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(RESEARCH ARTICLE)

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Corticosteroidal impacts on white blood cells differentials in ear-nose-throat admitted infected patients

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Abstract

Background/aim: It is well-established that the use of corticosteroidal agents in patients with Ear-Nose-Throat infections can lead to an increased risk of infection recurrence, while also potentially prolonging the duration of the infection. It is crucial to ensure a proper equilibrium between the advantages and drawbacks of the corticosteroidal agent. This study investigates the effects of corticosteroids on specific subsets of immune cells in patients admitted to the Ear-Nose-Throat department with infections.

Methods: This study was conducted retrospectively from March 2020 to September 2021. The variables that were measured and calculated were categorised into parametric and non-parametric data. The parametric data were compared between the two groups, Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II), using Independent, One-Sample T-Tests, and Chi-Square Test.

Results: The average age of the entire study cohort was 59.40±10.60 years. There was a slightly higher proportion of males compared to females, with a ratio of approximately 2.309:1. The haematological analysis revealed a decrease in the levels of white blood cells, absolute neutrophils, monocytes, and the monocytes to lymphocytes ratio in Cohort I when compared to Cohort II. The levels of prognosticator biomarkers and their ratios were significantly lower in Cohort I when compared to Cohort II. Cohort II exhibited a significantly reduced hospital length of stay and a lower mortality rate among admitted infected patients in the ear-nose-throat infection, in comparison to Cohort I.

Conclusion: Our analysis determined that Dexamethasone 6 mg/day provides a substantial survival advantage for patients with higher baseline risk upon admission. This benefit is associated with a decrease in the counts of neutrophils and monocytes, as well as a decrease in the ratio of these counts to lymphocyte count.

Keywords: Monocytes; Lymphocytes; Monocytes to Lymphocytes ratio; Ear-nose-throat infection

1. Introduction

Due to their slow and harmful progression, ear-nose-throat infections have strained the medical system. Due to their modernization and the involvement of other organs not related to respiration, ear-nose-throat infections are a major concern that requires collaboration. Some susceptible ear-nose-throat patients develop severe respiratory, cardiovascular, immune, and cerebral complications in addition to their usual symptoms. Four to five values are possible. Some patients with severe ear-nose-throat infections are admitted, causing hyperinflammation. Infection dissemination to the brain is a significant consequence of hyperinflammatory reactions, including increased production of pro-inflammatory cytokines like IL-6 and TNF-α. [9-10] Corticosteroids are the main treatment for infected ear-nose-throat patients. These agents target hyper-inflammatory cascades and oxidative stress, which are linked to overactive

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immune responses. They supplement supportive care and proposed anti-bacterial and anti-viral chemotherapies. Well-studied corticosteroidal agent dexamethasone, given at 6 mg per day, treats ear-nose-throat infections and their complications. 1-3.

Corticosteroidal agents in hyper-inflammatory oxidative stress can increase neutrophil production, inflating the Absolute Neutrophils Count. Monocytes and lymphocytes react inversely to corticosteroids, unlike neutrophils. The NLR and MLR are calculated by dividing the number of neutrophils and monocytes by the number of lymphocytes. Both NLR and MLR indicate pathogen-induced systemic inflammation. Viral infections lower NLR and MLR, while bacterial infections increase both. With corticosteroidal agents, the NLR to MLR ratio is 10:1, which is much higher in infected patients, including those with ear-nose-throat infections. Corticosteroids increase the neutrophil-to-lymphocyte ratio (NLR) but not the monocyte-to-lymphocyte ratio. According to empirical evidence, both ratios are used in clinical settings as biomarkers for diagnosis, prognosis, and differentiation between viral, bacterial, and non-infectious hyper-inflammatory oxidative stress conditions. A higher NLR or MLR indicates a higher risk of bacterial infection than non-infectious or viral-related systemic inflammatory response syndrome. [4-6]

It is well established that the use of corticosteroidal agents during viral infections can lead to prolonged viral shedding and, as a result, may be associated with reduced viral clearance. [20] Although these findings outline the potential hazards of using steroids to treat these infections, data on related inflammation suggest potential advantages. Specific areas of concern include the impact of corticosteroidal agents on different subsets and ratios of immune cells, as well as the resulting clinical consequences of these harmful changes in biochemical and clinical variables studied in infected patients admitted to the ear-nose-throat department. [7-8]

The main objective of this study was to examine the effects of corticosteroids on specific subsets of immune cells in patients admitted to the Ear-Nose-Throat department with infections. Additionally, our objective was to investigate the overall clinical effects of our examined cohort of infected patients admitted to the ear-nose-throat department, specifically in terms of their hospital stay duration and mortality rate.

2. Methods

This retrospective study was conducted at Jordan's King Hussein Military Hospital of the Royal Medical Services (RMS), which treats infected ear, nose, and throat patients. Our electronic medical record system (Hakeem) provided retrospective data on admitted and infected ear-nose-throat patients from March 2020 to September 2021. Patients under 18, with a hospital length of stay (LOS) of more than 7 days, taking a corticosteroidal drug regimen other than Dexamethasone 6 mg per day, and with missing variables were excluded from our study. Our study was retrospective, so a signed consent form was waived. Our institutional review board approved the study. All eligible ear-nose-throat infection patients in this study had moderate to severe disease severity. The eligible cohort's demographic, anthropometric, biochemical, and nutritional data were retrospectively retrieved from Hakeem. The primary retrievable data was also used to calculate prognosticator ratios like CRP: ALB, FER: ALB, NLR, and MLR. Piperacillin/Tazobactam (Tazocin®), Imipenem/Cilastatin (Tienam®), and Meropenem (Meronem®) doses were recorded. We determined the optimal antibiotic dosage based on the study patients' creatinine clearance (CrCl). Subtracting the calculated optimal dosing from the prescribed dosing yielded antibiotic dosing deficits. Based on blood glucose and pH, sodium and potassium levels were adjusted. The average of all biochemical data was calculated from at least two measurements. There were parametric and non-parametric variables to calculate. Independent and One-Sample T-Tests compared parametric data from Cohort I and Cohort II. Table 1-5 displays the analysis results as Mean±SD or Mean difference±SEM. For non-parametric variables, the Chi-Square Test was used. Number (Percentage) and odds ratio (OD) were used to express outcome results and relative risk estimates. Table 6-7 summarises these findings.

Table 1 Comparatively studied variables between Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II)

Studied Comparative Variables	**Overall Cohorts (N=781) Mean±SD**	**Cohort I (Non_Dexa Cohort) (N=376, 48.14%) Mean±SD**	**Cohort II (Dexa Cohort) (N=405, 51.86%) Mean±SD**	**Mean Differences ±SEM**	**P-Value**
Age (Yrs)	59.40±10.60	59.26±10.60	59.54±10.62	-0.28±0.76	0.71
BW (Kg)	73.73±10.02	74.05±10.31	73.43±9.75	0.62±0.72	0.39
BMI (Kg/m^2)	25.95±3.89	26.01±3.92	25.88±3.87	0.13±0.28	0.65
ALB $_1$ (g/dl)	2.21±0.38	2.38±0.37	2.04±0.31	0.35±0.02	0.00*
ALB $_2$ (g/dl)	3.19±0.64	3.45±0.64	2.94±0.54	0.52±0.04	0.00*
%ΔALB 12	44.7%±19.3%	45.5%±25.9%	44.0%±9.8%	1.4%±1.4%	0.304
HALB (g/day)	12.97±4.90	15.40±5.60	10.72±2.58	4.68±0.31	0.00*
Temp $_{avg1}$	37.95±0.69	37.62±0.72	38.25±0.50	-0.62±0.04	0.00*
Temp $_{avg2}$	37.47±0.47	37.49±0.54	37.45±0.39	0.04±0.03	0.20
PARA dose (g/day)	1.90±0.94	2.45±0.97	1.40±0.55	1.05±0.06	0.00*
SCr $_1$ (mg/dl)	1.12±0.18	1.08±0.19	1.15±0.16	-0.08±0.01	0.00*
BUN $_1$ (mg/dl)	13.16±2.20	12.62±2.34	13.66±1.93	-1.04±0.15	0.00*
BUN: SCr $_1$	11.76±0.40	11.68±0.48	11.84±0.29	-0.16±0.03	0.008
SCr $_2$ (mg/dl)	1.70±0.67	1.56±0.87	1.83±0.34	-0.27±0.05	0.00*
BUN $_2$ (mg/dl)	14.91±4.38	13.83±5.61	15.91±2.40	-2.08±0.30	0.00*
BUN: SCr $_2$	8.93±0.60	9.13±0.69	8.75±0.43	0.38±0.04	0.00*
CrCl $_{Jelliffe\ eq}$ (ml/min)	45.02±17.20	51.13±19.10	39.35±12.86	11.77±1.16	0.00*
BG $_1$ (mg/dl)	283.1±78.0	269.1±101.4	296.1±43.1	-27.0±5.5	0.00*
cNa $_1$ (mEq/l)	126.8±2.8	128.2±2.6	125.5±2.4	2.7±0.2	0.00*
BG $_2$ (mg/dl)	152.0±36.3	159.5±48.7	145.0±15.6	14.5±2.6	0.00*
cNa $_2$ (mEq/l)	137.8±4.4	140.2±4.0	135.6±3.5	4.5±0.3	0.00*
Insulin dose (IU/day)	32.10±1.96	32.79±2.16	31.46±1.50	1.32±0.13	0.00*
HLOS	11.23±2.85	12.14±3.55	10.38±1.58	1.76±0.19	0.00*
Data results of the comparative variables between Group I and Group II were statistically analyzed by independent T and One-Sample T-Test (at p-value< 0.05) and expressed as Mean±SD and Mean difference±SEM.					
1: Baseline. BW: Bodyweight. BMI: Body Mass Index. ALB: Albumin level. HALB: Human Albumin. SCr: Serum creatinine. BUN: Blood Urea Nitrogen.		CrCl: Creatinine Clearance. Temp: Temperature. PARA: Paracetamol. BG: Blood glucose level. cNa: Corrected sodium level. HLOS: Hospital length of stay.			

Table 2 (Continued). Comparatively studied variables between Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II)

Studied Comparative Variables	**Overall Cohorts (N=781) Mean±SD**	**Cohort I (Non_Dexa Cohort) (N=376, 48.14%) Mean±SD**	**Cohort II (Dexa Cohort) (N=405, 51.86%) Mean±SD**	**Mean Differences ±SEM**	**P-Value**
DBP $_{avg1}$ (mmHg)	54.70±3.83	55.75±4.45	53.72±2.81	2.03±0.26	0.00*
SI $_{avg1}$ (bpm/mmHg)	1.08±0.09	1.06±0.11	1.10±0.06	-0.04±0.01	0.00*
mSI $_{avg1}$ (bpm/mmHg)	1.49±0.15	1.46±0.18	1.52±0.10	-0.06±0.01	0.00*
DBP $_{avg2}$ (mmHg)	80.86±2.02	79.78±2.10	81.86±1.30	-2.08±0.12	0.00*
SI $_{avg2}$ (bpm/mmHg)	0.85±0.11	0.91±0.12	0.79±0.08	0.12±0.01	0.00*
mSI $_{avg2}$ (bpm/mmHg)	1.08±0.15	1.16±0.15	1.01±0.10	0.15±0.01	0.00*
%Δ DBP $_{avg12}$	48.8%±14.6%	44.4%±17.7%	52.8%±9.2%	-8.4%±1.0%	0.00*
%Δ SI $_{avg12}$	-20.5%±14.6%	-12.9%±14.9%	-27.5%±9.9%	14.7%±0.9%	0.00*
%Δ mSI $_{avg12}$	-26.5%±14.1%	-19.2%±14.5%	-33.3%±9.6%	14.1%±0.9%	0.00*
BIL $_1$ (mg/dl)	1.57±0.05	1.60±0.06	1.55±0.03	0.05±0.00	0.00*
BIL $_2$ (mg/dl)	2.57±0.19	2.66±0.21	2.48±0.12	0.18±0.01	0.00*
INR $_1$	1.53±0.05	1.55±0.05	1.51±0.03	0.04±0.00	0.00*
INR $_2$	2.59±0.12	2.65±0.13	2.54±0.08	0.10±0.01	0.00*
FLUD Input (ml/day)	2823±40	2831±49	2816±29	15±3	0.00*
ENF Input (ml/day)	291±171	355±177	230±141	125±11	0.00*
TCI (Cal/day)	572±219	629±235	518±187	110±15	0.00*
PD (g/100 Cal)	2.05±1.01	2.29±0.96	1.83±1.01	0.46±0.07	0.00*
CarbD (g/100 Cal)	20.04±4.62	18.96±4.39	21.05±4.61	-2.09±0.32	0.00*
pH $_1$	7.34±0.12	7.37±0.15	7.32±0.06	0.05±0.01	0.00*
cK $_1$ (mEq/l)	2.93±0.86	3.12±1.12	2.75±0.46	0.37±0.06	0.00*
pH $_2$	7.34±0.12	7.37±0.15	7.32±0.06	0.05±0.01	0.00*
cK $_2$ (mEq/l)	3.06±1.07	3.00±1.13	3.11±1.00	-0.11±0.08	0.15

•Data results of the comparative variables between Group I and Group II were statistically analyzed by independent T and One-Sample T-Test (at p-value< 0.05) and expressed as Mean±SD and Mean difference±SEM.

DBP: Diastolic blood pressure.
SI: Shock Index.
mSI: Modified Shock Index.
INR: International Normalized Ratio.
BIL: Bilirubin level.
FLUD: Total fluid (PO/IV) inputs.
ENF: Enteral Nutritional Feeding.
TCI: Total Calories Inputs.
PD: Protein Densities in g per 100 Cal.
CarbD: Carb Density in g/100 Cal.
cK: Corrected potassium levels.

Table 3 (Continued). Comparatively studied variables between Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II)

Studied Comparative Variables	**Overall Cohorts (N=781) Mean±SD**	**Cohort I (Non_Dexa Cohort) (N=376, 48.14%) Mean±SD**	**Cohort II (Dexa Cohort) (N=405, 51.86%) Mean±SD**	**Mean Differences ±SEM**	**P-Value**
WBC $_1$ (Cells/µl)	14036±3099	13388±3820	14638±2058	-1251±217	0.00*
TLC $_1$ (Cells/µl)	1635±798	1586±990	1681±562	-95±57	0.00*
ANC $_1$ (Cells/µl)	10902±2051	10374±2511	11392±1331	-1018±142	0.00*
MC $_1$ (Cells/µl)	1090±205	1037±251	1139±133	-102±14	0.00*
NLR $_1$	7.90±3.15	8.29±3.56	7.53±2.68	0.76±0.22	0.00*
MLR $_1$	0.79±0.32	0.83±0.36	0.75±0.27	0.08±0.02	0.00*
WBC $_2$ (Cells/µl)	15487±2851	14647±3275	16266±2115	-1620±196	0.00*
TLC $_2$ (Cells/µl)	2733±1298	2506±1545	2945±972	-439±92	0.00*
ANC $_2$ (Cells/µl)	10342±1973	10146±2408	10524±1437	-379±141	0.00*
MC $_2$ (Cells/µl)	819±156	853±198	786±90	67±11	0.00*
NLR $_2$	5.6±10.7	5.8±4.0	5.5±14.4	0.3±0.8	0.7
MLR $_2$	0.4±0.8	0.5±0.3	0.4±1.0	0.1±0.1	0.2
•Data results of the comparative variables between Group I and Group II were statistically analyzed by independent T and One-Sample T-Test (at p-value< 0.05) and expressed as Mean±SD and Mean difference±SEM.					
WBCs: White blood cells. TLC: Total lymphocytes counts. ANC: Absolute neutrophils count.		MC: Monocytes count. NLR: Neutrophils to Lymphocytes ratio. MLR: Monocytes to Lymphocytes ratio.			

Table 4 (Continued). Comparatively studied variables between Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II)

Studied Comparative Variables	**Overall Cohorts (N=781) Mean±SD**	**Cohort I (Non_Dexa Cohort) (N=376, 48.14%) Mean±SD**	**Cohort II (Dexa Cohort) (N=405, 51.86%) Mean±SD**	**Mean Differences ±SEM**	**P-Value**
Prescribed PIP/TAZ (mg/day)	11261±2375	11942±2338	10623±2233	1320±228	0.00*
Optimal** PIP/TAZ (mg/day)	15677±2565	16315±2658	15079±2328	1236±248	0.00*
Deficit*** PIP/TAZ (mg/day)	-4416±426	-4373±520	-4457±310	84±42	0.00*
% Deficit PIP/TAZ	-28.7%±4.1%	-27.2%±3.7%	-30.1%±4.1%	2.9%±0.4%	0.00*
Prescribed MER (mg/day)	2286±595	2566±597	2055±485	511±76	0.00*

Optimal** MER (mg/day)	4572±1190	5132±1195	4109±971	1023±153	0.00*
Deficit*** MER (mg/day)	-2286±595	-2566±597	-2055±485	-511±76	0.00*
% Deficit MER	-50.0%±0.0%	-50.0%±0.0%	-50.0%±0.0%	NA	NA
Prescribed IMI/CIL (mg/day)	1308±353	1411±348	1201±328	210±51	0.00*
Optimal** IMI/CIL (mg/day)	1850±451	1978±479	1718±379	259±65	0.00*
Deficit*** IMI/CIL (mg/day)	-542±140	-567±171	-517±92	-49±21	0.00*
% Deficit IMI/CIL	-29.8%±5.9%	-28.9%±5.5%	-30.9%±6.1%	2.0%±0.9%	0.024*
%Δ WBC $_{12}$	-14.4%±37%	8.0%±34.1%	-35.2%±24.6%	43.3%±2.1%	0.00*
%Δ TLC $_{12}$	149%±70.2%	148.4%±78.1%	148.4%±62.0%	0.0%±5.0%	0.995
%Δ ANC $_{12}$	-28.6%±38%	-5.2%±35.3%	-50.3%±25.8%	45.1%±2.2%	0.00*
%Δ MC $_{12}$	-36.1%±47%	-6.2%±42.0%	-63.8%±30.7%	57.7%±2.6%	0.00*
%Δ NLR $_{12}$	-33.7%±72%	-31.1%±29.2%	-36.2%±96.2%	5.1%±5.2%	0.322
%Δ MLR $_{12}$	-48.1%±52%	-43.2%±20.5%	-52.7%±68.5%	9.5%±3.7%	0.01*

•Data results of the comparative variables between Group I and Group II were statistically analyzed by independent T and One-Sample T-Test (at p-value< 0.05) and expressed as Mean±SD and Mean difference±SEM.

Optimal**: Optimal dosing of the selected antibiotics based on the calculated CrCl.

Deficit***: Deficit dosing of the corresponding antibiotics was calculated by subtracting the prescribed dose from the optimal dose and consequently the %Deficit was obtained by dividing the deficit dosing over the prescribed dose.

NA: Not-Applicable and statistically can't be computed.
WBCs: White blood cells.
TLC: Total lymphocytes counts.
ANC: Absolute neutrophils count.
MC: Monocytes count.

NLR: Neutrophils to Lymphocytes ratio.
MLR: Monocytes to Lymphocytes ratio.
PIP/TAZ: Piperacillin/Tazobactam (Tazocin®).
MER: Meropenem (Meronem®).
IMI/CIL: Imipenem/Cilastatin (Tienam®).

Table 5 (Continued). Comparatively studied variables between Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II)

Studied Comparative Variables	**Overall Cohorts (N=781) Mean±SD**	**Cohort I (Non_Dexa Cohort) (N=376, 48.14%) Mean±SD**	**Cohort II (Dexa Cohort) (N=405, 51.86%) Mean±SD**	**Mean Differences ±SEM**	**P-Value**
FER $_1$ (ng/ml)	746.5±310.7	692.8±404.9	796.3±170.4	-103.5±22.0	0.00*
FER: ALB $_1$	362.1±206.2	317.9±268.8	403.2±107.3	-85.3±14.5	0.00*
(FER: ALB): LNR $_1$	2514.0±829.3	2172.2±953.3	2831.4±523.9	-659.2±54.5	0.00*
(FER: ALB): LMR $_1$	251.4±82.9	217.2±95.3	283.1±52.4	-65.9±5.5	0.00*
FER $_2$ (ng/ml)	433.9±294.0	502.7±391.5	370.0±127.0	132.6±20.5	0.00*

FER: ALB $_2$	145.5±145.4	162.6±200.4	129.6±55.0	33.0±10.4	0.00*
(FER: ALB): LNR $_2$	673.0±801.2	745.9±559.7	605.2±969.0	140.7±57.2	0.00*
(FER: ALB): LMR $_2$	53.2±61.0	62.2±49.1	44.8±69.2	17.3±4.3	0.00*
%ΔFER $_{12}$	-39.6%±24.6%	-25.9%±26.4%	-52.4%±13.6%	26.4%±1.5%	0.00*
%ΔFER: ALB $_{12}$	-58.2%±15.5%	-48.8%±15.1%	-67.0%±9.6%	18.2%±0.9%	0.00*
%Δ (FER: ALB): LNR $_{12}$	-68.4%±47.1%	-61.3%±23.6%	-75.0%±60.6%	13.7%±3.3%	0.00*
%Δ (FER: ALB): LMR $_{12}$	-75.2%±34.1%	-68.3%±17.7%	-81.6%±43.2%	13.2%±2.4%	0.00*
CRP $_1$ (mg/dl)	73.24±31.21	67.64±40.57	78.44±17.24	-10.80±2.20	0.00*
CRP: ALB $_1$	35.57±20.60	31.09±26.81	39.74±10.77	-8.65±1.44	0.00*
(CRP: ALB): LNR $_1$	246.3±83.2	211.5±95.5	278.6±52.3	-67.1±5.5	0.00*
(CRP: ALB): LMR $_1$	24.6±8.3	21.2±9.6	27.9±5.2	-6.7±0.5	0.00*
CRP $_2$ (mg/dl)	41.59±29.06	47.61±38.98	36.00±12.46	11.61±2.04	0.00*
CRP: ALB $_2$	14.01±14.39	15.49±19.87	12.63±5.42	2.87±1.03	0.00*
(CRP: ALB): LNR $_2$	63.7±72.4	69.9±54.5	57.8±85.4	12.1±5.2	0.00*
(CRP: ALB): LMR $_2$	5.0±5.6	5.8±4.8	4.3±6.1	1.6±0.4	0.00*
%Δ CRP $_{12}$	-41.3%±24.2%	-28.6%±26.8%	-53.0%±13.1%	24.4%±1.5%	0.00*
%Δ CRP: ALB $_{12}$	-59.3%±14.8%	-50.6%±14.7%	-67.4%±9.2%	16.8%±0.9%	0.00*
%Δ (CRP: ALB): LNR $_{12}$	-69.4%±44.1%	-62.8%±22.7%	-75.6%±56.5%	12.9%±3.1%	0.00*
%Δ (CRP: ALB): LMR 12	-76.0%±32.0%	-69.5%±17.1%	-82.0%±40.4%	12.5%±2.2%	0.00*
•Data results of the comparative variables between Group I and Group II were statistically analyzed by independent T and One-Sample T-Test (at p-value< 0.05) and expressed as Mean±SD and Mean difference±SEM.					

FER: Ferritin level. ALB: Albumin level. CRP: C-Reactive protein level. CRP: ALB: C-Reactive Protein to Albumin levels Ratio.	FER: ALB: Ferritin to Albumin levels Ratio. LNR: Lymphocytes to Neutrophils Ratio. LMR: Lymphocytes to Monocytes Ratio.

3. Results

This study included 718 eligible ear-nose-throat infected patients admitted to our isolation departments at the King Hussein Military Hospital of the Royal Medical Services (RMS) in Jordan between March 2020 and September 2021. Of these, 247 (31.6%) had suspected infections and 534 (68.4%) had confirmed infections. Study participants had a mean age of 59.40±10.60 years, with the Non-Dexamethasone Cohort slightly younger than the Dexamethasone Cohort (59.26±10.60 years vs. 59.54±10.62 years, P-value=0.7 Males outnumbered females in the study by 2.309:1 (545 (69.8%) vs. 236 (30.2%), p-vale=0.829), with 69.4% (261 ear-nose-throat admitted infected patients infected men) and 30.6% (115). Retrospectively, 76 (9.7%), 332 (42.5%), 357 (45.7%), and 16 (2.0%) were on non-O2 supply, nasal cannula at 3-6 L/min, non-invasive mechanical ventilation, and invasive mechanical ventilation. Cohort I received more human albumin (15.40±5.60 g/day vs 10.72±2.58 g/day, +4.68±0.31, p-value=0.00) than Cohort II, but their serum albumin levels (%ΔALB 12) were not significantly different (45.5%±25.9% vs 44.0%±9.8%, +1.4%±1.4%, Cohort I displayed a significantly higher average Paracetamol dose (2.45±0.97 g/day vs 1.40±0.55 g/day, +1.05±0.06, p-value=0.00) and a higher IV distribution (246 (65.4%) vs 130 (34.6%)) than Cohort II (37 (9.1%) vs 368 (90.9%)). Cohort I had 181 (48.1%) and 195 (51.9%) non-Tazocin® antibiotics, while Cohort II had 197 (48.6%) and 208 (51.4%).

The Jelliffe equation showed that Cohort I had a significantly lower Tazocin® deficit than Cohort II (-4373±520 mg/day vs -4457±310 mg/day, +84±42 mg/day, p-value=0.00 In Cohort I, average corrected sodium levels (cNa) were higher (140.2±4.0 mEq/l vs 135.6±3.5 mEq/l, +4.5±0.3 mEq/l, p-value=0.00) and hyponatremia incidence was higher (368 (90.9%) vs 175 (46.5%), retrospectively, p- In Cohort I, blood glucose levels and insulin needs were significantly higher than in Cohort II (retrospective p-value=0.00, 159.5±48.7 mg/dl and 32.79±2.16 IU/day vs 145.0±15.6 mg/dl and 31.46±1.50. Cohort II patients had significantly lower bilirubin and INR levels than Cohort I (2.48±0.12 mg/dl and 2.54±0.08 vs 2.66±0.21 and 2.65±0.13, respectively, p-value=0.00). In Cohort I, calorie intake and protein density were significantly higher than in Cohort II (629±235 Cal/day and 2.29±0.96 g/100 Cal vs 518±187 Cal/day and 1.83±1.01 g/100 Cal, p-value=0.00). Compared to Cohort II (Dexamethasone Cohort), Cohort I (Non-Dexamethasone Cohort) had significantly lower reductions in white blood cell, absolute neutrophil, monocyte, and monocyte-to-lymphocyte ratios (%ΔWBCs12, %ΔANC12, %ΔMC12, and %ΔMLR12) [+8.0%±34.1%, -5.2%±35.3%, -6.2%±42.0%, and -43.2%± Cohort I had significantly lower reduction rates in FER: ALB and CRP: ALB compared to Cohort II (%ΔFER: ALB 12 and %ΔCRP: ALB 12, p-value=0.00). Cohort I had significantly lower inverse haematological ratios of lymphocytes to neutrophils (LNR) and monocytes (LMR) than Cohort II (-61%) when combined with two phase reactant ratios. Dexamethasone 6 mg/day significantly reduced hospital stay and mortality rates for ear-nose-throat infections in Cohort II (10.38±1.58 days and 20 (4.9%) vs. Cohort I). Both cohorts had similar baseline anthropometrics.

Table 6 (Continued). Comparatively studied variables between Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II)

Studied Comparative Variables		**Overall Cohorts (N=781) N (%)**	**Cohort I (Non_Dexa Cohort) (N=376, 48.14%) N (%)**	**Cohort II (Dexa Cohort) (N=405, 51.86%) N (%)**	**OD**	**P-Value**
Gender	F	236 (30.2%)	115 (30.6%)	121 (29.9%)	1.03 (95% CI; 0.76-1.4)	0.829
	M	545 (69.8%)	261 (69.4%)	284 (70.1%)		
	M: F ratio	2.309:1	2.27: 1	2.35: 1		
O2 Supply	None	76 (9.7%)	76 (20.2%)	0 (0.0%)	NA	0.00*
	NC (3-6 L/min)	332 (42.5%)	205 (54.5%)	127 (31.4%)		
	NIMV	357 (45.7%)	95 (25.3%)	262 (64.7%)		
	IMV	16 (2.0%)	0 (0.0%)	16 (4.0%)		
PARA	Oral	498 (63.8%)	130 (34.6%)	368 (90.9%)	0.05 (95% CI; 0.04-0.08)	0.00*
	IV	283 (36.2%)	246 (65.4%)	37 (9.1%)		
cNa	<140	543 (69.5%)	175 (46.5%)	368 (90.9%)	0.09 (95% CI; 0.06-0.13)	0.00*
	≥140	238 (30.5%)	201 (53.5%)	37 (9.1%)		
MORT	Survivors	626 (80.2%)	241 (64.1%)	385 (95.1%)	0.09 (95% CI; 0.06-0.15)	0.00*
	Non-Survivors	155 (19.8%)	135 (35.9%)	20 (4.9%)		
Data results of the comparative variables between the 2 tested cohorts were statistically analyzed by Chi-Square Test (at p-value< 0.05) and expressed as Number (Percentage).						
*: Significant (P-Value <0.05). N: Number of tested EAR-NOSE-THROAT ADMITTED INFECTED PATIENTS infected patients. NC: Nasal Cannula on an Oxygen flow rate of 3-6 L/min. NIMV: Non-Invasive Mechanical Ventilation. IMV: Invasive Mechanical Ventilation. cNa: Sodium level after correction with BG.				F: Female. M: Male. M: F: Male to Female ratio. 02: Oxygen. PARA: Paracetamol. NA: Not statistically applicable and can't be computed.		

Table 7 (Continued). Comparatively studied variables between Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II)

Studied Comparative Variables		**Overall Cohorts (N=781) N (%)**	**Cohort I (Non_Dexa Cohort) (N=376, 48.14%) N (%)**	**Cohort II (Dexa Cohort) (N=405, 51.86%) N (%)**	**OD**	**P-Value**
EAR-NOSE-THROAT ADMITTED INFECTED PATIENTS	Suspected	247 (31.6%)	116 (30.9%)	131 (32.3%)	0.93 (95% CI; 0.69-1.26)	0.654
	Confirmed	534 (68.4%)	260 (69.1%)	274 (67.7%)		
FER: ALB RSI	≥60	343 (43.9%)	80 (21.3%)	263 (64.9%)	0.15 (95% CI; 0.11-0.20)	0.00*
	<60	438 (56.1%)	296 (78.7%)	142 (35.1%)		
ABs Allocation	Non-Tazocin	378 (48.4%)	181 (48.1%)	197 (48.6%)	0.98 (95% CI; 0.74-1.29)	0.888
	Tazocin	403 (51.6%)	195 (51.9%)	208 (51.4%)		
	PIP/TAZ	403 (51.6%)	195 (51.9%)	208 (51.4%)	NA	0.551
	MER	201 (25.7%)	91 (24.2%)	110 (27.2%)		
	IMP/CIL	177 (22.7%)	90 (23.9%)	87 (21.5%)		
Isolated Gram Negative Bacteria	Non-Isolated	253 (32.4%)	122 (32.4%)	131 (32.3%)	NA	0.501
	Acinetobacter	49 (6.3%)	21 (5.6%)	28 (6.9%)		
	E. Coli	74 (9.5%)	35 (9.3%)	39 (9.6%)		
	Klebsiella	50 (6.4%)	20 (5.3%)	30 (7.4%)		
	Enterobacter	44 (5.6%)	22 (5.9%)	22 (5.4%)		
	Proteus	45 (5.8%)	22 (5.9%)	23 (5.7%)		
	Serratia	58 (7.4%)	23 (6.1%)	35 (8.6%)		
	Morganella	55 (7.0%)	29 (7.7%)	26 (6.4%)		
	Providencia	48 (6.1%)	30 (8.0%)	18 (4.4%)		
	Citrobacter	57 (7.3%)	31 (8.2%)	26 (6.4%)		
	Pseudomonas	48 (6.1%)	21 (5.6%)	27 (6.7%)		
Data results of the comparative variables between the 2 tested cohorts were statistically analyzed by Chi-Square Test (at p-value< 0.05) and expressed as Number (Percentage).						
PIP/TAZ: Piperacillin/Tazobactam (Tazocin®). IMI/CIL: Imipenem/Cilastatin (Tienam®). NA: Not statistically applicable and can't be computed. Dex: Dexamethasone.				•*: Significant (P-Value <0.05). •N: Number of tested EAR-NOSE-THROAT ADMITTED INFECTED PATIENTS patients. ABs: Selected Antibiotics. MER: Meropenem (Meronem®).		

4. Discussion

From March 2020 to September 2021, Royal Medical Services (RMS) in Jordan studied the Non-Dexamethasone Cohort (Cohort I) and Dexamethasone Cohort (Cohort II) of moderate-severe ear-nose-throat infected patients. Our study is unique in its multi-faceted tracking of biochemical dynamic changes of haematological immune subsets and other well-studied discrete and combined prognosticators in hospitalised ear-nose-throat admitted infected patients across two

cohorts and its secondary exploration of clinical outcomes in these comparable cohorts. Total lymphocyte counts (TLC) negatively correlate with clinical outcomes in observational studies. Over 2 weeks after symptom onset, lymphocyte counts rose in recovering patients. Infected ear-nose-throat patients with high-dose corticosteroids had decreased virological clearance and prolonged viral shedding, suggesting impaired antiviral immunity. A study of 138 infected ear-nose-throat patients. [9-10]

The Randomised Evaluation of Ear-Nose-Throat Admitted Patients trial found that dexamethasone 6 mg once daily improved survival by 17% in ARDS-afflicted patients who needed oxygen. In these severely ear-nose-throat admitted infected patients, Dexamethasone-derived cytokine storm mitigation propensity and mortality reduction rate likely dominated the positive clinical picture despite lymphopenia. Thus, corticosteroidal agents' oppositely infectious pathogenesis, lymphopenia-related negative effects on viral clearance and shedding, and cytokine storm mitigation capacity and survival benefit must be balanced. The crucial question is when to start corticosteroids in ear-nose-throat admitted infected patients. [11-13]

Corticosteroidal agents' dynamic effects should be assessed on CBC-related prognosticator ratios, NLR, MLR, TLC, ANC, and monocyte count. [31] Patients on Dexamethasone 6 mg/day (Cohort II) had higher baseline WBCs and immune-subsets of TLC, ANC, and MC (14638±2058, 1681±562, 11392±1331, and 1139±133) compared to the non-Dexamethasone cohort (13388±3820, 1586±990, 10374±). The immune subset quotients in NLR and MLR showed opposite results (7.53±2.68 and 0.75±0.27 vs 8.29±3.56 and 0.83±0.36, -0.76±0.22 and -0.08±0.02, p-value=0.000). A retrospective analysis of WBCs and immune subsets during hospitalisation for Dexamethasone and Non-Dexamethasone showed significant reductions in absolute neutrophil and monocyte counts in Cohort II compared to Cohort I (-50.3%±25.8% and -63.8%±30.7% vs -5.2%±35.3% and -6.2%±42.0%, respectively), but no significant changes in total lymphocyte counts. Cohort II patients had significantly lower baseline acute-phase reactants of FER: AL 1 and CRP: ALB 1 than Cohort I patients (385 (95.1%) vs 241 (64.1%), 0.09 (95% CI; 0.06-0.15), p-value=0.000).

5. Conclusion

Since corticosteroidal agents' effects on immune cell subsets and ratios and clinical effects are controversial, ear-nose-throat admitted infected patients must be monitored for these dynamic changes. Dexamethasone 6 mg/day improves survival in higher baseline risky patients upon admission and is associated with ANC, MC, and their ratios to TLC (NLR and MLR) downtrending. Retrospective design limits study. Large, multisite, prospective studies are needed to control multiple confounders. Our findings may contribute to the rapidly evolving controversial evidence despite these limitations.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest in this manuscript

Statement of ethical approval

There is no animal/human subject involvement in this manuscript

Statement of informed consent

Owing to the retrospective design of this study, the informed consent form was waived.

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