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Evaluating Efficacy of Hounsfield Unitmeasurement in Predicting Risk of Acutecerebral Venous Sinus Thrombosis on Thesinglenon-Enhancedctbrain

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I. INTRODUCTION

Cerebral venous thrombosis (CVT) is an uncommon condition, which over the past 5to10yearshasbeendiagnosedduetorisingclinicalawarenessandtheavailabilityofbetter non-invasive diagnostic techniques [1]. Cerebral vein and cerebral dural sinusthrombosis (CVT) is not a common cause for stroke than other types but it may bemore challenging to diagnose. Because of its nonspecific presentation as well as itsmanypredisposingcauses CVTisanelusivediagnosis.

There is no study in the literature based on the population of India stating exactincidence of acute CVST. There are many hospital-based studies regarding CVSTpublished in India. In the late 1970s, there is a hospital-based study from NorthernIndia in which frequency of CVT is 4.5/1000 in obstetric admissions[2]. In the late1960s, another population-based study from Southern India found that 25% of strokepatientswerelessthan(<)40yearsofageandwere primarilyyoungwomenhavingaCVTwhich had occurred inthepostpartumstage[3].

Cerebral venous sinus thrombosis can affect any age group even neonates with ayounger age at distribution than arterial stroke. It affects females more than males,particularly in the age group of 20 to 35, due to pregnancy, puerperium and oralcontraceptive use. Mean age in most larger studies was between 37 and 38 yearsthoughallagescanbeaffected[4][5].

Dural venous sinus thrombosis commonly affects the superior sagittal sinus (SSS)and/orthetransversesinuses[6].

There are many pathophysiological mechanisms and predisposing risk factors likehypercoagulable state, dehydration or pregnancy, the postpartum state ,extrinsiccompression or local invasion of a vein by tumor or an adjacent infectious process(e.g., mastoiditis), a slow-flow state within the venous sinus, and or dural sinuscompression[7][8].

Thereisalsoawidedistributioninthemodeofonsetofsymptoms,withapproximately28%acute(<48hours),42%subacute(between48hoursand30days),and30%chronic(>30days)[6].

Treatmentstrategiesareaimedtocontrolorresolvetheunderlyingpathology,controlling ICH and treatment of seizures or focal deficits caused by cerebral edemaorinfarction[12].

Because of its varied causes and presentations, CVT is a disease that may beencountered by neurologists and neurosurgeons as well as by emergency clinicians,internists,oncologists,hematologists,obstetricians,pediatricians,andfamilypractitioners.Inevery neuroradiologiccase,theevaluationforevidenceofCVTshouldbe included in the diagnostic checklist. The radiologist can be the first physician tosuggest the diagnosis, which is a radiological and not merely a clinical. So imagingplays a key role in the diagnosis. The imaging findings are easily overlooked if notspecificallysought.

Thoughangiographyisstillconsideredtobethe'goldstandard',MRIandMRvenographyiscurrentlythepreferredtechniquesformakingthediagnosisofCVT.MRimaginghasbeenreportedtohaveadvantagesoverCTandconventionalangiographyand was advocated as the test of choice for the definitive diagnosis of dural sinusthrombosis[13,14].

Conventional CT was the best noninvasive method of diagnosing CVT before thediscoveryofMRI[1].

CT venography is a very rapid, readily available and accurate technique for detectingcerebral venous thrombosis [15][16]. CT venography provides

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a highly detailed view ofthe cerebral venous system, superior to that available with conventional TOF MRvenography, and has at least similar accuracy for the detection of cerebral venousthrombosis[15].
Inthepresentera,CTisthefirstmodalityofchoiceforinvestigatingmostneurologicalconditions. CT is likely to remain the first or initial modality because of its widespreadavailability,comparativelylesserscantimeandlowercost.
CTimagesaremadeupofpixels,eachofwhichhasagrayscalevaluefrom1(black)to 256 (white). This value corresponds to the number of X-rays that pass through thestructureandcanbemeasuredandexpressedinHounsfieldunits(HU).
HUhassincebeenusedtoevaluateandquantifytissuesandfluids.Atstandardpressureandtemperature(STP),radiodensityofdistilledwaterisdefinedaszero Hounsfield units (HU), the radiodensity of air at STP is defined as -1000 HU,blood and other tissues have a positive HU, fat has a negative HU. This method canbe used to differentiate 256 shades of gray that are indistinguishable to the naked$_{eye}$[17].
HUvalueschangewithvaryingdensityoftheorganorfluid.HUvaluesareapproximatelyfixedforalltissueinthebody.ThisvariabilityoftheHUvaluesdependsonthedensityofthefluidandcanbeusedfordiagnosingthrombosis.
AtypicalimagingfindinginpatientswithCVSTisadirectvisualizationofahyperattenuating thrombus in the occluded sinus (dense sinus sign)[18,19]. The cordsigni.e.adirect signofCVSTisdefinedasahomogeneous,hyperattenuatedappearanceofthrombosedvenoussinusonnon-contrastCTscans,anditiscaused by the increased attenuation of the thrombotic material in the affected vessels[20–22].Thesefindingscanbeusedinthework-upofpatientswhoaresuspectedofdevelopinganacuteCVST.
HU value for blood ranges from + 35 to +60[23] .There are studies in which CTattenuationvalueshavebeenusedinthediagnosisofotheracutethromboticconditionsinnon-enhancedCT[24,25]
Cobellietal2005foundsimilarattenuationvaluesforacutepulmonaryemboli(mean,

74.25 HU; range, 57–93 HU) on unenhanced CT scans), and Goldstein et al 2012found similar HU values for acute abdominal venous thrombosis (mean, 67.12 HU;range, 53– 84 HU). [24,25] So the same principle can be used to diagnose at-riskpatientsofacutecorticalvenoussinusthrombosisonnonenhancedCT.

There are previous pilot studies which have used Hounsfield units of cerebral venoussinuses to diagnose cerebral venous sinus thrombosis(CVST) by using single nonenhancedCTbrain[26–28].
Astheapparentincreaseinsinusattenuationcansometimesbemisleadingandisnotalways visually picked up, it is more reliable to measure the attenuation of the sinusby measuring HU. Normalization of this increased attenuation by using hematocritvalue in the study may further increase the detection of true cases of CVST on non-contrastCTbrain.[27]
Accurate and prompt diagnosis of cerebral venous thrombosis is crucial becausetimely and appropriate therapy can reverse the disease process and significantlyreducetheriskofacutecomplicationsandlong-termsequelae.
Sointhesettingwhereonlynon-contrastCTisavailableandthepatientisneedinganurgent diagnosis for further work-up, HU measurement will help to evaluate at-riskpatientswithCVST.

II. AIMS AND OBJECTIVES

Primaryobjective:
1) To test the utility value of HU measurement in diagnosing acute cerebral venoussinusthrombosisinemergencysetup.

Secondaryobjectives:
1) CorrelationoftheHUvalueswithbiochemicallyderivedvaluesofhematocrit.
2) Evaluating the H: H ratio if sensitivity or specificity of study is increased in patientswithacuteCVST.

III. MATERIALS AND METHODS

Studydesign:Noninterventionalcross-sectionalobservationalstudy.
Periodofstudy:18months.
Setting: DepartmentofRadio-diagnosisinaTertiarycareteachinghospital.
Approximate subjects: approximately 200 patients were studied over a period of 18months.
Inclusioncriteriaforcases:

AnyadultpatientwhounderwentCTscanasadvisedbytherespectivephysician/surgeon and is suspected to have acute cerebral venous sinus thrombosisandfulfillingthebelow-mentioned criteria:

- Anysex,maleorfemale.
- Agemorethan18years.

- Patientshavingnormalserumcreatininevalue(0.3-1.4mg/dl).

- Patientsnon-allergictocontrast.
- Patienthavingregistrationatthisinstitute.

All patients suspected to have acute CVST were included in the study, irrespective ofthrombosisonCTvenography.

Exclusioncriteria:

- Anypatientnotwillingforthestudy.
- Anypatienthavingincreasedserumcreatininelevels(>1.4mg/dl).
- Anypregnantfemalepatients.
- Anypatienthavingahistoryofcontrastallergyreaction.
- Casesofintracranialhemorrhageorskullfractureadjacenttoduralsinuses.
- An increased intracranial pressure condition such as hydrocephalus, severebrain swelling, intra-axial or extra-axial mass, recent interventional or surgicaltreatment.
- Intra-venousorintra-arterialiodinatedcontrastmediaadministrationwithintheprevious24hr.

Ethics:

Properinformedconsentwas takenfromthepatientorfromrelativeifthepatientwasnot competent to give consent (in case of altered sensorium) after explaining to themaboutrisksandbenefitsofexamination.

StudyProcedure:

All CT scans which were assessed for the study were performed on Philips 64 sliceBrillianceComputeTomographyscanner.Allthec linicallysuspectedpatientsofCVSTwere scanned with NCCT brain plus venography. The serum creatinine value ofpatientwaschecked.

CT data were obtained with the following parameters:Fieldofview:250mm
Slicethickness:5mm

Increment: 5mmFilter:Standard(B)
Window:C:60 and W:360

Matrix:512
A weight-based low-dose CT protocol (120 kVp, 1000 mAs) was used. Scanning wasperformed from top of the skull to base of the skull. CT was performed in the cranio-caudaldirection.

CT Venography was performed 45s after administration of intravenous iodinatedcontrastat3-4mL/swithapprox.70-80ccofcontrastinjection.
Alltheimagedatawereanalyzedattheworkstation (PhilipsTera-recon).

All the study related data of suspected patients of acute CVST like HU values ofsuperior sagittal sinus, both transverse sinuses, torcula was obtained and maximumHUofamongthesesinuseswasrecorded.HU valuemeasurementwasdonebyusingcircle regions of interest (ROI) method on axial or coronal sections. The ROI was setto a limit of 1-30 mm^2 and used a circular ROI area as large as possible that could bemeasured and if HU values were in decimals then they were rounded off to a closestwholenumber.(image 17A,B,C)

CT venography scan was assessed for the presence of features of venous sinusthrombosis.TheCTfindingswererecordedinacaserecordform.

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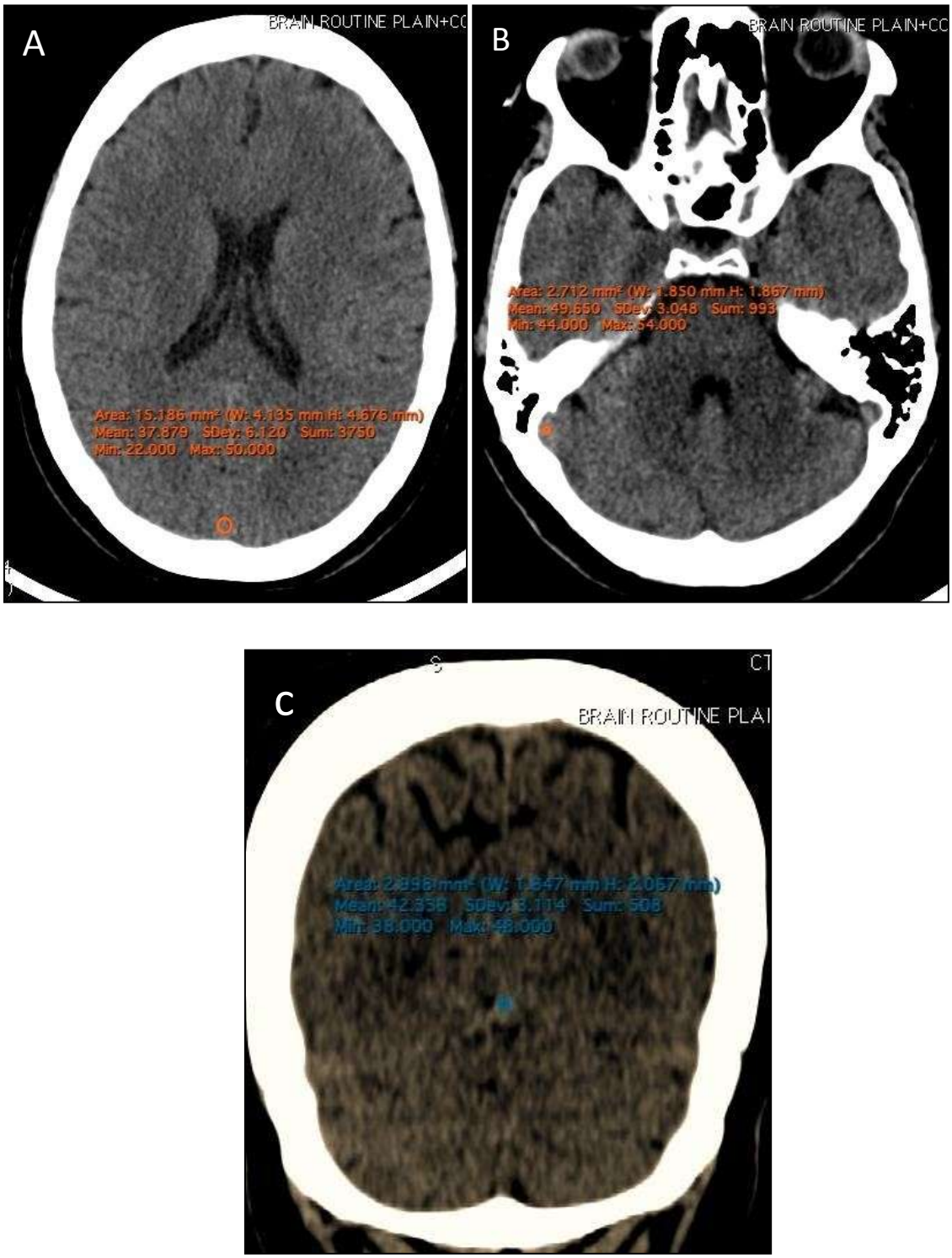

Image17 A, B, C: Axial and coronal sections of unenhanced CT scan showing amethod of measurement of HU using ROI's in SSS, transverse sinus and torcularespectively

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Before the scan, essential clinical history was obtained along with the hematocritvaluesofthosepatientsinwhomserumhematocrittestwasdoneforanotherpurpose.Blood collection was not done specifically for the study purpose. Hematocrit valuesweрerecorded.HU:hematocritratiowascalculated.

Statistical analysis:

We made two groups with patients in whom the diagnosis of CVST was excluded onCTvenographyasacontrolgroup.

Maximum HU value amongst the four sinuses (both transverse sinuses, SSS andtorcula) of the individual subject from the CVST patient group and the control groupwasusedforthestatisticalevaluation.

We compared both groups based on HU values and H: H ratio by Mann Whitney Utestandunpaired t-test.Ap-value<0.05wasconsideredtobestatisticallysignificant.

Simple regression analysis was used to evaluate the correlation between mean HUandhematocrit.

Based on the collected data, specificity and sensitivity of both HU and H: H ratio fordiagnosingacuteCVSTwerecalculatedwithCTvenographyasagoldstandardtest.

Receiver operating characteristic (ROC) curves were drawn to define the optimalcutoffvalueofHUandH:Hratio forwhichsensitivityandspecificitywere calculated.

Statistical analyses were done using software IBM SPSS V23 and Microsoft Excel2013.

IV. RESULTS

Resultsaredividedintofollowingsections

1. **Demography**
a) Agedistribution
b) Genderdistribution
c) Symptomwisedistribution
d) AcuteCVSTonCTvenographyamongsttotal,male andfemalestudypopulation
e) Sinuswisedistribution

2. **Comparisonofnormalgroupand diseasegroup byMannWhitneyUtestandunpairedt-testintotal, maleandfemalestudypopulationbasedon**
a) Age
b) Hematocrit
c) HU
d) H:H ratio

3. **Simpleregressionanalysisandscatterplot**
a) Max.HUvs.hematocrit
b) H:H ratiovs.max.HU

4. **Sensitivity,specificity,PPV,NPVof**
a) HU
b) H:Hratio

5. **Receiveroperatingcharacteristic(ROC)curve todeterminethecut-offvalue**
a) Sensitivityvs.false positive ofHU
b) Sensitivityvs.false positive ofH:Hratio

1. DEMOGRAPHY

Thestudywasconductedoveraperiodof18months.200 patientswhohadheadacheassociatedwithothersymptomslikeseizure,vertigoanddrowsinesswereincludedinthestudyandinvestigatedwithnonenhancedCTandCTvenography.

AgeDistribution

Belowtable6andgraph1show

- Ageofthepatientsincludedinthestudyrangedfrom18yearsto69years.
- Meanage was38years.
- Maximumnumberofpatientswereintheagegroup 30-50years(51%).
- Minimumnumberofpatientswereintheagegroup >50years(19%).

AGE GROUP(YEARS)	NO.OF PATIENTS	PERCENTAGE
<30	60	30%
30-50	102	51%
>50	38	19%

Table6:showingagewisedistributionoftotalpatientswiththepercentageinthreegroups.

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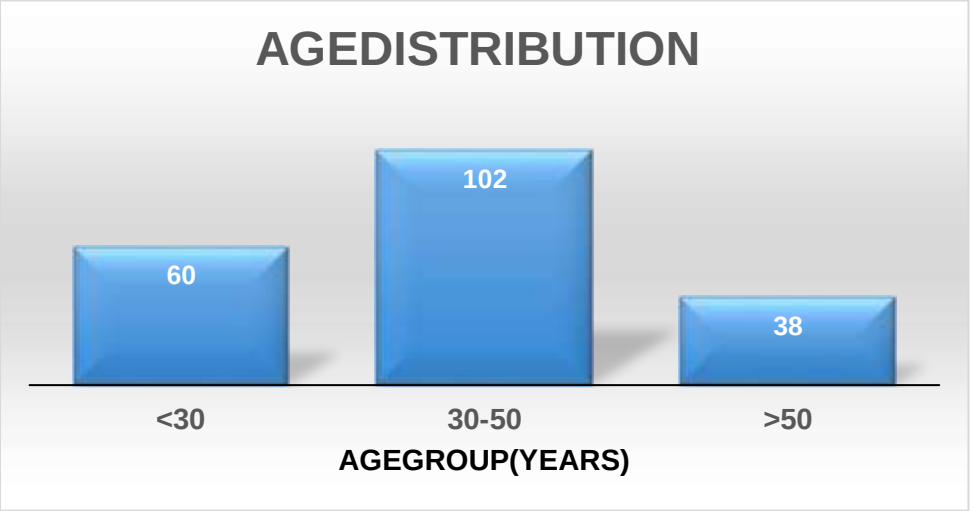


Graph1:Bardiagramshowingagedistributionamongthestudypopulation.

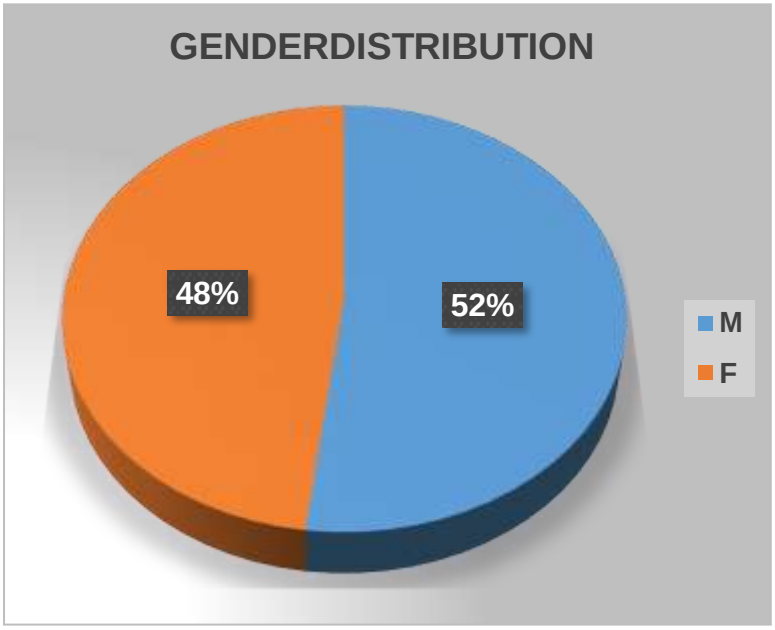
GENDERDISTRIBUTION

Belowtable7andgraph2show

- Outofthe200studypatients,104(52%)weremalesand96(48%)werefemales.
- Theoverallmaletofemaleratiowas1.083:1.

GENDER	NO OF PATIENTS	PERCENTAGE
MALE	104	52%
FEMALE	96	48%

Table7:showing gender-wisedistributionoftotalpatientswithapercentage.



Graph2:Piediagramshowinggenderdistributionamongthestudypopulation.

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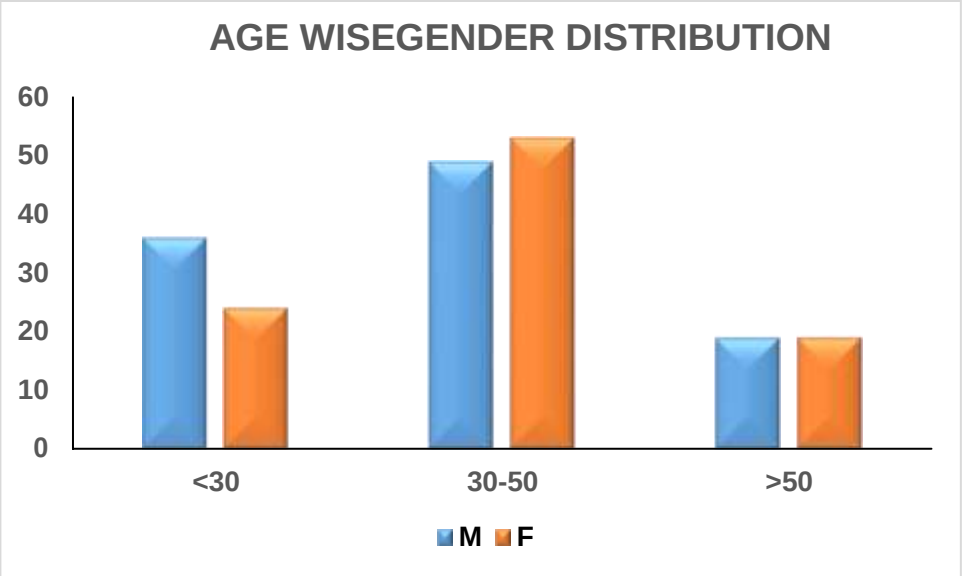
AGEWISEGENDERDISTRIBUTION
Table8andgraph3show

- Outof60patientsintheagegroupof<30years,36weremalesand24werefemales.
- Outof102patientsintheagegroupof30-50years,49weremalesand53werefemales.
- Outof38patientsintheagegroupof>50years,19weremalesand19werefemales.
- Both male and female patients who were suspected of acute CVST, maximummale,and femalepatientswerein30-50yearsagegroup.

AGE GROUP(YEARS)	MALE	FEMALE	TOTAL
<30	36	24	60
30-50	49	53	102
>50	19	19	38

Table8:showing agewisegenderdistributionoftotalpatients.



Graph3:Bardiagramshowingagewisegenderdistributionamongthestudypopulation

SYMPTOMWISEDISTRIBUTIONOFSTUDYPOPULATION
Headache was the most common clinical symptom in the study population.it waspresent in all 200patients. Headache was associated with other symptoms likeseizures,vertigo,anddrowsiness.

Among200patientswithheadachewhoweresuspected foracuteCVST,seizureswerepresentin93patients(46%),followedbydrowsiness(74patients:37%),followed byvertigo(33patients:17%).
(Belowtable9andgraph4)

SYMPTOMWISEDISTRIBUTION

SYMPTOMS	NO OF PATIENTS	PERCENTAGE
SEIZURES	93	46.5%
VERTIGO	33	16.5%
DROWSINESS	74	37%

Table9:showingsymptomwise distributionoftotalpatients.

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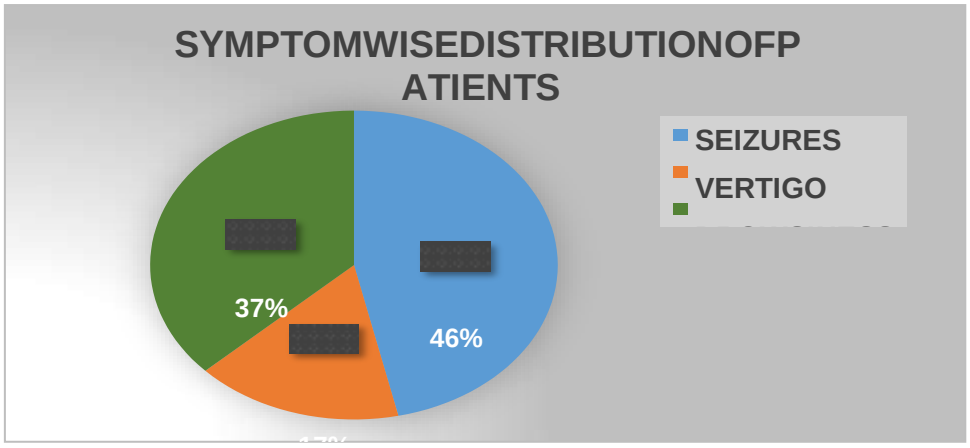


Graph4:Piediagramshowing symptomwisedistributionofpatientsamongthestudypopulation

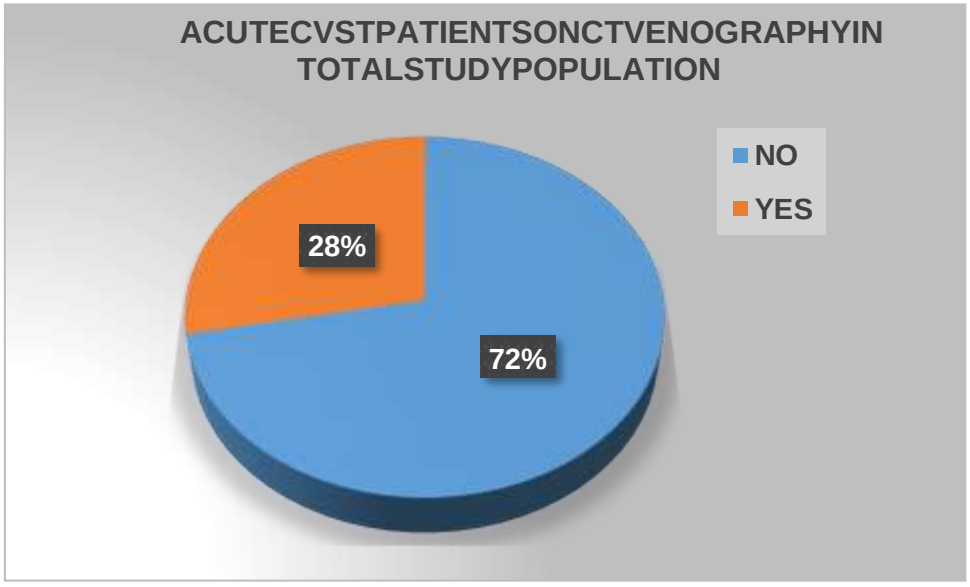
ACUTE CVST PATIENTS ON CT VENOGRAPHY AMONGST TOTAL STUDYPOPULATION

Belowtable10aandgraph5ashow

Outof200totalpatientswhoweresuspectedofhavingacuteCVST,56patients(28%)hadacutethrombosisineitheroneortwocorticalvenoussinuses.

ACUTECVSTON CTVENOGRAPHY	NOOF PATIENTS	PERCENTAGE
YES	56	28%
NO	144	72%

Table10a:showingacuteCVSTonCTvenographyamongstthetotalstudypopulation.



Graph5a:Piediagramshowingpatientswithacute CVSTonCTvenographyamongthestudypopulation

GENDER WISE DISTRIBUTION OF ACUTE CVST PATIENTS ON CTVENOGRAPHY

Belowtable10bandgraph5bshow

Outoftotalof56patientswithacuteCVSTonCTvenography,32(57%)patientsweremaleand24(57%)werefemale.

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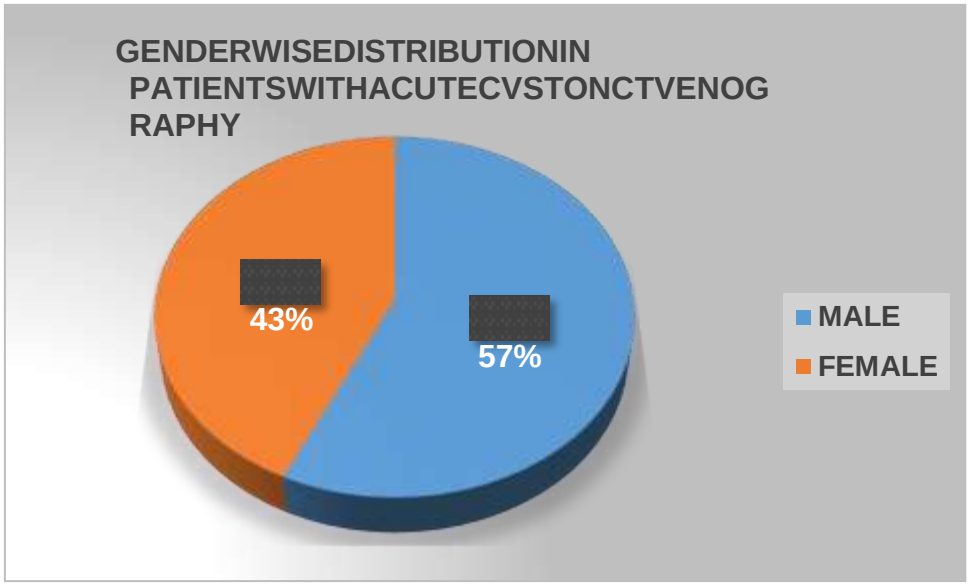
ACUTECVSTON CTVENOGRAPHY	NOOF PATIENTS	PERCENTAGE
MALE	32	57%
FEMALE	24	43%

Table10b:showinggender-wisedistributionofacuteCVSTonCTvenographyamongstthetotal studypopulation.



Graph5b: Piediagramshowinggender-wisedistributioninpatientswithacuteCVSTONCTvenography.

ACUTE CVST PATIENTS ON CT VENOGRAPHY AMONGST MALE STUDYPOPULATION

Belowtable11andgraph6show Outoftotal104malepatients,32patients(30%)hadacuteCVSTonCTvenography.

ACUTECVSTON CTVENOGRAPHY	NOOFMALE PATIENTS	PERCENTAGE
YES	32	30%
NO	72	70%

Table11:showingacuteCVSTonCTvenographyamongst malestudypopulation.

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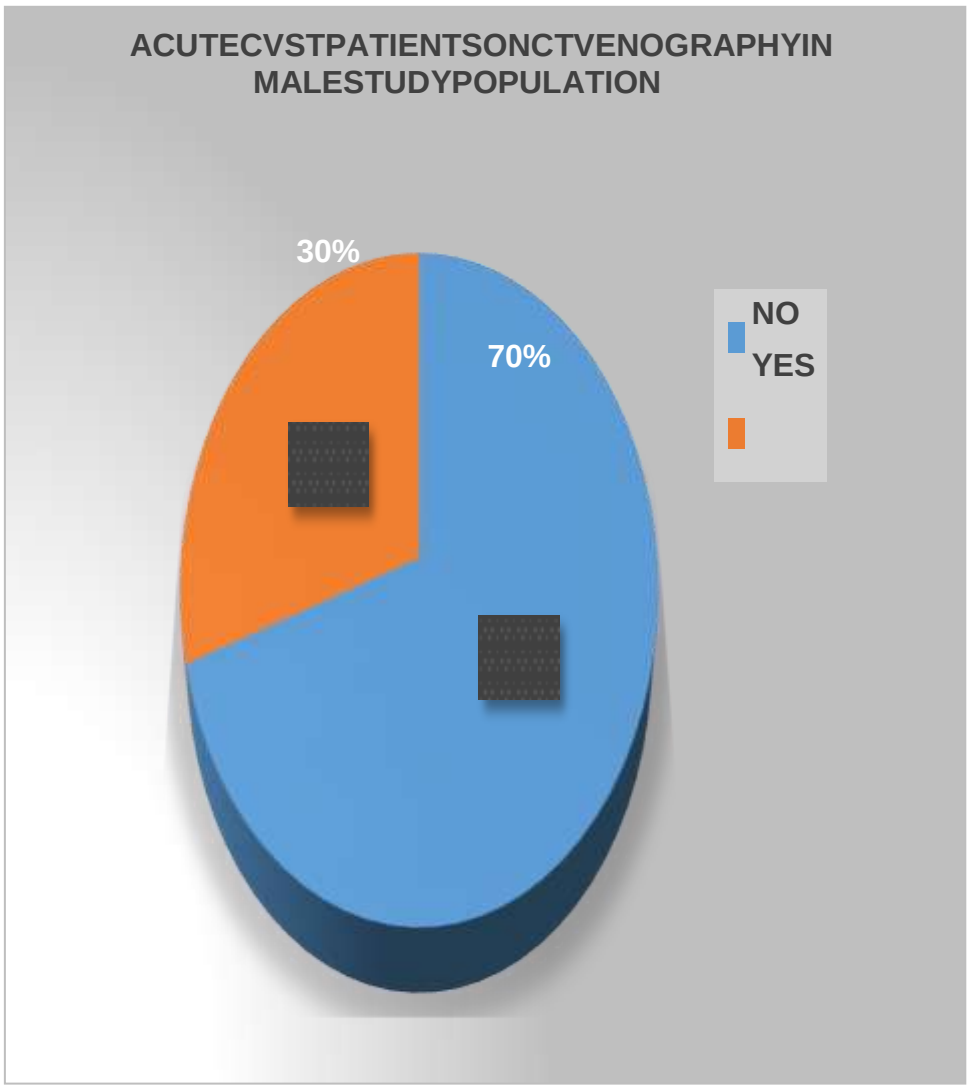

Graph6:PiediagramshowingpatientswithacuteCVSTonCTvenographyamongthe male studypopulation.

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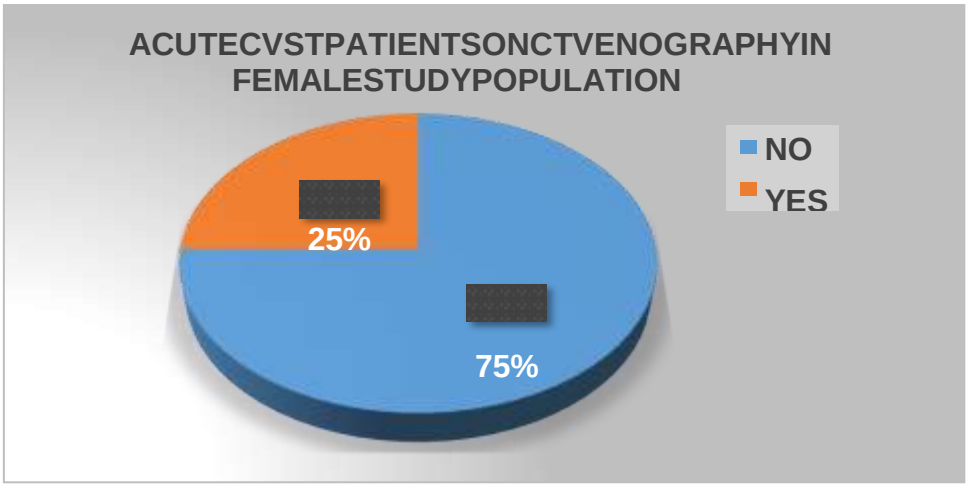
ACUTE CVST PATIENTS ON CT VENOGRAPHY AMONGST FEMALE STUDYPOPULATION

Belowtable12andgraph7show Outoftotal96femalepatients,24patients(25%)hadacuteCVSTonCTvenography.

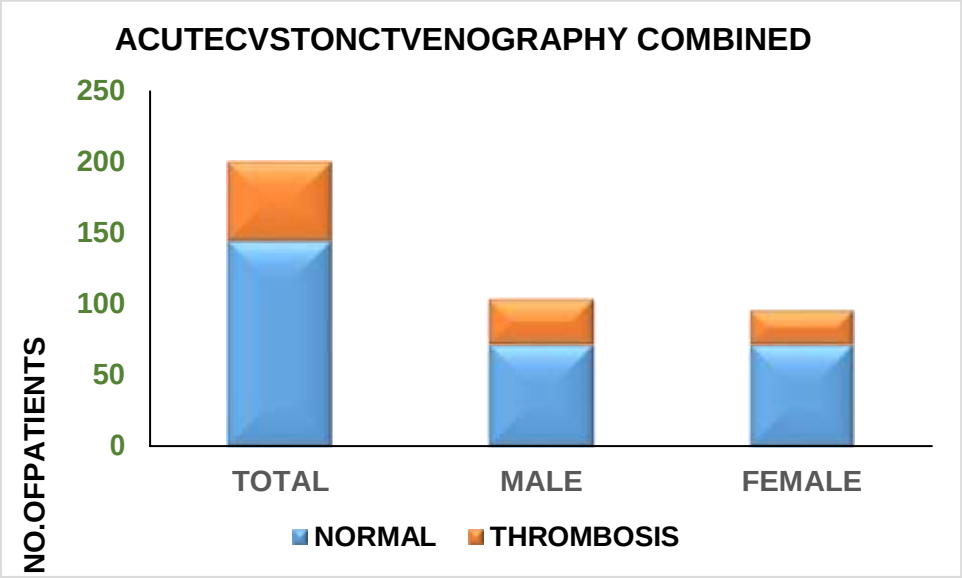
ACUTECVSTON CTVENOGRAPHY	NOOF FEMALE PATIENTS	PERCENTAGE
YES	24	25%
NO	72	75%

Table12:showingacuteCVSTonCTvenographyamongst femalestudypopulation.



Graph7:PiediagramshowingpatientswithacuteCVSTonCTvenographyamongthefemale studypopulation.

Belowthebardiagram(Graph8)showspatientsofcerebralvenous sinusthrombosisonCTvenographyinmaleandfemalestudypopulation.



Graph 8: bar diagram showing patients with acute CVST on CT venography amongtotal,maleandfemalethepopulation.

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SINUSINVOLVEMENT

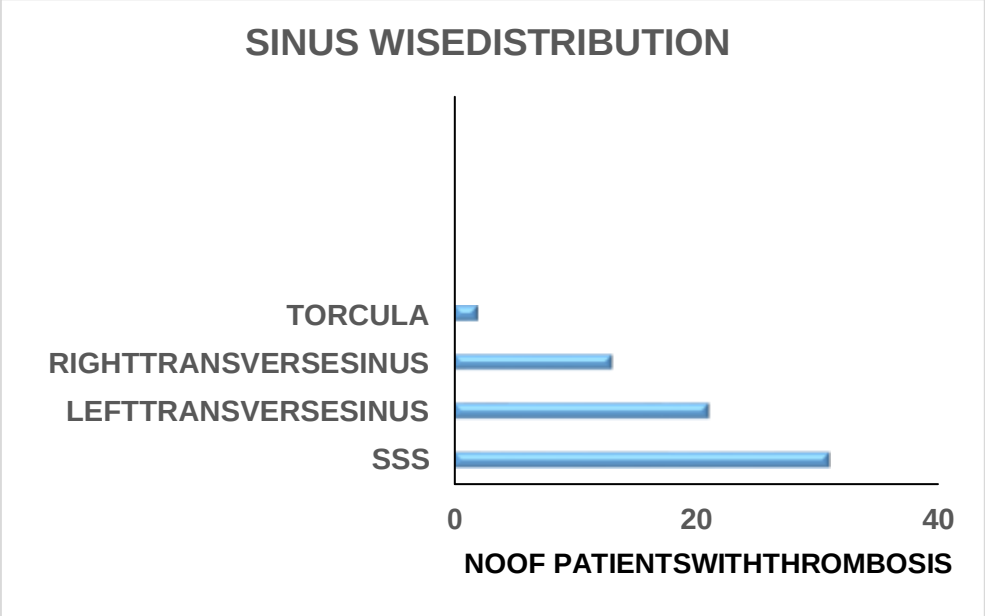
Belowtable13andgraph9show

Out of 56 patients, 31 patients had involvement of SSS, 21 had involvement of righttransversesinus,13oflefttransversesinusand2patientshadinvolvementoftorcula.

Thus, out of 56 patients presenting with acute CVST 31 i.e. 46% patients had SSSinvolvement, 31% had left transverse sinus thrombosis, 20% had right transversesinusthrombosis,3%hadthrombosisoftorcula.

SINUSINVOLVEMENT	Numberofpatients	PERCENTAGE
SSS	31	46%
LEFTTRANSVERSESINUS	21	31%
RIGHT TRANSVERSE SINUS	13	20%
TORCULA	2	3%

Table13:showing sinuswisedistributionofacuteCVSTpatients.



Graph9:Bardiagramshowingsinuswisedistributionofacutecvstpatients.

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2. COMPARISONOFTWOGROUPS

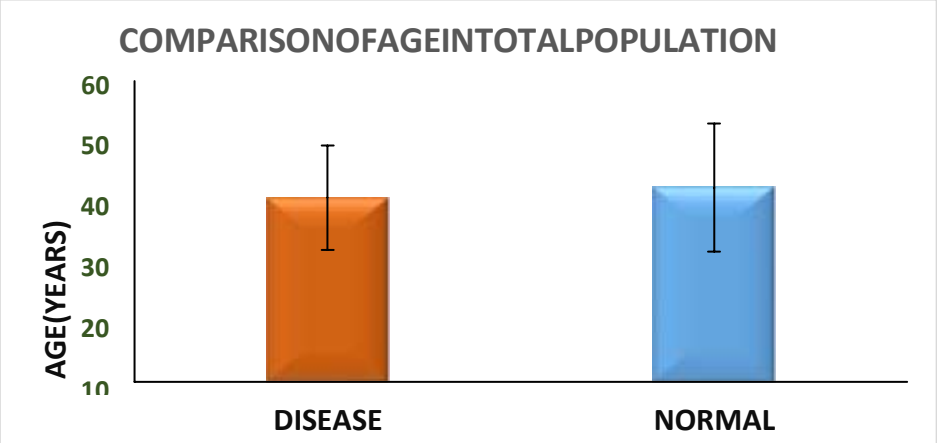
- **Comparisonofageintwostudygroupsinthetotal population.**

Wehavetakenatotalstudypopulation(200patients)aspatientswhoweresuspectedofhavingacuteCVSTbasedonclinicalsymptoms.

On the basis of CT venography findings, we have divided these 200 patients intodiseased i.e.patientswithacuteCVSTandintonormali.e.patientswithoutCVST.

On comparison of total population between two groups i.e. patients with thrombosis(disease patients group) and patients without thrombosis (normal patients group**)** atbaseline (Graph10), Twogroupswerecomparedby the**Mann–WhitneyUtestwithp-value =0.391.**

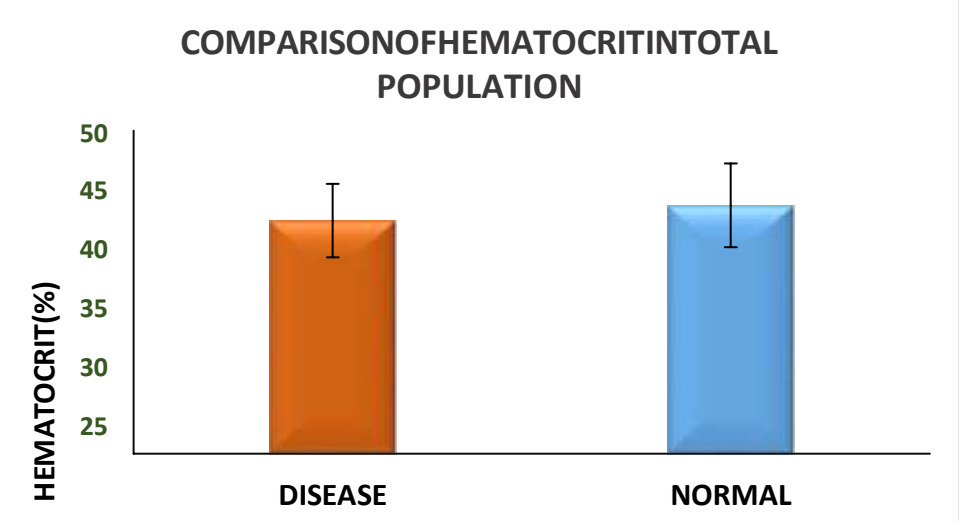
By comparing two groups i.e. normal and disease for age, both groups did not differbyagesignificantly.Sobothgroupswerecomparable.



Graph 10: Bar diagram showing a comparison of age between two groups by MannWhitneyUtestwith p-value =0.391 intotal populationwith mean ±SD.

- **Comparisonofhematocritintwostudygroupsinthetotalpopulation.**

For hematocrit values, both disease and the normal group were compared by **Mann–WhitneyU test.** Asp-valuewas0.07186(>0.05),boththegroupsdidnotdiffersignificantlyinhematocritvalues.(Graph11), SowehavecomparedboththegroupsbyHU,HU:hematocritratio(HHratio)inthetotalstudypopulation,malestudypopulationandinthefemale studypopulation**.**



Graph11:Bardiagramshowingacomparisonofhematocritvaluesbetweentwogroupsby MannWhitneyUtestwithp-value =0.07186withmean±SD.

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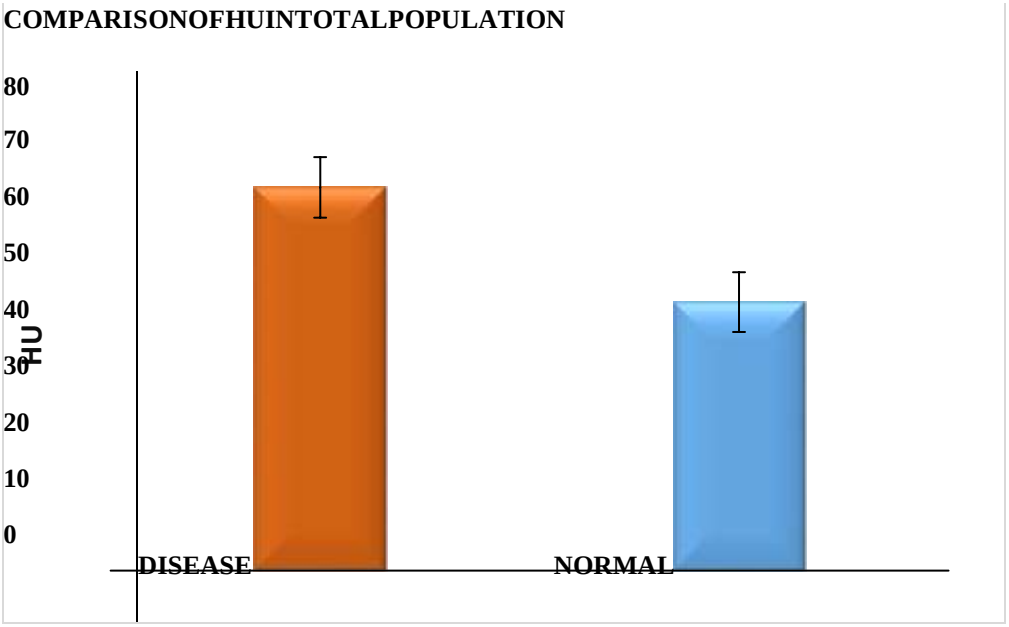
- **Comparisonof HU betweentwogroupsinthe totalpopulation.**

Belowgraph12shows

Aftercomparingagebetweentwogroupsinthetotalpopulation,HUvaluesbetweenthetwogroupswerecomparedbythe**Mann–WhitneyU testwithp-valuewas <0.0001.**

OncomparingtwogroupsforHU,ithasbeenfoundthat HUvaluewassignificantlyhigherinthedisease groupascomparedto the normal group.



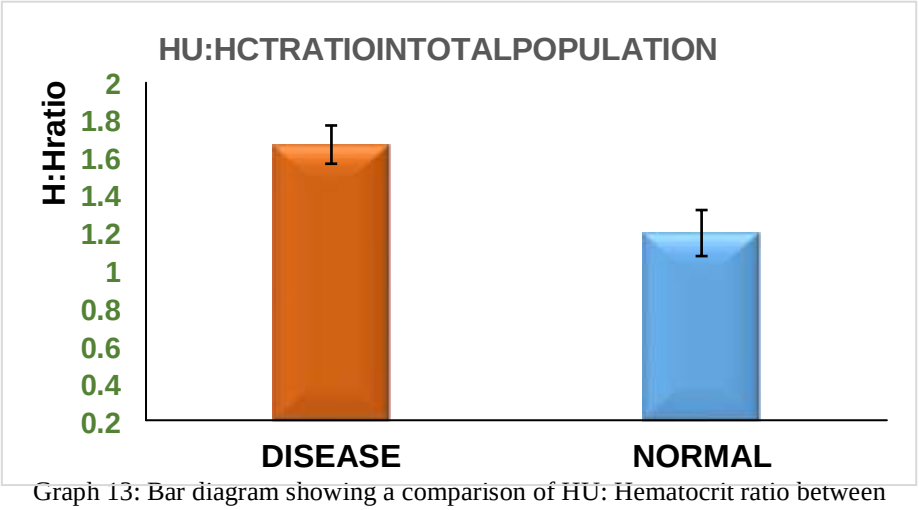
Graph12:BardiagramshowingacomparisonofHUbetweentwogroupsintotalpopulationbyMannWhitneyUtestwithp-value<0.0001withmean±SD.

- **ComparisonofH:H ratiobetweentwogroupsinthe totalpopulation.**

Belowgraph13shows

Aftercomparinghematocritbetweentwogroupsinthetotalpopulation,HU:Hematocrit ratio between two groups was compared by the **Mann–Whitney U testwithp-value was<0.00001.**

On comparing two groups for HU: Hematocrit ratio, it has been found that HU:Hematocrit ratio was significantly higher in the disease group as compared to thenormalgroup.



Graph 13: Bar diagram showing a comparison of HU: Hematocrit ratio between twogroupsintotalpopulationbyMannWhitneyUtestwithapvalue<0.00001withmean ±SD.

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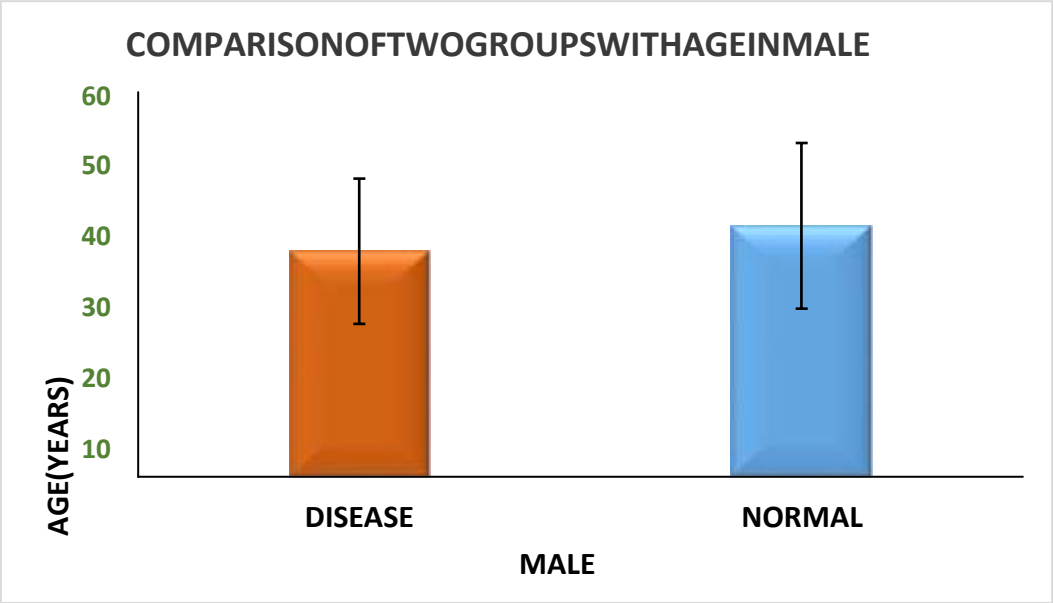
- **Comparisonofagebetweentwogroupsinthe malestudypopulation.**

BothgroupswerecomparedforagebyMannWhitneyU testwithpvalue=0.1556

Below bar diagram (graph 14) shows that mean age in male patients with diseasegroupwas35.18yrs(rangewasbetween30-66yrsandSDof11.33yrs).

Also,meanageinthenormalmalestudypopulationwas 39.15yrs(rangewasbetween19-69yrsandSDof12.91yrs)



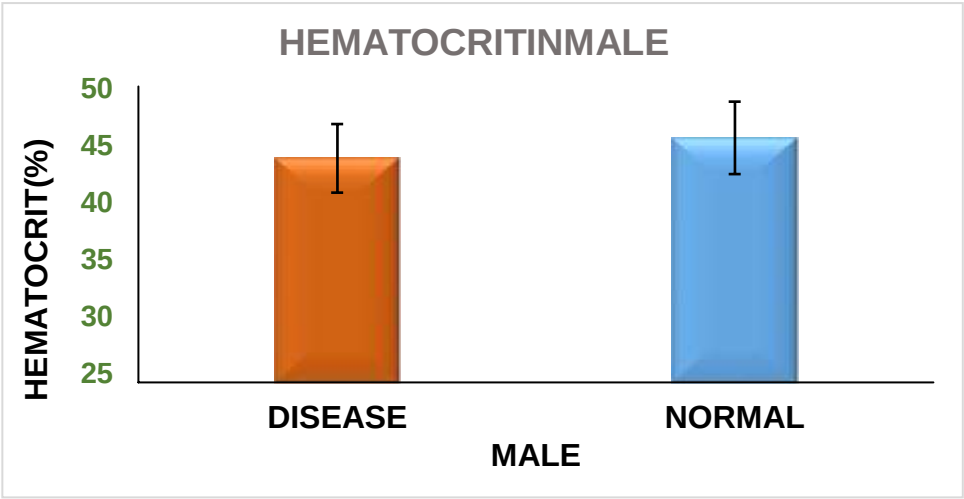
Graph 14: bar diagram showing a comparison of age by Mann Whitney test with pvalue= 0.1556 with mean, range and SD of disease group and control group in themalestudypopulation.

- **Comparisonofhematocritbetweentwogroups inthemalestudypopulation.**

BothgroupswerecomparedforhematocritbyMannWh itneyUtestwithpvalue=0.13Sobothgroupsdidn'tdiffe rsignificantlyforhematocritandsowerecomparable.

Belowthebardiagram(graph15)showsthatmeanhema tocritinmalepatientswithdiseasegroupwas42.71% (range wasbetween30-50%andSDof3.48%).

Also,meanageinthenormalmalestudypopulationwas 44.8%(rangewasbetween40-59%andSDof3.66%)



Graph 15: bar diagram showing a comparison of hematocrit by Mann Whitney testwith p value=0.13 with mean, range and SD of disease group and control group inthemale studypopulation.

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- **ComparisonofHU betweentwogroupsinthe male studypopulation.**

HUvaluesbetweentwogroupsinthemalestudypopulationwerecomparedby

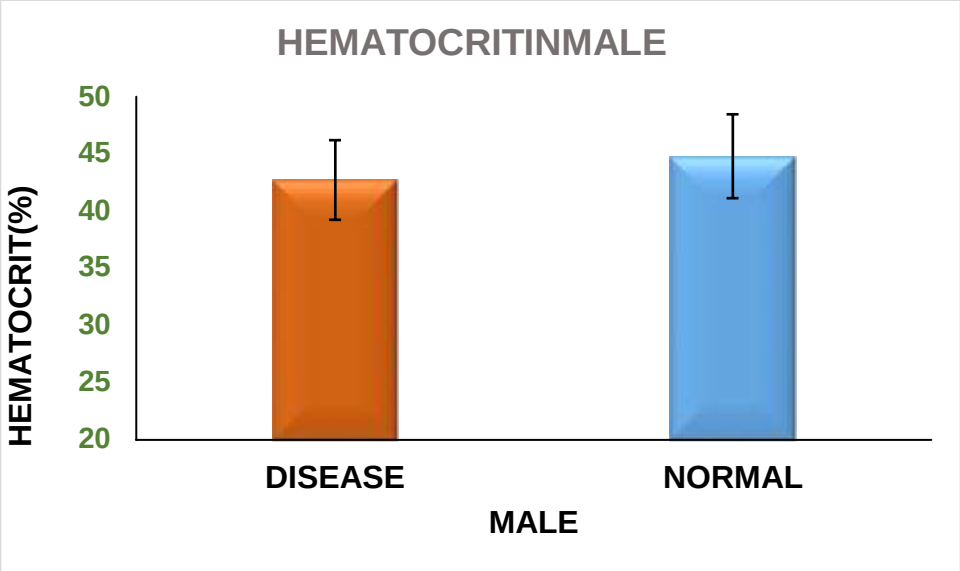
Mann–WhitneyU testwithp-valuewas<0.0001.

Belowgraph(graph16)showsthatHUvaluewassignificantlyhigherinthediseasegroupascomparedtothenormal groupinthemale population.

MeanHUinthediseased groupwas68.37(range:48-78andSD:6.28)andinnormal groupwas47.79(range:39-68and SD:5.17)

Belowthebardiagram(graph15)showsthatmeanhematocritinmalepatientswithdiseasegroupwas42.71% (range wasbetween30-50%andSDof3.48%).

Also,meanageinthenormalmalestudypopulationwas 44.8%(rangewasbetween40-59%andSDof3.66%)



Graph 15: bar diagram showing a comparison of hematocrit by Mann Whitney testwith p value=0.13 with mean, range and SD of disease group and control group inthemale studypopulation.

- **ComparisonofHU betweentwogroupsinthe male studypopulation.**

HUvaluesbetweentwogroupsinthemalestudypopulationwerecomparedby

Mann–WhitneyU testwithp-valuewas<0.0001.

Belowgraph(graph16)showsthatHUvaluewassignificantlyhigherinthediseasegroupascomparedtothenormal groupinthemale population.

MeanHUinthediseased groupwas68.37(range:48-78andSD:6.28)andinnormal groupwas47.79(range:39-68and SD:5.17)

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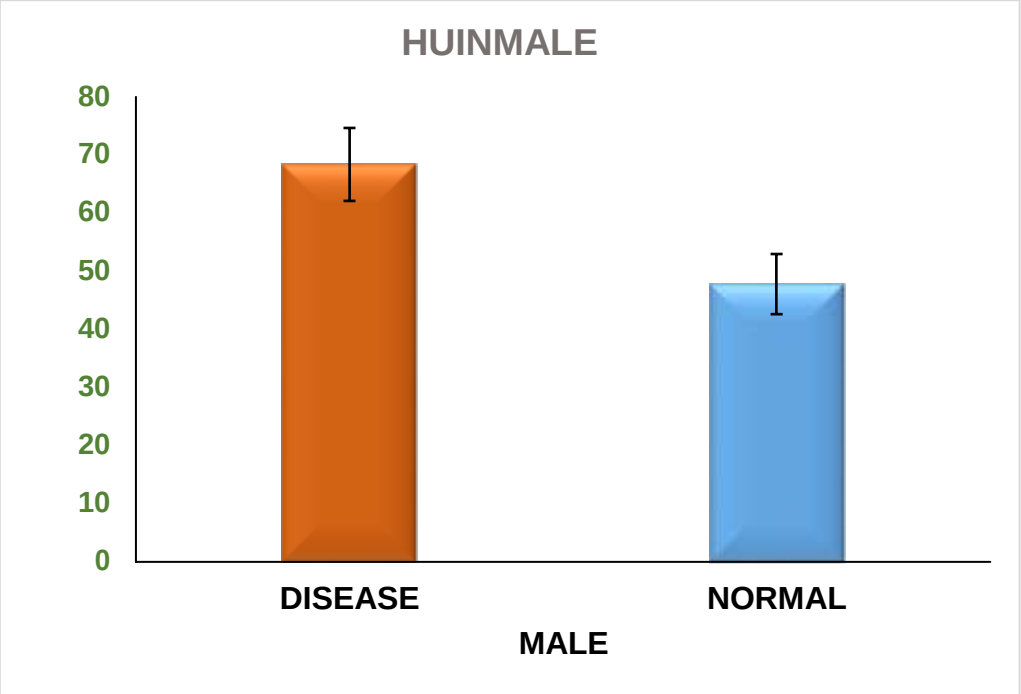
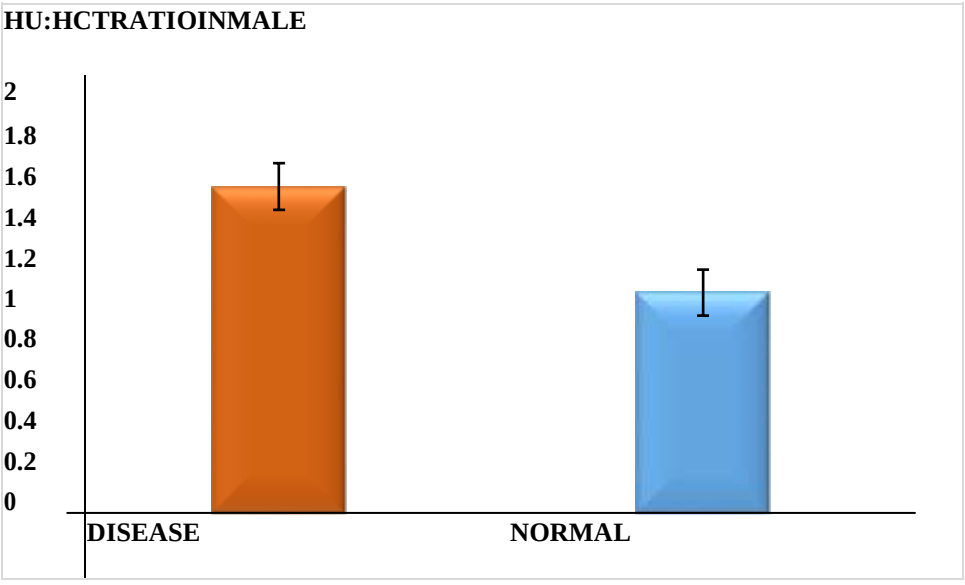


Graph16:bardiagramshowingacomparisonofHUvaluebyMannWhitneytestwithp-value<0.0001withmean,rangeandSDinthediseasegroupandinacontrolgroupofthe male studypopulation.

- **ComparisonofH:H ratiobetweentwogroupsinthemale population.**

HU:hematocritvaluesbetweentwogroupsinthemalest udypopulationwerecomparedby**Mann–WhitneyU testwithp-value was<0.00001.**
Below graph (graph 17) shows that HU: hematocrit value was significantly higher inthediseasegroupascomparedtothenormalgroupinth e male population.
Mean value of HU: hematocrit ratio in the diseased group was 1.6 (range: 1.26-1.8andSD:0.11)andinthenormal groupwas1.08(range:0.96-1.55and SD:0.11).



Graph 17: Bar diagram showing a comparison of HU: Hematocrit ratio by

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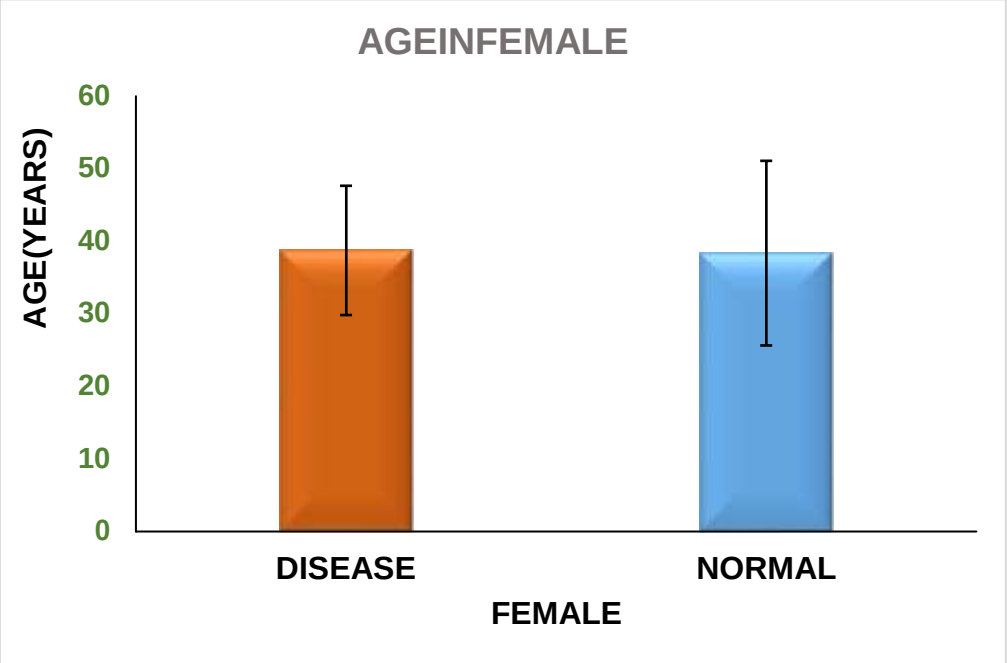
MannWhitneyUtestwithapvalue<0.00001betweentwogroupsinamalepopulationwithmean ±SD.

- **Comparisonofagebetweentwogroupsinthefemalestudypopulation.**

We have compared age distribution between disease group and normal group infemalepopulationby**unpairedt-test**with p-value of>0.05

Below the bar diagram (graph 18) shows that the mean age in female patients withdiseasegroupwas 38.75yrs(rangeisbetween24-56yrsandSD of8.9yrs). Also,meanageinthenormalfemalestudypopulationwas38.36yrs(rangeisbetween18-69yrsandSDof12.72yrs).



Graph18:bardiagramshowingacomparisonofagebyunpairedt-testwith p-value>0.05 with mean, range and SD of disease group and control group in the femalestudypopulation.

- **Comparisonofhematocritbetweentwogroups inthefemalestudypopulation.**

BothgroupswerecomparedforhematocritbyMannWhitneyUtestwithpvalue=0.053Sobothgroupsdidn't differsignificantlyforhematocritandsowerecomparable. Belowbardiagram(graph19)showsthatmeanhematocritinfemalepatientswithdiseasegroupwas40.2% (range wasbetween36-45%andSDof2.78%). Also,meanageinthenormalfemalestudypopulationwas41.98%(rangewasbetween35-53%andSDof3.85%).

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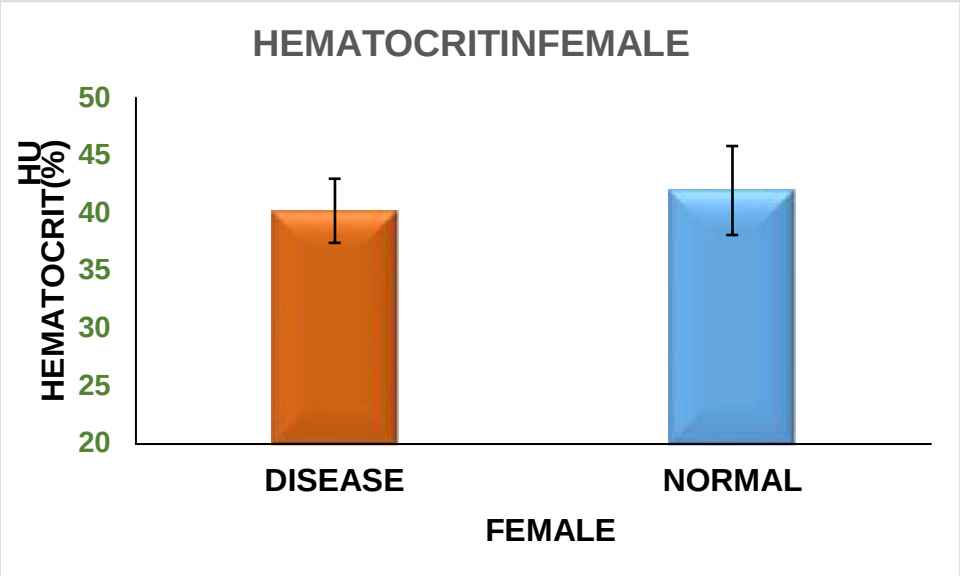
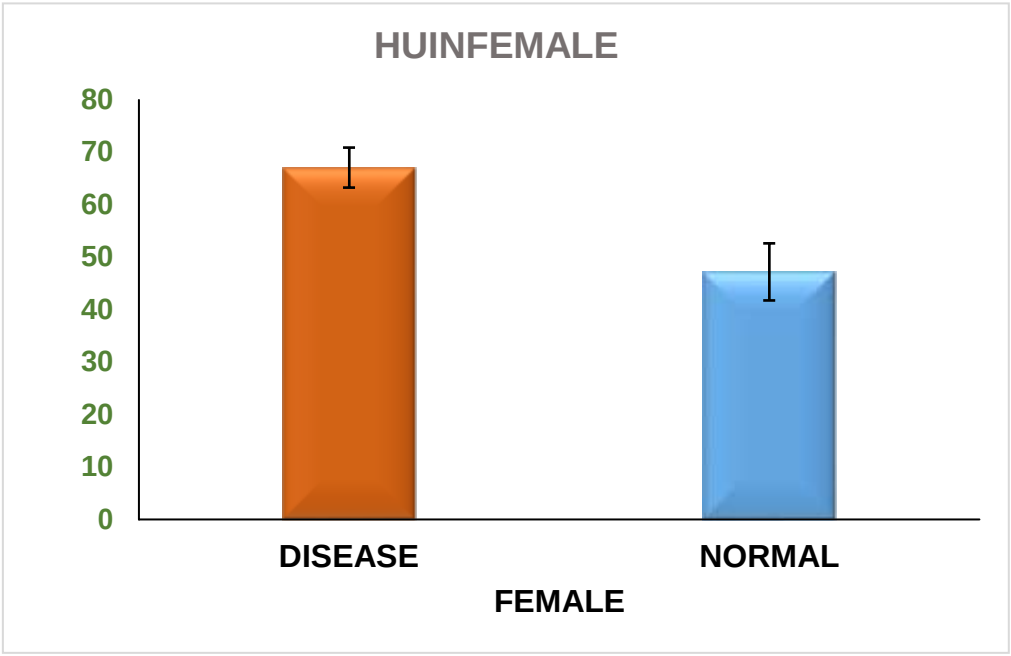


Graph 19: bar diagram showing a comparison of hematocrit by Mann Whitney testwith p value=0.053with mean, range and SD of disease group and control group inthefemale studypopulation.

- **ComparisonofHUbetweentwogroupsinthefemale studypopulation.**

HUvaluesbetweentwogroupsinthefemalestudypopulationwerecomparedby **Mann–WhitneyU testwithp-valuewas<0.0001.** Belowgraph(graph20)showsthatHUvaluewassignificantlyhigherinthediseasegroupascomparedtothe normalgroupinthefemale population. MeanHUinthediseasegroupwas67.13(range:61-75andSD:3.8)andinnormalgroupwas47.24(range:37-76andSD:5.44).



Graph 20: bar diagram showing a comparison of HU value by Mann Whitney U testwith p-value <0.0001 with mean, range and SD in the disease group and in controlgroupofthefemalestudypopulation.

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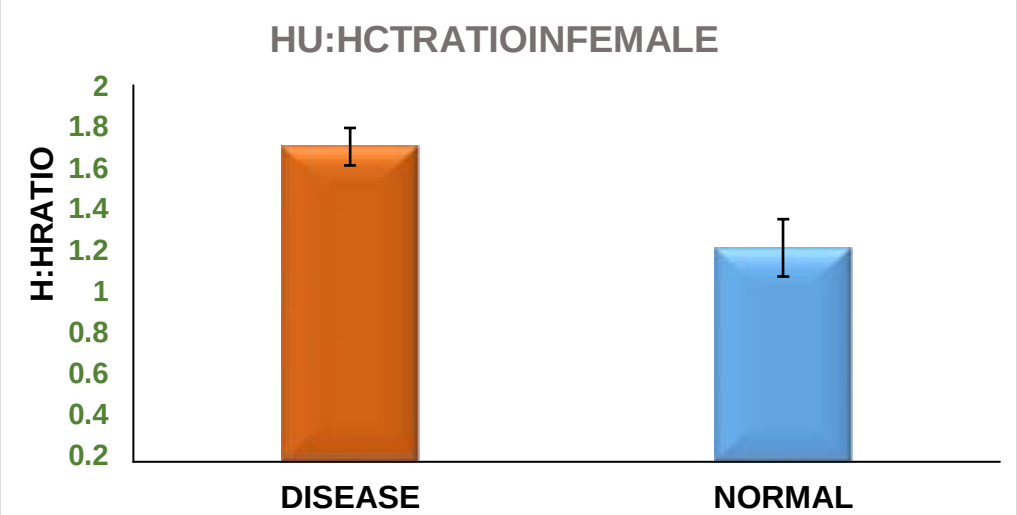
- **ComparisonofHU:hematocritbetweentwogroupsinthefemalestudypopulation.**

HU: hematocrit values between two groups in the female study population werecomparedby**Mann–WhitneyU testwithp-value was<0.00001.**

Below graph (graph 21) shows that HU: hematocrit value was significantly higher inthediseasegroupascomparedtothenormalgroupin thefemale population.

Mean value of HU: hematocrit ratio in the disease group was 1.67 (range: 1.48-1.92andSD:0.099)andinthenormalgroupwas1.13(range:0.85-1.95andSD:0.15).



Graph 21: Bar diagram showing a comparison of HU: Hematocrit ratio by MannWhitney U test with p-value <0.00001 between two groups in the female populationwithmean±SD.

3. SIMPLE REGRESSION ANALYSIS AND SCATTER PLOT

Linearregressionanalysisformax.HUandhematocrit

Belowtable14shows

Byapplyinglinearregressiontest,intotaldiseasedpopulation,changeinHUvaluewascontributedby hematocritby37%.

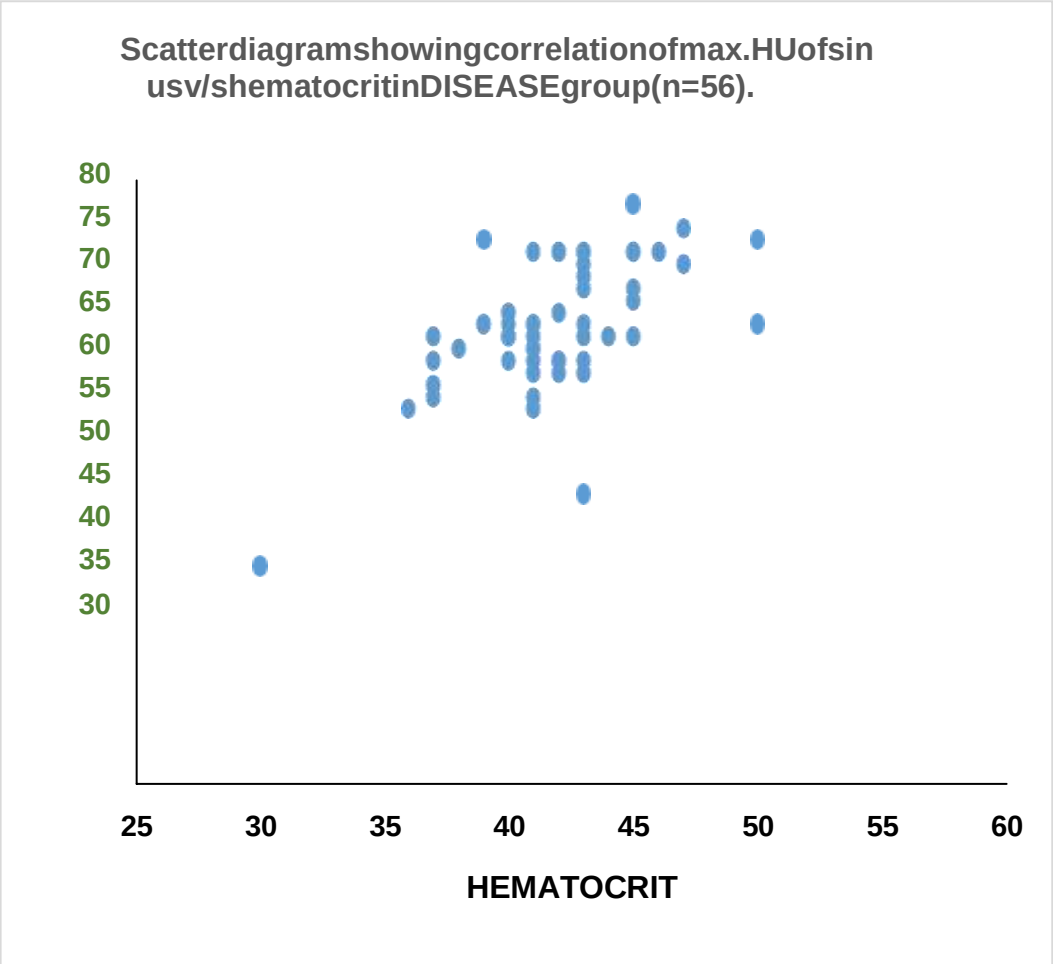
Inmalediseasedpopulation,changeinHUvaluewascontributedbyhematocritby41%.

In female diseased population, change in HU value was contributed by hematocritby30%.

	DISEASEPOPULATION		
	TOTAL	**MALE**	**FEMALE**
RVALUE	**0.61**	**0.64**	**0.55**
pVALUE	**<0.0001**	**0.0001**	**0.0053**
R^2	**0.37**	**0.41**	**0.30**

Table 14: coefficient of correlation, p-value and R^2value in disease population formax.HUandhematocrit.

Belowgraph(graph22)statesthattherewasasignificantpositivecorrelationbetweenthe hematocrit value and attenuation of sinuses (HU value) in disease group with acoefficientofcorrelation,r(54)=0.61andwithp<0.0001.



Graph 22: Scatter diagram showing a correlation of max. HU of sinus v/s hematocritinDISEASEgroup(n=56).

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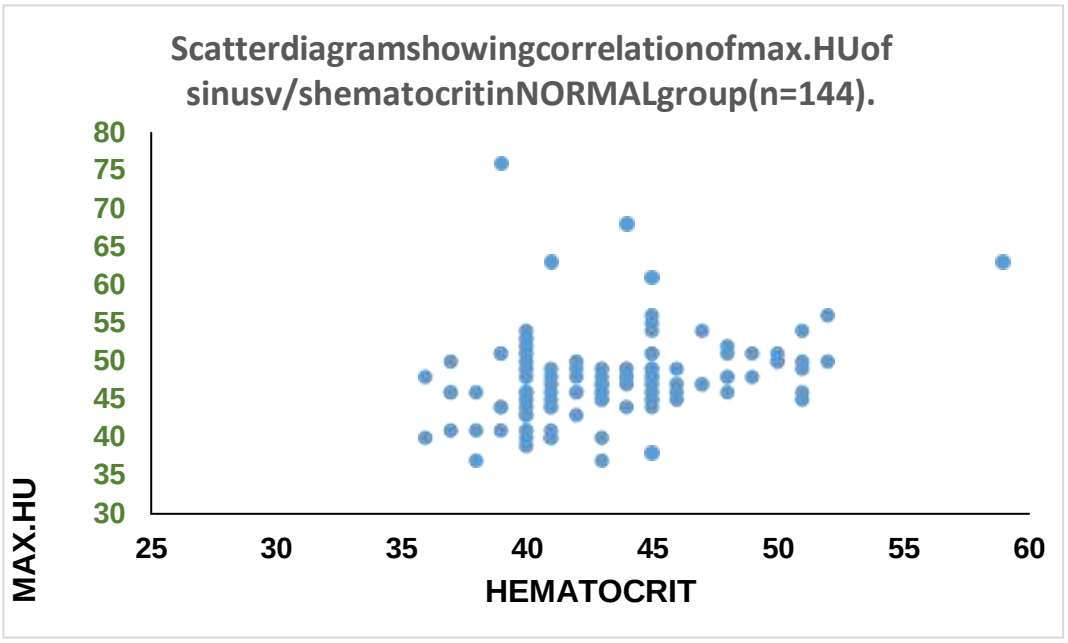
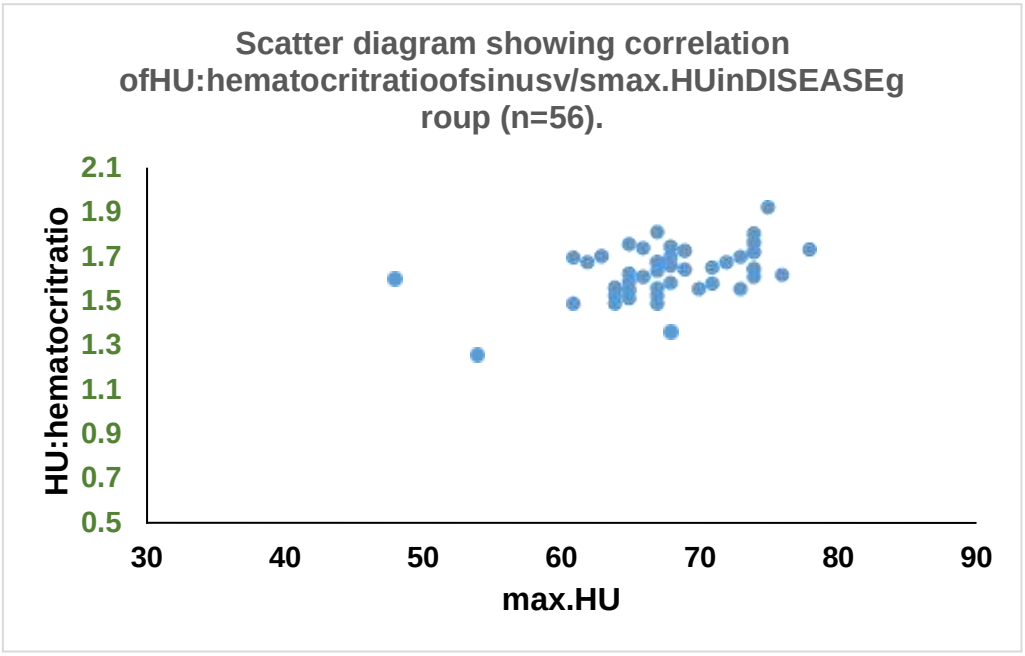
Belowgraph(graph23)statesthattherewasasignificantpositivecorrelationbetweenthe hematocrit value and attenuation of sinuses (HU value) in a normal group with r(142)=0.3andp<0.0002.



Graph 23: Scatter diagram showing a correlation of max. HU of sinus v/s hematocritinNORMALgroup(n=144).

Belowgraph(graph24)showsthattherewasasignificantpositivecorrelationbetweentheattenuationofsinuses(HUvalue)andHU:hematocritratioindiseasegroupwithr(54)=0.41andp<0.0015.



Graph 24: Scatter diagram showing a correlation of HU: hematocrit ratio of sinus v/smax.HUinDISEASEgroup(n=56).

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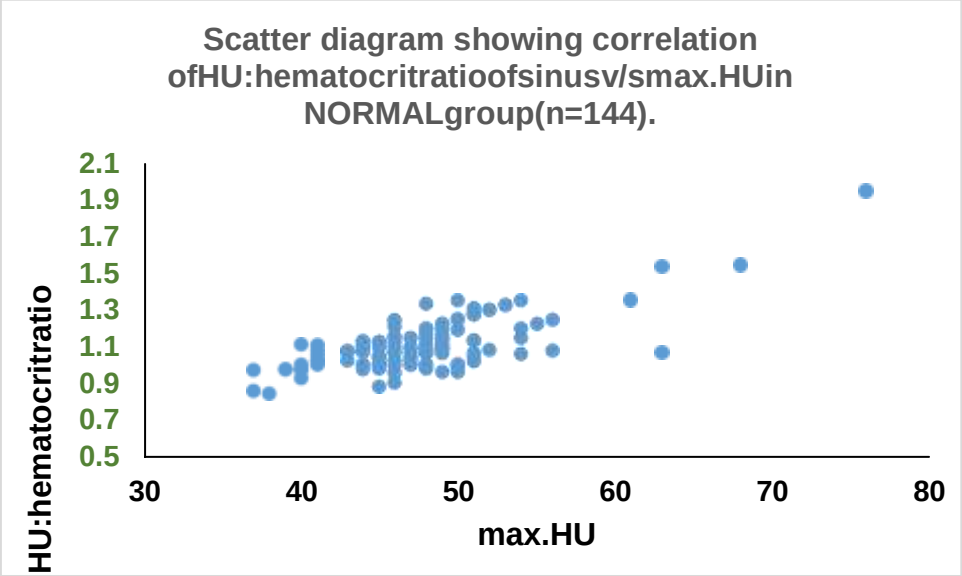
Belowgraph(graph25)statesthattherewasasignificantpositivecorrelationbetweentheattenuationofsinuses(HUvalue) andHU:hematocritratioinanormalgroupwithr(142)=0.71andp<0.0001.



Graph 25: Scatter diagram showing correlation of HU: hematocrit ratio of sinus v/smax.HUinNORMALgroup(n=56).

4. SENSITIVITY, SPECIFICITY, PPV, NPV OF HU AND H:H RATIOCalculationofsensitivity,specificitybased onHUvalueinthetotalpopulation

Belowgraph26aandtable15ashowsensitivityandspecificityinpercentage(%)ofmax.HUintotalpopulation96.42,96.52respectively.

BasedonHU value **TOTALPOPULATION(n=200)**	
SENSITIVITY(Sn)	96.42
SPECIFICITY(Sp)	96.52
POSITIVEPREDICTIVEVALUE(PPV)	91.52
NEGATIVEPREDICTIVEVALUE(NPV)	98.58

Table**1**5:sensitivity,specificity,PPV,NPVofHUvalueindiagnosingAcuteCVSTinthetotal population.

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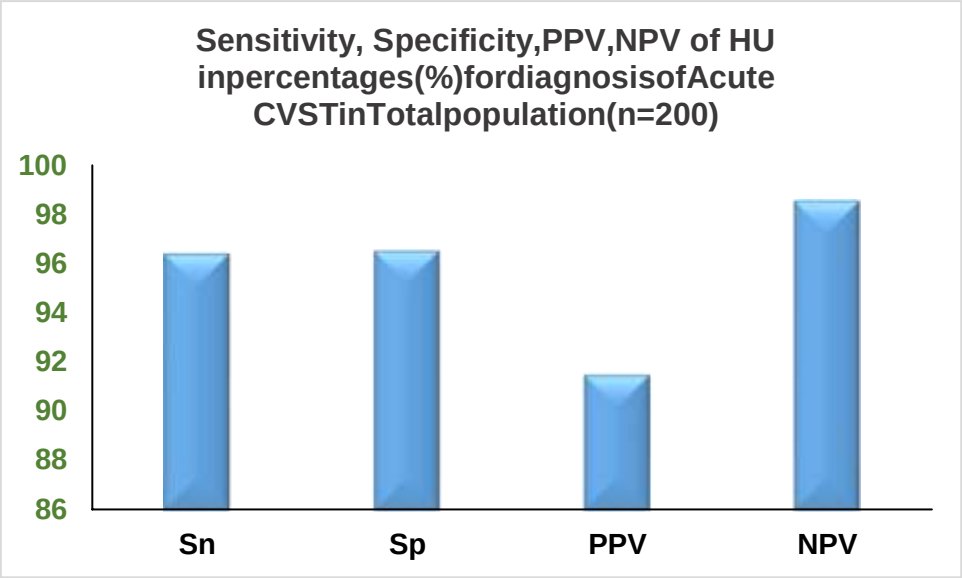


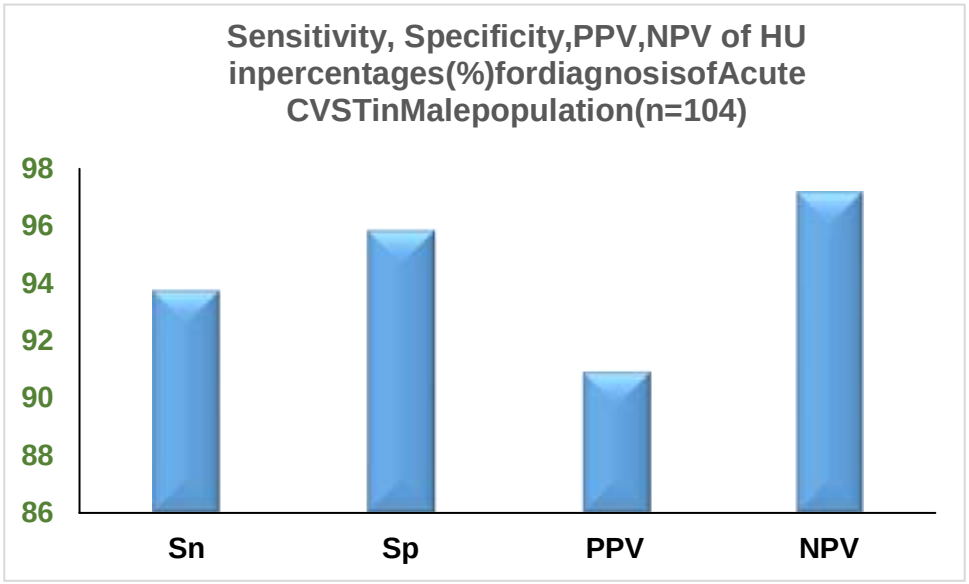
Graph 26a: Bar diagram showing Sensitivity, Specificity, PPV, NPV of max.HU inPercentage(%)fordiagnosisof AcuteCVSTinTotalpopulation(n=200).

Calculationofsensitivity,specificitybasedonHUvalue inthemalepopulation

Belowgraph26bandtable15bshowsensitivityandspecificityinpercentage(%)ofmax.HUinmalepopulation93.75,95.84respectively.

BasedonHU value **MALEPOPULATION (n=104)**	
SENSITIVITY(Sn)	93.75
SPECIFICITY(Sp)	95.84
POSITIVEPREDICTIVEVALUE(PPV)	90.9
NEGATIVEPREDICTIVE VALUE(NPV)	97.18

Table15b:sensitivity,specificity,PPV,NPVofHUvalueindiagnosingAcuteCVSTinthemale population.



Graph 26b: Bar diagram showing Sensitivity, Specificity, PPV, NPV of max.HU inPercentage(%)fordiagnosisof AcuteCVSTin Malepopulation(n=104).

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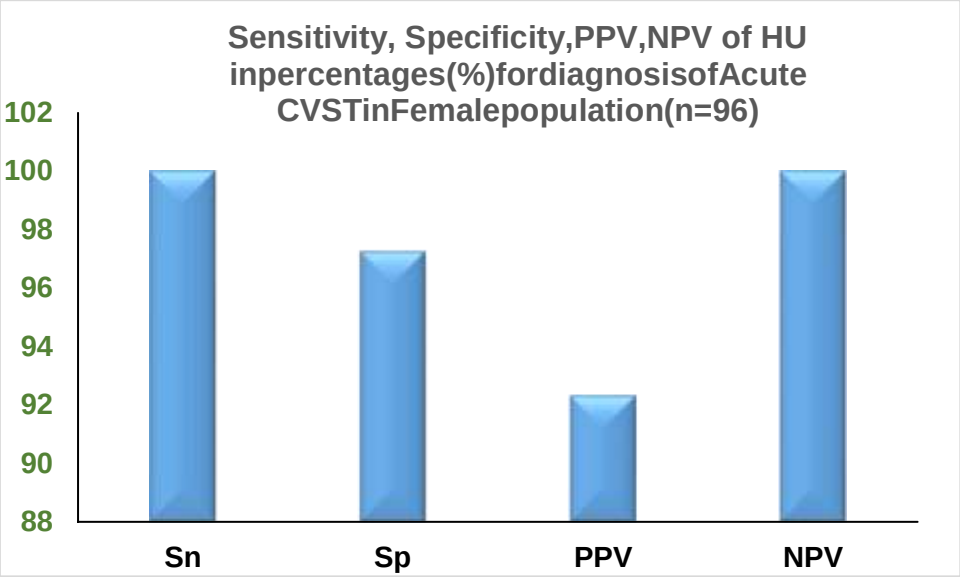
Calculationofsensitivity,specificitybasedonHUvalueinthefemalepopulation
Belowgraph26candtable15cshowsensitivityandspecificityinpercentage(%)ofmax.HUinfemalepopulation100,97.23respectively.

BasedonHUvalue **FEMALEPOPULATION (n=96)**	
SENSITIVITY(Sn)	100
SPECIFICITY(Sp)	97.23
POSITIVEPREDICTIVEVALUE(PPV)	92.3
NEGATIVEPREDICTIVEVALUE(NPV)	100

Table15c:sensitivity,specificity,PPV,NPVofHUvalueindiagnosingAcuteCVSTinthemale population.



Graph 26c: Bar diagram showing Sensitivity, Specificity, PPV, NPV of max.HU inPercentage(%)fordiagnosisof AcuteCVSTinfemalepopulation(n=96)

Calculationofsensitivity, specificitybasedon HU:hematocritratio (H:H)inthetotalpopulation
Graph27aandtable16ashowsensitivityandspecificityinpercentage(%)ofH:Hratiointotalpopulationof96.42,97.91 respectively.

BasedonH:Hratio **TOTALPOPULATION(n=200)**	
SENSITIVITY(Sn)	96.42
SPECIFICITY(Sp)	97.91
POSITIVEPREDICTIVEVALUE(PPV)	94.73
NEGATIVEPREDICTIVEVALUE(NPV)	98.6

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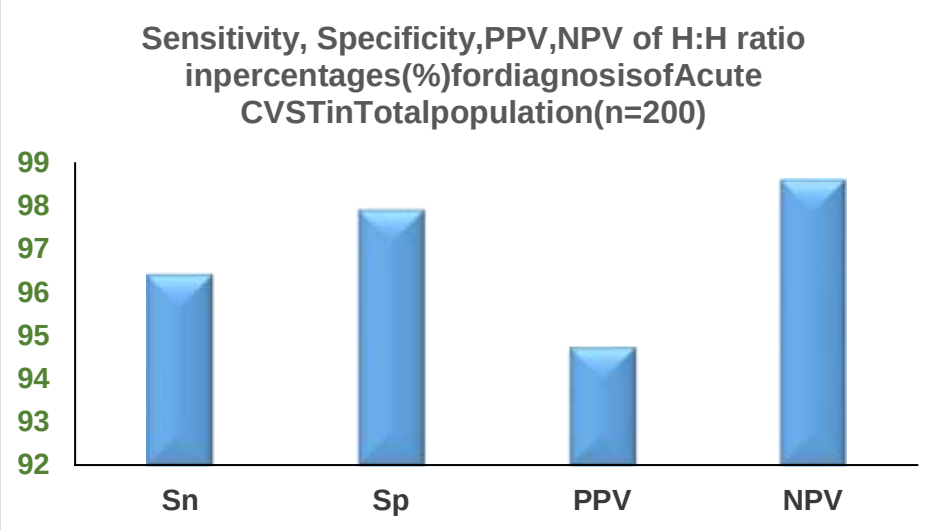
Table16a:sensitivity,specificity,PPV,NPVofH:HratioindiagnosingAcuteCVSTinthetotal population.

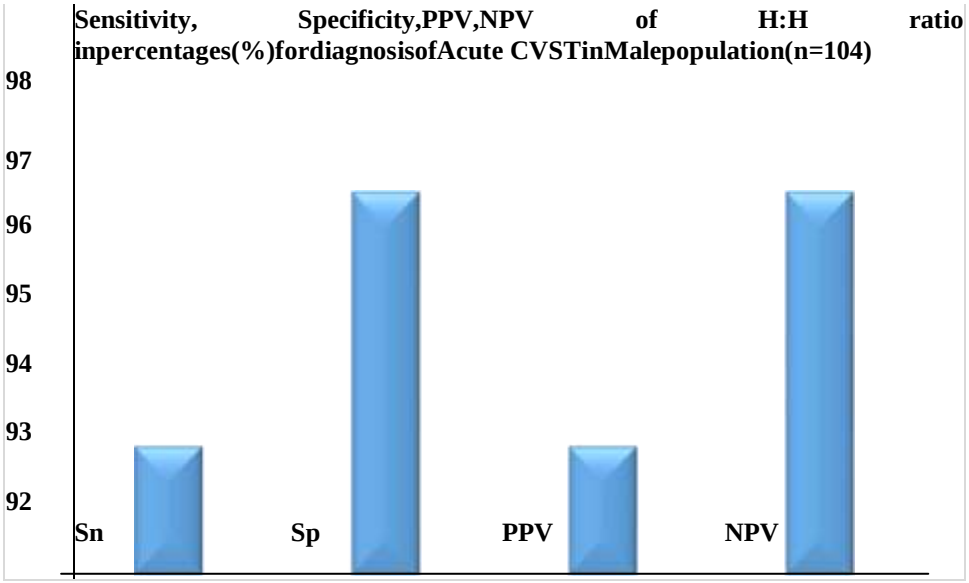


Graph 27a: Bar diagram showing Sensitivity, Specificity, PPV, NPV of H:H ratio inPercentage(%)for diagnosisofAcuteCVSTinTotalpopulation(n=200).

Calculationofsensitivity,specificity basedonHU:hematocritratio (H:H)inthemalepopulation
Graph27bandtable16bshowsensitivityandspecificityinpercentage(%)ofH:Hratioinmalepopulation93.75,97.23respectively.

BasedonH:Hratio **MALEPOPULATION(n=104)**	
SENSITIVITY(Sn)	93.75
SPECIFICITY(Sp)	97.23
POSITIVEPREDICTIVEVALUE(PPV)	93.75
NEGATIVEPREDICTIVEVALUE(NPV)	97.23

Table16b:sensitivity,specificity,PPV,NPVofH:HratioindiagnosingAcuteCVSTinthemale population.



Graph 27b: Bar diagram showing Sensitivity, Specificity, PPV, NPV of H:H ratio inPercentage(%)for

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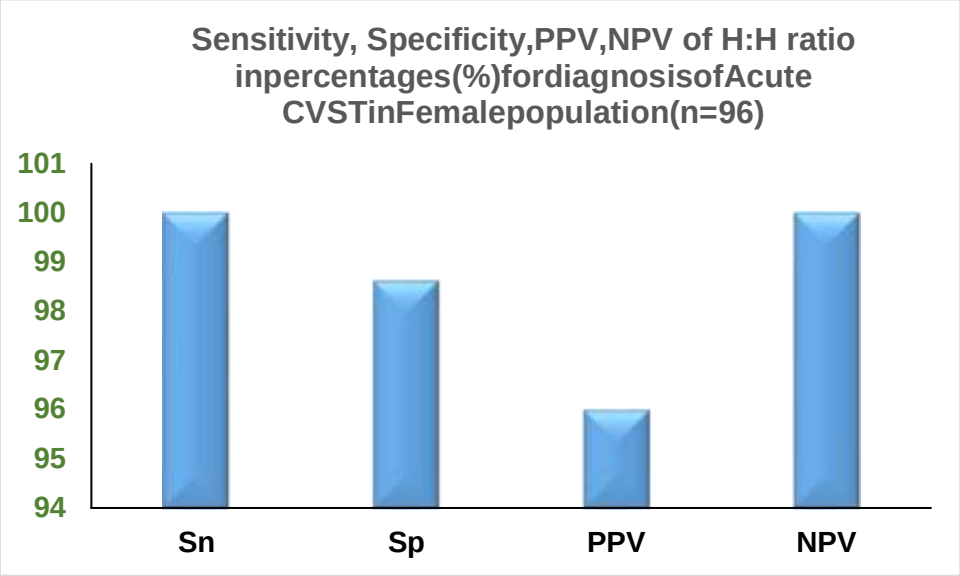
thediagnosisofAcute CVSTinTotalpopulation(n=104).

CalculationofsensitivityspecificitybasedonHU:haematocritratio(H:H)inthefemalepopulation
Graph27candtable16cshowsensitivityandspecificityinpercentage(%)ofH:Hratioinfemalepopulation100,98.62respectively.

BasedonH:Hratio **FEMALEPOPULATION(n=104)**	
SENSITIVITY(Sn)	100
SPECIFICITY(Sp)	98.62
POSITIVEPREDICTIVEVALUE(PPV)	96
NEGATIVEPREDICTIVEVALUE(NPV)	100

Table16c:sensitivity,specificity,PPV,NPVofH:Hratio indiagnosingAcuteCVSTinthemale population.



Graph 27c: Bar diagram showing Sensitivity, Specificity, PPV, NPV of H:H ratio inPercentage(%)fordiagnosisof AcuteCVSTin femalepopulation(n=96).

So after comparing both sensitivity and specificity for max. HU and H:H ratio fordiagnosing acute CVST patients, it was found that specificity is more if we use H:Hratio as a parameter for diagnosing patients with acute CVST with sensitivity for bothremainingthesame.
So in simple words, we can rule out true negative patients out of suspected acuteCVSTpatientsmoreefficientlywithH:Hratiorat herthanusingsinusattenuation(HU)alone.

5. Receiver operating characteristic (ROC) curve for calculation of the cut-offvalue

- **ROCcurveofsensitivityvs.falsepositive formax.HU**

ThevaluewhichismarkedwithredinbelowROCcurve(graph28)suggeststhatsinusattenuationvalue(HU)of61ormorewasmoresensitive(96.42%)indiagnosingacuteCVSTcaseswithsmallfalsepositiverate(3.4%).

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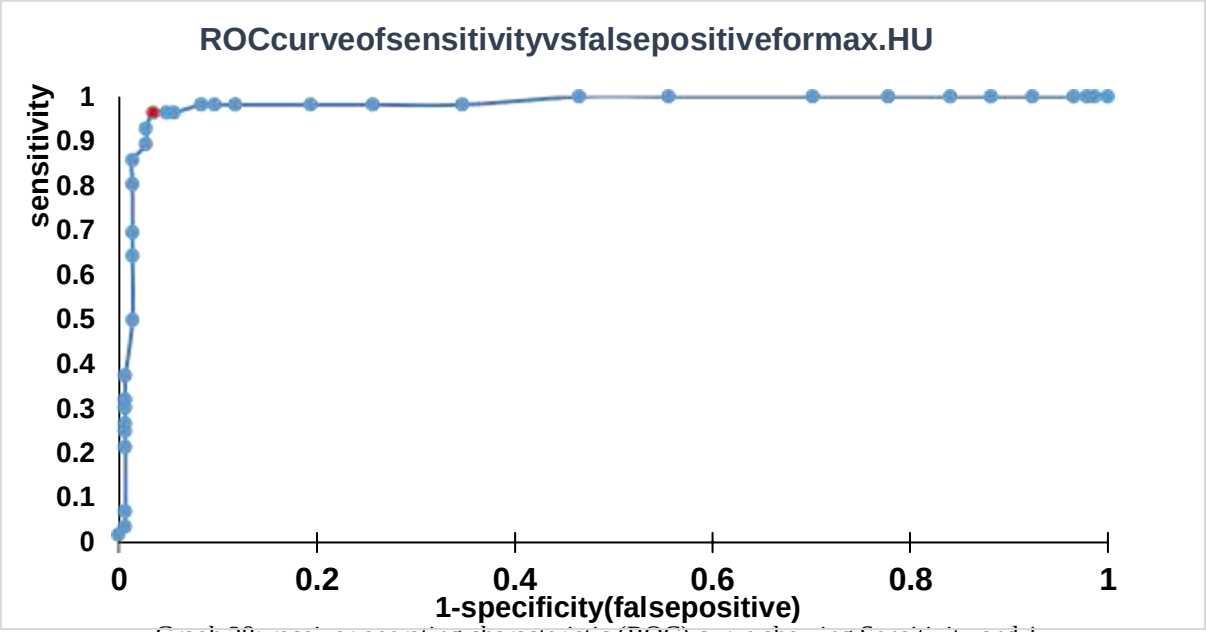
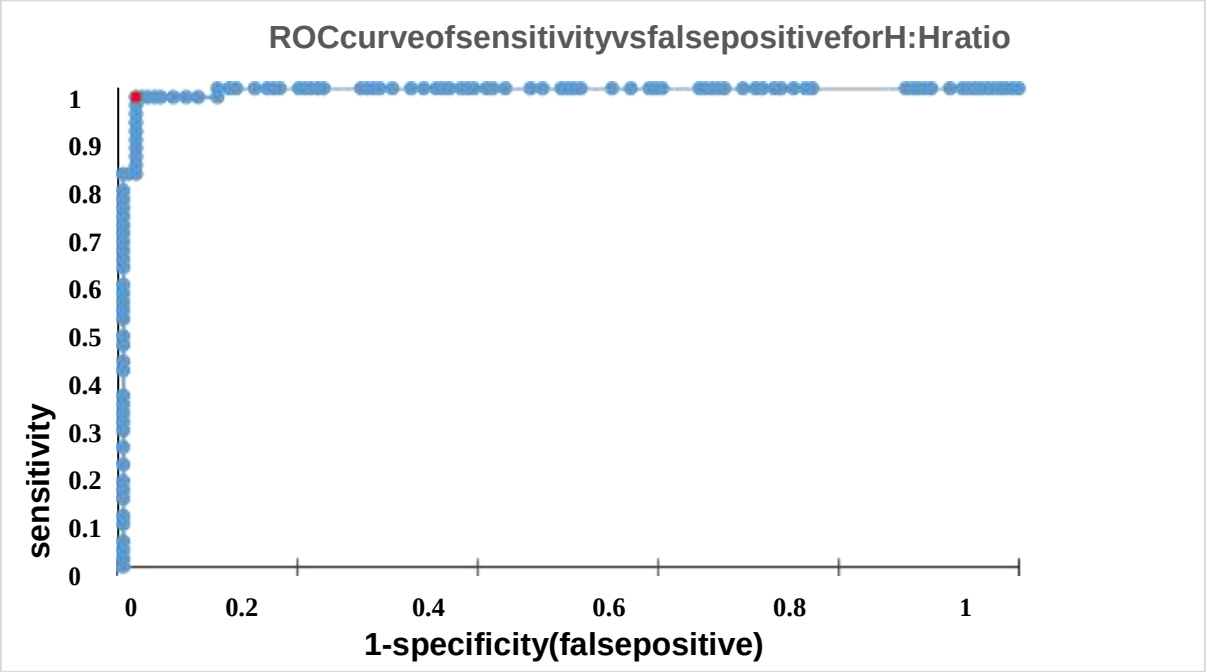


Graph 28: receiver operating characteristic (ROC) curve showing Sensitivity and 1-Specificity(falsepositive)ofmaximumHUforthediagnosisofAcuteCVSTinthetotalpopulation(n=200).

- **ROCcurveofsensitivityvs.false positiveforH:Hratio**

The value which is marked with red in above ROC curve (graph 29) suggests that H:Hratioof1.487ormorewasmoresensitive(96.42%)indiagnosingacuteCVSTcaseswithsmallfalsepositiverate(2%).



Graph 29: receiver operating characteristic (ROC) curve showing Sensitivity and 1-Specificity (false positive) of H: H ratio for the diagnosis of Acute CVST in the totalpopulation(n=200).

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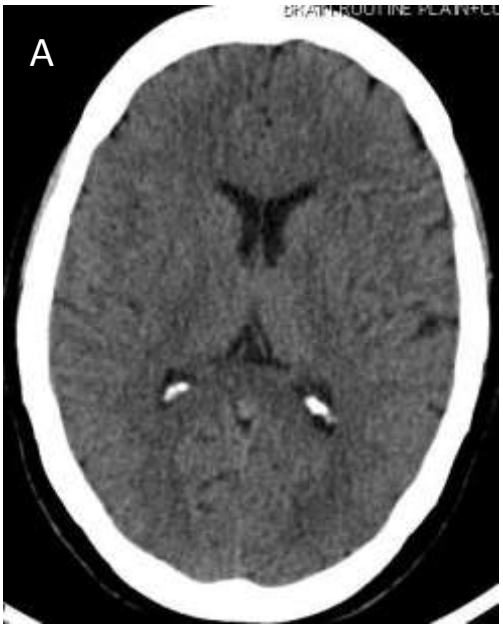
SamplecaseswithHUvaluesofSSS,transversesinusesinpatientswithandwithoutacuteCVST(fig 18,19,20).



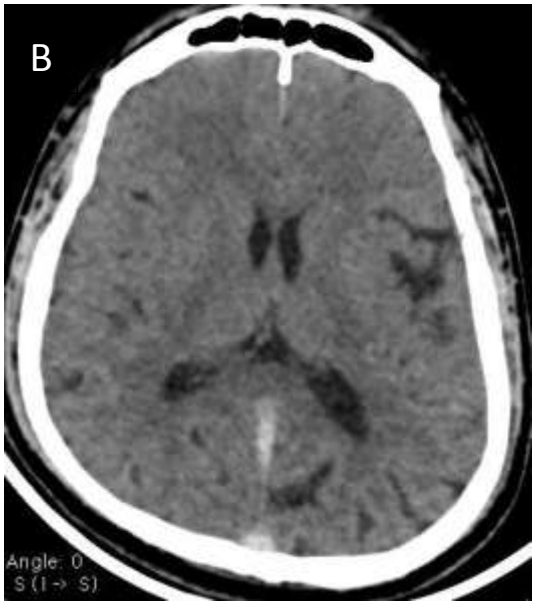


Image18AandB:axialsectionsofCTbrainshowingnormalSSS(A)andhyperattenuatingSSSinCVT(B)

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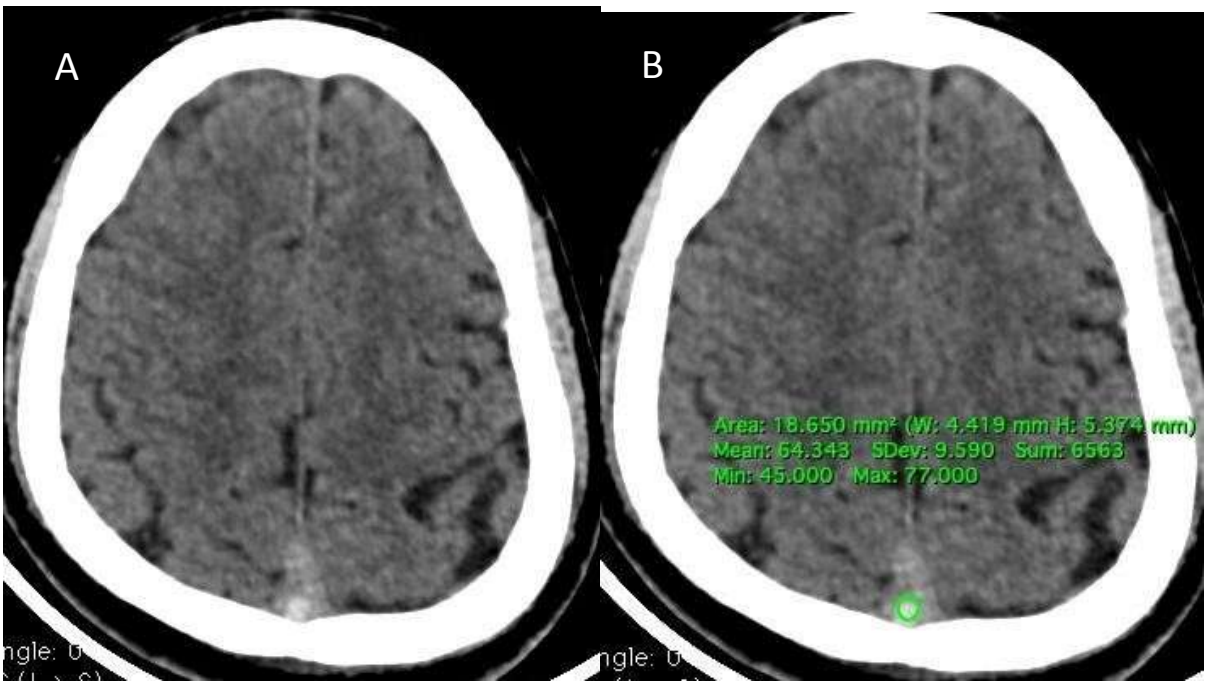

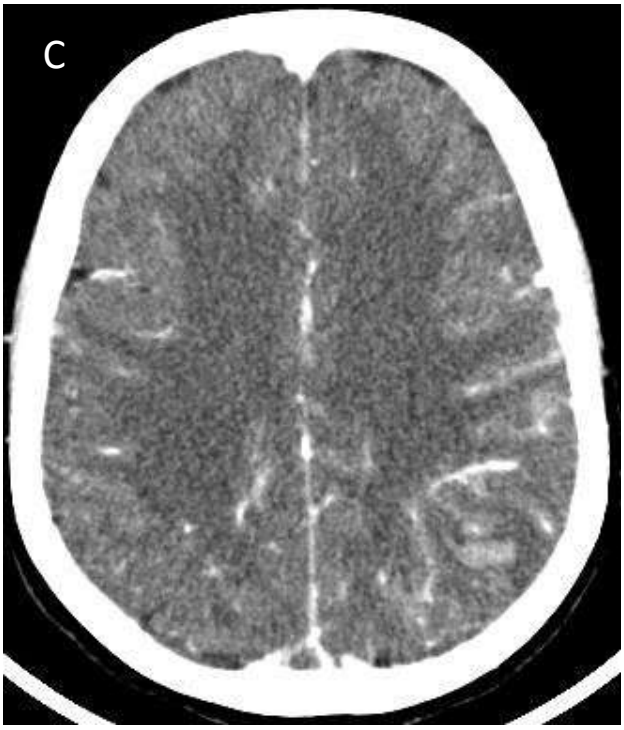

Image19A,B,C:axialsectionofCTbrainshowing denseSSS(A)withHUof64(B)andCEvenographyshowingcorresponding fillingdefectinSSS(C)s/othrombosis.

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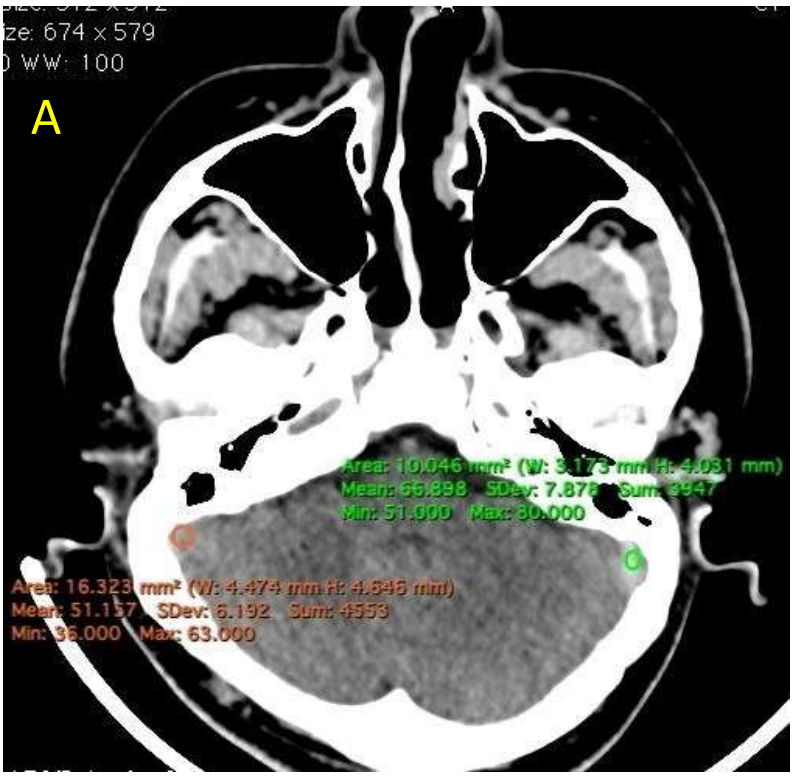

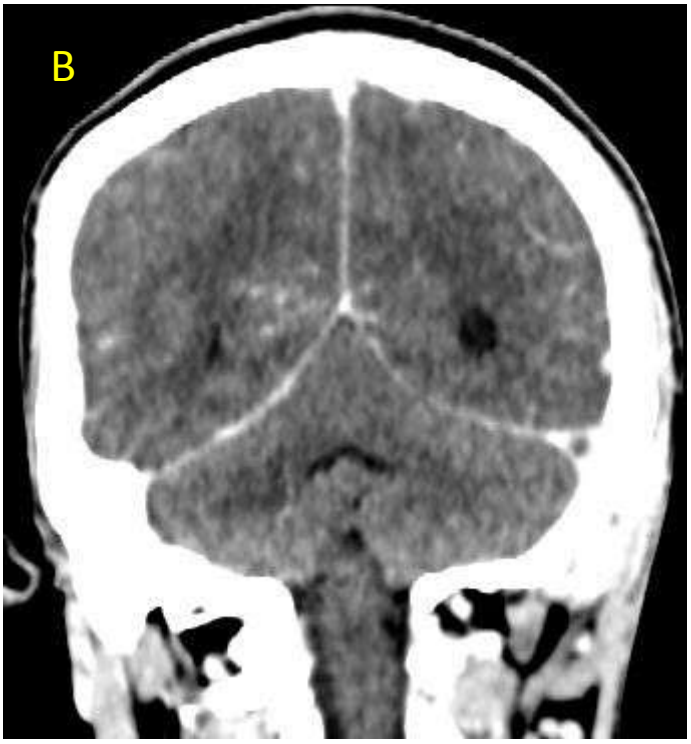

Image20AandB:axialsectionsofCTbrain(A)showingHUof67inlefttransversesinuswithacorresponding fillingdefectinit(B)onCTvenographys/othrombosis.

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V. DISCUSSION

Acute CVST is one of the no so common causes of stroke worldwide with varyingclinicalscenario.Soimagingplaysapivotalrol einguidingmanagement.

Both CT and MRI are sensitive imaging modalities when it comes to the detailedevaluationofacuteCVSTpatientswithinvasiv emethodslikeDSAcerebralvenographyisconsideredt hegoldstandard.However,duetowidespreadavailabili ty,lower cost, faster scanning times, and completion of NCCT, CT venography within 5-7minutesaswellasthefactthatmanypatientsareindrow sinessoralteredsensoriumand movement artifacts will render reading MRI scans less fruitful, CT is still a one-stop shopincasesofimagingofacuteCVST.

"Hyperattenuating sign" can be observed on non-contrast CT scans when acutethrombus has formed in the venous sinuses. In the literature, this sign was originallyfound in only a few of patients with CVST and was considered as a non-specific sign.Therewasanearlystudyreportedasensitivityofap proximately25%[22].WiththinnerCT sections and new advancement, however, this sign was detected much morefrequently.Anotherstudyreportedasensitivityof 64%oftheduralsinusforCVST[105].

This increase in attenuation is caused by clot retraction, with the elimination of waterand causing an increase in the concentration of hemoglobin and red blood cells. Thiscauses an increased attenuation of the thrombus to 60-90HU.[106] Also, interpretationofhyperattenuatedsinusonlyvisuallyca nsometimesmissthediagnosis,socalculating HU value by putting ROI in sinuses and measuring attenuation withinsinusesismorehelpfulindetectionofacuteCVS T.

SoourstudywillbeusefulinpatientswhodonothaveS.c reatininevaluesorpatientsinwhomcontrastiscontrain dicatedandinaninstitutionwheretheonlyfacilityofnon-contrastCTscanisavailable.Also,therearesimilarstud iesperformedinthewesternpopulation. But no such study has ever been published in the literature for Indianpopulation.

Ourstudyincluded200clinicallysuspectedcasesofacu teCVSTwhoseCTbrainwithvenography was performed. Scanning was performed from top of the skull to base ofthe skull and in the cranio-caudal direction. Before the scan, essential clinical historywasobtainedalongwithhematocritvaluesofthо sepatientsinwhomserumhematocrittestwasdonefor anotherpurpose.

Outofasampleof200inthestudy,sexdistributionwasof 104malescomprising52%and 96 females comprising 48% in the study with all those meeting inclusion criteriawere included. Age of the patients included in the study ranged from 18 years to 69years.Meanagewas38years.Amaximumnumberof patientswereintheagegroup30-50 years (51%). Minimum number of patients were in the age group >50 years(19%). In the age group of <30 years, males were more often affected than femalesand in the age group 30-50 years, female patients were more affected than male. Inagegroup>50years,therewasanequal numberofmaleandfemalepatients.

Inourstudyheadachewaspresentinallcasesfollowedb yseizures(46.5%),drowsiness(16.5%)andvertigo(37 %).

Out of 200 patients of suspected of acute CVST, 56 (28%) patients had the diseaseonCTvenography.Outofthese56patients,32w eremale and24were female.

The most common sinus involved was superior sagittal sinus (46%), followed by lefttransversesinus(31%),righttransversesinus(20%) andtorcula(3%)wasaffectedinverylessnumberofpati ents.

For statistical analysis, we divided study population into two groups, disease group(patients with acute CVST on CT venography) and normal i.e. control group (patientswithoutacuteCVSTonCTvenography)andth encomparedbothgroups.

Both groups were compared by the Mann-Whitney U test for age and hematocritvalues.Itwasfoundthatbothgroupsdidn't differbybothageandhematocritsignificantlyandwere comparable.

WefoundthatoncomparingtwogroupsforbothHUand H:Hratio,bothvalueswеresignificantlyhigherindisea segroupcomparedtothenormalgroup.

Themeanattenuationwas67.84HU(±5.36)inthedisea segroupand47.51HU(±5.3)in the normal group. In male and female patients with acute CVST mean attenuationwas68.37HU(±6.28)and67.13HU(±3.8)r espectively.

Cobellietal2005foundsimilarattenuationvaluesforac utepulmonaryemboli(mean, 74.25 HU; range, 57–93 HU) on unenhanced CT scans),[24] and Goldstein et al 2012found similar HU values for acute abdominal venous thrombosis (mean, 67.12 HU;range,53–84HU).[25]

Also, there are similar studies in which Buyck et al found that mean attenuation ofthrombosed sinuses was 73.9HU with a threshold of 62 HU which can be used todiscriminatepatientswithacuteCVSTfrompatients without.[106]

We found that value of H:H ratio was significantly

higher in acute CVST cases with ameanof 1.64(±0.11)andlowerinanormalgroupwith ameanof 1.1(±0.13). Inmale andfemalepatientswithacuteCVSTmeanH:Hratiowa s1.6(±0.11)and1.67(±0.09)respectively. There is no overlap of the H:H ratio distribution in patients with CVSTandwithoutCVST.

Black et al found mean H:H values of 2.2 in patients with CVST and 1.44 in patientswithout CVST and in their study there were only 8 patients with CVST and a cut offvalue of 1.8.[27]The study by Buyck et al found that mean H:H value of 1.91 ± 0.32 inpatients with CVST and 1.33 ± 0.12 and a cut off value of 1.52.[106] both studies wereretrospective studies, so they were prone to selection bias. Our study is a cross-sectionalstudy,so thechancesofselectionbiasarelesser.

Anemic patients have low hematocrit values and so low HU values even in case ofthrombosis.Similarly,conditionsinwhichthereishi ghhematocritvaluelikepolycythemiaveraordehydrati on,thereishighHUvalueevenifthereisnothrombosis. These findings are reported and are the most common cause of falsepositive or false negative results for acute CVST.[107] Therefore, to avoid this, HUvalues have to be correlated with hematocrit values as it corrects for the abnormalHCTlevel.HenceH:H ratiohasbeencalculated.

Inourstudy,therewasasignificantandpositivecorrelati onbetweenHUandhematocritvalues,thecoefficientof correlationwas0.61inpatientswithacuteCVST.

There are similar studies in which Buyck et al [106]and Lee et[26] al found a significantcorrelationwithbothhemoglobinandHCT withHU.

In our study, sensitivity and specificity for HU were 96.42 and 96.52 respectively.Sensitivity and specificity for H:H ratio was 96.42 and 97.91. This minor difference inspecificitysuggeststhatHUalonecanbeaverygoods ubstituteifhematocritvalueis not available and if we have both values then specificity of diagnosis of acute CVSTincreasessothattherewillbelesserfalsepositiver esults.

Wehaveplottedthereceiveroperatingcharacteristic(R OC)curves,inwhichwehavefoundathresholdof61HU whichcanbeusedtodifferentiatepatientswithacuteCV STfromthosewithout.OnthebasisofROCcurveforH: Hratio,thevalueofmorethan 1.48 suggests a strong likelihood of thrombosis in venous sinuses. So these cutoff orthreshold values can help in distinguishing patients with and without acute CVST onnon-contrastCTbraininanemergencysetup.

VI. LIMITATIONS:

This study has some limitations. First, for consistency, the ROIs were measured by asingle radiologist, so inter-observer variability for ROI measurement was not includedinthestudy. Second,theimmediatevicinityoftheskulltovenoussin usesmaycausepartialvolumeeffectsandcouldhaveca usedfalsepositivehigherHUvalues.

VII. SUMMARY AND CONCLUSION

Theexact prevalenceof acuteCVST inIndiaishithertounknown.Theclinicalpresentationo facute CVSTisvariable.

It is frequently seen between 35-40 years of age and CVST is slightly more commonin women, due to pregnancy, oral contraceptive use and in puerperium in the agegroup of 20 to 35. Also, many times in acute CVST patients no risk factor is found. ItisveryimportanttodiagnoseandtreatCVSTinpatient swithabsenceofco-morbidities.

Also,promptandaccuratediagnosisofcerebr alvenousthrombosisiscrucialbecausetimely and appropriate therapy can reverse the disease process and significantly canpreventmorbidcomplicationsandlong-termsequelae.

We studied 200 clinically suspected patients of acute CVST who were investigatedwith CT brain with venography. Our results demonstrated a significant and positivecorrelationbetweenhematocritandattenuatio nvaluesofsinuses.

We found that attenuation values (HU) and H: H ratio values were significantly higherinacuteCVSTpatientsthanwithoutacuteCVST patients.WefoundathresholdvalueofHUandH:Hratio abovewhichwecandiagnosepatientswithacuteCVST.

Inadditiontothis,wefoundhighersensitivity andspecificityforbothHUandH:Hratioin diagnosing acute CVST. Overall specificity of H: H ratio in diagnosing acute CVSTwas more as compared HU alone. So the conclusion is that patients who do not haveacuteCVSTarecertainlyruledoutonthebasisofH: Hratio.

This allows accurate pinpointing of acute CVST at unenhanced CT examination, andwe conclude that higher HU value predicts an increased risk of acute CVST in anappropriate clinicalscenario.

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