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Research Article

Assessment of Ventricular Function in Infants with Bronchiolitis

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Abstract

Background: Respiratory syncytial virus (RSV) can produce extra-pulmonary affection as well as its pulmonary effects. Cardiovascular involvement was considered the most common extrapulmonary affection of RSV infection.

Aim of the Study: Detection of cardiac affection in infants with acute bronchiolitis.

Methods: The study included 100 infants at Qena University Hospital, South Valley University. All of the infants were diagnosed as acute bronchiolitis, and were classified according to disease severity to mild (group I), moderate (group II) and severe (group III) bronchiolitis according to NSW Ministry of Health 2012). Full examination and laboratory investigations (ECG, CXR, cardiac troponin I and echocardiography with pulse wave Doppler echocardiographic assessments and calculation of the right ventricular function (Tei index), left ventricular fractional shortening and left ventricular diameters, tricuspid regurg velocity and pulmonary artery systolic pressure.

Results: The age of the studied cases ranged from 1.0-24.0 months, 58% had severe bronchiolitis, where (48%) had elevated pulmonary artery systolic pressure PASP for group I, group II, group III was (31.29 ± 7.43, 34.97 ± 3.65 and 35.58 ± 10.66 respectively), while (84.5%) of this group had elevated right ventricular Tei index values for group I, group II, group III was (0.26 ± 0.06, 0.29 ± 0.10 and 0.44 ± 0.14 respectively). Significant negative correlations were detected among patients of group III between (Tei index and pulse oxymetery) and between Tei index and pulmonary artery systolic pressure (PASP) ($P < 0.001$ and $P < 0.05$ respectively).

Conclusion: Elevated pulmonary artery systolic pressure was the most common cardiac affection among patients with acute bronchiolitis regardless the severity of the disease. Subclinical right ventricular dysfunction (indicated by elevated right ventricular Tei index) was common among patients with severe bronchiolitis. Left ventricular systolic and diastolic dimensions as well as left ventricular fractional shortening were not significantly affected in infants with bronchiolitis.

Keywords: *Bronchiolitis; Myocarditis; Tei index; ECG; Pulmonary Hypertension*

Abbreviations: BP: blood pressure, CBCD: Complete blood count with differential, CRP: C reactive protein, CXR: chest X ray, F.H: family history, NSW: New South Wales, PASP pulmonary artery systolic pressure, RSV: Respiratory syncytial virus, RV: right ventricle

Introduction

Bronchiolitis is considered the commonest lower respiratory tract disease in infants and it causes high morbidity during the first 2 years of life [1]. It is the first attack of wheezy chest in young children, in whom examination suggests viral cause of the respiratory infection, and also symptoms cannot be attributed to other cause [2]. Respiratory syncytial virus (RSV) is the commonest viral etiology of lower

respiratory infections during infancy and early childhood all over the world, also it has a high morbidity all over the world [3], rhino virus is the second common cause of bronchiolitis in infants [4]. Bronchiolitis is diagnosed clinically by appearance of coryza, poor feeding, cough, difficulty of breathing, wheeze and crepitations on auscultation [5].

Myocarditis was one of the manifestations of RSV infection, reported for the first time by Puchkov in 1972 [6]. Cardiac effects related to RSV infections extended from arrhythmias to myocardial failure [7-10]. Elevated level of cardiac enzymes (troponin I or T) when used as a predictors for myocardial damage, were detected among these patients where the damage may present with hypotension which need drugs to augment the myocardial contractility [9].

Patients and Methods

The present study is a prospective observational study included one hundred infants with acute bronchiolitis, admitted (68 admitted cases where all cases of group III and 10 cases of group II) to the Department of Pediatrics. And 32 attending to the Department of Pediatrics-Qena University Hospital-South Valley University, during winter season of 2014.

Strategy of the work

A total of 100 infant (68 males and 32 females) aged from 1month to 2 years old (84 infant aged 1-12 months and 16 infant aged 13-24months) were included in the study and were divided into the following three groups according to severity (NSW Ministry of Health 2012).

Group I (Mild bronchiolitis): Included 12 infant (8 males and 4 females) where they were examined at outpatient clinic found to have symptoms of mild bronchiolitis e.g. good general condition, mild tachypnea, normal heart rate, no cyanosis, no respiratory distress, oxygen saturation above 95% in room air with normal or mildly decreased oral intake.

Group II (Moderate bronchiolitis): Included 30 infant (20 males and 10 females) with more severe symptoms e.g. mild to moderate respiratory distress, oxygen saturation 90 - 95%, mild tachycardia, difficulty feeding but able to take more than 50% of normal feed and no cyanosis.

Group III (Severe bronchiolitis): Included 58 infant (40 males and 18 females) who have the most severe symptoms; including hypoxia with oxygen saturation < 90%, cyanosis, apnea or poor feeding. Mild and moderate bronchiolitis was used as a control group for comparison with severe bronchiolitis.

Inclusion Criteria

Previously healthy infants with no significant previous medical history, aged 1 - 24 months (16 patient older than 12 months, 10 belongs to group III and 6 belongs to group II) with acute bronchiolitis who were attending or admitted to the Department of Pediatrics, Qena University Hospital during the study period.

Exclusion Criteria

Presence of a chronic disease that increasing the risk of complications of respiratory infection, kidney or liver dysfunction, hemoglobinopathies, immunosuppression, genetic or neurological disorders or chronic pulmonary disorders, infant with diagnosed congenital heart disease or cardiomyopathy were excluded from the study population and also all newly discovered cases with congenital heart disease or cardiomyopathy during echocardiographic examination of infants with bronchiolitis were excluded, cases with is no detectable tricuspid regurgitation are excluded from the study.

All patients subjected to following

Meticulous Clinical History and Clinical Examination

Assessing severity of the disease: In particular, on the basis of previously published criteria of NSW Ministry of Health in 2012 [11], acute bronchiolitis was considered severe in the presence of all of the following:

1- O_2 saturation assessed by pulse oximetry ≤ 90%. 2- Respiratory rate of ≥ 70 breaths/min. 3-Marked accessory muscle use. 4- Nasal flare or grunting. 5- Heart rate of > 180 beats/min. 6- An inability to feed and a toxic appearance.

Methods

Blood samples: Complete blood count with differential (CBCD): Was measured by Sysmax KX-21, Sysmex, Japan.

CRP: It is done as one of the sepsis screen tests for excluding bacterial cause of chest infection. Negative results defined less than 6 mg/dl. By CRP ELIZA kit (human).

Serum cardiac (Troponin I): It was considered abnormal if the level was > 10 ng/L. All sera samples of the studied cases were tested for: detection of serum (Troponin I) by EIA Test kits as evidence of myocardial damage (myocarditis).

Imaging study

Electrocardiography (ECG): monitoring was routinely performed to detect arrhythmias (NIHON KOHDEN cardiofax C 3 channel).

Chest X ray (CXR): All patients with bronchiolitis underwent CXR searching for hyperinflation, peripheral atelectasis or any associated abnormalities. By Logic S6 General Electronics Health Care.

Echocardiography: By using phased array spectrum probe 6 MHz, Vivid S5 General Electronics Health Care. Using 2D, M mode, pulsed wave Doppler for measuring PVET and continuous wave Doppler for assessment of tricuspid regurge velocity, and color flow mapping for exclusion of shunt lesions and any flow abnormalities. Echocardiography was performed within 48 hours of admission for admitted cases (n = 68) all cases of group III and 10 patients of group II). All measurements were compared to echocardiographic measurements reported by Myung in 2008 [12]. The right ventricular Tei index was calculated as shown in (Figure 1, 2). An elevated Tei index indicating reduced right ventricular function was defined as an index of more than two standard deviations (SD) above the mean for children (non-age or sex dependant) of 0.24 (SD ± 0.04). Electrocardiography (ECG) monitoring was routinely performed throughout the admission.

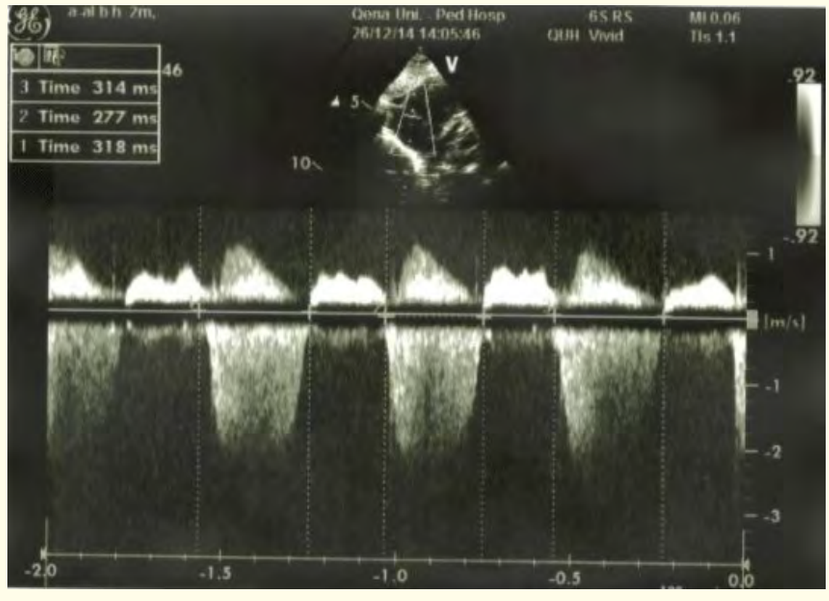

Figure 1.

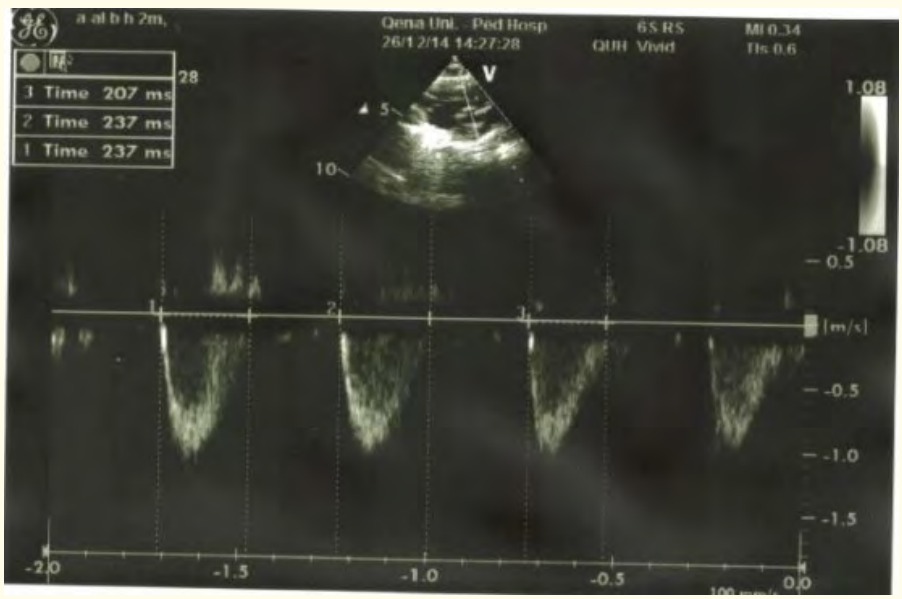

Figure 2.

Pulmonary artery systolic pressure (PASP) is measured from four chamber apical view from Tricuspid regurgitation velocity (TR) more than 2.9 m/s and considering right atrial pressure of 5 mmHg so PA systolic pressure more than 36 mmHg is considered pulmonary systolic hypertension.

Ethical Approval

The study was done after obtaining a written consent from the parents and under the approval of Ethics Committee of Qena University Hospital.

Statistical Analysis

The study data were statistically analyzed using the Statistical Package for Social version program (SPSS program-version 17.0 – SPSS Inc., Chicago, IL. USA). The difference between cases and control as regards quantitative variables was done using ANOVA, F test and Kruskal Wallis. For testing association between categorized variables chi square and Monte Carlo were used. Pearson's correlation test was done to study possible correlation between quantitative variables.

Results

Table 1 showing the percentage frequencies of demographic data of the studied cases according to the severity of bronchiolitis. It showed that age < 6 months was the only demographic factor that was associated with significantly higher percentage frequency of severe bronchiolitis among all cases.

N		Group I		Group II		Group III		Chi-square	
		%	N	%	N	%	X^2	P-value	
Age	< 6 month (N = 67)	5	41.7	7	23.3	55	94.8	49.669	< 0.05*
	6 months-2years (N = 33)	7	58.3	23	76.7	3	5.2		
Sex	Female (N = 32)	4	33.3	10	33.3	18	41.4	0.059	NS
	Male (N = 68)	8	66.7	20	66.7	40	58.6		
Residence	Rural	6	50.0	17	56.7	23	39.7	2.391	NS
	Urban	6	50.0	13	43.3	35	60.3		

Table 1: *The percentage frequencies of demographic data of the studied cases according to severity of bronchiolitis.*

*NS: Non-significant; * Significant P < 0.05; ** highly significant P < 0.001*

Table 2 showing the percentage frequencies of clinical signs among the studied cases: it showed that only two infants among the studied cases had clinical signs of heart failure and the two belonged to the group with severe bronchiolitis.

Vital signs			
Temperature (degree centigrade)	Range	37.5 - 40	
	mean ± SD	38.5 ± 0.5	
Heart rate (beat/ min)	Range	120-200	
	mean ± SD	146.6 ± 16.3	
Systolic BP (mmHg)	Range	60 - 95	
	mean ± SD	82.3 ± 5.8	
Diastolic BP (mmHg)	Range	40-65	
	mean ± SD	53.6 ± 5.3	
Respiratory rate (breath/min)	Range	40 - 90	
	mean ± SD	58.98 ± 10.1	
Chest examination			
Signs of respiratory distress	N	%	
Tachypnea	73	73.0	
Subcostal retraction	60	60.0	
Intercostal retraction	58	58.0	
Suprasternal retraction	58	58.0	
Grunting	49	49.0	
Cyanosis	12	12.0	
Air entry	Normal	N	%
		41	41.0
	decreased	59	59.0
Breath sound	Harsh vesicular	98	98.0
	Bronchial	2	2.0
Fine crepitation		94	94.0
Coarse crepitation.		85	85.0
Prolonged expiration		100	100
Expiratory Wheeze		100	100
Heart examination	Cardiomegaly	2	2.0
	Heart failure	2	2.0

Table 2: *The percentage frequencies of clinical signs among the studied cases.*

Table 3 Showing the percentage frequencies of various laboratory and imaging parameters among the studied cases in relation to the severity of bronchiolitis. Increased level of cardiac troponin (I) above the cutoff value was found in only 4 patients all belonged to group III (signifying myocardial damage). Frequencies of chest X ray abnormalities and Tei index were statistically significantly higher in group III in comparison to the other two groups (P < 0.001).

Laboratory investigations		Group I	Group II	Group III	Chi-square	
				X^2	P-value	
Cardiac treponin (I) (cut off value more than 10ng/L)		0 (0%)	0 (0%)	4 (6.9%)	3.017	NS
Imaging. Investigations						
CXR	Consolidation/atelectasis	0 (0%)	0 (0%)	29 (50%)	54.398	< 0.001**
	normal	12 (100%)	8 (26.7%)	1 (1.7%)		
	Hyperinflation	0 (0%)	22 (73.3%)	28 (48.3%)		
ECG abnormalities		0 (0.0%)	0 (0.0%)	5 (8.6%)	3.811	NS
Echocardiographic parameters					(ANOVA test)	
LVESd (millimeter)		15.3 ± 2.5	14.8 ± 2.7	14.4 ± 2.6	0.763	NS
LVEDd (millimeter)		25.2 ± 4.0	23.9 ± 3.5	23.6 ± 3.9	0.893	
LV FS (%)		38.5 ± 4.4	38.5 ± 5.2	36.8 ± 9.9	0.511	
LA diameter (millimeter)		16.8 ± 3.8	17.1 ± 3.0	15.8 ± 3.0	2.022	
Tei index		0.26 ± 0.06	0.29 ± 0.10	0.44 ± 0.14	19.917	< 0.001**
PASP (mmHg)		31.29 ± 7.43	34.97 ± 3.65	35.58 ± 10.66	2.273	NS
TR VELOCITY		3.0 ± 0.2	2.8 ± 0.5	2.6 ± 0.4	2.633	
TVCT (a)		256.3 ± 39.9	264.6 ± 38.3	284.1 ± 36.3	4.391	
PVET (b)		200.4 ± 30.3	203.9 ± 29.0	200.8 ± 32.0	0.115	

Table 3: *The percentage frequencies of various laboratory and imaging parameters among the studied cases in relation to the severity of bronchiolitis.*

LVEDd: Left Ventricular End Diastolic Diameter; LVESd: Left Ventricular End Systolic Diameter; LV FS: Left Ventricular Fractional Shortening; LA diameter: Left Atrial Diameter; PASP: Pulmonary Artery Systolic Pressure; PVET: Pulmonary Valve Ejection Time; TVCT: Tricuspid Valve Closure Time; TR velocity: Tricuspid Valve Regurge Velocity; m sec.: Millisecond; NS: Non-Significant

** significant P- value < 0.05*

*** highly significant P- value < 0.00*

Table 4 Showing percentage frequencies of pulmonary artery systolic pressure in the studied patients according to severity of bronchiolitis. It shows no significant statistical difference in pulmonary artery systolic pressure value among different groups of bronchiolitis.

PASP		Groups					
		Group I		Group II		Group III	
		N	%	N	%	N	%
≤ 36 (mmHg)		2	16.7	11	36.7	30	51.7
> 36 (mmHg)		10	83.3	19	63.3	28	48.3
Total		12	100.0	30	100.0	58	100.0
Chi-square	X^2	5.687					
	P-value	NS					

Table 4: *The percentage frequencies of pulmonary artery systolic pressure in the studied patients according to severity of bronchiolitis.*

PASP: Pulmonary artery systolic pressure

NS: Non-significant.

**significant P- value < 0.05*

*** highly significant P- value < 0.001*

Table 5 Showing percentage frequencies of Tei index values in the studied patients according to severity of bronchiolitis. Patients with severe bronchiolitis i.e. group III showed significantly higher percentage frequencies of those whose Tei index was > 0.32 (P < 0.001) in comparison to infants belonging to the other two groups.

Tei Index		Groups					
	Group I		Group II		Group III		
	N	%	N	%	N	%	
≤ 0.32		12	100.0	21	70.0	9	15.5
> 0.32		0	0.0	9	30.0	49	84.5
Total		12	100.0	30	100.0	58	100.0
Chi-square	X^2	42.925					
	P-value	< 0.001**					

Table 5: *The percentage frequencies of Tei index values in the studied patients according to severity of bronchiolitis.*

NS: Non-significant.

**significant P- value < 0.05*

*** highly significant P- value < 0.001*

Figure 3 Showing correlation coefficient between pulse oxymeter and Tei index for cases with severe bronchiolitis. Using correlation coefficient test (r-test), there was significant negative correlation between pulse oxymeter and Tei index (P < 0.05).

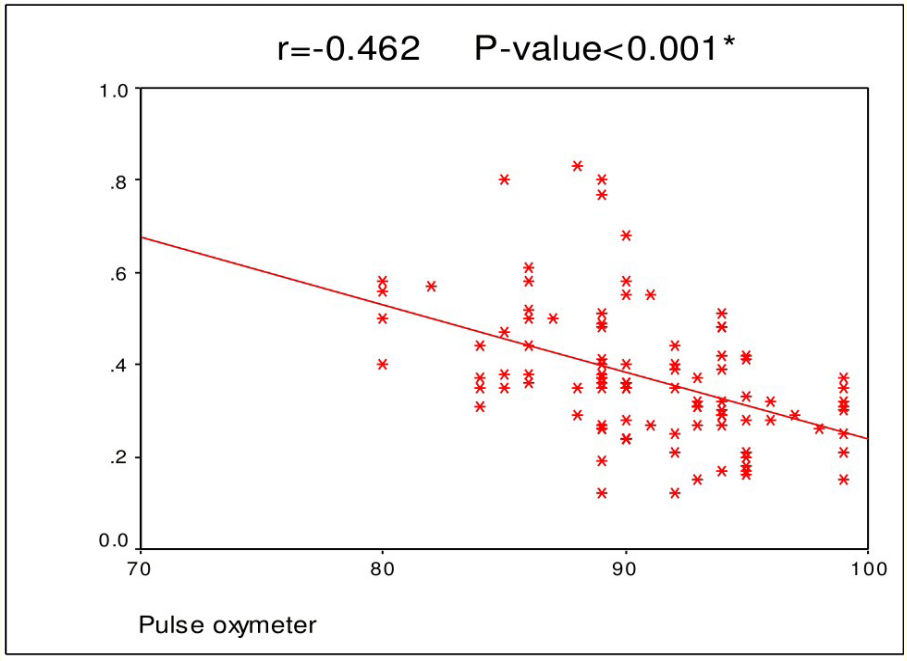

Figure 3: *Correlation coefficient between pulse oxymeter and Tei index for cases with severe bronchiolitis.*

Figure 4 Showing correlation coefficient between Tei index and pulmonary artery systolic pressure for cases with severe bronchiolitis. Using correlation coefficient test (r-test), significant negative correlation was detected between Tei index and pulmonary artery systolic pressure ($P < 0.05$).

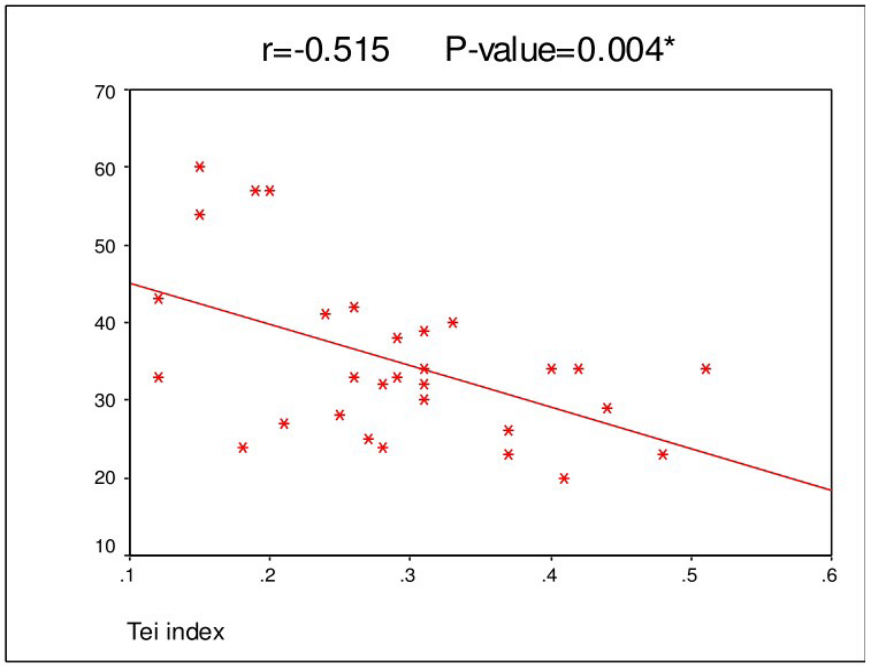

Figure 4: *Correlation coefficient between Tei index and pulmonary artery systolic pressure (PASP mmHg) for cases with severe bronchiolitis.*

Discussion

In the current study, it was found that bronchiolitis was significantly higher among infants younger than 6 months of age (Table 1), this was in agreement with Verma., *et al*. [13] who reported that bronchiolitis typically affects children younger than two years with a peak incidence between two and six months of age. Also, severe bronchiolitis was more common among infants belonging to low social class (Table 1). This was in agreement with Jansson., *et al*. [14] who reported that severe bronchiolitis was higher in patients from low social class areas. There was high association between complementary feeding and acute bronchiolitis also complementary feeding was associated with higher percentage frequency of severe bronchiolitis, this was in line with Dornelles., *et al*. [15] who reported that infants with bronchiolitis receiving exclusive breastfeeding had better clinical outcomes.

Cardiomegaly and manifestation of heart failure (tachypnea, tachycardia and enlarged tender liver) was detected among 2% of cases, those cases belonged to group of severe bronchiolitis (Table 2). Thorburn., *et al*. [16] reported that right ventricular dysfunction was detected among 20% of cases with severe bronchiolitis.

ECG abnormalities were detected among five cases, all of them belonged to severe bronchiolitis group, one case had sinus pause (sinoatrial block) which was asymptomatic, four cases who had elevated cardiac troponin level had abnormalities as the following; two

cases had supraventricular tachycardia and two had first degree heart block (Table 3). This was in agreement with Menchise [18] who reported that ECG changes in bronchiolitis, showed sinus tachycardia, supraventricular, and ventricular arrhythmias, as well as complete heart block, also this was in agreement with Esposito., *et al*. [19] reported that RSV seems associated with sinoatrial blocks and transient rhythm alterations even when the related respiratory problems are mild or moderate. On the other hand, this was in contrast to Thorburn., *et al*. [16] who did not report any arrhythmias or other ECG abnormalities among patients with normal or those with elevated cardiac troponin.

Echocardiographic examination done within the first 48 hour for the admitted 68 cases. Echocardiographic findings detected in this study: There was no significant statistical difference among the three groups regarding left ventricular systolic and diastolic dimensions, left atrial dimension and left ventricular fractional shortening (Table 3), this was in agreement with Thorburn., *et al*. [16] who reported that left ventricular and atrial dimensions, were similar in patients with and without reduced right ventricular function, also left ventricular fractional shortening was not different in patients with and without reduced right ventricular function. In the present study Tei index (right ventricular performance index) was ranging from 0.1-0.8 with mean ± SD 0.37 ± 0.15, this was in agreement with Thorburn., *et al*. [16] who assessed the right ventricular function in severe RSV infections that require ventilation support and reported an elevated Tei index (median Tei index: 0.46, range 0.33-0.92) consistent with reduced right ventricular function.

Pulmonary artery systolic pressure exhibited increased frequency but with no statistical difference among different groups (Table 4), this was in agreement with Bardi-Peti and Ciofu [20], who reported that pulmonary artery pressure was raised in infants with broncho-obstructive pathology specially bronchiolitis and attributed this to hyperinflation mechanical forces on pulmonary vessels. Pulmonary artery systolic pressure exhibited increased frequency but with no statistical difference among different groups (Table 4), this was in agreement with Bardi-Peti and Ciofu [20], who reported that pulmonary artery pressure was raised in infants with broncho-obstructive pathology specially bronchiolitis and attributed this to hyperinflation mechanical forces on pulmonary vessels.

In the present study, elevated Tei index was found in 84% of children with severe bronchiolitis (Table 5), this was much higher than that reported by Thorburn., *et al*. [16] who reported that an elevated Tei index was found in 20% of infants required assisted ventilation for RSV bronchiolitis and this was in line with right ventricular dysfunction. They noted that the dysfunction was independent to the degree of respiratory impairment and cardiac muscle damage. Regarding the results of cardiac troponin I which is an indicator of myocardial damage was found to be positive (cutoff value >10ng/L) in only 4 cases all of them belong to the group of severe bronchiolitis (Table 3), this denoting that right ventricular dysfunction found in the studied cases, was not related to myocardial damage (indicated by elevated cardiac troponin I), this was in agreement with Eiden *et al*. [17] who reported that high cardiac troponin levels (indicating cardiac muscle damage) were not the cause of reduced right ventricular function, as normal cardiac troponin level was detected in infants with troponin levels (indicating cardiac muscle damage) were not the cause of reduced right ventricular function, as normal cardiac troponin level was detected in infants with severe impairment of right ventricular function. Also, the present study detected no correlation between cardiac troponin I and left ventricular fractional shortening or the right ventricular Tei index. This was in agreement with Thorburn., *et al*. [16] who found no significant correlation between left ventricular or right ventricular function with cTnT.

In the present study, it was found that there was a significant negative correlation between pulse oxymeter values (as indicator of bronchiolitis severity) and Tie index for cases with severe bronchiolitis (Figure 3), this supported by Thorburn., *et al*. [16] who found that elevated Tei index was detected among infants with severe hypoxemia requiring ventilator support.

In the present study it was found that there was a negative correlation between Tei index and pulmonary artery systolic pressure (Figure 4), this was in agreement with Fitzgerald., *et al*. [21] who failed to prove a causal relation between pulmonary hypertension and the resultant right ventricular dysfunction, which was associated with severe bronchiolitis in many studies, but results of the present study were in disagreement with Tei., *et al*. [22] who reported that, the Tei index was done for use in patients with raised pulmonary artery pressure and may reflects pulmonary hypertension.

Conclusion

Echocardiographic changes were related mainly to the severity of bronchiolitis in structurally normal heart.

- Elevated pulmonary artery systolic pressure was the most common cardiac affection among patients with acute bronchiolitis regardless the severity of the disease.
- Subclinical right ventricular dysfunction (indicated by elevated right ventricular Tei index) was common among patients with severe bronchiolitis.
- Left ventricular systolic and diastolic dimensions together with left ventricular fractional shortening were not significantly affected in infants with bronchiolitis.
- Both myocarditis and ECG changes were limited to the patients with severe bronchiolitis only.

Recommendations

- Echocardiography should be done to all infants presented with respiratory distress especially those with severe bronchiolitis, for: Exclusion of congenital heart disease and cardiomyopathy and to assess right ventricular function and pulmonary artery systolic pressure.
- Patients with bronchiolitis who have impaired Tei index and those with elevated pulmonary artery systolic pressure should be closely observed for signs of right sided heart failure.
- Patients who developed myocarditis during the course of the disease should be followed up periodically, clinically and by echocardiographic assessment of cardiac function, to exclude post-myocarditis cardiomyopathy.
- Further researches and studies are recommended in this field, using other measures to assess right ventricular function as RV wall thickness and chamber dimensions, RV fractional area change together with Tei index which may yield a more indicative results about the right ventricular function.

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