EVALUATION OF BRAINSTEM AUDITORY EVOKED POTENTIALS IN CHRONIC KIDNEY DISEASE, HEMODIALYSIS AND RENAL TRANSPLANTATION PATIENTS

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CERTIFICATE

This to certify that the dissertation entitled **"EVALUATION OF BRAINSTEM AUDITORY EVOKED POTENTIALS IN CHRONIC KIDNEY DISEASE PATIENTS, HEMODIALYSIS PATIENTS AND RENAL TRANSPLANTATION PATIENTS"** by the candidate **Dr.D.PRIYADARSHINI** for **M.D Physiology (Branch V)** is a bonafide record of the research done by her during the period of study **(2014 -2017)** in the Department of Physiology and Experimental Medicine, Kilpauk Medical College, Chennai – 600010.

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DECLARATION

I**, Dr.D.PRIYADARSHINI** solemnly declare that this dissertation entitled **"EVALUATION OF BRAINSTEM AUDITORY EVOKED POTENTIALS IN CHRONIC KIDNEY DISEASE PATIENTS, HEMODIALYSIS PATIENTS AND RENAL TRANSPLANTATION PATIENTS"** was written by me in the Department of Physiology, Kilpauk Medical College, Chennai, under the guidance and supervision of **Prof. Dr. A. Shakeela Banu M.D.,** Professor and Head, Department of Physiology, Kilpauk Medical College, Chennai – 600 010.

This dissertation is submitted to **THE TAMILNADU Dr. M.G.R MEDICAL UNIVERSITY** Chennai, in partial fulfillment of the university regulations for the award of **DEGREE OF M.D PHYSIOLOGY (BRANCH V)** examinations to be held in **APRIL -2017**

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LIST OF ABBREVIATIONS

BAEP	-	Brainstem auditory evoked potentials
CKD	-	Chronic kidney Disease
HD	-	Hemodialysis
RT	-	Renal Transplantation
ESRD	-	End stage Renal Disease
NHANES	-	National Health And Nutrition Examination Survey
CRI	-	Chronic Renal Insufficiency
S.cr	-	Serum. Creatinine
MDRD	-	Modification of Diet And Renal Disease
GFR	-	Glomerular Filtration Rate
NGAL	-	Neutrophil Gelatinase Associated Lipocalin
IPL	-	Interpeak Latency.
AVCN	-	Anterior Ventral Cochlear Nucleus
PVCN	-	Posterior Ventral Cochlear Nucleus
DCN	-	Dorsal Cochlear Nucleus.

INTRODUCTION

Chronic kidney disease is defined as the presence of kidney damage or a decreased level of kidney function, for a period of three months or more .It can be divided into five stages depending upon how severe is the damage to kidneys or the level of decrease in renal function.In many renal diseases, the damage can be ascertained by the presence of Albuminuria, defined as albumin-creatinine ratio>30 mg /g in two of three spot urine collections.According to the level of GFR, Chronic kidney disease is divided into five stages.

Epidemiology of chronic kidney disease

According to a report based on Atherosclerosis risk in communities study (ARIC)[1], the incidence rate of CKD was 10,350 per 1 million person years, when incident CKD was defined as the MDRD estimated GFR of less than 60 ml/min/1.73 m^2.

The best data source for determining CKD prevalence has been the national health and nutrition examination survey in the united states (NHANES), according to which the prevalence was two order magnitude larger than the incident CKD patients[2].

In India there is no longitudinal study and there is limited data on the prevalence of CKD.

Agarwal et al studied south delhi urban population & reported the prevalence of stage 4 CKD to be 0.785 %.

Singh et al studied the prevalence of stage 5 CKD to be 4.2 % in both urban and semi urban population of Delhi.

In a recently published screening & early evaluation of Kidney Disease study, the prevalence of CKD according to various stages was studied and it was 7 %, 4.3%,4.4%,0.8%& 0.8 % respectively for stages I,II,III, IV, & V.

TABLE -1

STAGING OF CHRONIC KIDNEY DISEASE (national kidney foundation)[2]

STAGE	DESCRIPTION	GFR/ml/min/1.73m^2
1	Kidney damage with normal or GFR	≥90
2	Kidney damage with mild reduction in GFR	60-89
3	Moderate reduction in GFR	30-59
4	Severe reduction in GFR	15-29
5	Kidney failure	<15 or dialysis.

CKD, prevalence is complicated with difference in calibration of creatinine measurements.[3,4]. In late 2000's the same blood sample creatinine measurements differed by 0.2 or 0.3 mg/dl[5].

In the past 2 decades of NHANES surveys. creatinine has been measured in which different methods were used and systemic biases were introduced. Thus there was an apparent increase in prevalence of CKD from the period 1988 to 1994 to the period 1999 to 2004[6,7]

RISK FACTORS AND CAUSES OF CKD;

- The most common cause of CKD is Diabetic Nephropathy worldwide[8] .
- Hypertension is an important factor in the progression of CKD.
- Obesity is associated with hypertension, proteinuria and progressive renal disease[9,10]
- Metabolic syndrome has got an increased risk [11] of CKD.
- Complications of pregnancy especially preeclampsia causes renal damage.
- Renal disease progression[12] is accelerated by high protein diet.
- CKD is also associated with substantial increase in the risk of cardiovascular disease[13].

Among primary renal diseases autosomal dominant polycystic kidney disease was an independent predictor of a greater rate of GFR decline[14].

- Anaemia resulting from inherited hemoglobinopathy is associated with increased renal plasma flow, glomerular hyperfiltration and subsequent development of proteinuria, hypertension and ESKD[15].
- In Several studies, elevated levels of low density lipoprotein cholesterol (LDL) to High density lipoprotein cholesterol[16] and low HDL cholesterol levels[17] have been identified as both susceptibility and progression risk factor for CKD.
- Hyperuricemia is an independent risk factor for increased serum creatinine concentration [18].

It is also proposed that a small protein, neutrophil gelatinase associated lipocalin released by renal tubules in response to injury ,is an early marker which is elevated in proportion to the extent of renal damage in patients with CKD[19,20.]

OTHER RISK FACTORS

- Cigarette smoking[21]
- Alcohol consumption[22]
- Use of heroin,cocaine and other psychedelic drugs [23]
- Amyloidosis[24]
- Analgesic nephropathy
- Lead toxicity characterised by chronic interstitial nephritis[25]

DEMOGRAPHIC VARIABLES

- AGE; CKD increases with age since nephron loss is a part of normal ageing.[26]
- GENDER; United states renal data system shows increased incidence of CKD among males[27].
- ETHNICITY; There is higher incidence among African Americans[28,29]
- HEREDITORY FACTORS; Among 25,883 patients with incident CKD,22.8% reported family history[30].thus autosomal dominant polycystic kidney disease , Alports disease, Fabrys disease and congenital nephrotic syndrome account for a significant number of CKD cases.
- HEMODYNAMIC FACTORS; There were several studies which showed glomerular hypertension and hyperfiltration causing nephron loss [31] and chronic hyperglycemia[32] play crucial role in establishing CKD.
- DECREASED NEPHRON NUMBER; According to some autopsy studies ,there existed association between nephron number with both hypertension[33] and glomerulosclerosis[34]

Also, LBW is directly associated with reduced nephron number[35] and its an independent risk factor.

ACQUIRED NEPHRON DEFICIT

Removal of one of two normal kidney (uninephrectomy) predisposes individuals to other forms of CKD[36]

Acute kidney injury is also an important risk factor for CKD.

PATHOPHYSIOLOGY OF UREMIA

"Uremia is defined as the illness that would remain if the extracellular volume & inorganic ion concentrations were kept normal and the renal synthetic products ex.Erythropoietin were replaced in patients without kidneys". Its caused by accumulation of organic waste products which are usually excreted by kidneys. In most cited studies Johnson and colleagues[37] discovered that initiation of hemodialysis improved uremic symptoms.

Increased concentration of plasma urea cause ill effects by promoting carbomylation[38]

Increased ammonia production is a consequence of urea concentration .

Plasma level of D aminoacids increase in chronic kidney disease[39]

Proteins like β_2 Microglobulin and cystatin C with molecular weight 10 to 20 kDa are normally filtered by the glomerulus &hydrolysed in proximal tubular lysosomes.Their levels rise in proportion to creatinine levels as kidney fails.

HEMODIALYSIS

HD prolongs life for around 1 million patients throughout world, without which many would not survive more than few weeks[40] .

Graham (1805-1869) ,a Scottish chemistry professor invented the process of separating solutes invitro using semipermeable membranes & coined the term "Dialysis".[41]

"Abel" was the first to use the term artificial kidney[42]

In 1944, William kolff used extracorporeal dialysis to support patients with acute kidney failure[43].

Incidence and prevalence

According to US renal data system 5,35,160 patients in US had ESKD at the end of 2008.Of these 30 % had transplants & the rest were managed with dialysis. Highest prevalence of CKD was in Taiwan.

Statistics from USRDS ,states for patients starting dialysis in 2000 through 2001 show a 79% I year survival,65 % 2 year survival and 38 % 5 year survival[44]

According to current clinical practice dialysis can be commenced at an estimated GFR of less than 10 ml/min/1.73m^{2}.[45]

Vascular access;

Brescia and colleagues[46] eloborated the procedure to create an AV fistula in 1996 marking the viability of HD as a long term therapy for

CKD .Arm is the preferred site for fistula and grafts .In some patients ,leg is the preferred site[47]

The radiocephalic AV fistula is the access of choice for stage 5 CKD patients.

Types of vascular access;

a) AV fistulas are created by connecting vein to artery and the two vessels must be in proximity to each other

b) Vascular approach using ePTFE is the most prominent type of vascular access in United States.

Some small trials suggested fish oil use is effective in reducing thrombosis in grafts[48]

Another study supported the use of low dose Aspirin and Dipyridamole after placement of AV Grafts[49]

General principles of Hemodialysis

Therapeutically in hemodialysis solutes are removed essentially by diffusion and to a lesser extent by convection across a semipermeable membrane. The goals of dialysis are removal of accumulative fluid and toxic substances and the performance is analysed by clearance of the representative solutes.

Components of extracorporeal circuit

Modern HD machines have the size of a three to four drawer filing cabinet. Central to the system is the dialyzer or artificial kidney through which exchange between **blood** and dialysate occurs.

Blood circuit

During dialysis, the steady blood flow is obtained from a central venous catheter or from an AV Fistula or graft.

If a catheter is used, blood enters the extracorporeal circuit along the sides of double lumen catheter (arterial lumen) and return through the venous lumen.

An alternate dialysate delivery system uses a single needle in the vascular access or a single lumen catheter for dialysis[50]

Hemodialyzers

A Hemodialyzer called as an artificial kidney allows the flow of blood and dialysate preferably in opposite directions, through individual components separated by a semipermeable membrane. Conventionally blood which enters the hemodialyzer is arterial and the blood leaving hemodialyser is venous.

Dialysate circuit

Another function of the HD system is the preparation and delivery of dialysate to the dialyser. During HD, blood flows in one direction and

the isoosmotic dialysate flows in the opposite direction in the dialysate compartment. The temperature of dialysate is maintained between 35^{o} to 37^{o}c at the inlet.

Initiation of Dialysis

Dialysis is initiated in patients who lose weight and who have volume overload and uncontrolled acidosis or hyperkalemia.

Incision: After administering prophylactic antibiotics, Gibson incision which is made in the lower abdomen is extended to the flank or up to even 12^{th} rib. Most of the time, right side is preferred owing to the accessibility of the iliac vein ,which makes the operation easier.

Long term complication of Dialysis[51]

A) Vascular disease

B) Anemia

C) Renal osteodystrophy

D) Uremic neuropathy

E) Dialysis access failure

RENAL TRANPLANTATION

A successful renal transplant restores not merely life but also an acceptable quality of life to patients.

“Transplantation of kidney for renal failure was done as long as ago in 1945, when 3 young surgeons at peter bent hospital in Boston namely CHARLES HUFNAGEL, ERNEST LANDSTEINER and DAVID HUME joined the vessels of a cadaver kidney to brachial vessels of a young lady with CKD.

In 1954,the first successful kidney transplant was performed by late Joeseph murray at the peter bent hospital ,Boston.

On 1954, December 23rd the first twin to twin kidney transplant was done by boston[52]

Renal transplant operation and its surgical complications

It’s an elective surgical procedure performed in patients who have undergone careful preoperative assessment .The main goal is to prevent and limit the progression of CKD.

Operative technique

Meticulous surgical skill and techniques , strict aseptic procedure & perfect hemostasis are the basic requirements. It involves both vascular and ureteric anastamoses. Prior to transplantation proper history and physical examination are required to ensure that there is no contraindication to surgery. Prophylactic antibiotics are usually given to cover Skin infections & urinary tract contaminants[53].

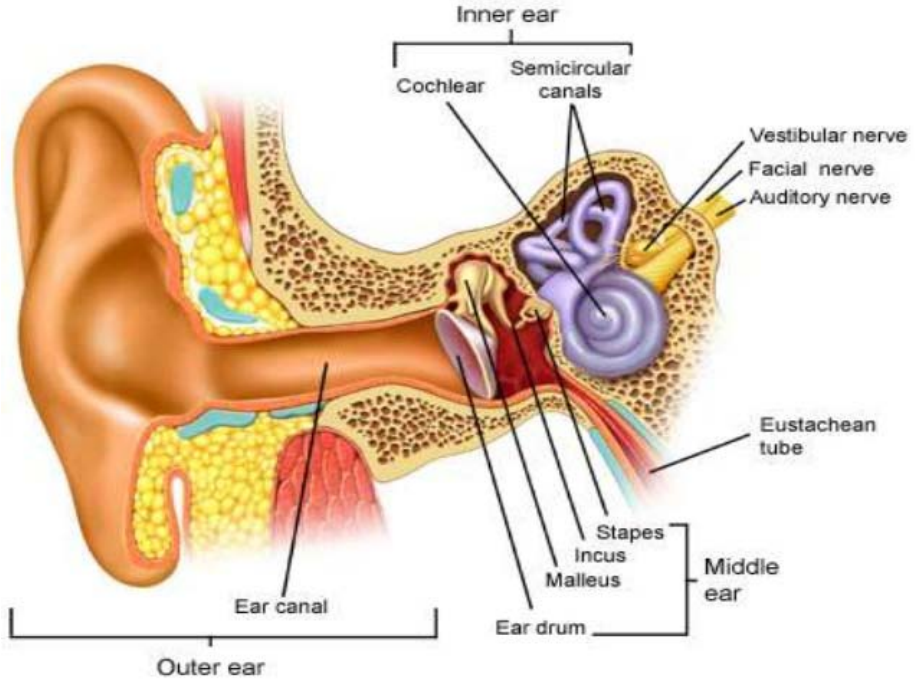
Post transplantation

Provided the graft function is adequate, after transplantation the peritoneal dialysis catheter could be capped off & left. The catheter is removed after 3 months if the kidney function is stable. When there is graft failure within 3 months, the catheter has to be flushed to remove debris and fibrin. A successful outcome following a renal transplant depends on the early perioperative management.

Main factors which affect the long term outcome are delayed graft function, acute rejection, early surgical complication like hematuria, urine leak, renal vein thrombosis.post operative haemorrhage and lymphocele.

PHYSIOLOGICAL ANATOMY OF EAR

Fig :1 Schematic diagram of anatomy of ear



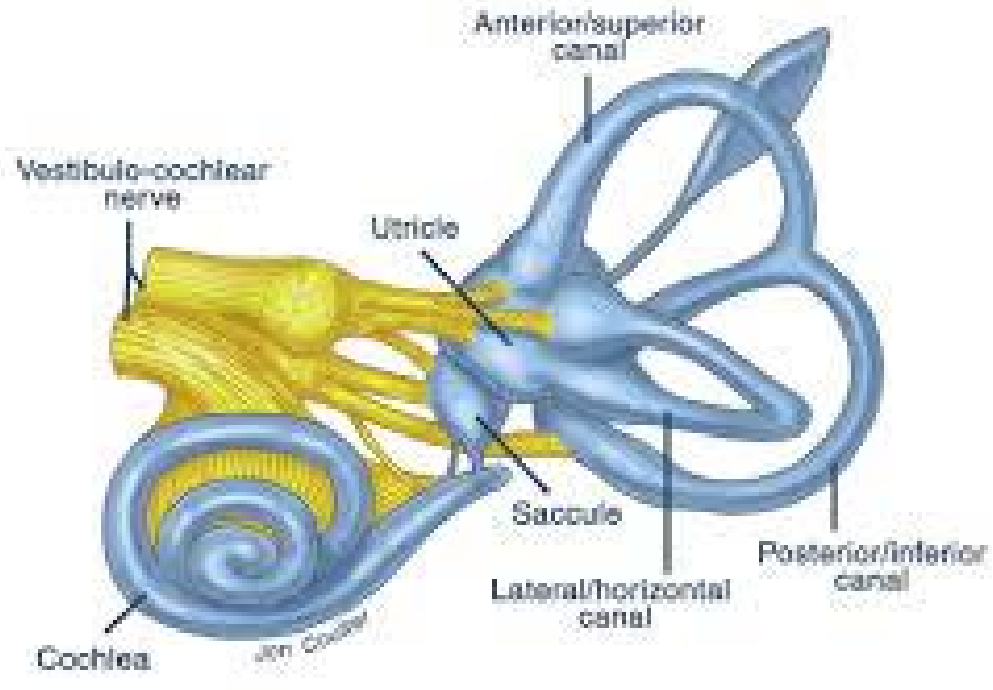
The peripheral auditory apparatus is the ear which can be divided into external ear, middle ear and internal ear[60].

External ear includes pinna, external auditory meatus and auditory canal.

The external ear is separated from the middle ear by tympanic membrane and the middle ear contains three ossicles namely malleus, incus and stapes

The tympanic membrane with the three ossicles act as the impedance matching device

Fig:2 Schematic diagram of inner ear



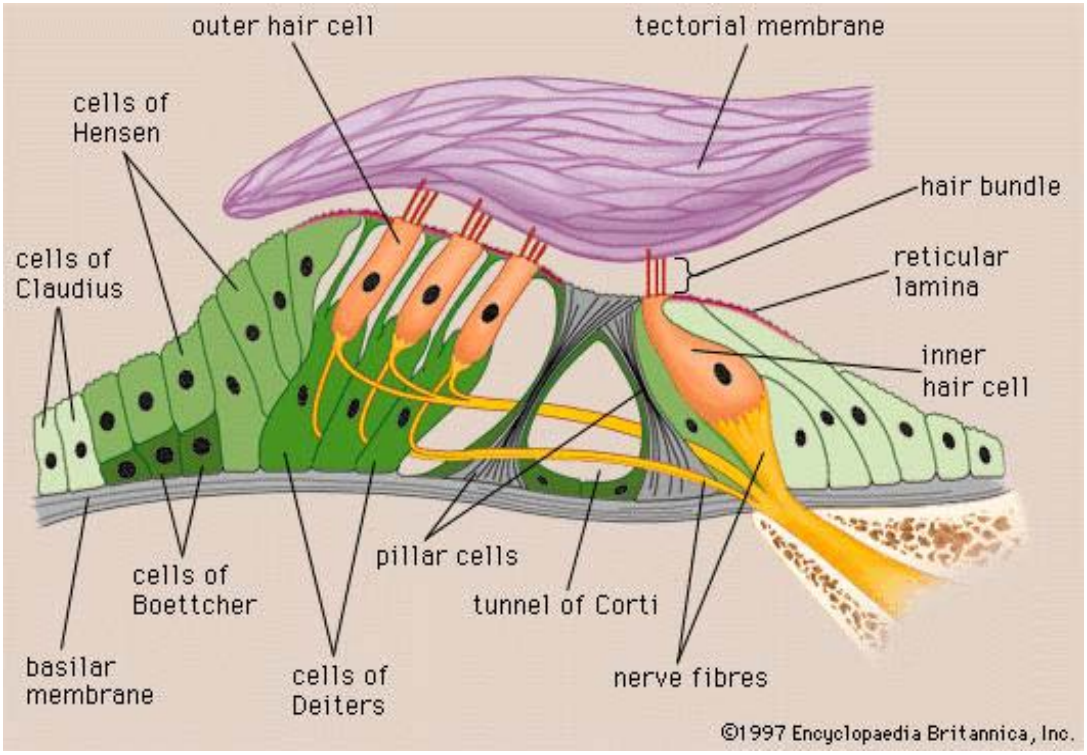
The inner ear includes bony and membranous labyrinths.[60] cochlea and vestibular apparatus are formed from bony and membranous labyrinths.

The neural apparatus responsible for transduction of sound is the organ of Corti which is within the cochlea.

Vestibular apparatus is composed of 3 semicircular canals namely horizontal, superior and posterior canals and 2 otolith organs utricle and saccule maintenance of equilibrium and posture

MECHANISM OF HEARING

Fig 3:Schematic diagram of organ of corti



Sound waves are transmitted from the external ear to the internal ear primarily through tympanic membrane causing vibration of stapes[61].

From tympanic membrane, sound waves are transmitted through air of middle ear cavity to reach scala tympani. This is air conduction.

Bone conduction is the transmission of sound waves from environment through the bones which reach the inner ear.

Sound waves get transmitted from footplate of stapes to the inner ear→ movement of stapes inward and outward→.movement of oval window→pressure in the perilymph of scala vestibuli increases →depression of reissners membrane→depression of basilar membrane →pressure wave transmitted to the perilymph of scala tympani outward movement of round window into the middle ear[61].

When the stapes move outward ..basilar membrane bulges and round window is pulled inward.

TRANSDUCTION OF SOUND WAVES

In resting state ,ear records 2 potentials.

RMP of the hair cells and endocochlear potentials

The basolateral RMP of hair cell is -60 mv. It is due to k efflux.

The hair cell, being a mechanoreceptor is very sensitive to the degree of movement of cilia. The lateral bending of shorter stereocilia towards taller cilia is the appropriate stimulus, which open the cation

channels, allowing k entry and ca entry into hair cel→. This causes depolarisation and increased opening of calcium channels→ release of neurotransmitter from the synaptic →cleft . generation of action potential→ When stereocilia are pushed away from taller cilia, the transduction channels close resulting in hyperpolarisation.

Hence, both depolarisation and hyperpolarisation depend upon movement of hairs.

AUDITORY PATHWAY

1) Nerve fibres from the spiral ganglion of corti enter the dorsal and ventral cochlear nuclei[62]

2) From cochlear nuclei second order neurons pass to the opposite side and terminate in the superior olivary nucleus.

3) From Superior olivary nucleus third order neurons pass upward through the lateral leminisci to inferior colliculi of both sides

4) Fibres from lateral leminisci bypass and pass to the medial geniculate body

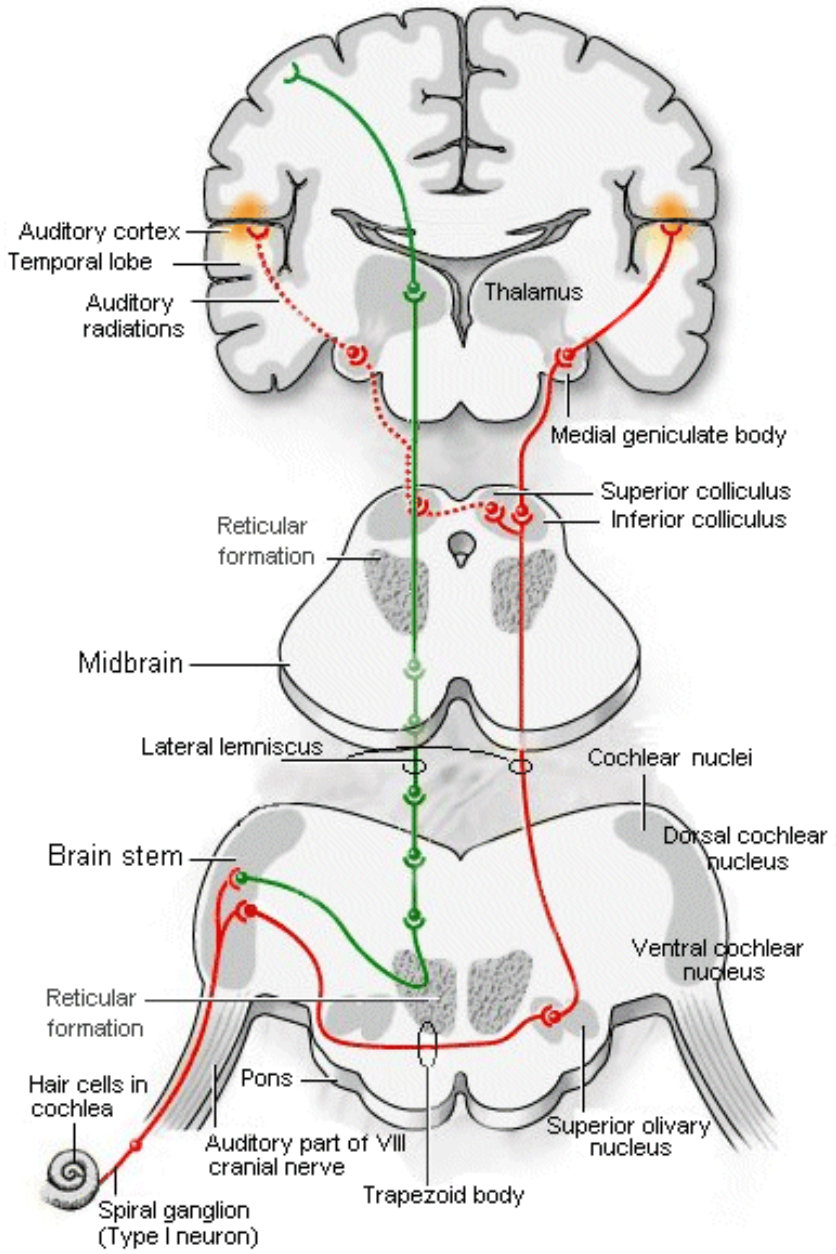
5) Fibres from MGB pass to the auditory cortex located in the superior temporal gyrus (area 41) & upper part of Sylvian fissure which includes both parietal and frontal opercula.

6) Primary auditory association areas; area 22,21 &20

a) Area 22 is the WERNICKE'S area located in the superior temporal gyrus[61]. It is concerned with understanding of auditory and visual information.

b) Area 21 &20 are located in middle and inferior temporal gyrus which interpret auditory short term memory.

Fig 4: Schematic diagram of auditory pathway



BIOPHYSICS

Nerve cell membrane have an equal distribution of positive ions outside and negative ions inside cell membrane. The action potential is due to the movement of Na^+ & K^+ Ions which is responsible for flow along cell membrane and is resisted by an intervening tissue which is called impedance.

1. ELECTRODES

There are 3 types of electrodes, active reference and ground which are made up of platinum, stainless steel, gold .The action potential is recorded between active and reference electrode and the ground electrode works as a zero voltage reference point.

Surface and needle electrodes are used in clinical practice.

2. AMPLIFIER

A 5 X 10 folds amplification is needed as the biological signals are very small and there exists an intrinsic impedance of the electrode and an impedance between the electrode and skin which reduce the amplitude of the signals.

3. FILTER

It is a device which restricts the frequency range of signals and is needed for elimination of noise and bringing out the optimal characteristics of waveforms.

4. AVERAGER

It is a device which extracts very small signals for example, evoked potentials are burried in EEG noise and sensory nerve action potential in EMG noise.

5. DISPLAY

The waveforms are displayed in two methods

i) Analogue oscilloscope display where the action potentials are displayed directly following amplification and filtering.

ii) Computer based digital video display where an analogue digital converter and a digital processing technique are used. Hence ,the signals can be redisplayed with greater sensitivity without losing accuracy of waveforms**.**

6. STIMULATOR

Electrical and magnetic stimulators are used in general Constant current type of electrical stimulator delivers constant current to the subject over a wide range of electrode impedance whereas a constant voltage type of electrical stimulator delivers a fixed voltage between anode and cathode.

Magnetic stimulator are used for noninvasive stimulation of motor cortex, peripheral nerves and spinal cord.

7. SENSITIVITY SWEEP SPEED

If the sensitivity is high, the latency of action potential shortens and increase in sweep speed also shortens the latency.

BRAINSTEM AUDITORY EVOKED POTENTIAL

The brainstem auditory evoked potentials are a series of potentials generated by sequential activation of different parts of auditory pathway[63].They are produced within 10 m.sec by a brief click stimuli.

Clinical significance of BAEP'S[63];

1) To assess the degree of hearing loss.

2) To assess the hearing in infants and young children suspected of being deaf.

3) The latencies and interpeak latencies provide information about tumours , in demyelination and in various drug induced traumatic disease processes.

ANATOMICAL &PHYSIOLOGICAL BASIS OF BAEPS

Organ of corti, rests upon the Cochlea with its receptor elements and hair cells. High frequency signals have impact on the basal end of Cochlea& low frequency sounds affect the apical end.

When cochlea is stimulated, the fibres of 8^{th} nerve which innervate the basilar membrane are set into vibration. The 8^{th} nerve neurons situated

in the spiral ganglia are bipolar,their axons reach the cochlear nucleus whereas dendrites go to hair cells.

There are three Subnuclei in the cochlear nucleus

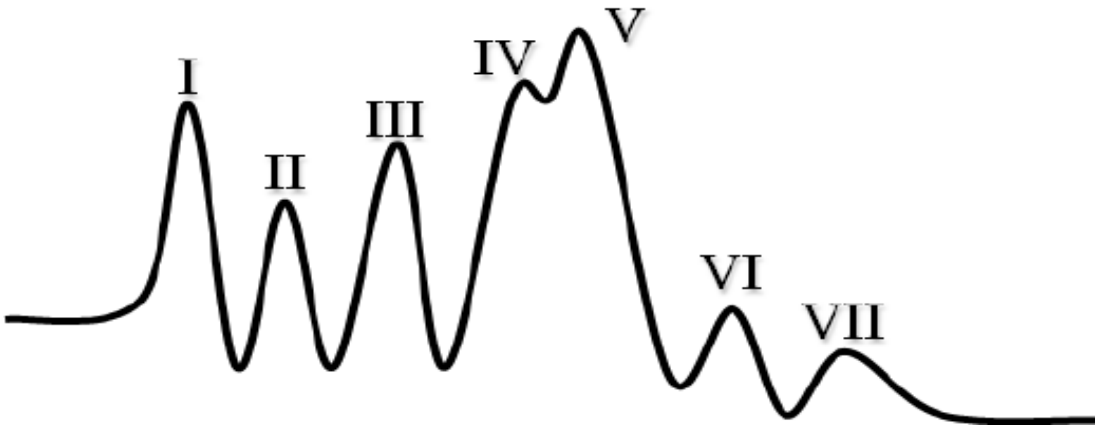
- Anterior Ventral Cochlear Nucleus (AVCN)
- Posterior Ventral Cochlear Nucleus (PVCN)
- Dorsal Cochlear Nucleus.

The Radiations from AVCN pass through the Ventral acoustic striae & the output from PVCN travel through middle and ventral Acoustic Striae to get terminated in the Superior Olivary Nuclei and Inferior Colliculus.

The output from DCN reach the Superior Olivary Nucleus via the Dorsal striae.

The impulses from the Inferior Colliculi reach the Auditory Cortex via the Medial geniculate body.

Fig 5: BAEP WAVEFORM



BRAINSTEM ELECTRICAL ACTIVITY AND ITS CORRELATION WITH BAEP

In first 10 ms after a brief acoustic stimuli, a series of potentials which corresponds to sequential activation of the peripheral, pontomedullary, pontine and midbrain portions of the auditory pathway are recorded.

The origin of the waveforms are,

Wave I	:	From the peripheral part of 8th cranial nerve adjacent to cochlea.
Wave II	:	From the Cochlear nuclei
Wave III	:	From the Superior olivary nucleus.
Wave IV	:	From the Lateral lemniscus
Wave V	:	From Inferior colliculi.
Wave VI	:	From medial geniculate body
Wave VII	:	From auditory cortex

Fig 6: ORIGIN OF BAEP WAVEFORM

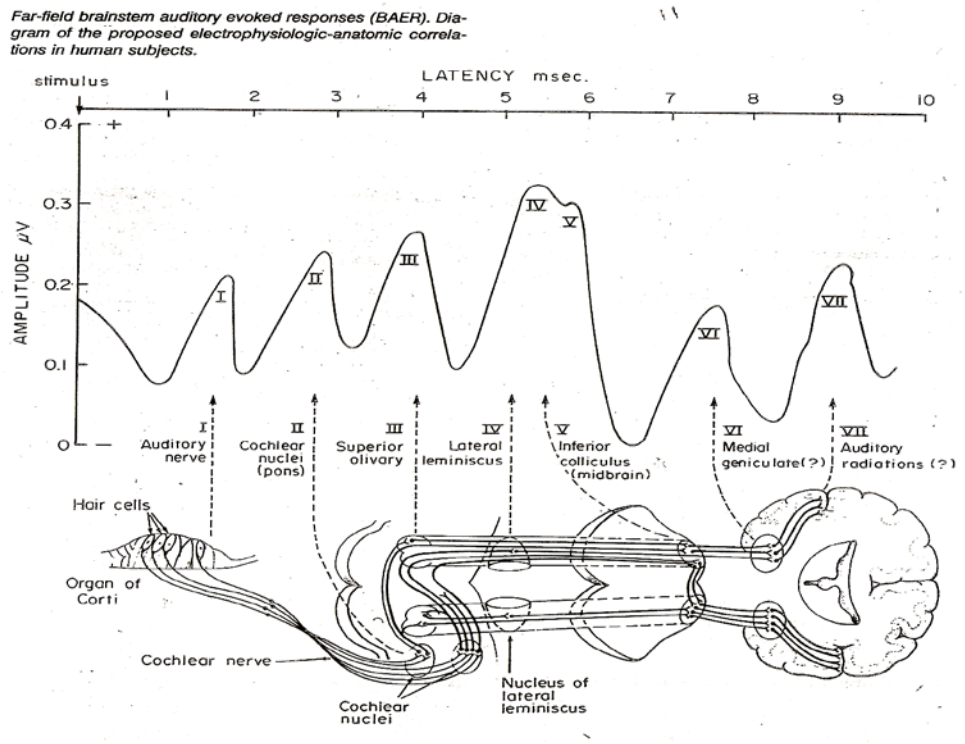
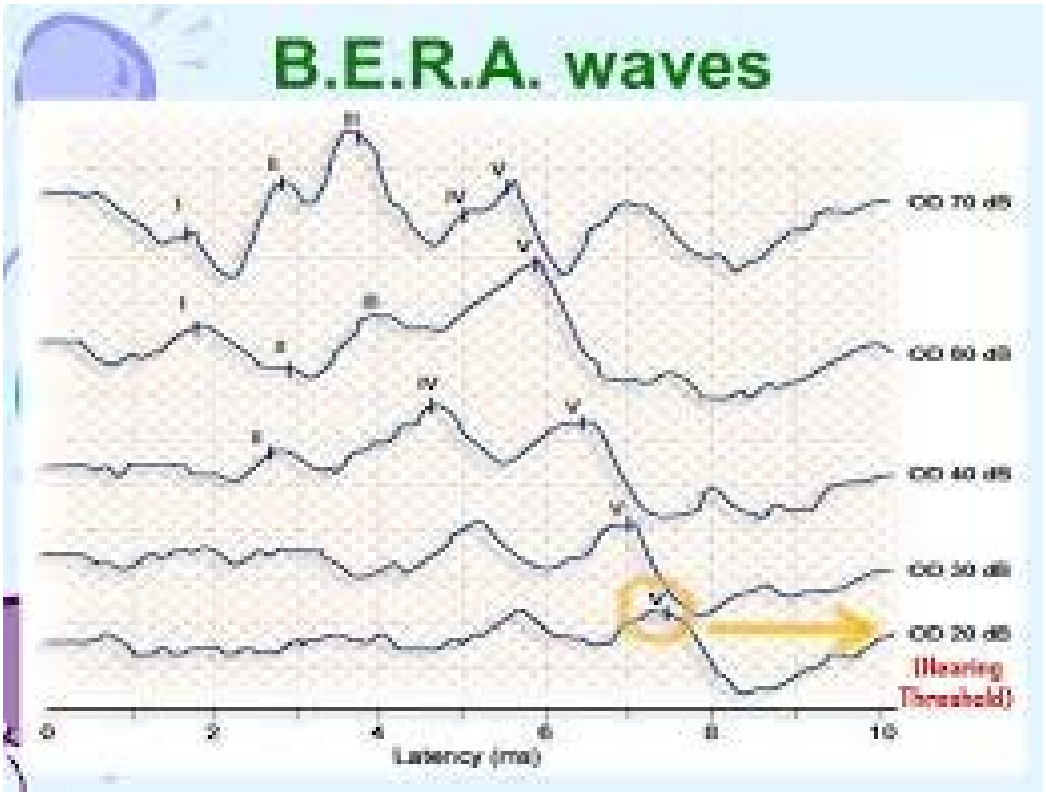


Fig 7: RECORDED BAEP WAVEFORMS



FACTORS AFFECTING BAEP WAVEFORMS

1. The latency of BAEP waveforms is age dependant up to two years. Older adults have prolonged I to IV interpeak latency compared to younger persons.[64]

2. Females have high amplitude and short latency waveforms.

3. The latency of BAEP waveforms decreases with increased temperature and increases with decreased temperature

4. Certain drugs like barbiturates and alcohol prolong the wave V latency by decreasing the body temperature and they do not directly act on the auditory pathway.[64]

5. Any hearing deficit should be ruled out prior to recording BERA.

CHARACTERISTICS OF WAVEFORMS OF BAEP

WAVE I: It is the first up going peak which appears 1.4 ms after the stimulus. The amplitude of the wave can be increased by using horizontal montage and an external canal needle electrode..As it originates from the 8^{th} nerve, this wave is preserved in patients with CNS problem alone. It is absent or reduced in patients with peripheral hearing impairment.

WAVE II: It is a poorly defined wave, which is absent in cochlear nucleus lesions

WAVE III: It is a prominent upgoing peak which appears as a bifid wave. It is reduced in superior olivary nuclear lesions

WAVE IV: It is a small wave which appears in the upgoing phase of wave V. It is absent in lateral leminisci lesions.

WAVE V: It is the most prominent peak which appears 5.5 ms after the auditory click. It disappears in inferior colliculi lesions.

Abnormal BAEP recordings are seen in

a) Absence of wave I is seen in 8th nerve tumour and ischaemia.

b) Absence of waves beyond wave I is seen in acoustic neuroma, meningioma.

c) Absence of waves 1V & V is seen in conditions like multiple sclerosis, hydrocephalus.

BAEP WAVEFORMS MEASUREMENT

The parameters used for analysing the BAEP Waveforms are

A) Absolute latency & amplitude

B) Interpeak latencies(I-III,I-V,III-V)

C) Amplitude ratio of V/I

Absolute latency & amplitude

Amplitude is measured as the height from the peak of a wave to the trough of the same wave & latency expressed in ms is measured from the beginning of the first wave to the peak of that wave.

Inter peak latencies

The commonly measured interpeak latencies are I-III,I-V & III-V.

I-V Inter peak latency

It indicates signal transduction from the proximal part of the eighth nerve to midbrain through pons. It has a normal value of 4.5 ms. It is prolonged in elderly males and in conditions like Demyelination, Degenerative diseases and Hypoxic brain damage.

I-III Interpeak latency

It measures the conduction of auditory radiation from the eighth nerve across the subarachnoid space to lower pons. It has a normal value of 2.5 ms and its prolonged in eighth nerve tumour, Guillain barre syndrome or any pontomedullary junction diseases.

III-V Interpeak latency

It denotes the conduction of impulses from lower pons to midbrain. It has a normal value of 2.4 ms .Its isolated prolongation is not significant

Amplitude ratio of V/I

This helps to assess whether the hearing impairment is peripheral or central..

Sohmer[54] et al in the year 1967 first recorded Auditory Brainstem Responses with surface electrodes.

Jewett[55] et al in the year 1971, interpreted BAEP recordings from the Absolute peak latencies and Interpeak Latencies.

Selters[56] et al in 1977, produced landmark findings of prolonged Inter peak latencies in tumour cases.

Hecox[57] et al stated that ABR could be used as a measuring tool for estimating hearing threshold in adults and infants.

It was Starr[58] et al in 1975 who first reported abnormal ABR findings due to central nervous system pathology in brainstem.

Sensorineuronal hearing loss has been documented in CKD Patients and Haemodialysis patients and the available studies report no retro cochlear component and the reports on reversibility of hearing impairment remains equivocal. Hence, I intend to proceed this study in order to document the electrophysiological changes in BAEP Waveforms and to determine the reversibility of the BAEP changes after renal transplantation.

REVIEW OF LITERATURE

An Evoked potential is an electrical potential recorded from the nervous system of a human following a brief stimuli. Such potentials are useful for electro diagnosis and monitoring. Signals can be recorded from the cerebral cortex, brainstem & spinal cord on the peripheral nerves.

Research History:

In 1967, Sohmer & Feinmesser[54] were the first to record Auditory Brainstem Responses with surface electrodes.

In 1971 Jewett & Williston[55] described BAEP and interpreted the Absolute and Inter peak latencies.

It was Lugigalvani who discovered the good conducting property of nerves in the year 1971.

In 1833, The Techniques of electrical stimulation in a neuromuscular disease was discovered by Duchne.

In 1977 Selters and Brackman[56] produced landmark findings on prolonged Interpeak latency in tumour cases.

1975, Hecox and Galambos[57] pointed out that ABR could be used for estimating the hearing threshold in adults and infants.

In the ARIC Study by Bash LD[1], Coresh et al ,it was discussed and compared the several definitions of incident chronic kidney disease by means of incidence, agreement and risk factors.

Hsc CY, Chertow GM[3] et al discussed the issues that define the prevalence of CRI which included the laboratory differences in ser.creatinine assays, within person measurement errors in s.cr & variations among different demographic groups.

Coresh J, Astor BC[4] et al studied that errors in caliberation make little difference in estimating severely decreased GFR (<30 ml/min/1.73 m^2), but in higher GFRs, they produce larger difference.

Murthy K, Stevens LA[5] made a study & concluded that recaliberation of serum creatinine assays improved the accuracy of GFR estimation using MDRD study though it was not practical for all clinical laboratories.

Coresh J, Selvin E[6] et al studied that prevalence of CKD in united states in 1999-2004 was higher compared to 1988-1994 which was attributed to the increased prevalence of DM &HT.

Coresh J, Astor BC[7] et al in their study analysed kidney function & damage & stages of CKD which was estimated from calibrated serum. creatinine level, spot urine albumin level, age, sex & race.

Jeon HG, Lee JW[8], et al made a study & concluded that nephron sparing surgery for small renal mass should be attempted to prevent CKD in all eligible patients especially those with diabetes.

Schmitz PG, Kasske[9] et al examined the effects of 30 week enalapril treatment on the development of glomerular disease in obese

zucker rats. It was concluded that there could be a possible restriction of glomerular growth.

Park SK, Kang SK[10] Suggested that obesity & hyperinsulinemia which are commonly associated with type II Diabetes can also be associated with glomerular capillary hypertension.

Chen J, Muntner P[11] et al in their study suggested that metabolic syndrome is an important risk factor for CKD.

Zatz, Meyer TW[12] et al made a study to indicate that metabolic disorder seen in stable moderately hyperglycemic diabetic rats does not lead to glomerulopathy as long as elevation in glomerular pressures are prevented.

Matsushita, Veldem[13] et al studied the quantitative data for use of both kidney measures for risk assessment & definition and staging of CKD.

Hunsicker LG, Greene T[14] et al examined the effects of dietary protein restriction & strict blood pressure control on the reduction in GFR.

Ataga KI, Orringer[15] et al studied that Sickle cell anemia and related hemoglobinopathies are associated with a large spectrum of renal abnormalities like impaired urinary concentrating ability, defects in urinary acidification and potassium excretion.

Mantarri M, Tiula E et al[16] in their study suggested that in addition to hypertension, serum lipids also accelerate the decline in renal function. It was noted that subjects with elevated HDL had a rapid regression of renal function.

Fox CS .Larson MG[17] in their study indicated the fact that cardiovascular risk factors are associated with new onset kidney disease development.

Eki K, Oshiro S[18] et al made a study to prove that high levels of serum uric acid levels was a positive factor to correlate high ser. creatinine in the Japanese population.

Bolignano D, Coppolino G[19] et al in their study demonstrated that NGAL, a protein had a direct relation to proteinuria and inverse relation to residual renal function.

Bolignano D, Coppnolino G [20] et al in their study stated that a stress protein –NGAL, plays a vital role in the pathophysiology of diabetic nephropathy.

Halim JM, Giraudeau B[21] et al did a study to illustrate the fact that chronic smokers, despite moderate smoking develop irreversible proteinuria.

Shankar K, Klein R[22], et al performed a cross sectional study to state that smoking along with consumption of alcohol per day is associated with chronic kidney disease.

Perneger TV, Klag MJ[23] et al, did a cross sectional study to throw lights over a neglected risk factor i.e lifetime use of addictive drugs like cocaine and heroin were increasingly related with ESRD.

Jaffe JA, Kimmel PL[24] studied that cocaine use led to renal injury in the form of hemodynamic changes, glomerular degradation and oxidative stress.

Muntner P, He J, Vupputuri[25] et al in their study described the link between high lead exposure with renal damage and CKD.

Lindeman RD, Tobin J[26] et al did a longitudinal study to explain the rate of reduction in renal function with ageing by showing a significant rise in creatinine clearance.

Kiberd BA, Clase CM[28] et al in their study determined the effect of CKD on life expectancy & compared that with the impact of breast cancer and prostate cancer in women and men's life expectancy respectively.

Klag MJ, Randall BL[29] et al, stated that high blood pressure and low socioeconomic status are the reasons for a four fold increase in CKD in African American men.

Freedman BJ, Volkova NV[30] et al, did a population based screening to make physicians aware of screening the family members to slow down the rate of growth of CKD.

Hostetter TH, Olson JL[31] et al in their study demonstrated the changes in glomerular hemodynamics after renal ablation & hyperfiltration of a single nephron led to maladaptive consequences by glomerular damage.

Zatz R, Dunn BR[32] et al in their study with two groups of diabetic rats, noticed the increase in weight of the kidney, GFR and plasma flow in both groups. One group of diabetic rats which were not treated with an ACE inhibitor enalapril showed structural abnormalities.

Keller G, Zimmer G [33] et al Proposed the fact that diminished number of nephrons contribute to primary hypertension

Mcnamara BJ, Diouf B[34] et al stated decrease in glomerular number & a large volume glomeruli increase the risk for renak hypertension in adult life.

Ataga KJ, Orringer EP [35] et al studied sickle cell anaemia & other Hemoglobinopathies are associated with renal abnormalities which included defects in concentrating urine, excreting potassium & the function of proximal tubule is supranormal i.e there is increased creatinine secretion with phosphorous reabsorption.

Steffes MW, Brown DM [36] et al did a study in control rats and rats which were induced diabetes with sttreptozocin. Both groups underwent unilateral nephrectomy. It was noticed after 3 to 4 months of surgery,

there was a marked thickening of the mesangial matris with deposition of IgG & C_3 in the diabetic rats.

Khadra MH, Pickard RS[37] et al did a prospective analysis of 1930 patients with hematuria and proved that renal tumours can be detected by combined use of Ultrasound and IVP & not by cystoscopy alone.

Karl Tryggvason, Jankko Patrakka[38] et al in their study concluded that patients with persistent microscopic hematuria develop thin basement membrane nephropathy.

S.Tian, E.Kusano[40] et al in their study suggested that measuring Cystatin C in both urine & serum is useful to estimate a mild decrease in GFR. It is also a marker for indicating the removal rate of a protein with low molecular weight &various types of flux membranes used in HD

Silkensen J, Kasiske BL[41] et al studied the Laboratory assessment of renal disease: clearance, urinalysis, and renal biopsy. In: Brenner BM, ed. Brenner and Rector's the kidney. Philadelphia: Saunders; 2004:1107-1150.

Sanger J, Kramer EL[42] et al did a study on Radionuclide quantitation of renal function. Urol Radiol. 1992;14:69-72.

Johnson WJ, Hagge WW, Wagoner RD[37], et al. narrated the effects of urea loading in patients with far-advanced renal failure. Mayo Clin Proc. 1972;47:21-29.

Kraus LM, Kraus AP[44] et al formulated a study to prove carbomylated molecules influence the fate of non-carbomylated molecules by blocking, enhancing or getting excluded from the metabolic pathways. Urea derived cyanate contribute to the toxic manifestations of uremia.

Nagata Y,Akino T[45] et al discussed in their study that elevation of plasma D aminoacid were observed in renal disease patients in proportion to the creatinine , β microglobulin levels and to the GFR.

Abel J, Rowntree L, Turner B[47]. On the removal of diffusible substances from the circulating blood of living animals by dialysis. J Pharmacol Exp Ther. 1914;5:275-316.

Haas G.[48] Dialysis of the flowing blood in the patient. Klin Wochenschr. 1888;70:1923.

Kolff WJ, Berk HT,[49] Welle M, et al.The artificial kidney: a dialyser with a great area. 1944 [classical article]. J Am Soc Nephrol. 1997;8:1959-1965.

U.S. Renal Data System. USRDS 2010 Annual Data Report:[50] Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2010.

National Kidney Foundation. K/DOQI[51] clinical practice guidelines and clinical practice recommendations for 2006 Updates: hemodialysis adequacy, peritoneal dialysis adequacy, and vascular access. Am J Kidney Dis. 2006;48(suppl 1):S1-S322.

Brescia MJ, Cimino JE, Appel K[52], et al did a study on Chronic hemodialysis using venipuncture and a surgically created arteriovenous fistula. N Engl J Med. 1966;275:1089-1092.

Antoniou GA[53], et al did a meta analysis & found out the occurrence of radial cephalic fistula failure in elderly patients which were less in the proximal brachiocephalic fistulas.

Sreedhara R, Himmelfarb J[54] et al discussed the. Impact of Anti-platelet therapy in graft thrombosis: results of a prospective, randomized, double-blind study. Kidney Int. 1994;45:1477-1483

Dixon, Beck[55] et al in their study discussed that those patients who received dipyridamole & aspirin therapy after a new arteriovenous graft for hemodialysis access showed significant reduction in the occurrence of graft stenosis.

Trakarnvanich T[56] et al, discussed the efficacy of single-needle versus double-needle hemodialysis in chronic renal failure. J Med Assoc Thai. 2006;89(suppl 2):S196-S206.

Murray JE, Merrill JP[58],et al made a study on kidney transplantation between 7 pairs of identical twins. Ann .surg. 1958;148;35359.

Cohen J, Rees AJ, Williams.[59] et al did a Prospective randomised control trial of perioperative antibiotic prophylaxis in renal transplantation .J hosp infect. 1988;11;357-363.

Newer MR, Aminoff [64]et al discussed the recommended standards for BAEP and submitted in the IFCN committee in the year 1994.

AIM AND OBJECTIVE

To Evaluate Brainstem Auditory Evoked potential in chronic Kidney disease, Hemodialysis and Renal transplantation patients.

OBJECTIVE:

A) To document the electrophysiological changes in BAEP waveforms.

B) To determine the reversibility of BAEP changes after Renal Transplantation.

MATERIALS AND METHODS

This study was conducted at the Department of Physiology in Kilpauk Medical College, Chennai.

STUDY DESIGN

Observational study.

SUBJECT SELECTION

Total sample size-80, controls-20,CKD Patients -20,Hemodialysis patients-20,Renal transplantation patients-20.

INCLUSION CRITERIA

1. Patients diagnosed to have Chronic kidney disease in the department of Nephrology with eGFR <60 with duration more than 3 months.
2. Chronic Kidney disease patients undergoing hemodialysis for more than one month in the department of Nephrology, KMC.
3. Chronic Kidney disease patients who underwent Renal transplantation in the department of Nephrology, KMC.
4. Male &female >18-70 years

EXCLUSION CRITERIA

- Ischemic heart disease.
- Cerebrovascular dise**ase**
- Alcoholism.
- Any neurological disease
- Previous history of Hearing impairment
- Alport syndrome

CONTROLS

Healthy volunteers who are age and sex matched were chosen as controls.

SCREENING PROCEDURES

- Patients who qualify under the inclusion criteria will be enrolled in the study (Appendix A).
- Blood pressure.
- Height.
- Weight.
- Brief history to rule out IHD, diabetes, hearing impairment, alcoholism, drug intake (Appendix B).
- General clinical examination (Appendix B).

CONSENT

A written informed consent was obtained from patients & controls after explaining the procedure and its significance in their vernacular language (Appendix F).

EQUIPMENT DETAILS

Brainstem auditory evoked potentials studies were carried out on a computerized Nerve conduction testing equipment: Medicaid, computerized physiolab, Neuroperfect plus**.**

ETHICAL CONSIDERATIONS

Institutional Ethical committee approval was obtained from Kilpauk medical college Chennai -10.

The settings were as follows:

STIMULUS PARAMETER;

- Click stimulus having intensity 70 db, was presented to both ears monoaurally. During stimulation of one ear, the other ear was masked by 40 db sound. A total of 2000 stimulations generated by passing 0.1 millisecond square pulse through shielded headphones with alternating polarity were applied on both ears monoaurally. Stimulus were at the rate of 11.1/sec.

- *filters :
- 1. low : 100 Hz
  2. high : 3 KHz

Stimulus polarity

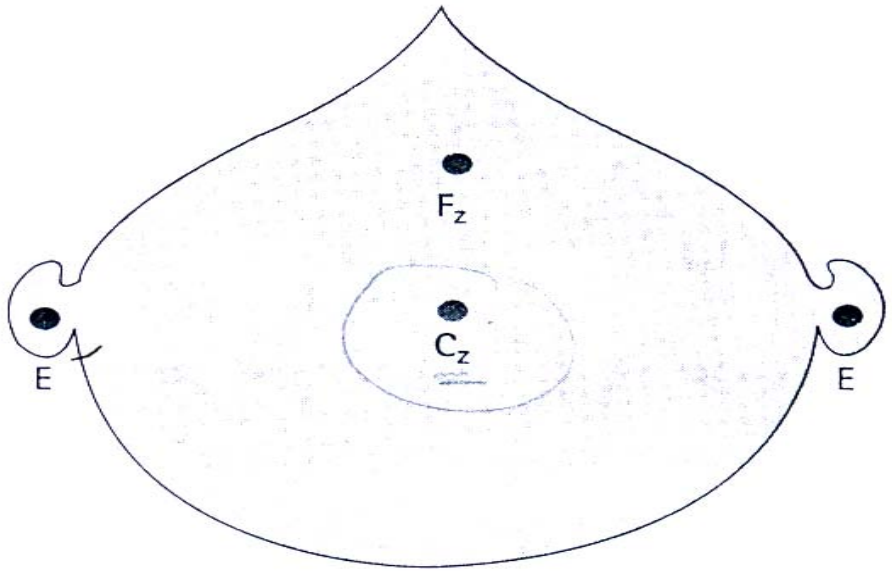
- Two types of clicks were produced.
- One, moving the earphone diaphragm away from the eardrum (rarefaction click).
- The other moving it in the opposite direction (condensation or compression click).

In this study, stimulus with rarefaction click is given.

Recording electrodes

- The volume-conducted evoked responses are picked up from scalp by electrodes. Two electrodes were attached, one to right mastoid and other to left one as ground electrode to forehead, termed as F_z. All the electrodes were pluged to the junction box. Skin-to-electrode impedance was monitored and kept below 5 kΩ.
- Recommended montage for BAEP :
- CHANNEL 1: mastoid, designated as A_i and A_c respectively; one reference electrode on vertex , labeled as C_z; and $C_z - A_i$
- CHANNEL 2 : C_Z - A_c
- GROUND : F_Z

Fig : 8 BERA –Placement of electrodes



- E – ear lobe recording, Cz – reference, Fz – ground electrodes

PREREQUISITES FOR THE STUDY

A) The subjects were advised to clean and keep their head oil free.

B) The research lab was made quiet and sound proof to the patients.

C) Subjects were made to remove their ornaments.

PROCEDURE:

The BAEP Recording was done in the research laboratory, in the Department of physiology, Kilpauk medical college using Neuroperfect Plus-Medicaid Physiolab. In al subjects both right and left ears were tested separately.

RECORDING OF BAEP-INSTRUMENT SETTING

The requirements are

1. Recording electrodes, 2.Amplifier and averager, 3. Electrode paste, 4.Ear phone

Equipment set up;

Suggested Montage;

1. Channel 1: Ai-Cz-Active electrodes
2. Channel 2 : Ac -Cz -ipsilateral ear (Ai), contralateral ear (Ac) or mastoid process
3. Ground : Fz-Reference electrode ;Cz, at vertex

Recording conditions

1. Filter, low filter cut at 10-100 Hz ,high at 3000 Hz
2. Amplification in the range of 2,00,000-5,00,000
3. Sweep speed at 1 msec/division
4. Electrode impedance kept below 5 kilo-ohms

Stimulation options

1. Sensitivity at 0.3uv/division
2. 60 db sensory level, the point at which the individual barely appreciates the stimulus.

B.Steps

1. The instrument is kept out of view of the subject.
2. The subject is allowed to sit comfortably on a chair.
3. Skin at the point where electrodes are placed is cleaned with spirit.
4. Using a conducting jelly or electrode paste the active recording electrodes are placed on both the ears ipsilateral ear (Ai) and contralateral ear (Ac) or mastoid process as per 10-20 international system of EEG electrode placement ;the reference electrode is placed at the vertex i.e at Cz..the ground electrode is placed at Fz
5. The electrodes are connected through the preamplifier to the cathode ray oscilloscope

6. A brief click stimulus, which is a square wave pulse of 0.1 msec duration is given. A click rate of 11-31 Hz is used mostly in clinical practice.

7. The effects of click intensity is observed and the BAEP waveforms are compared with the normal.

PARAMETERS STUDIED are the wave latencies I, II, III, IV & V and interpeak latency I-III, I-V, and III-V…Total duration of recording the waveforms is within 10 msec of stimulus. Thus brainstem auditory evoked potentials are recorded from the ear and scalp in response to a brief auditory stimuli. The evoked potentials that appear following transduction of acoustic stimulus by ear cells create an electric signal that is carried to the cerebral cortex via the auditory pathway.

TABLE : 2

ANTHROPOMETRIC MEASUREMENT OF CASES (CKD)

WITH CONTROLS

VARIABLES	CASE –CKD (20) Mean +SD	CONTROLS N=30	P VALUE
AGE (YRS)	49+ 12.73	31.60+9.95	0.000
WEIGHT(KG)	58.65+ 7.6	63.37+11	0.242

TABLE :3

ANTHROPOMETRIC MEASUREMENT OF CASES (HD) WITH CONTROLS

VARIABLES	CASE =HD (20) Mean +SD	CONTROLS (N=30) Mean +_SD	P VALUE
AGE (YRS)	36.75+_ 15.3	31.60+ 9.9	0.502
WEIGHT(KG)	58.05+_4.3	63.37+_11.8	0.822

TABLE: 4

ANTHROPOMETRIC MEASUREMENT OF CASES (RT) WITH CONTROLS

VARIABLES	CASE =RT (20) Mean +SD	CONTROLS (N=30) Mean +_SD	P VALUE
AGE (YRS)	45.15+_13	31.60+_9.9	0.002
WEIGHT(KG)	61.20+_6.925	63.37+_11.8	0.822

TABLE : 5

COMPARISON OF SERUM CREATININE IN CASES AND CONTROLS

SERUM. CREATININE	MEAN	SD	P VALUE
CONTROLS	0.712	0.1228	<0.001
CKD	6.325	1.3692	<0.001
DIALYSIS	6.280	1.3621	<0.001
RENAL TRANSPLANT	1.130	0.4842	0.418

'P' Value is significant for controls, CKD & HD patients.

TABLE: 6

COMPARISON OF ABSOLUTE PEAK LATENCIES OF RIGHT EAR- BETWEEN CHRONIC KIDNEY PATIENTS & CONTROLS

LATENCIES	CASE (CKD) MEAN +_SD	CONTROL MEAN+-SD	P VALUE
I	1.82+-0.24	1.75+-0.07	0.771
II	2.87+_0.14	2.83+_0.15	0.889
III	4.21+_0.31	3.98+_0.06	0.044
IV	4.99+_0.47	5.08+_0.17	0.859
V	5.61+_0.47	5.69+_0.17	0.902

Absolute peak latency of III waveform is significantly prolonged with a ‘p’ value of 0.044.

FIG - 9

COMPARISON OF ABSOLUTE PEAK LATENCIES OF RIGHT EAR- BETWEEN CHRONIC KIDNEY DISEASE PATIENTS & CONTROLS

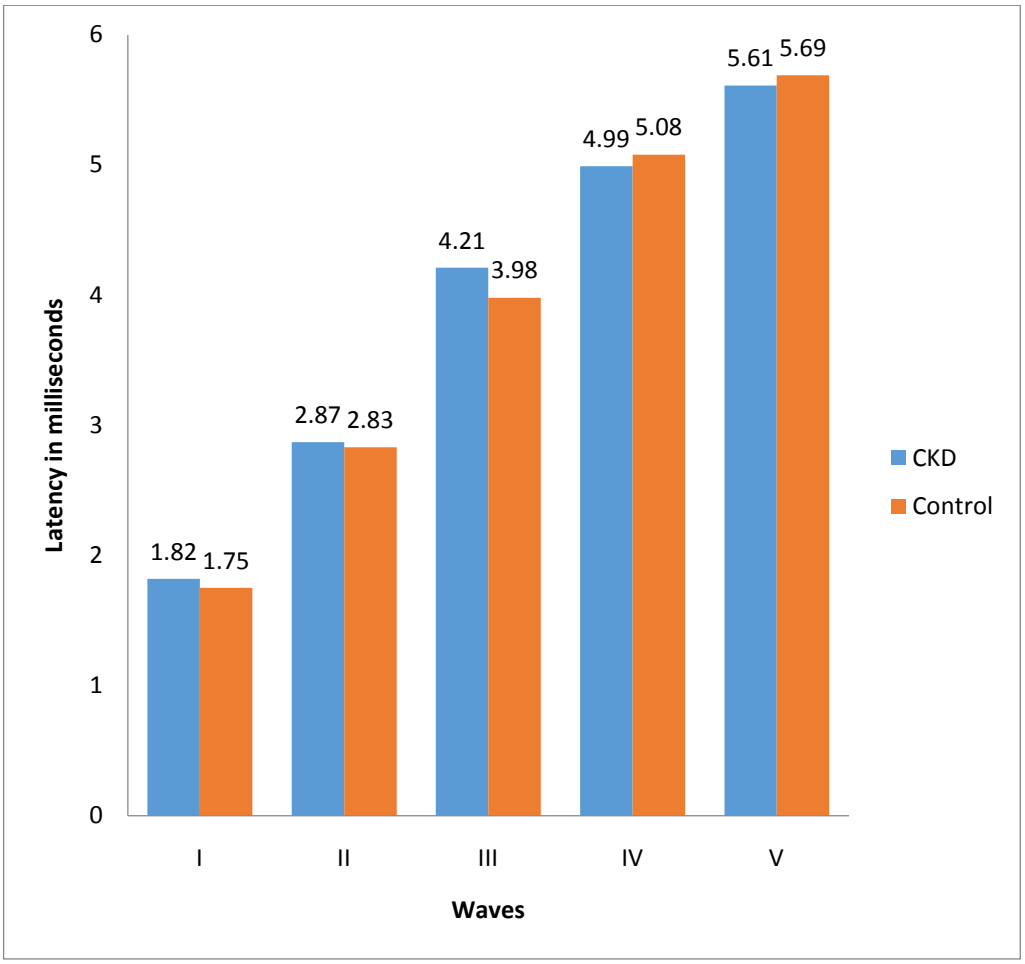


TABLE 7

COMPARISON OF ABSOLUTE PEAK LATENCIES OF RIGHT EAR-BETWEEN HEMODIALYSIS PATIENTS & CONTROLS

LATENCIES	CASE (HD) MEAN +_SD	CONTROL MEAN+-SD	P VALUE
I	1.98+_0.48	1.75+_0.07	0.013
II	2.79+_0.22	2.83+-0.15	0.891
III	3.72+_0.33	3.98+_0.06	0.020
IV	5.02+_0.15	5.08+_0.17	0.961
V	5.78+_0.29	5.69+_0.17	0.851

Absolute peak latency of waves I & III are prolonged with a ‘p’ value of 0.013 & 0.020.

FIG - 10

COMPARISON OF ABSOLUTE PEAK LATENCIES OF RIGHT EAR- BETWEEN HEMODIALYSIS PATIENTS & CONTROLS

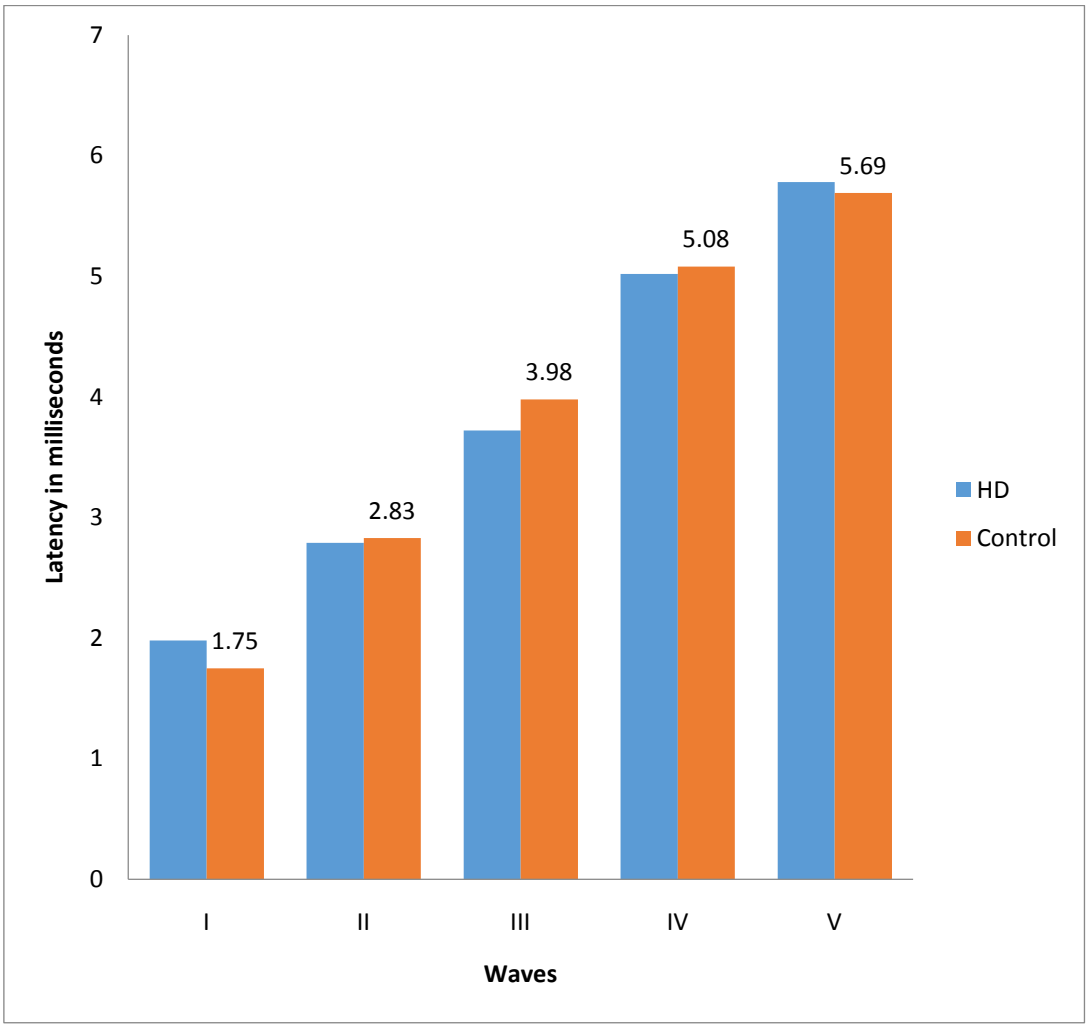


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TABLE: 8

COMPARISON OF ABSOLUTE PEAK LATENCIES OF RIGHT EAR-BETWEEN RENAL TRANSPLANTATION PATIENTS & CONTROLS

LATENCIES	CASE (HD) MEAN +_SD	CONTROL MEAN+-SD	P VALUE
I	1.74+_0.08	1.75+_0.07	1.000
II	2.78+_0.26	2.83+_0.15	0.749
III	3.87+_0.45	3.98+_0.06	0.564
IV	4.90+_0.64	5.08+_0.17	0.424
V	5.61+_0.63	5.69+_0.17	0.898

There is no significant prolongation of absolute peak latency.

FIG 11

COMPARISON OF ABSOLUTE PEAK LATENCIES OF RIGHT EAR- BETWEEN RENAL TRANSPLANTATION PATIENTS & CONTROLS

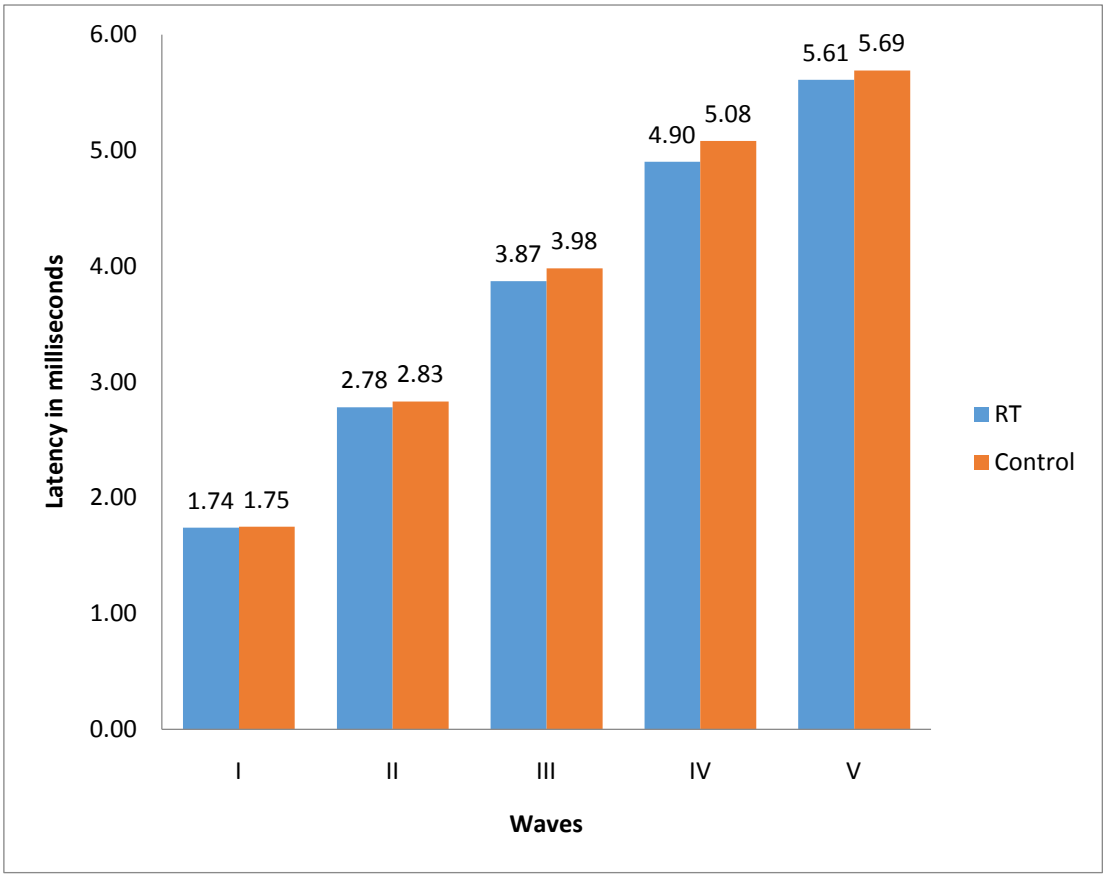

TABLE: 9

COMPARISON OF INTER PEAK LATENCIES OF RIGHT EAR-BETWEEN CHRONIC KIDNEY DISEASE PATIENTS & CONTROLS

LATENCIES	CKD PATIENTS	CONTROL	P VALUE
I-III	2.39+_0.49	2.23+_0.10	0.604
III-V	1.50+_0.35	1.70+-0.18	0.127
I-V	3.89+_0.24	3.92+_0.22	0.991

There is no significant prolongation of inter peak latencies..

FIG 12

COMPARISON OF INTER PEAK LATENCIES OF RIGHT EAR- BETWEEN CHRONIC KIDNEY DISEASE PATIENTS & CONTROLS

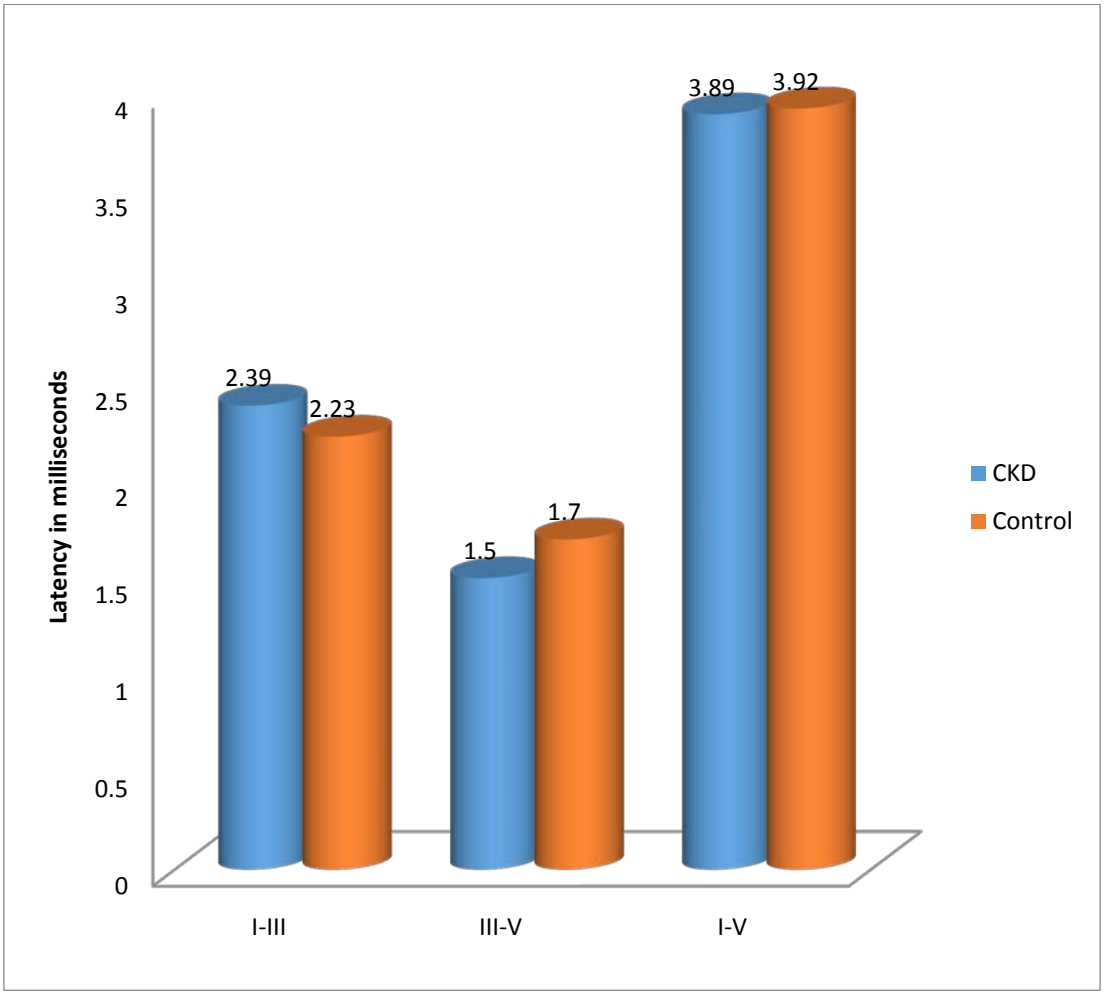

TABLE 10

COMPARISON OF INTER PEAK LATENCIES OF RIGHT EAR-BETWEEN HAEMODIALYSIS PATIENTS & CONTROLS

LATENCIES	CKD PATIENTS	CONTROL	P VALUE
I-III	1.79+_0.68	2.23+_0.10	0.005
III-V	2.15+_0.50	1.70+_0.18	0.000
I-V	3.84+_0.52	3.92+_0.22	0.901

There is significant prolongation of I-III & I-V interpeak latencies with ‘p’ value of 0.005 & 0.000.

FIG 13

COMPARISON OF INTER PEAK LATENCIES OF RIGHT EAR-BETWEEN HEMODIALYSIS PATIENTS & CONTROLS

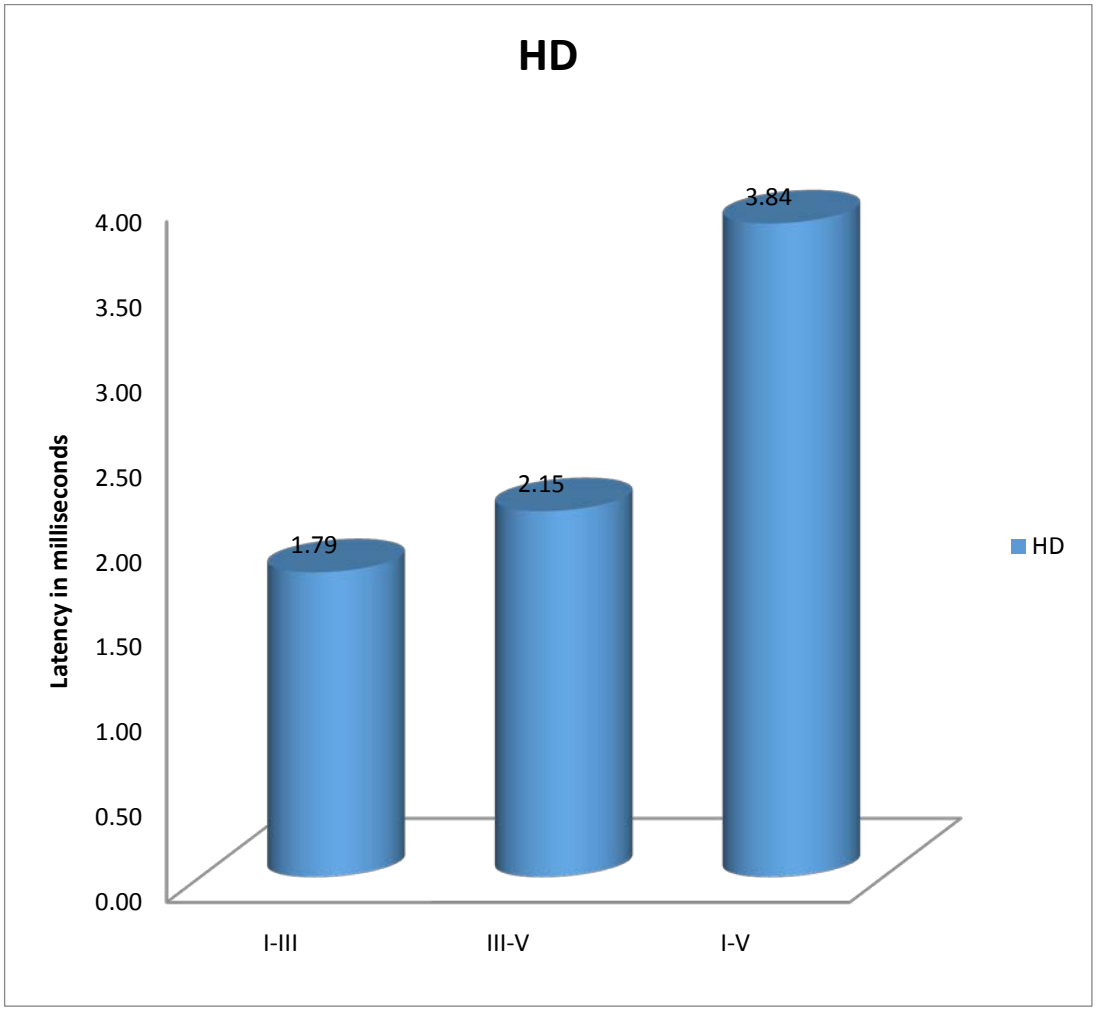

TABLE: 11

COMPARISON OF INTER PEAK LATENCIES OF RIGHT EAR- BETWEEN RENAL TRANSPLANTATION PATIENTS & CONTROLS

INTERPEAK LATENCIES	RT PATENTS	CONTROL	P VALUE
I-III	2.13+-0.43	2.23+_0.10	0.604
III-V	1.71	1.70+-0.18	0.127
I-V	3.89+_0.24	3.92+_0.22	0.991

There is no significant prolongation of interpeak latencies.

FIG :14

COMPARISON OF INTER PEAK LATENCIES OF RIGHT EAR-BETWEEN RT PATIENTS & CONTROLS

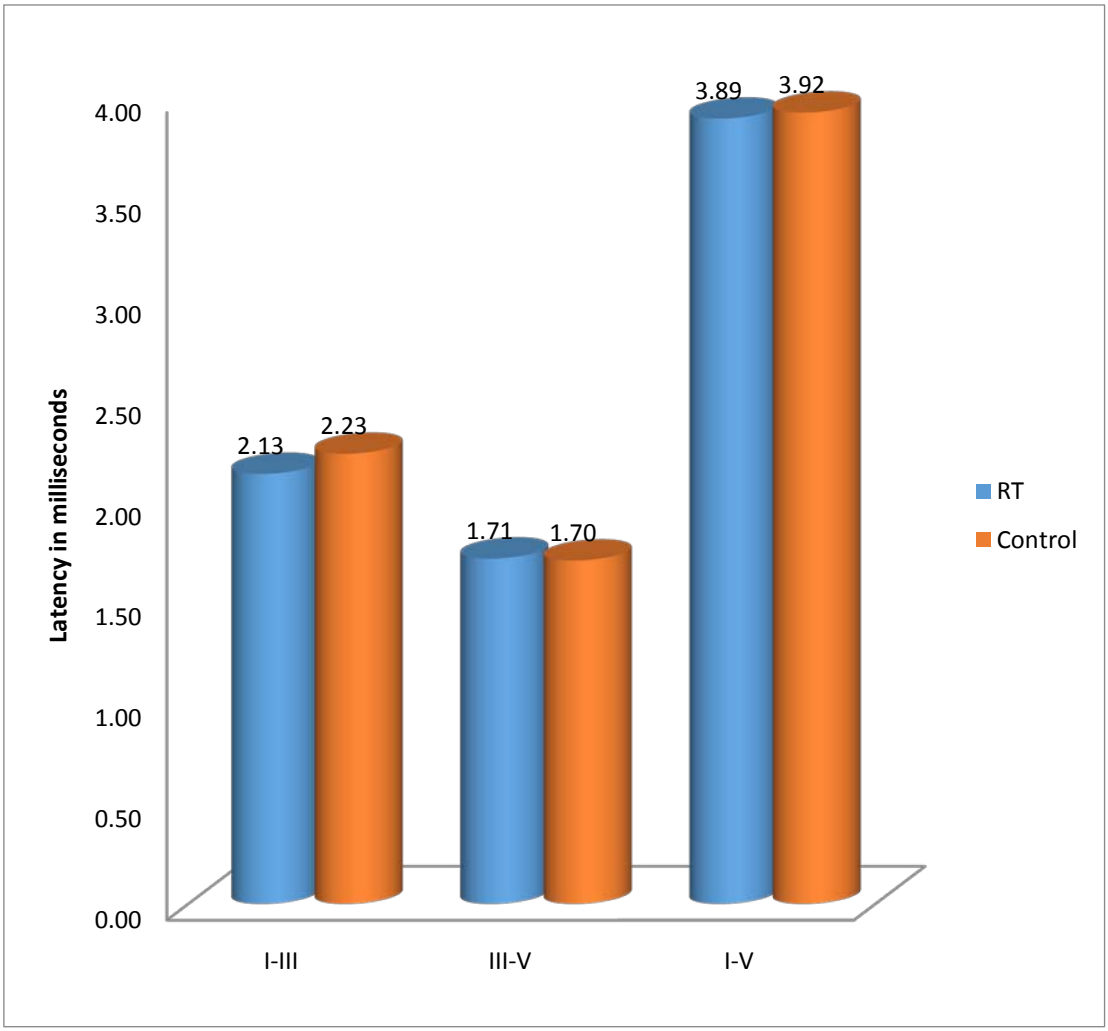

TABLE:12

COMPARISON OF ABSOLUTE PEAK LATENCIES OF LEFT EAR-BETWEEN CHRONIC KIDNEY DISEASE PATIENTS & CONTROLS

LATENCIES	CASE (CKD) MEAN +_SD	CONTROL MEAN+-SD	P VALUE
I	1.79+_0.06	1.74+_0.11	0.764
II	2.96+-0.26	2.85+_0.20	0.248
III	4.21+_0.31	3.98+_0.06	0.044
IV	4.96+_0.28	4.99+_0.52	0.994
V	5.79+_0.24	5.67+_0.58	0.717

The absolute peak latency of waveform III is prolonged with ‘p’ value 0.044.

FIG :15

COMPARISON OF ABSOLUTE PEAK LATENCIES OF LEFT EAR- BETWEEN CHRONIC KIDNEY DISEASE PATIENTS & CONTROLS

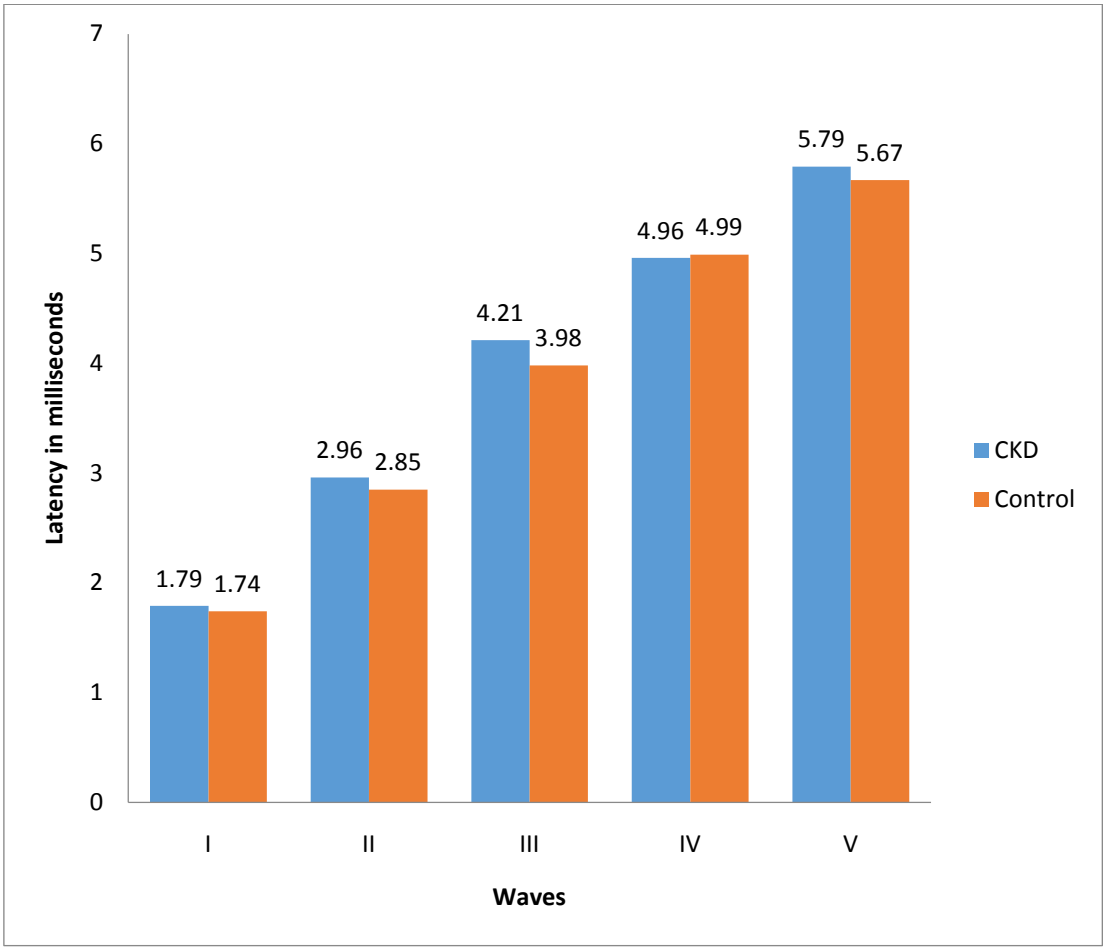

TABLE: 13

COMPARISON OF ABSOLUTE PEAK LATENCIES OF LEFT EAR- BETWEEN HAEMODIALYSIS PATIENTS & CONTROLS

LATENCIES	CASE (HD) MEAN +_SD	CONTROL MEAN+-SD	P VALUE
I	1.90+_0.36	1.74+_0.11	0.018
II	2.82+_0.21	2.85+_0.20	0.946
III	3.60+_0.38	3.93+_0.37	0.003
IV	4.91+_0.35	4.99+_0.52	0.898
V	5.80+_0.26	5.67+_0.58	0.661

There is significant prolongation of absolute peak latency of waveform I & III.

FIG :16

COMPARISON OF ABSOLUTE PEAK LATENCIES OF LEFT EAR-BETWEEN HAEMODIALYSIS PATIENTS & CONTROLS

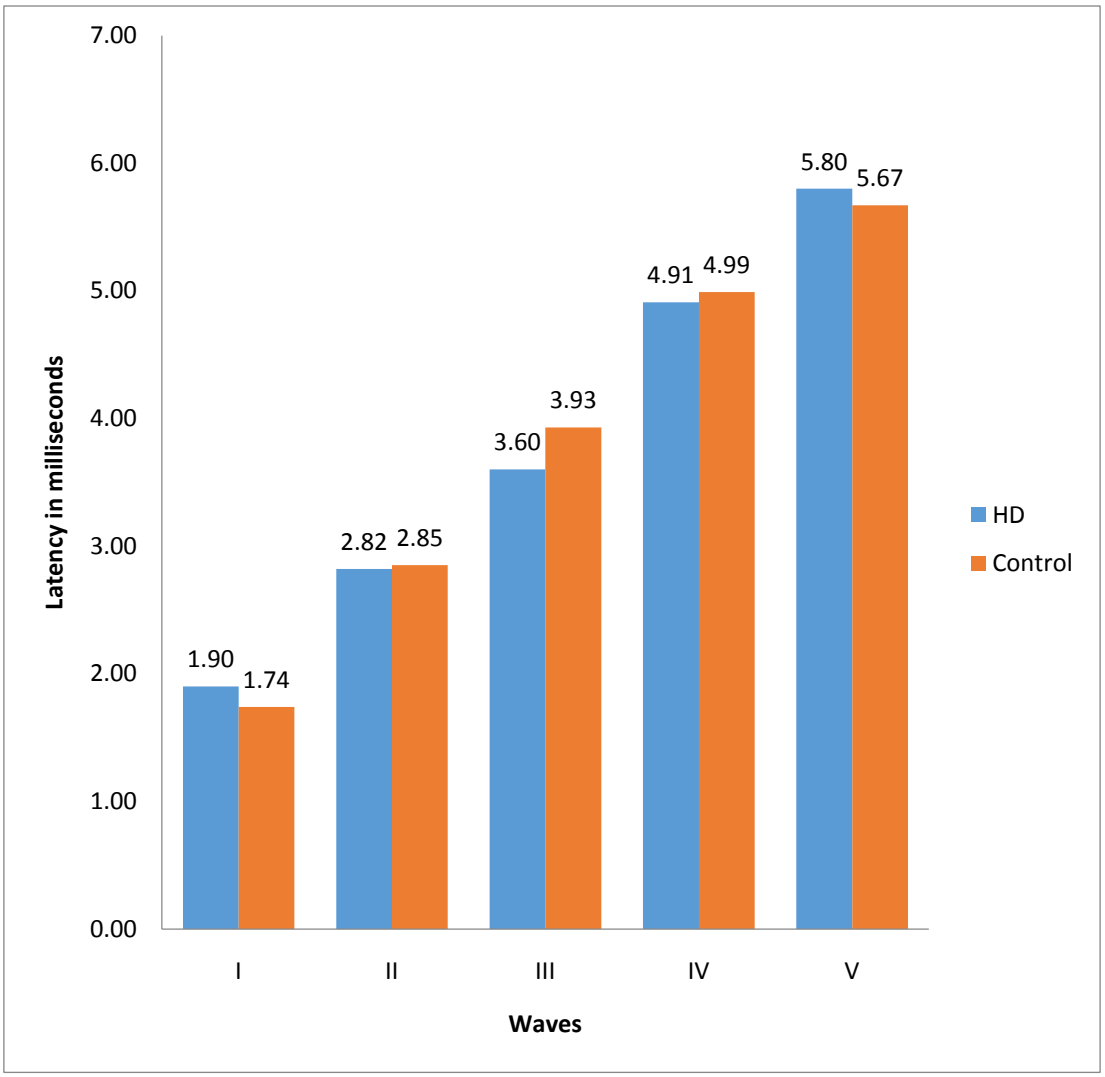

TABLE :14

COMPARISON OF ABSOLUTE PEAK LATENCIES OF LEFT EAR-BETWEEN RENAL TRANSPLANTATION PATIENTS & CONTROLS

LATENCIES	CASE (HD) MEAN +_SD	CONTROL MEAN+-SD	P VALUE
I	1.74+_0.07	1.74+_0.11	1.000
II	2.87+_0.07	2.85+_0.20	0.974
III	3.92+_0.23	3.93+_0.37	1.000
IV	5.06 +_0.14	4.99+_0.52	0.894
V	5.72+_0.26	5.67+_0.58	0.967

There is no significant prolongation of Absolute peak latencies

FIG :17

COMPARISON OF ABSOLUTE PEAK LATENCIES OF LEFT EAR-BETWEEN RENAL TRANSPLANTATION PATIENTS & CONTROLS

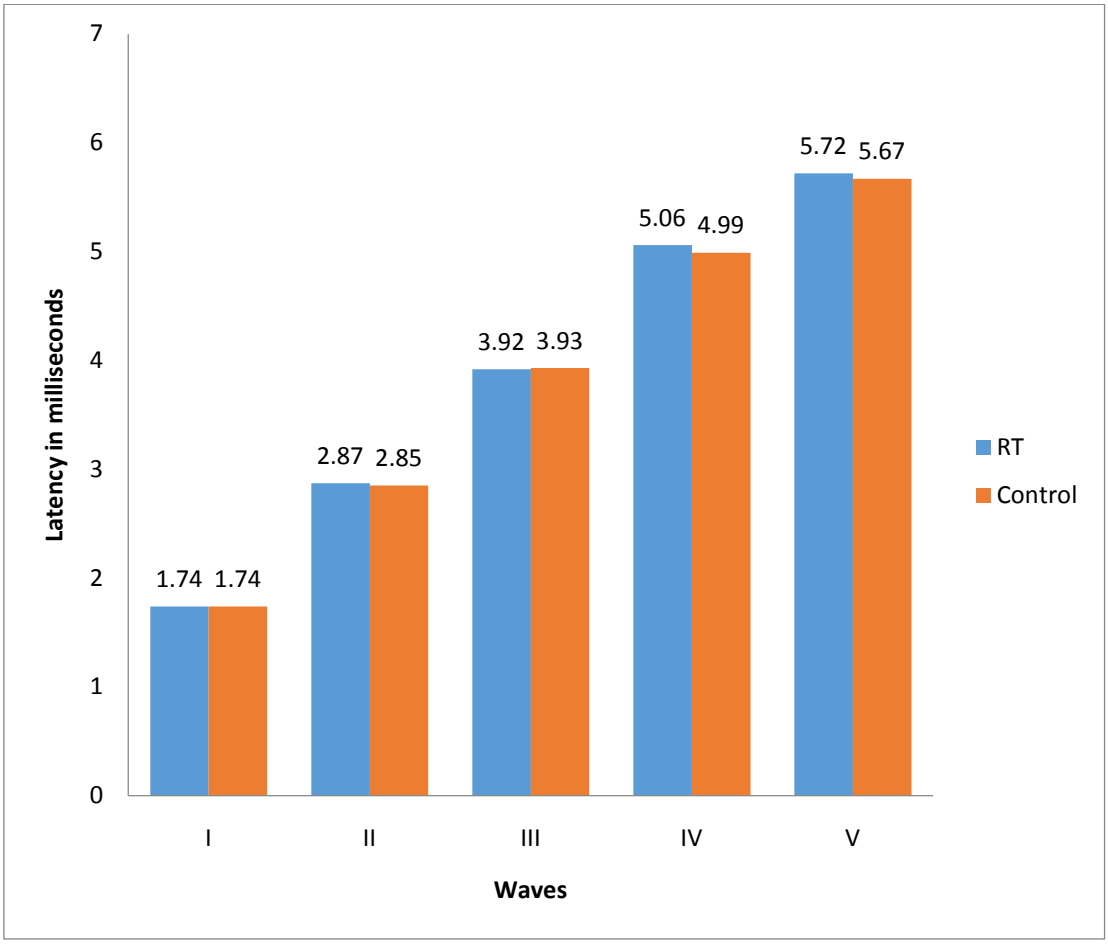

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TABLE: 15

COMPARISON OF INTER PEAK LATENCIES OF LEFT EAR-BETWEEN CHRONIC KIDNEY DISEASE PATIENTS & CONTROLS

INTERPEAK LATENCIES	RT PATIENTS	CONTROL	P VALUE
I-III	2.24+-0.19	2.18+_0.30	0.957
III-V	1.74+_0.31	1.75+_0.24	0.999
I-V	4.00+_0.22	3.93+_0.51	0.936

There is no significant prolongation of interpeak latencies.

FIG :18

COMPARISON OF INTER PEAK LATENCIES OF LEFT EAR- BETWEEN CHRONIC KIDNEY DISEASE PATIENTS & CONTROLS

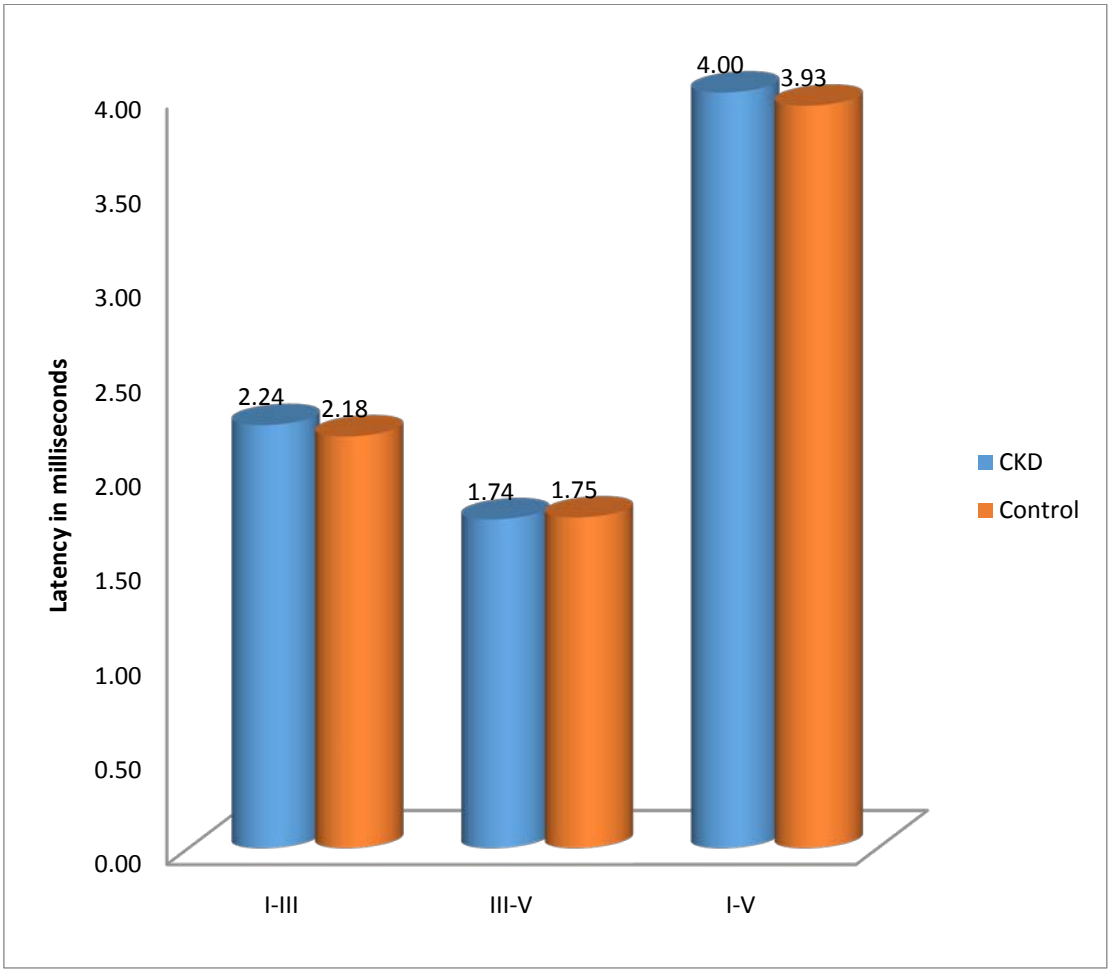


TABLE :16

COMPARISON OF INTER PEAK LATENCIES OF LEFT EAR-BETWEEN HEMODIALYSIS PATIENTS & CONTROLS

INTERPEAK LATENCIES	RT PATIENTS	CONTROL	P VALUE
I-III	1.78+_0.66	2.18+_0.30	0.003
III-V	2.20+_0.37	1.75+_0.24	0.000
I-V	3.84+_0.46	3.93+_0.51	0.881

There is significant prolongation of interpeak latencies I-III & III-V with a ‘p’ value of 0.003 & 0.000

FIG :19

COMPARISON OF INTER PEAK LATENCIES OF LEFT EAR-BETWEEN HEMODIALYSIS PATIENTS & CONTROLS

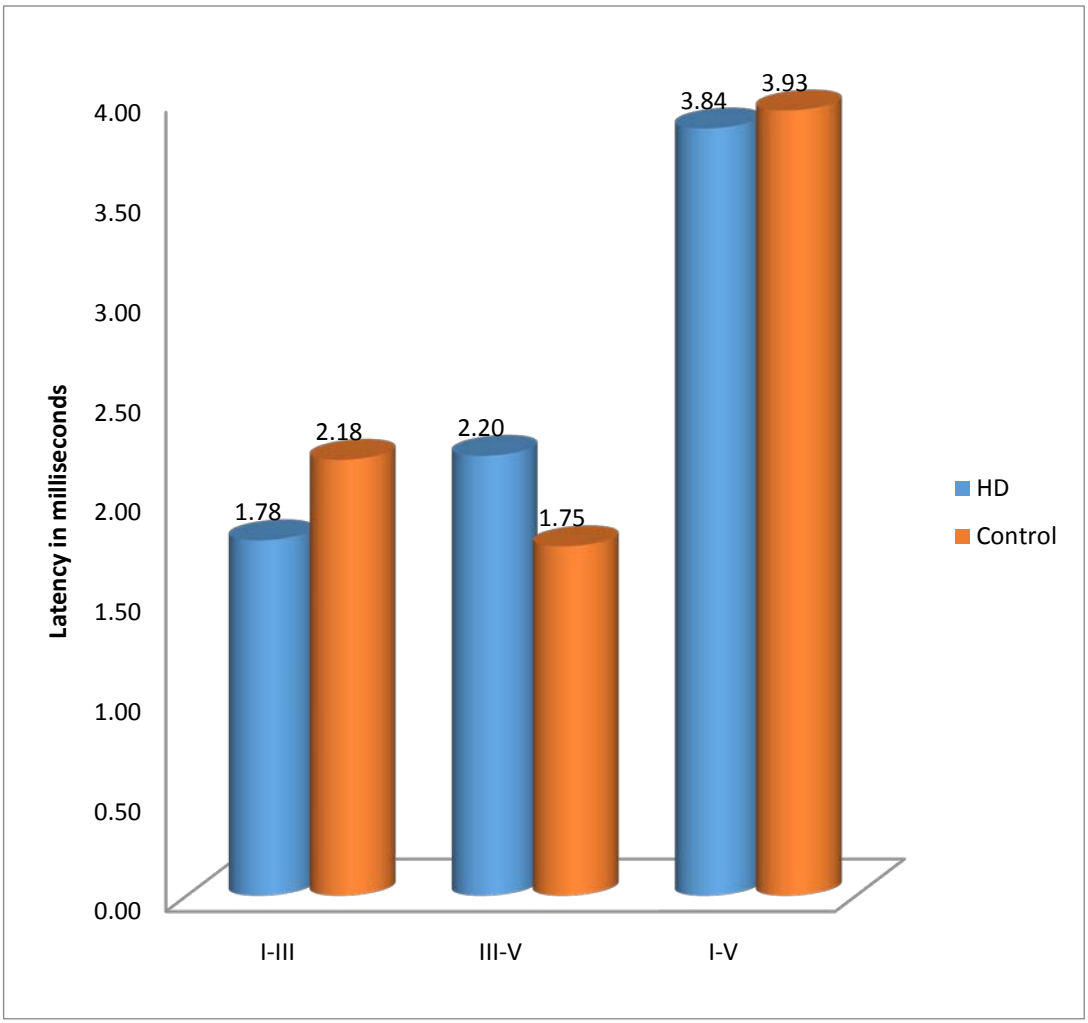


TABLE :17

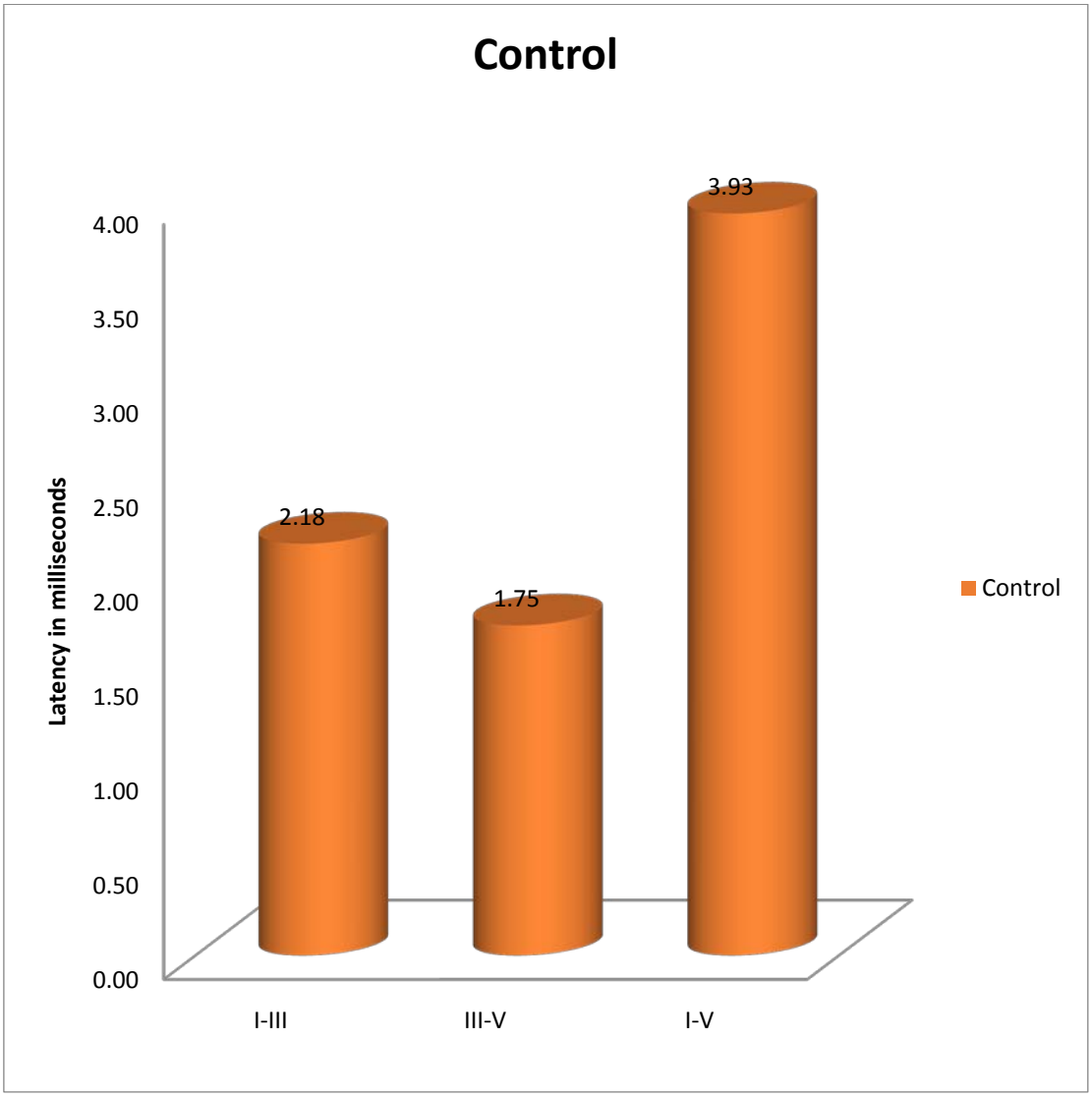
COMPARISON OF INTER PEAK LATENCIES OF LEFT EAR- BETWEEN RENAL TRANSPLANTATION PATIENTS & CONTROLS

INTERPEAK LATENCIES	RT PATIENTS	CONTROL	P VALUE
I-III	2.19+_0.25	2.18+_0.30	1.000
III-V	1.80+_0.20	1.75+_0.24	0.931
I-V	3.99+_0.27	3.93+_0.51	0..959

There is no significant prolongation of interpeak latencies.

FIG :20

COMPARISON OF INTER PEAK LATENCIES OF LEFT EAR- BETWEEN RENAL TRANSPLANTATION PATIENTS & CONTROLS



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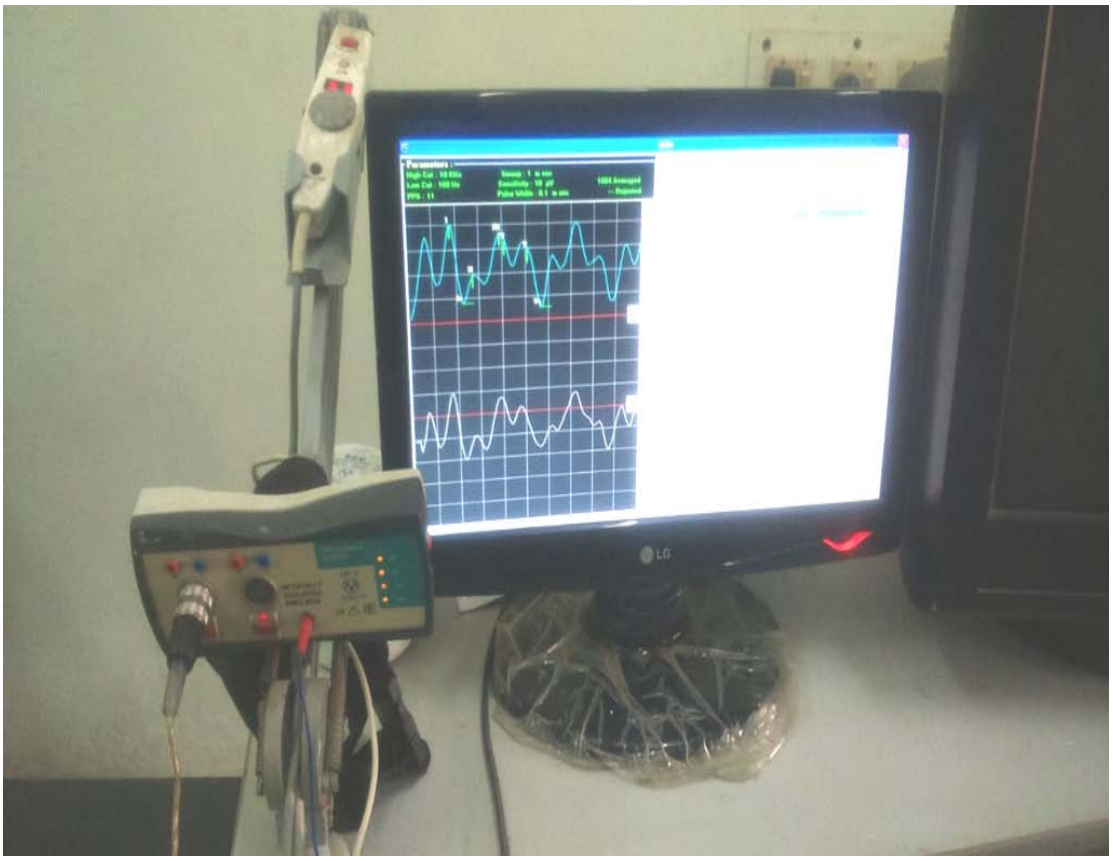
RECORDING OF BAEP WAVEFORMS



RECORDING OF BAEP WAVEFORM IN A SUBJECT.

RESULTS

CONTROL GROUP

There were 30 cases in the control group with average weight of 60.3 +_11.8 and creatinine 0.712 ± 0.12.

CHRONIC KIDNEY DISEASE GROUP

There are 20 CKD patients with an average weight of 58.65 +_7.6 kg and creatinine 6.32 ± 1.36.

HAEMODIALYSIS GROUP

There are 20 patients who were on haemodialysis in the department of nephrology, KMC with an average weight of 50.05+_4.3 kg and creatinine 6.2 ± 1.34.

RENAL TRANSPLANTATION GROUP

There are 20 patients who were treated with renal transplantation with an average weight of 60.20 +_6.9 kg and creatinine 1.13 ± 0.48.

CKD patients were graded on the basis of Creatinine and Gfr and the average values of BAEP with Absolute and Inter peak latencies were recorded and given in table 6,9,12 & 15.

The average value of Absolute peak latency and Inter peak latencies of HD patients were recorded and are given in table 7,10,13& 16.

The average value of Absolute peak latency and Inter peak latencies of RT patients were recorded and given in table 8, 11, 4 & 17.

In Chronic kidney disease group, there was a significant increase in the latencies of wave, III and inter peak latencies did not vary significantly in both ears.

In haemodialysis group there was a significant increase in the absolute peak latencies of I & III and inter peak latencies I-III, III-V in both the ears.

In renal transplantation group there was no significant change in either the absolute or the inter peak latencies in both the ears.

DISCUSSION

The aim of our study was to evaluate Brainstem Auditory Evoked potentials in Chronic Kidney Disease patients and patients on Haemodialysis and in those who have undergone Renal transplantation.

Quic CA, Fish A[65] Studied the relationship between Cochlea and Kidney and concluded that Cochlea and Kidney have the same physiological process, Active transport of fluid & electrolytes accomplished by Stria vascularis and glomerulus. They also attributed the similar effect of certain medications (ototoxic medication) on these two organs.

Alder et al in their study demonstrated the fact that there is a significant inhibition of Na^+K^+ATP ase in the inner ear of guinea pigs which had uraemia. They also suggested an inverse correlation between serum Creatinine levels and Na^+K^+ATP ase activity which is vital for maintaining the cationic gradients in the inner ear. Hence inhibition of this enzyme contributed to inner ear abnormalities in uremic patients.

In this study there is prolongation of Absolute and Inter peak Latencies in both the ears of Haemodialysis patients compared to Chronic Kidney Disease patients who were not started on Haemodialysis. This correlates with the study done by Naderpour M, Mortazavi F et al, in

which abnormal ABR recordings were seen in patients with Chronic kidney disease who were on Haemodialysis compared to chronic kidney disease patients who were yet to start on Haemodialysis.

The Present study showed prolongation of Absolute Peak Latencies I & III and Inter peak latencies I-III, III-V in patients undergoing Haemodialysis which correlates with the study done by Aspris ak, Thodi CD et al, who demonstrated the effects of chronic kidney disease on auditory function & changes in the auditory function following haemodialysis. It was seen that the absolute latency of wave III and inter peak latencies III-V & I-III were significantly prolonged than in Chronic Kidney disease patients not on Haemodialysis .This may be due to marked biochemical changes seen in CKD as this reverses after successful transplantation.

Hoth S, Weber FN et al in their study pointed out that the small increase in the ABR recordings were due to the broadening of the excited area & its shifting towards a more apical position of the hair cell population.

In this Study there is a highly significant improvement in hearing and Absolute & Inter peak latencies after successful renal Transplantation. This partially correlates with the study of Brain KS,

Chopra H et al who documented Brainstem evoked response audiometry in Chronic kidney disease patients who underwent Renal Transplantation. After transplantation, Compared with the pre-transplant values there was a significant improvement in the I, III V latencies and hence it was concluded that, there is a definite improvement in hearing and wave latencies after successful Renal Transplantation.

CONCLUSION

This study has documented BAEP Changes in CKD and HD patients.

The changes in BAEP Waveforms are in both cochlear and retro cochlear components of Auditory pathway.

The marked changes in BAEP Waveforms in patients undergoing Hemodialysis may reflect the intensity and fluctuation in biochemical changes related to CKD.

The reversal of BAEP changes after successful Renal transplantation throws light on the rehabilitatory potential of Renal transplantation on audiological dysfunction.

LIMITATIONS OF MY STUDY

The value of biochemical markers of CKD on the day of recording BAEP Could have been recorded which would have helped in explaining the marked changes seen in patients under Hemodialysis.

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ANNEXURE - A

PATIENT DATA COLLECTION

DEPARTMENT OF PHYSIOLOGY, KMC , CHENNAI.

1.DATE :

2.TIME :

3.ID NO :

4.NAME :

5.AGE (yrs) :

6.GENDER :

7.HEIGHT(cm) :

8.WEIGHT(kg) :

9.ADDRESS :

10.OCCUPATION :

11.CONTACT NUMBER :

ANNEXURE -B

BRIEF CLINICAL HISTORY & GENERAL CLINICAL EXAMINATION

DEPARTMENT OF PHYSIOLOGY, GKMC , CHENNAI**.**

NAME OF THE PATIENT :

AGE :

ID NO:

S.no	History / symptoms	Yes	no
1.	Chronic cough > 2 wks		
2.	H/O loss of appetite		
3.	H/O loss of weight		
4.	H/O diabetes		
5.	H/O hypertension		
6.	H/O alcohol intake		
7.	H/O drug intake		
8.	H/O any neurological disease or H/O treatment from neurologist		
9.	H/O thyroid disorder or H/O drug intake for thyroid disorder		

GENERAL EXAMINATION :

1.BP -

2.HEART RATE -

3.RESPIRATORY RATE -

4.TEMPERATURE -

5.ALERTNESS -

6. ANAEMIA -

7. CYANOSIS -

8.PEDAL EDEMA -

9.CLUBBING -

10.JAUNDICE -

11.CVS EXAMINATION :

12.RS EXAMINATION :

13.CNS EXAMINATION :

ANNEXURE - C

MEASURES OF BAEP ANALYSIS

WAVES	Rt EAR- latency in milliseconds	Lt EAR- latency in milliseconds
1		
II		
III		
IV		
V		
I-III		
III-V		
I-V		

ANNEXURE - D

PATIENT INFORMATION SHEET

We are conducting a study on Evaluation of Brainstem auditory evoked potentials in Chronic Kidney Disease, Hemodialysis and Renal transplantation patients in the Department of Physiology, KMC, Chennai – 600 010.The purpose of this study is to diagnose subclinical involvement of auditory pathway in the concerned patients. We are selecting some patients and if you are found eligible for this study, we do the Brainstem auditory evoked potential test for you to assess the functional integrity of auditory pathways, which in anyway do not affect your treatment. The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared. Taking part in this study is involuntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled. The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management.

Signature of investigator Signature of Participant

Date :

ANNEXURE - E

INFORMED CONSENT FORM

Title of the study : Evaluation of Brainstem auditory evoked potentials in chronic kidney disease Hemo dialysis and Renal transplantation patients.

Name of the participant : Age Sex :

IP No:

Name of the Principal investigator :

Name of the Institution : Department of Physiology, Kilpauk Medical College, Chennai – 600 010.

Documents of the informed consent

I_____ have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in **"Brainstem auditory evoked potential in chronic kidney disease, hemodialysis and renal transplantation patients.**

1. I have read and understood this consent form and the information provided to me.
2. I have had the consent document explained to me

3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.
5. I have been informed the investigator of all the treatments I am taking or have taken in the past including any native (alternative) Treatment.
6. I agree to cooperate with the investigator and I will inform her immediately if I suffer unusual symptoms.
7. I have not participated in any research study in the past
8. I am aware of the fact that I can opt out of the study at any time without having to given any reason and this will not affect my future treatment in this hospital.
9. I am also aware that the investigator may terminate my participation in the study at any time, for any reason, without my consent.
10. I hereby give permission to the investigators to release the inform obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt. agencies, and IEC. I understand that they are publicly presented.
11. I have understood that my identity will be kept confidential if my date are publicly presented.

12. I have had my questions answered to my satisfaction.

13. I have decided to be in the research study.

14. I am aware that if I have any question during this study, I should contact the investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

Signature & Date

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 19/2015 Dt: 02.11.2015
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval " Evaluation of brainstem auditory evoked potential in chronic kidney disease hemodialysis and renal transplantation patients". - For Project Work submitted by Dr.D.Priyadarshini,2nd Year MD, Physiology Post Graduate,Govt. Kilpauk Medical College, Chennai.

The Proposal is APPROVED.

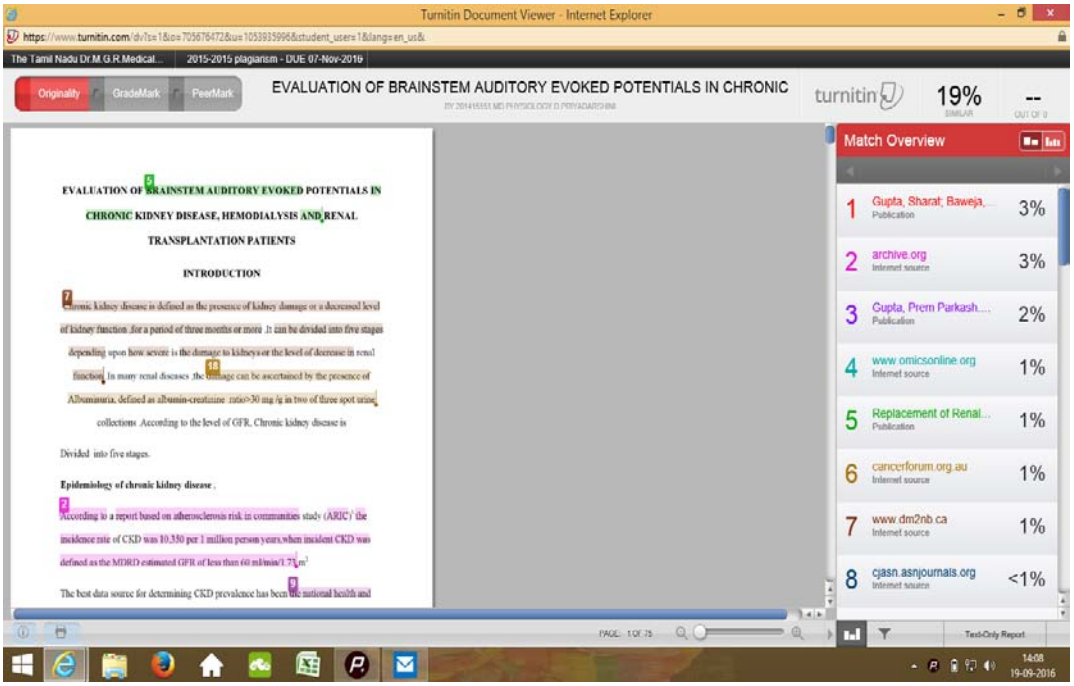
The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

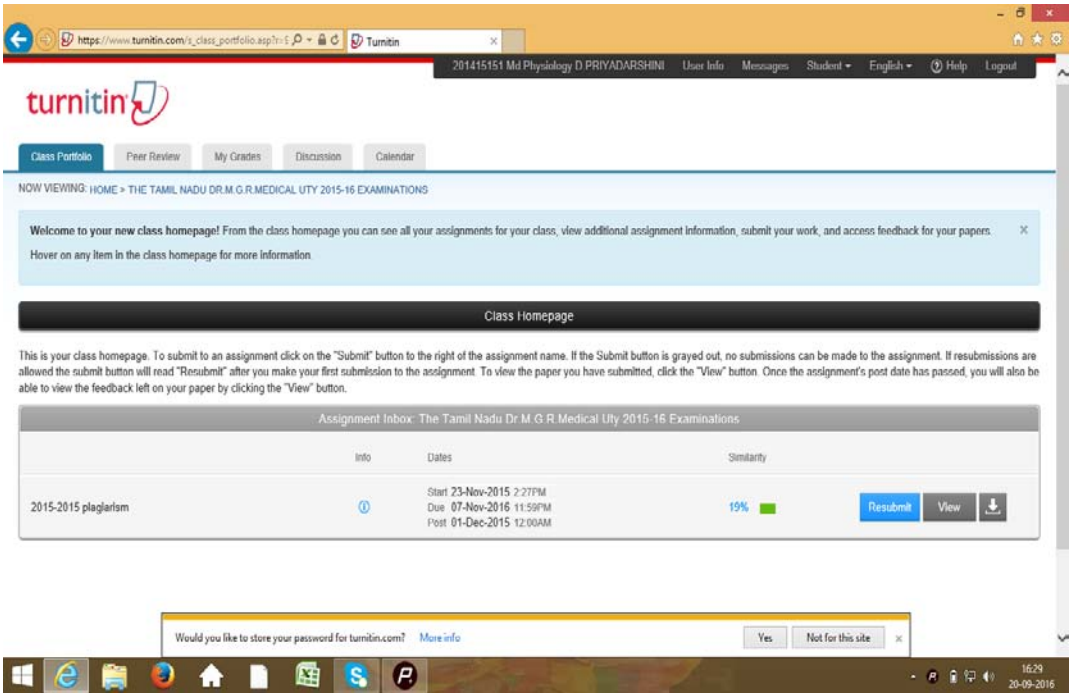
10/11/15

DEAN,
Govt.Kilpauk Medical College,
Chennai – 10.

10/12/15

TURNITIN DIGITAL RECEIPT





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EVALUATION OF BRAINSTEM AUDITORY EVOKED POTENTIALS IN CHRONIC KIDNEY DISEASE, HEMODIALYSIS AND RENAL TRANSPLANTATION PATIENTS

INTRODUCTION

Chronic kidney disease is defined as the presence of kidney damage or a decreased level of kidney function for a period of three months or more. It can be divided into two stages depending upon how severe the damage to kidneys or the level of decrease in renal function. In many renal diseases the damage can be ascertained by the presence of Albuminuria, defined as albumin excretion. More than 30 mg /g in two of three spot urine collections. According to the level of GFR, Chronic kidney disease is

Divided into five stages.

Epidemiology of chronic kidney disease :

According to a report based on observational cohort study (ARIC) the incidence rate of CKD was 11,350 per 1 million person years when incident CKD was defined as the MDRD estimated GFR of less than 60 ml/min/1.73 m²

The best data source for determining CKD prevalence has been the national health and nutrition examination survey (in the united states (NHANES),according to which the prevalence was five to twelve magnitude larger than the incident CKD patients.

நோயாளி ஒப்புதல் படிவம்

ஆராய்ச்சியின் விவரம்:

ஆராய்ச்சி மையம்:

நோயாளியின் பெயர்: நோயாளியின் வயது:

பதிவு எண்:

நோயாளி கீழ்கண்டவற்றுள் கட்டங்களை (✓) செய்யவும்

1. மேற்குறிப்பிட்டுள்ள ஆராய்ச்சியின் நோக்கத்தையும் பயனையும் முழுவதுமாக புரிந்துகொண்டேன். மேலும் எனது அனைத்து சந்தேகங்களையும் கேட்டு அதற்கான விளக்கங்களையும் தெளிவுபடுத்திக் கொண்டேன். ☐

2. மேலும் இந்த ஆராய்ச்சிக்கு எனது சொந்த விருப்பத்தின் பேரில் பங்கேற்கிறேன் என்றும், மேலும் எந்த நேரத்திலும் எவ்வித முன்னறிவிப்புமின்றி இந்த ஆராய்ச்சியிலிருந்து விலக முழுமையான உரிமை உள்ளதையும், இதற்கு எவ்வித சட்ட பிணைப்பும் இல்லை என்பதையும் அறிவேன். ☐

3. ஆராய்ச்சியாளரோ, ஆராய்ச்சி உதவியாளரோ, ஆராய்ச்சி உபயத்தாரோ, ஆராய்ச்சி பேராசிரியரோ, ஒழுங்குநெறி செயற்குழு உறுப்பினர்களோ எப்போது வேண்டுமானாலும் எனது அனுமதியின்றி எனது உள்நோயாளி பதிவுகளை இந்த ஆராய்ச்சிக்காகவோ அல்லது எதிர்கால பிற ஆராய்ச்சிகளுக்காகவோ பயன்படுத்திக்கொள்ளலாம் என்றும், மேலும் இந்த நிபந்தனை நான் இவ்வாராய்ச்சியிலிருந்து விலகினாலும் தகும் என்றும் ஒப்புக்கொள்கிறேன். ஆயினும் எனது அடையாளம் சம்பந்தப்பட்ட எந்த பதிவுகளும் (சட்டபூர்வமான தேவைகள் தவிர) வெளியிடப்படமாட்டாது என்ற உறுதிமொழியின் பெயரில் இந்த ஆராய்ச்சியிலிருந்து கிடைக்கப்பெறும் முடிவுகளை வெளியிட மறுப்பு தெறிவிக்கமாட்டேன் என்று உறுதியளிக்கின்றேன். ☐

4. இந்த ஆராய்ச்சிக்கு நான் முழுமனதுடன் சம்மதிக்கின்றேன் என்றும் மேலும் ஆராய்ச்சிக் குழுவினர் எனக்கு அளிக்கும் அறிவுரைகளை தவறாது பின்பற்றுவேன் என்றும் இந்த ஆராய்ச்சி காலம் முழுவதும் எனது உடல் நிலையில் ஏதேனும் மாற்றமோ அல்லது எதிர்பாராத பாதகமான விளைவோ எற்படுமாயின் உடனடியாக ஆராய்ச்சி குழுவினரை அணுகுவேன் என்றும் உறுதியளிக்கின்றேன். ☐

5. இந்த ஆராய்ச்சிக்குத் தேவைப்படும் அனைத்து மருத்துவப் பரிசோதனைகளுக்கும் ஒத்துழைப்பு தருவேன் என்று உறுதியளிக்கின்றேன். ☐

6. இந்த ஆராய்ச்சிக்கு யாருடைய வற்புருத்தலுமின்றி எனது சொந்த விருப்பத்தின் பேரிலும் சுயஅறிவுடனும் முழுமனதுடனும் சம்மத்திக்கின்றேன் என்று இதன் மூலம் ஒப்புக்கொள்கிறேன். ☐

நோயாளியின் கையொப்பம் / பெருவிரல் கைரேகை ஆராய்ச்சியாளரின் கையொப்பம்

இடம்: தேதி:

MASTER SHEET

Control Group

Sl.No.	AGE	GENDER	HEIGHT (cm)	WEIGHT (Kg)	S.CREATININE	BLOOD PRESSURE (mm Hg)	RIGHT EAR -LATENCY in milliseconds								LEFT EAR -LATENCY in milliseconds							
							WAVE 1	WAVE 2	WAVE 3	WAVE 4	WAVE 5	WAVES 1-3	WAVES 3-5	WAVES 1-5	WAVE 1	WAVE 2	WAVE 3	WAVE 4	WAVE 5	WAVES 1-3	WAVES 3-5	WAVES 1-5
1	32	F	163	59	0.6	120/70	1.69	2.93	4	5.14	5.87	2.31	1.87	4.18	1.69	2.94	3.98	5.22	5.94	2.29	1.96	4.25
2	57	M	160	60	0.8	140/80	1.68	2.94	4.06	5.24	5.88	2.38	1.82	4.2	1.76	2.95	4.02	5.09	5.86	2.2	1.9	4.1
3	25	F	154	48	0.61	110/70	1.7	2.96	4.09	5.33	5.39	2.39	1.3	3.69	1.79	2.88	4.09	4.9	5.78	2.3	1.69	3.99
4	31	F	156	45	0.64	130/80	1.68	2.8	4.08	5.34	5.9	2.4	1.82	4.22	1.8	2.87	4.08	4.99	5.89	2.28	1.81	4.09
5	42	F	165	88	0.8	130/86	1.71	2.88	3.99	4.86	5.91	2.28	1.92	4.2	1.84	2.85	3.99	5.34	5.56	2.15	1.57	3.72
6	36	F	152	56	0.66	124/80	1.76	2.78	3.95	4.87	5.49	2.19	1.54	3.73	1.85	2.84	3.89	5.21	5.6	2.04	1.71	3.75
7	41	F	160	78	1	130/86	1.79	2.9	3.97	5.05	5.47	2.18	1.5	3.68	1.76	2.91	3.9	4.97	5.66	2.14	1.76	3.9
8	53	F	160	54	0.92	120/86	1.68	2.95	3.89	5.02	5.54	2.21	1.65	3.86	1.69	2.93	3.94	4.98	5.76	2.25	1.82	4.07
9	33	F	174	74	0.8	130/70	1.85	2.96	3.9	5.14	5.52	2.05	1.62	3.67	1.66	2.84	3.97	5.09	5.9	2.31	1.93	4.24
10	35	F	176	76	0.68	120/80	1.88	2.89	3.99	5.32	5.65	2.11	1.65	3.77	1.7	2.82	3.99	5.26	5.8	2.29	1.81	4.1
11	26	F	174	60	0.6	110/66	1.68	2.88	3.91	4.99	5.66	2.23	1.75	3.98	1.81	2.86	3.89	5.31	5.89	2.08	2	4.08
12	18	M	176	75	0.64	120/80	1.78	2.78	3.9	5.06	5.76	2.12	1.86	3.97	1.74	2.88	4.02	4.98	5.76	2.28	1.74	4.02
13	23	M	175	80	1	134/84	1.76	2.91	3.9	4.97	5.66	2.14	1.76	3.9	1.67	2.82	4.03	5.32	5.56	2.36	1.53	3.89
14	18	F	166	62	0.6	130/82	1.69	2.93	3.94	4.98	5.76	2.25	1.82	4.07	1.69	2.94	4.07	5.27	5.67	2.38	1.6	3.98
15	33	M	170	70	0.68	110/76	1.66	2.84	3.97	5.09	5.9	2.31	1.93	4.24	1.3	1.85	2	2.35	2.65	0.7	0.65	1.35
16	34	F	166	50	0.66	110/60	1.7	2.82	3.99	5.26	5.8	2.29	1.81	4.1	1.85	2.96	4.05	4.94	5.9	2.2	1.85	4.05
17	20	M	168	56	0.6	120/80	1.81	2.86	3.89	5.31	5.89	2.08	2	4.08	1.7	2.88	4.1	4.86	5.87	2.4	1.77	4.17
18	42	F	156	56	0.7	120/80	1.7	2.88	4.1	4.86	5.87	2.4	1.77	4.17	1.8	2.84	3.99	4.99	5.74	2.19	1.75	3.94
19	46	M	170	72	0.6	120/80	1.8	2.84	3.99	4.99	5.74	2.19	1.75	3.94	1.82	2.8	3.92	5.03	5.61	2.1	1.69	3.79
20	25	F	163	61	0.8	120/80	1.88	2.79	3.91	5.33	5.93	2.03	2.02	4.05	1.85	2.79	3.93	4.89	5.71	2.08	1.78	3.86

CKD Group

Sl. NO.	AGE	GENDER	HEIGHT (cm)	WEIGHT (Kg)	S.CREATINE	BLOOD PRESSURE (mm Hg)	RIGHT EAR -LATENCY in milliseconds								LEFT EAR -LATENCY in milliseconds							
							WAVE 1	WAVE 2	WAVE 3	WAVE 4	WAVE 5	WAVES 1-3	WAVES 3-5	WAVES 1-5	WAVE 1	WAVE 2	WAVE 3	WAVE 4	WAVE 5	WAVES 1-3	WAVES 3-5	WAVES 1-5
1	57	M	160	60	6	140/90	1.72	2.9	4.02	5.12	5.89	2.3	1.87	4.17	1.7	2.82	4.51	5.01	5.55	2.31	1.04	3.85
2	52	F	168	66	4.8	130/86	2.8	3.08	3.38	4.6	5.88	0.58	2.5	3.08	1.79	2.9	4	5.1	5.59	2.21	1.59	3.8
3	35	M	172	70	7.2	140/82	1.69	2.92	4.47	5.36	5.79	2.78	1.32	4.1	1.8	2.9	4.03	4.99	5.52	2.23	1.49	3.72
4	43	F	166	60	5	130/90	1.7	2.86	4.07	5.33	5.94	2.37	1.87	4.24	1.8	3.2	4.2	4.99	5.95	2.42	1.73	4.15
5	68	F	150	58	4.2	120/86	1.72	2.92	4.51	4.89	5.89	2.79	1.38	4.17	1.75	3.2	4.32	5	5.96	2.57	1.64	4.21
6	63	M	168	60	7.8	140/78	1.75	2.84	3.99	4.88	5.65	2.24	1.66	3.9	1.79	2.97	3.91	4.99	5.51	2.12	1.6	3.72
7	23	M	170	68	8	156/90	1.77	2.89	4.5	5.09	5.6	2.73	1.1	3.83	1.75	2.8	3.95	4.89	5.5	2.2	1.55	3.75
8	64	M	160	56	6.8	160/88	1.69	2.94	4.51	5.06	5.6	2.82	1.09	3.91	1.82	2.85	4	5	5.49	2.13	1.49	3.67
9	48	F	155	50	6.6	140/74	1.79	2.99	3.97	5.1	5.55	2.18	1.58	3.76	1.79	3.14	4.27	5.3	5.97	2.48	1.7	4.18
10	35	M	156	52	9	146/80	1.79	2.97	3.91	4.99	5.51	2.12	1.6	3.72	1.84	3.1	4.35	5.1	5.95	2.51	1.6	4.11
11	40	F	158	54	6.6	130/80	1.88	2.95	4.5	5.19	5.77	2.62	1.27	3.89	1.8	2.9	4.03	4.99	5.52	2.23	1.49	3.72
12	45	M	160	61	7.2	120/80	1.66	2.88	3.99	5.27	5.59	2.33	1.6	3.93	1.88	3.14	4.12	4.93	5.99	2.24	1.87	4.11
13	56	F	154	50	4.7	150/86	1.79	2.78	3.94	5.33	5.66	2.15	1.72	3.87	1.79	2.98	4.17	4.9	6	2.38	1.83	4.21
14	34	M	168	56	6.4	140/86	1.83	2.9	4.46	5.1	5.96	2.63	1.5	4.13	1.8	3.2	4.22	4.99	5.95	2.42	1.73	4.15
15	48	F	160	60	5.6	154/90	1.88	2.95	4.5	5.19	5.77	2.62	1.27	3.89	1.7	2.9	3.9	5.27	5.45	2.2	1.55	3.75
16	68	M	164	78	3.8	160/94	1.8	2.82	4.4	4.99	5.6	2.6	1.2	3.8	1.74	3	3.9	5.36	6	2.16	2.2	4.26
17	66	F	158	54	5.8	158/86	1.82	2.34	4.06	4.99	5.59	2.24	1.53	3.77	1.66	2	3.5	4	5.8	1.84	2.3	4.14
18	50	M	150	48	6.2	154/70	1.81	2.9	4.06	3.13	3.71	2.25	1.65	3.9	1.86	3	3.8	4.6	5.9	1.94	2.1	4.04
19	45	F	156	50	8	160/80	1.8	2.84	4.5	5.1	5.65	2.7	1.15	3.85	1.88	3	4	4.8	6	2.12	2	4.12
20	40	M	165	62	6.8	154/70	1.7	2.82	4.51	5.01	5.55	2.81	1.04	3.85	1.9	3.1	3.98	5	6.2	2.08	2.22	4.3

Hemodialysis Group

Sl. NO.	AGE	GENDER	HEIGHT (cm)	WEIGHT (Kg)	S.CREATININE	BLOOD PRESSURE (mm Hg)	RIGHT EAR -LATENCY in milliseconds								LEFT EAR -LATENCY in milliseconds							
							WAVE 1	WAVE 2	WAVE 3	WAVE 4	WAVE 5	WAVES 1-3	WAVES 3-5	WAVES 1-5	WAVE 1	WAVE 2	WAVE 3	WAVE 4	WAVE 5	WAVES 1-3	WAVES 3-5	WAVES 1-5
1	57	M	160	56	4	160/90	1.5	2.6	3.7	5	5.8	2.2	2.1	4.3	1.4	2.7	3.8	5.1	5.9	2.2	2.1	4.3
2	62	F	156	50	7.6	120/80	1.8	2.9	4.03	4.99	5.52	2.23	1.49	3.72	1.9	3	4.04	5	5.62	2.14	1.58	3.92
3	50	M	160	60	4	110/78	2.2	2.72	3.08	5.45	5.98	1.78	2.9	3.78	1.9	2.08	3.05	4.6	5.72	1.15	2.67	3.82
4	25	F	156	56	6	120/80	2.05	2.5	3.4	4.95	5.65	1.45	2.25	3.6	1.82	2.6	3.52	4.85	5.8	1.7	2.28	3.98
5	31	F	163	60	6.2	110/90	1.87	2.8	3	5	5	1.13	2.8	3.93	2.84	2.8	3	4.02	5.88	0.16	2.88	3.04
6	25	F	158	56	4.8	120/90	2.9	2.9	3.25	4.72	5.89	0.35	2.64	2.99	2.38	2.8	3	4.75	5.8	0.62	2.8	3.42
7	16	M	168	60	5.4	130/80	2.88	2.72	3.72	5.08	5.9	0.84	3.08	3.02	1.85	2.98	3.7	5.38	5.82	1.85	2.12	3.87
8	18	M	170	62	6.6	130/88	2.7	3	3.6	5	5.6	0.9	2	2.9	1.8	2.8	3.2	4.8	5.4	1.4	2.2	3.6
9	20	F	166	62	7	140/92	2.94	3	3.4	4.9	6	0.46	2.6	3.06	2.76	3	3.44	4.4	5.88	1.04	2.44	3.12
10	35	M	158	54	7.8	150/92	1.4	2.8	3.6	5	6.2	2.2	2.6	4.8	1.5	2.9	3.7	5.1	6.3	2.2	2.6	4.8
11	23	F	164	58	9.6	140/90	2	2.9	3.8	5	6.4	1.8	2.6	4.4	2	2.8	3.8	4.94	6	1.8	2.2	4
12	45	M	166	57	4.5	150/80	1.76	2.78	3.95	4.87	5.49	2.19	1.54	3.73	1.85	2.84	3.39	5.21	5.6	2.04	1.71	3.75
13	56	M	162	56	5.8	146/82	1.68	2.05	3.89	5.02	5.54	2.21	1.65	3.86	1.7	2.82	3.99	5.26	5.8	2.29	2.29	4.1
14	40	F	150	48	7	150/82	1.6	2.8	4	4.9	6	2.4	2	4.4	1.86	2.8	3.54	5	6	2.68	2.46	4.14
15	60	M	155	58	6.6	140/86	1.7	2.8	3.99	4.99	5.79	2.29	1.8	4.09	1.8	2.9	4	5	5.89	2.29	1.8	4.09
16	56	M	168	65	5.4	158/90	1.69	2.94	3.98	5.22	5.94	2.29	1.96	4.25	1.86	3	3.8	5.5	6	1.94	2.2	3.14
17	28	F	167	65	6.6	150/86	1.76	2.95	4.02	5.09	5.86	2.2	1.9	4.1	1.6	3	4	4.6	5.8	2.4	1.8	4.2
18	34	F	156	56	7	150/82	1.76	2.91	3.9	4.97	5.66	2.14	1.76	3.9	1.72	2.92	4	5.04	6	2.28	2	4.28
19	32	M	160	60	6.7	148/90	1.74	2.88	4.02	4.98	5.76	2.28	1.74	4.02	1.8	2.6	3	4.6	5	1.2	2	3.2
20	22	M	162	62	7	150/86	1.69	2.94	4.07	5.27	5.67	2.38	1.6	3.98	1.7	3	4	5.1	5.8	2.3	1.8	4.1

Renal Transplantation Group

Sl.No.	AGE	GENDER	HEIGHT (cm)	WEIGHT (Kg)	S.CREATINE	BLOOD PRESSURE (mm Hg)	RIGHT EAR -LATENCY in milliseconds								LEFT EAR -LATENCY in milliseconds							
							WAVE 1	WAVE 2	WAVE 3	WAVE 4	WAVE 5	WAVES 1-3	WAVES 3-5	WAVES 1-5	WAVE 1	WAVE 2	WAVE 3	WAVE 4	WAVE 5	WAVES 1-3	WAVES 3-5	WAVES 1-5
1	31	M	175	75	1	120/80	1.65	1.72	2	2.25	3	0.35	1	1.35	1.65	2.86	3.93	5.23	5.46	2.32	1.43	3.85
2	46	M	170	67	1.2	130/80	1.7	2.8	4	4.96	5.8	2.3	1.96	4.1	1.8	2.9	4.09	5.07	5.86	2.29	1.77	4.06
3	25	M	172	70	2	126/88	1.86	2.9	3.84	5	5.8	2.14	1.96	4	1.81	2.96	3.89	4.9	5.87	2.08	1.98	4.06
4	30	F	167	66	0.6	120/80	1.76	2.76	3.9	5	5.69	2.14	1.79	3.93	1.8	2.88	3.9	5.24	5.9	2.1	2	4.1
5	43	F	156	56	0.78	110/70	1.8	2.8	4	4.8	5.5	2.2	1.5	3.7	1.66	2.86	3.92	5.3	5.79	2.26	1.87	4.13
6	52	F	160	60	0.66	100/80	1.8	2.9	3.9	5.19	5.78	2.1	1.88	3.98	1.68	2.78	3.98	4.94	5.87	2.3	1.89	4.19
7	43	F	166	56	1	120/80	1.66	2.8	3.9	5.14	5.77	2.3	1.87	4.11	1.67	2.79	4.04	4.99	5.95	2.37	1.91	4.28
8	57	M	168	68	1.4	110/80	1.86	2.9	3.88	4.94	5.76	2.02	1.88	3.9	1.7	2.8	4.06	4.97	5.87	2.36	1.81	4.17
9	68	F	158	56	1.5	110/70	1.85	2.83	4.05	5.08	5.97	2.2	1.92	4.12	1.8	2.9	3.99	5	5.88	2.19	1.89	4.08
10	63	M	170	72	1.6	120/80	1.79	2.73	4.07	4.94	5.63	2.28	1.56	3.84	1.65	2.77	3.9	4.99	5.45	2.25	1.55	3.8
11	58	M	166	60	1.8	110/86	1.8	2.9	4.04	5.2	5.79	2.24	1.75	3.99	1.85	2.89	3.99	5.06	5.55	2.14	1.56	3.7
12	55	M	158	57	0.63	120/80	1.8	2.9	3.99	5	5.98	2.19	1.19	4.18	1.69	2.93	4	5.14	5.87	2.31	1.87	4.18
13	60	M	165	65	0.64	120/70	1.77	2.76	3.97	4.86	5.45	2.2	1.43	3.68	1.68	2.94	4.06	5.24	5.88	2.38	1.82	4.2
14	45	M	168	66	0.68	110/76	1.66	2.87	3.94	5.26	5.76	2.28	1.82	4.1	1.7	2.96	4.09	5.33	5.89	2.39	1.8	4.19
15	52	M	158	56	1.6	110/80	1.69	2.94	4.07	5.27	5.67	2.38	1.6	3.98	1.79	2.9	3.97	5.05	5.47	2.18	1.5	3.68
16	35	F	162	60	2	120/80	1.66	2.84	3.97	5.09	5.9	2.31	1.93	4.24	1.71	2.88	3.99	4.86	5.91	2.28	1.92	4.2
17	31	F	154	54	0.62	110/70	1.76	2.92	3.88	4.96	5.64	2.12	1.76	3.86	1.78	2.78	3	4.84	5	1.22	2	3.22
18	25	F	158	50	1	120/80	1.56	2.84	4.08	4.96	5.66	2.52	1.58	4.1	1.85	2.96	3.9	5.14	5.52	2.05	1.62	3.67
19	28	M	162	54	1.2	110/70	1.79	2.79	3.94	5.22	5.86	2.15	1.92	4.07	1.8	2.94	3.8	5	6	2	2.2	4.2
20	56	F	156	56	0.68	110/70	1.66	2.67	3.89	4.92	5.72	2.23	1.83	4.06								