoffollicularneoplasmswereoperatedtoruleoutfollicularcarcinoma.Ofthe100cases,32caseweresubjected tototalorneartotalthyroidectomyandremaining68cases underwentsubtotalthyroidectomy

COMPLICATIONS:

5.8 ComplicationsinSTN&MNGCases

Sno	Complication		STN	MNG
1	Hemorrhage		0	0
2	Respiratoryobstruction		1	0
3	Recurrentlaryngealnerveinjury	Temporary	10	5
		Permanent	0	0
4	Parathyroidinsufficiency		6	8
5	Thyroidstorm		0	0
6	Woundinfection		0	0
7	Death		0	0

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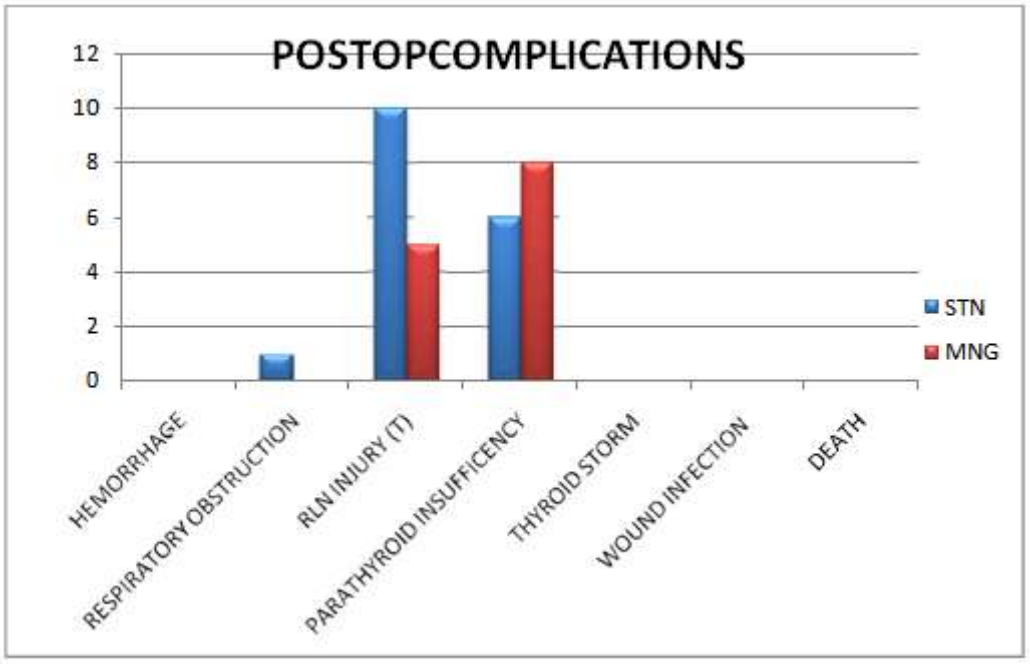
Figure5.6Barchartrepresentationofpostopcomplications



5.9PostOpHistopathologicalReportInSTNCases

Sno	TYPE	No.cases	Percentage
1	PapillaryCarcinoma	17	19.1
2	FollicularCarcinoma	3	3.37
3	Medullarycarcinoma	1	1.12
4	Follicularadenoma	30	33.7
5	Hurtlecelladenoma	1	1.12
6	Benigncolloidlesion	4	4.49
7	Colloidnodule	3	3.37
8	Adenomatoidnodule	10	11.11
9	Nodularcolloidgoitre	20	22.47
Total		89	

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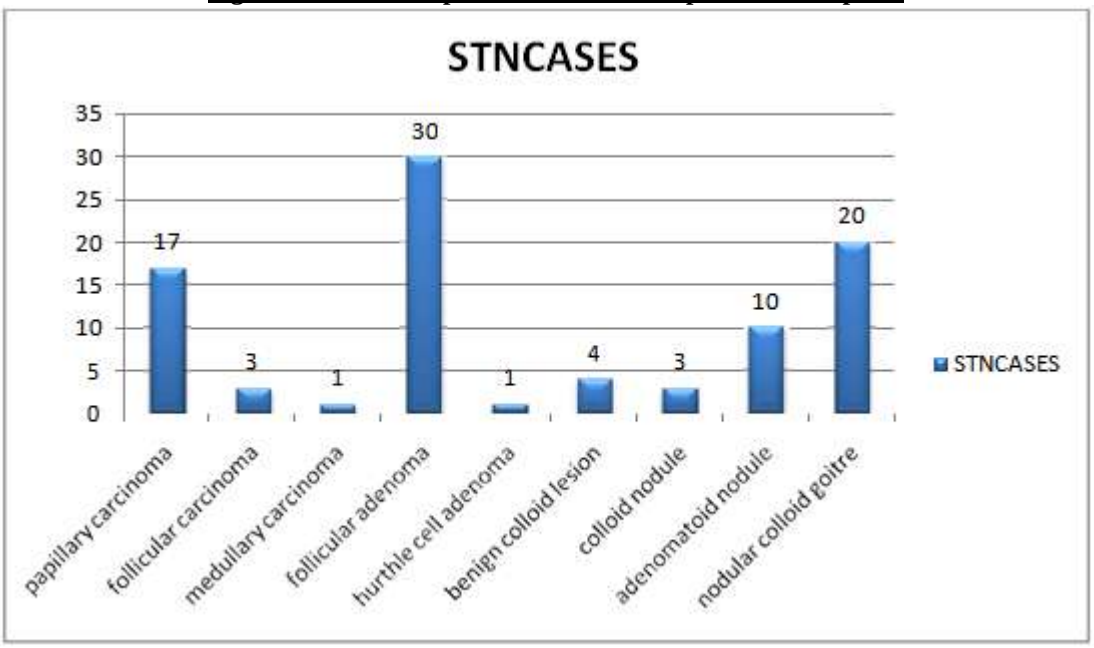
Figure5.7BarchartrepresentationofHPEreportsofSTNreports



5.10PostOpHistopathologyInMNGCases

Sno	HPEReport	Noofcases	Percentage
1	Colloidgoiter	78	78%
2	Hashimotosthyroiditis	6	6%
3	Follicularadenoma	6	6%
4	Follicularcarcinoma	2	2%
5	Papillarycarcinoma	7	7%
6	Medullarycarcinoma	1	1%
Total		100	

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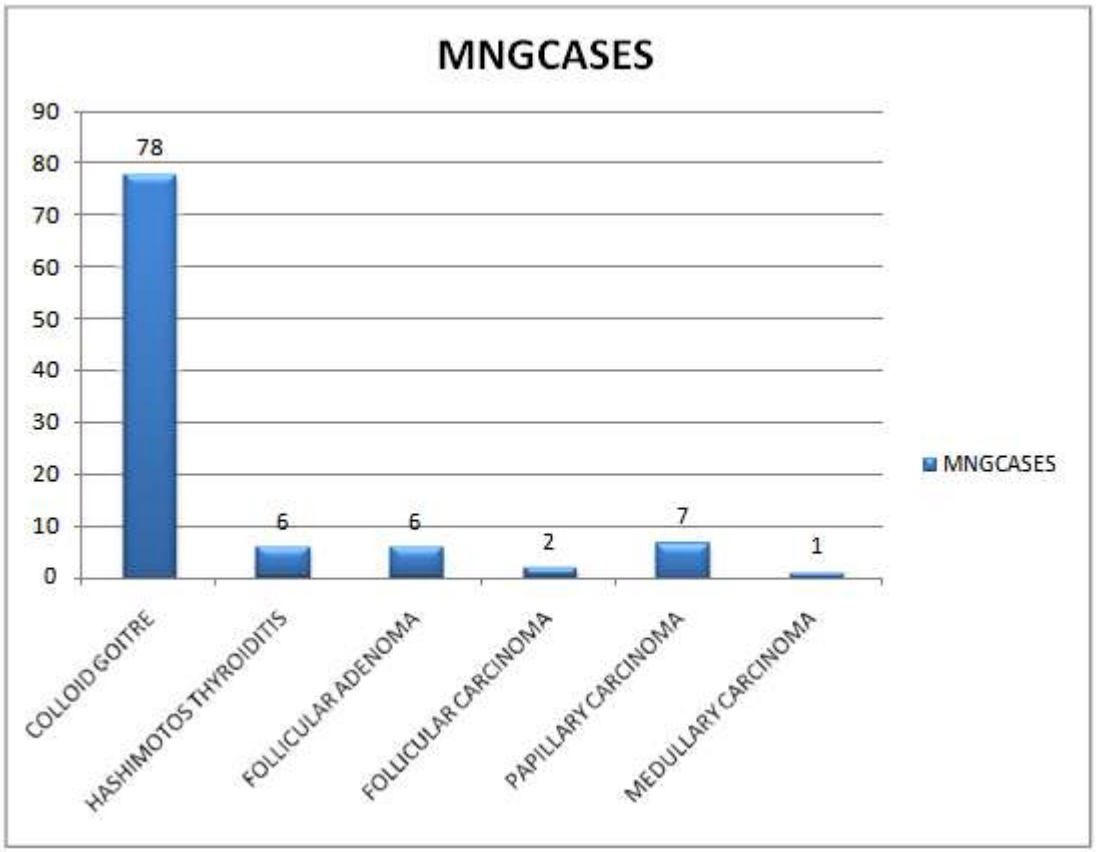
Figure5.8BarchartrepresentationofHPEofMNGcases



RADIOTHERAPY:

1patientofSTNwithskullsecondariesoffollicularcarcinoma& onepatient of MNGwithsternum secondariesoffollicular carcinomawassubjectedtoRadioiodine afterthroidectomy

GENETICANALYSIS:

Genetic analysis for RET mutation done in STN patient with afamily history .It is done to rule outwhether it is a sporadic case or familial case bymutation analysis of RET protooncogenereported asaheterozygous variationleadingtoaminoacidsubstitutionofCystieneto Tyrosineatcodon634wasdetectedinexonofRETgeneint hissubject

DISCUSSION

Thyroidnodulesareacommonclinicalproblem .Epidemiologicalstudieshave shown the prevalence of palpable thyroid nodules to be approximately 5% inwomenand1%inmenlivinginiodine-sufficientpartsoftheworld[1,2].

Thyroidnodulesare morefrequentinwomen,iniodine deficient regions,inolderagesIniodinedeficientareas,itisashigha s50%(Harrisons)

Thelifetimeriskofdevelopinga thyroid nodule is reported to be15%.[6]

Nevertheless,only5%oftheclinicallyapparentthyroidn odulesaremalignant.

Theclinicalimportanceofthyroidnodulesrestswiththen eedtoexcludethyroid cancer which occurs in 5–15% depending on age, sex, radiation exposurehistory,family history,andotherfactors.

Thyroidcarcinomaannualincidenceis1-2per100,000population,whichaccounts for 90% of the malignancies of the entire endocrine system, 1% of totalhumanmalignanciesand0.5%oftotaldeathsfromm alignancies.[10,11]

Althoughthyroidmalignanttumorsarenotusuallyaggressive,thyroidmalignanciesareresponsibleformoredeathsthanallothermalignanciesoftheendocrinesystem.
Inourstudyover2yearduration,wehaveencountered250 clinicallydiagnosed STN and600 MNGcases out of1200Thyroid patientspresentedtoGeneral Surgery OPDin thesame period. Excluding the patientswho did notcomeforfollowupandthosecaseswhicharediagnosedtobeDominantNoduleThyroid on ultrasonography of neck, we have done a prospective case series study on 258patients.Theanalysisofincidenceofmalignancywas doneamongthe89STN&100MNGcasesofoperatedpatientswithhistopathologicalevidence.
Total number of cases detected was increased when compared with previousseriesi.e,1000casesattendedOPDbetween2010to2012comparedto1200between2012to2014because ofimprovedclinicalorientationandincreasedawareness by thepatients.

Age&Sex:

The mean age ofthe patientsunderthe study was34.61 and 41.7 yearsinSTN& MNGrespectivelywhichcorrelated withthestudy ofother authors. Therange was16 to70 yearsand majorityof them werefemales, with femaletomaleratio being 10.2 : 1 & 7.33:1 in STN & MNG respectively. These observations aresimilartoobservationsofotherauthors.
. 4(57.14%) out of 7 men and 17(20.73%) out of 82 women were malignant inSTN.2outof12menand8outof88womenweremalignantinMNGweremalignant

6.1 ComparativeIncidenceOfMeanAgeInSTNCases

Studies	Meanage(yrs)
DasDK[85]	35
TalepoorM[86]	38.6
QariF[87]	36.17
PRESENTSTUDY	34.61

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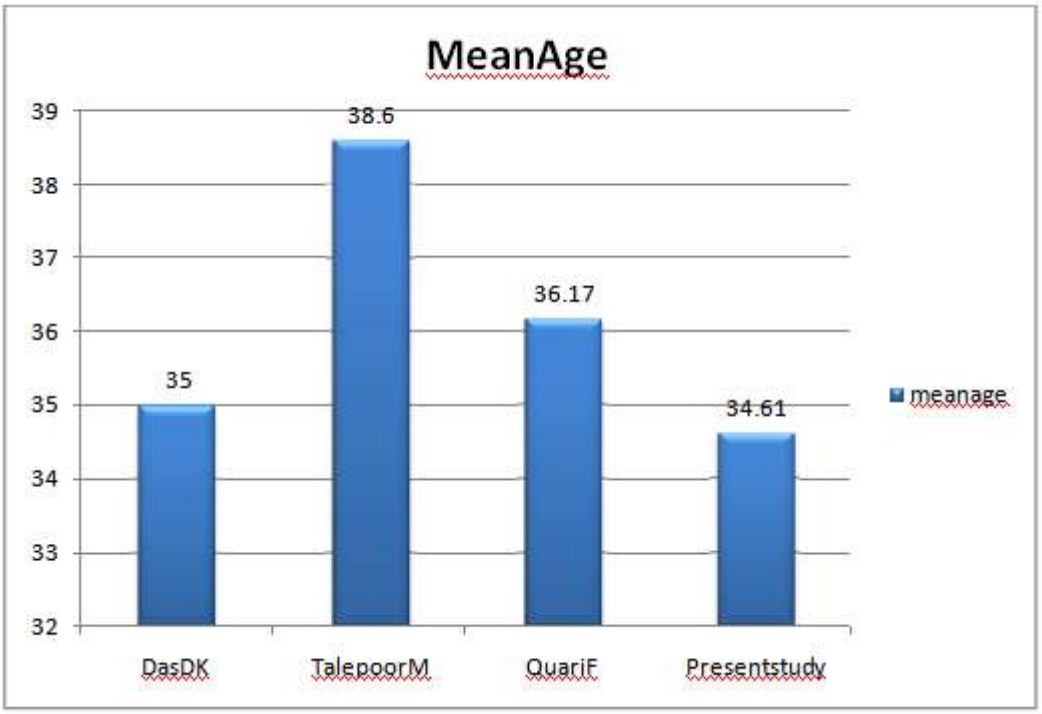

Figure6.1Barchartrepresentationofcomparativeincidenceofmeanageins TNcases

6.2 ComparisionOfIncidenceOfMeanAgeInMNGCases

Studies	Meanage(yrs)
MayorGetal[88]	45.0yrs
HallR,etal[89]	51.4yrs
Pradjes.JM.Etal[90]	38.4yrs
Presentstudy	41.7yrs

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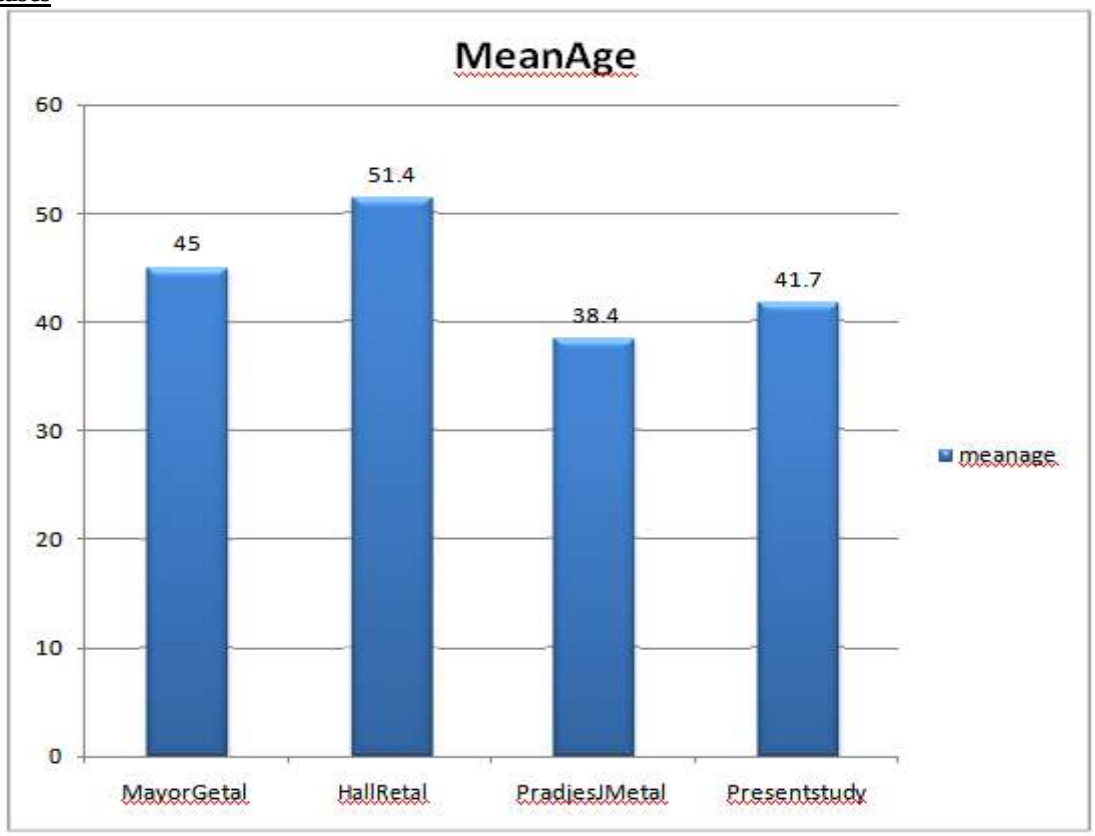
Figure6.2Barcharrepresentationofcomparativeincidenceofmeanagein MNGcases



The number of males in the present study was 14(8.86%) and the femaleswere144(91.14%) inSTN and itwasmales12and females88 inMNG casesshowingfemalepreponderance

6.3 ComparisionOfIncidenceOfSTNInFemalesAndMales

Studies	**Sexincidence (female:male)**
DorairajanN[107]	9.00:1
DasDK[85]	5.39:1
GuptaC[91]	5.00:1
PRESENTSTUDY	10.28:1

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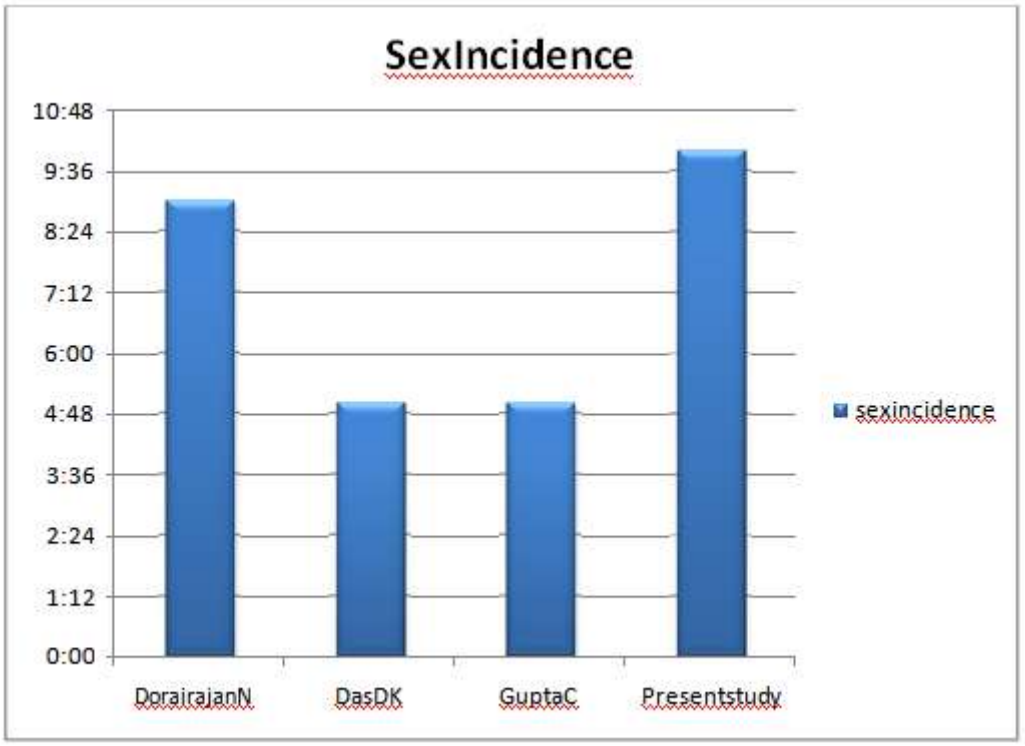
Figure6.3BarChartRepresentationOfSexIncidenceinSTN



ComparisionIncidenceOfMNGInFemalesAndMales

Studies	**Sexincidence(female:male)**
Tunbridgeetal[92]	13:1
BayerYetal[93]	9:1
PradjesJMetal[90]	7.4:1
PRESENTSTUDY	7.33:1

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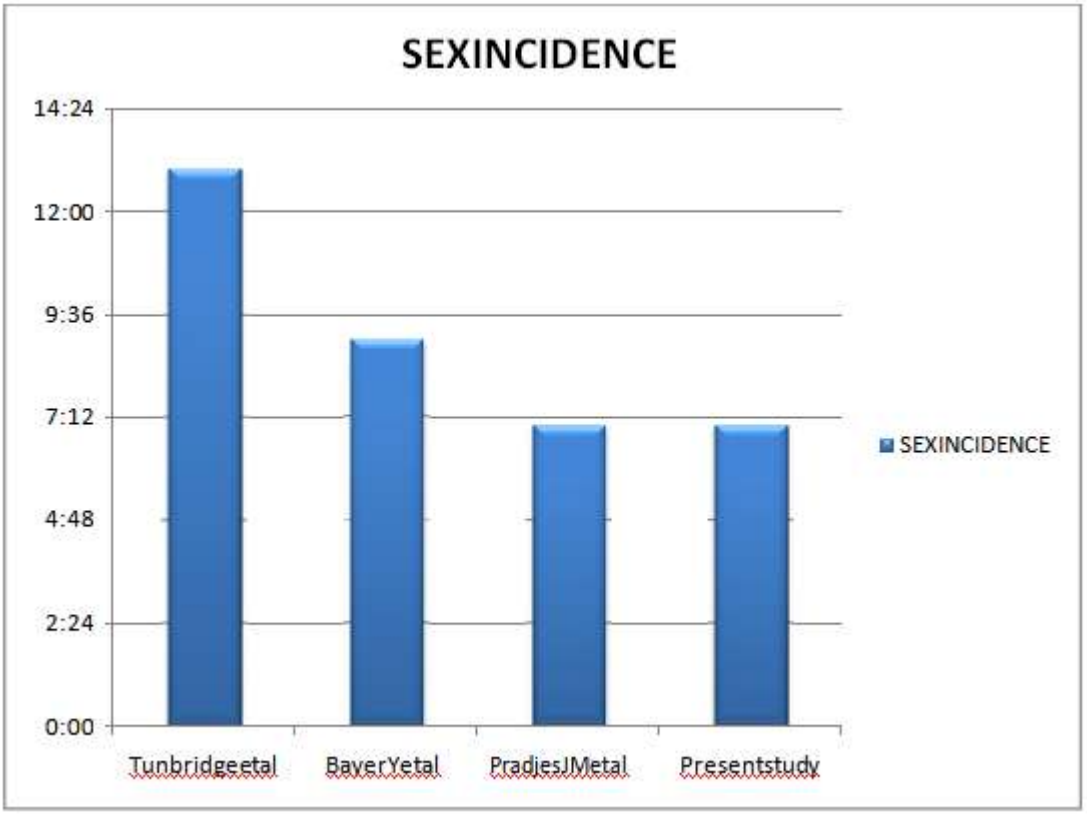

Figure6.4BarchartrepresentationofsexincidenceofMNG

Thesesmallvariationfromotherstudiescouldbeduetofac tthatoursamplecontainscomparatively lessnoofcases

Clinicalpresentation:

InSTNthecommonestclinicalpresentationisthepresenc eofswellinginfrontoftheneck(100%)andmajorityprese ntedbetween1weekto6months..NormanA.Methosen et al has also mentioned that the commonest presenting complaint isthyroidswelling[8].

Theseincidencesarecomparabletothoseobservedinthes tudybyTarrarAMetal[3]in2003.Andinthestudyconduct edbySimonHolzeretal·[94]in 1996inGermanyandpublishedin2000:

The ChiefcomplaintinMNGpatients (100 %) was swellinginfront of theneck.Howeverfewpatientshadassociatedlocalsympt omslikedifficultyinswallowingand/orbreathing.Durati on of swellingrangedfrom 20 daysto 15yearsand90%(90cases)wereseenintherangeof1mont hto5years

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6.4 ComparisionOfClinicalFeaturesAmongVariousStudies

Clinicalfeature	Simonetal	TarrarAMetal	Antoniorios etal	Present study	
				STN	MNG
Thyroidswelling	77%	99%	100%	100%	100%
Lymphnodes	5.6%	4%	16%	2.53%	6%
Hoarsenessofvoice	4.6%	14%	4%	0.63%	1%
Dysphagia	25%	8.9%	16%	3%	16%
Distantmetastases	0	12%	4%	0.63%	1%

ThesizeoftheswellingincreasedgraduallyinMNGin88cases(88%),rapidlyin4cases(4%) andwasstationaryin8cases(8%)..

Mostof the swellings–86 cases (86%)werenot associatedwithpainandonly14cases(14%)hadpain.

Pressure symptomswere seen in 22%(22 cases)asagainst 29%in Antoniorioetal(2005)study.[95] Patients noticed swelling swelling themselves in 57% cases in our study ,rest43% cases are noticed by third party. Thisincidence did not correspond to the studyperformed by Mc Mullen et al which postulated -Solitary thyroid nodules are mostcommonlydetectedbythepatientsthemselves(40%),followedbytheincidentaldiscovery of nodules on imaging studies performed for unrelated reasons (30%), andlastlyduetothird-partydiagnosisbyfamily,friends,acquaintances,ormedicalpractitioners(30%).[4]

InAndhraPradesh,incoastalareasandhillareas(agencyareas)theincidenceofthyroiddiseaseswashigh.Sotheincidenceofthyroiddiseaseswerehigh in Visakhapatnam, surrounding hilly areas and agency areas (Araku, Paderu,Chintapalli, Seeleru,Lambasing).

Patients come to our hospital from different types of areas like foothills, riverbeds, sea coast and fertile delta lands. Unlike in the western text books, where thethyroid diseases are said to be common close to the foot hills, this study shows thattheseproblemsarecommonbothinplainsandfoothills.

Therewasfamily history ofgoiterin4 casesinwhichthepatientsmothersand sistershadmultinodulargoiter and had undergone surgery inMNGandtwocasesoutofSTNhadfamilyhistoryoperatedoutofthem1wasproventobe

Medullarycarcinomathyoid.

Allthyroidswellingsinourstudy weremovingwithdeglutition.Bothlobeswere involved in 66 cases with predominantly involving right lobe and remaining 34casesinvolvingpredominantlyleftlobeinMNGInmajorityofthepatientsthesizetheglandwasin stage2 accordingto WHOclassificationi.e. swelling visiblewithneckinnormalposition.

Iodinedeficiency,goitrogenicdietanddrugs,irradiationtoheadandneckregions and I^{131} administration may cause goitre and induce carcinoma of the thyroidbut in our study, no etiological factor mentioned could be elicited exceptfor the rocksalttakencommonly by ourpatients.

Clinically,withsignsandsymptomsofdysphagia,horsenessofvoice,cervical lymphadenopathy, hardness ofnodule fixity andmetastasis , 7 casesout of89STNcasesoperatedwere suspected clinically asmalignantbut only 3 caseswereprovenmalignant.NormanA.Methosenetalal

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sohasmentionedthattheclinical diagnosis of malignancy based onhistory andphysical findingshasnot beenso successful[8].
Onesuchwithstrongclinicalsuspicionofmalignancywithbenign FNACprovedmalignancy.Hence,althoughtheaccuracyofclinicaldiagnosisofthyroidmalignancy is low patients with high clinical suspicion of malignancy need surgicaltreatmentwhatevertheFNACresultmay be.
Theclinicalfeaturesofthenodulewerenothelpfulinthediagnosisofmalignancy. There wasno correlation between the consistency, duration and size ofthenodulesandmalignancy.

X-ray of neck, AP and lateral views and X-ray of the chest were done in all thecases.Therewasonecaseoftracheal shifttoleftsideduetoagoiter,mainlyinvolvingrightlobeofthethyroid

FNAC:

Out of 258 cases, on FNAC 179 cases are benign ,67 are indeterminate andsuspiciousofmalignancy,12 casesare provenasmalignancy.Non neoplasticare179 and Neoplastic are 79 with a ratio of 2.26 : 1 are comparable with several otherstudiesasfollows,

6.5 ComparisionofRatioofNonneoplasticandNeoplasticcases

Series	Non-neoplastic	Neoplastic	Ratio
PepperGM[99]	84	18	4.66:1
DorairajanN[107]	78	20	3.99:1
DakDK[85]	346	85	4.07:1
KaurK[2]	32	15	2.13:1
DuekSD[96]	145	61	2.37:1
Hurtado-LopezLM[100]	80	50	1.60:1
NggdaHA[101]	51	18	2.83:1
ChaoCT[98]	276	264	1.04:1
PRESENTSTUDY	179	79	2.26:1
MNG	86	14	6.14:1
STN	93	65	1.43:1

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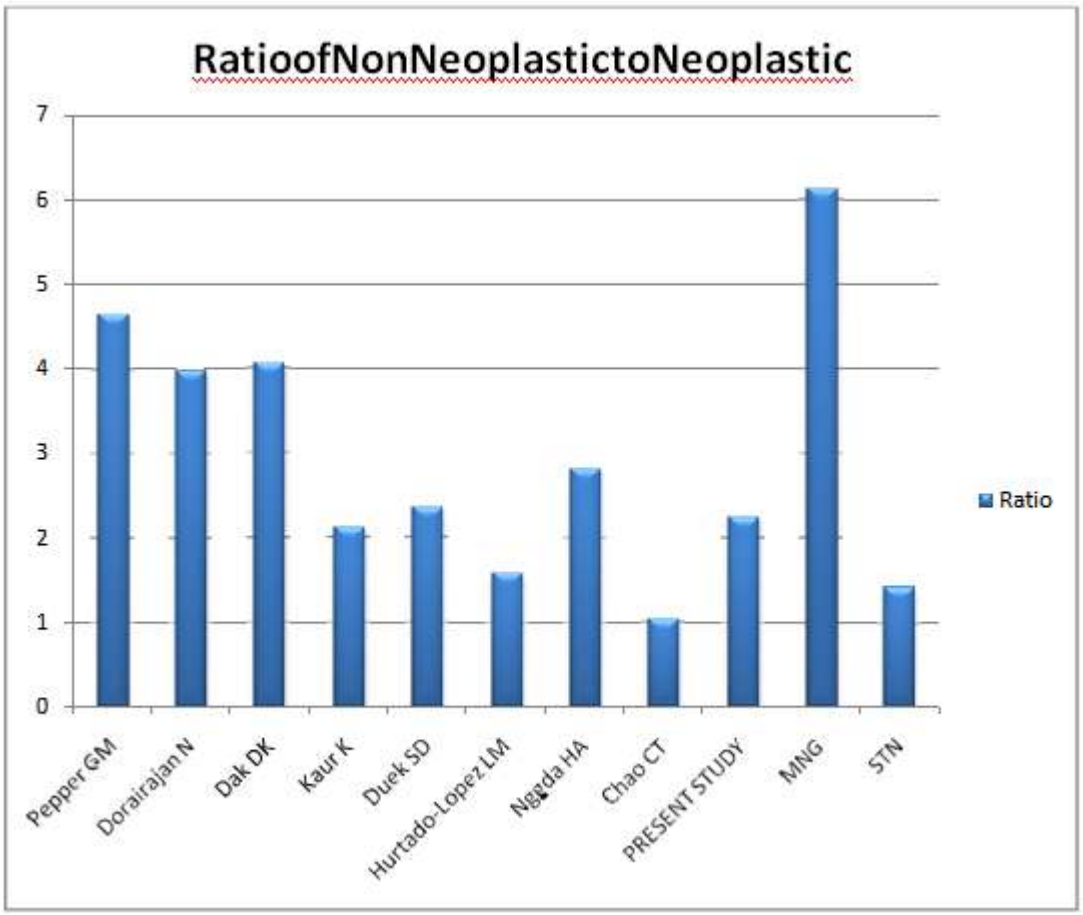
Figure6.5BarChartRepresentationofRatioofnonneoplastictoneoplastic onFNACdiagnosis



Out of 93 Non neoplastic STN cases, 69 are treated conservatively. Rest 24cases are operated for the reasons mentioned below. Total operated cases are 89include 24 non-neoplastic, 57 indeterminate and 8 neoplastic cases. These 89 casesFNAC are analysed to correlate with the histopathology to predict the accuracy ofFNAC.

Benignnodulesareoperatedwhen,a)clinicallysuspiciousofmalignancylike

- Hardtexture
- Fixity
- Recurrentlaryngealnervepalsy
- Lymphadenopathy

b) forcosmoses
c) pressuresymptoms
d) toxicnodule
e) recurrentcysts
f) patientmaynot/cannotbeonregularfollowup

TheratioofnonneoplastictoneoplasticinSTNcasesis1.43:1

Out of 100 MNG cases all are operated even in benign condition. Beningnconditions are operated for the reasons mentioned below In MNG main indicationfor surgery in our serieswas cosmetic problem. The next common indication wasfor pressure effects of the goiter like dysphagiaand dyspnoea. The six cases offollicularneoplasmswere operated torule out follicular carcinoma.Of the 100 cases,32 cases were subjected to total or near total thyroidectomy and remaining 68 casesunderwentsubtotalthyroidectomy

In 100 cases of MNG , FNAC proved 4 cases malignancy 10 cases as insignificantand suspicious,

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86 cases as benign therefore non neoplastic to neoplastic ratio is6.14:1

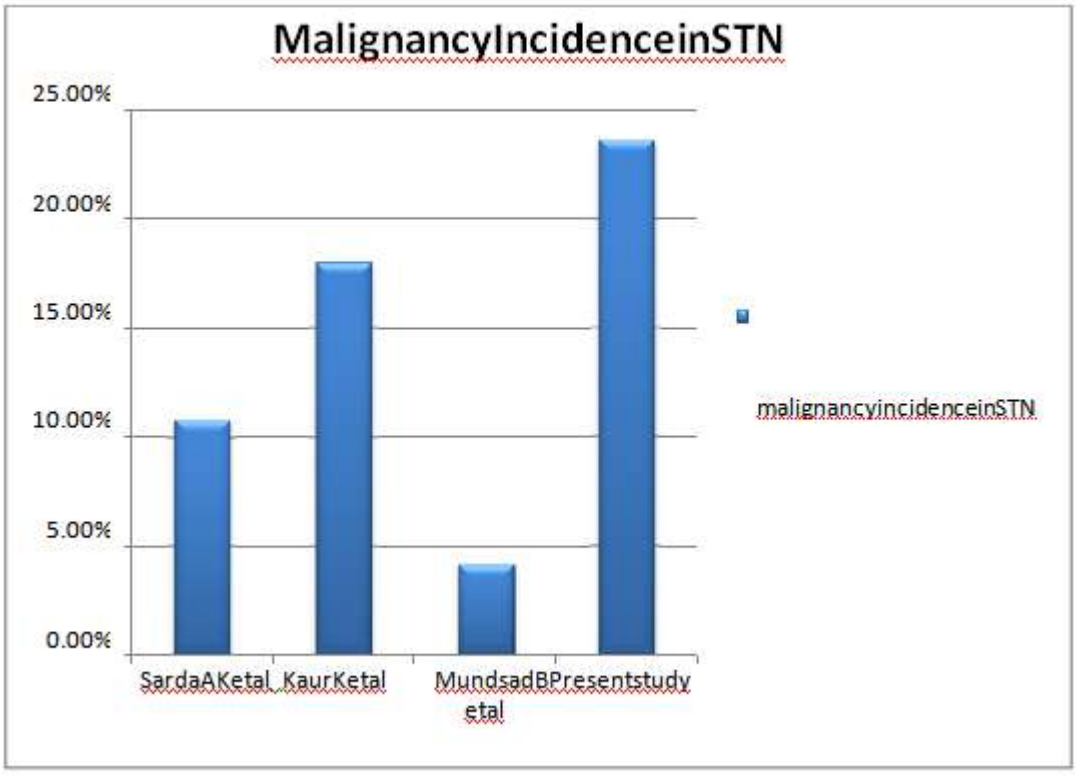
HISTOPATHOLOGY:
STNCASES:In89cases,21(23.59%)aremalignant,31(34.82%)areadenoma and restare37(41.57%).Commonestmalignancy ispapillary carcinoma17 cases constituting80.95%of 21 all carcinomas.Follicular adenoma(30 cases-33.70% of total cases) is commonest pathology observed in our study and nodularcolloidgoitreiscommonestnonneoplasticlesion 20cases–22.47%.

6.6 ComparisionOfIncidenceOfMalignanciesInSTN

IncidenceofmalignancyinSTN	PERCENTAGE
SardaAKetal[106]	10.8%
KaurKetal[105]	18.0%
MundsadBetal[97]	4.16%
PRESENTSTUDY	23.6%

Thehighincidenceofmalignancyinourstudymaybeduetothefactthatsurgerywasdonemainly onsuspiciousnodules

Figure6.6Barchartrepresentationofmalignancyincidenceof STN



In100casesofMNG,10(10%)aremalignant,78(78%)are colloidgoiter,6(6%)areHashimotosthyroiditis,and6(6%)areFollicularadenoma

Diagnosis of Follicular carcinoma preoperatively by FNAC was not possible asangioinvasionandcapsularinvasion,whicharefeature sofFollicularcarcinoma,which was evidentin 2% of cases on HPE. We had 6cases of MNG with thyroiditisandwereoperatedforcosmeticreasons.papillary carcinomaaccounts7 casesconstituting70%ofall 10carcinomacases

Akermanetalquotedfourreasonsforlowsensitivity.Theseinclude:

1. Tumorsmissedataspiration
2. Microscopicmisinterpretation
3. Diagnosisofcellularatypia
4. Indeterminatediagnosis[65]

Similarproblemswere also encountered during our present study. In the presentstudy,thespecificity ofFNAC of thyroidtumorswasfoundtobe highenoughtopermitsurgicalinterventionafteracyto-diagnosisofmalignancy.

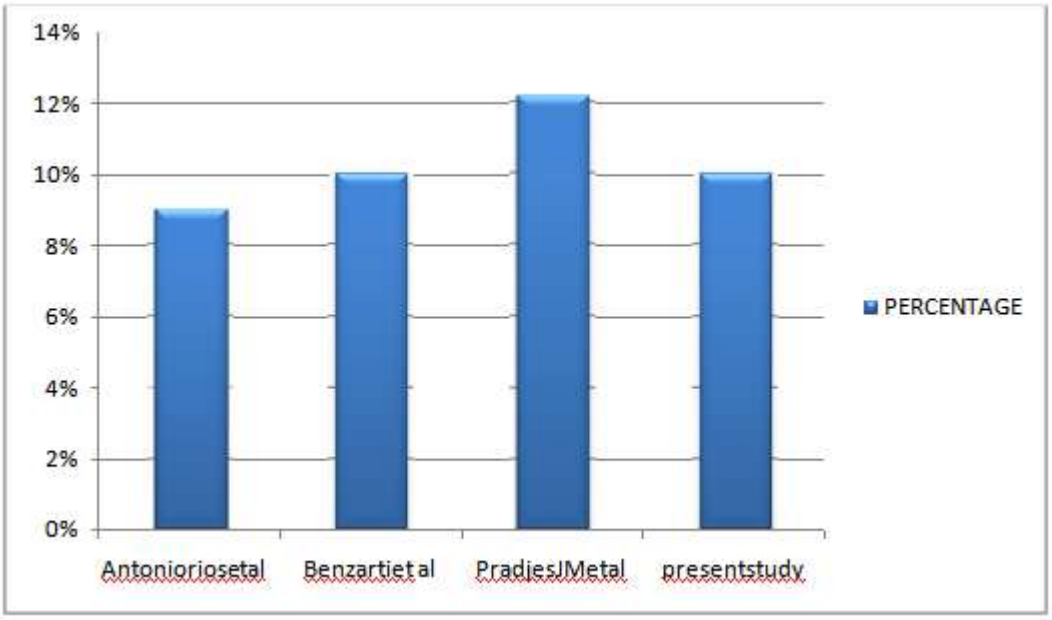
The most common variety of malignancy which has been documented in theliteratureispapillarycarcinoma[15,18].Theincidenceof carcinomain

MNG in our study was 10% and the most common type of malignancy whichwasobservedwaspapillarycarcinoma(60%).This wasconsistentwiththeobservationswhichweremadeby BenzartietalinTunis[102]

6.7 comparisionofincidenceofmalignancyinMNGcases

IncidenceofMalignancy	Percentage
Antoniorioseta1(2005)study.[95]	9%
BenzartietalinTunis[102.]	10%
Pradjes.JM.etal[90]	12.2%
Presentstudy	10%

Figure6.7BarchartrepresentationofmalignancyincidenceinMNG



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TREATMENT:

Benignlesions–

In MNG all benign lesions taken into study are operated in view of variousreasonsdiscuusedabove.

In 158 ofSTN cases 69 cases were treated conservatively in them 2 cases of21 benign cystic lesions conservatively treated have recurred and ultrasound guidedreaspiration was done and fluid sent for analysis . Nomalignancy wasdetected anddidnotrecurred again.DavidS. Cooper, M.D.etal(ATAGUIDELINES2009)recomendedreaspiration can be done upto 3 timesbefore subjecting to surgery9(18.75%) of 48 benign noduleshasdecreased in size, 9remained tobe static and12have slightly increased in size slowly(not more than 20% of diameter or 50% ofsize)withnoclinicalorradiologicalmalignantfeatures[7].Severalstudieswereconductedtodeterminethebenefitsofthyroxinesuppressivetherapyofpatientswith benignsolitarynodules.GharibandMazzaferrireviewed theliteratureandconcludedthatonly10%-20%patientsrespondtosuppressivetherapy.[66]

Operatedcases:

Commonestsurgeryperformedwashemithyroidectomyforbenignandindeterminate cases. Intraoperative frozen section biopsy was not done. 11 casesfurtherunderwentcompletionthyroidectomyformalignancy.11caseoftotalthyroidectomy doneforFNACprovenmalignancy amongst which3alsoincludedfunctionalneck dissection. OnecaseoffollicularcarcinomahasskullmetastasisforwhichsheunderwentsurgeryandfollowedbyRAITherapy. ThestudyconductedbyDepartmentofGeneralSurgery,SingaporeGeneralHospital,indicatedathree-foldhigherlikelihoodof Follicular ThyroidCancer having distant metastasesatpresentationthanPapillary ThyroidCancer.Skeletal metastasesaccountedforthemajority ofthedistantmetastasesatpresentationin FollicularThyroidCancer.

High incidence of follicular, poorly differentiated and anaplastic cancer hadbeenpreviouslyreportedfromareasofendemicgoiter duetoiodinedeficiency[9,12,85].

Contrary,tothishistopathologicfindingsin our serieshaveshowedhighrate of well differentiated papillary type as 17 cases of papillary carcinoma and 3casesoffollicularcarcinomaand1medullaryandnoanaplasticcarcinoma.

It was reported that exogenous iodine intake has induced a significant change inhistological type of nodule as an increase in papillary and a decrease in follicularandanaplastictypes.[9,**96,103,91,83**]Slowinska-Kleckaetal[**9**]andBurgessetal[10,11] havereportedthatadecreaseinthediagnosisoffollicularneoplasmandcarcinoma, and an increase in the diagnosis of papillary type have been induced byroutineiodineintakeinordertocorrectitsdeficiency.ThereforeitwaspostulatedbyEMINGURLEYIKetalthatexogenousiodinesupplementationinducesincreasedrateofwelldifferentiated(papillary)cancerisscomparablewithmystudy.

GENETIC ANALYSIS

Medullary carcinoma thyroid accounts for about 5% of thyroid malignancies.Mostpatientsarepresentbetween50to60years.Mostofthemoccursporadically,approximately25%occurwithinthespectrum ofseveralinheritedsyndromessuchasfamilialMTCs,MEN2AandMEN2B.Allthesevariantsarekowntoresultsecondarytogermlinemutationin RETprotooncogeneInthepresentcasethereismutationon634codonofexon11ofRETprotooncogenewith no other endocrine involvement and with no familial history most probably casemaycomeunderMEN2Awithnootherendocrineabnormalitiesatpresent[88,89]

POST OPERATIVE COMPLICATIONS

Inourstudypostoperativecomplicationswereveryfew.

Transienthypoparathyroidismwasseenin14patients(5.42%)whichwasobserved during the first post-operative week and all recovered completely with oralcalcium and I.V. calcium therapy. There was no permanent hypoparathyroidism. T.A.Day et al (2006) shows that there was 8% of temporary hypocalcemia and 0.9% withpermanenthypocalcemia.

Temporaryrecurrentlaryngealnervepalsywasseenin21cases(8%),bothofwhichrecoveredwithinamonth.whichwassimilartothestudybyChangWFetalinwhichUnilateralvocalcordpalsyoccurredin5.5%(15patients)ofwhichallrecoveredcompletelyexcept2patient.[**104**]Therewasnopermanentrecurrentlaryngealnervepalsypostoperatively inthepresent study.Temporary RLNpalsywasseenin8%,permanentRLNpalsywasseenin0.9%inT.A.Dayetal(2006).

Thyroidmalignancieshaveaverygoodprognosis,owingtotheirearlydetectionbytheanatomicallocation,limitedspreadbeyondtheneckandthedefinitivemanagementoptions

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6.9ComparisionOfIncidenceOfTemporaryRLNPalsy

STUDY	TemporaryRLNpalsy%
ChangWFetal[104]	5.5%
T.A.Dayetal(2006)	8%
Presentstudy	8%

SUMMARY

Thepresent'CLINICOPATHOLOGICALSTUDYOF CARCINOMAINMULTI NODULARGOITREvsSOLITARYTHYROIDNODULEisaprospectivestudy'carriedoutattheDepartmentofGeneralSurgery,KingGeorgeHospital,Visakhapatnam during the period of 24 months extending between July 2012 to june2014.objectivesbeingtoevaluatetheSTNandMNG casesclinicallyandpathologically,to study theincidence of carcinomainbothSTN and MNG,toStudythe clinicalpresentationof carcinomainbothSTNandMNG, correlation ofFNACwithHPE, toknow which pathological variant of carcinomamost commonly occurringinboth cases. This studyincluded atotalof258 cases,100MNGallofcaseswhich were operated& 158 STN of which 89 cases operated and 69 conservativelymanaged.

1. Themeanageofpresentationwas34.61yearsforSTN &41.7yearsforMNGwitharangebetween16and 70years.
2. Inourstudy,femalepreponderanceisseenwithfemaletomaleratiobeing10.28:1inSTNanditis 7.33:1inMNG
3. Swellinginfrontofneckiscommonest syptomand presentinallpatients(100%)
4. Noneofpatientshadirradiationexposureintheirpast.
5. 45%ofpatientsuserocksaltintheirdiet and32%areresidentsof hillyareas.
6. Only2.5%0fpatientswithSTNand6%ofpatientswithMNGhadcervicallymphadenopathy.
7. 1patientof STNpresentedwithskull metastasis and 1patientof MNGpresentedwithsternumsecondariesbothofwhichwerediagnosedasfollicularcarcinoma
8. Clinical diagnosis of malignancuy based on history and physical findings arenotvery successful.
9. Only1casewithtoxicnoduleinSTNand6 casesoftoxicMNGwasstudied,restofthemareeuthyroid
10. 23.59% of the patients were found to have malignancy in histopathologicalreportinSTN.And10%ofpatients inMNG.
11. 4(57.14%) out of 7 men and 17(20.73%) out of 82 women were malignant inSTN.2(16.16%)outof12menand8(9.19%)outof 88womenweremalignantinMNG.
12. Amongst 21 cases of benign cyst, after aspiration only 2 reappeared. Afterreaspirationnonereccured.
13. Inbenignnodulesonthyroxinesuppression,only18 %caseshaveregressedin size.Nonehasincreasedin sizesignificantly tomorethan50%theinitialvolume.All areonfollowup.
14. Extentofthesurgerydependsonthenatureofthelesion
15. Temporaryrecurrentlaryngealnervepalsywasthecommonestpostoperativecomplicationofthesurgery.
16. Outof189casesoperated,189casesarefolloweduptoperiodofstudy

CONCLUSION

Fromthisstudywehavecometothefollowingconclusions:

1. Thyroid swellings and thyroid carcinomas are more common in femalesbutathyroidswellinginmaleshavehighchancestobecomemalignant
2. TheriskofmalignancyishighinSTN(23.59%)

3. Amongst the malignant lesionsmost commonwas papillary carcinomainbothSTNandMNGcases(80.95%)
4. Long term survival or recurrence in malignant cases and the diseaseprogressioninbenigncasescouldnotbeassessedbythis2yearstudy.
5. Counseling is a must to all patients and attendants with thyroiddisordersregarding:

a. incidenceofmalignancyinthenodules.

b. Regardingunavailabilityofonesinglediagnostictesttoruleoutpreoperativemalignancyandtherebyneedforsurgerytoruleoutmalignancyasinindeterminatecases.
c. Inbenigncasesonmedicalmanagementandalsopostoperativepatients,theneedfor regularfollowup.

6. ExclusionofmalignancyisofprimeimportanceinSTN&MNGevaluation.
7. Thedetectionofthyroidnoduleshasbeenontheraiseinrecentdecades may be due to wide spread use of neck imaging or due toincreaseinawarenessamongthepublicregarding malignancy.
8. .Fine-NeedleAspirationcytologyisconsideredtobethe"goldstandard"intheselectionofpatientsforsurgery.
9. Ultrasonography (US) can be used to determine changes in the size ofnodulesduringfollow-uportodetectrecurrentlesionsinpatientssuspected forthyroid malignancy, although there are no specificUSfindingsthatsuggestmalignancy.
10. ThefavoureddiagnosticstrategyintheworkupofpatientswithaThyroidSwellinginclude determinations of serum TSH combined withserumT4and/orfreeT4followedbyFNACand UStogetherwithscintigraphy.
11. Incaseofclinicalfactorsraisingthelikelihoodofmalignancy,themajorityrecommendeddiagnosticthyroidectomydespiteFNACsuggestingabenigncondition.

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