A prospective study from a tertiary care facility in North India on the function of vascular endothelial growth factor in tuberculous meningitis

1.P.SASIKALA*, Asst. Professor, DEPT OF Pharmacy Practice
2. **B.SYED SALMAN,** Asso. Professor, DEPT OF Pharmaceutics
3. A. Ravi Kumar, Asso. Professor, DEPT OF Pharmacology
4. **Dr.k.Kishore kumar,professor** DEPT OF Pharmaceutics,SWATHI COLLEGE OF PHARMACY,NELLORE.
5.**Dr.M.SREENIVASULU**,PRINCIPAL,NARAYANA PHARMACY COLLEGE
[1,2,3,5] NARAYANA PHARMACY COLLEGE, CHINTHA REDDY PALEM, NELLORE

Abstract:
The part that vascular endothelial-derived growth factor (VEFG) plays in the onset of tuberculous meningitis (TBM) is still mostly unknown. We evaluated the role of VEFG in serum and CSF in TBM prospectively. PARTICIPATES AND METHODS: In this prospective study, researchers observed patients at a hospital in northern India from January 2018 to June 2019. 82 consecutive drug-naive TBM patients who were diagnosed using modified Ahuja's criteria were included in the study. 49 healthy controls (n = 49) were used to compare the results. Serum and cerebral fluid levels of VEFG were assessed in both patients and controls. 34 patients had their blood VEFG levels rechecked three months after completing antitubercular therapy. The levels of VEFG were determined using the human VEFG enzyme-linked immunosorbent assay kit.29.9 ± 13.1 years was the average age. These are the outcomes. The study group consisted of 33 men and 49 women (59.8% and 40.2%, respectively). Seventy-three patients (89%) had positive multiplex TB polymerase chain reaction tests, while thirteen patients (18%) had positive BACTEC MGIT960 tests. Patients with TBM did not have greater levels of VEFG in their serum or cerebrospinal fluid than the control group. Serum VEFG level declines during follow-up were not linked to the final result in TBM. In conclusion, VEFG may not have a major role in the emergence of TBM. Future studies with larger sample numbers could be able to clarify the VEFG status in TBM further.

Keywords: Treatment for tuberculosis, outcome, TB meningitis, VEFG

Introduction

Despite years of intensive research, the prognosis for tuberculous meningitis (TBM) remains poor, with around one-third of survivors experiencing significant residual disability and 25% of patients dying.1–3 The host's immune response to a tubercular bacilli infection might be either positive or negative. The Creative Commons Attribution NonCommercial ShareAlike 4.0 License governs the distribution of the papers published in this open-access publication. As long as appropriate credit is given and the new works are licensed under the same terms, this license allows others to alter, adapt, and produce works based on the original work without receiving payment. either nice or bad, depending on how terrible it is. One of the main causes of death and other issues in tuberculosis (TBM) is the host immune system's response to tubercular bacilli. An excellent illustration of this is the widespread use of steroids in combination with antitubercular treatment (ATT) for tuberculosis (TBM) [4].Cerebral infarction will occur in around 40% of those with TBM, making it a major cause of several issues.One of the most One of the main causes of brain infracts is intracranial vascular strangulation and occlusion, which is brought on by the discharge of viscous exudates from the base of the brain. This has led to the association of VEFG, chemokines, and cytokines with the pathogenesis of cerebral infarctions in TBM.From 5 to 8 Vascular endothelial-derived growth factor (VEGF) or vascular permeability factor is a 36–46 kDa homodimeric glycoprotein that regulates the

permeability of the vascular endothelium. TBM develops as a result of inflammation and oedema in the brain caused by disruption to the blood-brain barrier (BBB). VEFG does contribute to BBB impairment in brain infarctions, CNS neoplasms, and bacterial meningitis.[6] However, only a limited number of studies have looked at the role of VEFG in TBM [9–11]. Other issues with these studies were a small sample size and the use of computed tomography scans rather than magnetic resonance imaging (MRI) to detect brain infarcts. Because there is little information from well planned prospective studies, the function of VEFG in the development of TBM is still unknown. If VEFG is shown to have a substantial pathogenic role in CNS TB, then future treatment regimens based on anti-VEFG medications may provide improved outcomes in TBM. As a result, VEFG's role in TBM was evaluated prospectively.

Aimsandobjectives

Theaimsandobjectivesofthestudyweretodetermine theroleofVEGFinthepathogenesisofTBM.

Patients and Methods

ThepresentprospectivestudywasdoneatauniversitystandardhospitalfromJanuary2018toJune2019.DiagnosisofTBMwas madeonthebasisofthemodifiedAhuja's criteria.[1,2]We included 82 consecutive newlydiagnosedpatientsofTBMwhohadnotreceivedATT before the collection of samples. The results werecomparedtohealthycontrols(*n*=49)consistingofpatientswhounderwentcerebrospinalfluid(CSF)examinationfordiagnosticpurposesandduringsurgeryunder spinal anesthesia. Control subjects did not haveany active CNS disease or any other disease which isknowntoelevateVEGFlevels.Thestudywasapprovedby the Ethics Committee of the institute wide ordernumberNK/4247/MD/2666-67.Patientsandcontrolswere included and excluded based on the followingcriteria.

Inclusioncriteria

a. Agemorethan14years
b. PatientsbeingdiagnosedasTBMusingmodifiedAhuja's criteria.

Exclusioncriteria

1. Pregnancy
2. Presenceoforganismsotherthan*Mycobacteriumtuberculosis*
3. Patients on antitubercular therapy or other forms ofimmunosuppressivetherapy
4. Presenceofdisorders(otherthanTBM)whichmay elevateVEGFlevels.

A history was taken, and each patient underwent a thorough systemic and neurological examination.Every detail was recorded on a pre-made proforma. Haemoglobin, total and differential leukocyte counts, erythrocyte sedimentation rate, platelet counts, blood sugars, renal, liver, and thyroid function tests, serum electrolytes, and serum calcium and phosphorus were among the many biochemical and hemogrammatic analyses performed on each patient. Adenosine deaminase, multiplex polymerase chain reaction (PCR) for bacterial DNA, forcells, protein, glucose, acid-fastbacillus (AFB) smear, GeneXpert for MTB, culture, and drug susceptibility tests for MT were all examined in the CSF.BonLowenstein-Jensen medium, BACTEC automated blood culture systems, bacterial and fungal cultures, and cryptococcus antigen testing, among other things.Every patient had a baseline MRI brain with contrast.The four medications used in ATT (antituberculous therapy) were rifampicin, isoniazid, pyrazinamide, and streptomycin (RHZS) in combination with steroids for each patient. Where necessary, ventriculoperitoneal hunting was carried out. Following three months of therapy, the patients were reviewed by radiological examination and clinical assessment each month.Additionally, they received clinical examination and neuroimaging on an as-needed basis.The Glasgow Outcome Scale [12] and the Schwab and England Activities of Daily Life (SandEADL) Scale were used to establish the final result.[13] The grade of TBM was determined using the British Medical Research Council guidelines.[14] If the main subject was younger than 18

or had a sensory impairment, the authors acquired written informed permission from all participants or their family.

All patients had five millilitres of blood and seven to eight millilitres of CSF taken at baseline under strict aseptic conditions in order to estimate their VEGF levels.Following three months of ATT therapy, blood samples were taken in order to estimate VEGF.After obtaining permission, two millilitres of CSF were extracted from controls during a lumbar puncture performed for anaesthetic reasons during surgery. Blood was used to extract serum, which was then placed in an autoclaved tube.After centrifuging it for 10 minutes at 3000 revolutions per minute, it was stored at -80°C. The human VEGFDIACLONE enzyme-linked immunosorbent test kit, a solid-phase kit intended to measure VEGF level, was used to quantify the VEGF.

Statistical analysis

AlldatawereanalyzedusingtheIBMStatisticalPackage fortheSocialSciences(SPSS)forWindows,version 25.0. Armonk, NY: IBM Corp. Demographic data wereanalyzed using mean, median, and range. To analyzediscretevariables,theChi-squaretestwasutilized,whereas the Mann–Whitney test was used to analyzecontinuousvariables.Statisticalsignificancewasdefinedas $P \leq 0.05$. The Student's *t*-test was used to compareVEGFlevels atbaselineand3 monthsafter ATT.

Results

Demographicandclinicalprofile

ThemeanageofTBMpatients(29.9±13.1years)wassignificantlyless($P<0.01$)thancontrolpopulation(41.8±9.5years). Therewere33(40.2%)men and49(59.8%)womenintheTBMgroupand22(44.9%)menand27women(55.1%)inthecontrolgroup.The

Table1:Clinicalanddemographicprofileofpatients withtuberculousmeningitis

Parameters	Numberofpatients (*n*=82),*n*(%)
Age(years),mean±SD	29.9±13.1
Male sex	30 (40.2)
Fever	79 (96.3)
Headache	80 (97.6)
Vomiting	64 (78)
Durationofillness(days),mean±SD	48.1±52.2(range7–360)
GCSscore 3(3.7)	

andclinical data are summarized inTable 1.Altered sensorium

Radiological and cerebrospinal fluid data BaselineMRI(*n*=77)wasabnormalin76(98.7%)patients. The most common MRI abnormality includedthepresenceofexudatesseenin85.7%ofpatientsfollowedbyhydrocephalusin62.2%ofpatients.Evidenceofbraininfarctionwasseenin24.4%.CSFwasabnormalin76/82(92.7%)ofpatients.Theremainingsixpatientshadunmistakableevidenceofcnstuberculosisonneuroimaging.AFBculture(BACTECMGIT960)waspositivein15(18%)patientswhilemultiplexPCRfortubercularbacilluswaspositivein73(89%)patients.The MRIand CSF results are shown inTable 2.

Finaloutcomeamongpatientswithtuberculousmeningitis

ThefinaloutcomeinTBMwasdefinedeitherby:

1. Death(*n*=24)oralive(*n*=58)or
2. UsingtheGlasgowOutcomeScalescore(good–5,
   Lowermotorneurontype offacial
   weakness
   ADLScalescore(100%–80%–good,60%–70%
   – moderate, and <60% – poor). The outcome wastakenaspooriftherewasdeathorifanyscalerevealedpooroutcome,moderateifanyscalerevealedmoderateoutcome, andgoodifbothscaleshavegoodoutcome.

Overall, death occurred in24(29.3%) patients.Forty (48.8%), 12 (14.6%), and 30 (36.6%) patients hadgood,moderate, andpooroutcomes,respectively.

Table2:Cerebrospinalfluidandradiologicaldataof patientswithtuberculousmeningitis

Radiologcaldata	
Parameter	**Numberof patients(*n*=77),*n*(%)**
Anyabnormality	76 (98.7)
Hydrocephalus	51 (62.2)
Exudates	66 (85.7)
Cerebralinfarcts	20 (24.4)
Border-zoneencephalitis	5(6.1)
Meningealenhancement	60 (73.2)
Tuberculomas	39 (26.7)
Militarymottling	5(6.1)
Cordinvolvement	16 (20.8)
Optochiasmaticarachnoiditis	3(3.9)
Cerebraledema	23 (29.9)
CSFdata	
Parameters	**Numberofpatients withTBM(*n*=82),*n*(%)**
Antitubercular therapy-inducedhepatitis	
Hydrocephalus 51 (62.2)	
Ventriculoperitonealshunt	16 (19.5)Staging ofTBM
StageITBM	20 (24.4)
StageIITBM	41 (50)
StageIIITBM	21 (25.6)
BACTECculturepositivity	15 (18)
MultiplexTBPCRpositivity	73 (89)
TypeofTBM	
Definitive	73 (89)
Highlyprobable	9(11)
Extraneural TBon PET	
Brain	40 (70.2)
Lung	44 (77.2)
Consolidation	23
Fibrocavitarylesions	13
Militarymottling	13

Pleuralinvolvement	5
Lymphadenopathy	44 (77.2)
Mediastinallymphadenopathy	30
Cervicallymphadenopathy	26
Axillary	11
Mesenteric	15
Para-aortic	17
Bone	10 (17.5)
Pericardial	1(1.7)
Adnexa	2(3.5)
Prostate	4(7)
Gastrointestinal	6(10.5)
Liver	1(1.7)
Pancreas	1(1.7)

TB=Tuberculosis, PET=Positron emission tomography, SD=Standarddeviation, GCS=Glasgow Coma Scale, TBM=Tuberculous meningitis,PCR=Polymerase chainreaction

Determinantsofpooroutcome

Wefurtheranalyzedastoifvariousclinical,biochemical,CSF,orradiologicalparameters[Table3]canpredictthefinal outcome in TBM. The following associations werefound as follows:

1. PositiveassociationbetweenlowGlasgowComa Scaleanddeathas wellaspoorfinal outcome
2. Trends between TBM Stage III and death (P = 0.08)andpooroutcomewithoutdeathonanyofthescalescomparedtolower clinical stage of TBM
3. Trend(P=0.08)betweenalteredsensoriumandpoor outcomeasdefinedbyeitherofthetwoscales
4. Atrend toward death andthepresence ofexudates(P=0.06)andcerebraledema(P=0.09)
5. Positiveassociationbetweenpooroutcome(oneither of the scales) and the presence of cerebralinfarcts (P =0.02)
6. Positiveassociationbetweenthepresenceofcerebral tuberculomasandgoodoutcome(determinedbythepresence or absence of mortality) (P = 0.02) and atrendbetweenthepresenceofcerebraltuberculomasand good outcome as defined by either of the twoscales (P = 0.06).

CSFpleocytosis	76(92.7)
Lymphocytic predominance	42
Polymorphonuclear predominance	34
Lowglucose	72 (87.8)
CSFglucose≤30mg/dL	46 (56.1)
RaisedCSFprotein(>50mg/dL)	71 (86.6)
AFB culture	15/82
AFB staining	Nil
CSFhigh ADA(>10)	54
CSF TBPCR	73

CSF=Cerebrospinalfluid,AFB=Acid-fastbacillus,ADA=Adenosine deaminase,PCR=Polymerasechainreaction,TB=Tuberculosis, TBM=Tuberculousmeningitis

VEGFinserumandcerebrospinalfluidsamplesof tuberculous meningitis and controls*ComparisonofserumandcerebrospinalfluidVEGFincasesversus controls*

Inthepresentstudy,weevaluatedtheroleofVEGFin the pathogenesis of TBM. The levels of serum andCSFVEGFweremeasuredinTBMandcomparedwith controls. On analysis, serum and CSF VEGF weregreater (though statistically insignificant; P = 0.01) inTBMthancontrols [Table 4].

CorrelationbetweenVEGFandvariousclinical parameters

WealsocomparedserumandCSFVEGFwiththestageof TBM and with the final outcome among patients withTBM.Onanalysis,therewasnocorrelationoftheseverityofTBM(assuggestedbyclinicalstaging)orfinaloutcomeofTBM with either serum or CSFVEGF.

Table3:Correlationofclinicalandradiologicalparameterswithfinaloutcomeintuberculousmeningitis

Parameters	"Finaloutcomeas definedbydeath oralivedead"	*P*	"FinaloutcomeasdefinedbyEngl andscoreofGOS Schwab andscore		*P*
			Good	Poor	
GCS					
15	6	0.01	25	10	0.05
8–14	15		14	17	
<7	3		1	3	
TBMstage					
1 or2	14	0.06	6	34	0.09
3	10		11	19	
Altered sensorium					
Present	17	0.5	21	19	0.08
Absent	7		21	9	
Radiologicalparameters					
Cerebralinfarct					
Infarctabsent		NS	43	14	0.02
Infarctpresent			6	12	
Exudates					
Present	12	0.06	12	15	0.07
Absent	8		28	11	
Cerebraledema					
Present	9	0.09	-	-	-
Absent	11		-	-	
Cerebraltuberculomas					
Present	6	0.02	25	9	0.06
Absent	14		15	17	

NS=Notsignificant,TBM=Tuberculousmeningitis,GCS=GlasgowComaScale

Table4:Serumandcerebrospinalfluidvascularendothelial-derived growth factor in patients withtuberculousmeningitisversuscontrols

Parameter	Mean±SD(pg/mL)	*P*

CorrelationbetweenVEGFandvariousradiological parameters

WedeterminedtheroleofVEGFinradiologicalcompilations of TBM such as hydrocephalus, exudates,infarcts,tuberculomas,borderzoneencephalitis,andcerebraledema.Analysisrevealedapositiveassociation(*P*=0.01)betweenserumVEGFandexudateson MRI. There was no correlation between serum andCSFVEGFwithanyotherradiological parameter.

Follow-upserumVEGFlevels

Inthispresentstudy,wealsodeterminedlevelsofserumVEGF at follow-up. Follow-up VEGF testing was donein34patients.Atfollow-upserumVEGFdecreasedonlyin15(44.1%)patients.Whencompared,changeinserumlevels of VEGF did not have any bearing on the finaloutcome.These results are shown inTable 5.

to VEGF A, a 45 kDa glycoprotein produced by manydifferent cell types. Primarily released from vascularendothelialcellsinresponsetohypoxia,VEGFpotentlystimulatesangiogenesis.Incerebralischemia,VEGFcanhavebothpathogenicandprotectiverolesdependingonthestageofdiseaseprocess.While,inearlystages,VEGFcontributestobraindamagethroughincreaseinvascularpermeabilitywithconsequentcerebralinflammationandedema; in the late stages, it protects against ischemiathroughtheformationofnewbloodvessels.AsdisruptionofBBB(withincreasedvascularpermeabilityandinfluxofinflammatorycells)remainsamajorfactorforcerebraldamageinTBM,itislikelythatVEGFcontributestothepathology of TBM at least in the early stages of diseaseprocess.VEGFalsostimulatesthegenesisofnitricoxideresulting in vasodilatation with increased blood flowandconsequentcerebralvasodilatation.Accordingly,itis imperative to study the role of VEGF in TBM wherevascular complications are important determinants ofdeathandotherdisablingsequelae.[9-11]

Matsuyama*etal*.[9] foundasignificantincreasein VEGF(inbloodandCSF)inTBM(*n*=28)thanotherCNS

Table5:Follow-upserumvascularendothelial-derivedgrowthfactorlevelsandtheirinfluenceontheoutcomeasdefinedbydeadoralive

Parameter	Finaloutcomeasdefinedby dead oralive (*n*=38)Alive	Dead	*P*
DecreaseinserumVEGF	15	0	0.6
Increaseinserum VEGF	18	1	

Parameter	"Finaloutcomeasdefinedby SchwabandEnglandADLsorGOS(*n*=38)			*P*
	Good	Moderate	Poor	
DecreaseinserumVEGF	11	3	1	0.4
Increaseinserum VEGF	13	2	4	

VEGF=Vascular endothelial-derived growth factor, ADLs=Activities of dailyliving, GOS=GlasgowOutcomeScale

infections(*n*=31).Follow-upVEGFlevelsdecreasedin patients who showed clinical improvement (*n* = 12).They stressed on the importance of VEGF in TBM. Inanother study conducted on pediatric population,[10]CSFVEGFwassignificantlyhigherinTBM(*n*=26)thanhealthychildren(*n*=20).Therewasapositivecorrelationbetween CSF mononuclear cell count and VEGF levels.Thus,inflammatorycellsinCSFsecreteVEGFwhich,inturn,damagesBBB.Theauthorssuggestedthatsteroidsmayexerttheirbenefitin TBMbyantagonizingtheeffectsof VEGF. Husain *et al*.[11]reported significantly higherblood and CSF VEGF in ongoing (*n* = 20) compared toinactive TBM (*n* =20).

Thedemographic,clinical,laboratory,positronemission tomography, and MRI data of the present study wereconsistentwiththatreportedpreviouslyfromourcenter.[1,2,15]RegardingserumandCSFVEGF,ourresultscontrastedwith previousstudiesaswedidnotfindaroleof VEGF in the pathogenesis of TBM. Although bloodandCSFVEGFweremoreinTBMthanhealthysubjects,the difference did not reach statistical significance. OurresultsweresimilartothoseofMisra*etal*.[6]whoreportedinsignificantly higher serum VEGF in TBM (*n* = 40)patients compared to controls. Similar to Misra *et al*.,[6]the present study did not find any correlation betweenVEGFlevelsanddiseaseseverityortimeofpresentation.

Amongvariousradiologicalparameters,wedidfinda significant correlation between basal exudates andserumVEGFlevelsbutnotwithCSFVEGFlevels.The association between increased serum VEGF andbasal exudates can be explained due to VEGF-inducedvasodilatationandincreasedvascularpermeability.However,theaboveinferenceisputativeastherewasnoassociationbetweenCSFVEGFlevelsandthepresenceofbasalexudates.Similartothestudy byMisra*etal*.,[6]wedidnotfindanyeffectofcorrelationbetweenthepresenceorabsenceofcerebralinfarctionandVEGFlevelsinTBM.

Inourstudy,wecomparedchangeinthevalueofVEGFaftertreatmentwithATTfor3months.Unlikeapreviousstudy,[9]wedidnot findanycorrelationbetweendecreaseinlevels of VEGFwith thefinal outcome.

Ourfindingsaresignificant.Ourresultscouldnotreiteratethepreviouslysuggestedroleplayedbyelevated VEGFinthepathogenesisofTBM.Thelikely reason could be the unique genetic structure ofourpopulationwhereinadifferentsetofcytokinesratherthanVEGFmaybemoreoperativeinthepathogenesis of TBM. The point in favor of the abovehypothesisisthefactthatapreviousstudyfromIndiansubcontinentalsodidnotfindasignificantroleofVEGFinTBM.

Conclusion

In summary, our analysis was unable to find any evidence of VEFG's substantial contribution to the emergence of TBM.
The high sample size and the fact that all patients had brain magnetic resonance imaging (MRI) at baseline and follow-up evaluations were two of our study's best qualities. The conclusion that 89% of patients had verified TBM is a strength of our research. Future studies using larger sample sizes may help clarify the precise role of VEFG in TBM.
References

1. ModiM,SharmaK,PrabhakarS,GoyalMK,TakkarA,SharmaN,*etal*.Clinicalandradiologicalpredictorsofoutcomeintubercularmeningitis: A prospective study of 209 patients. Clin NeurolNeurosurg2017;161:29-34.

2. SharmaS,GoyalMK,SharmaK,ModiM,SharmaM,KhandelwalN,*etal.*Cytokinesdoplayaroleinpathogenesisoftuberculousmeningitis:Aprospective studyfromatertiarycarecenterin India. J NeurolSci 2017;379:131-6.
3. ThwaitesGE,TranTH.Tuberculousmeningitis:Manyquestions, toofewanswers.LancetNeurol2005;4:160-70.
4. Rock RB, Olin M, Baker CA, Molitor TW, Peterson PK. Centralnervous system tuberculosis: Pathogenesis and clinical aspects.Clin Microbiol Rev 2008;21:243-61.
5. ThwaitesGE,Macmullen-PriceJ,TranTH,PhamPM,NguyenTD,SimmonsCP,*etal.*SerialMRItodeterminetheeffectofdexamethasoneonthecerebral pathologyoftuberculous meningitis: An observational study. Lancet Neurol2007;6:230-6.
6. Misra UK, Kalita J, Singh AP, Prasad S. Vascular endothelialgrowthfactorintuberculousmeningitis.IntJNeurosci2013;123:128-32.
7. KalitaJ,MisraUK,NairPP.Predictorsofstrokeanditssignificanceintheoutcomeoftuberculousmeningitis.JStroke Cerebrovasc Dis 2009;18:251-8.
8. Misra UK, Kalita J, Srivastava R, Nair PP, Mishra MK, Basu A.Astudyofcytokinesintuberculousmeningitis:ClinicalandMRIcorrelation.NeurosciLett 2010;483:6-10.
9. MatsuyamaW,HashiguchiT,UmeharaF,MatsuuraE,Kawabata M,Arimura K,*etal.*Expression ofvascularendothelial growth factor in tuberculous meningitis. J NeurolSci2001;186:75-9.
10. van der Flier M, Hoppenreijs S, van Rensburg AJ, Ruyken M,Kolk AH, Springer P, *et al.* Vascular endothelial growth factorand blood-brain barrier disruption in tuberculous meningitis.Pediatr Infect Dis J 2004;23:608-13.
11. HusainN,AwasthiS,HarisM,GuptaRK,HusainM.Vascular endothelialgrowthfactorasamarkerofdiseaseactivityin neurotuberculosis.JInfect2008;56:114-9.
12. JennettB,BondM.Assessmentofoutcomeafterseverebrain damage. Lancet 1975;1:480-4.
13. RamakerC,MarinusJ,StiggelboutAM,VanHiltenBJ.Systematicevaluationofratingscalesforimpairmentanddisabilityin Parkinson's disease. Mov Disord 2002;17:867-76.
14. Lamba PA, Bhalla JS, Mullick DN. Ocular manifestations oftubercular meningitis: A clinico-biochemical study. J PediatrOphthalmolStrabismus 1986;23:123-5.
15. Jain A, Goyal MK, Mittal BR, Sood A, Singh H, Vyas S, *et al.*18FDG-PETissensitivetoolfordetectionofextracranialtuberculousfociincentralnervoussystemtuberculosis–PreliminaryobservationsfromatertiarycarecenterinNorthernIndia.JNeurolSci 2020;409:116585.