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# Role of cholesterol, lipoproteins, and neutrophilic-lymphocytic ratio in patients with pneumonia

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## Abstract

**Background:** Lipids play numerous functions in lung biology and pathophysiology of infection, in addition to their role in lipid transport, lipoproteins share in innate immunity that is the most important way for the host to defend against microbes. The NLR (neutrophil-lymphocytic ratio) is a good indicator of systemic inflammation and infection.

**Objective:** To evaluate the role of cholesterol, lipoproteins, and neutrophilic-lymphocytic ratio in the assessment of patients with pneumonia.

**Patients and methods:** This prospective case–control study included 52 subjects; they were categorized into 2 groups. Group A included 42 patients with pneumonia admitted to the Chest Department, Menoufia University, and group B included 10 healthy people during the period from May 2019 to December 2019. History taking, clinical examination, laboratory investigation in the form of CBC and lipid profile, and radiological investigation in the form of CXR and CT chest if needed were done to all subjects of the study.

**Results:** The mean cholesterol level in group A was  $149.76 \pm 42.79$  which was statistically significantly lower as compared with group B ( $165.90 \pm 45.50$ ) ( $p = 0.039$ ). The mean HDL level in group A was  $43.16 \pm 6.32$  which was statistically significantly lower as compared with group B ( $50.51 \pm 9.60$ ) ( $p = 0.026$ ). No statistically significant difference was found in the triglyceride level, LDL level and VLDL between the subjects in the two studied groups ( $p = 0.479, 0.792,$  and  $0.606$ ), respectively, but all levels were still within normal levels. Mean NLR in group A was  $7.04 \pm 7.98$  which was statistically significantly higher as compared with group B ( $3.04 \pm 1.6$ ) ( $p = 0.004$ ). Roc curve of neutrophil–lymphocyte ratio shows that the cutoff point is 1.94 and the N/L ratio had area under curve of 78% with 79.6% sensitivity and 67.8% specificity.

**Conclusion:** Serum cholesterol and high-density lipoprotein levels significantly decreased in patients with pneumonia when compared to the control group but were still within normal range. Lipid profile is affected by different variables like smoking index, body mass index, and sex. The neutrophil–lymphocyte at cutoff point is 1.94, and N/L ratio had area under curve of 78% with 79.6% sensitivity and 67.8% specificity.

**Trial registration:** TCTR, [TCTR20220524001](https://www.tctrcr.com/record/TCTR20220524001). Registered on 24 May 2022, retrospectively registered.

**Keywords:** Pneumonia, Neutrophilic-lymphocytic ratio, Cholesterol, HDL, BMI, Smoking index

## Introduction

Pneumonia is defined as an inflammatory disease of the lungs that affects the alveoli. Symptoms include a combination of productive or dry cough, chest pain, fever, and dyspnea. The severity of the illness varies. Pneumonia is

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most commonly caused by viruses and bacteria, but it can also be caused by other microbes [1].

Lipoproteins are classified as chylomicrons, very-low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) according to their relative density. Lipoproteins play a major function in innate immunity, which is the most critical line of protection against pathogens, in addition to transporting lipids [2].

In addition, anti-inflammatory effects of lipoproteins, especially HDL, have been demonstrated both in vitro and in vivo studies. Circulating lipoproteins detoxify lipopolysaccharide and toxins of gram-negative and lipoteichoic acid of gram-positive bacteria [3, 4].

In patients with infection there was a decrease in the serum levels of total cholesterol, LDL, and HDL. These changes were independent of the underlying disease or microorganisms [5].

The neutrophil-lymphocyte ratio (NLR) is a low-cost, basic diagnostic of systemic inflammation that can predict prognosis in a variety of diseases. It is determined by dividing the absolute neutrophil count by the absolute lymphocyte count, which is obtained from CBC [6].

The aim of the work was to evaluate the role of cholesterol, lipoproteins, & neutrophilic-lymphocytic ratio in the assessment of patients with pneumonia.

## Patients and methods

### Study design

A prospective case-control study was done on a group of 42 cases with pneumonia admitted to the Chest Department of Menoufia University and El Mahalla Chest hospital (group A). In addition, a group of 10 healthy people was included as a free group (Group B) during the duration from May 2019 to December 2019. A written informed consent was obtained from every participant or his representatives prior to inclusion in the study after a detailed explanation of the work, and approval from Menoufia Ethical Committee was obtained.

Inclusion criteria include the following: presence of a major infection criterion (productive cough, body temperature more than 37.8 °C) or 2 minor infection criteria (pleurisy, dyspnea, pulmonary consolidation by clinical examination), leukocytosis  $> 10^3/\text{mm}^3$ , and pulmonary consolidation verified by chest radiography [7].

Exclusion criteria include the following: any other chest diseases. Previously diagnosed with dyslipidemia. & patients received therapy for lipids.

### Methods

History taking, clinical examination, and laboratory investigation were done to all participants of the study.

### CBC

CBC with automated differential counts, including WBCs, neutrophils, and lymphocytes, were made on admission to define neutrophil-to-lymphocyte ratio (NLR), and blood samples were collected before giving any antibiotics. WBCs ( $3.0\text{--}10 \times 10^3/\text{mm}^3$ ), neutrophil count (43–76%), and lymphocyte count (17.0–48.0%) were the normal standard levels.

### Lipid profile

Fasting blood sample was obtained from all study individuals the day after admission. And serum levels of lipids were measured and compared between the cases and control groups. Blood samples were tested within one hour since they were taken from the patients or within 2 h when samples were been put in the refrigerator.

Pneumonia was diagnosed clinically by major criteria of infection (cough, sputum production, body temperature more than 37.8 °C) or two minor criteria (chest pain due to pleurisy, dyspnea, and pulmonary consolidation by examination), increase WBCS count of more than  $10^3/\text{mm}^3$ , with consolidation in an x-ray, and radiologically by presence of opacity in chest x-ray which was diagnosed as bronchopneumonia or lobar pneumonia, also para pneumonic effusion detected in some cases as opacity obliterating costophrenic angle.

## Results

This prospective study included 42 cases with pneumonia from the Chest Department of Menoufia University and El Mahalla Chest hospital (group A); in addition, a group of 10 healthy people was included as a control group (group B). In group A (patients), there were eighteen males (42.9%) and twenty-four females (57.1%) while in group B (controls), there were three (30%) males and seven (70%) females. In group A, the mean age of the patients was  $51.07 \pm 14.33$  years and group B was  $47.70 \pm 15.78$  years with no statistically significant difference between the two studied groups ( $p = 0.516$ ). The mean smoking index in group A was  $458.8 \pm 259.9$  and group B was  $275 \pm 176.78$  with no statistically significant difference between the studied groups ( $p = 0.35$ ). The mean weight in group A was  $72.8 \pm 7.9$  while in group B, it was  $77.1 \pm 8.7$  ( $p = 0.769$ ). The mean height in group A was  $164.9 \pm 6$  and group B was  $167.0 \pm 7.70$  ( $p = 0.424$ ); the mean BMI in group A was  $26.7 \pm 2.9$  and it was  $26.9 \pm 3.4$  in group B ( $p = 0.714$ ) with no statistical difference, as shown in Table 1.

The mean temperature in group A was  $38.7 \pm 1.77$  which was higher than the mean temperature in group B ( $37.1 \pm 0.37$ ) with no statistical significance difference. The mean heart rate in group A was  $98.72 \pm 10.64$

**Table 1** The data of the studied groups

Data		Groups				$\chi^2$	P value
		Patients (A)		Controls (B)			
		No	%	No	%		
Sex	Male	18	43.9%	3	30.0%	Fisher's exact test 0.641	0.495
	Female	23	56.1%	7	70.0%		
Age (years)	Range Mean $\pm$ SD	51.07 $\pm$ 14.33		47.70 $\pm$ 15.78		0.655	0.516
Smoking (pack/day)	Yes	6	14%	1	10.0%	3.48	0.036
	No	36	86%	9	90.0%		
Smoking index	Mean $\pm$ SD	458.8 $\pm$ 259.9		275 $\pm$ 176.78		0.961	0.350
Weight (kg)	Range	60–85		64–90		0.295	0.769
	Mean $\pm$ SD	72.8 $\pm$ 7.9		77.1 $\pm$ 8.7			
Height (cm)	Range	158–175		157–180		0.806	0.424
	Mean $\pm$ SD	164.9 $\pm$ 6		167.0 $\pm$ 7.70			
BMI (kg/cm <sup>2</sup> )	Range	23.4–32.1		23.2–30.2		0.369	0.714
	Mean $\pm$ SD	26.7 $\pm$ 2.9		26.9 $\pm$ 3.4			

$\chi^2$  Chi-square test, *FET* Fisher's exact test, *SD* Standard deviation, *BMI* Body mass index

P value (Ns, Non significant  $p$  value > 0.05). S significant (\*)  $p$  value < 0.05. Hs Highly significant (\*\*)  $p$  value < 0.001

which was statistically significantly higher as compared with group B ( $89.90 \pm 4.72$ ) ( $p = 0.014$ ). The mean respiratory rate in group A was  $25.08 \pm 2.95$  which was statistically significantly higher as compared with group B ( $18.23 \pm 5.60$ ) ( $p = 0.015$ ).

The mean WBC count in group A was  $14.67 \pm 2.47$  which was statistically significantly higher as compared with group B ( $9.46 \pm 2.03$ ) ( $p = 0.005$ ). The mean neutrophil count in group A was  $74.21 \pm 13.35$  which was statistically significantly higher as compared with group B ( $59.57 \pm 6.25$ ) ( $p = 0.021$ ). The mean lymphocyte in group A was  $19.52 \pm 13.11$  which was statistically significantly lower as compared with group B ( $26.94 \pm 8.68$ ) ( $p = 0.024$ ). The mean NLR in group A was  $7.04 \pm 7.98$  which was statistically significantly higher as compared with group B ( $3.04 \pm 1.6$ ) ( $p = 0.004$ ), as shown in Table 2.

There was a significantly positive correlation between weight and N/L ratio ( $P = 0.008$ ). Otherwise, no statistically significant differences were found ( $p > 0.05$ ), as shown in Table 3.

The mean N/L ratio was significantly higher in females than in males ( $10.4 \pm 6.8$ ,  $4.5 \pm 2.8$ , respectively;  $p = 0.017$ ). The mean N/L ratio in smokers was higher than non-smokers ( $4.7 \pm 2.8$ ,  $3.95 \pm 2.8$ , respectively;  $p = 0.575$ ), with no statistical significance difference, as shown in Table 4.

In the Roc curve of N/L ratio in the case group, the cutoff point is 1.94, and N/L ratio had area under curve of 78% with 79.6% sensitivity and 67.8% specificity, as shown in Table 5 and Fig. 1.

**Table 2** Laboratory investigations in the studied groups

Lab	Group A	Group B	t-test	P-value
WBCs			2.7	0.005**
Mean $\pm$ SD	14.67 $\pm$ 2.47	9.46 $\pm$ 2.03		
Range	10.5–31.9	5.7–10.2		
Neutrophile (%)			19.63	0.021*
Mean $\pm$ SD	79.21 $\pm$ 13.35	59.57 $\pm$ 6.25		
Range	42–92	53–76.9		
Lymphocyte (%)			20.1	0.024*
Mean $\pm$ SD	19.52 $\pm$ 13.11	26.94 $\pm$ 8.68		
Range	5.6–30	19.4–37		
N/L ratio			1.56	0.004**
Mean $\pm$ SD	7.04 $\pm$ 7.98	3.04 $\pm$ 1.6		
Range	0.8–18.4	1.7–6.03		
SPO2 (%)				
Mean $\pm$ SD	90.10 $\pm$ 18.36	96.50 $\pm$ 2.90		
Range	82–95	96–99	–2.39	0.021*

t-test Student's t-test,

SD Standard deviation, WBCs White blood cells, N/L Ratio neutrophil-lymphocyte ratio

P value (Ns Non significant  $p$  value > 0.05). s significant (\*)  $p$  value < 0.05. Hs Highly significant (\*\*)  $p$  value < 0.001

The mean cholesterol level in group A was  $149.76 \pm 42.79$  within the normal range but statistically significantly lower than group B ( $165.90 \pm 45.50$ ) ( $p = 0.039$ ). The mean HDL level in group A was  $43.16 \pm 6.32$  within the normal range which was statistically significantly lower than group B ( $50.51 \pm 9.60$ ) ( $p = 0.026$ ). The triglyceride level, LDL level, and VLDL

**Table 3** Correlation between N/L ratio and demographic data

	N/L ratio	
	R	P value
Age	0.204	0.112
Smoking index	0.350	0.141
weight	0.403	0.008**
height	-0.206	0.142
BMI	0.064	0.654

SD Standard deviation, R Correlation, N/L Ratio neutrophil-lymphocyte ratio, BMI Body mass index

P value (Ns Non significant p value > 0.05). s significant (\*) p value < 0.05. Hs Highly significant (\*\*) p value < 0.001

**Table 4** Relation between Mean N/L ratio and sex and smoking

	Mean N/L ratio	P value
<b>Sex</b>		
• Male	4.5 ± 2.8	0.017
• Female	10.4 ± 6.8	
<b>Smoking</b>		
• None	3.95 ± 2.8	0.575
• Current	4.7 ± 2.8	

P value (Ns Non significant p value > 0.05). s significant (\*) p value < 0.05. Hs Highly significant (\*\*) p value < 0.001

N/L ratio Neutrophil-lymphocyte ratio

were within normal but lower than group B with no statistically significant difference ( $110.61 \pm 25.51$ ,  $94.26 \pm 47.56$ , and  $21.68 \pm 11.33$  and  $120.40 \pm 51.86$ ,  $103.26 \pm 103.94$ , and  $23.33 \pm 8.45$ , respectively, as shown in Table 6).

There was a significant difference between males and females regarding cholesterol levels but there was no statistically significant difference between males and females regarding the rest of the lipid profile. Cholesterol, HDL, and LDL levels were higher in females than in males ( $171.04 \pm 47.4$ ,  $52.87 \pm 12.12$ , and  $104.03 \pm 52.51$  and  $145.11 \pm 33.26$ ,  $48.70 \pm 7.09$ , and  $102.54 \pm 149.95$ , respectively). Triglyceride was higher in males than in females ( $112.16 \pm 30.78$  and  $110.78 \pm 39.63$ , as shown in Table 7).

**Table 5** Roc curve of N/L ratio in the case group

Area	Sensitivity	Specificity	Cut off point	Asymptotic	Asymptotic 95% confidence interval	
					Lower bound	Upper bound
78%	79.6%	67.8%	1.94	0.042	0.356	0.792

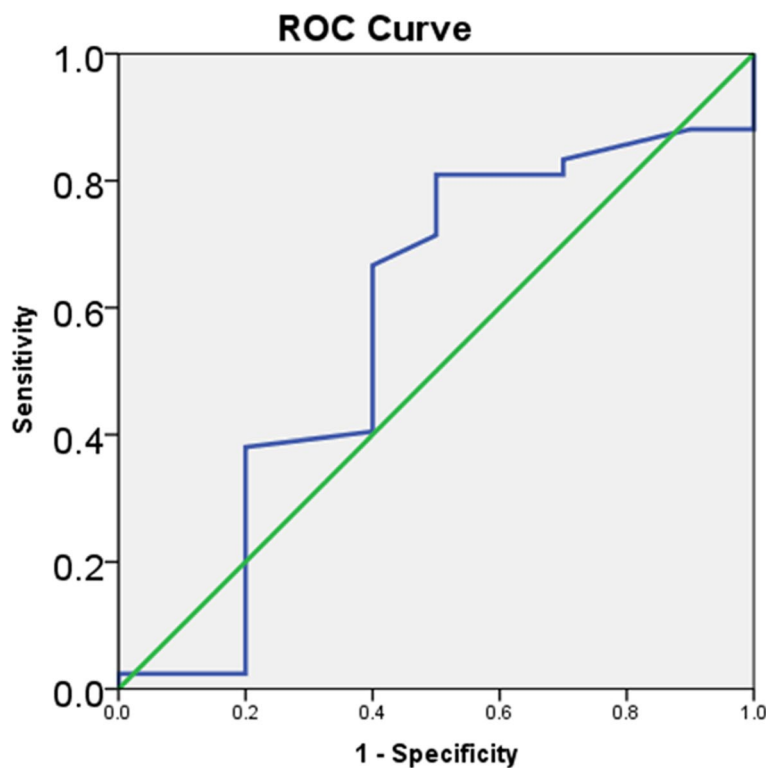
Roc curve Receiver operating characteristic curve, N/L ratio Neutrophil-lymphocyte ratio

There were negative correlations between HDL and age, weight, and BMI ( $-0.166$ ,  $-0.095$ , and  $-0.181$ , respectively) with no statistical significance difference, but there was a negative correlation with smoking index with statistical significance difference ( $-0.181$ ,  $p=0.001$ ). There were positive correlations between cholesterol and smoking index, weight, and BMI ( $0.792$ ,  $0.433$ , and  $0.784$ , respectively) with statistical significance difference ( $p=0.001$ ,  $p=0.004$ , and  $p=0.001$ ). There were positive correlations between triglyceride and smoking index, weight, and BMI ( $0.765$ ,  $0.434$ , and  $0.784$ , respectively). There was a negative correlation between triglyceride and height ( $-0.493$ ,  $p=0.001$ ) with a statistical significance difference. There were positive correlations between LDL and smoking index, weight, and BMI ( $0.750$ ,  $0.422$ , and  $0.789$  and  $p=0.001$ ,  $p=0.005$ , and  $p=0.001$ , respectively) with statistical significance difference. There was a negative correlation between LDL and height ( $-0.514$ ) with a statistical significance difference ( $p=0.001$ ). There were positive correlations between VLDL and smoking index, weight, and BMI ( $0.776$ ,  $0.458$ ,  $0.799$ , respectively) with statistical significance difference ( $p=0.001$ ,  $p=0.002$ , and  $p=0.001$ ). There was a negative correlation between VLDL and height ( $-0.468$ ) with a statistical significance difference ( $p=0.002$ ) as shown in Table 8.

**Discussion**

Pneumonia is an inflammation of the lungs that affects the alveoli or small air sacs. Cough, productive or dry, chest pain, fever, and dyspnea are common symptoms. The severity of the illness varies. Pneumonia is caused by either a viral or bacterial infection. It can be difficult to identify the causative agent. Diagnosis is based on symptoms and physical examination. Chest x-rays, blood tests, and sputum cultures can help confirm the diagnosis. Diseases can be categorized according to where they were obtained. Examples: community-acquired infections, nosocomial infections, or healthcare-associated pneumonia [1].

On laboratory investigations in the studied groups, our results reported that WBCs, neutrophil count, and NLR were statistically significantly higher in group A, while lymphocyte count decreases in group A than in group B with a statistically significant difference. In agreement,



Diagonal segments are produced by ties.

Fig. 1 Roc curve sensitivity and specificity

Table 6 Lipid profile in studied groups

Lipid profile	Group A	Group B	t test	P value
Cholesterol			2.403	0.039*
Mean ± SD	149.76 ± 42.79	165.90 ± 45.50		
Range	88–250	133–250		
Triglyceride			−0.714	0.479
Mean ± SD	110.61 ± 25.51	120.40 ± 51.86		
Range	59–180	61–181		
HDL			2.295	0.026*
Mean ± SD	43.16 ± 6.32	50.51 ± 9.60		
Range	34–98	35–52.3		
LDL			0.266	0.792
Mean ± SD	94.26 ± 47.56	103.26 ± 103.94		
Range	14–146.8	44–177		
VLDL			0.519	0.606
Mean ± SD	21.68 ± 11.33	23.33 ± 8.45		
Range	11.8–47	7–36.2		

t-test Student's t-test, SD Standard deviation, HDL High-density lipoprotein (40–70), LDL Low-density lipoprotein (≤ 130), VLDL Very-low-density lipoprotein (≤ 30)

P value (Ns Non significant p value > 0.05). s significant (\*) p value < 0.05. Hs highly significant (\*\*) p value < 0.001

some studies mentioned by Jennings et al., Ruuskanen et al., and Albrich et al. showed that WBC significantly increased in individuals with bacterial pneumonia. Lee et al. found that NLR was highest in bacterial pneumonia patients [4.1 (2.4–7.0)] than in healthy [1.5 (1.2–2.2)] [8–11].

In the present study, there was a positive non-significant correlation between N/L ratio and age either male or female, smoking index, and BMI. In our study, there was a significantly positive correlation between weight and N/L ratio ( $P=0.008$ ). There was a negative non-significant correlation between N/L ratio and height ( $p=0.142$ ) with no statistically significance difference. NLR was reported by de Jager et al. and Lee et al. as a marker of inflammation in cases with pneumonia [12, 13].

Moreover, multiple cancer studies for survival mentioned by Sarraf et al. and Walsh et al. also mentioned that NLR is a significant predictor of overall and disease-specific survival in patients [14, 15].

As regards Roc curve of N/L ratio in the case group, we found that at cutoff point is 1.94, and N/L ratio had area under curve of 78% with 79.6% sensitivity and 67.8% specificity. Ge et al. mentioned that the AUC of NLR was

**Table 7** Comparison between lipid profiles regarding sex in group A

	Lipid profile				
	Cholesterol	Triglyceride	HDL	LDL	VLDL
<b>Sex</b>					
• Male	145.11 ± 33.26	112.16 ± 30.78	48.70 ± 7.09	102.54 ± 149.95	23.81 ± 8.58
• Female	171.04 ± 47.40	110.78 ± 39.63	52.87 ± 12.12	104.03 ± 52.51	23.28 ± 8.55
• P value	0.056	0.904	0.176	0.965	0.845

P value (Ns Non significant  $p$  value > 0.05). s significant (\*)  $p$  value < 0.05. Hs Highly significant (\*\*)  $p$  value < 0.001

HDL High-density lipoprotein (40–70), LDL Low-density lipoprotein ( $\leq$  130), VLDL Very-low-density lipoprotein ( $\leq$  30)

**Table 8** Correlation between lipid profile and demographic data

	Lipid profile									
	Cholesterol		Triglyceride		HDL		LDL		VLDL	
	R	P value	r	P value	R	P value	R	P value	r	P value
Age	0.001	0.997	0.103	0.522	-0.166	0.298	0.001	0.995	0.079	0.622
Smoking index	0.792**	0.001	0.765**	0.001	-0.181	0.001	0.750**	0.001	0.776**	0.001
Weight	0.433**	0.004	0.434**	0.004	-0.095	0.548	0.422**	0.005	0.458**	0.002
Height	-0.485**	0.001	-0.493**	0.001	0.088	0.578	-0.514**	0.001	-0.468**	0.002
BMI	0.784**	0.001	0.784**	0.001	0.181	0.250	0.789**	0.001	0.799**	0.001

P value (Ns Non significant  $p$  value > 0.05). s significant (\*)  $p$  value < 0.05. Hs Highly significant (\*\*)  $p$  value < 0.001

R Correlation, HDL High-density lipoprotein (40–70), LDL Low-density lipoprotein ( $\leq$  130), VLDL Very-low-density lipoprotein ( $\leq$  30), BMI Body mass index

0.81 (95% CI 0.73 to 0.89), the sensitivity was 81.00%, and the specificity was 72.8%. NLR is superior to CURB-65 in unfavorable prognosis prediction. NLR and CURB-65 improve the sensitivity and specificity (89.40% versus 91.30%) [16].

In the present study, there was positive non-significant relation between N/L ratio and smoking ( $p=0.575$ ). the same result was reported by Mukta Pujani et al. There was no significant difference in the NLR among the smokers and non-smokers ( $2.61 \pm 1.99$ ), ( $2.48 \pm 2.30$ ) respectively. [17].

In the present study, there was a positive significant difference between the mean N/L ratio and sex as it was  $4.5 \pm 2.8$  and  $10.4 \pm 6.8$  between males and females, respectively. On contrary to the present study, Lin BD et al. mentioned that women with lower mean NLR levels than men [18].

HDL and cholesterol levels decrease in group A with a statistically significant difference, while there was no statistically significant difference in the triglyceride level, LDL level, and VLDL between the subjects in the two study groups ( $p=0.479$ ,  $0.792$ , and  $0.606$ , respectively). In agreement with our study, Ko et al. found that a low level of total serum cholesterol at admission in the pneumonia group with a statically significant difference. In disagreement with our study, Chien et al. found that serum HDL,

cholesterol, and LDL on admission had no significant difference between the two studied groups [19, 20].

In our study, cholesterol, HDL, and LDL levels were higher in females than in males ( $171.04 \pm 47.4$ ,  $52.87 \pm 12.12$ , and  $104.03 \pm 52.51$  and  $145.11 \pm 33.26$ ,  $48.70 \pm 7.09$ , and  $102.54 \pm 149.95$ , respectively). Triglyceride was higher in males than females ( $112.16 \pm 30.78$ ,  $110.78 \pm 39.63$ ) with no statistical significance difference. Cholesterol level was higher in smokers than in non-smokers ( $167.58 \pm 47.85$ ,  $125.83 \pm 20.95$ , respectively) with a statistical significant difference. Triglyceride, LDL, and VLDL were higher in smokers than in non-smokers ( $134.50 \pm 31.16$ ,  $126.99 \pm 129.45$ , and  $26.90 \pm 6.23$ , respectively) with no statistical significance difference. According to a study done by Freitas et al., cholesterol, LDL, and triglyceride were higher in males than in females ( $153 \pm 45.3$ ,  $79 \pm 15.5$ , and  $135 \pm 10.3$ , respectively) while HDL was higher in females than in males ( $56 \pm 12.09$ ,  $49 \pm 7.09$ , respectively). HDL levels showed decreased levels in smokers than in non-smokers ( $51 \pm 6.08$ ,  $54 \pm 6.30$ , respectively) with a statistically significant difference [21].

In our study, there were positive correlations between cholesterol, triglyceride, LDL, VLDL, and BMI ( $p=0.001$ ) with a statistically significant difference, while there was a negative correlation between HDL and BMI ( $r= -0.181$ ,

$p=0.250$ ) with no statistically significant difference. According to Reddy RR and Nambiar S., it was observed that there was a positive correlation between TC, LDL, and BMI with a statistically significant difference [22].

## Conclusion

There was a significant decrease in serum cholesterol and HDL in cases with pneumonia when compared to the control group but still within the normal range. Lipid profile is affected by different variables like smoking index, body mass index, and sex. The neutrophil-lymphocyte ratio (NLR) is a cheap diagnostic tool in the assessment of patients with pneumonia in daily practice at a cutoff point of 1.94 and N/L ratio with 79.6% sensitivity and 67.8% specificity.

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Not applicable.

## Authors' contributions

Hesham E. Abd El-Aaty: conceptualization, methodology, supervision. Ibrahim I. El-Mahallawy: data curation, methodology, supervision. Fatma G. Abd Elmaksoud: writing—review and editing. Gehan A. Abdelaal: visualization, investigation, validation, supervision. The authors read and approved the final manuscript.

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## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

A written informed consent was obtained from every participant or his representatives prior to inclusion in the study after detailed explanation of the work, and approval from Menoufia Ethical Committee was obtained.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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