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Comparison of Correlation between Serum Uric Acid and Blood Pressure in Offspring's of Patients with Essential Hypertension and in Healthy Controls

Sandhya H.P.*, Suma H.P., Noorjehan Begum*****

Abstract

Background: Studies have suggested a tight linear correlation between the SUA and SBP, DBPin children with pre-hypertension. Many factors, including family history, genetics, insulin resistance and BMI, play a role in the development of essential hypertension. **Aims and Objectives:** 1) To assess the SUA, BPin offspring's of patients with essential hypertension (cases), and in age and sex matched healthy controls. 2) To compare and thereby to test the hypothesis that a *"significant correlation is present between the SUA and BP"*. **Methodology:** Thirty cases and thirty controls without history of essential hypertension in the family were randomly selected. Out of thirty subjects in each group, ten females and twenty were males aged between 17-25years.SUA, blood urea, serum creatinine, triglycerides, total cholesterol, FBS and BP were measured in both groups along with anthropometric measurements viz., height, weight, BMI, waist- hip ratio. Data was tabulated and statistically analysed using SPSS software. **Results and Conclusions:** It was found that both groups were well matched with respect to age, sex, BMI, and waist-hip ratio. The two groups also did not differ much in their lipid parameters, renal parameters, FBS (except serum creatinine). BP (systolic and diastolic, $p<0.001$, $p=0.075$) was significantly higher in cases in comparison to controls. Further analysis did not reveal any positive correlation between SUA and SBP in cases($r=-0.265$, $p=0.157$). So it was concluded that the correlation between SUA and SBP has been distorted in cases due to confounding factors like age, etc.

Keywords: BP; Essential hypertension; SUA.

Introduction

Essential hypertension affects upto 25% of adults and significantly increases the risk of myocardial infarction, stroke, congestive heart failure, and renal failure. The development of the disease process has been clearly shown to begin in childhood.[1]

Many factors such as family history, genetics, insulin resistance, and a high body mass index play a role in the development of essential hypertension. The family history is an important risk factor for essential hypertension seen in children.[2]

Epidemiological studies have demonstrated an association between serum uric acid levels and the incident as well as prevalent hypertension in diverse populations including Asians.[3] A significant correlation between elevated uric acid levels (5.5 mg/dl) and blood pressure has been demonstrated in children and adolescents. Earlier studies have also shown an association between higher serum uric acid levels with higher diastolic blood pressure and lean body mass in children and young adults.[1]

Hence the present study was done to determine the association between the serum uric acid levels and the blood pressure in apparently normal offsprings of patients of essential hypertension. This study helps in understanding early stages

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of the relationship and therefore in early identification and prevention of hypertension.

Materials and Methods

Thirty offspring's of patients of essential hypertension (diagnosed based on their blood pressure measurements and clinical manifestations) and thirty age and sex matched healthy controls without history of essential hypertension in the family, were randomly selected from the general population for the study, as per the inclusion and exclusion criteria.

Inclusion Criteria

- Healthy offsprings of patients of essential hypertension in the age group of 17-25 years.
- Healthy age and sex matched control subjects are selected from general population.
- Subjects who are willing to participate in the study and give consent for the same.

Exclusion Criteria

- Smokers, alcoholics.
- Any history of diabetes, metabolic syndrome, hypertension, coronary heart disease, stroke, gout, renal colic, chronic kidney disease.
- Non-cooperation by the subjects.

This study was done after taking ethical clearance from the institute.

Out of the thirty subjects in each group, ten were females and twenty were males. Informed written consent was taken from all the subjects. Detailed (family, dietary and personal) history was taken from all the subjects and medical examination was also done. The anthropometric measurements like height (in cms), weight (in kgs), were done and body mass index (kg/sq.m) was calculated. Also waist circumference was measured at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest; hip circumference measurement was taken around the widest portion of the buttocks (WHO, 2008b).[4] Then the waist-hip ratio was calculated for all the subjects. Heart rate and blood pressure were also recorded.

Measurement of Blood Pressure

Blood pressure was measured manually using mercury sphygmomanometer by palpatory and auscultatory method. The subject was made to sit comfortably on a chair with back supported, legs uncrossed and upper arm bared. Subject's arm was supported at heart level. It was ensured that the cuff bladder encircled 80% or more of the arm circumference (size of cuff used 12.5*23 cm). Then the cuff is inflated by raising the mercury column and then deflated at 2-3 mm of Hg/second. The level of the mercury column at which the radial pulse reappears is noted as the systolic blood pressure.

After placing the chestpiece of the stethoscope over the arm medial to the tendon of biceps blood pressure of the subject was then recorded by auscultatory method. The first and the last audible korotkoff sounds were recorded as systolic and diastolic blood pressure respectively. Measurements were taken to the nearest 2mm Hg. Neither the subject nor the examiner talk during the procedure. The recordings were made in two different sittings and the lowest of the two recordings was taken in to consideration.[5]

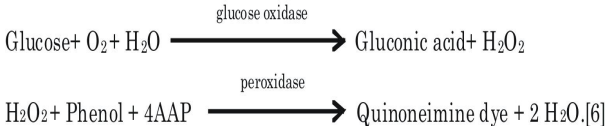
Analysis of the Blood Sample

About 3 ml of blood sample was collected from the ante cubital vein of all the subjects (after 8 hours of overnight fasting) under aseptic precautions and the following parameters were measured at Central Laboratory, Vijayanagar Institute Of

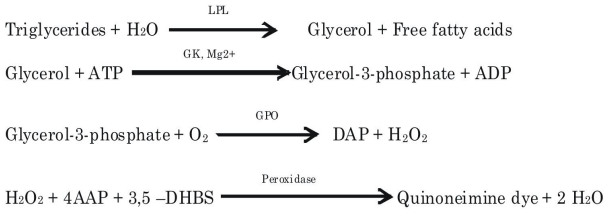
Medical Sciences.

- Fasting blood glucose (Trinder's method),
- Triglycerides (GPO–Trinder method),
- Total cholesterol (by CHOD-PAP method),
- Blood urea (GLDH–Urease method),
- Serum creatinine (Jaffe's method),
- Serum uric acid (Modified Trinder's method),

Trinder's Method: Glucose in sample is oxidised to yield gluconic acid and hydrogen peroxide in the presence of glucose oxidase. The enzyme peroxidase catalyses the oxidative coupling of 4-aminoantipyrine with phenol, to yield a coloured quinoneimine complex, with absorbance proportional to the concentration of glucose in sample.

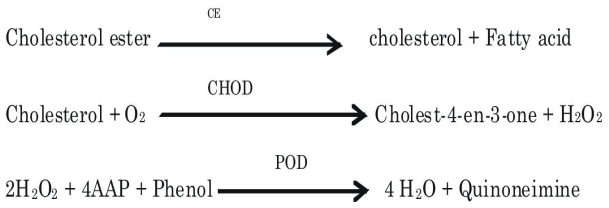


GPO–Trinder Method: Its principle involves the following reactions.



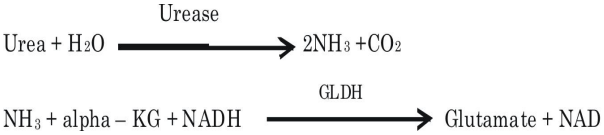
The intensity of chromogen (quinoneimine) formed is proportional to the trigycerides concentration in the sample when measured at 505 nm.[7,8,9,10]

CHOD-PAP Method: the estimation of cholesterol involves the following enzyme catalysed reactions.



The absorbance of quinoneimine so formed is directly proportional to the cholesterol concentration in the specimen.[11,12]

GLDH–Urease Method: The estimation of urea in serum involves the following enzyme catalysed reactions:

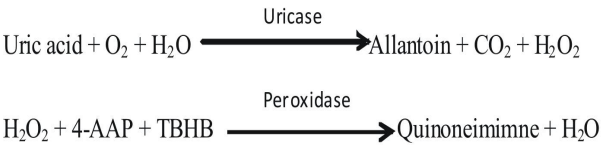


The rate of decrease in absorbance is monitored at 340 nm and is directly proportional to urea concentration in the sample.[13,14,15,16]

Jaffe's Method: Creatinine reacts with alkaline picrate to produce an orange yellow colour (the Jaffe reaction). Specificity of the assay has been improved by the introduction of an initial rate method. However, cephalosporin antibiotics are still major interferants.

The absorbance of the orange yellow colour formed is directly proportional to creatinine concentration and is measured photometrically at 540 nm.[17,18,19,20]

Modified trinder method: the following reactions are involved in its principle.



The intensity of chromogen (Quinoneimine) formed is proportional to the uric acid concentration in the sample when measured at 505 nm.[21,22,23,24,25, 26,27,28]

Statistical Analysis

Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%).

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale

between two groups (Inter group analysis) on metric parameters. Leven1s test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Pearson correlation of BP and FBS with uric acid is also performed.

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data.[29,30,31,32]

Results

Table 1 shows the comparison of baseline variables of the offsprings of patients of essential hypertension and that of controls. There was a significant difference between the two groups with respect to their mean age. The mean age of the offsprings of patients of essential hypertension was 19 +1.80 years and that of controls was 17.97 +1.22 years.

Table 1: Comparison of Baseline Variables in Two Groups Studied

Baseline variables	Offspring's of essential hypertension	Healthy controls	P value
Age	19.00±1.80	17.97±1.22	0.012*
BMI	20.75±3.47	19.61±1.77	0.115
Waist Cir	68.17±7.48	66.57±4.28	0.313
Hip Cir	89.50±7.99	88.93±4.31	0.734
W/H ratio	0.76±0.05	0.75±0.03	0.223

Table 2: Comparison of FBS in Two Groups Studied

FBS	Offspring's of essential hypertension		Healthy controls	
	No	%	No	%
<100	21	70.0	16	53.3
100-126	9	30.0	14	46.7
>126	0	0.0	0	0.0
Total	30	100.0	30	100.0
Mean ± SD	91.77±11.45		101.27±7.96	

P=<0.001**

But the two groups did not differ much with respect to their BMI, and waist – hip ratio.

Table 2 shows the comparison of fasting blood glucose levels of the two groups studied.

From the table it is evident that the fasting blood glucose levels, was significantly higher in controls in comparison to that of offsprings of patients of essential hypertension; though being within normal limits in the two groups.

Table 3 shows the comparison of lipid parameters between the two groups studied. As can be observed from the table the two groups did not differ much with respect to their total cholesterol and triglyceride levels(both were within limits).

Table 4 demonstrates the comparison of renal parameters between the two groups studied. From the table it can be observed that, the two groups did not differ significantly with respect to their urea and serum uric acid levels (both within normal range).But the serum creatininelevels were significantly higher in offsprings of patients of essential hypertension in comparison to controls. The values of the parameters were within normal range in both the groups.

Table 5 shows the comparison of vital parameters between the two groups studied. From the table it can be seen that the two groups did not differ significantly with respect to their pulse rate; and was within normal range in both groups. But the SBP and the DBP was significantly higher in offsprings of patients of essential hypertension in comparison to controls. Both SBP and DBP were within normal range in both the groups. These findings were similar to those found by Kilic Z, Tutuncu RT, Ozdeimer G et al. [2] Similar findings were also found by Arnold B, Alper Jr, Chen W et al.[1]

Statistical analysis further did not reveal any correlation between the SUA levels and the BP in offsprings of patients of essential

Table 3: Comparison of Lipid Parameters in Two Groups Studied

Lipid parameters	Offspring's of essential hypertension	Healthy controls	P value
Total cholesterol	149.40±22.46	146.07±10.48	0.464
TGL	72.30±30.15	65.10±16.14	0.254

Table 4: Comparison of Renal Parameters in Two Groups Studied

Renal parameters	Offspring's of essential hypertension	Healthy controls	P value
Urea	19.83±4.57	20.83±3.33	0.337
Creatinine	0.83±0.25	0.69±0.08	0.005**
Uric acid	4.28±0.89	3.98±0.57	0.123

Table 5: Comparison of Vital Parameters in Two Groups Studied

Vital parameters	Offspring's of essential hypertension	Healthy controls	P value
PR (bpm)	85.70±14.48	82.17±8.67	0.256
SBP (mm Hg)	118.23±12.10	107.67±9.79	<0.001**
DBP (mm Hg)	76.62±8.82	73.27±5.00	0.075+

hypertension.

Discussion

Several studies have already demonstrated the close association between SUA levels and the blood pressure in patients of essential hypertension. But there are a few studies conducted on normotensive offsprings of patients of essential hypertension to evaluate the relationship between the SUA levels and the blood pressure. Such studies have been done on western population.Hence the present study was taken up in Indian population to determine the association between SUA levels and the BP in apparently normal offsprings (adolescents) of patients of essential hypertension.

In the present study both the groups were well matched with respect to their age and gender. But there was a significant difference in their mean age.

The fasting blood glucose was significantly higher in controls in comparison to that of offsprings of patients of essential hypertension even though it was within normal range in both the groups. The exact cause of this is not known.

The total cholesterol and the triglycerides levels were higher in offsprings of patients of essential hypertension compared to controls; but the difference between the two groups was not significant. Both the parameters were within normal range in the two groups.

In the present study serum uric acid and serum creatinine (significantly high) levels were higher in the offsprings of patients of essential hypertension compared to controls (both within normal range). Uric acid in high concentrations is associated with development of renal disease. Elevated uric acid (3.1+0.2mg/dL in rats) is known to cause glomerular hypertension and cortical vasoconstriction. These changes then induce glomerular damage and tubular ischemia. In addition, uric acid stimulates inflammatory mediators in vascular smooth muscle cells including CRP, MCP-1 and vasoconstrictive factors such as

thromboxane.[33,34]

The offsprings of patients of essential hypertension had significantly high systolic and diastolic blood pressure compared to controls. But both were within normal limits in the two groups studied.SUA has been correlated with BP in childhood primary HTN. Uric acid enters the vascular smooth muscle cells and stimulates a number of factors including PDGF and MAPK. These factors induce proliferation of vascular smooth muscles and pre-glomerular arteriolopathy. Once a vascular lesion is established, salt sensitivity persists despite correction of SUA levels and is attributed to renal ischemia that leads to activation of renin–angiotensin system, renal vasoconstriction, increased sodium absorption. Increased uric acid levels also cause an increase in juxtaglomerular renin production and a decrease in macula densa nitric oxide synthase expression and both of these mechanisms directly lead to increased BP.[1,33,34]

In the present study the significant positive correlation between SUA and blood pressure could not be established[1.uric acid vs SBP, r= -0.265, p = 0.157, 2. Uric acid vs DBP, r = -0.074, p = 0.697].This is probably because this study was conducted on a small sample, or the correlation between the two parameters might have been distorted by some of the confounding factors such as age, gender, race, and BMI.

The analysis of the association between SUA and BP among youth is complicated by the observed developmental changes in SUA and urinary uric acid excretion. SUA is known to increase with age and BMI during childhood. Gender and racial differences have already been noted. Gender differences in normal SUA levels become most obvious during adolescence and have been attributed the effect of estrogen.

In addition, there occurs age, size, and gender related changes in BP that makes analysis of BP in youth difficult.[35]

Conclusions

Though the present study has shown a significant rise in SBP, DBP, and in serum creatinine levels (within normal range) in offsprings of patients of essential hypertension, a significant positive correlation between SUA and BP could not be established in them. Hence further studies are suggested in this regard with a large sample size and 24 hour ambulatory BP monitoring.

Limitations

1) The present study was done on a small sample size.
2) 24 hour ambulatory BP was not monitored which reflects the variations in SBP and DBP.
3) Single determination of SUA was made in this study which can cause bias, as there occurs variation in SUA when measured repeatedly.

List of Abbreviations

1. Alpha-KG- alpha ketoglutarate
2. ATP- Adenosine tri phosphate
3. 4-AAP- 4 Amino antipyrine
4. BMI- Body mass index
5. BP- Blood Pressure
6. CE- Cholesterol esterase
7. CHOD- Cholesterol oxidase
8. Cm- Centimetres
9. CRP- C Reactive Protein
10. DAP- Dihydroxyacetone phosphate
11. DBP – diastolic blood pressure
12. DHBS- 3,5- Dichloro-2-hydroxybenzene sulfonate
13. FBG- Fasting blood glucose
14. GK- Glycerol kinase

15. GLDH- Glutamate dehydrogenase
16. GPO- Glycerol phosphate oxidase
17. GTT- Glucose tolerance test
18. HMP- Hexose monophosphate shunt
19. Kg- Kilograms
20. LPL- Lipoprotein lipase
21. MAPK – mitogen activated protein kinase
22. MCP-1- Monocyte chemo attractant protein -1
23. ml- Millilitre
24. SD- Standard Deviation
25. SBP – systolic blood pressure
26. SUA- Serum uric acid
27. TBHB- 2,4,6,-tribromo-3-hydroxy benzoic acid
28. URAT-1- Urate anion exchanger-1
29. WHO- World Health Organisation

References

1. Arnold B, Alper Jr, Chen W, Yau L, Srinivasan RS, Gerald S, *et al*. Childhood uric acid predicts adult blood pressure. *Hypertension*. 2005; 45: 34-38.
2. http://www.uni-kiel.de/aepc/2011/aepcHandouts/Handdout_565pdf. accessed on 12/06/2013.
3. Feig DI. The role of uric acid in the pathogenesis of hypertension in the young. *J Clin Hypertens (Greenwich)*. 2012; 14(6): 346-352.
4. *http://www.whqlibdoc.who.int/publications/2011/9789241501491_eng.pdfý* accessed on 24/08/2013.
5. Smith L. Practice guidelines. New AHA Recommendations for Blood Pressure Measurement. *Am Fam Physician*. 2005; 72(7): 1391-1398.
6. Trinder, P. *Ann Clin Biochem*. 1969; 6(24).
7. Product Data Sheet, Triglyceride-G code no.997-69801, WAKO Pure chemical industries Ltd., Dallas,TX.
8. McGowan MW, *et al*. *Clin Chem*.1983; 29: 538.
9. Fossati P. *Ann Clin Biochem*. 1969; 6: 24-7.
10. Trinder P. *Ann Clin Biochem*. 1969; 6: 24-7.
11. Allian CC, Poon LS, Chan CSG, *et al*. *Clin Chem*. 1974; 20(470).
12. Roeschalu P, Bernt E, Gruber WA. *Clin Chem Clin Biochem*. 1974; 12(226).
13. Take H, Schubert, Klin GE. *Wochschr*. 1965; 19(43): 174.
14. Tiffany TO, Jansen J, Burtis CA, *et al*. *Clin Chem*. 1972; 18: 829.
15. Young DS. Effects of drugs on clinical laboratory tests. Third edition. 1990; 21: 5.
16. Tietz N. Fundamentals of clinical chemistry. Philadelphia, PA: WB Saunders Co.: 1976.
17. Bowers LD. *Clin Chem*. 1980; 26: 551.
18. Bartel H. *Clin Chem Acta.* 1972; 37: 193.
19. Slot C, Scand. *J Clin Lab Invest*. 1965; 17: 381.
20. Young DS. *Clin Chem*. 1975; 21: 266D.
21. Searcy RL. Diagnostic biochemistry. Newyork, NY: Mc.Graco-Hill; 1969.
22. Henry RJ, Common C & Winkelman JW. Clinical Chemistry: Principles & Techniques. Hagerstown, MD: Harper & Row; 1974.
23. Balis ME. *Adv Clin Chem*. 1976; 18(213).
24. Trivedi R, Berta E, Rebar L. *Clin Chem*. 1976; 22: 1223.
25. Kabasakalian P, Kalliney S, Wescott A. *Clin Chem*. 1973; 19: 522.
26. Trinder P. *J Clin Pathol*. 1949; 22: 246.
27. Young DS. Clin Chem. 1972; 18: 10.
28. Shephard MD, Mezzachi RD. *Clin Biochem Revs*. 1983; 4: 61-7.
29. Rosner B. Fundamentals of Biostatistics, 5th Edition. Duxbury: 2000; 80-240.
30. Riffenburg RH. Statistics in Medicine, Second edition. Academic Press; 2005: 85-125.
31. Sunder Rao PSS, Richard J. An Introduction to Biostatistics, A manual for students in health sciences, 4th edition. New Delhi: Prentice Hall of India; 2006, 86-160.

32. Suresh KP and Chandrasekhar S. Sample Size estimation and Power analysis for Clinical research studies. *Journal Human Reproduction Science*. 2012; 5(1): 7-13.
33. Heinig M, Johnson RJ. Role of uric acid in hypertension, renal disease and metabolic syndrome. *Clevland Clinic Journal of Medicine*. 2006; 73(12): 1059-1064.
34. Mazzali M, Hughes J, Kim GY, *et al*. Elevated uric acid increases blood pressure in the rat by a novel crystal independent mechanism. *Hypertension*. 2001; 38: 1101-1106.
35. Jones DP, Phyllis A, Richey BS, Alpert, Li R. Serum uric acid and ambulatory blood pressure in children with primary hypertension. *Pediar Res*. 2008; 64(5): 556-561.

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Electrocardiographic Changes in Relation to Body Mass Index

Arpana Bhide*, Noorjehan Begum, Latheef Kasala***, Vanajakshamma Velam******

Abstract

Introduction: There are various physiological factors that affect ECG waveforms which include sex, age, ethnicity, height, weight, body mass index, and pregnancy and produce inter individual variability in ECGs. **Hypothesis:** The present study was done to find out the electrocardiographic changes in relation to body mass index. **Approach:** The study was conducted in the Physiology department, VIMS, Bellary. 30 normal, 30 overweight and 30 obese individuals, each between ages 18-30 years were selected from student population, VIMS, Bellary and also from general population to find out electrocardiographic changes in relation to body mass index. The ECG was recorded and was evaluated for different parameters like heart rate, P wave, PR interval, QRS complex, QRS axis, QT interval, QT_c interval, and results were drawn. **Results:** There was statistically significant increase in heart rate, PR interval, QT interval, QT_c interval, in overweight and obese individuals when compared to normal individuals and decrease in QRS axis in overweight and obese individuals when compared to normal individuals. **Conclusions:** The study shows that there are a variety of adaptations/alterations in cardiovascular system with increase in body mass index which bring about changes in ECG in the absence of any cardiac disease.

Keywords: ECG; Body mass index; Physiological changes.

Introduction

An important factor to consider when reading electrocardiograms (ECGs) for clinical decision making is that the waveforms are influenced by normal physiological and technical factors as well as by pathophysiological factors. Physiological factors that affect ECG waveforms include sex, age, ethnicity, height, weight, torso morphology, body mass index (BMI) and pregnancy. Such characteristics account for the differences among individuals and produce inter individual variability in ECGs.[1]

Obesity is a complex multifactorial chronic disorder that develops from an interaction of genotype and the environment. The health hazards of obesity have been recognized for centuries. Populations in industrialized countries are becoming more overweight as a result of changes in lifestyle. Both overweight and obesity must be regarded as serious medical problems in our time since obesity is associated with reduced life expectancy. Indeed, obesity represents an independent predictor of cardiovascular disease (CVD) and this association is more pronounced in individuals under 50 years of age. The presence of obesity may limit the accuracy of the physical exam. Jugular venous pulse

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is often not seen, and heart sounds are usually distant.

Obesity has the potential to affect the ECG in several ways:

1) displacement of the heart by elevating the diaphragm in the supine position,
2) increasing the cardiac workload and
3) increasing the distance between the heart and the recording electrodes.[2]

Currently over weight and obesity are classified by Body Mass Index (BMI = weight in kilograms/square of the height in meters). In adults, overweight is defined as BMI of 25.0 to 29.9kg/m^2; obesity is defined as BMI>/=30kg/m^2.[3]

The objective of the present study is to determine electrocardiographic changes in overweight and obese individuals. This study is undertaken to highlight the effects of BMI on the ECG and thereby help to differentiate from that of pathological changes.

Subjects and Methods

This study was conducted in the department of Physiology, VIMS, Bellary. Study population divided into 3 groups such as normal, overweight and obese. Each group contains 30 subjects who are aged between 18-30 years were selected from student population, VIMS, Bellary and also from general population to find out ECG changes in relation to their BMI.

Following an explanation about the nature and purpose of the study, those subjects who were willing to participate in the study were included after obtaining informed consent.

A detailed history was taken from all the subjects which were followed by a detailed physical examination. A pretested structured proforma was used to record relevant information from each individual.

Physical examination included measuring height in centimeters, weight in kilograms, recording resting pulse rate by palpating radial artery and blood pressure recording with a mercury sphygmomanometer. Clinical examination of cardiovascular and respiratory systems was done in detail.

Following detailed assessment of the subjects, they were screened for the presence of inclusion and exclusion criteria and dropped if any exclusion criteria were present.

Individuals with heart diseases like valvular heart disease, myocardial infarction, congenital heart disease, arrhythmias, and hypertension, respiratory diseases like chronic obstructive pulmonary disease, corpulmonale, individuals with anaemia, thyroid disorders and individuals on medication were excluded.The instrument used to record electrocardiogram is the Magic R 12 channel electrocardiograph designed by Mediline's team of biomedical engineers. Following detailed assessment of the subject, a 12 lead ECG was recorded during the resting state.The ECG was recorded and was evaluated for different parameters like heart rate, P wave, PR interval, QRS complex, QRS axis, QT interval, QT interval and results were drawn.

Statistical Analysis

The data was compiled in Microsoft excel and analyzed using SPSS (Statistical Package for Social Sciences) version15 (SPSS Inc. Chicago, IL, USA). Data was presented as mean ± SD for continuous data. The changes in ECG in overweight and obese when compared to normal were examined using ANOVA test, Chi square test and Fischer exact test. Differences were considered as significant if p-value<0.05.

Results

The distribution of study population based

Figure 1: Age-wise Distribution of Study Subjects based on BMI (at Column Width)

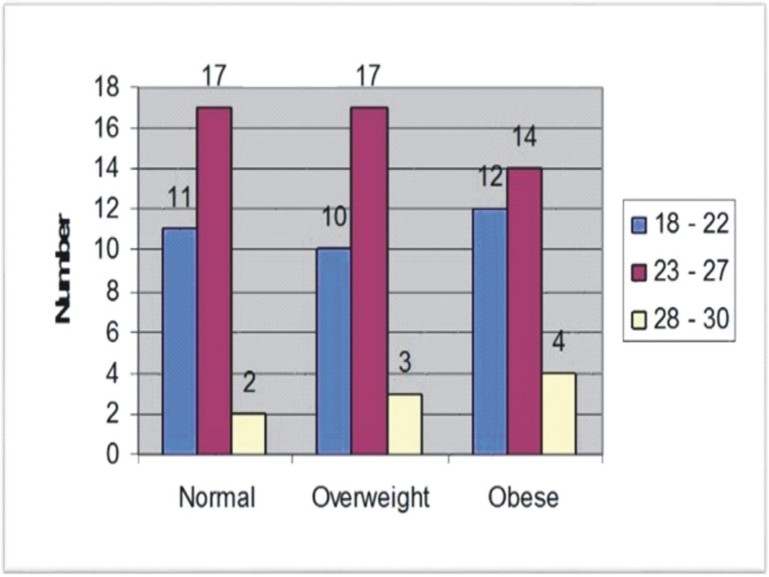

Table 1: Comparison of Pulse (bpm), Blood Pressure (mmHg), Heart Rate (bpm) and Respiratory Rate between Normal, Overweight and Obese Individuals

Variables	(Mean ± SD)			'F' value*	p-value	p-value (Multiple comparisons#)		
	(A) Normal	(B) Overweight	(C) Obese			A & B	A & C	B & C
SBP	118.80±2.7	121.87 ± 13.5	122.07 ± 2.5	13.47	0.00	0.00	0.00	0.27
DBP	79.67± 1.4	78.87 ± 3.3	80.93 ± 1.4	6.77	0.00	0.37	0.00	0.06
Heart rate	78.83 ± 3.0	75.13 ± 14.9	90.00 ± 3.4	56.43	0.00	0.00	0.00	0.00
Respiratory rate	15.93 ± 0.5	16.10 ± 0.5	15.87 ± 0.9	0.20	0.81	0.80	0.94	0.94

*ANOVA test applied, # post-hock Tuke test applied P>0.05 – not significant, P<0.05 – significant

Table 2: Comparison of 'P' Wave between Normal, Overweight and Obese Individuals

P wave	(Mean ± SD)			'F' value*	p-value	p-value (Multiple comparisons#)		
	(A) Normal	(B) Overweight	(C) Obese			A & B	A & C	B & C
Duration	0.080 ± 0.002	0.081 ± 0.004	0.082±0.006	3.19	0.08	0.72	0.07	0.31
Amplitude	1.00 ± 0	1.01±0.05	1.03±0.06	2.17	0.12	0.55	0.09	0.55

*ANOVA test applied, # post-hock Tuke test applied P>0.05 – not significant, P<0.05 – significant

Figure 2: Comparison of PR, QRS, QT and Qt_c Intervals between Normal, Overweight and Obese Groups (at Column Width)

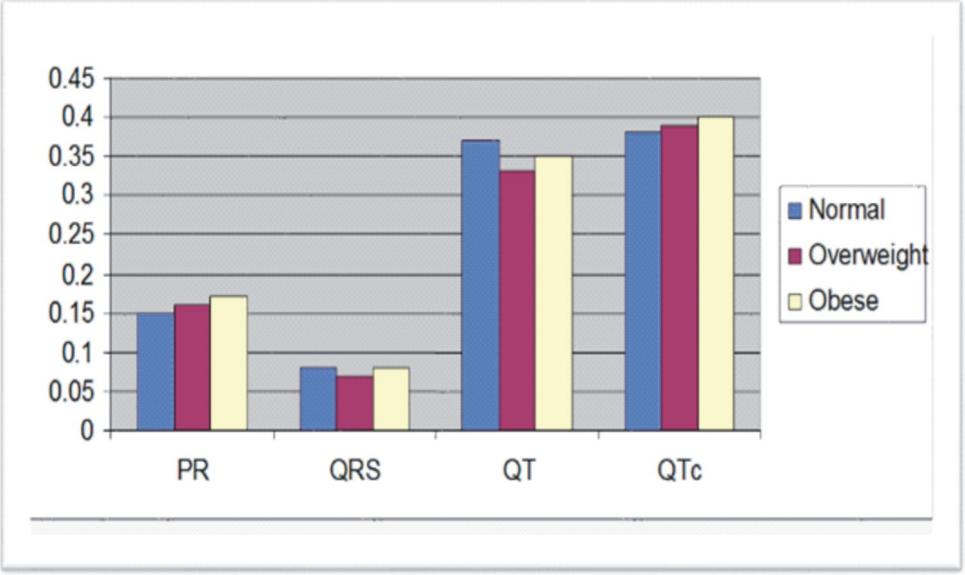

Table 3: Comparison of PR interval (Sec), QRS Complex(Sec), QT Interval (Sec), QTc Interval (Sec) and QRS Frontal Axis (Degree) between Normal, Overweight and Obese Individuals

Variables	(Mean ± SD)			'F' value*	p-value	p-value(Multiple comparisons#)		
	(A) Normal	(B) Overweight	(C) Obese			A & B	A & C	B & C
PR interval	0.15 ± 0.009	0.16 ± 0.00	0.17± 0.01	24.12	0.00	0.36	0.00	0.00
QRS complex	0.08 ± 0.003	0.07± 0.003	0.08± 0.009	1.42	0.24	0.55	0.80	0.22
QT interval	0.37 ± 0.02	0.33 ± 0.02	0.35± 0.03	12.59	0.00	0.00	0.02	0.04
QTc interval	0.38 ± 0.01	0.39 ± 0.006	0.40± 0.01	21.85	0.00	0.00	0.00	0.00
QRS axis	65.23 ± 7.29	50.20 ± 8.49	36.40± 11.86	70.51	0.81	0.80	0.00	0.00

*ANOVA test applied, # post-hock Tuke test applied, P>0.05 – not significant, P<0.05 – significant

on their age was summarized in Figure 1. Mean age was 23.4 ± 3.1, 23.6 ± 3.2 and 23.6 ± 3.4 years in normal, overweight and obese groups respectively (p = NS).Heart rate showed statistically significant increase in overweight and obese when compared to normal individuals (75.13±14.9, 78.83±3.00 and 90.0±3.4; p<0.01). There was also statistically significant increase in heart rate in obese individuals when compared to overweight individuals (78.83±3.00 vs 90.0±3.4; p<0.01) (Table 1).

Table 2 showing comparison of P wave between 3 groups. There is no statistically significant difference between 3 groups in P wave duration (0.08±0.002, 0.081±0.004 and 0.083±0.06; p =0.08).There is no statistically significant increase in P wave duration in obese when compared to normal (0.08±0.002 vs0.083±0.06; p<0.07). The P wave amplitudes (in mm) were 1.00±0.00, 1.01±0.05 and 1.03±0.06 among normal, overweight and obese individuals respectively. There was no statistically significant difference among the three groups (p = 0.12).

PR intervals (in seconds) were 0.15±0.009, 0.16±0.00 and 0.17±0.01 among normal, overweight and obese individuals respectively (Table 3). There was statistically significant increase in PR

interval among normal, overweight and obese groups ($p<0.01$). There was no statistically significant increase in PR interval in overweight when compared to normal individuals ($p=0.36$), but there is a significant increase in PR interval between normal and obese groups ($p<0.01$) and overweight and obese groups ($p<0.01$).

The durations of QRS complex were 0.08±0.003, 0.07±0.003 and 0.08±0.009 among normal, overweight and obese individuals respectively (Table 3, Figure 2). There was no statistical difference in duration of QRS complex among the three groups ($p = 0.24$).

Axis measurements (in degrees) were 65.23±7.29, 50.20±8.49 and 36.40±11.86 among normal, overweight and obese individuals respectively (Table 3). The QRS axis showed decrease in both overweight and obese when compared to normal individuals though there was no statistical significance when three values were compared($p = 0.81$).

There was statistically significant decrease in QRS axis in obese individuals when compared to normal (36.40±11.86 vs 65.23±7.29; $p<0.01$) and when compared to overweight (36.40±11.86 vs 50.20±8.49; $p<0.01$) groups. QT interval values (in seconds) were 0.33±0.02, 0.35±0.03 and 0.37±0.02 among normal, overweight and obese individuals respectively (Table 3, Figure 2). There was statistically significant increase in QT interval among overweight and obese individuals when compared to normal individuals ($p<0.01$). Also, there was statistically significant increase in QT interval in obese individuals when compared to normal (0.37±0.02 vs 0.33±0.02; $p=0.02$) and when compared to overweight (0.37±0.02 vs 0.35±0.03; $p=0.04$) individuals and also statistically significant increase in QT interval among overweight when compared to normal (0.35±0.03 vs 0.33±0.02; $p<0.01$) individuals.

QT interval values (in seconds) were 0.38±0.01, 0.39±0.006 and 0.40±0.01 among normal, overweight and obese individuals respectively (Table 3, Figure 2). There was statistically significant increase in QT interval among overweight and obese individuals when compared to normal individuals ($p<0.01$).

There was statistically significant increase in QT interval in obese individuals when compared to overweight (0.40±0.01 vs 0.39±0.006; $p<0.01$) and when compared to normal individuals (0.40±0.01 vs 0.38±0.01; $p<0.01$) and also statistically significant increase in QT interval in overweight individuals when compared to normal (0.39±0.006 vs 0.38±0.01; $p<0.01$) individuals.

Discussion

Many physiological factors affect the electrocardiographic waveforms. In this study, statistically significant increase in heart rate was found in both overweight and obese when compared to normal individuals. There was a positive correlation between body mass index and heart rate. Similar findings were reported by multiple studies, Alberto Salvadori *et al*,[4] Hugh R. Peterson *et al*,[5] Krzyszt of Narkiewicz *et al*[6] and Gilles Paradis *et al.*[7]

Activation of the sympathetic nervous system occurs early in the course of obesity and the autonomic nervous system is an important contributor to the regulation of both the cardiovascular system and energy expenditure as mentioned in multiple studies mentioned above. These studies also showed that heart rate increases with increase in percentage of body fat. A 10% increase in body weight is associated with a decline in parasympathetic tone accompanied by a rise in mean heart rate and conversely, heart rate declines during weight reduction. This is of importance because higher heart rate is associated with increased mortality rates.[8]

P Wave

P wave duration and amplitude

measurements did not show any statistically significant difference in overweight and obese individuals when compared to normal individuals.

PR Interval

In this study, PR interval showed statistically significant increase in overweight and obese individuals when compared to normal individuals. Similar findings were reported by Frank S *et al*[9] and Paul Poirier[2] in their study.

The reason for increased PR interval is not yet known and further studies are required to find the cause for increased PR interval in overweight and obese.

QRS Complex

The duration of QRS complex did not show any statistically significant difference in overweight and obese individuals when compared to normal individuals.

QRS Axis

In this study, QRS axis showed statistically significant decrease in obese individuals when compared to normal and overweight individuals. However, there was no statistically significant decrease in overweight individuals when compared to normal individuals.

The decrease in QRS axis in obese individuals is attributed to upward shift of diaphragm resulting in more horizontal position of heart and also to increased cardiac workload.[1,2]

Similar findings were reported by Hamoda MGA *et al*[1], Paul Poirier[2], Alpert MA *et al.*[10]

QT Interval

In this study, QT interval showed statistically significant increase in overweight and obese individuals when compared to normal individuals.

This was attributed to various factors primarily caused by obesity like left ventricular hypertrophy, left ventricular diastolic dysfunction, increased degree of myocardial repolarization in homogeneity, changes in sympathetic- vagal balance, increase in catecholamine levels, increase in free fatty acid levels which affect repolarization.[11]

Similar findings were reported by Bilora F *et al*[12], Seyfeli E *et al*[13], Carella MJ *et al*[14] and Boban Mathew *et al.*[11]

QT_c Interval

In this study ,QT_c interval showed statistically significant increase in overweight and obese individuals when compared to normal individuals.

This may be due to increased heart rate and also due to increased degree of myocardial repolarization in homogeneity, increase in free fatty acid levels which affect repolarization.[52]

Similar findings were reported by Frank S *et al*[9], Paul Poirier[2], Seyfeli E *et al*[13], Alaa El-Gamal *et al*[15], Carella MJ *et al*[14], Boban Mathew *et al.*[11].

Conclusion

- There was statistically significant increase in heart rate in overweight and obese individuals when compared to controls. There was also statistically significant increase in heart rate in obese when compared to overweight individuals.
- There was statistically significant increase in PR interval among overweight and obese individuals when compared to normal individuals. There was statistically significant increase in PR interval in obese individuals when compared to normal and overweight individuals.
- The QRS axis showed decrease in both

overweight and obese when compared to normal individuals though there was no statistical significance when three values were compared.

There was statistically significant decrease in QRS axis in obese individuals when compared to normal individuals and also when compared to overweight individuals.

- There was statistically significant increase in QT and QT_c intervals among overweight and obese individuals when compared to normal individuals.

There was statistically significant increase in QT andQT_c intervals in obese individuals when compared to overweight and normal individuals and also statistically significant increase in QT and QT_c intervals in overweight individuals when compared to normal individuals.

Though our study is by no means exhaustive, it does provide a glimpse into the variety of adaptations/alterations in cardiovascular system with increase in body mass index which bring about changes in ECG in the absence of any cardiac disease. Although we understand to some extent these changes and also since few studies have been done on this aspect, further research is needed to study the effect of body mass index on electrocardiogram.

Acknowledgement

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References

1. Hamoda MGA, Caldwell MA, Stotts NA, Drew BJ. Factors to consider when analyzing 12 lead electrocardiograms for evidence of acute myocardial ischaemia. *Am J Crit Care*. 2003; 12: 9-18.
2. Poirier P. Abdominal obesity: an important risk factor in clinical and interventional cardiology. *Official Journal of the International Chair on Cardiometabolic Risk*. 2008; 2(1): 7-14.
3. Clinical Guidelines on identification, evaluation and treatment of overweight and obesity in adults: The evidence report: National Institutes of Health. *Obes Res*. 1998; Suppl 2: 51S-209S.
4. Salvodori A, Fanari P, Mazza P, Agosti R, Longhini E. Work capacity and cardiopulmonary adaptation of the obese subjects during exercise testing. *Chest*. 1992; 101: 674-679.
5. Peterson HR, Rothschild M, Weinberg CR, Fell RD, Mcleish KR, Pfeifer MA. Body fat and the activity of the autonomic nervous system. *N Engl J Med*. 1988; 318: 1077-1083.
6. Narkiewicz K, Vande PJH, Cooley RL, Dyken ME, Somers VK. Sympathetic activity in obese subjects with and without obstructive sleep apnoea. *Circulation*. 1998; 98: 772-776.
7. Paradis G, Lambert M, O'Loughlin J, Lavallee C, Aubin J, Delvin E. Blood pressure and adiposity in children and adolescents. *Circulation*. 2004; 110: 1832-1838.
8. La Rovere MT, Bigger JT, Marcus FI, Mortara A, Schwartz PJ. Baroreflex sensitivity and heart rate variability in prediction of total cardiac mortality after myocardial infarction. ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) Investigators. *Lancet*. 1998; 351: 478-484.
9. Frank S, Colliver JA, Frank A. The electrocardiogram in obesity; statistical analysis of 1029 patients. *J Am Coll Cardiol*. 1986; 7: 295-99.
10. Alpert MA, Terry BE, Cohen MV, Hamm CR, Fan TM, Massey CV, *et al*. The electrocardiogram in morbid obesity. *Am J Cardiol*. 2000; 85: 908-910.
11. Mathew B, Francis L, Kayalar A, Cone J. Obesity: effects on cardiovascular disease and its diagnosis. *The Journal of the American Board of Family Medicine*. 2008; 21(6): 562-568.
12. Bilora F, Vettore G, Barbata A, Pastorello M, Petrobelli F, San Lorenzo I. Electrocardiographic findings in obese subjects. *Minerva Gastroenterol Dietol*. 1999;

45(3): 193-197.

13. Seyfeli E, Duru M, Kuvandik G, Kaya H, Yalcin F. Effect of weight loss on QT_c dispersion in obese subjects. *Anadolu Kardiyol Derg*. 2006; 6: 126-129.
14. Carella MJ, Mantz SL, Rovner DR, Willis PW, Gossain VV, Bouknight RR *et al*. Obesity, adiposity and lengthening of QT interval: improvement after weight loss. *International Journal of Obesity*. 1996; 20(10): 938-942.
15. Gamal AE, Gallagher D, Nawras A, Gandhi P, Gomez J, Allison DB *et al*. Effects of obesity on QT, RR and QT_c intervals. *Am J Cardiol*. 1995; 75(14): 956-959.

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Application of Physiology in Physical Therapy- Evidence for Efficacy of Pain Neurophysiology Education

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Abstract

Poor knowledge about pain and underestimation of patients' ability to understand pain-related information represented barriers to reconceptualization of chronic pain problem and hence this short communication was aimed at providing a descriptive summary of evidence for pain neurophysiology education (PNE) as an effective intervention through studies retrieved from PubMed. PNE was shown to be effective in one study on fibromyalgia, four studies on chronic low back pain (one pilot study, one single case study, one randomized controlled trial, one systematic review), and one study on chronic whiplash. The ensuing paradigm shift towards mechanism-based classification of pain and mechanism-based physical therapy warranted establishing mechanism-based treatment guidelines so that treatments not only aim at symptom control but also enhancement of quality of life in people.

Keywords: Manual therapy; Applied physiology; Therapeutic physiology; Clinical physiology; Pain neurophysiology.

Although both healthcare professionals and patients could understand the neurophysiology of pain, professionals tend to underestimate patients' ability to understand. This would imply:

(1) a poor knowledge of currently accurate information about pain and

(2) the underestimation of patients' ability to understand currently accurate information about pain represent barriers to reconceptualization of the problem in chronic pain.[1]

Fibromyalgia

van Ittersum *et al*[2] studied 41 participants with fibromyalgia (FM) who were given pain neurophysiology educational booklet and found that they had notable improvements in illness coherence, emotional representations, pain and fatigue levels, with no positive effects on illness perceptions, catastrophizing or impact of FM on daily life.

Chronic Low Back Pain

Ryan *et al*[3] in their pilot RCT investigated the effect of pain biology education and group exercise classes compared to pain biology education alone for individuals with chronic low back pain (CLBP) who were randomised to a pain biology education and group exercise classes group (EDEX) [n = 20] or a pain biology education only group (ED) [n = 18].

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The authors found short-term effectiveness of pain biology education alone for pain and pain self-efficacy than a combination of pain biology education and group exercise classes. However the between-group effects were not evident at 3-months follow-up.

Moseley *et al*[4] compared two groups:individual education sessions on neurophysiology of pain (experimental group) and back anatomy and physiology (control group) and found important beneficial treatment effects on Survey of Pain Attitudes (revised) (SOPA-R),Pain Catastrophizing Scale (PCS), Roland Morris Disability Questionnaire (RMDQ), straight leg raise (SLR) and forward bending. Education about pain neurophysiology was found to change pain cognitions and physical performance and was recommended for inclusion in wider pain management programs.

Clarke *et al*[5] searched MEDLINE, CINAHL and AMED and found two moderate quality RCTs (n=122)suggesting very low quality evidence that PNE is beneficial for pain, physical-function, psychological-function, and social-function. Meta-analysis showed that PNE reduced short-term pain by 5 mm on 100 mm visual analogue scale.

Whiplash-Associated Disorders

Van Oosterwijck *et al*[6] performed a single-case study (A-B-C design) with six patients with chronic whiplash associated disorders (WAD) where periods A and C represented assessment periods, while period B consisted of the intervention (pain neurophysiology education). A significant decrease in kinesiophobia (Tampa Scale for Kinesiophobia), the passive coping strategy of resting (Pain Coping Inventory), self-rated disability (Neck Disability Index), and photophobia (WAD Symptom List) was observed with increased pain pressure thresholds and improved pain-free movement performance (visual analog scale on Neck Extension Test and Brachial Plexus Provocation Test).

Nijs and Van Houdenhove[7] explained that "manual therapy might be able to influence the process of chronicity in three different ways.

(I) In order to prevent chronicity in (sub)acute musculoskeletal disorders, it seems crucial to limit the time course of afferent stimulation of peripheral nociceptors.

(II) In the case of chronic widespread pain and established sensitisation of central pain pathways, relatively minor injuries/trauma at any locations are likely to sustain the process of central sensitisation and should be treated appropriately with manual therapy accounting for the decreased sensory threshold. Inappropriate pain beliefs should be addressed and exercise interventions should account for the process of central sensitisation.

(III) However, manual therapists ignoring the processes involved in the development and maintenance of chronic widespread pain/FM may cause more harm than benefit to the patient by triggering or sustaining central sensitisation."

The ensuing paradigm shift towards mechanism-based classification of pain[8] and mechanism-based physical therapy[9] warranted establishing mechanism-based treatment guidelines so that treatments not only aim at symptom control but also enhancement of quality of life in people.[10]Nijset al[11] provided mechanism based clinical guidelines for the recognition of central sensitization in patients with musculoskeletal pain by which manual therapists can apply the science of nociceptive and pain processing neurophysiology to the practice of manual therapy.

References

1. Moseley L. Unraveling the barriers to reconceptualization of the problem in chronic pain: the actual and perceived ability of patients and health professionals to understand the neurophysiology. *J Pain*. 2003; 4(4): 184-9.
2. van Ittersum MW, van Wilgen CP, Groothoff JW, van der Schans CP. Is appreciation of written education about pain neurophysiology related to changes in illness perceptions and health status in patients with fibromyalgia? *Patient Educ Couns*. 2011; 85(2): 269-74.
3. Ryan CG, Gray HG, Newton M, Granat MH. Pain biology education and exercise classes compared to pain biology education alone for individuals with chronic low back pain: a pilot randomised controlled trial. *Man Ther*. 2010; 15(4): 382-7.
4. Moseley GL, Nicholas MK, Hodges PW. A randomized controlled trial of intensive neurophysiology education in chronic low back pain. *Clin J Pain*. 2004; 20(5): 324-30.
5. Clarke CL, Ryan CG, Martin DJ. Pain neurophysiology education for the management of individuals with chronic low back pain: systematic review and meta-analysis. *Man Ther*. 2011; 16(6): 544-9.
6. Van Oosterwijck J, Nijs J, Meeus M, Truijen S, Craps J, Van den Keybus N, Paul L. Pain neurophysiology education improves cognitions, pain thresholds, and movement performance in people with chronic whiplash: a pilot study. *J Rehabil Res Dev*. 2011; 48(1): 43-58.
7. Nijs J, Van Houdenhove B. From acute musculoskeletal pain to chronic widespread pain and fibromyalgia: application of pain neurophysiology in manual therapy practice. *Man Ther*. 2009; 14(1): 3-12.
8. Kumar SP, Saha S. Mechanism-based Classification of Pain for Physical Therapy Management in Palliative care: A Clinical Commentary. *Indian J Palliat Care*. 2011; 17(1): 80-6.
9. Kumar SP, Prasad K, Kumar KV, Shenoy K, Sisodia V. Mechanism-based classification and physical therapy management of persons with cancer pain- a prospective case series. *Indian J Palliat Care*. 2013; 19(1): 27-33.
10. Kumar SP, Jim A. Physical therapy in palliative care: from symptom control to quality of life: a critical review. *Indian J Palliat Care*. 2010; 16(3): 138-46.
11. Nijs J, Van Houdenhove B, Oostendorp RA. Recognition of central sensitization in patients with musculoskeletal pain: Application of pain neurophysiology in manual therapy practice. *Man Ther*. 2010; 15(2): 135-41.

Revised Rates for 2014 (Institutional)

Title	Freequency	Rate (Rs): India	Rate ($):ROW
Dermatology International	2	2500	280
Gastroenterology International	2	3500	360
Indian Journal of Agriculture Business	2	4500	300
Indian Journal of Anatomy	2	3200	260
Indian Journal of Ancient Medicine and Yoga	4	6600	330
Indian Journal of Anesthesia and Analgesia	2	4000	600
Indian Journal of Anthropology	2	8000	500
Indian Journal of Applied Physics	2	3500	400
Indian Journal of Biology	2	1500	170
Indian Journal of Cancer Education and Research	2	4500	500
Indian Journal of Communicable Diseases	2	1000	58
Indian Journal of Dental Education	4	3200	288
Indian Journal of Forensic Medicine and Pathology	4	12500	576
Indian Journal of Forensic Odontology	4	3200	288
Indian Journal of Genetics and Molecular Research	2	5000	262
Indian Journal of Law and Human Behavior	2	5000	500
Indian Journal of Library and Information Science	3	7500	600
Indian Journal of Maternal-Fetal & Neonatal Medicine	2	4500	400
Indian Journal of Mathematics and Statistics	2	3000	200
Indian Journal of Medical & Health Sciences	2	1800	120
Indian Journal of Obstetrics and Gynecology	2	2000	200
Indian Journal of Pathology: Research and Practice	2	3000	915
Indian Journal of Plant and Soil	2	5000	1700
Indian Journal of Preventive Medicine	2	3200	270
Indian Journal of Reproductive Science and Medicine	4	3000	180
Indian Journal of Scientific Computing and Engineering	2	3300	280
Indian Journal of Surgical Nursing	3	1800	70
Indian Journal of Trauma & Emergency Pediatrics	4	6500	302
International Journal of Agricultural & Forest Meteorology	2	8000	800
International Journal of Food, Nutrition & Dietetics	2	3200	900
International Journal of History	2	6000	500
International Journal of Neurology and Neurosurgery	2	7500	276
International Journal of Political Science	2	5000	400
International Journal of Practical Nursing	3	1500	70
International Physiology	2	4000	240
Journal of Animal Feed Science and Technology	2	3500	280
Journal of Cardiovascular Medicine and Surgery	2	5500	238
Journal of Orthopaedic Education	2	2500	190
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Mitochondrial Function and Dysfunction in Diabetic Peripheral Neuropathy: An Updated Overview of Studies to Implicate Physiological Basis of Neuropathological Condition

Nisha Rani Jamwal, Kumar Senthil P.*, Kumar Anup,Adhikari Prabha***, Jeganathan PS****, D'Souza Mariella*****

Abstract

This short communication article was aimed to provide an evidence-informed overview and a scoping review of the role of mitochondrial function/dysfunction in diabetic peripheral neuropathy (DPN). From the reviewed studies, it is apparently evident that mitochondria played a comprehensive role not only in predisposing oxidative stress but also in programmed cell death or apoptosis in DPN.

Keywords: Mitochondrial function; Oxidative stress; Pathophysiology; Diabetic neuropathy.

This short communication article was aimed to provide an evidence-informed overview and a scoping review of the role of mitochondrial function/dysfunction in diabetic peripheral neuropathy (DPN).

4-Hydroxy-2-nonenal induces mitochondrial dysfunction: Akude *et al*[1] tested the hypothesis that exposure of cultured adult rat sensory neurons to 4-hydroxy-2-nonenal (4-HNE) would result in the formation of amino acid adducts on mitochondrial proteins and that this process would be associated with impaired mitochondrial function and axonal regeneration. 4-HNE was shown to induce formation of protein adducts on cytoskel *et al* and mitochondrial proteins, and impaired axon regeneration by approximately 50% at 3 micro M while initiating formation of aberrant axonal structures and caused the accumulation of mitochondria in these dystrophic structures.

Chowdhury *et al*[2] summarized the major features of mitochondrial dysfunction in neurons and Schwann cells in human diabetic patients and in experimental animal models (primarily exhibiting type 1 diabetes) and emphasized, "hyperglycemia in diabetes triggers nutrient excess in neurons that, in turn, mediates a phenotypic change in mitochondrial biology through alteration of the AMP-activated protein kinase (AMPK)/peroxisome proliferator-activated receptor ã coactivator-1á (PGC-1á) signaling axis. This vital energy sensing metabolic pathway modulates mitochondrial function, biogenesis and regeneration.

Fernyhough et al[3] summarized the nature of sensory and autonomic nerve dysfunction in diabetes-induced nerve degeneration mediated by alterations in mitochondrial ultra structure, physiology and trafficking. A reduction in electron

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transport chain capability might predispose mitochondria to generate elevated reactive oxygen species (ROS), which would deleteriously alter the bio-energetic status of neurons.

Fernyhough *et al*[4] demonstrated that insulin and neurotrophin-3 (NT-3) modulate mitochondrial membrane potential in cultured adult sensory neurons and Diabetes caused a significant loss of mitochondrial membrane potential in all sub-populations of sensory neurons which was treated with insulin or NT-3. Their results showed that in adult sensory neurons, treatment with insulin could elevate the input of reducing equivalents into the mitochondrial electron transport chain, which lead to greater mitochondrial membrane polarization and enhanced ATP synthesis.

Adenosine monophosphate-activated protein kinase: Roy Chowdhury *et al*[5] assessed the deficits in adenosine monophosphate-activated protein kinase/ peroxisome proliferator-activated receptor ã coactivator-1á (PGC-1á) signalling in sensory neurons in rodent models of type 1 and type 2 diabetes. The study had following findings: "Phosphorylation and expression of adenosine monophosphate-activated protein kinase/PGC-1á and mitochondrial respiratory chain complex proteins were down regulated in dorsal root ganglia of both streptozotocin-diabetic rats and db/db mice. The bioenergetics profile (maximal oxygen consumption rate, coupling efficiency, respiratory control ratio and spare respiratory capacity) was aberrant in cultured sensory neurons from streptozotocin-diabetic rats and was corrected by resveratrol treatment."

Ciliary neurotrophic factor: Salehet al[6] tested the hypothesis that Ciliary neurotrophic factor (CNTF) protects sensory neuron function during diabetes through normalization of impaired mitochondrial bioenergetics. Neurite outgrowth of sensory neurons derived from streptozotocin (STZ)-induced diabetic rats was reduced compared to neurons from control rats and exposure to CNTF for 24 h enhanced neurite outgrowth. The authors proposed that the ability of CNTF to enhance axon regeneration and protect peripheral nerve from structural and functional indices of diabetic peripheral neuropathy was associated with targeting of mitochondrial function, and in part via NF-êB activation, and improvement of cellular bioenergetics.

Srinivasan *et al*[7] opined that diabetic sensory neuropathy was associated with activation of apoptosis and concomitant mitochondrial dysfunction. These findings were confirmed by the presence of basal mitochondrial membrane potential (deltapsi) being more positive in DRG neurons from diabetic rats.

Chaperones: Urban *et al*[8] proposed that modulating the activity and expression of heat shock proteins (Hsp) might be of benefit in treating DPN. KU-32 was found to improve physiological and morphologic markers of degenerative neuropathy and drug efficacy might be related to enhanced mitochondrial bioenergetics in sensory neurons.

Vincent *et al*[9] reported a greater number of mitochondria in both myelinated and unmyelinated dorsal root axons in a well-established model of murine diabetic neuropathy by examining mitochondrial biogenesis and fission in response to hyperglycemia in the neurites of cultured DRG neurons. The study demonstrated overall mitochondrial biogenesis via increases in mitochondrial transcription factors and increases in mitochondrial DNA in both DRG neurons and axons. The authors concluded that "during acute hyperglycemia, mitochondrial fission was a prominent response, and excessive mitochondrial fission might result in dysregulation of energy production, activation of caspase 3, and subsequent DRG neuron injury. During more prolonged hyperglycemia, there was evidence of compensatory mitochondrial biogenesis in axons."

From the reviewed studies, it was apparently evident that mitochondria played a comprehensive role not only in predisposing oxidative stress but also in programmed cell death or apoptosis in DPN.

References

1. Akude E, Zherebitskaya E, Roy Chowdhury SK, Girling K, Fernyhough P. 4-Hydroxy-2-nonenal induces mitochondrial dysfunction and aberrant axonal outgrowth in adult sensory neurons that mimics features of diabetic neuropathy. *Neurotox Res*. 2010; 17(1): 28-38.
2. Chowdhury SK, Smith DR, Fernyhough P. The role of aberrant mitochondrial bioenergetics in diabetic neuropathy. *Neurobiol Dis*. 2013; 51: 56-65.
3. Fernyhough P, Roy Chowdhury SK, Schmidt RE. Mitochondrial stress and the pathogenesis of diabetic neuropathy. *Expert Rev Endocrinol Metab*. 2010; 5(1): 39-49.
4. Fernyhough P, Huang TJ, Verkhratsky A. Mechanism of mitochondrial dysfunction in diabetic sensory neuropathy. *J Peripher Nerv Syst*. 2003; 8(4): 227-35.
5. Roy Chowdhury SK, Smith DR, Saleh A, Schapansky J, Marquez A, Gomes S, *et al*. Impaired adenosine monophosphate-activated protein kinase signalling in dorsal root ganglia neurons is linked to mitochondrial dysfunction and peripheral neuropathy in diabetes. *Brain*. 2012; 135(Pt 6): 1751-66.
6. Saleh A, Roy Chowdhury SK, Smith DR, Balakrishnan S, Tessler L, *et al*. Ciliary neurotrophic factor activates NF-êB to enhance mitochondrial bioenergetics and prevent neuropathy in sensory neurons of streptozotocin-induced diabetic rodents. *Neuropharmacology*. 2013; 65: 65-73.
7. Srinivasan S, Stevens M, Wiley JW. Diabetic peripheral neuropathy: evidence for apoptosis and associated mitochondrial dysfunction. *Diabetes*. 2000; 49(11): 1932-8.
8. Urban MJ, Pan P, Farmer KL, Zhao H, Blagg BS, Dobrowsky RT. Modulating molecular chaperones improves sensory fiber recovery and mitochondrial function in diabetic peripheral neuropathy. *Exp Neurol*. 2012; 235(1): 388-96.
9. Vincent AM, Edwards JL, McLean LL, Hong Y, Cerri F, Lopez I, *et al*. Mitochondrial biogenesis and fission in axons in cell culture and animal models of diabetic neuropathy. *Acta Neuropathol*. 2010; 120(4): 477-89.

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[2] Twetman S, Axelsson S, Dahlgren H, Holm AK, Källestål C, Lagerlöf F, et al. Caries-preventive effect of fluoride toothpaste: A systematic review. Acta Odontol Scand 2003;61:347-55.

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[3] Fleischer W, Reimer K. Povidone iodine antisepsis. State of the art. Dermatology 1997;195 Suppl 2:3-9.

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[4] American Academy of Periodontology. Sonic and ultrasonic scalers in periodontics. J Periodontol 2000;71:1792-801.

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[5] Garoushi S, Lassila LV, Tezvergil A, Vallittu PK. Static and fatigue compression test for particulate filler composite resin with fiber-reinforced composite substructure. Dent Mater 2006.

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[6] Hosmer D, Lemeshow S. Applied logistic regression, 2nd edn. New York: Wiley-Interscience; 2000.

Chapter in book

[7] Nauntofte B, Tenovuo J, Lagerlöf F. Secretion and composition of saliva. In: Fejerskov O, Kidd EAM, editors. Dental caries: The disease and its clinical management. Oxford: Blackwell Munksgaard; 2003. p. 7-27.

No author given

[8] World Health Organization. Oral health surveys - basic methods, 4th edn. Geneva: World Health Organization; 1997.

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