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# CORRELATION OF ANTHROPOMETRIC PARAMETERS WITH QTc INTERVAL IN MALNOURISHED CHILDREN

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**Abstract :** Various studies have reported the effect of severe malnutrition on electrolyte levels and electrocardiographic parameters. However, only a few have reported these findings in mild and moderate grades of malnutrition in children. Therefore, the objective of this study was to assess the effect of malnutrition (mainly mild and moderate grades) on corrected QT interval (QTc) and QT dispersion (QTcd) and electrolyte changes. A total of 20 malnourished children in the age group of 2-11 yrs were enrolled in the study group and 20 age and sex matched healthy children were taken as controls. Anthropometry, serum levels of albumin & electrolytes were determined. QTc and QTcd (difference between maximum & minimum corrected QT interval) were measured with the help of RMS Polyrite D. Our results have shown that body weight, height, body mass index (BMI), serum levels of albumin, potassium & calcium were lower ($P<0.01$) in malnourished children. QTc ($P<0.01$) & QTcd ($P<0.01$) were significantly greater in malnourished children than controls. We concluded that increase in QTc and QTcd intervals is associated with electrolyte disturbances in malnourished children. Electrolyte disturbance correction and appropriate nutrition therapy followed by further cardiac evaluation must be taken into account in the management of these patients.

**Key words :** malnutrition children body mass index corrected QT interval QT dispersion electrolytes

## INTRODUCTION

Protein energy malnutrition (PEM) has been identified as a major health and nutrition problem in India (1). It is largely the byproduct of poverty, ignorance, insufficient education, lack of knowledge regarding the nutritive value of foods, inadequate sanitary environment, large family size, high rate of maternal morbidity, still births & low birth weight babies (2).

PEM is a complex health problem that may be caused by simultaneous deficiency of

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protein-calories, micronutrients & vitamins. The great majority of cases of PEM, nearly 80 percent, are the 'intermediate' ones, that is the mild and moderate cases which frequently go unrecognized. What makes the problem even more serious is that its main victims are children under the age of 15 years (3). Although PEM affects virtually every organ system, this study primarily focuses on its cardiac manifestations. Malnourished children suffer several altercations in body composition that could produce cardiac abnormalities like hypotension, cardiac arrhythmias, myocardiopathy, cardiac failure & sudden death. Electrolytic changes have also been observed in children with PEM (4).

Previous study has shown that corrected QT interval (QTc) and QT dispersion (QTcd) were significantly greater in malnourished children. QTc & QTcd have shown increased values related with cardiac depolarization & repolarization alterations (5, 6).

This study was designed to compare the electrolyte changes and electrocardiographic parameters between a group of malnourished children and a control group of same age and to investigate which are the anthropometric or metabolic variables that may determine the cardiac findings. We have focused mainly on the mild to moderate grades of malnutrition.

## MATERIAL AND METHODS

The study was conducted in research laboratory of Department of Physiology in collaboration with Departments of Pediatrics and Pathology, Subharti Medical College and associated C.S.S. Hospital, Meerut. A total of 20 malnourished children in age group 2-11 yrs, selected on the basis of anthropometrical parameters including height, weight & mid arm circumference, comprised the study group, which consisted of the children of labourers, residing in temporary accommodations and working at construction sites in Subharti Campus. The control group consisted of age & sex matched, 20 healthy subjects, who were wards of the faculty members residing in the Subharti campus. Following approval from our Institutional Research and Ethical Clearance Committee, written informed consent was obtained from all guardians of the subjects, recruited for this study.

A thorough history and complete clinical examination was done of all the subjects.

### Inclusion criteria

The weight & height was marked on the CDC (Centre's for Disease Control) growth charts. The CDC growth charts represent the revised version of 1977 NCHS (National Centre for Health Statistics) weight for age, height for age & BMI for age charts (7).

In children below five years of age, malnutrition was defined by WHO Classification: A low height for age can be taken as one that is 1 Standard Deviation (SD) below the median height for age of the reference population. The same principle applies to the other indicator, weight for age.

In children above five years of age, malnutrition was defined by IAP Classification: A weight of more than 80% of expected for age is designated as normal. The grades of malnutrition are: Grade

I – 71 -80%, Grade II – 61-70%, Grade III – 51- 60% & Grade IV - <50% (8,9).

**Exclusion criteria**

Subjects with congenital anomalies, endocrinal disorders leading to short stature, liver disease, cardiac disease, central nervous system damage and patients receiving diuretics or drugs that prolong QT interval were excluded from the study (10).

**Anthropometric measurements**

Body weight (Kg) was measured using a weighing machine (Krups) while subjects wore light clothing and no shoes, height (cms) was measured using a stadiometer with sliding head board while the subject stood with his bare feet together on the fixed foot board. Body Mass Index was calculated using Quetelet's index. (BMI = Wt./$(Ht)^2$ in ($Kg/m^2$).

**Biochemical assay**

Estimations of serum proteins (albumin & globulin) were done using reflectance spectrophotometry method & serum electrolytes (sodium, potassium & calcium) were done using ions selective electrode method with the help of automatic analyzer (Johnson & Johnson Vitros 250).

**Brief procedure**

The subjects and their guardians were explained in brief about the experimental procedure. Experiments were done in a quiet room during which subjects lay supine, awake and breathing normally and following recordings were done.

**Electrocardiographic measurements**

Single lead (lead II) ECG was recorded at (25 mm/s & voltage at 10 mm/mV) for 330 seconds, using RMS Polyrite D software. Corrected QT interval (QTc) was obtained after the analysis of ECG (Polyrite D software). We considered that this parameter was increased if it was greater than 440 ms. QT dispersion (QTcd) was defined as the difference between maximum & the minimum corrected QT interval (11).

**Statistical analysis**

All values were expressed as Mean±SD. Differences between the study group and controls were examined using the unpaired Student's t- test. Chi-square test was used to evaluate differences in gender between the groups. Pearson's correlation coefficients were used to assess associations between continuous variables. Step wise multiple regression analyses were performed with cardiac findings as dependent variables and anthropometric and biochemical data as independent variables. A two tailed test ($P<0.05$) was considered statistically significant. The data were analyzed using the statistical package of Analytical Software SPSS (version 11.5).

## RESULTS

**General and biochemical parameters**

There was no significant difference in age, gender & levels of serum sodium between the two groups. However, body weight, height, BMI, serum levels of albumin & calcium were significantly lower ($P<0.01$)

in malnourished children than in the control group as shown in Table I.

The serum potassium levels were found to be on the lower side of the normal range in the malnourished group. But, as compared to the control group, the values were significantly lower (P< 0.001) as shown in Table I.

**ECG parameters**

Table II shows electrocardiographic measurements in both groups.

The ECG analysis showed that QTc interval and QTcd was significantly greater (P<0.01) in the malnourished group than in the controls.

**Correlation values**

Main correlations found between ECG and anthropometric or biochemical variables are shown in Table III. There is a strong negative correlation between BMI & $Ca^{2+}$ and QTc interval. To avoid casual associations, step wise multiple regression analyses were performed with these variables in the entire group of malnourished and healthy children (Table IV). Serum $Ca^{2+}$ & BMI together explained 41.5% of QTc variability. No significant contribution of weight, serum levels of albumin or potassium was found in the regression analysis for QTc. Serum $K^{+}$ & BMI together explained 27.7% of QTcd variability. No significant contribution of weight, serum levels of albumin or calcium was found in the regression analysis for QTcd.

TABLE I: General characteristics & biochemical parameters in malnourished & control groups (n=20 in each group).

| *Parameters* | *Malnourished group* | *Control group* | *P value* |
|---|---|---|---|
| Age (years) | 6±2.07 | 7.75±2.53 | 0.6895 |
| Gender (Male/Female) | 10M+10F | 11M+9F | 0.10## |
| Body weight (kg) | 15.47±4.45 | 30.60±9.70 | 0.0038* |
| Height (cm) | 107.65±14.27 | 129.5±14.49 | 0.0003** |
| BMI (Kg/m$^2$) | 13.19±1.85 | 17.73±2.33 | 0.0053* |
| Albumin (g/dL) | 3.3±0.376 | 4.17±0.219 | 0.0015* |
| Sodium (mEq/L) | 138.45±1.76 | 139.1±1.44 | 0.4891 |
| Potassium (mEq/L) | 3.87±0.19 | 4.33±0.28 | 0.0008** |
| Calcium (mg/dL) | 8.9±0.202 | 9.79±0.38 | 0.0018* |

Data presented are mean±SD; BMI: Body Mass Index. The analysis of data was done using unpaired student's t test; *P<0.01; **P<0.001; ##Chi-square test was used to evaluate differences in gender between the groups: $\chi^2 = 0.10$; P>0.01.

TABLE II: Electrocardiographic findings in malnourished and control groups (n=20 in each group).

| *Parameters* | *Malnourished* | *Control* | *P value** |
|---|---|---|---|
| QTc(s) | 0.455±0.021 | 0.419±0.020 | 0.0007** |
| QTcd(s) | 0.164±0.094 | 0.085±0.053 | 0.0091* |

Data presented are mean±SD; QTc: corrected QT interval in lead II; QTcd: corrected QT interval dispersion (max-min.) in lead II. The analysis of data was done using unpaired student's t test: *P<0.01; **P<0.001.

TABLE III: Main Pearson correlations between cardiac and anthropometric and biochemical data in malnourished and control groups.

| *Parameters* | *QTc* | *QTcd* |
|---|---|---|
| Weight | –0.545* | –0.304 |
| BMI | –0.566** | –0.409 |
| Height | –0.513* | –0.309 |
| Albumin | –0.541* | –0.253 |
| Potassium | –0.456* | –0.498* |
| Calcium | –0.606** | –0.289 |

QTc: corrected QT interval in lead II; QTcd; corrected QT interval dispersion (max-min.) in lead II; BMI: Body mass index (kg/m$^2$). The P value less than 0.05 was considered significant: **P<0.01; *P<0.05.

TABLE IV : Step wise multiple regression between dependent (QTc & QTcd) and independent (anthropometric and biochemistry) variables.

| *Dependent variable* | *Independent variable* | $R^2$ | *P* |
|---|---|---|---|
| QTc | | | |
| Step 1 | BMI | 0.320 | 0.000** |
| Step 2 | BMI | 0.320 | |
| | Calcium | 0.415 | 0.000** |
| Excluded: Weight, height, albumin and potassium | | | |
| QTcd | | | |
| Step 1 | BMI | 0.168 | 0.009* |
| Step 2 | BMI | 0.168 | |
| | Potassium | 0.277 | 0.002* |
| Excluded: Weight, height, albumin and calcium | | | |

QTc: corrected QT interval in lead II; QTcd: corrected QT interval dispersion (max-min.) in lead II; BMI: body mass index (Kg/m$^2$). P<0.05 was significant : ***P<0.001, *P<0.01.

## DISCUSSION

Malnutrition is a complex phenomenon caused by several etiologies that produce, on the whole, body composition alterations, with important losses of heart and skeletal muscle mass, complicated by electrolytic disorders and mineral or vitamin deficiencies (12). According to the IAP classification, out of the twenty children in the study group, seven (35%) had mild (Grade I), twelve (60%) had moderate (grade II) malnutrition and only one (5%) child had severe (Grade III) malnutrition. Previous studies have focused mainly on severe malnutrition.

The present study has revealed that malnourished children had significantly lower body weight, height, BMI, serum albumin, potassium and calcium levels as compared to the control group (Table I). However, serum potassium level was not much decreased and was found to be on the lower side of the normal range. This may be explained by the fact that nineteen out of twenty children in the study group did not have severe malnutrition, according to the IAP classification. Olivares et al have also observed that body weight, BMI, plasma levels of albumin, serum potassium & calcium were lower and QTc & QTcd were greater in the malnourished group (13). Fuenmayor, et al conducted a study for nutritional assessment & ECG changes in twenty malnourished Venezuelan children & twenty control children. Malnourished children had lower plasma protein & electrolyte concentration and greater QTd than the controls (14).

Cardiac repolarization process may change depending on the ventricular regions. These variations determine the QT interval variability, the difference between the maximum & minimum QT interval, defined as QT dispersion (QTd) when QT is measured in any of the ECG leads. QTd has emerged as a noninvasive measurement for quantifying the degree of myocardial inhomogeneity in ventricular repolarization (15, 16). QTd has been linked as a risk indicator for arrhythmic cardiac deaths in patient populations having coronary artery disease, myocardial infarction, sustained ventricular arrhythmia, ventricular fibrillation, unstable angina pectoris, long QT syndrome, chronic heart failure, peripheral vascular disease, drug arrhythmogenicity & hypertrophic cardiomyopathy (16).

Our results show that, in malnourished children, QTc and QTcd has increased values related with depolarization and repolarization alterations (Table II). Electrolytic changes and cardiac repolarization

alterations, consisting of QTc interval and QTd prolongation have been observed previously in children with kwashiorkor (17) and in adolescents with anorexia nervosa (18,19). The association of torsade de pointes, prolonged QT interval and sudden death with dieting or severe malnutrition is well known (20).

The reasons for a prolonged QTc and QTcd intervals in this study may be the electrolytic changes. It is a well documented fact that hypocalcaemia typically prolongs the QT interval (21). And because cardiac repolarization relies on potassium influx, hypokalemia lengthens the action potential and increases QT dispersion (22). In a study by coworker, oral potassium supplementation in patients of anorexia nervosa lead to a significant reduction in QT dispersion (18, 19).

Significant correlations were found between QTc and QTcd and both anthropometric and biochemical variables in this study (Table III). However, when step wise multiple regression analyses were performed to avoid casual associations and to find which are the main predictive variables of these ECG changes, the BMI and calcium were found to be the most powerful predictors of QTc, together accounting for 41.5% of the variability in QTc. The BMI and potassium together explained 27.7% of the variability in QTcd. The BMI alone explained 32% of the QTc variability and 16.8% of the QTcd variability (Table IV). BMI alone was found to be the strong predictor of QTc and QTcd (39.1% & 13.1% respectively) in a study by coworkers, Olivares et al. (13).

However, there are limitations in our study as single lead II ECG was recorded for measuring QTc and QTcd. In previous studies, 12 lead ECG have been recorded.

We have found important electrocardiographic abnormalities and electrolyte changes in association with the anthropometrical parameters in the malnourished children in this study. Further study should assess whether the ECG abnormalities still persist after electrolyte disturbance correction and appropriate nutrition therapy is given to these malnourished children. In the present study, the parents/guardians of the malnourished children were counseled and referred to the pediatrician for further evaluation and treatment.

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## REFERENCES

1. Park K. Nutrition and Health. In: Park's textbook of Preventive and Social Medicine. 20th ed. Park K (Editor). Banarsidas Bhanot Publishers: Jabalpur. 2009: 552.
2. Jelliffe DB. In WHO (ed) : The assessment of the nutritional status of the community. World Health Organization Monograph Sr. No. 53: 1966.

3. Gopalan C, Rao KJ. In WHO : Prevention in childhood of health problem in adult life. F Falkner (ed), Geneva, World Health Organization, 1980.

4. Sims BA. Conducting tissue of the heart in kwashiorkor. *Br Heart J* 1972; 34: 828–829.

5. Lund K, Perkiomaki J, Brohet C, et al. The prognostic accuracy of different QT interval measures. *Ann Noninvasive Electrocardiol* 2002; 17: 10–16.

6. Zabel M, Franz MR. The electrophysiological basis of QT dispersion: global or local repolarization? *Circulation* 2000; 101: 235–236.

7. National center for Health Statistics Growth Charts. In WHO (ed): Measuring changes in nutritional status, guidelines for assessing the impact of supplementary feeding for vulnerable groups. Geneva, World Health Organization. 1983.

8. Ghai OP, Gupta P, Paul VK. Growth and development. In: Essential pediatrics VI ed, Eds, Ghai OP, Gupta P, Paul VK. New Delhi: CBS publishers and distributors. 2004: 10–42.

9. Gupta P, Shah D. Nutrition and Macronutrient disorders. In: Essential pediatrics VI ed, Eds, Ghai OP, Gupta P, Paul VK. New Delhi: CBS publishers and distributors. 2004: 101–102.

10. Roder DM. Drug induced prolongation of the QT interval. *N Engl J Med* 2004; 350: 1013.

11. Hill JA, Freidman PL. Measurement of QT interval & QT dispersion. *Lancet* 1997; 349: 894–895.

12. Leung AK, Robson WM, Fagan JE. Assessment of the child with failure to thrive. *Am Fam Physician* 1993; 48: 1432–1438.

13. Vazquez M, Olivares JL, Fleta J, Rodriguez G, Samper P. Electrocardiography and echocardiography findings in malnourished children. *JACN* 2005; 24: 38–43.

14. Fuenmayor AJ, Mora RE, Fuenmayor AC, Fuenmayor AM. QT – Interval dispersion in malnourished children. *Clin Cardiol* 1998; 21: 201–205.

15. Heikki V. Huikuri. QT dispersion – What does it mean ? *Cardiovasc Drugs Ther* 2001; 15: 299–300.

16. Malik M, Velislav B. QT dispersion. In: Clinical Approaches to Tachyarrhythmia series, Eds, A. Jonn Camm, Futura publishing company, New York, 2000; 12: 3–13.

17. Olowonyo MT, Akinbami FO, Ogunkunle OO, Jaiyesimi F. The electrocardiographic changes in kwashiorkor. *Ann Trop Paediatr* 1993; 13: 293–298.

18. Vazquez M, Olivares JL, Fleta J, Lacambara I, Gonzalez M. Cardiac disorders in young women with anorexia nervosa. *Rev Esp Cardiol* 2003; 56: 669–673.

19. Seim HC, Mitchell JE, Pomeroy C. Electrocardiographic findings associated with very low calorie dieting. *Int J Obes Relat Metab Disord* 1995; 19: 817–819.

20. Day CP, McComb JM, Campbell R WF. QT dispersion: an indication of arrhythmia risk in patients with long QT intervals. *Br Heart J* 1990; 63: 342–344.

21. Goldberger LA. Electrocardiography. In: Harrison's Principles of Internal Medicine 16th ed. Editors, Kasper LD, Braunwald E, Fauci SA, Hauser LS, Longo LD, Jameson LJ. New York: Mc Graw Hill. 2005: 1319.

22. Macdonald JE, Struthers AD. What is the optimal serum potassium level in cardiovascular patients? *J Am Coll Cardio*l, 2004; 43: 155–161.