Society for Science and Education
United Kingdom

ISSN: 2055 - 1266
Volume 5 No 4
August 2018

Journal of Biomedical Engineering and Medical Imaging

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SOCIETY FOR SCIENCE AND EDUCATION UNITED KINGDOM

JBEMi JOURNAL OF BIOMEDICAL ENGINEERING AND MEDICAL IMAGING

ISSN: 2055-1266
VOLUME 5 ISSUE 4

Trends and Out Look for Clinical Diagnostic Testing

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PREPHASE

There are several approaches are being used in clinical diagnosis including routine laboratory tests as conventional methods and also rapid and robust modern methods. Both the approaches have their significance in the clinical diagnosis of a disease. The conventional approaches largely depend on microscopy and staining of microorganism responsible for disease while modern methods are based on molecular signature and findings. In the current scenario, there is a need for rapid and robust diagnostics as global disease burden is prevailing. At the same time, there is the continuous emergence of new and complex infectious pathogens, and hence early diagnosis provides ease in disease management. Recently, use of nanotechnology and enzyme-based diagnostic became popular and shown satisfactory results. The use of diagnostic become an integral part of modern medicine and involves molecular biology and cutting-edge bio-engineering as well. The integration of information technology in diagnostic is an added advantage to minimize time and ensure precise data interpretation.

***Keywords*:** Polymerase chain reaction (PCR), Nucleic acid-based tests, A rapid diagnostic test (RDT), Readymade diagnostic kits, Patient compliance, genomics

1 Introduction

Medical diagnosis is the condition explains a person's symptoms and signs (1). It is most often referred to as diagnosis with the medical context being implicit. There are several means of diagnosis of diseases including symptomatic, molecular and genomics (2). The conventional way of clinical diagnosis is still in practice provide first and basic information regarding disease and causative agents as well. (3) Integration is influenced by the clinical syndrome, the availability of and access to appropriate diagnostics, the place of service, and the experience and knowledge of the healthcare provider (4). The goal of the chapter is to increase awareness of the current and potential value of infectious diseases diagnostics for patient care and public health and to promote further development of needed diagnostics.

DOI: 10.14738/jbemi.54.4848
Publication Date: 25th July 2018
URL: http://dx.doi.org/10.14738/jbemi. 54.4848

The credit goes to Antonie van Leeuwenhoek (1632–1723), the "father of the microscope." (5). . The field of clinical microbiology is currently in transition, and standard-of-care testing is now a hybrid of old and new methodologies (6). The evolution of infectious diseases diagnostics has resulted from advances in chemistry, immunology, molecular biology, engineering, automation, and nucleic acid amplification. (7). Individual pathogens can be readily identified in a wide variety of specimen types including blood, urine, tissue, mucosal swabs, cerebrospinal fluid (CSF), respiratory secretions, and stool samples. The modern diagnostic is quick, robust and precise in finding cause for candidate disease and allow ease in data studies (8).

One basic and very old method is the identification of a microorganism simply by looking at it under a microscope. Most samples are treated for stains. Stains are special dyes that color the microorganisms, causing them to stand out from the background (11). Doctors add substances to the dish or testtube to stop the growth of microorganisms that donot cause the disease . (12). Many microorganisms, such as the bacteria that cause urinary tract infections or strep throat, can easily be grown in culture. Some bacteria, such as the bacteria that cause syphilis, cannot be cultured at all (13). They are produced by certain types of white blood cell when these white blood cells encounter a foreign substance or cell (14).If a person has antibodies to a particular microorganism, it means that the person has been exposed to that microorganism and has mounted an immune response (15). Antigen tests detect the presence of a microorganism directly so that doctors can diagnose an infection quickly, without waiting for a person to produce antibodies in response to the microorganism (16). If there are antigens from that microorganism in the person's sample, they attach to the test antibody (17). D This genetic material consists of nucleic acids: deoxyribonucleic acid (DNA) or ribonucleic acid (RNA). The polymerase chain reaction (PCR) is an example of this type of test (18).

Thus, these tests are done only when a doctor already suspects a particular disease. Most nucleic acid-based tests are designed to identify the presence of a microorganism (called qualitative testing) (19). However, a few of these tests can measure the amount of genetic material present (called quantitative testing) in certain microorganisms, such as HIV and hepatitis C, and thus determine how severe the infection is. Quantitative tests can also be used to monitor how well treatment is working. Nucleic acid-based tests can sometimes be used to check the microorganisms for genes or gene mutations that make the microorganism resistant to a drug (20) Enzymes produced by the microorganism (which help the microorganism infect cells or spread through tissues faster) (21). For many diseases, the clinical laboratory provides essential diagnostic information (22).A rapid diagnostic test (RDT) is a medical diagnostic test that is quick and easy to perform. RDTs are suitable for preliminary or emergency medical screening and use in medical facilities with limited resources (23). Malaria RDTs detect specific antigens (proteins) produced by malaria parasites that are present in the blood of infected individuals. Some RDTs detect a single species (either P. falciparum or P. vivax), some detect multiple species (P. falciparum, P. vivax, P. malariae and P. ovale) and some further distinguish between P. falciparum and non-P. Falciparum infection, or between specific species. Blood for the test is commonly obtained from a finger-prick and results are available within 15-30 minutes (24)With the use of conventional diagnostic methods and new cutting-edge modern tools in clinical diagnosis outcomes are- Rapid clinical diagnosis Robust tests and higher reproducibility ,Readymade diagnostic kits ,Ready to use, Ease in sample

processing ,Digital output ,Ease of data interpretation ,Low title volume Patient compliance and Low cost

2 History and Mechanism

Patient safety agenda is gaining momentum in the health care systems of all developed countries. However, adverse event detection systems and initiatives to reduce error rates in medicine are in their infancy. Laboratory services play a crucial role in both individual and population-based healthcare, and clinical laboratories use many different methods to reduce errors, ensure patient safety, and improve quality including quality control procedures, quality assurance programs, accreditation of laboratories and certification of education programs. Considerable advances in analytical techniques, laboratory instrumentation, information technologies, automation and organization have granted an exceptional degree of analytical quality over the past 50 years. This, in turn, has resulted in a significant decrease in error rates, analytical error rates in particular. There is consolidated evidence that nowadays, most laboratory errors fall outside the analytical phase, and that pre- and post-analytical processes are more vulnerable to error than analytical processes. The first recorded examples of medical diagnosis are found in the writings of Imhotep (2630–2611 BC) in ancient Egypt (the Edwin Smith (25) Babylonianmedical textbook, the Diagnostic Handbook written by Esagil-kin-apli (fl.1069–1046 BC), introduced the use of empiricism, logic and rationality in the diagnosis of an illness or disease (26) Traditional Chinese Medicine, as described in the Yellow Emperor's Inner Canon or Huangdi Neijing, specified four diagnostic methods: inspection, auscultation-olfaction, interrogation, and palpation.(27)Hippocrates was known to make diagnoses by tasting his patients' urine and smelling their sweat (28) The credit goes to Antonie van Leeuwenhoek (1632–1723), the “father of the microscope,” changed the course of infectious diseases when he enabled the visualization of the microbial world, a world no one had imagined. Medical diagnosis is the process of determining which disease or condition explains a person's symptoms and signs (29). It is most often referred to as diagnosis with the medical context being implicit. The diagnosis is the first step in the process of therapeutics prescription. There are several means of diagnosis of diseases including symptomatic, molecular and genomics (30). Diagnostic tests play a major role in the clinical care of patients with infectious diseases, including detection of specific pathogens, the discovery of new pathogens, determining appropriate therapy, monitoring response to therapy, assessing prognosis, and disease surveillance (31). Integration is influenced by the clinical syndrome, the availability of and access to appropriate diagnostics, the place of service, and the experience and knowledge of the healthcare provider (32). The goal of the chapter is to increase awareness of the current and potential value of infectious diseases diagnostics for patient care and public health and to promote further development of needed diagnostics.

3 Major Advances and Discoveries

Advanced clinical diagnostics has fully equipped with ware housing, animal facilities, clean room, high speed and ultra centrifuges, iso environmental chambers for various atmospheric conditions of temp and air mixtures, fer mentors with high speed filtration and separation, laminar flow biosafty and equipped for biological, microbiology, tissue culture, large scale cryopreservation, biochemical, analytical, virology, immunology, food and safety, cryopreservation of biological materials and other investigative work The old and new diagnostic tests to diagnose pathogenic parasites , viruses,bacteria

are observing parasites,ova,cysts, blood smear,MRI,CAT,ELISA (Enzyme linked immunosorbent assay),HA(Hem agglutination),CF (Complement fixation) FAST(Falcon assay screening test),DOT-ELISA,RDTS (Rapid antigen detecting system),LIPS(Luciferase Immunoprecipitation system, PCR(Polymerase chain reaction),RT-PCR (Real time Polymerase chain reaction),LAMP (Loop mediated isothermal Amplification) etc are the major diagnostic tests.

4 Ideas Where the Research Go Next

The clinical diagnosis is a first and most crucial step in the process of finding therapeutics for a disease. There are several approaches are being used in clinical diagnosis including routine laboratory tests as conventional methods and also rapid and robust modern methods. Both the approaches have their significance in the clinical diagnosis of a disease. The conventional approaches largely depend on microscopy and staining of microorganism responsible for disease while modern methods are based on molecular signature and findings. In 19 the current scenario, there is a need for rapid and robust diagnostics as global disease burden is prevailing. At the same time, there is the continuous emergence of new and complex infectious pathogens, and hence early diagnosis provides ease in disease management. Recently, use of nanotechnology and enzyme-based diagnostic became popular and shown satisfactory results. The use of diagnostic become an integral part of modern medicine and involves molecular biology and cutting-edge bio-engineering as well. The integration of information technology in diagnostic is an added advantage to minimize time and ensure precise data interpretation.

A medical error is a preventable adverse effect of care, whether or not it is evident or harmful to the patient.Laboratory blood studies can reveal a little information about organ systems throughout the body. The amount of blood taken for a laboratory test is not harmful . Human body manufactures a couple of milliliters of new blood every day. Blood studies may give information about the levels of sodium, potassium, calcium and other chemicals . Presence of certain enzymes and information about the coagulation characteristics , levels of sugar, urea, cholesterol, alcohol , protein, and other drugs of patients blood sample.

Diagnostic error can be defined as a diagnosis that is missed, wrong or delayed, as detected by some subsequent definitive test or finding. The ensuing harm results from the delay or failure to treat a condition present when the working diagnosis was wrong or unknown, or from treatment provided for a condition not actually present.

5 Significant Gap in Research

Mistakes and failures are integral part of any great effort worth the mention.Your best teacher is your last mistake. Developing new manifolds by revitalizing old ideas. The quality of thinking action decide your strength. Is it a sin or boon to admit patient in a hospital for treatment? . Medical error is not included on death certificates or in rankings of cause of death. Hospital is expected to be a safe place. When you take a sick patient to the hospital, you expect that the patient is in good hands and under the umbrella of experienced doctors. Errors in diagnosis, misdiagnosis of psychological disorder, competency, education and training are the main features causing fatal deaths. These are the common misconceptions about adverse events, and the arguments and explanations against those misconceptions are noted in parentheses: "Bad apples" or incompetent health care providers are a common cause. (Although human error is commonly an initiating event, the faulty process of delivering

care invariably permits or compounds the harm, and is the focus of improvement.(33) High risk procedures or medical specialties are responsible for most *avoidable* adverse events. (Although some mistakes, such as in surgery, are harder to conceal, errors occur in all levels of care. Even though complex procedures entail more risk, adverse outcomes are not usually due to error, but to the severity of the condition being treated(34) However, USP has reported that medication errors during the course of a surgical procedure are three times more likely to cause harm to a patient than those occurring in other types of hospital care(35) If a patient experiences an adverse event during the process of care, an error has occurred. (Most medical care entails some level of risk, and there can be complications or side effects, even unforeseen ones, from the underlying condition or from the treatment itself) (36)

6 Current Debate

Incorrect laboratory tests account for significant harm. Researchers estimated that the number of patients suffering from missed diagnostic tests are annually in thousands. These are potentially preventable, subject to the condition if proper attention is paid.

Diagnosing diseases and disorders requires highly developed skill on the part of the physician or other medical professional .Usually the diagnosis calls for systematic use of instruments and diagnostic aids, various tests, and , often with sophisticated instruments and machines.

Quality systems are the mainstay of clinical laboratory management. The comprehensive laboratory testing process must be continually monitored and evaluated to ensure reliable test results and set the foundation for quality improvement. While such efforts have resulted in significant improvements in many of the processes, errors still occur. In order to implement corrections and improve the testing process, the laboratorian must identify the various sources of errors.

Last two decades has witnessed phenomenal advances in the field of medicine following revolutionary changes taking place in the application of technology and as a consequence, Biochemistry and Microbiology have evolved as the most important branch of evidence based medicine.

The quality of any laboratory test result is dependent on many variables, It begins with skill, and knowledge when preparing the patient and specimen are essential to the provision of the highest quality standards for testing and services. The patient must first be properly prepared so that the best possible specimen can be collected. Next, the actual collection of the specimen must be completed. Then, the specimen should be properly processed, packaged and transported to the laboratory in a timely manner and under environmental conditions that will not compromise the integrity of the specimen. After all of these activities take place, a quality analysis can be performed.

Some common reasons of not getting quality and reliable results are 1. Lack of commitment on part of staff performing the tests 2. Poor management and supervision 3. Poor understanding of quality assurance concepts 4. Analysts do not understand the concepts of assay principles 5. Reagents used are not high quality 6. Poor quality of instruments 7. Procedures are not followed as recommended 8. Under staff leads to high error rate. 9. Lack of equipment. 10. Mislabeling blood sample. 11. Un labeling blood sample.

REFERENCES

[1] Ross AGP, Bartley PB, Sleigh AC, Olds GR, Li Y, Williams GM, McManus DP. Schistosomiasis. N Eng J Med 2002;346:1212-9.

[2] Gryseels B, Polman K, Clerinx J, Kestens L. Human schistosomiasis. Lancet 2006;368:1106-18.

[3] Steinmann P, Keiser J, Bos R, Tanner M, Utzinger J. Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. Lancet Infect Dis 2006;6:411-25.

[4] King CH, Dickman K, Tisch DJ. Reassessment of the cost of chronic helminthic infection: a meta-analysis of disability-related outcomes in endemic schistosomiasis. Lancet 2005;365:561-9.

[5] King CH, Dangerfield-Cha M. The unacknowledged impact of chronic schistosomiasis. Chronic Illness 2008;4:65-79.

[6] Mas-Coma S, Valero MA, Bargues MD. Climate change effects on trematodiases, with emphasis on zoonotic fascioliasis and schistosomiasis. Vet Parasitol 2009;163:264-80

[7] Leshem E, Meltzer E, Marva E, Schwartz E. Travel-related schistosomiasis acquired in Laos. Emerg Infect Dis 2009;15:1823-6.

[8] Ross AG, Vickers D, Olds GR, Shah SM, McManus DP. Katayama syndrome. Lancet Infect Dis 2007;7:218-24.

[9] Wynn TA, Thompson RW, Cheever AW, Mentink-Kane MM. Immunopathogenesis of schistosomiasis. Immunol Rev 2004;201:156-67.

[10] Burke ML, Jones MK, Gobert GN, Li YS, Ellis MK, McManus DP. Immunopathogenesis of human schistosomiasis. Parasite Immunol 2009;31:163-76.

[11] Carod-Artal FJ. Neurological complications of Schistosoma infection. Trans R Soc Trop Med Hyg 2008;102:107-16.

[12] Ferrari TC. Involvement of the central nervous system in the schistosomiasis. Mem Inst Oswaldo Cruz 2004;99:59-62.

[13] McManus DP, Gray DJ, Li YS, Feng Z, Williams GM, Stewart D, et al. Schistosomiasis in the Peoples' Republic of China: the era of the Three Gorges Dam. Clinic Microbiol Rev 2010;23:442-66.

[14] Katz N, Chaves A, Pellegrino J. A simple device for quantitative stool thick-smear technique for schistosomiasis mansoni. Rev Inst Med Trop Sao Paulo 1972;14:397-400.

[15] Oliveira LM, Santos HL, Gonçalves MM, Barreto MG, Peralta JM. Evaluation of polymerase chain reaction as an additional tool for the diagnosis of low-intensity Schistosoma mansoni infection. Diagn Microbiol Infect Dis 2010;68:416-21.

[16] Wichmann D, Panning M, Quack T, Kramme S, Burchard GD, Grevelding C, Drosten C. Diagnosing schistosomiasis by detection of cell-free parasite DNA in human plasma. PLoS Negl Trop Dis 2009;3:e422.

[17] Gomes LI, Dos Santos Marques LH, Enk MJ, de Oliveira MC, Coelho PM, Rabello A. Development and evaluation of a sensitive PCR-ELISA system for detection of Schistosoma infection in feces. PLoS Negl Trop Dis 2010;4:e664.

[18] Ellis MK, Li Y, Hou X, Chen H, McManus DP. sTNFR-II and sICAM-1 are associated with acute disease and hepatic inflammation in schistosomiasis japonica. Int J Parasitol 2008;38:717-23.

[19] Bergquist R, Johansen MV, Utzinger J. Diagnostic dilemmas in helminthology: what tools to use and when? Trends Parasitol 2009;25:151-6.

[20] Chand MA, Chiodini PL, Doenhoff MJ. Development of a new assay for the diagnosis of schistosomiasis, using cercarial antigens. Trans R Soc Trop Med Hyg 2010;104:255-8.

[21] Stothard JR, Sousa-Figueiredo JC, Standley C, Van Dam GJ, Knopp S, Utzinger J, et al. An evaluation of urine-CCA strip test and fingerprick blood SEA-ELISA for detection of urinary schistosomiasis in schoolchildren in Zanzibar. Acta Trop 2009;111:64-70.

[22] Doenhoff MJ, Cioli D, Utzinger J. Praziquantel: mechanisms of action, resistance and new derivatives for schistosomiasis. Curr Opin Infect Dis 2008;21:659-67. [PubMed]

[23] Cioli D, Pica-Mattoccia L. Praziquantel. Parasitol Res 2003;90:S3-S9. [PubMed]

[24] Hou XY, McManus DP, Gray DJ, Balen J, Luo XS, He YK, et al. A randomized, double-blind, placebo-controlled trial of safety and efficacy of combined praziquantel and artemether treatment for acute

[25] "Edwin Smith Papyrus". Retrieved 2015-02-28.

[26] H. F. J. Horstmanshoff, Marten Stol, Cornelis Tilburg (2004), Magic and Rationality in Ancient Near Eastern and Graeco-Roman Medicine, p. 97-98, Brill Publishers, ISBN 90-04-13666-5.

[27] Jingfeng, C. (2008). "Medicine in China". Encyclopaedia of the History of Science, Technology, and Medicine in Non-Western Cultures. pp. 1529–1534. doi:10.1007/978-1-4020-4425-0_8500. ISBN 978-1-4020-4559-2.

[28] "What Would Hipocrates Do?". Retrieved February 28, 2015.

[29] Ross AGP, Bartley PB, Sleigh AC, Olds GR, Li Y, Williams GM, McManus DP. Schistosomiasis. N Eng J Med 2002;346:1212-9.

[30] Gryseels B, Polman K, Clerinx J, Kestens L. Human schistosomiasis. Lancet 2006;368:1106-18.

[31] Steinmann P, Keiser J, Bos R, Tanner M, Utzinger J. Schistosomiasis and water resources development: systematic review, meta-analysis, and estimates of people at risk. Lancet Infect Dis 2006;6:411-25.

[32] King CH, Dickman K, Tisch DJ. Reassessment of the cost of chronic helminthic infection: a meta-analysis of disability-related outcomes in endemic schistosomiasis. Lancet 2005;365:561-9.

[33] Weingart SN, Wilson RM, Gibberd RW, Harrison B; Wilson; Gibberd; Harrison (March 2000). "Epidemiology of medical error". *BMJ*. **320** (7237): 774–7. doi:10.1136/bmj.320.7237.774. PMC 1117772 . PMID 10720365

[34] Gardner, Amanda (6 March 2007). "Medication Errors During Surgeries Particularly Dangerous". The Washington Post. Retrieved 2007-03-13.

[35] US Agency for Healthcare Research & Quality (2008-01-09). "Physicians Want To Learn from Medical Mistakes but Say Current Error-reporting Systems Are Inadequate". Retrieved 2008-03-23.

[36] Institute of Medicine (2000). *To Err Is Human: Building a Safer Health System*. Washington, DC: The National Academies Press. doi:10.17226/9728. ISBN 978-0-309-26174-6

SOCIETY FOR SCIENCE AND EDUCATION UNITED KINGDOM

JBEMi JOURNAL OF BIOMEDICAL ENGINEERING AND MEDICAL IMAGING

ISSN: 2055-1266
VOLUME 5 ISSUE 4

Application of Artificial Neural Network to Live Predict Brain Lesions like Multiple Sclerosis, Glioma, Glioblastoma and Metastases and Superiority of Refractive Index Over other Parameters

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ABSTRACT

Artificial Neural Network an extremely authoritative method of Supervised Machine Learning was applied to detect the different pathological lesions in the brain, like multiple sclerosis MS, glioma of different grades and metastasis. Structural changes in the brain lesions may be noticed in MR images. MR spectroscopic graph may be informative to some extent but is not so easy to diagnose the disease accurately always. Use of ANN helps identifying the condition in doubtful cases. ANN train different data collected from various patients such as – Refractive Index, T2 relaxation values, Apparent Diffusion Coefficient (ADC), Creatine (CR), Choline (CHO), NAA (N-Acetyl Aspartate), ratio of CR/NAA, LIP/LAC (Lipid/lactate), MI (Myoinositol), CHO/CR and T2 value in the periphery of lesion. Prediction by ANN after training the data, shows high accuracy in diagnosis. RI was found to be unique and most accurate amongst these parameters.

Keywords: Artificial Neural Network (ANN); Magnetic Resonance Imaging (MRI); Metabolites of MR Spectroscopy; Refractive Index (RI); Independent Numeric and dependent Variable; Prediction.

1 Introduction

For proper treatment of different brain lesions correct diagnosis is needed. Tissue discrimination is not possible by noting the morbid changes in the MR images only without performing a brain biopsy (Figure1) [1,2]. Glioma in different stages, Glioblastoma, metastasis from primary cancer site and benign diseases like multiple sclerosis (relapsing remitting or tumefactive multiple sclerosis) sometimes create confusion [2]. Even MR Spectroscopy (MRS) fails to detect the exact character of the lesion from the graph generated by the peak of different metabolites along with the quantity [3,4].

1.1 Artificial Neural Network (ANN)

Live prediction of the lesions or characterization of the tissue is possible by data analyzing method of ANN [5]. From the prior research work of the authors [6-8] data like Refractive indices (RI) , T2 relaxation and Apparent Diffusion Coefficient (ADC) values determined from the MRI and different

DOI: 10.14738/jbemi.54.4919
Publication Date: 29th July 2018
URL: http://dx.doi.org/10.14738/jbemi. 54.4919

chemical metabolites available from the MRS like N Acetyl Aspertate (NAA), Choline (CHO),Creatine(CR), Lipid (Li), Lactate (La) Myoinisitol(MI) along with ratio of these metabolites have been tabulated [4]. These data were used as input for ANN to get output value or prediction of lesions [6-10].

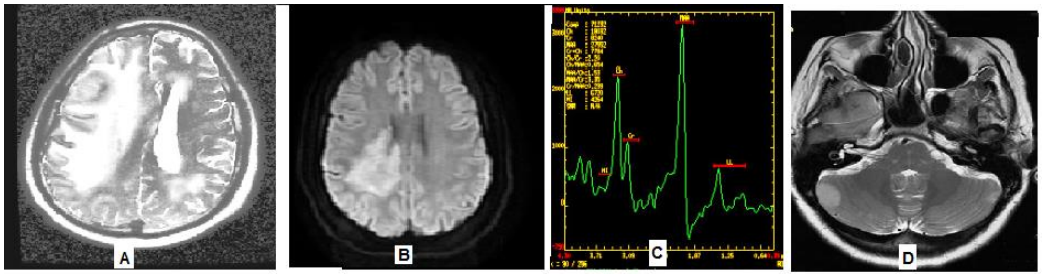


Figure 1. a-Glioblastoma b. Diffusion weighted image of Tumefactive MS mimicking Tumor c. MRS of MS. d. Lesion in the right cerebellar hemisphere-diagnosed as metastasis, biopsy shows benign lesion.

2 Background of ANN

ANN, one of the important strategies of Supervised Machine Learning was implemented as data analyzing method for live prediction of diseases [11]. In the Excel spread sheet the data collected were tabulated as inputs column (**Independent numeric variables**) and rows and **Dependent variable** to be predicted as disease or different tissues in the extreme left of the column. If the supporting data are available ANN can predict the diseases 95 to 98% correctly [12]. Program of Neural network includes artificial intelligence to analyze the data by applying algorithms that replicate basic brain neuronal (cortical cell) functions to study the structure of data and to discriminate data patterns [13] . This is regarded as training of the Data Set. New information then can be utilized by the program of ANN to predict the output of problems using "untrained data".

2.1 Prediction by ANN

PNN or Probabilistic Neural Network technique is a nonlinear method with training of a category dependent variables. A Probabilistic Neural Net will be trained. A "node" represents the element of the NET of the training case [10]. A prediction for a case with unknown dependent value is obtained by interpolation from training cases with neighbouring cases giving more weight after dividing the data set into training and testing subsets[11-14].

Optimal interpolation parameters were found during training [11]. It was implemented to assess the virtual pathological condition from the data obtained. ANN having amazing exceptionality in data analyzing and handling skill, nonlinearity and knowledge of simplification, was used to characterize or to classify the disease [8, 9]. Therefore multiple input nodes (ten) or independent numeric variables were used.

ANN represents one layer (hidden) having ten nodes [10]. It has output of 7 different nodes of brain tissue (such as gray and white matters, CSF) and diseases (or pathological abnormalities). These diseases were MS, low and high grade glioma and metastasis. By running the predict command specifies settings for predicting values were used with a trained neural net [11,12].

The data like T2 relaxation value, ADC values, metabolites generated directly from the MR Magnet and RI value determined by the Abbey Refractometer would be used as inputs. Output is the Dependent

numeric variables like diseases and tissues [6]. A schematic diagram is given in the Figure2 about the independent numeric variable and Dependent numeric variable [6, 9].

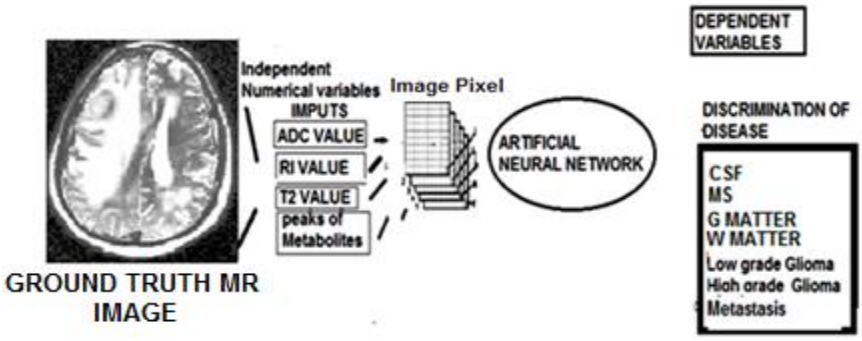


Figure 2. ANN for live prediction of diseases as Dependent variables using independent numerical variables as inputs [Ref 6].

2.2 To recapitulate the inputs and outputs [6]

2.2.1 Independent variables as inputs:

RI values ,T2 value ,ADC value ,Quantities of metabolites , (Choline,Creatine,MI ,NAA, Lipid/ lactate)

Ratio of Choline NAA ,Ratio of Creatine NAA,Ratio of Cho Cr

2.2.2 To live predict (Output or decision) :

Diseases like MS, Glioma, Glioblastoma (Grade III/IV Astrocytoma), metastasis and tissues like Gray /white matters, CSF are regarded as dependent variables [6,9].

3 Methods

After taking proper institutional ethics, 137 patients of different age (from 7 to 81 years) and gender were examined in a 3 Tesla MR Magnet (SIGNA HDxt, GE,USA). Materials collected from the Stereotaxic and post surgery biopsies were sent for histo-pathological diagnosis. At the same time following sets data or parameters were collected:

3.1 Parameters

3.1.1 RI Values

RI of tissues collected from biopsies of brain materials were determined by Abbe Refractometer (Suprashes Model AAR-33, India)[6-8]. RI map of a T2 weighted image (Figure 3.f) can be generated from the T2 values from a linear relationship between them. RI =4.338 X1/T2 value + 1.3338 [6,8].

3.1.2 T2 Relaxation Values

In the said 3T MR, T2 mapping was done with the help of multi ECHO read out train (with different echo times 30,60,90,120,150,180ms respectively) keeping a TR of 4000ms.T2 relaxation value of various brain tissue and brain lesions were generated from the map by exploiting the formula:

$S=S_0\, e^{-TE/T2}$ [8]. T2 map was thus generated by the inbuilt program (tool) of the MR Scanner. By placing the cursor in the Region of Interest (ROI), T2 values of the gray/white matter, CSF and tumours were determined from the T2 map as well [6] (Figure 3a). T2 values within the tumour and in the perilesional edema was also noted [6].

3.1.3 ADC (APPARENT DIFFUSION COEFFICIENT)

By making ADC map in the MR magnet, ADC values of the tissues are measured applying Stejstal-Tanner Equation $S=S_0e^{(-b.ADC)}$, which measure rate of diffusion of water within the tissues in units of mm^2/sec (Figure3c) . The ***b-value*** is a factor that reflects the strength and timing of the gradients used to generate diffusion-weighted images. S is the signal intensity [6,9,10] (Figure3b).

3.1.4 Metabolites Quantification of MR Spectroscopy (MRS)

Quantification of metabolites like CHO,CR,NAA,MI, Lipid, Lactate, CHO NAA,CHO CR and CHO NAA ratio were determined by single or multi voxel Spectroscopy applying PRESS technique. TR- 9602 and TE-35 to 144ms were used [3,4,6,9] (Figure3d)

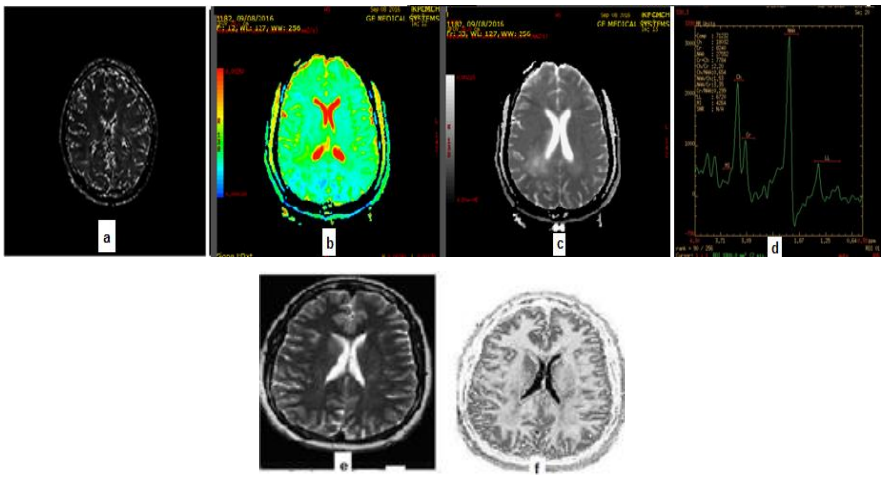


Figure 3a. T2 Mapping b. ADC Mapping c. DWI image d. MRS showing quantification of metabolites e. T2W and f. RI mapping of Brain

The values were then tabulated (Table1) in the Excel Spread Sheet for the application of **NEURAL TOOL 7.5** (Palisade Inc. UK). Column A to K represents independent variables and L depicts dependent variable or diseases.

3.1.5 Ground Truth MR Input Image

Therefore a **Ground Truth MR image** contains information like RI values (derived from RI mapping), T2 values (from T2 mapping) and ADC values (from ADC mapping) and metabolites from the MRS quantification (Table1) [6,7].

TABLE 1. Data of RI, T2, ADC Value,CHO, CR, CR/ NAA,CHO/NAA,CH/CR from Column A to K as Independent Variable and column L represent Dependent variable as Diseases . A column has influence on the L column or disease/tissues outcome

	A	B	C	D	E	F	G	H	I	J	K	L
1	RI	T2	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
2	1.3333	400	1010	300	1400	0.346	1400	910	1.13	400	0.402	CSF
3	1.3334	395	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF
4	1.3335	390	1700	330	1967	0.389	1600	1076	1.15	390	0.432	CSF
5	1.3336	384	1890	340	1989	0.411	1675	1080	1.14	384	0.498	CSF
6	1.3421	340	11750	145	8320	0.557	4160	2912	1.40	240	0.779	MS
7	1.3439	328	8904	135	2800	0.433	4490	5576	3.15	241	1.39	MS
8	1.3498	316	7896	124	4560	0.225	3570	3536	1.73	243	0.389	MS
9	1.3497	304	5947	120	5400	0.7396	6766	4294	1.1	245	0.389	MS
10	1.3589	249	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	MS
11	1.3641	245	1610	73	2212	0.941	1440	364	0.495	227	0.465	MS
12	1.3956	130	1601	76	2209	0.938	1441	363	0.491	166	0.461	g.matter
13	1.3956	125	1601	77	2208	0.937	1440	362	0.491	168	0..460	g.matter
14	1.3957	123	1589	78	2219	0.941	1467	345	0.491	167	0.459	g.matter
15	1.3952	121	1458	80	2320	0.878	1443	321	0.494	169	0.456	g.matter
16	1.4251	95	1180	70	2443	0.788	1345	312	0.488	148	0.453	w.matter
17	1.4256	89	1108	71	2435	0.771	1341	320	0.468	146	0.447	w.matter
18	1.4259	85	1098	77	2387	0.774	1211	321	0.467	150	0.445	w.matter
19	1.3741	160	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema
20	1.3823	182	1331	180	2321	0.787	1011	321	0.456	243	0.442	edema
21	1.3821	182	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema
22	1..3822	184	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema
23	1.4331	90	1443	127	2243	0.766	989	310	0.423	175	0.431	GLIOMA
24	1.4446	99	1.365	177	2254	0.712	917	300	0.343	170	0.341	GLIOMA
25	1.4551	110	2655	156	2112	0.678	900	311	0.311	195	0.332	G.BLASTOMA
26	1.4512	116	2774	142	3280	1.06	2240	312	0.844	190	0.907	G.BLASTOMA
27	1.4562	118	2661	140	3189	1.02	2134	314	0.7881	185	0.89	G.BLASTOMA
28	1.4611	123	1281	139	2998	1.01	2098	316	0.7662	175	0.876	G.BLASTOMA
29	1.4768	135	1321	127	2532	0.654	1011	340	0.432	200	0.432	METS
30	1.4834	147	1388	139	2211	0.667	1021	341	0.445	219	0.411	METS
31	1.4911	151	1411	131	2019	0.713	119	356	0.449	223	0.423	METS

NOTE: MS= Multiple sclerosis g. matter-Gray Matter w. matter=White matter

G BLASTOMA= Glioblastoma METS= Metastases

3.2.1. Neural Network [11,12,13,14]

Trial version of Neural Tool 7.5 (Palisade Inc) was applied to perform the prediction. The method of working of the Neural Tool is shown in the Figure.4.

1. In the Excel spread sheet the values derived from the ground truth MR images are tabulated (Table 1) in such a way that the Dependent Variables (disease or tissues) remain in the extreme left column (L column) and Independent Numeric variable (Usually RI, T2, ADC values, Choline : NAA ratio etc) in the right side of the column (A through K).The efficacy of the parameter in the A column clearly influences the accuracy of prediction rate.

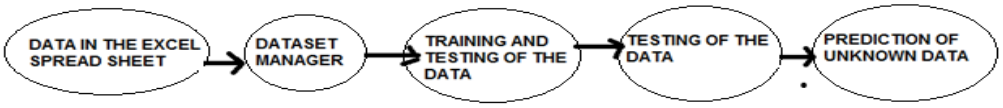


Figure 4. Steps of events occuring in Neural net work

3.2.2 A **data set manager** was created from the values tabulated in the excel spread sheet (Figure 5).

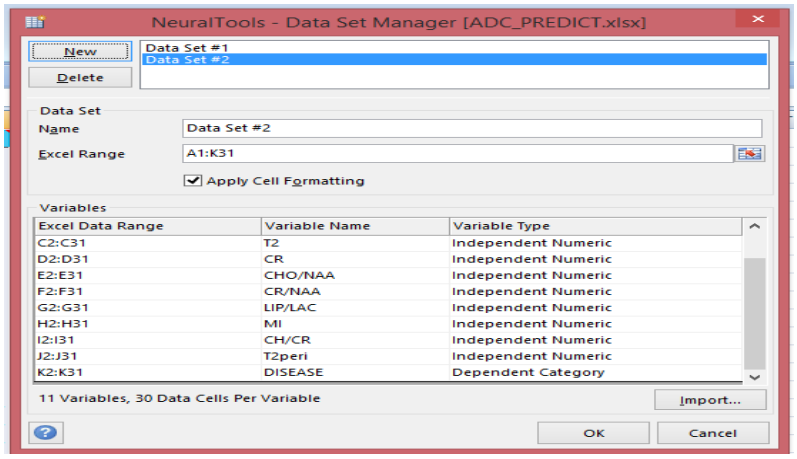
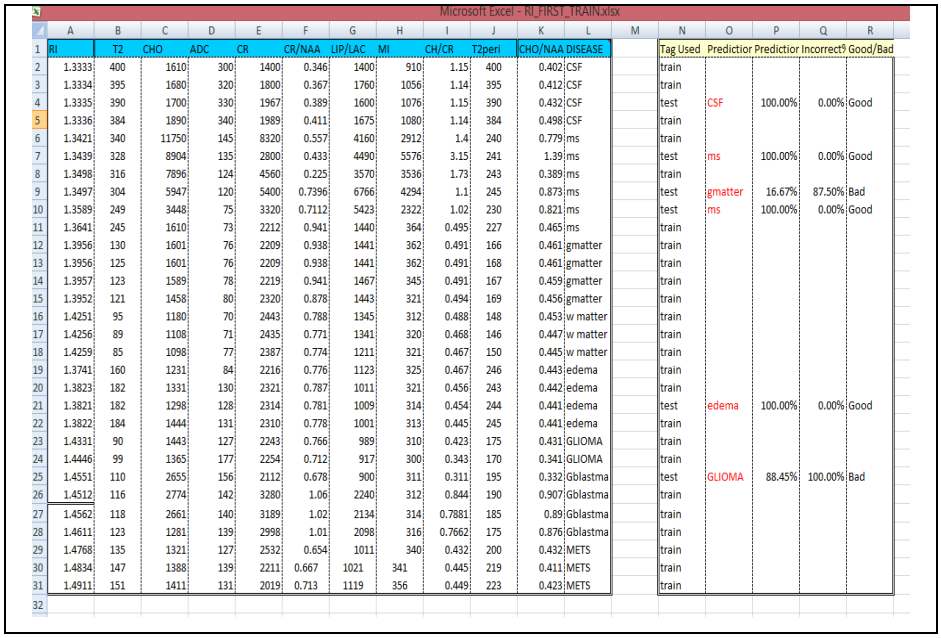


Figure 5. Data set manager [13].

3.2.3. Training and Testing

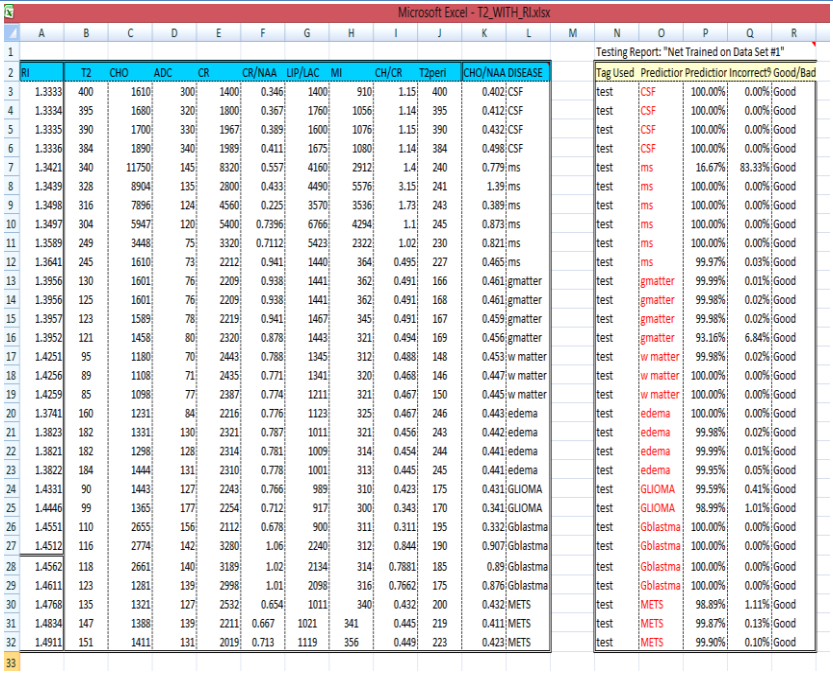
Training and testing of the data of the table were executed keeping RI, T2, ADC values, CHO, CHO /CR, CHO / NAA ratio one by one in the "**A"** column (Extreme right side of the table) and running the NET to assess the effectiveness of the parameters as efficacy of the parameters may vary (Figure 6 and 7). 12 independent variables (Table 2) of different parameters were kept away from the training.



Microsoft Excel - RI_FIRST_TRAIN.xlsx

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1	RI	T2	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE		Tag Used	Predictior	Predictior	Incorrect%	Good/Bad
2	1.3333	400	1610	300	1400	0.346	1400	910	1.15	400	0.402	CSF		train				
3	1.3334	395	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF		train				
4	1.3335	390	1700	330	1967	0.389	1600	1076	1.15	390	0.432	CSF		test	CSF	100.00%	0.00%	Good
5	1.3336	384	1890	340	1989	0.411	1675	1080	1.14	384	0.498	CSF		train				
6	1.3421	340	11750	145	8320	0.557	4160	2912	1.4	240	0.779	ms		train				
7	1.3439	328	8904	135	2800	0.433	4490	5576	3.15	241	1.39	ms		test	ms	100.00%	0.00%	Good
8	1.3498	316	7896	124	4560	0.225	3570	3536	1.73	243	0.389	ms		train				
9	1.3497	304	5947	120	5400	0.7396	6766	4294	1.1	245	0.873	ms		test	gmatter	16.67%	87.50%	Bad
10	1.3589	249	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	ms		test	ms	100.00%	0.00%	Good
11	1.3641	245	1610	73	2212	0.941	1440	364	0.495	227	0.465	ms		train				
12	1.3956	130	1601	76	2209	0.938	1441	362	0.491	166	0.461	gmatter		train				
13	1.3956	125	1601	76	2209	0.938	1441	362	0.491	168	0.461	gmatter		train				
14	1.3957	123	1589	78	2219	0.941	1467	345	0.491	167	0.459	gmatter		train				
15	1.3952	121	1458	80	2320	0.878	1443	321	0.494	169	0.456	gmatter		train				
16	1.4251	95	1180	70	2443	0.788	1345	312	0.488	148	0.453	w matter		train				
17	1.4256	89	1108	71	2435	0.771	1341	320	0.468	146	0.447	w matter		train				
18	1.4259	85	1098	77	2387	0.774	1211	321	0.467	150	0.445	w matter		train				
19	1.3741	160	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema		train				
20	1.3823	182	1331	130	2321	0.787	1011	321	0.456	243	0.442	edema		train				
21	1.3821	182	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema		test	edema	100.00%	0.00%	Good
22	1.3822	184	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema		train				
23	1.4331	90	1443	127	2243	0.766	989	310	0.423	175	0.431	GLIOMA		train				
24	1.4446	99	1365	177	2254	0.712	917	300	0.343	170	0.341	GLIOMA		train				
25	1.4551	110	2655	156	2112	0.678	900	311	0.311	195	0.332	Gblastma		test	GLIOMA	88.45%	100.00%	Bad
26	1.4512	116	2774	142	3280	1.06	2240	312	0.844	190	0.907	Gblastma		train				
27	1.4562	118	2661	140	3189	1.02	2134	314	0.7881	185	0.89	Gblastma		train				
28	1.4611	123	1281	139	2998	1.01	2098	316	0.7662	175	0.876	Gblastma		train				
29	1.4768	135	1321	127	2532	0.654	1011	340	0.432	200	0.432	METS		train				
30	1.4834	147	1388	139	2211	0.667	1021	341	0.445	219	0.411	METS		train				
31	1.4911	151	1411	131	2019	0.713	1119	356	0.449	223	0.423	METS		train				
32																		

Figure 6. Screen shot image of Neural Tool data viewer showing training and testing of the data along with Training Report :Prediction accuracy with Good or Bad remark.



RI	T2	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
1.3333	400	1610	300	1400	0.346	1400	910	1.15	400	0.402	CSF
1.3334	395	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF
1.3335	390	1700	330	1967	0.389	1600	1076	1.15	390	0.432	CSF
1.3336	384	1890	340	1989	0.411	1675	1080	1.14	384	0.498	CSF
1.3421	340	11750	145	8320	0.557	4160	2912	1.4	240	0.779	ms
1.3439	328	8904	135	2800	0.433	4490	5576	3.15	241	1.39	ms
1.3498	316	7896	124	4560	0.225	3570	3536	1.73	243	0.389	ms
1.3497	304	5947	120	5400	0.7396	6766	4294	1.1	245	0.873	ms
1.3589	249	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	ms
1.3641	245	1610	73	2212	0.941	1440	364	0.495	227	0.465	ms
1.3956	130	1601	76	2209	0.938	1441	362	0.491	166	0.461	gmatter
1.3956	125	1601	76	2209	0.938	1441	362	0.491	168	0.461	gmatter
1.3957	123	1589	78	2219	0.941	1467	345	0.491	167	0.459	gmatter
1.3952	121	1458	80	2320	0.878	1443	321	0.494	169	0.456	gmatter
1.4251	95	1180	70	2443	0.788	1345	312	0.488	148	0.453	w matter
1.4256	89	1108	71	2435	0.771	1341	320	0.468	146	0.447	w matter
1.4259	85	1098	77	2387	0.774	1211	321	0.467	150	0.445	w matter
1.3741	160	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema
1.3823	182	1331	130	2321	0.787	1011	321	0.456	243	0.442	edema
1.3821	182	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema
1.3822	184	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema
1.4331	90	1443	127	2243	0.766	989	310	0.423	175	0.431	GLIOMA
1.4446	99	1365	177	2254	0.712	917	300	0.343	170	0.341	GLIOMA
1.4551	110	2655	156	2112	0.678	900	311	0.311	195	0.332	Gblastma
1.4512	116	2774	142	3280	1.06	2240	312	0.844	190	0.907	Gblastma
1.4562	118	2661	140	3189	1.02	2134	314	0.7881	185	0.89	Gblastma
1.4611	123	1281	139	2998	1.01	2098	316	0.7662	175	0.876	Gblastma
1.4768	135	1321	127	2532	0.654	1011	340	0.432	200	0.432	METS
1.4834	147	1388	139	2211	0.667	1021	341	0.445	219	0.411	METS
1.4911	151	1411	131	2019	0.713	1119	356	0.449	223	0.423	METS

Tag Used	Predictior	Predictior	Incorrect%	Good/Bad
test	CSF	100.00%	0.00%	Good
test	CSF	100.00%	0.00%	Good
test	CSF	100.00%	0.00%	Good
test	CSF	100.00%	0.00%	Good
test	ms	16.67%	83.33%	Good
test	ms	100.00%	0.00%	Good
test	ms	100.00%	0.00%	Good
test	ms	100.00%	0.00%	Good
test	ms	100.00%	0.00%	Good
test	ms	99.97%	0.03%	Good
test	gmatter	99.99%	0.01%	Good
test	gmatter	99.98%	0.02%	Good
test	gmatter	99.98%	0.02%	Good
test	gmatter	93.16%	6.84%	Good
test	w matter	99.98%	0.02%	Good
test	w matter	100.00%	0.00%	Good
test	w matter	100.00%	0.00%	Good
test	edema	100.00%	0.00%	Good
test	edema	99.98%	0.02%	Good
test	edema	99.99%	0.01%	Good
test	edema	99.95%	0.05%	Good
test	GLIOMA	99.59%	0.41%	Good
test	GLIOMA	98.99%	1.01%	Good
test	Gblastma	100.00%	0.00%	Good
test	Gblastma	100.00%	0.00%	Good
test	Gblastma	100.00%	0.00%	Good
test	Gblastma	100.00%	0.00%	Good
test	METS	98.89%	1.11%	Good
test	METS	99.87%	0.13%	Good
test	METS	99.90%	0.10%	Good

Figure 7. Screen shot image of Neural Tool data viewer showing testing of the data along with Testing Report: Prediction accuracy as Good or Bad remark.

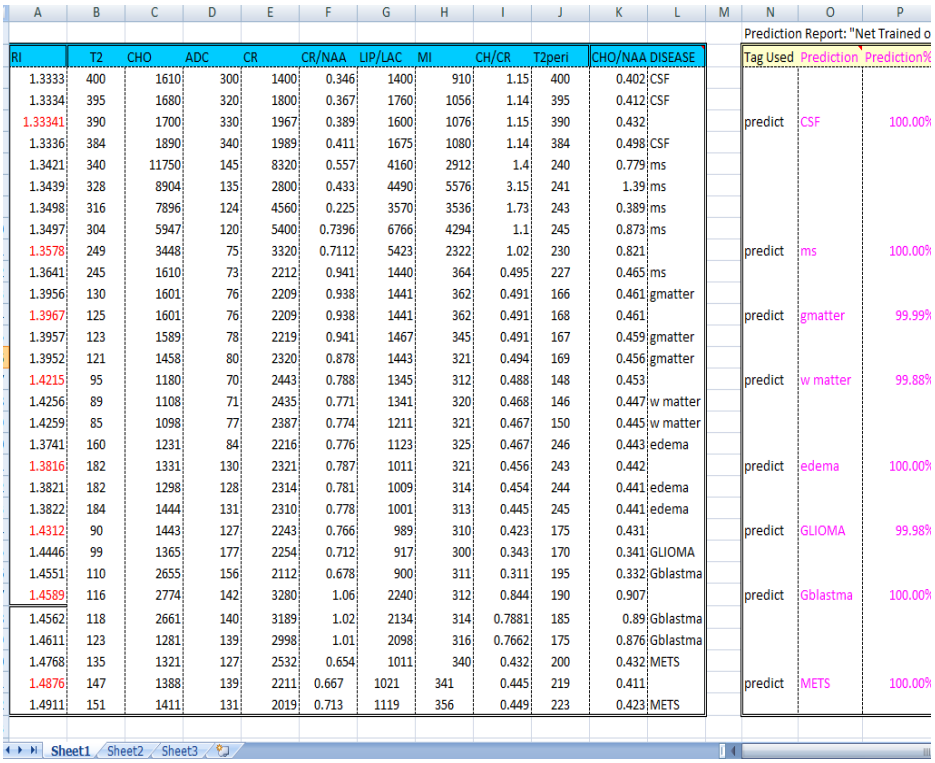
3.2.4. Prediction

After training and testing**,** untrained values (Table2) of RI,T2,ADC or metabolites of various diseases and tissues were put into the Column A one by one and net was run for prediction.

TABLE 2. Untrained Variables (in Red) to be used in the A column one after another to note the prediction accuracy.

T2	RI	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
387	1.33345	1704	333	1976	0.388	1589	1078	1.47	387	0.423	CSF
384	1.3338	1878	332	1987	0.414	1675	1084	1.42	378	0.489	CSF
331	1.3482	8878	134	2878	0.432	4491	5478	3.15	241	1.88	ms
311	1.3441	5975	122	5401	0.7389	6756	4289	1.11	244	0.874	ms
233	1.3611	1613	74	2211	0.913	1439	359	0.487	226	0.461	ms
119	1.387	1589	78	2219	0.941	1467	345	0.491	167	0.459	gmatter
87	1.4312	1154	74	2431	0.772	1342	319	0.479	144	0.441	wmatter
179	1.3823	1331	132	2315	0.777	1019	320	0.456	241	0.4429	edema
88	1.4321	1441	127	2231	0.775	978	311	0.421	177	0.432	glioma
100	1.4456	1323	167	2251	0.713	915	300	0.342	170	0.334	glioma
119	1.4566	2656	141	3178	1.03	2133	315	0.7868	182	0.887	gblastoma
141	1.4876	1320	129	2543	0.659	1011	332	0.435	210	0.431	mets

Prediction thus created by the Neural Tool was shown in the Figure 8a,b,c using different parameters like RI, T2 and ADC values and metabolites . To scrutinize the accuracy (percentage) of Prediction "untrained data set" of different variable in this Column **A** was tried one by one.

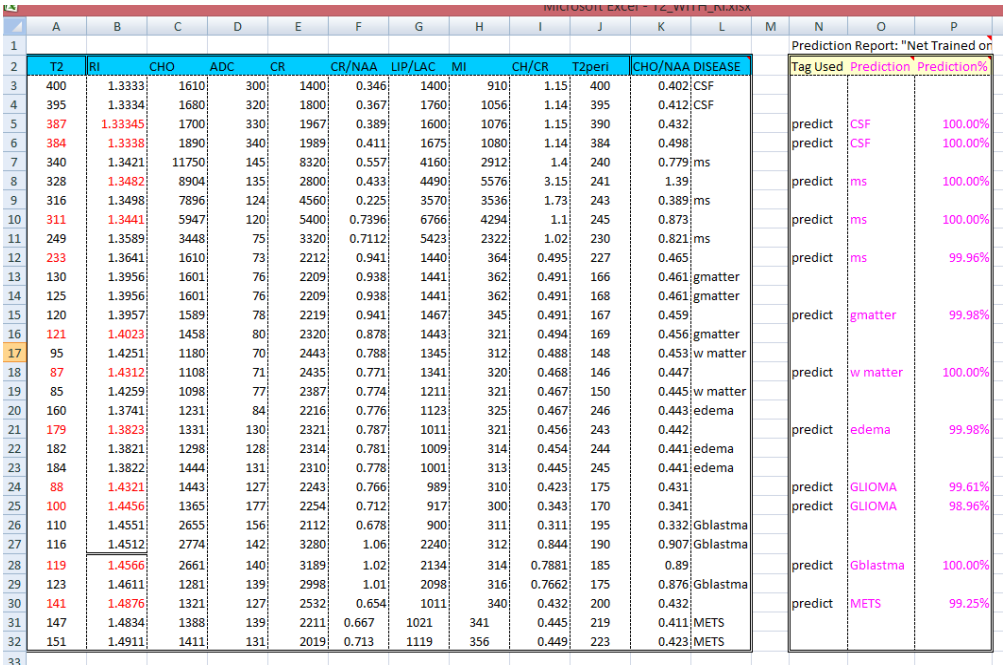


RI	T2	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
1.3333	400	1610	300	1400	0.346	1400	910	1.15	400	0.402	CSF
1.3334	395	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF
1.33341	390	1700	330	1967	0.389	1600	1076	1.15	390	0.432	
1.3336	384	1890	340	1989	0.411	1675	1080	1.14	384	0.498	CSF
1.3421	340	11750	145	8320	0.557	4160	2912	1.4	240	0.779	ms
1.3439	328	8904	135	2800	0.433	4490	5576	3.15	241	1.39	ms
1.3498	316	7896	124	4560	0.225	3570	3536	1.73	243	0.389	ms
1.3497	304	5947	120	5400	0.7396	6766	4294	1.1	245	0.873	ms
1.3578	249	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	
1.3641	245	1610	73	2212	0.941	1440	364	0.495	227	0.465	ms
1.3956	130	1601	76	2209	0.938	1441	362	0.491	166	0.461	gmatter
1.3967	125	1601	76	2209	0.938	1441	362	0.491	168	0.461	
1.3957	123	1589	78	2219	0.941	1467	345	0.491	167	0.459	gmatter
1.3952	121	1458	80	2320	0.878	1443	321	0.494	169	0.456	gmatter
1.4215	95	1180	70	2443	0.788	1345	312	0.488	148	0.453	
1.4256	89	1108	71	2435	0.771	1341	320	0.468	146	0.447	w matter
1.4259	85	1098	77	2387	0.774	1211	321	0.467	150	0.445	w matter
1.3741	160	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema
1.3816	182	1331	130	2321	0.787	1011	321	0.456	243	0.442	
1.3821	182	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema
1.3822	184	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema
1.4312	90	1443	127	2243	0.766	989	310	0.423	175	0.431	
1.4446	99	1365	177	2254	0.712	917	300	0.343	170	0.341	GLIOMA
1.4551	110	2655	156	2112	0.678	900	311	0.311	195	0.332	Gblastma
1.4589	116	2774	142	3280	1.06	2240	312	0.844	190	0.907	
1.4562	118	2661	140	3189	1.02	2134	314	0.7881	185	0.89	Gblastma
1.4611	123	1281	139	2998	1.01	2098	316	0.7662	175	0.876	Gblastma
1.4768	135	1321	127	2532	0.654	1011	340	0.432	200	0.432	METS
1.4876	147	1388	139	2211	0.667	1021	341	0.445	219	0.411	
1.4911	151	1411	131	2019	0.713	1119	356	0.449	223	0.423	METS

Prediction Report: "Net Trained o

Tag Used	Prediction	Prediction%
predict	CSF	100.00%
predict	ms	100.00%
predict	gmatter	99.99%
predict	w matter	99.88%
predict	edema	100.00%
predict	GLIOMA	99.98%
predict	Gblastma	100.00%
predict	METS	100.00%

Figure8a. Screen shot image of Neural Tool data viewer showing Prediction using RI in the Column A.

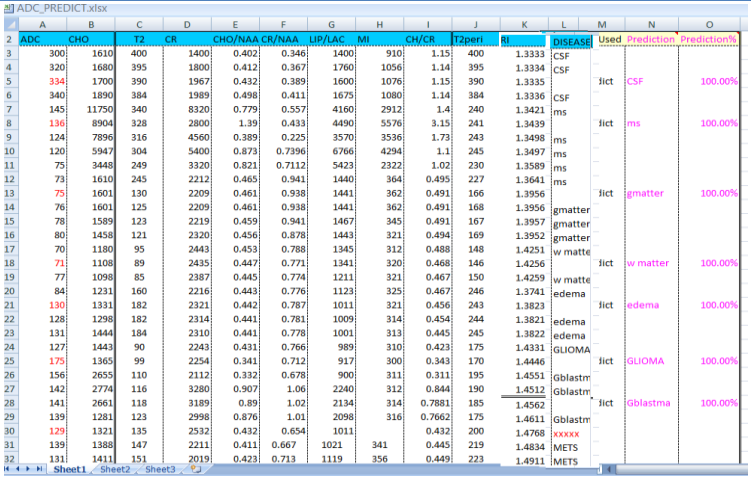


T2	RI	CHO	ADC	CR	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	CHO/NAA	DISEASE
400	1.3333	1610	300	1400	0.346	1400	910	1.15	400	0.402	CSF
395	1.3334	1680	320	1800	0.367	1760	1056	1.14	395	0.412	CSF
387	1.33345	1700	330	1967	0.389	1600	1076	1.15	390	0.432	
384	1.3338	1890	340	1989	0.411	1675	1080	1.14	384	0.498	
340	1.3421	11750	145	8320	0.557	4160	2912	1.4	240	0.779	ms
328	1.3482	8904	135	2800	0.433	4490	5576	3.15	241	1.39	
316	1.3498	7896	124	4560	0.225	3570	3536	1.73	243	0.389	ms
311	1.3441	5947	120	5400	0.7396	6766	4294	1.1	245	0.873	
249	1.3589	3448	75	3320	0.7112	5423	2322	1.02	230	0.821	ms
233	1.3641	1610	73	2212	0.941	1440	364	0.495	227	0.465	
130	1.3956	1601	76	2209	0.938	1441	362	0.491	166	0.461	gmatter
125	1.3956	1601	76	2209	0.938	1441	362	0.491	168	0.461	gmatter
120	1.3957	1589	78	2219	0.941	1467	345	0.491	167	0.459	
121	1.4023	1458	80	2320	0.878	1443	321	0.494	169	0.456	gmatter
95	1.4251	1180	70	2443	0.788	1345	312	0.488	148	0.453	w matter
87	1.4312	1108	71	2435	0.771	1341	320	0.468	146	0.447	
85	1.4259	1098	77	2387	0.774	1211	321	0.467	150	0.445	w matter
160	1.3741	1231	84	2216	0.776	1123	325	0.467	246	0.443	edema
179	1.3823	1331	130	2321	0.787	1011	321	0.456	243	0.442	
182	1.3821	1298	128	2314	0.781	1009	314	0.454	244	0.441	edema
184	1.3822	1444	131	2310	0.778	1001	313	0.445	245	0.441	edema
88	1.4321	1443	127	2243	0.766	989	310	0.423	175	0.431	
100	1.4456	1365	177	2254	0.712	917	300	0.343	170	0.341	
110	1.4551	2655	156	2112	0.678	900	311	0.311	195	0.332	Gblastma
116	1.4512	2774	142	3280	1.06	2240	312	0.844	190	0.907	Gblastma
119	1.4566	2661	140	3189	1.02	2134	314	0.7881	185	0.89	
123	1.4611	1281	139	2998	1.01	2098	316	0.7662	175	0.876	Gblastma
141	1.4876	1321	127	2532	0.654	1011	340	0.432	200	0.432	
147	1.4834	1388	139	2211	0.667	1021	341	0.445	219	0.411	METS
151	1.4911	1411	131	2019	0.713	1119	356	0.449	223	0.423	METS

Prediction Report: "Net Trained or

Tag Used	Prediction	Prediction%
predict	CSF	100.00%
predict	CSF	100.00%
predict	ms	100.00%
predict	ms	100.00%
predict	ms	99.96%
predict	gmatter	99.98%
predict	edema	99.98%
predict	GLIOMA	99.61%
predict	GLIOMA	98.96%
predict	Gblastma	100.00%
predict	METS	99.25%

Figure 8b. Screen shot image of Neural Tool data viewer showing Prediction using T2 in the Column A.



ADC_PREDICT.xlsx

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
2	ADC	CHO	T2	CR	CHO/NAA	CR/NAA	LIP/LAC	MI	CH/CR	T2peri	RI	DISEASE	Used	Prediction	Prediction%
3	300	1610	400	1400	0.402	0.346	1400	910	1.15	400	1.3333	CSF			
4	320	1680	395	1800	0.412	0.367	1760	1056	1.14	395	1.3334	CSF			
5	334	1700	390	1967	0.432	0.389	1600	1076	1.15	390	1.3335		fict	CSF	100.00%
6	340	1890	384	1989	0.498	0.411	1675	1080	1.14	384	1.3336	CSF			
7	145	11750	340	8320	0.779	0.557	4160	2912	1.4	240	1.3421	ms			
8	136	8904	328	2800	1.39	0.433	4490	5576	3.15	241	1.3439		fict	ms	100.00%
9	124	7896	316	4560	0.389	0.225	3570	3536	1.73	243	1.3498	ms			
10	120	5947	304	5400	0.873	0.7396	6766	4294	1.1	245	1.3497	ms			
11	75	3448	249	3320	0.821	0.7112	5423	2322	1.02	230	1.3589	ms			
12	73	1610	245	2212	0.465	0.941	1440	364	0.495	227	1.3641	ms			
13	75	1601	130	2209	0.461	0.938	1441	362	0.491	166	1.3956		fict	gmatter	100.00%
14	76	1601	125	2209	0.461	0.938	1441	362	0.491	168	1.3956	gmatter			
15	78	1589	123	2219	0.459	0.941	1467	345	0.491	167	1.3957	gmatter			
16	80	1458	121	2320	0.456	0.878	1443	321	0.494	169	1.3952	gmatter			
17	70	1180	95	2443	0.453	0.788	1345	312	0.488	148	1.4251	w matte			
18	71	1108	89	2435	0.447	0.771	1341	320	0.468	146	1.4256		fict	w matter	100.00%
19	77	1098	85	2387	0.445	0.774	1211	321	0.467	150	1.4259	w matte			
20	84	1231	160	2216	0.443	0.776	1123	325	0.467	246	1.3741	edema			
21	130	1331	182	2321	0.442	0.787	1011	321	0.456	243	1.3823		fict	edema	100.00%
22	128	1298	182	2314	0.441	0.781	1009	314	0.454	244	1.3821	edema			
23	131	1444	184	2310	0.441	0.778	1001	313	0.445	245	1.3822	edema			
24	127	1443	90	2243	0.431	0.766	989	310	0.423	175	1.4331	GLIOMA			
25	175	1365	99	2254	0.341	0.712	917	300	0.343	170	1.4446		fict	GLIOMA	100.00%
26	156	2655	110	2112	0.332	0.678	900	311	0.311	195	1.4551	Gblastm			
27	142	2774	116	3280	0.907	1.06	2240	312	0.844	190	1.4512	Gblastm			
28	141	2661	118	3189	0.89	1.02	2134	314	0.7881	185	1.4562		fict	Gblastma	100.00%
29	139	1281	123	2998	0.876	1.01	2098	316	0.7662	175	1.4611	Gblastm			
30	129	1321	135	2532	0.432	0.654	1011		0.432	200	1.4768	xxxxx			
31	139	1388	147	2211	0.411	0.667	1021	341	0.445	219	1.4834	METS			
32	131	1411	151	2019	0.423	0.713	1119	356	0.449	223	1.4911	METS			

Sheet1 Sheet2 Sheet3

Figure 8c. Screen shot image of Neural Tool data viewer showing Prediction using ADC in the Column A.

4 Results and Discusion

4.1. It is evident that the 100 % prediction or characterization of tissue and pathological lesions when RI values are regarded as **independent numerical value** (in the column A) (Figure8 a). T2 also produces high accuracy. The prediction accuracy depends on the independent numeric variables or different physical or chemical parameters [6,13-16].

4.2. The NET depicts the statistical aspect of the prediction by RI in the Table 3. Minimum error was noted between 0.15 to 0.2 units. On the contrary, prediction is 20% to 60% in the context of ADC values (Figure8c) or Choline-Creatine ratio. Therefore the dataset had been trained in Neural Net and Auto tested in such a way that the wrong prediction reached the least amount and then the trained model data was run for testing (Table 3).

Table 3. Neural Tool : Net Training and auto testing

Location	This Workbook
Independent Category Variables	0
Independent Numeric Variables	**11 (RI, T2, CHO, ADC, CR, CR/NAA, LIP/LAC, MI, CH/CR, T2peri, CHO/NAA)**
Dependent Variable	Category Var. (DISEASE)
Training	
Number of Cases	24
Training Time	0:00:00
Number of Trials	108
Reason Stopped	Auto-Stopped
% Bad Predictions	0.0000%
Mean Incorrect Probability	0.0057%
Std. Deviation of Incorrect Prob.	0.0114%
Testing	
Number of Cases	6
% Bad Predictions	33.3333%
Mean Incorrect Probability	31.2500%
Std. Deviation of Incorrect Prob.	44.3412%
Data Set	
Name	Data Set #1
Number of Rows	30
Manual Case Tags	NO

4.3 Ten Fold Cross Validation

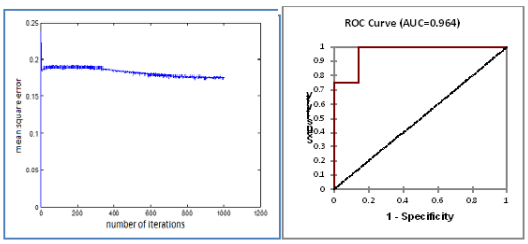
Cross-validation technique was adapted to evaluate predictive models by partitioning the original sample into a training set to train the model in relation to different samples of independent variable and a **test** set to evaluate it (Table4) [4,16,17].

10 fold cross validation method was used for wrong prediction, sensitivity and specificity and classification rate. The classification rate is quite high and very few blunders have been noticed in the prediction of test samples [11,12, 17]. Table 4 also discerns the consequent sensitivity and specificity. RI and T2 values produced the best results.

Table 4. Ten Fold Cross Validation [6]

Sample Number	In relation to different Independent Numeric variables	No. of incorrect Prediction (out of 24)	Classification Rate (in %)	Specificity (in%)	Sensitivity (in %)
1.	CR	4	83.33	86	78
2	CHO/NAA	3	87.5	91	76
3	T2 PERI	6	75.38	76.47	71.43
4	MI	4	83.33	87.5	75
5	RI	1	95.83	95	100
6	CHO/CR	3	87.52	85	100
7	ADC	3	87.55	88.89	83.33
8	T2	2	91.67	89.47	100
9	LIP/LAC	4	83.35	84.21	80
10	CHO	3	87.52	88.89	83.33

In most of the cases sensitivity is slightly lower than the specificity. However, in a few exceptional cases the sensitivity has reached 100% where all the diseased samples are identified. Hence, it can be concluded that the types of disease depend on RI and T2 values of the tissues, ADC values, metabolites like NAA, Choline, Creatine, Lipid and Lactate and their ratios [16,17]. From the Figure 9a it is noticed that the mean square error of the data during training decreases with iteration and finally becomes constant [6,17].



a b

Figure 9 a. Mean square error versus number of iteration b. Sensitivity versus specificity curve [6]

4.4 Pearson PHI(p Values)

Results derived from ANN was extracted statistically by **XLSTAT© (ADDINSOFT,** France**)** program to know "Correlation Tests" particularly of the continuous variables (for malignancies) and selected quantitative variables derived from the ground truth input images . **"p-values"** (Pearson Phi) [18] are shown in the Table 5a and b Figure 10.

Table5a. Correlations of the continuous variables (For malignancy) with the selected quantitative variables (Pearson's Phi) [6]:

Column2	Column3	Column4	Column5	Column6
Variable labels	Correlation coefficient	Test value	p-values	Variable labels
RI	0.687	4.261	0.000	RI
T2	-0.606	3.373	0.001	T2
MI	-0.249	0.750	0.230	MI
CH/CR	-0.247	0.741	0.233	CH/CR
LIP/LAC	-0.224	0.585	0.282	LIP/LAC
CR/NAA	0.210	0.495	0.313	CR/NAA
CHO	-0.116	-0.209	0.582	CHO
CR	-0.090	-0.443	0.669	CR
CHO/NAA	-0.064	-0.726	0.762	CHO/NAA
ADC	0.041	-1.043	0.846	ADC

Table 5.b p-values (Pearson)/ Group 1 Correlation test between the variables :

p-values (Pearson) / Group 1:

Variables	ADC	CHO	CR	CH/CR	CHO/NAA	CR/NAA	LIP/LAC	MI	RI	T2
ADC	**0**	0.861	0.733	0.599	0.600	0.603	0.687	0.221	0.557	0.508
CHO	0.861	**0**	0.469	0.485	0.447	0.509	0.401	0.292	0.176	0.240
CR	0.733	0.469	**0**	**0.010**	**0.011**	**0.010**	**0.005**	0.620	0.733	0.515
CH/CR	0.599	0.485	**0.010**	**0**	**0.001**	**0.000**	**0.009**	0.531	0.820	0.618
CHO/NAA	0.600	0.447	**0.011**	**0.001**	**0**	**0.003**	**0.006**	0.505	0.785	0.592
CR/NAA	0.603	0.509	**0.010**	**0.000**	**0.003**	**0**	**0.012**	0.551	0.841	0.632
LIP/LAC	0.687	0.401	**0.005**	**0.009**	**0.006**	**0.012**	**0**	0.538	0.693	0.500
MI	0.221	0.292	0.620	0.531	0.505	0.551	0.538	**0**	0.791	0.914
RI	0.557	0.176	0.733	0.820	0.785	0.841	0.693	0.791	**0**	0.052
T2	0.508	0.240	0.515	0.618	0.592	0.632	0.500	0.914	0.052	**0**
Values in bold are different from 0 with a significance level alpha=0.05										

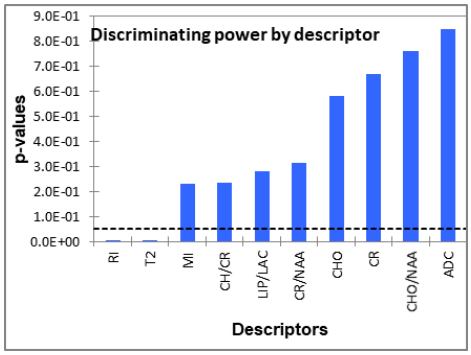
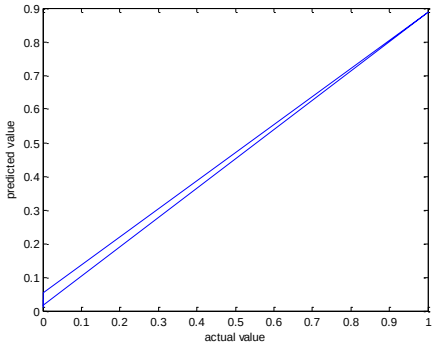


Figure10. p- values and discriminating power by descriptors[6]

4.5 Sensitivity and Specificity in ANN

From the results it has been found that Sensitivity is 87 to 89% whereas specificity is around 93 to 95%.From the various input data a presumptive diagnosis could be made which could be of immense help for the management of the patients [6] (Figure9b).



b

Figure 11. Actual versus predicted value in relation to RI [6]

4.6 Relationship of Predicted versus Actual Values

In this data set there are 240 samples. In this figure only one of them (RI—variable) has been plotted. The plot shows the number of prediction of disease (diagnosis) versus number of actual histopathological diagnosis from biopsy in the curve. Similar curves can be obtained for other samples as well. From the graph (Figure 11) it is observed that the actual and predicted values generate a straight slope.

5 Conclusion

ANN, an important data analytical process of Supervised Machine Learning method helps differentiating different disease process and brain tumors. To discriminate different issues in this regard, RI was regarded as superior to all other parameters like T2 values, ADC values and important metabolites and their ratio. Thus a presumptive diagnosis can be made from the Data derived from the ground tooth images before the biopsy. ANN can reduce the frequency of Stereotaxic Biopsy and its potential hazards to patients [19].

ACKNOWLEDGEMENT

We are thankful to the ISPUB (Internet Journal of Radiology) to kindly allow to use some data, phrases and facts of our previously published articles (Reference No 6,7,8,9). We also thank Palisade Inc (UK) and Addinsoft (France) for providing their free trial version.

REFERENCES

[1] Taghpour Zahir SH, Rezaei sadrabadi Dehghani F, *Evaluation of Diagnostic Value of CT Scan and MRI in Brain Tumors and Comparison with Biopsy*, Iranian Journal of Pediatric Hematology Oncology 2011 ;1.(4):121-125

[2] Hagen T, Nieder C, Moringlane JR. Feiden W,Konig J, *Correlation of preoperative neuroradiologic with postoperative histological diagnosis in pathological intracranial process*. Der Radiologe, Nov 1995; 35(11):808-15

[3] Horská Alena and Barker Peter B., *Imaging of Brain Tumors: MR Spectroscopy and Metabolic Imaging*, Neuroimaging Clin N Am. 2010 ; 20(3): 293–310.

[4] Jansen JF, Backes WH, Nicolay K, Kooi ME. *1H MR spectroscopy of the brain: absolute quantification of metabolites*.Radiology2006; 240 (2): 318–32.

[5] Stuart J. Russell, Peter Norvig (2010) *Artificial Intelligence: A Modern Approach, Third Edition*, Prentice Hall ISBN 9780136042594.

[6] T K Biswas, R Bandopadhyay, A Dutta*, Validating The Discriminating Efficacy Of MR T2 Relaxation Value Of Different Brain Lesions And Comparison With Other Differentiating Factors: Use Of Artificial Neural Network And Principal Component Analysis*. The Internet Journal of Radiology. 2017 Volume 20 Number 1. ISPUB DOI**:** 10.5580/IJRA.52614

[7] Biswas TK, Gupta A. *Retrieval of true color of the internal organ of CT images and attempt to tissue characterization by refractive index : Initial experience. Indian Journal of Radiology and Imaging* 2002;12:169-178

[8] Biswas TK, Luu T *In vivo MR Measurement of Refractive Index, Relative Water Content and T2 Relaxation time of Various Brain lesions With Clinical Application to Discriminate Brain Lesions***.** The Internet Journal of Radiology 2009;13(1).

[9] T K Biswas, S R Choudhury, A Ganguly, R Bandopadhyay, A Dutta, *Refractive Index As Surrogate Biological Marker Of Tumefactive And Other Form Of Multiple Sclerosis And Its Superiority Over Other Methods,* Internet Journal of Radiology, https://print.ispub.com/api/0/ispub-article/46167.

[10] Kono K*,* Inoue Y*,* Nakayama K*, et al. The role of diffusion-weighted imaging in patients with brain tumors.* AJNR Am J Neuroradiol 2001*;* 22*:* 1081–1088*.*

[11] G. James *Variance and Bias for General Loss Functions, Machine Learning* 2003; 51, 115135. (http://www-bcf.usc.edu/~gareth/research/bv.pdf

[12] Haykin S., *Neural Networks: A Comprehensive Foundation*, 2nd edition, Pearson Educ. Asia, Hong Kong, 2001.

[13] *Neural Network*,http://www.palisade.com/neuraltools/neural_networks.asp.

[14] Bishop C.M., *Neural Networks for Pattern Recognition*, Clarendon Press, Oxford, 1995.

[15] Jain Sparsh, Biswas Tapan K, Bandyopadhyay Rajib; *Diagnosis of Brain Lesions, Glioma, Multiple-Sclerosis and Metastases from MRI: An efficient classifier-aided method using Refractive Index as a surrogate Biological Marker*. Journal of Biomedical Engineering and Medical Imaging, 2018;5 (3) :19-26

[16] Samuel, Arthur*, Some Studies in Machine Learning Using the Game of Checkers*. IBM Journal of Research and Development,1959;Vol **3**(3): 210–229

[17] Stone, Mervyn, *Asymptotics for and against cross-validation*. *Biometrika* 1977;**64** (1): 29–35.

[18] Ronald L Wasserstein, Nicole Lazar. A *The ASA's Statement on p-Values: Context, Process, and Purpose* 2016; 70(2): *129-133.*

[19] Wells, S Lillian, *Stereotaxic Brain Biopsy*, https://neurosurgery.ufl.edu/residency/about-us/clinical-specialties/stereotactic-brain-biopsy/

SOCIETY FOR SCIENCE AND EDUCATION UNITED KINGDOM

JBEMi JOURNAL OF BIOMEDICAL ENGINEERING AND MEDICAL IMAGING

ISSN: 2055-1266
VOLUME 5 ISSUE 4

Urinary Tract Infection (UTI) still a Force to be Reckoned with

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PREPHASE

Burning pain ,frequent urge to urinate is the first sign of a UTI. It is due to bacteria in the urethra or bladder. Frequent urination is another red flag for an infection. Urine produces peculiar even foul odor and smoky, cloudy. Urine appears pinkish or reddish due to the presence of blood.Young women are commonly infected.Prostate hypertrophy is linked to male disease. It is affecting almost 4 million people in US alone. The chance of UTI is more in women.In females, it affects the bladder and urethra. Women who use diaphragms, spermicidal agents are more at risk. Menopause women are more vulnerable to infection. Infection of upper urinary tract,consisting of the kidney and pelvis ,is known as pyelonephritis.Infection of the lower tract may involve the bladder (Cystitis),urethra (Urethritis) or prostate (Prostatitis) Intercourse is common association of UTI. Catheters increase the risk.Obstruction of urinary flow increase the risk.Bacterial adherence favors persistence.Fever is usually absent.Enterobacteriaceae and gram positive bacteria appear with complications.Back and perirectal pain are the signs of UTI.Pyuria suggests UTI but not specific.Chronic disease is the source of cystitis.Kidney infection results in permanent kidney damage. Take plenty of water/fluids to flush out bacteria.Wipe front to back. This helps the spread of bacteria from the anus into the bladder. Decreased estrogen levels during menopause cause changes that make the urinary tract more susceptible to bacteria. Most patients with UTI have uncomplicated cystitis, which is one of the most common infections in the United States, especially in sexually active women. Escherichia coli is the most common cause of urinary tract infection. Staphylococcus saprophyticus is a frequent cause of cystitis in women, probably related to its occurrence as a part of normal vaginal flora. Klebsiella, Enterobacter, Proteus, and Serratia are the primary opportunistic and often nosocomial pathogens. Pseudomonas aeruginosa is an opportunistic pathogen and a major cause of hospital-acquired infections.

Keywords: Escherichia coli ,Klebsiella, Pseudomonas aeruginosa, Enterobacteriaceae, uncomplicated cystitis, , cefaclor,

DOI: 10.14738/jbemi.54.5121
Publication Date: 03rd Sep 2018
URL: http://dx.doi.org/10.14738/jbemi.54.5121

1 Introduction

Invasion of rectal bacteria by direct extension or by lymphogenous or hematogenous spread may also constitute other possible routes.(1)Due to several anatomical and hormonal changes, pregnant women are more susceptible to develop Urinary tract infections (UTI) (2). UTI is a major health problem,it has been reported among 20% of the pregnant women and it is the most common cause of admission in obstetrical wards.(3)

Although various microorganisms can cause UTI, Escherichia coli is the most common cause of disease in 80%–90% of cases. (4,5)

Staphylococcus saprophyticus as a second agent is a distant second to E.coli,causing 5 to 10% of infections.S.saprophyticus presents as a more aggressive disease with more approximately one half of the patients showing involvement in the upper urinary tract. (6) Urinary tract infections also account for up to 40% of nosocomial infections catheters these hospital acquired infections tend to be more serious because the bacteria resistant to drug treatment and patients are often in poor general health.(7)

Clinical characteristics, etiology and antimicrobial susceptibility patterns may differ from country to country.(8)

Antibiotics are administered only if gas formation is localized in the renal pelvis and there is no invasion in the kidney parenchyma. .(9). During urinary tract infections, invading bacteria may either promote or prevent host cell death by interfering with cell death pathways.(10)

Uncomplicated urinary tract infections (UTIs) are common in otherwise healthy individuals. Half of all women will get one or more UTIs before reaching their mid-30s, and recurrent infections are frequent also in women without any anatomical abnormalities in the urinary tract (11,12)

Urinary tract infections (UTIs) are a severe public health problem and are caused by a range of pathogens, but most commonly by Escherichia coli, Klebsiella Pneumoniae, Proteus mirabilis, Enterococcus faecalis andisand Staphylococcus saprophyticus..(13)

As the most common bacterial infection that requires medical care, UTIs vary greatly by clinical presentation and therapeutic management. Urinary tract infections affect a variety of patients with different biological and procedural risk factors(e.g., age, sex, pregnancy, catheters and urologic interventions).However, not all bacteria require antibiotic therapy,particularly in the presence of ASB. Antibiotic stewardship practices are essential to promote judicious antibiotic use for UTIs. This can significantly reduce antibiotic resistance because UTIs are the most common infections leading to an antibiotic prescription.(14)

Procalcitonin (PCT) as a potential biomarker that can help in differentiating between lower UTI and pyelonephritis in the pediatric age group.(15)

Uropathogenic Escherichia coli is the causative agent for >80%of uncomplicated urinary tract infections (UTIs). Uropathogenic E. coli strains express a number of virulence and fitness factors that allow successful colonization of the mammalian bladder.(16)

,MAPK activators, and lymphocyte signaling molecules.(17)

Diseases Group of the French Pediatric Society set up an active surveillance network in pediatric centers across France in 2014.(18)

Clear instructions for the interpretation of urine cultures by the laboratory technicians are indispensable to obtain standardized, reliable, and clinically useful results.(19)

Congenital abnormalities of the kidney and urinary tract have a high prevalence (3.5-43% in pediatric population.(20)

2 History

It was described by the Egyptians as "sending forth heat from the bladder.(22) Effective treatment did not occur until the development and availability of antibiotics in the 1930s before which time herbs, bloodletting and rest were recommended (21)
Urinary tract infections have been described since ancient times. The first written description, found in the Ebers Papyrus, dates to around the 1550 BC.(23)The Egyptians described a urinary tract infection as "sending forth heat from the bladder(24)

Herbs, bloodletting, and rest were the common treatments until the 1930s, when antibiotics became available.(23)

3 Significant Gap in Research

In most cases, UTIs can be diagnosed just from the symptoms and there is no need for laboratory testing.. The urine is tested for urinary nitrites, white blood cells (leukocytes), or leukocyte esterase.. However, women with negative cultures can still improve with antibiotic treatment (25) UTI symptoms in old people can be vague, and diagnosis can be difficult as there is no really reliable test (26) It is a common urological condition. Sometimes it is impossible to eradicate it because of the development of drug-resistant bacteria. So the wrong therapy is likely to make sensitive organism resistant to drugs. Hence prior isolation of causative organisms and their sensitivity to antimicrobial drugs should be done before any rational treatment is given to the patient.(27)

Staphylococcus saprophyticus is a frequent cause of cystitis in women, probably related to its occurrence as a part of normal vaginal flora. Klebsiella, Enterobacter, Proteus, and Serratia are the primary opportunistic and often nosocomial pathogens. Pseudomonas aeruginosa is an opportunistic pathogen and a major cause of hospital-acquired infections such as UTI, particularly in patients who have been subjected to catheterization, instrumentation, surgery, or renal transplantation or to prior antibiotic therapy.(28)

4 Major Advances and Discoveries

Infected children, men, and those who experience UTI relapse should be investigated with intravenous pyelography to allow detection and correction of any factor causing predisposition to infection.(29)The risk of UTI, both cystitis, and pyelonephritis, can be increased by several factors, especially sexual intercourse, particularly with a new sexual partner. Immunodeficiency and urogenital tract anatomical abnormalities have been considered the essential risk factors for recurrent UTI. In healthy women,Voiding dysfunction and behavioral factors also increase the risk of recurrent UTI.Sexual intercourse and estrogen deficiency in postmenopausal women might have the strongest association

with recurrent UTI.. Vaccines for recurrent UTI are recommended by the latest guidelines and are available on the market.(30)

Recent research has revealed many novel concepts in recurrent UTI including pathogenesis, risk factors, biomarkers, and prevention. Nowadays recurrent UTI may be considered a distinct disease and patients with recurrent UTI should be managed aggressively.

5 Ideas where the Research go Next?

Together, these mechanisms work in concert to help eradicate a UTI. In all likelihood, these mechanisms are constantly being utilized by our urinary tract to ward off invading pathogens without a single symptom or invasive infection.(31)

UTI are the some of the most common bacterial infections,resulting in billions of dollars in health care annually (32)

The only effective treatment option available-antibiotics (33,34) These are considered complicated UTIs, defined as those in the presence of factors that predispose to persistent or relapsing infection, such as foreign bodies (calculi, indwelling catheters), obstruction, renal failure, and urinary retention.(35)

Initial therapy is based on the local susceptibility patterns of *E. coli* and other uropathogens. For the treatment of cystitis, an adequate urinary antibiotic concentration is important to ensure response to therapy Nitrofurantoin is recommended for the treatment of cystitis. It is highly active against *E. coli*, with 0.9% resistance among female outpatients.Trimethoprim/sulfamethoxazole remains a highly effective agent for the treatment of uncomplicated cystitis, with cure rates of 90%–100%.Fluoroquinolones (e.g., levofloxacin or ciprofloxacin) are recommended for the treatment of uncomplicated pyelonephritis

6 Current Debate

Fosfomycin trometamol has in vitro activity against most Enterobacteriaceae spp. including ESBL-producing isolates and *Enterococcus* spp.Studies of β-lactam antibiotics (e.g., amoxicillin/clavulanate, cefaclor, cefdinir, cefpodoxime, and ceftriaxone) report lower efficacy than with fluoroquinolones and trimethoprim/sulfamethoxazole.(36) Depending on the susceptibility of isolated strains, different oral relay possibilities were available: 30% of isolates were susceptible to cotrimoxazole, 50% were susceptible to ciprofloxacine and only 37% were resistant to both antibiotics, which led to the prescription of a non-orthodox combination.(37). Thus urine culture should be performed as screening and diagnostic tool of UTI in pregnancy in this setting.(38) UTIs vary greatly by clinical presentation and therapeutic management.Urinary tract infections affect a variety of patients with different biological and procedural risk factors (e.g., age, sex, pregnancy, catheters and urologic interventions). However, not all bacteriurias require antibiotic therapy, particularly in the presence of ASB. Antibiotic stewardship practices are essential to promote judicious antibiotic use for UTIs. This can significantly reduce antibiotic resistance because UTIs are the most common infections leading to an antibiotic prescription.(39)

Foreign bodies (calculi, indwelling catheters), obstruction, renal failure, and urinary retention. (40)

REFERENCES

[1] Domingue, G. J. &Hellstrom, W. J. G. (1998). Prostatitis. Clin Microbiol Rev 11, 604–613.

[2] Dafnis E, Sabatini S: The effect of pregnancy on renal function: physiology and pathophysiology. Am J Med Sci 1992, 303(3):184-205.

[3] Bacak SJ, Callaghan WM, Dietz PM, Crouse C: Pregnancy-associated hospitalizations in the United States, 1999-2000. Am J ObstetGynecol2005, 192(2):592-597.

[4] Elder JS. Urinary tract infections. In: Kliegman RM, Stanton BF, St.Geme JW III, Schor NF, Behrman RE, editors. Nelson textbook of pediatrics. 20th ed. Philadelphia (PA): Elsevier Saunders, 2016:2554-63.

[5] Wald ER. Cystitis and pyelonephritis. In: Feigin RD, Cherry J, Demmler-Harrison GL, Kaplan SL, editors. Feigin and Cherry's text book of infectious diseases. 6th ed. Philadelphia (PA): Elsevier Saunders, 2009:554-69.

[6] Agace, W., Hedges, S., Andersson, U. et at.. (1993). Selective cytokine production by epithelial cells following exposure to Escherichia coll.Infection and Immunity ,61, (2), 602-609.

[7] Al Mamun, A. A. M., Tominaga, A. and Enomoto, M. (1996). Detection and characterization of the flagellar master operon in the four Shigella subgroups. Journal of Bacteriology 178: 3722-3726.

[8] Cheol-In Kang, Jieun Kim, Dae Won Park, Baek-Nam Kim, U-Syn Ha, Seung-Ju Lee,JeongKyun Yeo, Seung Ki Min, Heeyoung Lee, and Seong-HeonWie.Clinical Practice Guidelines for the Antibiotic Treatmentof Community-Acquired Urinary Tract Infections. Infect Chemother 2018;50(1):67-100.

[9] Aboumarzouk OM, Hughes O, Narahari K, Coulthard R,Kynaston H, Chlosta P, Somani B. Emphysematous pyelonephritis:Time for a management plan with an evidence-basedapproach. Arab J Urol 2014;12:106-115.

[10] Diego Martin-Sanchez, Miguel Fontecha-Barriuso, Maria Dolores Sanchez-Niño, Adrian M. Ramos, Ramiro Cabello, Carmen Gonzalez-Enguita, Andreas Linkermann, Ana BelénSanz, and Alberto Ortiz.Cell death-based approaches in treatmentof the urinary tract-associated diseases: afight for survival in the killing fields. Martin-Sanchez et al. Cell Death and Disease, 2018, 9118, 1-14.

[11] Hooton, T. M. 2001. Recurrent urinary tract infection in women. Int. J. Antimicrob.Agents 17: 259-268.

[12] Foxman, B. 1990. Recurring urinary tract infection: incidence and risk factors.Am. J. Public Health 80: 331-333.

[13] Ana L. Flores-Mireles, Jennifer N. Walker, Michael Caparon, and Scott J. Hultgren.

[14] Urinary tract infections: epidemiology, mechanisms of infection and treatment options. *Nat Rev Microbiol*. 2015 May ; 13(5): 269–284.

[15] Helen S. Leeand Jennifer Le. Urinary Tract Infections. PSAP 2018 Book 1,Infectious Diseases, 7-28.

[16] Neha Nanda and ManishaJuthani-Mehta. Novel Biomarkers for the Diagnosis of Urinary TractInfection-a Systematic Review. Biomarker Insights 2009:4 111-121.

[17] Kelsey E. Sivick, Matthew A. Schaller, Sara N. Smith andHarry L. T. Mobley. The Innate Immune Response toUropathogenicEscherichia coli InvolvesIL-17A in a Murine Model of Urinary TractInfection. J Immunol2010; 184:2065-2075.

[18] Benjamin L. Duell, Alison J. Carey, Chee K. Tan, XiangqinCui, Richard I. Webb, MakrinaTotsika, Mark A. Schembri,Petra Derrington, Helen Irving-Rodgers, Andrew J. Brooks,Allan W. Cripps, Michael Crowley and Glen C. Ulett. Innate Transcriptional Networks Activated inBladder in Response to Uropathogenic*Escherichia coli* Drive Diverse BiologicalPathways and Rapid Synthesis of IL-10 forDefense against Bacterial Urinary TractInfection. *J Immunol*2012; 188:781-792.

[19] FouadMadhi*et al*, 2018.Febrile urinary-tract infection due toextended-spectrum beta-lactamase-producing Enterobacteriaceae in children: AFrench prospective multicenter study. PLoS One. 2018 Jan 25;13(1):e0190910.

[20] MatthijsOyaert, Britt Van Meensel, ReinoudCartuyvels, Johan Frans, WimLaffut, Patricia Vandecandelaere, Hans De Beenhouwer.Laboratory diagnosis of urinary tract infections: Towards a BILULUconsensus guideline. Journal of Microbiological Methods 146 (2018), 92-99.

[21] Song R and Yosypiv I V 2011. Genetics of congenital anomalies of the kidney and urinary tractPediatr. Nephrol. 26(3),353-64.

[22] *Al-Achi, Antoine (2008). An introduction to botanical medicines : history, science, uses, and dangers. Westport, Conn.: Praeger Publishers. p. 126. ISBN 978-0-313-35009-2. Archivedfrom the original on 2016-05-28*

[23] *Wilson...], [general ed.: Graham (1990). Topley and Wilson's Principles of bacteriology, virology and immunity: in 4 volumes (8. ed.). London: Arnold. p. 198. ISBN 0-7131-4591-9.*

[24] *Al-Achi, Antoine (2008). An introduction to botanical medicines : history, science, uses, and dangers. Westport, Conn.: Praeger Publishers. p. 126. ISBN 9780313350092.*

[25] Wilson...], general ed.: Graham (1990). *Topley and Wilson's Principles of bacteriology, virology and immunity: in 4 volumes* (8. ed. ed.). London: Arnold. p. 198. ISBN 0713145919.

[26] Nicolle LE (2008). "Uncomplicated urinary tract infection in adults including uncomplicated pyelonephritis". *Urol Clin North Am* **35** (1): 1–12, v. doi:10.1016/j.ucl.2007.09.004. PMID 18061019

[27] Woodford, HJ; George, J (2011 Feb). "Diagnosis and management of urinary infections in older people.". *Clinical medicine (London, England)* **11** (1): 80-3. PMID 21404794

[28] The short textbook of Medical Microbiology,Satish Gupte, Ninth Edition, Jaypee Brothers, Medical Publishers(p) LTD PP-454

[29] Lippincott's illustrated reviews,Richard A.Harvey,Pamela.C.Champe,Microbiology second Edition,PP374-375.

[30] Sherris Medical Microbiology ,fifth Ed,Kenneth .J.Ryan,C.George Ray,Nafees ahmad,W.Lawrence Drew, James.J.Plorde, Mcgraw Hill-Medical,pp-939-941

[31] Jia-Fong Jhang, Hann-ChorngKuo.Recent advances in recurrent urinary tract infection from pathogenesis and biomarkers to prevention. Tzu Chi Medical Journal 2017; 29(3): 131-137.

[32] John David Spencer, Andrew L. Schwaderer,Brian Becknell,Joshua Watson,and David S. Hains.The innate immune response during urinary tract infection and Pyelonephritis. PediatrNephrol. 2014 July ; 29(7): 1139-1149.

[33] StammWE,NorrbySR,Urinary tract infections:Disease panorama and changes.J.of.Inf.disease ,2001:183,Suppl,:si,s4 (pubmed)

[34] Chen YH,Ko.WC,Hsueh PR,Emerging resistance problems and future perspectives in pharmacotherapy for complicated urinary tract infections.Expert Opin Pharmacother:2013,14:587-596

[35] Kostakioti M,Hultgren SJ,Hadjifrangiskou,M.Molecular blue print of ureopathogenic Escherichia coli virulence provides clues toward the development of anti virulence therapeutics. Virulence 2012:3:592-594(pubmed)

[36] Levison ME, Kaye D. Treatment of complicated urinary tract infections with an emphasis on drug-resistant gram-negative uropathogens. *Curr Infect Dis Rep.* 2013;15(2):109-115.

[37] Helen S. Lee and Jennifer Le. Urinary Tract Infections. PSAP 2018 Book 1.Infectious Diseases, 7-28.

[38] Fouad Madhi *et al.* Febrile urinary-tract infection due to extended-spectrum beta-lactamase-producing Enterobacteriaceae in children: A French prospective multicenter study. PLoS One. 2018 Jan 25;13(1): e0190910.

[39] Hamdan Z Hamdan, Abdel Haliem M Ziad, Salah K Ali, Ishag Adam. Epidemiology of urinary tract infections and antibiotics sensitivity among pregnant women at Khartoum North Hospital. Annals of Clinical Microbiology and Antimicrobials 2011, 10:2, 1-5.

[40] Sanchez GV, Babiker A, Master RN, et al. Antibiotic resistance among urinary isolates from female outpatients in the United States in 2003 and 2012. Antimicrob Agents Chemother 2016;5:2680-3.

[41] Levison ME, Kaye D. Treatment of complicated urinary tract infections with an emphasis on drug-resistant gram-negative uropathogens. *Curr Infect Dis Rep.* 2013;15(2):109-115.

SOCIETY FOR SCIENCE AND EDUCATION UNITED KINGDOM

JBEMi JOURNAL OF BIOMEDICAL ENGINEERING AND MEDICAL IMAGING

ISSN: 2055-1266
VOLUME 5 ISSUE 4

Local Reference of Splenic Volume in Healthy Sudanese Subjects Sonographically

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ABSTRACT

This study was carried out to estimate normal linear dimensions and volume of the spleen in Sudanese using ultrasonography, and to keep it as standards reference for diagnostic purposes.

This prospective study was done at Radiology Department, National Ribat University Hospital, Khartoum, Sudan, conducted on 108 volunteers **(**72 males and 36 females**)**.All linear dimensions of spleen were measured, and splenic volume was calculated using ultrasonography. The splenic volume was then analyzed with age and body parameters using the Pearson's correlation coefficient. Results of this study revealed that the mean values of the age, height, weight of subjects, spleen length (SL), spleen width (SW), spleen thickness (ST) and spleen volume were calculated were found to be 38.74±18.898years,163.11±17.747mm,65.33±15.431kg,91.07±11.330mm,37.59±7.440mm, 37.78±8.085mm and 70.63±31.924cm^3 respectively. Age had no significant effect on spleen volume **(***p*=0. 684**)**. There was a significant positive correlation, using Pearson's correlation coefficient, between the spleen volume, and other parameters **(**height *p*=0.000, and weight *p*=0.002**.**The present study concluded that a local reference of spleen dimensions was established with a different range of values reported previously.

Keywords: Spleen Size, ultrasound, Local Reference

1 Introduction:

The spleen is the largest organ in the reticulo endothelial system [1] Spleen size is important in the evaluation of gastrointestinal and hematological diseases for both radiologists and clinicians.[2] A normal spleen weighs 150-200 g, and is 10.9 ± 1.4 cm long, 4.0 ± 0.45 cm deep, and 6.8 ± 0.71 cm in diameter. The spleen volume can be measured by various techniques such as radiography, scintigraphy, CT, MRI, and ultrasonography. [3, 4] Ultrasonography is the first imaging method to assess splenomegaly.[5,6]

There are several studies about normal internal organs character [7, 8].All of these are from the populations of Caucasoid and from the populations of Asian, Japan, China, Korea, and India. In the past, Thailand normally used references from American or European references. The problem is that the

DOI: 10.14738/jbemi.54.4836
Publication Date: 30th August 2018
URL: http://dx.doi.org/10.14738/jbemi.54.4836

differences of these factors make the indicators different: race, body structure, genetic, environment, living condition, life style, and food. [9, 10].Spleen size varies widely according to age also many diseases can affect their size, including infections and malignancy [11, 12].Radiography and radionuclide studies expose the patient to gamma radiation [13,14,15].

Ultrasound is considered as one of the first lines of diagnosis of many abdominal organs, for its various facilities in detection and measurement; many of splenic disease may associate with incrimination of its volume and sometimes without causing and morbidity of the patient, therefore the measurement of normal spleen volume may assist in early diagnosis of its pathological condition as well as providence of reference standard for spleen volume.

This study was carried out to estimate normal linear dimensions and volume of the spleen in Sudanese using ultrasonography, to correlate splenic volume with age and body parameters: age, height, and weight, in order to keep it as standards reference for diagnostic purposes.

This study was carried out to estimate normal linear dimensions and volume of the spleen in Sudanese using ultrasonography, and to keep it as standards reference for diagnostic purposes.

2 Material and method

2.1 Subjects

The study was performed at the Radiology Department, National Ribat University Hospital, Khartoum, Sudan, between December 2016 and April 2017, conducted on 108 volunteers (72 males and 36 females) not known to have any conditions likely to be associated with splenomegaly, and verbal informed consent was taken for each case. Ethical approval was obtained from the Research Council of the college of Medical Radiological science.

2.2 Exclusion criteria

Subjects underwent a physical examination and completed a short standardized interview questionnaire to exclude any previous or current conditions that might involve the size of the spleen.

2.3 Methods of the Study

Baseline data including age, gender, height, and weight were recorded for all participants. All ultrasonographic examinations were performed by experienced senior sinologists. The examinations were performed using Siemens Aplio MX ultrasound machine equipped with 3.5 MHz curvilinear probes (Erlangen, Germany).The subjects were placed and examined in the supine and right posterior oblique positions, and the spleen was scanned during suspended respiration. Splenic length, thickness and width measurement methods used in this study. D1= Splenic length D2= Splenic width, D3= Splenic thickness, Fig. (1)

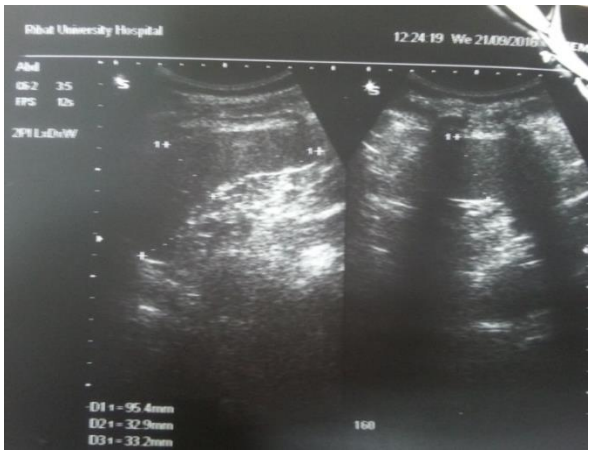

Figure 1. Splenic length, thickness and width measurement methods used in this study. D1= Splenic length D2= Splenic width, D3= Splenic thickness,

2.4 Statistical analysis

The data was entered into a spread sheet and analyzed using the SPSS Statistics for Windows, version 16. The means (± standard deviation), ranges, were all calculated.

The relationship between the splenic index and each of the variables (age, height, and weight) was assessed with the Pearson's correlation coefficient.

The significance threshold was set at 0.05. The XY scatter plots were generated by Microsoft Excel 2010.

3 Results

This prospective study conducted on 108 volunteers (72 males and 36 females).All linear dimensions of spleen were measured, and splenic volume was calculated using ultrasonography. The splenic volume was then analyzed with age and body parameters using the Pearson's correlation coefficient. the mean values of the age, height, weight of subjects, spleen length (SL), spleen width (SW), spleen thickness (ST) and spleen volume were calculated were found to be 38.74±18.898years,163.11±17.747mm,65.33±15.431kg,91.07±11.330mm,37.59±7.440mm, 37.78±8.085mm and 70.63±31.924cm3 respectively. Age had no significant effect on spleen volume (p=0. 684). There was a significant positive correlation, using Pearson's correlation coefficient, between the spleen volume, and other parameters (height p=0.000, and weight p=0.002.The present study concluded that a local reference of spleen dimensions was established with a different range of values reported previously

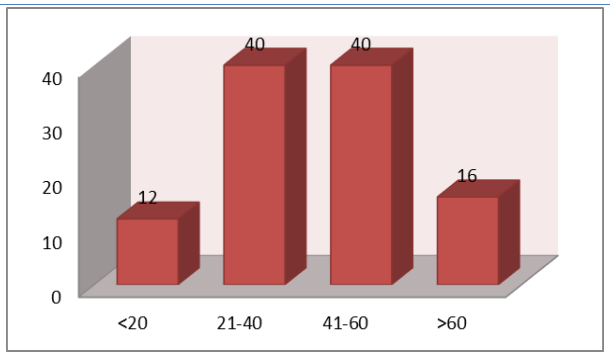

Figure 2 shows the distribution of the subject's age groups

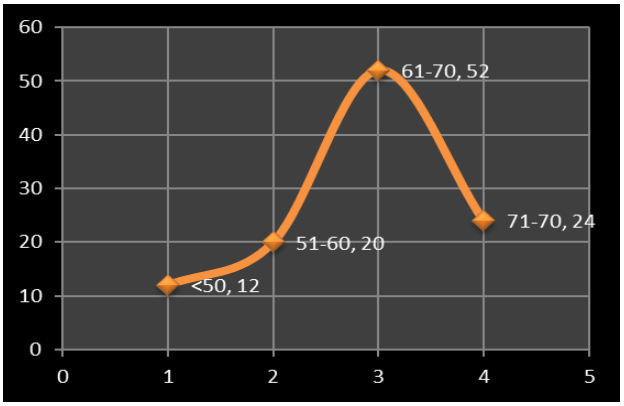

Figure 3 shows the distribution of the subject's weight (in Kgs)

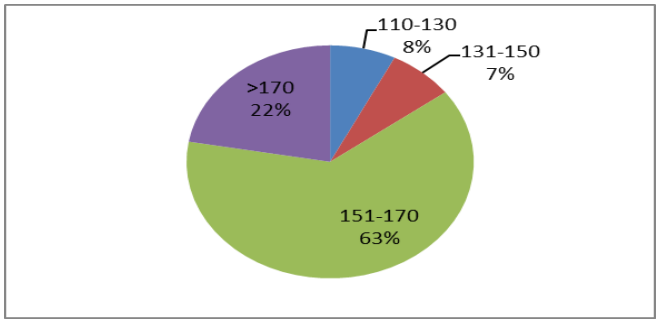

Figure 4 shows the distribution of the subject's height (in cm)

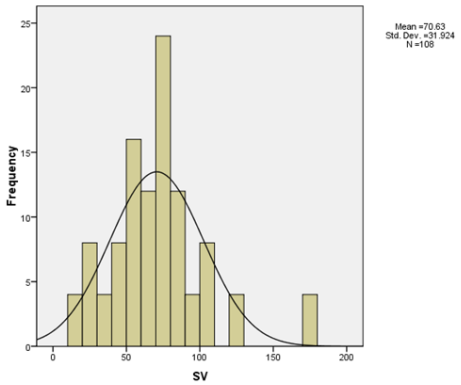

Figure 5 shows the distribution of spleen volume (mm3) in all participants. The x-axis shows measurement of spleen length, and the y-axis shows the number of subjects

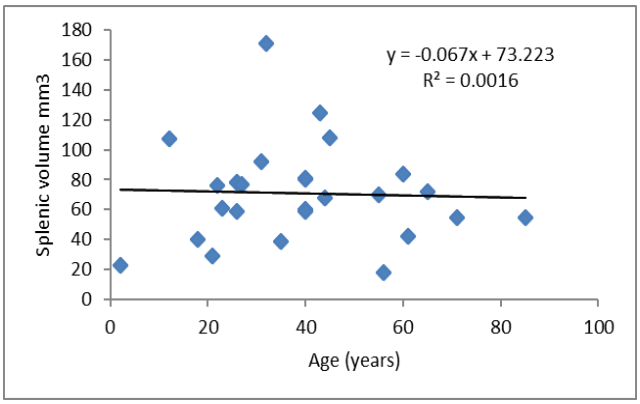

Figure 6 shows the correlation between age groups and spleen volume

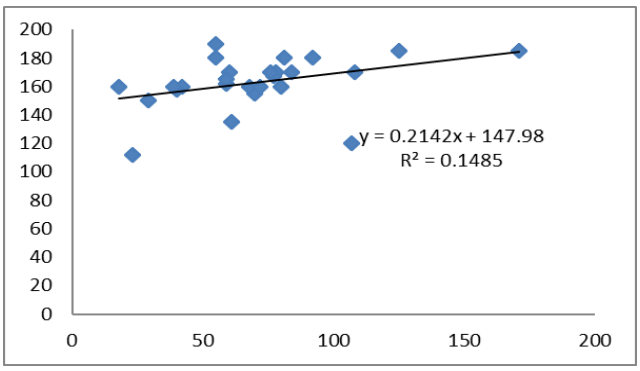

Figure 7 shows the relation between body height and spleen volume.

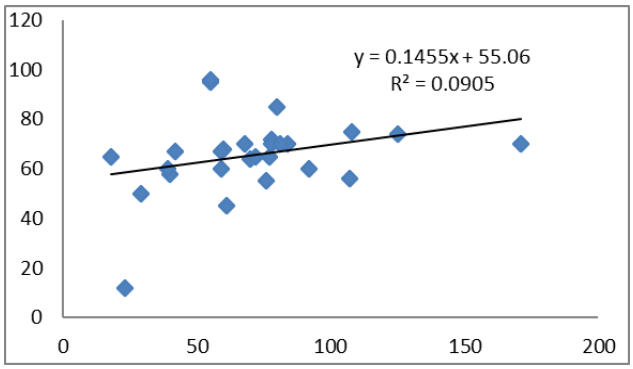

Figure 8 shows the relation between body weight and spleen volume.

Table 1. Characteristics of spleen from 108 subjects (72 males and 36 females' ages 2–85 years).

		Age (years)	Spleen length mm	Spleen width-mm	Spleen depth-mm	Splenic volume mm3	Subjects height(M)	Subjects Weight (Kg)
N	Valid	108	108	108	108	108	108	108
	Missing	0	0	0	0	0	0	0
Mean		38.74	91.07	37.59	37.78	70.63	163.11	65.33
Std. Deviation		18.898	11.330	7.440	8.085	31.924	17.747	15.431
Range		83	48	30	36	153	78	84
Minimum		2	74	22	17	18	112	12
Maximum		85	122	52	53	171	190	96

Table 2 illustrates Proximity Matrix of correlation between variables.

		Age (years)	Spleen length (mm)	Spleen width-(mm)	Spleen depth-mm	Splenic volume mm3	Subjects height(M)	Subjects Weight (Kg)
Age (years)	Pearson Correlation	1	.178	-.082	-.009	-.040	.538**	.733**
	Sig. (2-tailed)		.065	.398	.925	.684	.000	.000
	N	108	108	108	108	108	108	108
Spleen length (mm)	Pearson Correlation	.178	1	.576**	.454**	.735**	.609**	.487**
	Sig. (2-tailed)	.065		.000	.000	.000	.000	.000
	N	108	108	108	108	108	108	108
Spleen width-(mm)	Pearson Correlation	-.082	.576**	1	.661**	.880**	.394**	.281**
	Sig. (2-tailed)	.398	.000		.000	.000	.000	.003
	N	108	108	108	108	108	108	108
Spleen depth-mm	Pearson Correlation	-.009	.454**	.661**	1	.838**	.181	.261**
	Sig. (2-tailed)	.925	.000	.000		.000	.061	.006
	N	108	108	108	108	108	108	108
Splenic volume mm3	Pearson Correlation	-.040	.735**	.880**	.838**	1	.385**	.301**
	Sig. (2-tailed)	.684	.000	.000	.000		.000	.002
	N	108	108	108	108	108	108	108
Subjects height(M)	Pearson Correlation	.538**	.609**	.394**	.181	.385**	1	.766**
	Sig. (2-tailed)	.000	.000	.000	.061	.000		.000
	N	108	108	108	108	108	108	108
Subjects Weight (Kg)	Pearson Correlation	.733**	.487**	.281**	.261**	.301**	.766**	1
	Sig. (2-tailed)	.000	.000	.003	.006	.002	.000	
	N	108	108	108	108	108	108	108
**. Correlation is significant at the 0.01 level (2-tailed).								

4 Discussion

The wide range of normal spleen size values reported in the literature makes the establishment of normal ranges more difficult. The Sudanese's population is a cosmopolitan society of approximately 40 million people where the vast majority is Sudanese, and the rest are refugees and immigrants from nearby countries. Only Sudanese were included in this study. In this study population,

The majority of the sample under study was male 72 patients (81%) and female 36 patients forming the (19%).In this study the average age of the patients studied was 38.74 years. The majority of patients studied were from Khartoum state (81%), Central Sudan (7%), and Western Sudan (7%), and Eastern Sudan (5%). The subjects' characteristic data were comparable to the mean values reported in the literature (Table 1)

Table 3 illustrates the subjects characteristic data comparable to the mean values reported in the literature

Authors	N	Age.range(years)	L±SD	W±SD	T±SD	V±SD	country
current study	108	2–85	9.107±1.133	3.759±.744	3.778±8.09	70.63±31.92	Sudan
Nouri et al , 2013[16]	215	7–13	NR	NR	NR	9.0 ± 1.2	Sudan
Ezeofor1 et al ,2014[17]	1315	5 - 17	10.1±1.4	NR	NR	NR	Nigeria
Badran, et al , 2015[18]	205	NR	10.72±1.37	7.40±1.52	4.40±1.47	184.15±79.56	Jordan
Çeliktas et al 2015[19]	150	18- 76	9.87±1.28	7.58±1.56	3.34□0.79	136.05±61.14	Turkey
Tanna et al , 2012[20]	80	NR	9.70□0.15	NR	NR	NR	India
Mustapha et al 2010[21]	375	NR	8.9±1.3	4.9±1.2	5±0.9	119.5±55.7	Nigeria
Serter et al 2010[22]	2179	17-42	10,76±1,8	NR	NR	NR	Turkey
Singh and Kumari, 2016[23]	NR	NR	2.5 ± 0.3	1.7 ± 0.1	1 ± 0.1	NR	India
Chakraborti et al in 2016[24]	146	17- 95	8.85±1.54	NR	NR	NR	India

The means of splenic dimensions were fairly similar to those recorded by Turkish and Nigerian populations[19,20]and less than the data from Jordan [18] implicating that ethnicity could be attributed in part to the wide ranges of normative data registered by different populations this recent study performed on Jordan adults. To estimate normal linear dimensions and volume of the spleen in Jordanians using ultrasonography, and to correlate splenic volume with age and body parameters: height, weight, body surface area **(**BSA**)**, and body mass index **(**BMI**)**. [18]. Splenomegaly is considered as moderate if the biggest dimension is 11-20 cm, and severe if the biggest dimension is greater than 20 cm.18 However, this study recorded a the mean of spleen length of normality in Sudanese is 9.107cm. Therefore, caution is required in defining splenomegaly in our population.

A likely decrease in the size of the spleen due to aging reported in the previous literature was not evident in this study [25], Arora et al. 2010). However, our findings were in agreement with the results described in Africans and Indians studies [22]. Moderate positive relationships between splenic volume and height, weight were observed; this was similar to the data from spleen sonography and autopsy [26, 27]. Graphic representation of the data showed some variability of the spleen volume by height; weight (**Figs (7,8)**, it also showed the unmistakable trend for spleen volume to increase in parallel with the increase in the body parameters. So the variations of body parameters could be attributed to different splenic measurements in different areas. Previous studies showed that the longitudinal measurements of the spleen were best correlated only with body height [28]. On the other hand, studies of African adults and Turkish males found no correlation between spleen volume and body parameters [21,22]. From a physiological perspective, our findings would make more sense; as patients with a bigger body habitus will have a larger blood volume requiring larger spleens for filtration.As there is a positive correlation between the body parameters and the splenic volume.

This study measured the splenic length, width, thickness and volume among Sudanese and the results were compared to other populations. The mean values of splenic length and width were 9.107cm and 3.759cm

The Africans, Rajasthan population and Thai population having lower, and Nigerians having greater values than this study. The study results are different from to those of these investigations, except the Thai population when comparing splenic width results.

Moreover, mean values of splenic thickness were reported between 3.33 cm and 6 cm in Thai population, Indians, Africans, Americans and Nigerians [21, 28,29] In this study this value was 3.778cm. According to this data of the present result is similar to Thai population.

Splenic volume was calculated in males and 136.05 cm3 in females. In a studying consisting of Nigerians, in males mean value of splenic volume were 202.7 cm3 and in females 153.7 cm3 respectively (Ehimwenma & Tagbo, 2011).

Moreover, the same value was 119.5 cm3 in African population [21, 29] determined that the splenic volumes were 288.36 cm3 and 217.44 cm3 in males and females respectively. Furthermore, the mean volume of the spleen was 132 cm3 and 113 cm3 respectively in Japanese males and females whereas; same dimensions were 134.2 cm3 and 115.6 cm3 in males and females respectively in Thai adults [29]. However, same value was 344 cm3 in the USA [30].

Due to these data, this study found differences in the mean values of the splenic volume of Sudanese, Nigerians, Japanese population.

We consider that these discrepancies could be a result of such factors like race, genetic variables, nutritional status, socioeconomic status and demographic variables including age, weight, and height. Moreover, we found that all dimensions were greater in males than females and splenic length decreased with increase in age in both genders. As we mentioned before, there were no differences in the mean values of the spleen volume between two calculation methods.

Among the different techniques employed for assessment of normal or otherwise spleen size, ultrasonographic measurements have been considered to be the most feasible and accurate. Ultrasonography can be a useful technique as it is noninvasive and does not involve any risk of radiation. Ultrasound, therefore, has become the most common practice to differentiate pathologically enlarged or reduced spleen in patients.

5 Conclusion

The precise knowledge of the spleen morphology with USG may be essential for safe and accurate diagnose of many disorders such as infections, splenomegaly, malignant conditions and viral illnesses for surgeons and radiologist. Therefore, the observations presented in this study have defined anatomic parameters that need to be taken into consideration for evaluating splenic problems and guidelines to determine the reference values.

The data obtained in this study can provide crucial information for surgeons and radiologists about spleen, and they can be used as reference values for evaluating pathologic changes in the spleen region.

A local reference of spleen dimensions was established in this study with a different range of values reported previously. Setting a higher cutoff point for defining splenomegaly in Sudanese should be considered.

REFERENCES

[1] Cesta MF. Normal structure, function, and histology of the spleen. Toxicol Pathol 2006; 34: 455-465.

[2] Niederau C, Sonnenberg A, Muller JE, Erckenbrecht JF, Scholten T, Fritsch WP. Sonographic measurements of the normal liver, spleen, pancreas, and portal vein. Radiology 1983; 149: 537-540.

[3] Benter T, Kluhs L, Teichgraber U. Sonography of the spleen. J Ultrasound Med 2011; 30: 1281-1293.

[4] Sutherland T, Temple F, Galvin A, Hennessy O. Contrast-enhanced ultrasound of the spleen: an introduction and pictorial essay. Insights Imaging 2011; 2: 515-524.

[5] Yildiz AE, Ariyurek MO, Karcaaltincaba M. Splenic anomalies of shape, size, and location: pictorial essay. Scientific World Journal 2013; 2013: 321810.

[6] Inoue Y, Nakajima A, Mizukami S, Hata H. Effect of breath holding on spleen volume measured by magnetic resonance imaging. PLoS One 2013; 8: e68670.

[7] Ludwig J. Current methods of autopsy practice. Philadelphia: Saunders; 1979: 647-89.

[8] Sunderman WF, Boerner F. Normal va lues in clinical medicine. Philadelphia: Saunders; 1949.

[9] Chirachariyavej T, Ouyswat K, Sanggar njanavanich S, Tiensuwan M, Peonim V, Sirikulchayanonta V. Normal internal organ weight of Thai adults correlated to body length and body weight. J Med Assoc Thai 2006; 89: 1702-12.

[10] Piyanun Mathuramon, Thamrong Chirachariyavej,AVM Vichan Peonim, Mana Rochanawutanon. Correlation of Internal Organ Weight with Body Weight and Length in Normal Thai Adults J Med Assoc Thai 2009; 92 (2): 250-8.

[11] Krestin GP, Brennan RP. Ultrasound diagnosis of the abdomen. Ther Umsch.1992; 49(6):395-404.

[12] Joshi R, Singh A, Jajoo N, Pai M, Kalantri SP.Accuracy and reliability of palpation and percussion for detecting hepatomegaly: a rural hospital based study. Indian J Gastroenterol 2004; 23: 171-74.

[13] French J, Camitta BM. Splenomegaly. In:Behrman RE, Kliegman RM, Jenson HB (ed). Nelson Textbook of Pediatrics. 17th ed. Philadelphia, Pa: Saunders; 2004. p.1675.

[14] Mimouni F, Merlob P, Ashkenazi S,Litmanovitz I,Reisner SH. Palpable spleens in newborn term infants. Clin Pediatr (Phila) 1985; 24: 197-98.

[15] Megremis SD, Vlachonikolis LG, Tsilimigaki AM.Spleen length in childhood with US: Normal values based on age, sex and somatometric parameters. Radiology 2004; 23:129-34.

[16] Maha Nouri, Caroline Edward Ayad, Elsaffi Ahmed Balla & Samih Kajok(2013) , Establishment Local Reference of Spleen Length in Sudanese Normal School Age Children Sonographically, Global Journal of Medical research Radiology, Diagnostic, Imaging and Instrumentation 13 (2)

[17] SN Ezeofor, EN Obikili1, GE Anyanwu, AC Onuh, SO Mgbor(2014), Sonographic assessment of the normal limits of the spleen in healthy school children in South-East Nigeria , Nigerian Journal of Clinical Practice • 17 -4(484-488)

[18] Darwish H. Badran, , Heba M. Kalbouneh, Maher T. Al-Hadidi, Amjad T. Shatarat, Emad S. Tarawneh,Azmy M. Hadidy, Waleed S. Mahafza(2015). Ultrasonographic assessment of splenic volume and its correlation with body parameters in a Jordanian population ,Saudi Med J; Vol. 36 (8): 967-972

[19] Çeliktas, M.; Özandaç, S.; Göker, P. & Bozkir, M. G(2015). Sonographic determination of normal spleen size in Turkish adults. Int. J. Morphol., 33(4):1401-1405,

[20] Tanna Nita A, Ambiye M V, Tanna Vilpa A, Joshi Himanshu A(2012), Ultrasonic Measurement OF Normal Splenic Size in Infants and Children in Paediatric Indian Population, National Journal of Community Medicine,Volume 3,Issue 3,.(529-533)

[21] Mustapha Z, Tahir A, Tukur M, Bukar M, Lee WK(2010). Sonographic determination of normal spleen size in an adult African population. Eur J Radiol; 75: e133-e135.

[22] Selim Serter, Cengiz Ceylan, Özüm Tunçyürek, ebnem Örgüç, Yüksel Pabuçcu (2010), Sonographic evaluation of spleen size and prevalence of accessory spleen in a healthy male Turkish population, Turk J Hematol; 27: 25-8)

[23] Singh A, Ansari H, Das JK, Chandra N(2011). Ultrasonographic measurement of splenic length in relation with height in Bihari adult population. A prospective study. J Anat Soc India; 60: 188-189.

[24] Somnath Chakraborti, Nirmalya Saha, Biplab Debbarma, Snigdha Das, Diana Leishram(2016), Normal Spleen Length by Ultrasonography in Adults of Tripura, IOSR-JDMS, Volume 15, Issue 1 Ver. I, PP 55-60

[25] Asghar A, Naaz S, Agrawal D(2014). Estimation of standard splenic index (SI) in Indian population: A CT scan based study. Indian Journal of Basic and Applied Medical Research; 3: 332-337.

[26] Caglar V, Kumral B, Uygur R, Alkoc OA, Ozen OA, Demirel H(2014). Study of volume, weight and size of normal pancreas, spleen and kidney in adults autopsies. Forensic Medicine and Anatomy Research; 2: 63-69.

[27] Arora N, Sharma PK, Sahai A, Singh R(2013). Sonographic measurement of the spleen: splenic length in adults and its correlation with different parameters. J Anat Soc India; 62: 57-61.

[28] Asghar A, Agrawal D, Yunus SM, Sharma PK, Zaidi SH, Sinha A(2011). Standard splenic volume estimation in north Indian adult population: Using 3d reconstruction of abdominal CT scan images. Anat Res Int; 707325.

[29] Srisajjakul, S.; Prapaisilp, P. & Laorratkul, N(, 2012). Normal splenic volume assessment on CT in 426 adults. Siriraj Med. J.,64(2):43-6.

[30] Tonelli, A. R; Yadav, R.; Gupta, A.; Arrossi, A. V.; Heresi, G. A. & Dweik, R. A(2013). Spleen size in idiopathic and heritable pulmonary arterial hypertension. Respiration, 85(5):391-9,

[31] Serter S, Ceylan C, Tunçyürek , Pabuçcu Y(2010). Sonographic evaluation of spleen size and prevalence of accessory spleen in a healthy male Turkish population. Turk J Hematol; 27: 25-28.