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Serum Endocan Level in Preterm Neonates with Respiratory Distress Syndrome

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ABSTRACT

Background: In the early newborn period, hyaline membrane disease (HMD) or respiratory distress syndrome (RDS) is a leading cause of morbidity and mortality. It occurs in 7% - 50% of neonates. Our objective was to determine serum endocan role in the diagnosis and the prognosis of RDS in neonates.

Methods: This prospective controlled study was carried out on 80 preterm neonates ≤ 34 weeks gestation at Neonatal Intensive Care Unit. They were diagnosed with RDS, and were classified into two groups: **Group I** consisted of 40 preterm newborns diagnosed with RDS, two blood samples were withdrawn. 1st at birth (1st day) and 2nd after 4 days. **Group II** consisted of 40 healthy preterm neonates, blood samples were withdrawn at day1.

Results: There was a significant high serum endocan level in dead cases in comparison with survived cases (P=0.001). Serum endocan level in RDS group showed an area under the curve of 0.867, which gave very good performance (p value was 0.001) at a cut of value > 450 ng/ml. Serum endocan level had a sensitivity of 88% (was able to identify 88% of cases that had RDS) and a specificity of 83% (identified 83% of cases that did not have RDS), with positive predictive value of 83%, negative predictive value of 87%, and accuracy 85%.

Conclusions: Levels of serum endocan are significantly elevated in preterm neonates with RDS. Serum endocan level had positive correlation with severity of RDS. Serum endocan levels decreased after 3 days in preterm neonates with RDS.

Keywords: Serum endocan level, Preterm neonates, respiratory distress syndrome.

INTRODUCTION

The leading cause of morbidity and mortality in the early newborn period is hyaline membrane disease (HMD) or respiratory distress syndrome (RDS). It affects between 7 and 50 % of newborns, and responsible for 30% - 40% of their hospital admission [1]. Depending on gestational age, the incidence of NRDS differs from 57% for newborns born at 30–31 weeks to 92 % for newborns delivered at 24–25 weeks [2].

The anatomical immaturity of the lungs, as well as developmental inadequacy of production and function of surfactant, are the causes of RDS. It can also be caused by a genetic disorders of the surfactant protein [3]. RDS risk rises with numerous births, maternal diabetes, caesarean section, hypoxia, premature delivery, a maternal history of previously affected babies, and cold stress. Preterm male or white newborns are the most susceptible. Prolonged rupture of membranes, pregnancies with chronic or pregnancy-associated hypertension, antenatal corticosteroid prophylaxis, and maternal heroin use have a reduced risk of RDS [4].

RDS usually occurs during the 1st hours of neonatal life, often immediately following birth. Neonates with marked respiratory distress clinically suffer with tachypnea, suprasternal, intercostal, and/or subcostal retractions, grunting, and nasal flaring [5]. Surfactant and respiratory support are the foundation of treatment for cases with RDS [i.e. Nasal Continuous Positive Airway Pressure (NCPAP) and Mechanical Ventilation (MV)] [6]. In complicated cases, Bronchopulmonary Dysplasia can occur leading to asthma, recurrent wheeze, and higher rates of hospitalization later in life [4].

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Endocan, is a soluble 50-kDa dermatan sulfate proteoglycan (initially known as endothelial cell-specific molecule-1) that can be detected in human blood and is constitutively expressed by endothelial cells in kidneys and lungs [7]**.** It plays a crucial function in endothelial homeostasis, able to control endothelial permeability, leukocyte migration, and cell adhesion from the circulation into the tissues [8]. It is released in response to activation by cytokines, namely interleukin-1 (IL-1), tumor necrosis factor, and microbial lipopolysaccharide, in addition to proangiogenic factors including vascular endothelial growth factor [9]. It is considered a new tissue- and blood-based biomarker as it represents endothelial activity and dysfunction. As a result, it is being studied and assessed across a broad spectrum of healthy and disease pathophysiological processes [10].

Our objective was to determine serum endocan role in the diagnosis and the prognosis of RDS in neonates.

PATIENTS AND METHODS

This prospective controlled study was conducted at Neonatal Intensive Care Unit (NICU) of Tanta University Hospital from October 2020 to September 2021.

Inclusion criteria: Preterm neonates ≤ 34 weeks gestation, diagnosed with RDS.

Exclusion criteria: Neonates > 34 weeks gestation, hemodynamically significant Patent Ductus Arteriosus, chromosomal anomalies, hypoxic ischemic encephalopathy, sepsis, major-congenital anomalies and IUGR.

Eighty preterm neonates born < 34 weeks gestation [11] were enrolled and further classified into two groups: **Group I** consisted of 40 preterm newborns diagnosed with RDS, two blood samples were withdrawn. 1st at birth (1st day) and 2nd after 4days. **Group II:** consisted of 40 healthy preterm neonates, blood samples were withdrawn at day1.

RDS diagnostic criteria:

Newborns were diagnosed with RDS if they exhibited respiratory distress with tachypnea, grunting, suprasternal, intercostal, and/or subcostal retractions, nasal flaring, cyanosis, and increased oxygen need within the first hours of life, in addition to radiological abnormalities on chest X-ray [12].

The hallmark radiographic RDS findings include a peripheral air bronchograms and reticulogranular (i.e., ground-glass) pattern. The lungs in severe cases may appear completely white, with total loss of the cardiac borders. Low lung volume is another cardinal feature [12]. Radiographic stages of RDS [13]:

- **Stage I:** Fine homogenous ground glass shadowing.
- **Stage II:** Widespread air bronchogram bilaterally.
- **Stage III:** Confluent shadowing of the alveoli.
- **Stage IV:** Shadowing of the alveoli obscuring cardiac border.

All included preterm infants underwent: Complete history taking: **Prenatal history** (length of gestation, maternal age, parity, previous abortion and any maternal insults or illnesses during gestation as medications, antenatal steroid, PROM, DM and hypertension). **Natal history** as mode of delivery, difficulties in delivery anthropometric measurements (weight, length and head circumference), Apgar score at birth and surfactant administration. **Postnatal history** as assessment of method of respiratory support (nasal cannula, CPAP or mechanical ventilation). **Clinical examination:** Assessing the gestational age using new Ballard score, assessment of general condition, detecting any related neonatal problems and assessing degree of respiratory distress.

Radiological investigations: Chest x-ray, chest anterior-posterior (AP) radiographs were taken in supine position to confirm the diagnosis and exclude other causes of respiratory distress, Echocardiography examination of enrolled neonates to exclude HsPDA.

Routine laboratory investigations: Complete blood picture (CBC) was performed

using automated hematology system (Sysmex XE 5000). Arterial blood gases (ABG) with the Wondfo's blood gas analyzer test card (electrochemistry), C-reactive protein (CRP), renal function tests and liver function tests.

Specific laboratory investigations: Serum Endocan level in the 1st and 4th day of life using ELIZA kits (Shanghai Korain Biotech Co., Ltd, Shanghai, China).

Sampling:

Skilled medical personnel collected 2 ml of peripheral venous blood under complete aseptic conditions, the collected blood was allowed to clot by leaving it undisturbed for 15-30 minutes at room temperature. The sample was centrifuged for approximately 15 minutes at 2000-3000 RPM. The serum was collected carefully and stored at -20 to -80°C. We avoided repeated freeze/thaw cycles.

Principles of the assay:

The kit was an Enzyme–linked Immunosorbent Assay (ELIZA). Human ESM–1 antibody had been used to pre-coat the plate. ESM-1 from the sample was introduced and subsequently bound to anti-bodies coated on the wells. Then, Biotinylated human ESM–1 Antibody was added to the sample and bound to ESM -1. Then, streptavidin–HRP was added and conjugated to the Biotinylated ESM-1 antibody. After incubation, during a washing step, unbound Streptavidin–HRP was washed away. Then, substrate solution was added and in proportion to the amount of human ESM-1, a color was developed. By adding acidic stop solution, the reaction was terminated, and absorbance was measured at 450 nm.

Preparing reagent:

The reagents were prepared before their usage by bringing them to room temperature.

For generating 1200 ng/L standard stock solution, standard reconstitute the 120 µl of the standard (2400 ng/L) with 120 µl of standard diluents was performed. Before producing dilutions, standard was allowed to sit for 15 minutes with gentle agitation. Duplicate standard points were prepared by serial dilution of the standard stock solution (1200 ng/L) 1:2 with standard diluents serves as the zero standard (0 ng/L). Any leftover solution was kept frozen at -20 ℃ and utilized within one month. The proposed dilutions of standard solution are:

Assay procedure

All standard solutions, reagents and samples were prepared as instructed. Before usage, all reagents were brought to room temperature. The assay is conducted at room temperature. The number of strips needed was determined, then inserted for use in the frames, while storing the unused ones at 2-8℃.

To standard well, add 50 µl standard (Antibody should not be added to the standard well since the standard solution already includes biotinylated antibody). To sample wells, add 40 µl sample, then add 10 µl anti-ESM-1 antibody. Then, add to sample wells and standard wells 50 µl streptavidin-HRP (NOT blank control well). Mix well. Seal the plate with the sealant. The incubation was performed at 37℃ for 60 minutes. The sealant was removed and the plate was thoroughly washed with wash buffer five times. The wells were soaked for each wash for 30 seconds to 1 minute with at least 0.35 ml of wash buffer. For automated washing, aspirate all wells and wash with wash buffer five times, overfilling wells with wash buffer. Use paper towels or another absorbent material to blot the plate.

To each well, add 50 µl of substrate solution A followed by adding 50 µl of substrate solution B. Plates should be covered with a new sealant and incubated in the dark at 37 °C for 10 minutes. Add 50 µl of stop solution to each well; the colour will immediately change from blue to yellow. Using a microplate reader set to 450 nm, immediately determine the optical density (OD value) of each well within 10 minutes after adding the stop solution.

Ethical approval: The Ethics Committee of Faculty of Medicine, Tanta University approved the conduction of this trial (approval code: 32597/09/18). Every patient's parents or legal guardians provided their written informed consent. The Helsinki Declaration was followed throughout the study's conduction.

Statistical analysis

SPSS v 27 was used for the statistical analysis of the data (IBM©, Armonk, NY, USA). To assess the normality of the data distribution, histograms and Shapiro-Wilks test were used. Qualitative data were expressed as frequency and percentage (%) and analyzed using the Chi-square test. Quantitative parametric data were expressed as mean and standard deviation (SD) and analyzed by ANOVA (F) test with post hoc test (Tukey). A two tailed P value ≤ 0.05 was deemed statistically significant. Linear Correlation coefficient (r) was used to detect the correlation between two quantitative variables in one group. To determine the overall predictivity of parameter in and to determine the best cut-off value, with detecting specificity and sensitivity at this cut-off value. Receiver operating characteristic (ROC curve) analysis was used.

RESULTS

There was a significant variation as regards Apgar score at 1st minute and gestational age, which were higher in control group compared to RDS group.

As regards the clinical presentation, 3 (7.5 %) cases were presented with tachypnea, 5 (12.5%) cases with retraction, 26 (65%) cases with grunting and 6 (15 %) cases were presented with central cyanosis. As regards type of respiratory support, 4 (10 %) babies received CPAP, 6 (15%) received oxygen via high flow nasal cannula (HFNC), 2 (5%) received nasal intermittent positive pressure ventilation (NIPPV), 20 (50 %) were put on mechanical ventilation (MV) and 8 (20%) were put on high frequency oscillatory ventilation (HFOV). The mean of the duration of mechanical ventilation was 6.4 ± 2.54 days, while the mean of the duration of hospitalization was 17.6 ± 10.45 days. As regards outcome in RDS group, 32 (80%) babies improved, while 8 (20%) of babies died. Concerning radiological grading of RDS in RDS group, grade I was found in 3 cases (7.5 %) of, grade II was found in 5 cases (12.5 %), grade III was reported in 26 cases (65%) and grade IV was found in 6 cases (15%) (Table 1**)**.

Table (1): Demographic data, clinical characteristics, and radiological grading of RDS of the studied group

Variables	Cases (n=40)	Control (n=40)	t/X^2	P
Gestational age (weeks)			3.979	<0.001*
Mean ±SD	30.53±2.19	32.20±1.51		
Birth weight (Kgs)			1.807	0.075
Mean ±SD	1.55±0.46	1.76±0.58		
Gender:			1.289	0.256
Males	21 (52.5%)	26 (65.0%)		
Females	19 (47.5%)	14 (35.0%)		
Mode of delivery			2.669	0.111
Normal vaginal	15 (37.5%)	13 (32.5%)		
Cesarean	25 (62.5%)	27 (67.5%)		
Apgar score first minute			2.371	0.023*
Mean ±SD	3.93±1.38	4.5±1.198		
Apgar score 5 minutes			0.298	0.767
Mean ± SD	7.28±1.11	7.35±1.14		
Antenatal steroid Yes No	16(40%) 24(60%)	27 (32.5%) 13 (67.5%)		

Clinical presentation		
Tachypnea	3	7.5
Retraction	5	12.5
Grunting	26	65
Central cyanosis	6	15
Type of respiratory support		
CPAP	4	10
HFNC	6	15
NIPPV	2	5
M.V	20	50
HFOV	8	20
Duration of mechanical ventilation(days)		
Range	4-15	
Mean ±SD	6.4±2.54	
Duration of hospitalization (days)		
Range	5-63	
Mean ±SD	17.6±10.45	
Complications		
BPD	2	5
ROP		
Stage I	2	5
Stage II	1	2.5
Stage III	1	2.5
Stage IV	0	0
NEC		
Stage I	1	2.5
Stage II	2	5
Stage III	1	2.5
Pneumothorax	3	7.5
Pulmonary He	2	5
IVH		
Stage I	4	10
Stage II	3	7.5
Stage III	1	2.5
Stage IV	0	0
Administrated surfactant		
Yes	24	60
No	16	40
Outcome		
Improved	32	80
Died	8	20

Variables		**Number (n=40)**	**%**
CXR Grading	I	3	7.5
	II	5	12.5
	III	26	65
	IV	6	15

*Statistically significant at $p \leq 0.05 X^2$: Chi square test t: student t-test. HFOV = High frequency oscillatory ventilation. CPAP = Continuous positive airway pressure. ROP = Retinopathy of prematurity. NEC = Necrotizing enters colitis. BPD = Bronchopulmonary dysplasia. IVH = Intraventricular hemorrhage.

As regards parameters of CBC, there was insignificant difference as regards haemoglobin level, WBCs and platelets count. As regards serum electrolyte where there was insignificant variation between both groups (Table 2).

Table (2): Laboratory investigations and serum electrolytes of studied groups at day 1

Variables	Cases	Control	t	P
Hemoglobin:			1.488	0.141
Mean ±SD	15.04± 1.81	15.65± 1.87		
Platelets (X 10^3):			1.572	0.121
Mean ±SD	178.58 ±40.17	192.45 ±38.99		
Total leucocyte count (X 10^3)			1.664	0.201
Mean ±SD	15.45± 4.7	15.09± 5.7		
Calcium			1.502	0.138
Mean ±SD	1.81±0. 80	2.03±0. 43		
Magnesium			0.007	0.934
Mean ±SD	2.30±0. 49	2.29±0. 61		
Sodium			1.113	0.269
Mean ±SD	138.35 ±4.56	139.42 ±4.04		
Potassium			0.011	0.917
Mean ±SD	4.77±1. 22	4.73±0. 90		

*****Statistically significant at $p \leq 0.05$, t: student t-test, SD: standard deviation

Regarding the initial ABG, a significant variation between the two groups was reported as regards pH, PCO_2 and HCO_3 level (Table 3).

Table (3): Initial arterial blood gases in studied groups at enrollment:

Variables	**Cases**	**Control**	**t**	**P**
pH				
Mean ±SD	7.278± 0.060	7.29± 0.48	1.252	<0.001*
PCO_2				
Mean ±SD	52.83± 7.77	34.95± 3.54	8.982	<0.001*
HCO_3				
Mean ±SD	14.92± 5.12	21.21± 3.73	6.287	<0.001*

*****Statistically significant at $p \leq 0.05$, t: student t-test, SD: standard deviation

Serum Endocan level had significantly decreased in day 4 compared to day 1 in RDS group (mean Endocan levels were 375.15 Vs 604.25 ng/ml respectively, p=0.001). A significant elevation of serum Endocan in RDS group day 1 was reported compared to control group (mean Endocan levels were 604.25 Vs 397.20 ng/ml respectively, p=0.001). There was insignificant difference between serum Endocan level in RDS group day 4 and control group (Table 4).

Table (4): Serum Endocan level in studied groups

S. Endocan	**Group I (Day 1)**	**Group I (Day 4)**	**Group II Control**
Mean ± SD (ng/mL)	604.25 ± 173.37	375.15 ± 36.59	397.20 ± 58.95
f. test	**44.723**		
p. value	**0.001***		
Group I (Day 1) and (Day 4)	**Group I (Day 1) and Control**	**Group I (Day 4) and Control**	
0.001*	**0.001***	**0.411**	

*****Statistically significant at $p \leq 0.05$, t: student t-test

Table (5) showed that in the RDS group, there was insignificant correlation between serum Endocan level and gestational age. A significant negative correlation was reported between serum Endocan level with (APGAR 1 m, APGAR 5 m) and a significant positive correlation between serum Endocan level and CXR grading was also reported.

Table (5): Serum Endocan level in D1 and different parameters in RDS group

	S. endocan	
	R	p
Gestational age	0.290	0.135
APGAR 1m.	- 0.475	0.015*
APGAR 5m.	- 0.423	0.021*
CXR grading	0.616	0.001*

*****Statistically significant at $p \leq 0.05$, r: spearman coefficient

Table (6) showed the relation of serum endocan level and sex where insignificant difference was reported**.**

Table (6): Comparison between serum Endocan level and sex

S. endocan	Male	Female
Mean ± SD (ng/mL)	624.52 ± 177.58	581.85 ± 170.51
T. test	0.598	
P. value	0.444	

* Statistically significant at p ≤ 0.05t: student t-test.

There was a significant high serum endocan level in dead cases in comparison with survived cases (mean 736.75 ± 99.51 ng/mL Vs 442.31 ± 78.94 ng/mL respectively P=0.001 (Table 7).

Table (7): Serum Endocan level in day 1 and outcome in RDS group

S. endocan	Improved	Died
Mean ± SD	442.31 ± 78.94	736.75 ± 99.51
T. test	15.906	
P. value	0.001*	

* Statistically significant at p ≤ 0.05t: student t test

ROC of serum endocan level in RDS group showed an area under the curve (AUC) = 0.867, which gave very good performance, (p value was 0.001) at a cut off value of > 450 ng/ml, serum Endocan level had a sensitivity of 88% (was able to identify 88% of cases that has RDS) and a specificity of 83% (identified 83% of cases that did not have RDS). Moreover, the positive predictive value (PPV) was 83%, while the negative predictive value (NPV) was 87% and the accuracy was 85% (Table 8).

Table (8): ROC curve of serum endocan level in RDS

	AUC	cut off value	Sensitivity%	Specificity%	PPV%	NPV%	Accuracy%
S. endocan	0.867	450	88	83	83	87	85

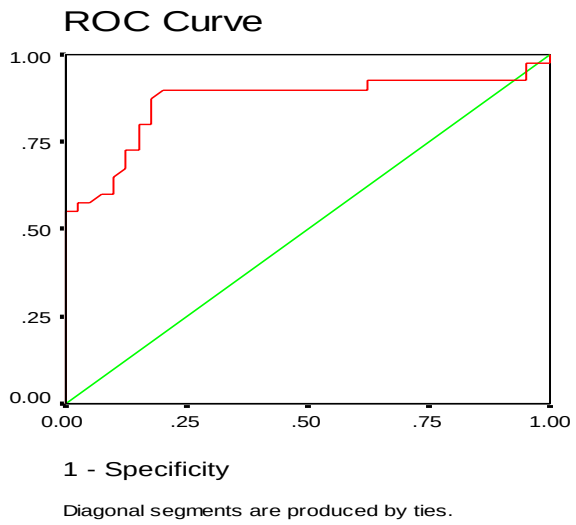

Fig. (1): ROC curve of serum endocan level in RDS group

DISCUSSION

Recent data suggests that Endocan is involved in multiple pathophysiological processes, such as tumor growth and inflammatory diseases, and in the control of key cellular functions, such as adhesion, angiogenesis, and migration **[14].**

The present research investigated the predictive value of serum Endocan level in the

diagnosis and follow up of RDS in preterm neonates. Regarding the mode of delivery in the RDS group in our study, 25 cases (62.5%) were delivered by cesarean section (CS) and 15 cases (37.5%) were delivered vaginally, with RDS being more significantly common in newborns delivered by CS. Similarly, **Nakahara *et al.*** [15] reported that newborn delivered by CS have higher incidence of RDS than those delivered vaginally.

Our study included 14 female (35%) and 26 male (65%) neonates. Similarly, **Niesłuchowska-Hoxha *et al.*** [16] reported that in preterm newborns, females had a lower incidence of RDS.

Apgar score in the 1st minute was significantly lower in newborns with RDS compared to newborns without RDS. Similarly, **Luerti *et al.*** [17] found that low Apgar score in the 1st minute was related to a higher RDS risk.

As regards Apgar score in the 5th minute, an insignificant difference between both studied groups was reported. This coincides with **Canpolat *et al.*** [18] study, which involved 83 premature infants, divided into RDS group consisted of 44 preterm infants and the control group consisted of 39 preterm neonates without RDS**.** They found an insignificant variation between both groups. Contrarily, **Luerti *et al.*** [17] found that low Apgar score in the 5th minute was related to a higher risk of RDS.

In this study, as regards types of respiratory support, 4 patients (10 %) were on CPAP, 6 patients (15 %) were on HFNC, 2 patients (5%) were on NIPPV, 20 patients (50%) were on MV and 8 patients (20%) were on HFOV. Regarding the days of MV, the mean was 6.4 ± 2.54 days. The mean of the duration of hospitalization was 17.6 ± 10.45 days. Antenatal steroid was received in 16 patients (40%) of cases.

Our results showed an insignificant variation between both groups as regards CBC (Hb, WBCs and platelet count) at enrollment. This is in agreement with **Canpolat *et al.*** *[18]* who found an insignificant variation between both group as regards Hb and platelets count. In contrast, **Tigabu *et al.*** [19] found that thrombocytopenia was found in 49.3% of patients with RDS, which is similar to research performed in Bellevue Hospital, USA and in India where they detected thrombocytopenia in 42% of newborns with RDS [20]**.**

Our data showed a significant variation between both groups as regards ABG at enrollment in the RDS group, which showed respiratory and metabolic acidosis. Also, this coincides with **Niesłuchowska-Hoxha *et al.*** [16] study in which blood gas analysis showed oxygen tension/fraction of inspired oxygen ratio (PaO2/FiO2) ≤ 26.7 kPa, hypercapnia, and hypoxia in preterm newborns.

Regarding the outcome in RDS group, 8 preterm neonates died, and 32 patients were discharged.

In our study, as regards serum Endocan level, we noticed a significant variation between day 1 and day 4 in the RDS group where the levels of serum endocan was significantly elevated in the 1st day compared to the 4th day. Also, there was a significant difference between day 1 in the RDS group and day 1 in the control group, as the level of Endocan in day 1 in RDS group was higher than its level in day 1 in the control group. The mean of Endocan level was 604.25± 173.37 ng/mL VS. 397.20 ± 58.95 ng/mL respectively with P value = 0.001. However, an insignificant difference was reported as regards serum Endocan level between day 4 in the RDS group and day 1 in the control group. Our results coincide with some studies, which done to detect the role of Endocan in different diseases. **Tayman *et al.*** [21] found an elevated levels of serum Endocan in newborns with BPD compared to the control group, and reported an elevated levels of serum Endocan in newborns with BPD before hydrocortisone medication and reduced following appropriate treatment throughout the consecutive days.

In our study, we didn't report a correlation between the levels of serum Endocan and gestational age. This is in agreement with **Szpera-Goździewicz *et al.*** [22] observational case-controlled study, which enrolled 237 cases (after 20 weeks of gestation), and found an insignificant correlation between the levels of serum Endocan and gestational age. Also,

there were statistically insignificant correlation between the level of serum Endocan and gender.

A significant negative correlation was reported between the level of serum Endocan in the RDS group and the Apgar score in 1st and 5th minute. This coincides with **Kucukbas *et al.*** [23] who conducted their study on 47 healthy pregnancies and 44 pregnancies complicated with IUGR. A negative weak correlations was reported between Endocan level and 5th (r = 0.256; p =0.015) and 10th minute APGAR scores (r = 0.215; p =0.042).

Our study showed positive significant correlations between serum Endocan level and CXR grading. Similarly, **Tayman *et al.*** [21] studied 148 infants, 74 as controls and the remaining with BPD (moderate/severe), where the severe BPD group had higher levels of Endocan than moderate BPD group. Moreover, BPD groups had remarkably higher serum levels of Endocan than control group. And also come in agreement with **Kao *et al.*** [24] who found that APACHE II, Pneumonia Severity Index (which are the indicators of the severity of the disease) were associated with high Endocan values.

Our study reported a significant variation between the level of serum Endocan and outcome, as there was a significant high serum Endocan level in dead neonates in comparison with survived cases. This comes in agreement with **Abd El Halim *et al.*** [25] who found that in patients with ventricular associated pneumonia (VAP), the dead VAP group had significantly higher mean values of Endocan compared to the survivor VAP group on the two groups' first day.

In our study, analysis of ROC curve of serum Endocan level as a diagnostic test for RDS group showed an AUC of 0.867 (p value was 0.001) at a cut of value > 450 ng/ml serum endocan level with a sensitivity of 88% (was able to identify 88%. of cases that has significant RDS) and a specificity of 83% (identified83% of cases that did not have significant RDS). Moreover, PPV has been calculated and was 83%, while NPV was 87%. In **Tayman *et al.*** [21] study, ROC analysis was conducted to determine the predictive diagnostic value of the levels of serum Endocan in cases with moderate BPD. AUC was 0.984 (P =.0001). Endocan had the cut-off value of 450, with sensitivity 95%, specificity 100%, PPV 100.0% and NPV 70.3%. In cases with severe BPD. AUC was 0.975 (P =0.001). The Endocan cut-off value was 553.3, with sensitivity 92%, specificity 100%, PPV 100.0% and NPV 100%.

Our study had limitations as being single center study, including relatively small number of population, and lack of randomization.

CONCLUSIONS

Serum levels of Endocan are significantly elevated in preterm neonates with RDS. Serum Endocan level had positive correlation with severity of RDS. Serum Endocan levels decreased after 3 days in preterm with RDS. Serum endocan was significantly high in died preterm suffered from RDS compared to survived ones. Further larger multicenter researches are needed to investigate the potential role of serum endocan in management modalities in RDS cases.

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