TISSUE DOPPLER ECHOCARDIOGRAPHY IN INFANTS WITH PNEUMONIA

By

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ABSTRACT

Background: *Pneumonia is a major public health and economic problem with a considerable impact on morbidity and mortality in children. The single largest and the most common infectious cause of death in children worldwide.*

Aim and objective:; *to assess left ventricular functions among infants with pneumonia using Tissue Doppler Echocardiography.*

Subjects and methods: *this cross sectional case control study was conducted at AL Hussein and Al-Sayed Galal Al-Azhar university hospitals from Jan 2022 to May 2022 on 50 cases. 16 were males and 14 were females. Patients' ages ranged from 2 months to less than 1 year admitted as respiratory distress diagnosed as pneumonia. The control group consisted of 20 matched healthy infants of the same gender and age. Routine 2D echo was done, pulsed Doppler and tissue Doppler imaging (TDI) was done at the level of mitral valve, Tricuspid annular plan systolic excursion (TAPSE) using Philips EPIQ 7C*

Result: *the most prevalent finding on our study is slight overall affection of ventricular functions (MPI) in cases compared to control, also Systolic dysfunction was detected in the cases by S wave affection (<10 cm/s), and decline of TAPSE as indicator of overall myocardial function of both right and left ventricles. Diastolic function is preserved and couldn't be detected by tissue Doppler in our study.*

Conclusion: *TAPES and MPI were a useful indicator of systolic and diastolic dysfunction as a part of cardiovascular complication of pneumonia in infants and could be detected by tissue Doppler imaging as new imaging technique of echocardiography. Systolic dysfunction can be detected in in cases by S wave affection (<10 cm/s), diastolic function is reserved with no tissue Doppler parameters of diastolic dysfunction. but elevation of MPI as indicator of overall function of left ventricle and decline of TAPSE as indicator of overall myocardial function of both right and left ventricles, both can be used as predictors of diastolic dysfunction that's can't be detected by parameters of tissue Doppler in our study.*

Keywords: *Tissue Doppler echo, left ventricular functions, pneumonia, pediatrics.*

INTRODUCTION

Pneumonia, defined as inflammation of the lung parenchyma, is the leading cause of death globally among children younger than age 5 yr., accounting for an estimated 1.2 million (18% total) deaths annually. The incidence of pneumonia is more than 10-fold higher and the number of childhood-related deaths from pneumonia ≈2,000 fold higher, in developing than in developed countries **(Matthew et al., 2020)**.

The respiratory and cardiovascular systems cannot be thought of independently. Several previous series demonstrated myocardial involvement with pneumonia. Some may attribute this to the state of septicemia that may cause septic or toxic myocarditis while others may relate this dysfunction to the presence of post-infectious antibody mediated sequel **(Tralhão & Póvoa 2020)**.

Echocardiography has become the most important non-invasive technique for the diagnosis and follow-up of heart disease in children **(Nimdet and Techakehakij, 2020)**.

Tissue Doppler (TDI) measurements are considered as a practical echocardiographic tool in Pediatrics as it is non-invasive, hardly time-consuming, relatively available, and software-independent compared to other measurements **(Doyon A, et al., 2019)**.

Tissue Doppler imaging is a technique which has been recently used in the assessment of myocardial dysfunctions, and results can be retrieved immediately during examination. Moreover, TDI can assess both systolic and diastolic myocardial motions which render it a sensitive indicator of any myocardial subtle dysfunction **(Tissot C, et al., 2017)**.

The European Society of Cardiology and the American Society of Echocardiography recommend the use of tissue Doppler imaging for the evaluation of both diastolic and systolic functions **(McMurray JJ, et al., 2012)**.

The aim of this study: was to assess left ventricular functions among infants with pneumonia using Tissue Doppler Echocardiography.

PATIENTS AND METHODS

This case-control cross sectional study was conducted at AL Hussein and Al-Sayed Galal Al-Azhar university hospitals from Jan 2022 to May 2022 on 30 cases 16 were males and 14 were females and 20 matched healthy

infants of the same gender and age. Patients' ages ranged from 2 months to less than 1 year.

Inclusion criteria: Age: from 2 months up to 1 year, symptoms suggestive of pneumonia. e.g.; Fever, cough, dyspnea, signs of respiratory distress, diminished air entry, crackles, irritability, and decreased feeding, with CXR and laboratory confirmation.

Exclusion criteria: children < 2 months or > 1 years, children with chronic diseases e.g.: hepatic, renal diseases or congenital heart diseases and Children suspected to have COVID-19 infection according to Egyptian protocol for management of COVID-19 in pediatrics.

Tools of Assessment: The including children subjected to the following:

A. History:

- Personal history: name, age, sex, residence, socioeconomic status, parent education, contact with animal or source of pollution.
- Past history of recurrent chest infection or hospital admission.
- Family history, vaccination history, developmental and dietetic history.

B. Examination:

- The vital signs including blood pressure, heart rate, respiratory rate, SpO_2 and body temperature were recorded.
- Anthropometric measurements (height & weight).
- General examination: Head & neck, abdomen, back, UL and LL.
- Local examination: Chest and cardiac examination; by inspection, percussion, auscultation of both heart and chest.

C. Investigations:

- Complete blood count by Sysmex x5-800 (Sysmex Corporation, Japan).
- Radiological imaging: Chest x ray to all patients while CT chest was done only when indicated.
- Quantitative assessment of Creactive protein (CRP) by latex agglutination test (TURBOX plus Orion Diagnostica, Finland).

Echocardiography:

Echo-Doppler examination was performed for all cases in a supine or left lateral position using Philips EPIQ 7C (multifrequency transducer 4-8 MHz) according to

the age of patient, having tissue velocity imaging capabilities.

A. Conventional Echo Doppler measures:

The examination was performed by pediatric cardiologists who are experts in echocardiography. The examination was consisted of M mode, 2-D, pulsed, continuous wave and color Doppler blood flow velocity measurements of the heart valves.

For M-mode the following:

Measurements we M-mode measurements were done at the level of the tips of the mitral valve leaflets in the parasternal long-axis view of the left ventricle. Left ventricular dimensions (LVEDD and LVESD), left ventricular fractional shortening (FS) and ejection fraction (EF) were measured. Left atrial (LA) dimension was also measured using parasternal long axis view at the level of the aorta and left atrium. Tricuspid annular plan systolic excursion (TAPSE) at tricuspid annulus, as well as mitral annular plan systolic excursion (MAPSE) at lateral mitral annulus in apical 4 chamber view.

Conventional Doppler measurements:

Doppler velocities were measured for the mitral valve using apical four-chamber view; for the aortic valve using the apical 5 chamber view. The following Doppler parameters were measured: Mitral peak S, E and A wave velocities.

Tissue Doppler imaging (TDI):

Pulsed wave Tissue Doppler imaging (PW-TDI) was done, the following parameters were measured: Systolic (S′) and diastolic (E′, A′, E′/A′ ratio) myocardial velocities at the basal segments of the LV septal wall.

(Tei index) was calculated and is defined as the sum of isovolumic contraction time (IVCT) and isovolumic relaxation time (IVRT) divided by ventricular ejection time (ET). Toper form that continuous wave cursor line was placed midway between anterior mitral leaflet and left ventricular outflow tract.

Ethical considerations:

1. A written informed consent was obtained from parents or the legal guardians before the study.
2. An approval by the local ethical committee was obtained before the study.
3. The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

4. All the data of the patients and results of the study are confidential & the patients have the right to keep it.
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Statistical Analysis: Data were analyzed using MedCalc© version 18.2.1 (MedCalc© Software ltd, Ostend, Belgium).

Continuous numerical variables were presented as mean ± SD and inter-group differences were compared using the unpaired t test for two-group comparisons or one-way analysis of variance (ANOVA) for multiple-group comparisons.

Categorical variables were presented as ratio or number and percentage and differences were compared using Fisher's exact test.

Correlations were tested using the Pearson product-moment correlation.

Table (1): Interpretation of correlation coefficient

Correlation coefficient	Strength of correlation
<0.2	Very weak
0.2 – 0.39	Weak
0.4 – 0.59	Moderate
0.6 – 0.79	Strong
0.8 – 1.0	Very strong

P-values <0.05 were considered statistically significant.

RESULTS

Table (2): Demographic Characteristics of studied Cases and Controls

Variables	**Acute pneumonia cases (n=30)**	**Control (n=20)**	p-value*
Age (months)	5.50 ± 3.72	6.93 ± 3.67	0.250
Gender (M/F)	16/14	14/6	0.239
***BSA (m^2)**	0.33 ± 0.05	0.35 ± 0.05	0.430
Weight (Kg)	6.35 ± 1.59	7.05 ± 2.14	0.313
Height (cm)	62.23 ± 4.69	62.30 ± 1.78	0.069

*Unpaired t-test unless otherwise indicated. #Fisher's exact test.
*BSA= Body Surface Area

BSA = $\sqrt{(Height(cm) \times weight(kg))/3600}$

This table shows insignificant difference between cases and controls as regard demographic data.

Table (3): Clinical and Laboratory Characteristics of Patient Group (n=30)

Variable	**Acute pneumonia cases (n=30)**
PRESS score	
Mild	8 (26.6 %)
Moderate	16 (53.3 %)
Severe	6 (20 %)
Vital data	
Heart rate (beats/min.)	149.08 ± 10.77
Respiratory rate	66.31 ± 5.47
O2 saturation (%)	91.92 ± 4.73
Temperature (^oC)	38.40 ± 0.94
Laboratory	
WBCs	15.68 ± 5.88
Hemoglobin	9.98 ± 0.81
Platelets count	526.38 ± 177.96
CRP	24.46 ± 17.05

*Unpaired t-test unless otherwise indicated.
*PRESS score: pediatric respiratory severity score

This table shows: That the majority of cases had moderate respiratory distress (53.3 % had moderate PRESS score). It also shows that there's mild hypoxemia (SPO2 level = 91.92 ± 4.73) & There's also marked leukocytosis (15.68 ± 5.88) and elevated CRP level (24.46 ± 17.05).

Table (4): Outcome and Survival of Patient Group N=30

OUTCOME	
Cured (%)	24 (80 %)
Complicated (%)	4 (13.3 %)
Died (%)	2 (6.7 %)
OVERALL SURVIVAL	
Discharged (%)	28 (93.3 %)
Died (%)	2 (6.7 %)

This table shows that only 2 case died out of 30 and 4 cases were complicated with all survival rate = 93.3%.

Table (5): Comparison of echocardiographic parameters in cases and controls

Variables	**Acute pneumonia cases (n=30)**		**Control (n=20)**		p-value*
	Mean	SD	Mean	SD	
LA/AO	1.20	0.09	1.70	0.06	0.164
LVEDD (mm)	22.16	1.34	21.66	2.22	0.592
LVESD(cm)	1.30	0.22	1.23	0.07	0.195
EF%	70.06	3.93	68.88	2.96	0.233
FS%	40.75	3.38	39.81	1.23	0.172
MAPSE (cm)	0.77	0.14	0.69	0.23	0.174
TAPSE (cm)	1.45	0.13	1.69	0.22	**<0.001**
E (cm/s)	79.60	22.17	96.35	10.09	**0.022**
A (cm/s)	88.32	32.77	70.31	3.45	0.072
E/A ratio	1.02	0.57	1.37	0.16	**0.044**
IVCT	38.00	6.40	47.65	3.80	**<0.001**
IVRT	47.54	3.69	42.40	3.12	**<0.001**
MPI	0.54	0.13	0.46	0.03	**0.042**
S (cm/s)	6.59	.62	8.06	0.56	**<0.001**
E' (cm/s)	8.78	2.27	10.06	0.91	0.074
E/e	9.38	3.01	9.62	1.03	0.788
A' (cm/s)	8.08	2.12	8.09	1.19	0.994
ET	164.62	34.69	195.55	7.43	**0.008**

Unpaired t-test.

LVEDD = left ventricle end diastolic diameter, LVESD= left ventricle end diastolic diameter, EF= ejection fraction, FS= fraction shortening. E= Peak early mitral inflow velocity, E'= peak mitral annular velocity during early diastole; normal septal ≥8cm/s, while normal E/e'<8 (septal), A'= peak annular velocity during late diastole, TAPSE= Tricuspid annular plan systolic excursion, MAPSE= mitral annular plan systolic excursion, IVRT= isovolumetric relaxation time, IVCT = isovolumetric contraction time, and ET = the ejection time of LV.

Table 5: shows that TAPSE parameter by Conventional Echo, Conventional Doppler and tissue Doppler derived parameters namely E/A' ratio, S and Tei index (MPI) of left ventricle among other echocardiographic parameters were able to differentiate cases from controls.

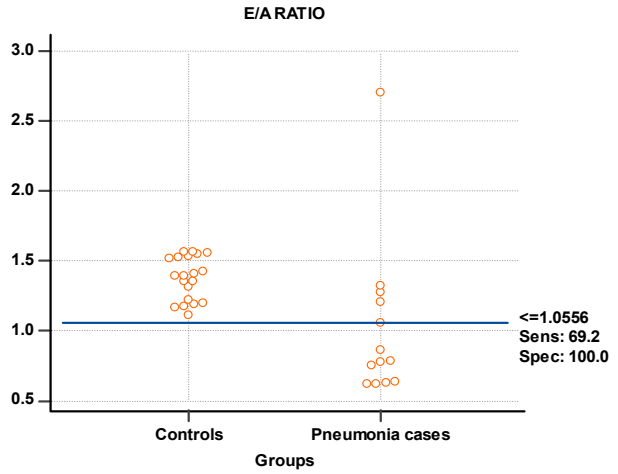

Figure (1): Interactive dot diagram showing E/A in cases and controls

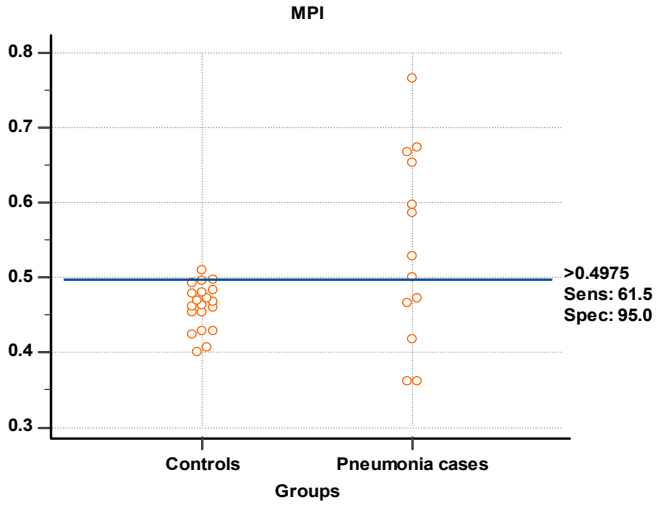

Figure (2): Interactive dot diagram showing MPI in cases and controls

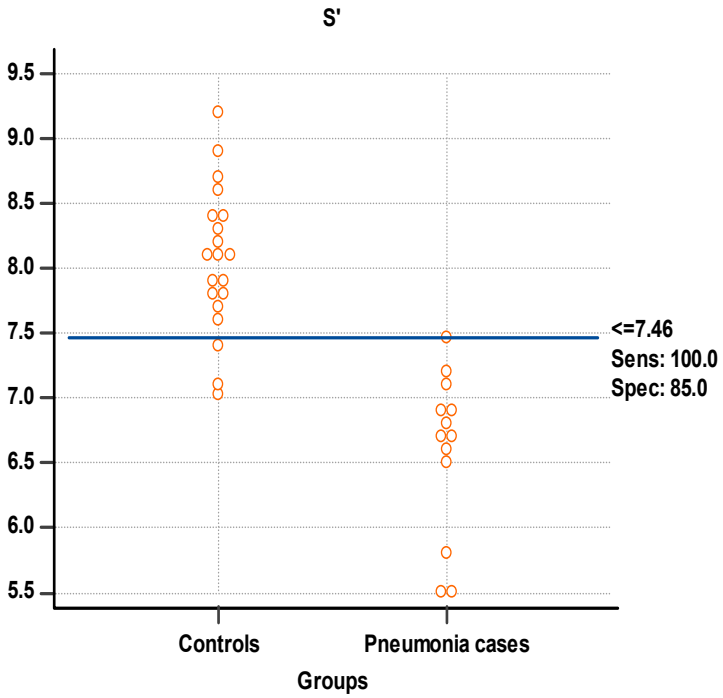

Figure (1): Interactive dot diagram showing S' in cases and controls

FIGURES 1, 2, 3 showed that E/A, S and MPI can differentiate cases from control.

Table (6): Relation between doppler or echocardiographic measures and outcome of pneumonia

Variable	Discharged		Died		Difference	95% CI		p-value*
	Mean	SD	Mean	SD		Lower limit	Upper limit	
LA/AO	1.20	.09	1.23	.03	-.03-	-.18-	.12	0.369
LVED	2.21	.14	2.25	.07	-.03-	-.11-	.05	0.713
LVES	1.30	.23	1.19	.01	-.04-	-.27-	.19	0.529
EF	75.15	4.09	72.80	1.70	-.04-	-.26-	.18	0.450
FS	43.06	4.42	38.70	.42	.11	-.26-	.47	0.202
MAPSE	.77	.14	.73	.07	.11	-.04-	.25	0.682
TAPSE	1.46	.23	1.40	.14	2.35	-4.21-	8.91	0.727
E	82.48	20.46	69.65	34.86	2.35	-2.56-	7.26	0.460
A	89.76	33.79	112.00	57.98	4.36	-2.68-	11.40	0.440
E/A ratio	1.05	.58	.63	.01	4.36	1.50	7.22	0.340
IVCT	38.42	6.50	32.50	.71	.04	-.18-	.27	0.237
IVRT	47.42	3.82	48.50	.71	.04	-.18-	.26	0.706
MPI	.55	.13	.42	.08	.06	-.31-	.44	0.200
S'	6.55	.63	6.30	1.13	.06	-.44-	.56	0.646
E'	8.86	2.35	7.35	.64	12.83	-23.81-	49.48	0.397
E/E'	9.68	2.93	9.72	5.58	12.83	-239.15-	264.82	0.990
A'	8.07	2.23	6.50	2.40	-22.24-	-82.86-	38.37	0.382
ET	163.83	36.11	198.00	33.94	-22.24-	-442.50-	398.02	0.237

*Unpaired t test.

This table shows: Pulsed & tissue Doppler imaging and relevant echocardiographic parameters are not predictive of the outcome of Pneumonia.

DISCUSSION

Identifying patients with asymptomatic cardiac dysfunction may allow the implementation of non-pharmacological or pharmacological interventions aiming at reversing heart functional and structural abnormalities.

In this aspect we assessed our patients' systolic function using M-Mode echocardiography. LA/AO, EF and FS showed no significant difference in pneumonia cases compared to control.

Several reasons may explain such finding, but the most important of which is the lack of Sensitivity and specificity of M-mode derived parameters; for the following reasons:

- Do not represent global LV shortening in the presence of

regional wall motion abnormalities (RWMA).

- Overestimation of overall LV function is possible if conclusions are made based on contractility of basal segments alone because basal segments contract adequately even in a significant LV systolic dysfunction **(Chengode, 2016)**.

Tissue Doppler imaging allows evaluation of myocardial velocities. Peak systolic annular velocity (S′ wave) measured at the level of the mitral annulus reflects left ventricular contractility. S′ value is considered as a reliable qualitative measure of global left ventricular systolic function, and the normal value in adults is ≥10 cm/s.

According to **(A. Thorstensen et al., 2011)** Peak systolic velocity indices were more sensitive in detecting contraction changes, and therefore, it may be suggested that peak systolic velocity indices are more sensitive to detect changes of cardiac function also in clinical practice.

In our study we detect that Peak systolic velocity (S′wave) showed significant decrease in pneumonia cases compared to controls ($p<0.001$) which is indicator of systolic dysfunction caused by pneumonia, our finding is correlated with **(Gitonga et al., 2022)** who report left ventricular dysfunction occurred in children with severe pneumonia.

Also an important finding in our assessment of left ventricular function using Tissue Doppler echocardiography was a higher Myocardial Performance Index (MPI) that showed significant increase in pneumonia cases compared to control but results are within normal ranges in children.

Diastolic Function was measured in our patients using combined Doppler derived and Tissue Doppler derived septal E/e' ratio.

In our study measures of pulse Doppler: E and E/A ratio showed significant decrease in pneumonia cases compared to control ($p=0.022$ & 0.044 respectively), this denote Impairment of myocardial relaxation leads to a reliance on filling during late diastole according to **(Holley., 2013)**.

In our series, Septal E/e' parameter showed no statistically significant difference between cases and controls.

These finding describe overall affection of myocardial function of right and left ventricles detected by decreased measurement of TAPSE in cases compared to

control and normal range in pediatric group.

The previous finding describe systolic function affection of pneumonic cases compared to control , also detect diastolic dysfunction in pneumonia in comparison to cases by pulsed wave conventional echo which goes in agreement with Kalra et al series which proved that diastolic dysfunction in the context of pneumonia precedes systolic impairment **(Kalra et al., 2013)**.

Tissue Doppler parameters of diastolic assessment in our study are within normal range according to age group.

CONCLUSION

The current study points towards the ability of tissue Doppler imaging to act as a screening parameter for pneumonia cases with myocardial functions of left ventricle. Left ventricular affection as a part of cardiovascular complication of pneumonia in infants could be detected by tissue Doppler imaging: systolic dysfunction can be detected in in cases by S wave affection (<10 cm/s), diastolic function is reserved with no tissue Doppler parameters of diastolic dysfunction. but elevation of MPI as indicator of overall function of left ventricle and decline of TAPSE as indicator of overall myocardial function of both right and left ventricles, both can be used as predictors of diastolic dysfunction that's can't be detected by parameters of tissue Doppler in our study.

RECOMMENDATIONS

1. The use of Routine Tissue Doppler is useful in early detection of myocardial changes in pneumonia in infancy.
2. Regular assessment and follow up of Oxygen saturation by pulse oxyemeter is an important test in pneumonia in infancy.
3. Diagnosis and management of cardiovascular complications in these patients may improve overall outcome of pneumonia in infancy.
4. Further studies are needed to elucidate the spectrum of cardiovascular changes and their clinical and therapeutic implications in cases with pneumonia.

LIMITATION

This was a single-center, case control study with enough sample size. However, we are aware that heart disease is a complication of chest disease and our study has some limitations. One of the limitations of the study was the acquisition of tissue Doppler

echocardiographic images, especially in children < 1 years old. In addition, imaging was performed by pediatric cardiology specialists under strict infection-control regulations. Another controversial issue is the impact of high heart rate in infant with pneumonia groups on the accuracy of the diastolic parameter assessment. But further studies are needed to evaluate the long-term cardiac involvement of these patients.

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