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ORIGINAL RESEARCH

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Evaluation of Three Clinical Decision Rules in Pediatric Patients with Minor Head Injury: PECARN, CHALICE and CHATCH

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Abstract

Objective: In this study, we aimed to evaluate the diagnostic accuracy of the Pediatric Emergency Care Applied Research Network (PECARN), Canadian Assessment of Tomography for Childhood Head Injury (CATCH), and children's head injury algorithm for the prediction of important clinical events guidelines in identifying clinically important traumatic brain injury (ciTBI) in pediatric patients with minor head injury.

Materials and Methods: This single-center, prospectively designed study was performed in the emergency department (ED) of a tertiary hospital. The study included patients under 18 years old who presented to the ED with head trauma and a GCS of 14-15. The primary outcome of the study was the relationship between the decision rules and ciTBI.

Results: The study was completed with 502 patients. It was found that the PECARN algorithm was 80% sensitive in detecting ciTBI in patients younger than 2 years of age, and 84.55% in patients aged 2 years or older. While this rate decreased (50.0%) in CATCH, it was higher (89.54%) in CHALICE. In the detection of patients without a risk (specificity), all 3 algorithms found good detections, and the specificity rates were between 82% and 90%.

Conclusion: ciTBI risk prediction models will assist in clinical decision making and establish an accurate neuroimaging strategy. According to the results of our study, all three clinical decision rules can be safely used in the management of pediatric minor head trauma patients.

Keywords: Pediatrics, emergency department, clinically important traumatic brain injury

Introduction

Head injuries are common in children and are one of the leading causes of morbidity and mortality among pediatric patients. Head injuries mostly occur due to mechanisms such as falls, impact with a hard object, or striking a hard surface. Children with head injuries present to emergency departments (EDs) with complaints such as headache, nausea-vomiting, and bleeding [1].

The diagnosis of traumatic intracranial injuries is important and cranial computed tomography (CT) is the gold standard for their diagnosis [2]. Most patients with minor head injuries can be discharged after a period of observation, but a small proportion of their condition deteriorates and brain surgery intervention is required for intracranial hematoma. The use of CT in EDs is important for early diagnosis of these intracranial hematomas [3]. The lack of evidence to assist in identifying children with significant injuries and the concern of clinicians missing such an injury has led to uncertainty as to which patients require investigation. The increased availability and decrease in the time required for cranial CT has led to an increase in CT usage rates [4]. As a result, CT usage has become increasingly widespread while diagnostic yield remains low. The increased use of CT significantly increases health care costs and exposes a large number of children to the potentially harmful effects of ionizing radiation every year [3]. The lifetime cancer death risk attributed to the ionizing radiation dose from a single cranial CT is approximately 1 in 1.500 per year and 1 in 5.000 at age 10. Exposure of a child's brain to ionizing radiation can affect cognitive abilities in adulthood.

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Children with head injuries may be uncooperative due to fear or agitation and may require sedation that carries the risk of airway and hemodynamic compromise [4]. Three clinical decision rules have been developed to assist clinicians in reducing CT scans while determining all relevant injuries, to identify children with high risk of intracranial injury: Canadian Assessment of Tomography for Childhood Head Injury (CATCH), Pediatric Emergency Care Applied Research Network (PECARN), and children's head injury algorithm for the prediction of important clinical events (CHALICE) [5]. The PECARN rule is recommended for patients under 18 years of age, presenting within 24 hours, with blunt head trauma and a Glasgow Coma scale (GCS) score of 14-15. It helps in decision making for CT scans, observation, and discharge. The CATCH rule is used for patients presenting within the first 24 hours with a GCS score of 13-15, including those with blunt head trauma. CT scans are recommended if at least one of the criteria is present. The CHALICE rule can be used for all children with head trauma. It assists in decision making based on the history, physical examination, and mechanism of injury. If there is one of the criteria, a CT scan is recommended. If none of them are present, the patient has a low risk of intracranial injury. In this study, the aim was to evaluate the diagnostic accuracy of PECARN, CATCH, and CHALICE rules in determining clinically important traumatic brain injuries (ciTBI) in children with minor head trauma.

Materials and Methods

This study, which was designed as a single-center and prospective study, was conducted at the Emergency Medicine Clinic of University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital between July 1, 2022 and November 1, 2022. The Clinical Research Ethics Committee of the University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital approved this study (approval number: 2022/514/228/2, date: 30.06.2022). Relatives of all participants were informed in detail before starting the study and approval was obtained via written informed consent forms.

The study included patients under 18 years old who presented to the ED with head trauma and a GCS of 14-15. Patients over 18 years old, patients with a GCS of 13 or below, patients with multiple trauma, patients taking anticoagulant drugs, and patients who could not be followed up were not included in the study.

A form was created by the researchers involved in the study to record the study data. The effectiveness of PECARN, CHALICE, and CATCH scores was compared. Variables in CATCH, CHALICE, and PECARN are provided in Table 1. All the variables for these scores were included in the study form. The forms were filled out only on days when the researchers were working. The data of patients who presented to the ED with minor head trauma was recorded in the form by the researchers in the

Table 1. Variables of CATCH, CHALICE, and PECARN

CHALICE	CATCH	PECARN	
History **1.** Witnessed LOC >5 minutes **2.** History of amnesia >5 minutes **3.** Abnormal drowsiness **4.** Over 3 discrete vomits **5.** Physician suspicion of non-accidental injury **6.** First ever seizure after injury **Examination** **7.** GCS <14 or <15 if under 1 year **8.** Suspicion of penetrating or depressed skull injury or tense fontanelle **9.** Signs of basil skull fracture **10.** Positive focal neurological finding **11.** Presence of bruise, swelling, or laceration >5 cm if <1 year old **Mechanism** **12**. Dangerous mechanism (MVA >40 mph, fall >3 meters, high speed projectile injury	CT head is required only for children with minor head injury (injury within the past 24 hours associated with witnessed LOC, definite amnesia, witnessed disorientation, persistent vomiting, or persistent irritability) plus any one of the following **High risk** **1.** GCS<15 two hours post injury **2.** Suspected open or depressed skull fracture **3.** History of worsening headache **4.** Irritability on examination **Medium risk** **5.** Any sign of basal skull fracture **6.** Large boggy hematoma of the scalp **7.** Dangerous mechanism (MVA, fall >3 ft/0.9 m, or from 5 stairs, fall from bicycle with no helmet)	**Children younger than 2 years** **1.** GCS ≤14 **2.** Signs of altered mental status (agitation, somnolence, repetitive questioning, slow to respond to questions) **3.** Palpable skull fracture **4.**Occipital, parietal, or temporal scalp hematoma **5.** History of LOC ≥5 s **6.** Dangerous mechanism (MVA with ejection or death of other occupant or rollover, pedestrian or cyclist struck without helmet, falls over 3 ft/0.9 m, or struck by high-impact object) **7.** Parental concern	**Children 2 years and older** **1.** GCS ≤14 **2.** Signs of altered mental status (agitation, somnolence, repetitive questioning, slow to respond to questions) **3.** Signs of basilar skull fracture **4.** History of LOC **5.** History of vomiting **6.** Dangerous mechanism (MVA with ejection or death of other occupant or rollover, pedestrian or cyclist struck without helmet, falls over 5 ft/1.5 m, or struck by high-impact object) **7.** Severe headache

CATCH: Canadian Assessment of Tomography for Childhood Head Injury, CHALICE: Children's head injury algorithm for the prediction of important clinical events, PECARN: Pediatric Emergency Care Applied Research Network, GCS: Glasgow Coma scale, LOC: Level of consciousness, MVA: Motor vehicle accident

triage section of the ED. The patients were then redirected to the trauma section of the ED, where their management was performed by another physician who was not involved in the research. Finally, the outcomes of the patients were obtained from digital medical records and/or by contacting the patients' relatives by telephone.

Any of the following definitions are considered ciTBI; death from traumatic brain injury (TBI), neurosurgical intervention for TBI (intracranial pressure monitoring, elevation of depressed skull fracture ventriculostomy, hematoma evacuation, lobectomy, tissue debridement, dura repair), intubation of more than 24 hours for TBI, hospital admission of 2 nights or more for the TBI in association with TBI on CT.

Any of the following definitions were considered TBI on CT; intracranial hemorrhage or contusion, cerebral edema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus, and skull fracture depressed by at least the width of the table of the skull.

Statistical Analysis

To perform statistical analysis, SPSS v. 25.0 software package (SPSS Inc., Chicago, IL, USA) and MedCalc ver. 12.5 (MedCalc Software Ltd, Ostend, Belgium) were used. While evaluating the study data, the data were summarized by using descriptive statistical methods (frequency, percentage). Receiver operating characteristic analysis was applied for PECARN, CHALICE, and CATCH effectiveness in clinical decisions. Sensitivity and specificity calculated from the analysis were reported with their 95% confidence intervals. Area under the curve, pulse pressure variation and negative predictive value were also given to distinguish diagnostic efficiencies of PECARN, CHALICE, and CATCH.

The Fisher's exact test was applied for the independency of 2x2 crosstabs two categorical variables to determine relationships of PECARN, CHALICE, CATCH and the present of TBI on CT.

Results

After excluding 23 patients who did not meet the inclusion criteria of the study, the study was completed with 502 patients. Of these patients, 155 were under the age of 2, and 347 were 2 years old or older. Tables 2-4 show the distribution of variables in PECARN, CHALICE, and CATCH clinical decision-making algorithms among the included patients. The PECARN algorithm showed that the highest changes in consciousness and scalp hematoma were found in patients under 2 years of age. In patients over 2 years old, a history of vomiting and changes in consciousness were found more frequently compared to others. In the CATCH algorithm, larger and swollen scalp hematomas and high energy trauma classification were found to be more frequent than others. In the CHALICE algorithm, it appears that the presence of ecchymosis, swelling, laceration and abnormal sleepiness in patients is more commonly encountered compared to other conditions in younger patients.

Table 5 shows the sensitivity and specificity rates and 95% confidence intervals found for the PECARN, CHALICE, and CATCH clinical decision-making algorithms in order to measure their effectiveness in making the correct decision in the study. It was found that the PECARN algorithm was 80% sensitive in detecting ciTBI in patients under 2 years of age, and 84.55% sensitive in patients 2 years old or older. The rate decreased in CATCH (50.0%), while it was higher in CHALICE (89.54%). In detecting patients without risk (specificity), all three algorithms performed well, with specificity rates ranging from approximately 82% to 90%.

In terms of detecting TBI with CT, PECARN has the best sensitivity with a range of 80-82.26%, while the sensitivity of CATCH and CHALICE decreases. All algorithms have high specificity rates in this detection. In conclusion, the PECARN algorithm has more stable detections in terms of sensitivity compared to CATCH and CHALICE and that all three algorithms have roughly equal and high specificity rates in the range of 80-90%. Diagnostic accuracy of PECARN, CATCH, and CHALICE clinical decision rules were found to be statistically significant (p values respectively; 0.0046-0.0133, 0.0085 and 0.0001) (Table 5).

Discussion

In this study, analyses were performed regarding the risk classification of head injuries in children under the age of 18 using the PECARN, CATCH and CHALICE algorithms. According to the analyses, the PECARN, CATCH and CHALICE algorithms were successful in detecting high-risk head injuries.

Various risk algorithms are used for early diagnosis and rapid intervention in patients admitted to ED [6-8]. The risk algorithms should have high sensitivity and high negative predictive value in detecting the injury, meaning that if a patient is scored as having low risk, they should not actually have a serious head injury. Results of the study showed that PECARN has high sensitivity in both age groups (under 2 and over 2), and similar results were seen in other studies [9,10]. Sensitivity of CATCH and CHALICE algorithms was found to be slightly lower compared to results reported in other studies (86-100% for CATCH and 91-100% for CHALICE in the mentioned studies) [11,12]. Additionally, the negative predictive values of these 3 risk scales were found to be 82-90% in the analysis.

Clinically, severe traumatic head injuries have a significant place in the healthcare system. According to our results regarding PECARN, patients who came with serious head injury in the under-2 age group were generally present with

Table 2. Distribution of variables found in the PECARN clinical decision algorithm among patients in the study

PECARN	Frequency	Percentage	TBI detected on CT		p values
			Absent n (%)	Present n (%)	
<2 years patients; Glasgow Coma scale <15					
Absent	154	99.4	138 (89.6)	16 (10.4)	0.897
Present	1	0.6	1 (100)	0 (0)	
<2 years patients; signs of altered mental status					
Absent	146	94.8	130 (89)	16 (11)	0.407
Present	8	5.20	8 (100)	0 (0)	
<2 years patients; palpable skull fracture					
Absent	152	98.7	138 (90.2)	14 (9.2)	0.010
Present	2	1.30	0 (0)	2 (100)	
<2 years patients; occipital, parietal, or temporal scalp hematoma					
Absent	146	94.8	134 (91.8)	12 (8.2)	0.004
Present	8	5.20	4 (50)	4 (50)	
<2 years patients; history of loss of consciousness ≥5 s					
Absent	153	99.4	137 (89.5)	16 (10.5)	0.896
Present	1	0.6	1 (100)	0 (0)	
<2 years patients; dangerous mechanism					
Absent	148	96.1	133 (89.9)	15 (10.1)	0.488
Present	6	3.9	5 (83.3)	1 (16.7)	
<2 years patients; parental concern					
Absent	148	96.1	132 (89.2)	16 (10.8)	0.512
Present	6	3.9	6 (100)	0 (0)	
>2 years patients; GCS <15					
Absent	349	99.7	328 (94)	21 (6)	0.940
Present	1	0.3	1 (100)	0 (0)	
>2 years patients; signs of altered mental status					
Absent	334	95.2	315 (94.3)	19 (5.7)	0.270
Present	17	4.80	15 (88.2)	2 (11.8)	
>2 years patients; signs of basilar skull fracture					
Absent	349	100.0	328 (94)	21 (6)	-
>2 years patients; history of loss of consciousness					
Absent	348	99.1	328 (94.3)	20 (5.7)	0.169
Present	3	0.9	2 (66.7)	1 (33.3)	
>2 years patients; history of vomiting					
Absent	327	93.7	312 (95.4)	15 (4.6)	0.001
Present	22	6.30	16 (72.7)	6 (27.3)	
>2 years patients; dangerous mechanism					
Absent	342	98.0	322 (94.2)	20 (5.8)	0.355
Present	7	2.0	6 (85.7)	1 (14.3)	
>2 years patients; severe headache					
Absent	346	98.6	325 (93.9)	21 (6.1)	0.733
Present	5	1.40	5 (100)	0 (0)	

PECARN: Pediatric Emergency Care Applied Research Network, GCS: Glasgow Coma scale, CT: Computed tomography, TBI: Traumatic brain injury

Table 3. Distribution of variables found in the CATCH clinical decision algorithm among patients in the study

CATCH	Frequency	Percentage	TBI detected on CT		
			Absent n (%)	Present n (%)	p values
Glasgow Coma scale <15 two hours post injury					
Absent	501	99.8	466 (93)	35 (87)	0.072
Present	1	0.2	0 (0)	1 (100)	
Suspected open or depressed skull fracture					
Absent	502	100.0	466 (92.8)	36 (7.2)	-
History of worsening headache					
Absent	501	99.8	465 (92.8)	36 (7.2)	0.928
Present	1	0.2	1 (100)	0 (0)	
Irritability on examination					
Absent	501	99.8	464 (92.8)	36 (7.2)	0.928
Present	1	0.2	1 (100)	0 (0)	
Any sign of basal skull fracture					
Absent	502	100.0	466 (92.8)	36 (7.2)	-
Large boggy hematoma of the scalp					
Absent	463	92.2	443 (95.7)	20 (4.3)	0.000
Present	39	7.8	23 (59)	16 (41)	
Dangerous mechanism*					
Absent	489	97.4	455 (93)	34 (7)	0.238
Present	13	2.6	11 (84.6)	2 (15.4)	

*Motor vehicle accident, fall >3 ft/0.9 m, or from 5 stairs, fall from bicycle with no helmet, CT: Computed tomography, TBI: Traumatic brain injury, CATCH: Canadian Assessment of Tomography for Childhood Head Injury

scalp hematoma and changes in consciousness. In the over-2 age group, nausea and changes in consciousness were also identified as clinical presentations. In a study done by Runde and Beiner [13], it was mentioned that younger patients in the groups evaluated as high risk had more scalp hematomas or palpable fractures or confusion, while older children had admission due to changes in consciousness or GCS scores below 14. In a study done by Hennelly et al. [14], it was emphasized that when determining an appropriate imaging strategy for children with minor head trauma, one must consider the quality of life based on health status and radiation risk in their analysis of the management of these cases. In a similar study, it was stated that PECARN's algorithm can help in the clinical decision-making stage for children patients who are isolated with a GCS score of 14 or with consciousness disturbance and who are identified as high risk [15]. In a study done by Bressan et al. [16], information was provided about determining risk with different predictive combinations in the PECARN medium and high-risk groups in traumatic head injuries, supporting the study that we carried out. Studies have shown that the use of PECARN has resulted in a significant decrease in the rate of CT scans in places with high rates of CT scans, and has not caused any increase in places with low rates of CT scans [17]. When compared, a cost-effectiveness study conducted by Nishijima et al. [18] in the United States showed that PECARN was seen as the dominant and effective strategy compared to general clinical understanding (CT scan rate at 33.8%). In another similar analysis conducted by Holmes et al. [19] in England, both CHALICE and PECARN were emphasized and it was noted that both were effective approaches. As in the literature studies, it was concluded that all three decision rules were useful in this study.

Study Limitations

The results of our study should be evaluated taking into account the limitations. The numerical scarcity of the patient population that came with traumatic head injury, suitable for our age group, caused a wide confidence interval in the calculation of some predictive signs. As in other studies related to PECARN [9], we did not exclude children who were injured from our population due to small injury mechanisms, falling from the same level or running/walking injuries caused by stable objects. Although the rate of serious traumatic head injury is low in low-risk injury mechanisms, in our study, there were cases that resulted in intracranial injury even in such an injury. The results of our study should not be generalized to the general public due to factors such as the doctors at our center being more experienced in managing pediatric trauma patients.

Table 4. Distribution of variables found in the CHALICE clinical decision algorithm among patients in the study

CHALICE	Frequency	Percentage	TBI detected on CT		p values
			Absent n (%)	Present n (%)	
Witnessed LOC >5 minutes					
Absent	496	98.8	461 (92.9)	35 (7.1)	0.362
Present	6	1.2	5	1	
History of amnesia >5 minutes					
Absent	495	99.0	461 (92.9)	35 (7.1)	0.313
Present	5	1.0	4 (80)	1 (20)	
Abnormal drowsiness					
Absent	479	95.4	445 (92.9)	34 87.1)	0.503
Present	23	4.6	21 (91.3)	2 (8.7)	
Over 3 discrete vomits					
Absent	492	98.2	458 (93.1)	34 (6.9)	0.131
Present	9	1.8	7 (77.8)	2 (22.2)	
Physician suspicion of non-accidental injury					
Absent	499	100.0	463 (92.8)	36 (7.2)	-
First ever seizure after injury					
Absent	500	100.0	464 (92.8)	36 (7.2)	-
Glasgow Coma scale <14 or <15 if under 1 year					
Absent	501	100.0	465 (92.8)	36 (7.2)	-
Suspicion of penetrating or depressed skull injury or tense fontanelle					
Absent	500	100.0	464 (92.8)	36 (7.2)	-
Signs of basil skull fracture					
Absent	502	100.0	466 (92.8)	36 (7.2)	-
Positive focal neurological finding					
Absent	501	99.8	465 (92.8)	36 (7.2)	0.928
Present	1	0.2	1 (100)	0 (0)	
Presence of bruise, swelling, or laceration >5 cm if <1 year old					
Absent	126	81.3	443 (93.9)	29 (6.1)	0.003
Present	29	18.3	22 (75.9)	7 (24.1)	
Dangerous mechanism					
Absent	495	98.6	461 (93.1)	34 (6.9)	0.084
Present	7	1.4	5 (71.4)	2 (28.6)	
Fall >3 meters					
Absent	501	100.0	465 (92.8)	36 (7.2)	-
High speed projectile injury					
Absent	499	99.4	463 (92.8)	36 (7.2)	0.800
Present	3	0.6	3 (100)	0 (0)	

CHALICE: Children's head injury algorithm for the prediction of important clinical events, CT: Computed tomography, TBI: Traumatic brain injury, LOC: Level of consciousness

Table 5. Diagnostic accuracy of PECARN, CATCH, and CHALICE clinical decision rules

	PECARN		CATCH	CHALICE
	<2 years	≥2 years	All patients	All patients
	n=155	n=347	n=502	n=502
ciTBI				
Sensitivity (95% CI)	80.0 (68.4-90.5)	84.55 (76.9-90.4)	50.00 (24.7-75.3)	89.54 (61.2-97.3)
Specificity (95% CI)	82.26 (74.4-88.5)	88.48 (84.5-91.7)	89.54 (86.2-92.3)	86,13 (82.4-89.3)
TBI on CT				
Sensitivity (95% CI)	80.00 (55.3-85.3)	82.26 (74.4-88.5)	55.56 (38.5-75.5)	51.85 (31.9-71.3)
Specificity (95% CI)	80.95 (72.6-87.2)	89.06 (78.8-95.5)	90.51 (83.9-98.7)	91.06 (87.7-95.8)
AUC	0.721	0.836	0.672	0.743
p values	0.0046	0.0133	0.0085	0.0001
NPV	92.00	95.43	95.98	94.42
PPV	80.77	84.44	66.67	83.33

CI: Confidence interval, ciTBI: Clinically important traumatic brain injury, TBI on CT: Traumatic brain injury on computed tomography, PECARN: Pediatric Emergency Care Applied Research Network, AUC: Area under the curves, CHALICE: Children's head injury algorithm for the prediction of important clinical events, CATCH: Canadian Assessment of Tomography for Childhood Head Injury, PPV: Positive predictive value, NPV: Negative predictive value

Conclusion

ciTBI risk prediction models will assist in clinical decision making and in establishing an accurate neuroimaging strategy. According to the results of our study, all three clinical decision rules can be used safely in the management of pediatric minor head trauma patients. More studies are needed to demonstrate reliability and accuracy in hospitals with non-specialized doctors or healthcare professionals in pediatric patients.

Ethics

Ethics Committee Approval: The Clinical Research Ethics Committee of the University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital approved this study (approval number: 2022/514/228/2, date: 30.06.2022).

Informed Consent: Relatives of all participants were informed in detail before starting the study and approval was obtained via written informed consent forms.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.D.E., N.B.Ç., S.K., S.G., Concept: A.U.S., R.A., S.K., Design: R.A., H.D.E., A.Y.K., N.B.Ç., Data Collection or Processing: S.G., H.D.E., A.Y.K., S.K., Analysis or Interpretation: N.B.Ç., A.U.S., S.G., Literature Search: R.A., A.Y.K., H.D.E., S.G., Writing: R.A., A.Y.K., A.U.S., H.D.E.

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References

1. Bressan S, Eapen N, Phillips N, Gilhotra Y, Kochar A, Dalton S, et al. PECARN algorithms for minor head trauma: Risk stratification estimates from a prospective PREDICT cohort study. Acad Emerg Med. 2021;28:1124-33.
2. Babl FE, Bressan S. Physician practice and PECARN rule outperform CATCH and CHALICE rules based on the detection of traumatic brain injury as defined by PECARN. Evid Based Med. 2015;20:33-4.
3. Caceres JA, Goldstein JN. Intracranial hemorrhage. Emerg Med Clin North Am. 2012;30:771-94.
4. Lyttle MD, Crowe L, Oakley E, Dunning J, Babl FE. Comparing CATCH, CHALICE and PECARN clinical decision rules for paediatric head injuries. Emerg Med J. 2012;29:785-94.
5. Babl FE, Borland ML, Phillips N, Kochar A, Dalton S, McCaskill M, et al. Accuracy of PECARN, CATCH, and CHALICE head injury decision rules in children: a prospective cohort study. Lancet. 2017;389:2393-402.
6. Kılıç M, Ak R, Dalkılınç Hökenek U, Alışkan H. Use of the AIMS65 and pre-endoscopy Rockall scores in the prediction of mortality in patients with the upper gastrointestinal bleeding. Ulus Travma Acil Cerrahi Derg. 2022;29:100-4.
7. Kılıç M, Ak R, Alışkan H. The utility of hemoglobin, albumin, lymphocyte and platelet (HALP) score in predicting mortality among COVID-19 patients: a preliminary study. Signa Vitae. 2023;19:143-7.
8. Ak R, Hökenek NM. Comparison of AIMS65 and Glasgow Blatchford scores in predicting mortality in patients with upper gastrointestinal bleeding. Rev Assoc Med Bras (1992). 2021;67:766-70.
9. Gambacorta A, Moro M, Curatola A, Brancato F, Covino M, Chiaretti A, et al. PECARN Rule in diagnostic process of pediatric patients with minor head trauma in emergency department. Eur J Pediatr. 2022;181:2147-54.
10. Kuppermann N, Holmes JF, Dayan PS, Hoyle JD Jr, Atabaki SM, Holubkov R, et al. Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study. Lancet. 2009;374:1160-70.
11. Osmond MH, Klassen TP, Wells GA, Correll R, Jarvis A, Joubert G, et al. CATCH: a clinical decision rule for the use of computed tomography in children with minor head injury. CMAJ. 2010;182:341-8.

12. Nigrovic LE, Stack AM, Mannix RC, Lyons TW, Samnaliev M, Bachur RG, et al. Quality improvement effort to reduce cranial CTs for children with minor blunt head trauma. Pediatrics. 2015;136:227-33.

13. Runde D, Beiner J. Calculated decisions: PECARN pediatric head injury/trauma algorithm. Pediatr Emerg Med Pract. 2018;15(Suppl 6):CD3-CD4.

14. Hennelly KE, Mannix R, Nigrovic LE, Lee LK, Thompson KM, Monuteaux MC, et al. Pediatric traumatic brain injury and radiation risks: a clinical decision analysis. J Pediatr. 2013;162:392-7.

15. Dalziel K, Cheek JA, Fanning L, Borland ML, Phillips N, Kochar A, et al. A cost-effectiveness analysis comparing clinical decision rules PECARN, CATCH, and CHALICE with usual care for the management of pediatric head injury. Ann Emerg Med. 2019;73:429-39.

16. Bressan S, Eapen N, Phillips N, Gilhotra Y, Kochar A, Dalton S, et al. PECARN algorithms for minor head trauma: Risk stratification estimates from a prospective PREDICT cohort study. Acad Emerg Med. 2021;28:1124-33.

17. Yang K, Zhao M, Sun J, Nie X. Accuracy of PECARN decision rule in minor blunt head trauma in pediatric emergency department: a meta-analysis. Int J Clin Pract. 2021;75:e14586.

18. Nishijima DK, Yang Z, Urbich M, Holmes JF, Zwienenberg-Lee M, Melnikow J, et al. Cost-effectiveness of the PECARN rules in children with minor head trauma. Ann Emerg Med. 2015;65:72-80.

19. Holmes MW, Goodacre S, Stevenson MD, Pandor A, Pickering A. The cost-effectiveness of diagnostic management strategies for children with minor head injury. Arch Dis Child. 2013;98:939-44.

ORIGINAL RESEARCH

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Correlation Between Age Shock Index and Perfusion Index with Emergency Severity Index and its Predictive Value on In-hospital Mortality

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Abstract

Objective: Perfusion index (PI), shock index (SI), modified SI (MSI), and age SI (ASI) are valuable markers used to predict the clinical course and mortality of patients in various intensive care units and emergency departments (ED). We investigated the relationship between these markers and emergency severity index (ESI) and their value in predicting in-hospital mortality.

Materials and Methods: In this prospective, cross-sectional, single-centered study, the vital values of the patients and the PI were measured and categorized according to ESI. The correlation between SI, MSI, ASIs, and PI among the ESI categories and their predictive values for in-hospital mortality were calculated.

Results: We established statistically significantly lower PI values and significantly higher values in the ASI in the group with in-hospital mortality compared to survivors (p=0.001, <0.001, respectively). The area under curve score for in-hospital mortality of the PI of 0.723 and ASI are 0.723 and 0.807, respectively. The specificity of PI and the sensitivity of ASI are 91.62% and 91.67%, respectively, and negative predictive values of those are 98.66% and 99.67%, respectively.

Conclusion: Adding PI and ASI to existing triage scores, such as ESI, may improve triage specificity in unselected patients who are admitted to the ED.

Keywords: Perfusion index, shock index, mortality, triage

Introduction

Emergency departments (ED) have the most important place for the global health crisis worldwide due to their easy accessibility; they have become the preferred admission points to healthcare services. As a solution to this crowded environment of EDs, triage practices have been developed to reduce crowding and to ensure that critically ill patients receive accurate and effective treatment on time. In triage systems, the patient's history, vital signs, and resource requirements take an important place in scoring. Vital signs are the most crucial markers in identifying critically ill patients. However, vital signs begin to change whenever the compensation mechanisms are insufficient. Studies have been performed that aim to test the state of tissue perfusion in a non-invasive, rapid way, such as perfusion index (PI), brachial index, and thoracic impedance, to establish tissue perfusion state before the compensation mechanisms occur. Therefore, rapid assessment of tissue perfusion status guides the clinician in identifying critically ill patients.

Recently, the shock index (SI) has been used to predict the prognosis of high-energy trauma, shock, sepsis, and pneumonia with high mortality. Many studies have demonstrated that SI is superior to only systolic blood pressure (SBP) or only pulse measurement in predicting the prognosis [1,2]. Failure to take into account the patient's diastolic blood pressure (DBP) in the calculation of SI was considered a deficiency; as a result, a modified SI (MSI) was developed [3]. Later, age SI (ASI) was

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defined because comorbidities and medications used in elderly patients affect the pulse and blood pressure values [4].

This study aimed to obtain information about the clinical significance of SI, MSI, ASI, and PI values in addition to standard vital parameters and to determine their role in predicting mortality in patients admitted to ED.

Materials and Methods

After the approval of the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee no: 2022.02.37, subject no: KAEK/2022.02.37, a prospective cross-sectional study was performed in the ED of University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital between 10/02/2022 and 30/10/2022. Patients who were admitted outpatient or by ambulance were evaluated by triage nurses and doctors who had more than 10 h of practical and theoretical training, and patients at the age of 18 and above who gave consent were included in the study. Patients were accepted consecutively, and participants in each ESI category were aimed to be in similar numbers. Thirty-seven patients with uncertain clinical outcomes (19 patients who left without permission and 18 patients who refused treatment) were excluded from the study (Figure 1).

Heart rate, SpO_2, and blood pressure were measured after 5 min of resting in the sitting position and avoiding patients' speech. PI was measured non-invasively from the distal phalanx of the second finger of the right hand until the value on the display stabilized or by waiting for at least 10 s via Lifescope, BSM-3562 device; by Nihon Koden, Tokyo, Japan. The respiratory rate (RR) was measured by visual inspection of the patient's chest wall motion for 1 min. The patients were divided into five groups based on their vital signs according to the ESI classification. PI data, patient's age, gender, consciousness status, comorbidities, Glasgow Coma score (GCS) value, and vital signs (blood pressure, body temperature, pulse, SpO_2, RR) were recorded in the study form. Then, with these obtained values, SI, MSI, and ASI were calculated. The patients' hospitalization status, emergency operation requirement, discharge status, and in-patient and 1-month mortality were followed. Hospitalization was defined as the admission of patients either to the inpatient service or to the intensive care unit (ICU) after evaluation in the ED. The outcome measure for mortality was defined as death from any cause within 30 days of hospital admission and was determined based on hospital records or, in some cases, telephone interviews.

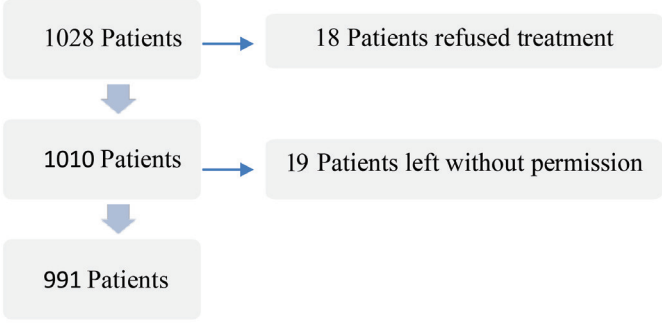

Figure 1. Patient flow chart

Statistical Analysis

Categorical data will be displayed as number and percentages. The Shapiro-Wilk or Kolmogorov-Smirnov tests will examine the conformity of continuous variables to normal distribution. Normally, distributed data will be shown as mean ± standard deviation, and non-normally distributed data as median (min-max) or (interquartile range). In comparisons between groups with and without in-hospital mortality, vital parameters, perfusion index, SI, MSI, and ASI were calculated using the Student's t-test and ANOVA test for normally distributed parameters and Mann-Whitney U test with Kruskal-Wallis test for non-normally distributed parameters. The cut-off value is determined according to the receiver operating characteristic (ROC) curve for the parameters found to be statistically significant between the groups. The data were analyzed in the SPSS Statistics 24.0 (IBM Inc., New York, USA) program. $P<0.05$ is considered statistically significant in this study.

Results

A total number of 991 patients, 525 (53.0%) female and 466 (47.0%) male, were included in our study. According to the ESI classification, 191 (19.3%) were in the first category, 192 (19.4%) were in the second category, 198 (20.0%) were in the third category, 210 (21.2%) were in the fourth category, and 200 (20.2%) were in the fifth category.

In the clinical follow-ups of the patients, 706 (71.2%) were discharged, 173 (17.5%) were referred to the ICU, 98 (9.9%) were admitted to the inpatient service, and 12 (1.2%) were undergone emergent operation; 2 (0.2%) of them died in the operation room. In-hospital and 30-day mortality rates in patients were 2.4% (24) and 7.2% (71), respectively. The distribution of age, vital parameters, and shock indices of the patients according to the ESI categories are given in Table 1. According to the results of the ANOVA test, which had been performed depending on the ESI categories, statistical significance in age, SBP, and PI values were estimated ($p<0.001$, <0.001, <0.001, respectively). There is no statistically significant difference estimated between the ESI categories and DBP, mean arterial pressure, and pulse ($p=0.190$, 0.079, and 0.065, respectively). In the results of the Kruskal-Wallis test conducted between the ESI categories, there was statistical significance in RR, SpO_2, and ASI values ($p<0.001$, 0.001, 0.001, respectively), while there was no statistical significance in temperature, SI, and MSI values ($p=0.169$, 0.066, 0.333, respectively).

A comparison of the variables according to the in-hospital mortality status is shown in Table 2. Differences in the PI and ASI scores between the mortal and survival groups are statistically significant. Statistically significant lower PI values and statistically significant higher values in the ASI are found in the group with in-hospital mortality compared with the survival group. The age of the patients was higher in the in-hospital mortality group, the RR was statistically significantly higher, and the DBP and SpO_2 values were low in the in-hospital mortality group.

ROC analysis is performed for the statistically significant variables in patients grouped according to in-hospital mortality status. For the perfusion and ASI, we calculated the area under the curve, sensitivity, specificity, and positive and negative predictive values (Table 3, Figures 2 and 3).

Discussion

Our department is one of the most crowded EDs in Turkey, with 535,045 patients admitted between 01/02/2022 and 01/11/2022 and accepting an average of 59,450 patients per month. It is important to recognize quickly critically ill and high-risked patients to provide treatment as soon as possible to reduce mortality rates in busy ER. In this study, which indices may be applicable in predicting in-hospital mortality, statistically significantly higher values were found in ASI, whereas there were statistically significantly lower PI values in the group with mortality compared with the survival group.

Recent studies have showed a significant and positive relationship between in-hospital mortality and ASI in patients with stroke patients [5]. In a study conducted in Korea, ASI had the power to predict in-hospital mortality better than SI or MSI in geriatric trauma patients admitted to ED [6]. In another study, the ASI value in patients over 55 years of age may be useful in predicting early mortality and increasing the need for blood transfusion [7]. In a study by Agerskov et al. [8], which included 1.338 patients who required emergent surgery, found that those with a PI ≤0.5 had a 19% mortality, and those with a PI ≥0.5 had a 10% 30-day mortality.

Er et al.'s [9] research studied the 60-day mortality of patients receiving mechanical ventilation and found the mortality of patients with a low PI value at the 12th h to be high. Savastano et al. [10] calculated the mean PI value of 346 patients who had spontaneous respiratory return after cardiopulmonary resuscitation. The mean PI value was found to be high in

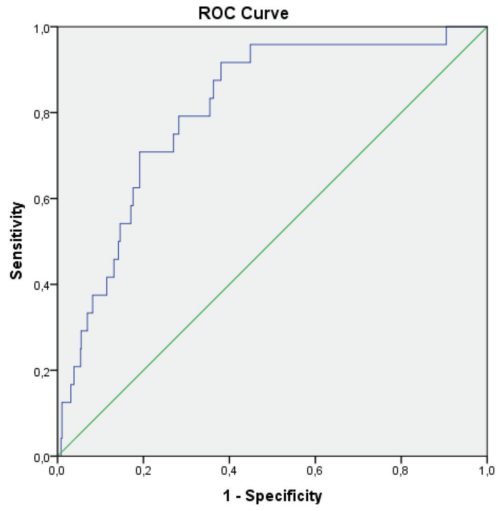

Figure 2. ROC curve of age shock index

ROC: Receiver operating characteristic

Table 1. Analysis of age, vital parameters, and shock indices according to ESI

Parameters	ESI categories					p values
	1 (191)	2 (192)	3 (198)	4 (210)	5 (200)	
Age	60.48±19.83	56.27±21.57	52.84±21.27	37.98±14.67	36.31±13.98	**<0.001**
SBP	133.19±36.62	139.68±33.43	132.42±24.41	128.33±20.19	129.29±16.86	**<0.001**
DBP	75.53±19.67	78.68±16.12	76.65±13.31	77.52±12.87	78.58±11.86	0.190
MAP	94.75±24.28	99.01±20.67	95.24±15.60	94.46±13.95	95.48±12.20	0.079
Pulse	93.14±24.13	89.23±17.50	88.80±17.78	89.02±10.86	89.71±10.04	0.065
Temperature	36.5 (36.0-39.2)	36.5 (36.0-39.4)	36.5 (35.0-40.0)	36.5 (34.5-38.4)	36.6 (35.7-38.8)	0.169
Respiratory rate	20 (10-40)	18 (12-34)	16 (12-30)	14 (11-25)	14 (12-20)	**<0.001**
SpO_2	92 (53-100)	97 (83-100)	98 (85-100)	98 (92-100)	98 (92-100)	**<0.001**
GCS	15 (3-15)	15 (10-15)	15 (11-15)	15 (14-15)	15 (15-15)	**<0.001**
Perfusion index	1.38±1.00	1.76±1.52	1.99±1.33	2.39±1.11	2.37±1.06	**<0.001**
Shock index	0.68 (0.22-2.39)	0.66 (0.29-1.26)	0.68 (0.29-1.29)	0.70 (0.33-1.15)	0.70 (0.42-1.14)	0.066
Modified shock index	0.93 (0.32-3.35)	0.91 (0.45-1.89)	0.93 (0.43-1.85)	0.95 (0.52-1.52)	0.95 (0.60-1.53)	0.333
Age shock index	39.68 (12.18-165.97)	34.30 (9.50-104.21)	32.39 (8.67-78.10)	24.39 (9.80-56.37)	23.69 (8.40-63.39)	**<0.001**

ANOVA test, Kruskal-Wallis test, parametric values shown as mean ± SD; non-parametric data shown as median (min-max) (interquartile range). SD: Standard deviation, ESI: Emergency severity index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, GCS: Glasgow Coma score

those who survived 30 days. Recent studies have shown that PI is a significant marker for mortality in trauma patients [11]. The findings of this study were found to be compatible the literature. Although there is systemic vasodilation secondary to sympathetic nervous system hyperstimulation in septic patients, this is not the case for peripheral vessels. Thus, we believe that the peripheral PI value is estimated to be low [12].

Almost twenty-nine percent of the cases were hospitalized, 11.1% were admitted to inpatient service, and 17.5% were admitted to the ICU. In the study of Rivers et al. [13], it has been reported that 100 million ED admissions annually constitute

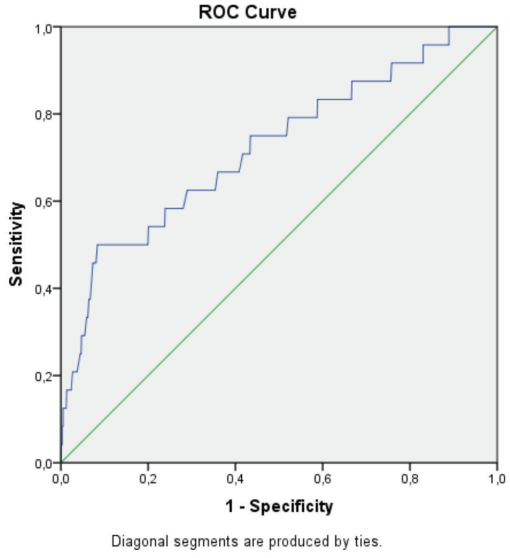

Figure 3. ROC Curve of perfusion index

ROC: Receiver operating characteristic

Table 2. Analysis of variables with in-hospital mortality

Parameters	In-hospital mortality		p values
	Yes (24)	No (967)	
Perfusion index	1.13±1.03	2.01±1.27	**0.001**
Shock index	0.68 [0.30]	0.69 [0.22]	0.386
Modified shock index	0.93 [0.45]	0.94 [0.28]	0.318
Age shock index	48.56 [24.53]	29.68 [18.98]	**<0.001**
Age	67.67±15.45	48.02±20.80	**<0.001**
SBP	123.13±42.32	132.71±26.92	0.281
DBP	71.33±20.16	77.55±14.81	**0.044**
MAP	88.60±27.14	95.94±17.51	0.200
Pulse	89.75±22.38	89.96±16.63	0.965
Fever	36.4 [0.48]	36.5 [0.40]	**0.026**
RR	20 [2]	16 [5]	**<0.001**
SpO_2	92 [9]	97 [3]	**<0.001**

Independent sample t-test, Mann-Whitney U test, parametric values shown as mean ± SD; non-parametric data shown as median [interquartile range]. SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, RR: Respiratory rate

40% of hospitalizations, and 25% of these patients are critically ill. In this study, in-hospital mortality was estimated at 2.4%, and 30-day mortality was 7.2%; the rate of 30-day mortality and hospitalization were low compared to other studies. This is considered because this study is single-centered with a limited number of patients.

In this study, PI, temperature, RR, DBP, SpO_2 value, and ASI were found to be statistically significant variables for in-hospital mortality. Studies showed a significant correlation between PI and the core-to-toe temperature difference [14]. Torabi et al. [15] also examined patients in the ESI category three and found that SBP and ASI values were better in determining mortality than SI and MSI. In another study, a non-linear correlation between baseline DBP and in-hospital mortality in patients with acute myocardial infarction was found, and a decrease in DBP within the first three days in patients who had a mortal course [16]. Lee et al. [17] determined that the SpO_2/RR ratio is an independent prognostic factor for 28-day mortality in patients with sepsis or septic shock. Another study found that nocturnal RR measures in patients aged 65 and over may be a risk marker for mortality [18]. Daş et al. [19] demonstrated that the SI value had a clear advantage over some vital measures for estimating 30-day mortality but was not useful in estimating hospitalization and showed that a lower PI value was associated with both hospitalization and 30-day mortality. In another study, conventional vital signs and SI values were compared to determine acute critical illnesses in ED, and they concluded that a more than 0.9 unit abnormal increase in SI values of 36 patients was closely associated with hospitalization and intensive treatment after hospitalization [20]. SI and MSI values are found to be potentially useful for predicting in-hospital and out-of-hospital massive bleeding and defining hemorrhagic shock [21]. Laaksonen et al. [22] showed that it could be used to predict 30-day mortality by dividing the ASI value by the GCS in seriously injured patients in the pre-hospital setting. ASI and SI are found to be valuable in predicting mortality in acute heart failure [23]. The ASI value is calculated to be high due to the decrease in physiological reserve, metabolic and hormonal response with advanced age, and the decrease in the body's response to trauma [4,6]. In another study, they found that SpO_2 <90 in coronavirus disease-2019 patients was a strong indicator of in-hospital mortality [24]. Studies are conducted in variable patient groups of different populations that explain the discrepancy of findings.

Study Limitations

A limited number of patients were included, as it was a single-centered, cross-sectional study conducted in a limited time frame with a limited number of patients. These are considered to be the limitations of our study.

Table 3. ROC analysis of the perfusion index and age shock index

	AUC	p values	95% CI		Sensitivity	Specificity	PPV	NPV	Accuracy
			Lower bond	Upper bond					
Perfusion index <0.505	0.723	0.000	0.608	0.838	50%	91.62%	12.9%	98.66%	90.62%
Age shock index >34.21	0.807	0.000	0.728	0.887	91.67%	61.94%	5.64%	99.67%	62.66%

ROC: Receiver operating characteristic, AUC: Area under curve score, CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

Conclusion

We recommend using PI and ASI with existing triage category systems for easier recognition and early treatment of critically ill patients in busy EDs.

Ethics

Ethics Committee Approval: After the approval of the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee no: 2022.02.37, subject no: KAEK/2022.02.37.

Informed Consent: Patients at the age of 18 and above who gave consent were included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.S.K., S.D., Design: B.S.K., S.D., A.F.B.K., V.A., Data Collection or Processing: B.S.K., A.F.B.K., M.G., M.U., Analysis or Interpretation: B.S.K., S.D., S.F., V.A., Literature Search: B.S.K., A.F.B.K., M.G., Writing: B.S.K., V.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Paladino L, Subramanian RA, Nabors S, Sinert R. The utility of shock index in differentiating major from minor injury. Eur J Emerg Med. 2011;18:94-8.
2. Yasaka Y, Khemani RG, Markovitz BP. Is shock index associated with outcome in children with sepsis/septic shock?*. Pediatr Crit Care Med. 2013;14:372-9.
3. Liu YC, Liu JH, Fang ZA, Shan GL, Xu J, Qi ZW, et al. Modified shock index and mortality rate of emergency patients. World J Emerg Med. 2012;3:114-7.
4. Rau CS, Wu SC, Kuo SC, Pao-Jen K, Shiun-Yuan H, Chen YC, et al. Prediction of massive transfusion in trauma patients with shock index, modified shock index, and age shock index. Int J Environ Res Public Health. 2016;13:683.
5. Demir A, Eren F. The relationship between age shock index, and severity of stroke and in-hospital mortality in patients with acute ischemic stroke. J Stroke Cerebrovasc Dis. 2022;31:106569.
6. Kim SY, Hong KJ, Shin SD, Ro YS, Ahn KO, Kim YJ, et al. Validation of the shock index, modified shock index, and age shock index for predicting mortality of geriatric trauma patients in emergency departments. J Korean Med Sci. 2016;31:2026-32.
7. Zarzaur BL, Croce MA, Fischer PE, Magnotti LJ, Fabian TC. New vitals after injury: shock index for the young and age x shock index for the old. J Surg Res. 2008;147:229-36.
8. Agerskov M, Thusholdt ANW, Holm-Sørensen H, Wiberg S, Meyhoff CS, Højlund J, et al. Association of the intraoperative peripheral perfusion index with postoperative morbidity and mortality in acute surgical patients: a retrospective observational multicentre cohort study. Br J Anaesth. 2021;127:396-404.
9. Er MC, Kaya C, Ustun YB, Sahinoglu AH. Predictive value of perfusion index for mortality in mechanically ventilated patients. Aging Male. 2020;23:1251-8.
10. Savastano S, Baldi E, Contri E, De Pirro A, Sciutti F, Compagnoni S, et al. Post-ROSC peripheral perfusion index discriminates 30-day survival after out-of-hospital cardiac arrest. Intern Emerg Med. 2021;16:455-62.
11. Ozakin E, Yazlamaz NO, Kaya FB, Karakilic EM, Bilgin M. Perfusion Index measurement in predicting hypovolemic shock in trauma patients. J Emerg Med. 2020;59:238-45.
12. Elshal MM, Hasanin AM, Mostafa M, Gamal RM. Plethysmographic peripheral perfusion index: could it be a new vital sign? Front Med (Lausanne). 2021;8:651909.
13. Rivers EP, Nguyen HB, Huang DT, Donnino MW. Critical care and emergency medicine. Curr Opin Crit Care. 2002;8:600-6.
14. Lima AP, Beelen P, Bakker J. Use of a peripheral perfusion index derived from the pulse oximetry signal as a noninvasive indicator of perfusion. Crit Care Med. 2002;30:1210-3.
15. Torabi M, Moeinaddini S, Mirafzal A, Rastegari A, Sadeghkhani N. Shock index, modified shock index, and age shock index for prediction of mortality in emergency severity index level 3. Am J Emerg Med. 201634:2079-83.
16. Huang S, Luo Y, Liang L, Guo N, Duan X, Zhou Q, et al. The baseline and repeated measurements of DBP to assess in-hospital mortality risk among critically ill patients with acute myocardial infarction: a retrospective cohort study. Medicine (Baltimore). 2022;101:e30980.
17. Lee CU, Jo YH, Lee JH, Kim J, Park SM, Hwang JE, et al. The index of oxygenation to respiratory rate as a prognostic factor for mortality in sepsis. Am J Emerg Med. 2021;45:426-32.
18. Baumert M, Linz D, Stone K, McEvoy RD, Cummings S, Redline S, et al. Mean nocturnal respiratory rate predicts cardiovascular and all-cause mortality in community-dwelling older men and women. Eur Respir J. 2019;54:1802175.
19. Daş M, Bardakci O, Siddikoglu D, Akdur G, Yilmaz MC, Akdur O, et al. Prognostic performance of peripheral perfusion index and shock index combined with ESI to predict hospital outcome. Am J Emerg Med. 2020;38:2055-9.
20. Rady MY, Nightingale P, Little RA, Edwards JD. Shock index: a re-evaluation in acute circulatory failure. Resuscitation. 1992;23:227-34.
21. Terceros-Almanza LJ, García-Fuentes C, Bermejo-Aznárez S, Prieto-Del Portillo IJ, Mudarra-Reche C, Sáez-de la Fuente I, et al. Prediction of massive bleeding. Shock index and modified shock index. Med Intensiva. 2017;41:532-8.
22. Laaksonen M, Björkman J, Iirola T, Raatiniemi L, Nurmi J. The effect of time of measurement on the discriminant ability for mortality in trauma of a pre-hospital shock index multiplied by age and divided by the Glasgow Coma score: a registry study. BMC Emerg Med. 2022;22:189.

23. Castillo Costa Y, Cáceres L, Mauro V, Fairman E, Fernández A, Soricetti J, et al. Shock index, modified shock index, and age-adjusted shock index as predictors of in-hospital death in acute heart failure. Sub analysis of the ARGEN IC. Curr Probl Cardiol. 2022;47:101309.

24. Mejía F, Medina C, Cornejo E, Morello E, Vásquez S, Alave J, et al. Oxygen saturation as a predictor of mortality in hospitalized adult patients with COVID-19 in a public hospital in Lima, Peru. PLoS One. 2020;15:e0244171.

ORIGINAL RESEARCH

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Impact of the Presence of Chronic Respiratory Diseases on the Mortality of Hospitalized Patients with COVID-19 Pneumonia: A Single Center Experience

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Abstract

Objective: The influence of coexisting chronic respiratory diseases (CRDs) on the prognosis of patients with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection is debatable. This study aimed to investigate the consequences of CRDs on the mortality of coronavirus disease-2019 (COVID-19) pneumonia inpatients.

Materials and Methods: Hospitalized patients with confirmed SARS-CoV-2 infection were included. The data were derived from electronic medical records retrospectively and patients with and without CRD past history were analyzed concerning in-hospital mortality.

Results: In 1.529 patients with COVID-19 pneumonia, 54 (58.1%) were male and the mean age was 61.18±15.03 years. A total of 245 individuals were diagnosed with CRD. The CRD group consisted of asthma (128 cases, 52.24%), chronic obstructive pulmonary disease [(COPD), 79 cases, 32.37%], lung cancer (15 cases, 6.14%), obstructive sleep apnea syndrome (12 cases, 4.91%), and interstitial lung disease [(ILD), 11 cases, 4.5%]. Mean age, female gender, respiratory rate, and supplemental oxygen requirement were significantly higher in the CRD group ($p=0.001$; $p<0.01$ for all). In-hospital mortality was 11.8% (29 cases) in the CRD group and 8.4% (108 cases) in the group without CRD. In univariate analysis, there was no significant difference in-hospital mortality between the two groups ($p>0.05$). Although CRD patients had a similar mortality ratio compared with non-CRD patients on multivariate logistic analysis [odds ratio (OR): 0.262, 95% confidence interval (CI): 0.071-0.968; $p=0.045$]; COPD and ILD subgroups exhibited 2.1 fold (OR: 2.1, 95% CI: 1.13-3.92; $p=0.017$) and 3.87 fold (OR: 3.87, 95% CI: 1.015-14.772; $p=0.033$) increased risk of in-hospital mortality respectively.

Conclusion: Even though patients with COVID-19 pneumonia and CRDs do not have a higher mortality rate, it is crucial to closely monitor these patients because of the elevated mortality risk associated with COPD and ILD.

Keywords: COPD, asthma, OSAS, interstitial lung disease, COVID-19 pneumonia, mortality

Introduction

Specifying characteristics linked to poor prognosis and identifying vulnerable individuals with higher susceptibility are crucial in the struggle against coronavirus disease-2019 (COVID-19). Age, male gender, comorbidities, and metabolic abnormalities are risk factors associated with poor prognosis in COVID-19 [1]. Following cardiovascular disease and diabetes mellitus (DM) as the leading causes of mortality among the comorbidities, chronic respiratory diseases (CRDs) have been witnessed. It has been demonstrated that prognosis varies among CRDs as well [2,3]. There are still conflicting data about the prevalence of CRDs among COVID-19 patients [4,5].

According to a study comparing hospitalized COVID-19 and influenza cases in France, despite CRDs being reported less frequently in COVID-19 than influenza cases, patients with CRDs had more severe COVID-19 development risk and a higher mortality rate [6]. Previous studies were reporting that

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the prevalence of CRD was higher in Middle East respiratory syndrome (MERS) than in severe acute respiratory syndrome (SARS); the prevalence of CRD in influenza was higher than COVID-19, and there was increased susceptibility for MERS coronavirus (CoV) infection in smokers and chronic obstructive pulmonary disease (COPD) cases [6,7]. COPD is defined as a risk factor for severe disease and high mortality in COVID-19 cases [8], whereas asthma is not defined as a risk factor for severe disease and mortality [9].

The issue remains unclear today although numerous researches have been published on the impact of CRD on COVID-19 prognosis. Therefore, the purpose of our study was to determine the association between COVID-19 and CRD and how CRD affects the prognosis of patients with SARS-CoV-2 pneumonia.

Materials and Methods

This retrospective single-center cohort study was carried out at Prof. Dr. Murat Dilmener Emergency Hospital in İstanbul on 1.938 confirmed COVID-19 patients who were recruited from September 1st, 2020 to December 31st, 2020. Based on the instructions from the World Health Organization (WHO), SARS-CoV-2 infection was determined [10]. They were administered in accordance with the Republic of Turkey Ministry of Health's COVID-19 treatment plan [11]. This research was approved by the Local Ethics Committee, University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital (2021/164/2021-06-40/15.03.2021).

Data of patients were extracted retrospectively from the inpatient electronic medical records. Demographic characteristics, clinical variables, coexisting medical conditions, laboratory parameters, chest computed tomography (CT) scan results, and clinical outcomes were recorded. Patients were classified as having moderate and severe illness [12]. On the chest CT scan, the pulmonary involvement was categorized as low, moderate, and severe [13]. The research consisted of 1.529 inpatients (>18 years) with COVID-19 pneumonia.

Comorbidities were classified as hypertension, DM, coronary artery disease (CAD), valvular heart disease, congestive heart failure (CHF), atrial fibrillation, peripheral artery disease, cerebrovascular disease, neurodegenerative disease, dyslipidemia, chronic kidney disease, rheumatic disease, malignancy, and CRD. The following diseases were considered CRDs: asthma, COPD, lung cancer, obstructive sleep apnea syndrome (OSAS), and interstitial lung disease (ILD). Patients were divided into groups based on whether they had a CRD or not. The primary endpoint of this trial was defined as in-hospital mortality.

Statistical Analysis

Analyses were performed using the Number Cruncher Statistical System program. Continuous variables were presented by mean ± standard deviation or median (min-max). Categorical variables are expressed as numbers (%). Comparison of characteristics between the two groups was performed using the student t-test and Mann-Whitney U test for continuous variables. Categorical variables were compared using the Pearson chi-square test and Fisher's exact test. Multivariable logistic regression analysis was performed to investigate risk factors for mortality. Receiver operating characteristic (ROC) analysis and Binomial exact test were used to evaluate the mortality. A p value <0.05 was considered significant.

Results

One thousand five hundred and twenty nine adults, 889 male (58.1%) and 640 female (41.96%) with a mean age of 61.18±15.03 were included in the cohort (age >18 years) between September 1, 2020 and December 31, 2020. One thousand five hundred and twenty nine patients, had comorbidities mainly including hypertension (737, 48.2%), DM (512, 33.5%), and CAD (221, 14.5%). 245 people (16%) had underlying CRDs. In CRDs, the most common respiratory diseases were asthma (128 cases - 52.24%), COPD (79 cases - 32.37%), and lung cancer (15 cases - 6.14%). In overall patients, asthma 8.37% (128/1529), COPD 5.2% (79/1529), lung cancer 1% (15/1.529), OSAS 0.8% (12/1.529), and ILD 0.7% (11/1.529) were found. (Tables 1, 2). Table 1 summarizes general information and baseline patient characteristics, Table 2 presents the distribution of CRDs.

The mean respiratory rate (breaths per minute) was 21.06±5.23, the oxygen saturation (SpO_2) while receiving oxygen was 94.33±1.95, and oxygen support was 4.95±7.14 L/per min.

Based on established categories 830 (54.3%) patients were classified as moderate and 699 (45.7%) patients as severe. Pulmonary involvement in chest CT scans was low in 329 (21.5%), moderate in 738 (48.3%), and severe in 462 (30.2%) patients. In-hospital death was found to be 9% (137/1.529 cases) and overall intensive care unit (ICU) admission was 11% (168/1.529) in this study. The duration of the length of stay was 11.52±6.81 days (range, 1-64 days).

The clinical characteristics of patients with and without CRD were compared. The mean age was 64.69±13.78 in patients with CRD vs. 60.51±15.16 in patients without CRD (p=0.001; p<0.01). The gender difference was statistically significant in two groups; female gender was higher in patients with CRD (p=0.001; p<0.001). Hypertension, CHF, and malignancy were more common in patients with CRD (p=0.008; p=0.001; p=0.001; p<0.01; respectively). No significant difference was observed between the two groups concerning other comorbidities (p>0.05). Respiratory rate and supplemental

oxygen requirement was significantly higher in the CRD group (p=0.001; p<0.01 for both). There were no significant differences in body temperature, SpO_2 while receiving oxygen support, pulse rate, or diastolic/systolic blood pressure between patients with and without CRD (p>0.05) (Table 1).

Total cholesterol, high-density lipoprotein, cholesterol and D-dimer concentrations were significantly higher in the CRD group (p values, respectively 0.031; 0.008, and, 0.008). On the other hand, calcium, aspartate aminotransferase, alanine aminotransferase, albumin, lactate dehydrogenase (LDH), and ferritin levels were observed to be significantly lower in those with CRD than in another group (p values, respectively 0.003; 0.002; 0.019; 0.012; 0.041; 0.002). Other laboratory test results revealed no differences between patients with and without CRD (p>0.05). Although cases with CRDs had a significantly higher disease severity status than the other group (p=0.003;

Table 1. Baseline characteristics of the patients

		All patients (n=1529)	CRD (n=245)	No CRD (n=1284)	p
Age, years	Mean ± SD	61.18±15.03	64.69±13.78	60.51±15.16	[a]0.001**
	Median (min-max)	61 (20-103)	65 (32-97)	60 (20-103)	
Sex, n (%)	Female	640 (41.9)	128 (20.0)	512 (80.0)	[b]0.001**
	Male	889 (58.1)	117 (13.2)	772 (86.8)	
Physical findings					
Body temperature, °C	Mean ± SD	36.92±0.67	36.86±0.63	36.93±0.68	[c]0.316
	Median (min-max)	36.7 (35.9-40)	36.7 (35.9-40)	36.7 (36-39.4)	
Systolic blood pressure, mmHg	Mean ± SD	126.80±18.60	126.57±18.16	126.85±18.69	[a]0.830
	Median (min-max)	126 (70-208)	127 (81-182)	126 (70-208)	
Diastolic blood pressure, mmHg	Mean ± SD	70.65±10.46	70.42±9.95	70.7±10.55	[a]0.699
	Median (min-max)	70 (37-123)	70 (44-99)	70 (37-123)	
Heart rate, per minute	Mean ± SD	83.14±15.20	82.65±13.68	83.23±15.48	[a]0.580
	Median (min-max)	82 (45-206)	82 (48-130)	82 (45-206)	
Respiratory rate, breaths per minute	Mean ± SD	21.06±5.23	22.01±5.13	20.87±5.23	[c]0.001**
	Median (min-max)	20 (12-40)	22 (12-40)	20 (12-40)	
SpO_2, under oxygen support, mean	Mean ± SD	94.33±1.95	94.37±1.85	94.32±1.97	[a]0.718
	Median (min-max)	94 (86-99)	94 (89-99)	94 (86-99)	
Oxygen support, L/per min	Mean ± SD	4.95±7.14	6.11±7.56	4.73±7.04	[c]0.001**
	Median (min-max)	3 (0-30)	4 (0-30)	2 (0-30)	
Comorbidities, n (%)		1151 (75.3)	-	-	-
Hypertension		737 (48.2)	137 (56)	600 (46.7)	0.008**
Diabetes mellitus		512 (33.5)	88 (36)	424 (33)	[b]0.379
Coronary artery disease		221 (14.5)	37 (15)	184 (14.3)	[b]0.753
Atrial fibrillation		87 (5.7)	17 (6.9)	70 (5.5)	[b]0.357
Congestive heart failure		94 (6.1)	28 (11.4)	66 (5.1)	[b]0.001**
Valvular heart disease		11 (0.7)	1 (0.4)	10 (0.8)	[d]1.000
Peripheral artery disease		10 (0.7)	3 (1.2)	7 (0.5)	[d]0.207
Cerebrovascular disease		54 (3.5)	5 (2)	49 (3.8)	[b]0.168
Neurodegenerative disease		62 (4)	13 (5.32)	49 (3.82)	[b]0.460
Dyslipidemia		73 (4.8)	9 (3.7)	64 (5)	[b]0.378
Cerebrovascular disease		54 (3.5)	5 (2)	49 (3.8)	[b]0.168
Neurodegenerative disease		62 (4)	13 (5.32)	49 (3.82)	[b]0.460
Chronic kidney disease		71 (4.6)	11 (4.50)	60 (4.68)	[b]0.901
Rheumatic disease		27 (1.8)	8 (3.3)	19 (1.5)	[d]0.063
Malignancy		76 (5.0)	25 (10.2)	51 (4)	[b]0.001**

[a]Student's t-test, [b]Pearson chi-square test, [c]Mann-Whitney U test, [d]Fisher's exact test, *p<0.05, **p<0.01, SpO_2: Oxygen saturation, SD: Standard deviation, CRD: Chronic respiratory disease, min-max: Minimum-maximum range

p<0.01), regarding chest CT score, there was no difference between CRD cases and those without CRD (p=0.707; p>0.05) (Table 3). Table 3 displays laboratory results, chest CT results, disease severity status, and patient outcomes.

Among 1.529 patients with COVID-19 of, 137 (9%) died during hospitalization. In-hospital mortality was found to be 11.8% (29/245) in patients with CRD, 8.4% (108/1.284) in patients without CRD; ICU admission was 14.3% (35/245) in patients with CRD, 10.4% (133/1.284) in cases with no CRD. In-hospital mortality and ICU admission did not significantly differ between CRD and non-CRD patients (p>0.05). It was discovered that patients with CRD had greater hospital length of stay (13.69±9.17 vs. 11.11±6.17 days, p= 0.001; p<0.01) (Table 3).

When the variables considered to have an effect on mortality in the univariate analysis were assessed with backward stepwise logistic regression analysis, the model was determined to be significant (p=0.001; p<0.01). According to the results of multivariate analysis, age, respiratory rate, fibrinogen, C-reactive protein (CRP), LDH, and the presence of malignancy significantly affect mortality (p values, respectively 0.001; 0.001; 0.049; 0.021; 0.002; 0.013; p<0.05). The coefficient of determination of the model was 96.5%, the sensitivity was 58.5% and the specificity was 99.1%. CRDs were not associated with the risk of in-hospital death. The presence of malignancy multiplied the risk of death by more than 6.43 [%95 confidence interval (CI): 1.483-27.940] (Table 4). Table 4 provides univariate ve multivariate regression analysis for in-hospital mortality in the study population.

In ROC analysis, respiratory rate presented the highest AUROC (0.916; 95% CI: 0.893-0.935), followed by age (0.731; 95% CI: 0.698-0.763) and CRP (0.669; 95% CI: 0.633-0.703) in predicting mortality (Table 5, Figure 1). The binomial exact test figured out the respiratory rate in predicting mortality as a superior reference, compared with age, fibrinogen, and CRP (p=0.001). Similarly taking age as a reference, age was superior compared with fibrinogen in predicting mortality (p=0.045).

Multivariable logistic regression model analysis revealed no increase in death in patients with both SARS-CoV-2 pneumonia and CRD (OR: 0.26; 95% CI: 0.071-0.968; p=0.045). When CRDs were divided into five distinct disorders, several CRDs had a considerable risk of in-hospital mortality. Patients with COPD and ILD showed 2.1-fold [odds ratio (OR): 2.1, 95% CI: 1.13-3.92; p=0.017] and 3.87-fold (OR: 3.87, 95% CI: 1.015-14.772; p=0.033) higher risk of in-hospital mortality of COVID-19 pneumonia compared with those without. Although OSAS had a remarkable OR of 2.047, it was not statistically significant (p=0.293). Asthma and lung cancer were not associated with in-hospital mortality in COVID-19 patients (p>0.05) (Table 6). Table 6 shows the risk of mortality for inpatients with COVID-19 according to CRD.

Table 2. Distribution of CRDs

	CRD n=245 (%)	All patients n=1529 (%)
Any CRDs	245	245 (16.0)
Asthma	128 (52.24)	128 (8.37)
Chronic obstructive pulmonary disease	79 (32.37)	79 (5.2)
Lung cancer	15 (6.14)	15 (1.0)
Obstructive sleep apnea syndrome	12 (4.91)	12 (0.8)
Interstitial lung disease	11 (4.50)	11 (0.7)

CRD: Chronic respiratory disease

Discussion

Investigating the effect of CRDs on COVID-19 pneumonia-related hospital mortality was the goal of this study. In our cohort, the prevalence of CRD was 16% (245/1.529). The distribution of CRDs was as follows: asthma 8.37% (128/1.529), COPD 5.2% (79/1.529), lung cancer 1% (15/1.529), OSAS 0.8% (12/1.529), and ILD 0.7% (11/1.529).

Our cohort demonstrated a prevalence of 5.2% for COPD, which was markedly lower than the general population in Turkey (19%), although the prevalence of asthma was concordant in the general population (8.37% and 2-17%, respectively) [14,15]. The prevalence of COPD varies from 3-21%, while the prevalence of asthma is 1-18% globally [16].

While Guan et al. [4] demonstrated a prevalence of 2.8% for any CRD, 1.6% for COPD, and 0.6% for asthma, a greater number of patients with both asthma (10.4%) and CRDs (26.8%)

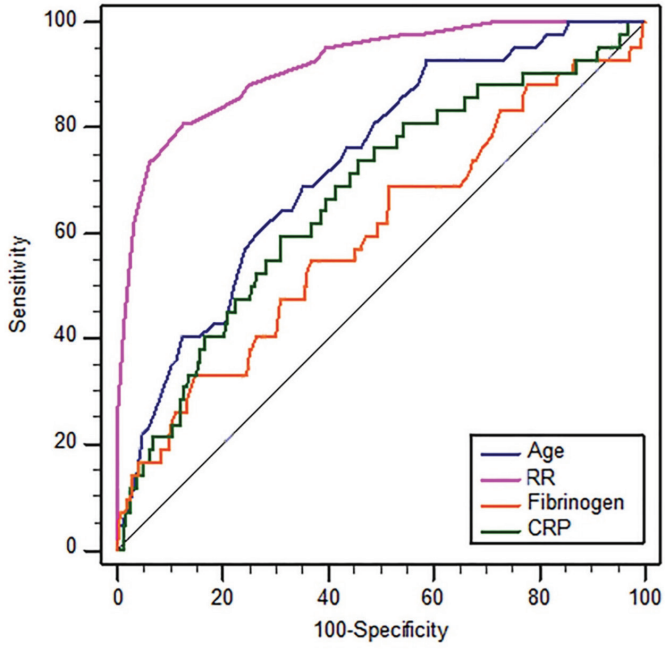

Figure 1. Receiver operating characteristic curves for age, respiratory rates, fibrinogen and CRP for mortality

CRP: C-reactive protein, RR: Respiratory rate

Table 3. Laboratory findings, chest CT scan results, disease severity status and outcomes of the patients

Laboratory findings		All patients (n=1529)	CRD (n=245)	No CRD (n=1284)	p
Neutrophil count, cells/mL	Mean ± SD	5.58±3.04	5.89±3.5	5.52±2.84	[c]0.415
Median (min-max)	Median (min-max)	5 (0.87-23.67)	5.2 (0.9-18.8)	4.9 (1.1-23.7)	
Lymphocytes count, cells/mL	Mean ± SD	1.19±0.62	1.17±0.66	1.20±0.61	[c]0.175
Median (min-max)	Median (min-max)	1.06 (0.15-6.9)	0.99 (0.3-4.7)	1.1 (0.2-6.9)	
Neutrophil/lymphocytes ratio	Mean ± SD	6.31±5.88	6.95±6.85	6.18±5.67	[c]0.280
Median (min-max)	Median (min-max)	4.46 (0.35-47.95)	4.9 (0.6-47.95)	4.4 (0.35-46.33)	
Platelet count, $10^3/mm^3$	Mean ± SD	248.76±112.83	246.5±103.83	249.2±114.51	[c]0.972
Median (min-max)	Median (min-max)	229 (0.7-1207)	237 (0.9-571)	228 (0.7-1207)	
Hematocrit, %	Mean ± SD	37.43±4.99	36.94±5.05	37.5±5.08	[a]0.113
Median (min-max)	Median (min-max)	37.7 (0.38-58.9)	36.9 (23.5-58.9)	37.8 (0.4-52)	
Glucose, mg/dL	Mean ± SD	153.04±71.97	149.99±70.56	153.62±72.25	[c]0.233
Median (min-max)	Median (min-max)	127.2 (11.3-791)	123 (62.9-526.7)	128.1 (11.3-791)	
Urea, mg/dL	Mean ± SD	42.86±29.73	43.91±28.32	42.66±30	[c]0.438
Median (min-max)	Median (min-max)	35 (10-328)	36 (10.8-204)	35 (10-328)	
Creatinine, mg/dL	Mean ± SD	0.99±0.86	0.94±0.76	0.99±0.88	[c]0.271
Median (min-max)	Median (min-max)	0.8 (0.07-11.98)	0.8 (0.4-11.2)	0.8 (0.1-12)	
Alanine transaminase, ALT, U/L	Mean ± SD	42.65±39.07	37.66±32.02	43.61±40.22	[c]0.019*
Median (min-max)	Median (min-max)	29 (4-321)	26 (4.8-271)	30 (4-321)	
Aspartate aminotransferase, AST, U/L	Mean ± SD	43.19±31.2	38.46±24.41	44.1±32.26	[c]0.002**
Median (min-max)	Median (min-max)	34 (4.8-356)	31 (4.8-170)	35 (9-356)	
Lactate dehydrogenase, LDH, U/L	Mean ± SD	353.71±155.48	345.72±165.58	355.23±153.51	[c]0.041*
Median (min-max)	Median (min-max)	318 (2.3-1386)	297 (125-1103)	323 (2.3-1386)	
Potassium, mEq/L	Mean ± SD	4.22±0.53	4.23±0.5	4.22±0.54	[a]0.798
Median (min-max)	Median (min-max)	4.2 (1.1-6)	4.2 (2.6-5.8)	4.2 (1.1-6)	
Sodium, mEq/L	Mean ± SD	137.14±5.38	137.37±3.96	137.09±5.61	[c]0.168
Median (min-max)	Median (min-max)	137 (38-237)	138 (121-147)	137 (38-237)	
Calcium	Mean ± SD	8.71±0.63	8.62±0.66	8.72±0.63	[c]0.003**
Median (min-max)	Median (min-max)	8.7 (3.4-12.2)	8.6 (4.3-11)	8.7 (3.4-12.2)	
C-reactive protein, CRP, mg/L	Mean ± SD	105.16±78.08	100.77±79.63	106±77.78	[c]0.288
Median (min-max)	Median (min-max)	95.8 (0.3-620.2)	83.8 (0.3-620.2)	97 (0.6-476)	
Procalcitonin, ng/mL	Mean ± SD	0.45±2.87	0.24±0.7	0.51±3.11	[c]0.786
Median (min-max)	Median (min-max)	0.1 (0-68)	0.1 (0.01-10.2)	0.1 (0.01-68)	
Ferritin, µg/L	Mean ± SD	525.93±582.41	455.39±559.92	539.39±585.85	[c]0.002**
Median (min-max)	Median (min-max)	350 (0.8-5357)	276.6 (5.7-4075)	363.6 (0.8-5357)	
D-dimer, µg FEU/mL	Mean ± SD	0.87±1.10	1.01±1.22	0.84±1.07	[c]0.008**
Median (min-max)	Median (min-max)	0.4 (0-8.82)	0.5 (0-8.82)	0.4 (0-7.99)	
Fibrinogen, mg/dL	Mean ± SD	514.81±135.23	515.51±129.23	514.68±136.4	[a]0.929
Median (min-max)	Median (min-max)	507 (187-1195)	504 (212-1104)	507 (187-1195)	
International normalized ratio, INR	Mean ± SD	1.07±0.21	1.08±0.22	1.07±0.21	[c]0.593
Median (min-max)	Median (min-max)	1 (0.2-3.7)	1 (0.5-2.9)	1 (0.2-3.7)	
Troponin I, ng/mL	Mean ± SD	28.04±177.22	38.19±267.54	26.25±156.05	[c]0.616
Median (min-max)	Median (min-max)	6 (0-3896)	7 (1-3896)	6 (0-3816)	
Albumin, g/L	Mean ± SD	35.61±5.54	34.8±5.57	35.77±5.52	[a]0.012*
Median (min-max)	Median (min-max)	35.5 (1.5-59.3)	34.7 (3.8-49.1)	35.5 (1.5-59.3)	

Table 3. Continued

Laboratory findings		All patients (n=1529)	CRD (n=245)	No CRD (n=1284)	p
Total cholesterol, mg/dL	Mean ± SD	158.73±42.50	163.68±41.17	157.80±42.69	[c]0.031*
	Median (min-max)	155 (64-477)	158.5 (72-310)	154 (64-477)	
HDL, HDL cholesterol, mg/dL	Mean ± SD	34.05±10.04	35.63±9.95	33.75±10.03	[a]0.008**
	Median (min-max)	33 (9-95)	35 (13-82)	33 (9-95)	
Disease severity status, n (%)					
Moderate		830 (54.3)	112 (45.7)	718 (55.9)	[b]0.003**
Severe		699 (45.7)	133 (54.3)	566 (44.1)	
CT involvement, n (%)					
Low		329 (21.5)	52 (21.2)	277 (21.5)	
Moderate		738 (48.2)	114 (46.5)	624 (48.6)	[b]0.707
Severe		462 (30.2)	79 (32.2)	383 (29.8)	
Clinical outcomes, n (%)					
Hospital length of stay, d	Mean ± SD	11.52±6.81	13.69±9.17	11.11±6.17	[c]0.001**
	Median (min-max)	10 (1-64)	11 (1-64)	10 (1-42)	
ICU admission		168 (11.0)	35 (14.3)	133 (10.4)	[b]0.072
ICU ex		118 (7.7)	25 (10.2)	93 (7.2)	[b]0.111
Discharge from hospital		1392 (91.0)	216 (88.2)	1176 (91.6)	[b]0.088
Death		137 (9.0)	29 (11.8)	108 (8.4)	[b]0.088

[a]Student's t-test, [b]Pearson chi-square test, [c]Mann-Whitney U test, [d]Fisher's exact test, *p<0.05, **p<0.01, CT: Computed tomography, SD: Standard deviation, CRD: Chronic respiratory disease, min-max: Minimum-maximum range, AST: Aspartate aminotransferase, ICU: Intensive care unit

was reported by the ISARIC WHO study [5]. In a previous study in Italy, diabetes was reported in 20.3% of COVID-19 patients who died, however, COPD was not listed as a comorbidity for any patient [17]. Reporting of COPD at a lower prevalence might have been caused by missed diagnosis, poor recognition due to failure to perform a proper lung function test, and lack of documentation. Asthma and COPD are heterogeneous diseases with many overlapping clinical and pathophysiologic diagnostic features. Another likely explanation for the low presentation of CRDs in COVID-19 could be that this vulnerable group of patients might have behaved more cautiously to prevent COVID-19 and that ICSs, often used to treat COPD and asthma, could protect them [5]. Under these circumstances, it seems hard to compare the prevalence of separate CRDs in patients with COVID-19 pneumonia.

According to our results, there was no increase in the mortality of COVID-19 pneumonia in hospitalized patients due to CRDs. However, patients with COPD and ILD had a higher risk of hospital death compared with those without. Even though CRD was not associated with in-hospital mortality in COVID-19, Oh and Song [3] suggested that COPD and lung disease due to external agents had a greater risk of hospital death in patients with COVID-19, and also patients with ILD and OSAS may have an increased risk of COVID-19. The fact that lung disease due to external agents was not classified separately and this group of patients was included in ILD in our study may be the reason why we have reached similar results to the study mentioned above.

Another study also published that CRD was associated with the risk of reaching the combined endpoint (invasive ventilation, ICU, or death within 30 days after hospitalization) but not particularly of death from COVID-19 [4]. In contrast, Aveyard et al. [2] identified an association between preexisting CRDs (including COPD, lung cancer, asthma, bronchiectasis, and idiopathic pulmonary fibrosis) and a higher risk of hospitalization and death. The same study noted that COPD and ILD were associated with a 50% greater risk of developing severe COVID-19, although asthma did not appear significantly associated with a higher risk of COVID-19 severity.

Many studies have classified COPD as pathology associated with severe disease and poor outcomes, such as ICU treatment and death, based on our findings [2,3,5,8,18,19]. The exact pathophysiology of how COPD increases the severity of COVID-19 pneumonia is not clear; underlying lung malfunction, the presence of increased expression of angiotensinconverting enzyme 2 (ACE-2) receptors, endothelial cell dysfunction, and increased coagulation have all been implicated [20].

Table 4. Univariate and multivariate logistic regression analysis for risk factors on mortality

	Univariate analysis				Multivariate analysis			
	OR	%95 CI		p	OR	%95 CI		p
		Lower	Upper			Lower	Upper	
Age	1.073	1.057	1.089	0.001**	1.095	1.046	1.147	0.001**
Respiratory rate	1.520	1.435	1.610	0.001**	1.508	1.323	1.717	0.001**
Fibrinogen	1.002	1.000	1.003	0.007**	1.004	1.000	1.009	0.049*
CRP	1.006	1.004	1.008	0.001**	0.990	0.981	0.998	0.021*
LDH	1.004	1.003	1.005	0.001**	1.004	1.001	1.007	0.002**
CRD	1.462	0.946	2.258	0.087	0.262	0.071	0.968	0.045*
Malignancy	2.121	1.184	4.131	0.013*	6.437	1.483	27.940	0.013*
Heart rate	1.014	1.003	1.025	0.011*				
Oxygen support	1.152	1.130	1.176	0.001**				
PLT	0.997	0.995	0.999	0.003**				
NLR	1.110	1.085	1.136	0.001**				
Troponin I	1.002	1.001	1.003	0.003**				
D-dimer	1.347	1.191	1.523	0.001**				
INR	4.229	2.293	7.800	0.001**				
Ferritin	1.001	1.000	1.001	0.001**				
Urea	1.022	1.017	1.027	0.001**				
Creatinine	1.413	1.234	1.619	0.001**				
Calcium	0.525	0.405	0.682	0.001**				
Albumin	0.912	0.883	0.941	0.001**				
Hypertension	2.743	1.875	4.014	0.001**				
CAD	3.120	2.105	4.625	0.001**				
AF	5.111	3.105	8.411	0.001**				
CHF	3.754	2.259	6.237	0.001**				
CVD	4.265	2.286	7.958	0.001**				
CKD	2.666	1.444	4.921	0.002**				
Chest CT score								
Low	2.768	1.541	4.970	0.001**				
Moderate	2.008	1.383	2.914	0.001**				
Severe	3.537	2.468	5.068	0.001**				
Severe illness	48.524	17.845	131.947	0.001**				

*p<0.05, **p<0.01, OR: Odds ratio, CI: Confidence interval, CRP: C-reactive protein, LDH: Lactate dehydrogenase, CRD: Chronic respiratory disease, PLT: Platelet count, NLR: Neutrophil/lymphocytes ratio, INR: International normalized ratio, CAD: Coronary artery disease, AF: Atrial fibrillation, CHF: Congestive heart failure, CVD: Cerebrovascular disease, CKD: Chronic kidney disease, CT: Computed tomography

Our study revealed that the presence of ILD was associated with a 3.8-fold higher risk of in-hospital mortality. Similarly, previous studies have revealed that the presence of ILD was associated with older age, obesity, and male gender with higher mortality, severe disease, and ARDS [2,3,21]. Contrary to these findings, Guiot et al. [22] found that only 1% of patients with ILD were hospitalized for COVID-19, with no increase in the incidence of severe illness. Patients with ILD are susceptible to respiratory viral infections, and SARS-CoV-2 could exacerbate underlying ILDs and lead to poor outcomes. On the other hand, it is thought that viral infections may contribute to the pathogenesis of ILD by causing inflammation in the lung tissue [23].

Similar to our findings, numerous studies have reported that asthma was not associated with elevated risks of serious pneumonia and death in patients with COVID-19 [2,9]. Since our cohort group consists of half of CRD patients with asthma, this may be the reason for similar mortality in the CRD group. Conversely, it was reported that the risk of COVID-19 mortality

Table 5. ROC analysis for mortality

	AUROC (95% CI)	Standard error	p
Age	0.731 (0.698-0.763)	0.0373	0.001**
Respiratory rate	0.916 (0.893-0.935)	0.0227	0.001**
Fibrinogen	0.596 (0.560-0.632)	0.0492	0.036*
CRP	0.669 (0.633-0.703)	0.0444	0.001**

*p<0.05; **p<0.01, AUROC: Area under the receiver operating characteristic, CI: Confidence interval, CRP: C-reactive protein

Table 6. Risk of mortality for patients hospitalized COVID-19 according to CRD

			95% CI	
	p	OR	Lower	Upper
Asthma	[b]0.560	0.820	0.419	1.602
COPD	[b]**0.017***	**2.106**	1.130	3.925
Lung cancer	[d]0.638	1.572	0.351	7.037
OSAS	[d]0.293	2.047	0.444	9.440
ILD	[b]**0.033***	**3.873**	1.015	14.772

[b]Pearson chi-square test, [d]Fisher's exact test,*p<0.05: significantly increased prevalence, COVID-19: Coronavirus disease-2019, CRD: Chronic respiratory disease, CI: Confidence interval, COPD: Chronic obstructive pulmonary disease, OSAS: Obstructive sleep apnea syndrome, ILD: Interstitial lung disease, OR: Odds ratio

was increased in patients who had recently required oral corticosteroid treatment or were hospitalized with severe asthma [5]. Untreated asthma patients may have reduced airway ACE-2 expression and transmembrance protease serine 2 mRNA expression due to type 2 inflammation. A previous study reported that the differences in disease severity and mortality between asthma and COPD may be related to different ACE-2 expression pathways [24].

Although our cohort did not show any relationship between OSAS and mortality in COVID-19 pneumonia, previous studies stated that patients with OSAS had an increased rate of COVID-19, hospitalization, critical illness and mortality related to COVID-19 [3,25]. Hypertension, heart failure, coronary heart disease, cerebrovascular disease, obesity, DM, age, and male gender are all cluster risk factors for OSAS and all these comorbidities have been associated with poor outcomes in COVID-19 [18,26]. OSAS leads to a reduction of respiratory functions, an increase of inflammatory lung disease and a higher incidence of thromboembolic disease [27]. Hypoxia leads to higher ACE-2 expression due to damage in the renin-angiotensin system in patients with OSAS. This mechanism may lead to a rise in death and disease severity in patients with both COVID-19 and OSAS [28].

Oncology patients are vulnerable to SARS-CoV-2 infections due to an immunocompromised state from cancer or its therapies including corticosteroids, older age, and comorbidities. The severity of disease, prolonged hospitalisation, pulmonary complications, and need for ICU and mechanical ventilation have been higher in patients with lung cancer compared with the general population and other malignancies reported with a death rate of 17.7-55% [29]. Death rates were reported to be 33% and 25%, respectively, in Europe and the US. Similar to lung cancer, patients with hematological malignancies have an increased risk of mortality compared with other cancer types [30].

In line with earlier research, age, respiratory rate, fibrinogen, CRP, LDH, and malignancy emerged as independent risk factors for in-hospital mortality in this cohort [2-6,8,18,19,21,24,26,30].

Study Limitations

There are some potential limitations to our analysis. It is a single-center study with a retrospective design that only involves hospitalized patients with moderate to severe illness. There was no available information about previous medication or lung function test results, the severity of CRD, or smoking status. It was not possible to perform lung function tests due to pandemic measures.

Conclusion

Our study shows that only COPD and ILD types of CRD lead to an increase in the mortality of COVID-19 infection. Therefore, these patients group should be closely monitored during COVID-19 infection to decrease the poor outcomes. Most importantly, they should be given priority in immunization programs for such infectious diseases. Still, further detailed studies are needed in this field.

Ethics

Ethics Committee Approval: This research was approved by the Local Ethics Committee, University of Health Sciences Turkey, Bakırköy Dr. Sadi Konuk Training and Research Hospital (2021/164/2021-06-40/15.03.2021).

Informed Consent: Retrospective study.

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Authorship Contributions

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References

1. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708-20.

ORIGINAL RESEARCH

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Impact of the Presence of Chronic Respiratory Diseases on the Mortality of Hospitalized Patients with COVID-19 Pneumonia: A Single Center Experience

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Abstract

Objective: The influence of coexisting chronic respiratory diseases (CRDs) on the prognosis of patients with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection is debatable. This study aimed to investigate the consequences of CRDs on the mortality of coronavirus disease-2019 (COVID-19) pneumonia inpatients.

Materials and Methods: Hospitalized patients with confirmed SARS-CoV-2 infection were included. The data were derived from electronic medical records retrospectively and patients with and without CRD past history were analyzed concerning in-hospital mortality.

Results: In 1.529 patients with COVID-19 pneumonia, 54 (58.1%) were male and the mean age was 61.18±15.03 years. A total of 245 individuals were diagnosed with CRD. The CRD group consisted of asthma (128 cases, 52.24%), chronic obstructive pulmonary disease [(COPD), 79 cases, 32.37%], lung cancer (15 cases, 6.14%), obstructive sleep apnea syndrome (12 cases, 4.91%), and interstitial lung disease [(ILD), 11 cases, 4.5%]. Mean age, female gender, respiratory rate, and supplemental oxygen requirement were significantly higher in the CRD group ($p=0.001$; $p<0.01$ for all). In-hospital mortality was 11.8% (29 cases) in the CRD group and 8.4% (108 cases) in the group without CRD. In univariate analysis, there was no significant difference in-hospital mortality between the two groups ($p>0.05$). Although CRD patients had a similar mortality ratio compared with non-CRD patients on multivariate logistic analysis [odds ratio (OR): 0.262, 95% confidence interval (CI): 0.071-0.968; $p=0.045$]; COPD and ILD subgroups exhibited 2.1 fold (OR: 2.1, 95% CI: 1.13-3.92; $p=0.017$) and 3.87 fold (OR: 3.87, 95% CI: 1.015-14.772; $p=0.033$) increased risk of in-hospital mortality respectively.

Conclusion: Even though patients with COVID-19 pneumonia and CRDs do not have a higher mortality rate, it is crucial to closely monitor these patients because of the elevated mortality risk associated with COPD and ILD.

Keywords: COPD, asthma, OSAS, interstitial lung disease, COVID-19 pneumonia, mortality

Introduction

Specifying characteristics linked to poor prognosis and identifying vulnerable individuals with higher susceptibility are crucial in the struggle against coronavirus disease-2019 (COVID-19). Age, male gender, comorbidities, and metabolic abnormalities are risk factors associated with poor prognosis in COVID-19 [1]. Following cardiovascular disease and diabetes mellitus (DM) as the leading causes of mortality among the comorbidities, chronic respiratory diseases (CRDs) have been witnessed. It has been demonstrated that prognosis varies among CRDs as well [2,3]. There are still conflicting data about the prevalence of CRDs among COVID-19 patients [4,5].

According to a study comparing hospitalized COVID-19 and influenza cases in France, despite CRDs being reported less frequently in COVID-19 than influenza cases, patients with CRDs had more severe COVID-19 development risk and a higher mortality rate [6]. Previous studies were reporting that

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Effect of Disease Severity on the Clinical Course, Maternal and Perinatal Outcomes in Pregnancy in COVID-19 Infection

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Abstract

Objective: The purpose of the present study was to evaluate the clinical course and maternal and perinatal outcomes of coronavirus disease-2019 (COVID-19) in pregnant women to determine the effects of the severity of the disease on these results.

Materials and Methods: The present study was planned retrospectively, and 303 patients between the ages of 16 and 46 who were admitted by Adana City Training and Research Hospital, Clinic of Gynecology and Obstetrics between 15.03.2020 and 01.10.2021 and diagnosed with COVID-19 with reverse transcription-polymerase chain reaction test, pregnant patients and newborns of those who gave birth among these patients were included in it.

Results: The mean age of pregnant women in the severe and critical disease group was found to be significantly higher than that of pregnant women in the mild disease group. The mean gestational week of the patients who were included in the study was 33.8±6.6 years. It was found that the pregnant women in the severe and critical disease group had a lower gestational week than the pregnant women in the mild disease group, and this difference was significant.

Conclusion: It was determined that maternal age was higher in pregnant women who had severe and critical COVID-19 disease than in those with mild disease. It was determined that the presence of obesity and comorbid disease in pregnant women with COVID-19 did not correlate with the severity of the disease.

Keywords: COVID-19, pregnancy, disease severity, preterm birth, perinatal outcomes

Introduction

Coronavirus disease-2019 (COVID-19) is caused by a highly pathogenic virus from the β-coronavirus group of the Coronaviridea family called severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) and was first described in China in 2019. The virus is transmitted among people through droplets as a disease that is easily transmitted and patients usually have mild to moderate symptoms. Severe conditions such as pneumonia and acute respiratory distress syndrome may also develop in some patients [1,2]. The disease may progress more severely in patients who have comorbidities such as underlying heart disease, chronic lung disease, and diabetes [3]. According to World Health Organization data, 659.124.900 people have been diagnosed with COVID-19 since the declaration of a pandemic, and 6.676.181 deaths have occurred due to COVID-19. Around the world, approximately one million people are diagnosed of COVID-19 every day, and approximately 4.000

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people die of of COVID-19 [4]. Very serious restrictions were applied in this respect. Although SARS-CoV-2 was first detected in patients with unexplained pneumonia, it was later shown in studies that it can cause different clinical manifestations, from multi-organ failure, because of the cytokine storm caused by this virus, and it was shown that it can target many tissues. It is now known that it can also cause serious complications and death. Physiological adaptation mechanisms of pregnancy that develop during pregnancy are considered to be a high-risk process because of cardiovascular, immunological, and respiratory changes, and therefore, many studies try to uncover the differences in the clinical course of the disease in pregnancy from that in the normal population. Although some studies speculated that pregnancy is a risk factor affecting the clinical course of COVID-19 negatively, the evidence on this subject is insufficient. In addition, the data in the literature show that the increased severity of COVID-19 in pregnant women significantly increases maternal and fetal complications [5-7]. All the effects of SARS-CoV-2 in pregnancy have not yet been demonstrated. There is a need for collaborative studies to be conducted worldwide to determine the effects of SARS-CoV-2 on implantation, fetal growth and development, and birth and neonatal health [6]. The clinical experience of pregnant women with SARS and Middle East respiratory syndrome (MERS) infections from other coronaviruses in the past caused pregnant women to be identified as a risk group because of more complications and risk of serious disease, and it was recommended that additional precautions must be taken [6,8]. The purpose of the present study was to evaluate the clinical course and maternal and perinatal outcomes of COVID-19 in pregnant women, to determine what kind of effects the severity of the disease causes on these results, and to contribute to the literature by revealing the maternal and fetal negative effects of COVID-19 that occurs during pregnancy, to reduce complications as much as possible and to raise awareness on this issue.

Materials and Methods

The present study was planned retrospectively, and 303 patients between the ages of 16 and 46 who were admitted by Adana City Training and Research Hospital, Clinic of Gynecology and Obstetrics between 15.03.2020 and 01.10.2021 and diagnosed with COVID-19 with reverse transcription-polymerase chain reaction (RT-PCR) test, pregnant patients and newborns of those who gave birth among these patients were included in it. This study was approved by University of Health Sciences Turkey, Adana City Training and Research Hospital, Clinical Research Ethics Committee (date: 04.11.2021, meeting number: 92, decision no: 1628). Patients' ages, gestational weeks, body mass index (BMI) scores, troponin, C-reactive protein (CRP), procalcitonin, ferritin, D-dimer, urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), sodium, potassium, hemoglobin, platelet, leukocyte, neutrophil, lymphocyte, and their laboratory findings including monocytes, international normalized ratio, fibrinogen values, presence of chronic disease, symptoms, gestational week, whether or not the patient gave birth during hospitalization, if she did, the type and timing of the delivery, indications for cesarean section, hospitalization in the intensive care unit, oxygen support, mechanical ventilation or ECMO, whether the patient received support, the presence of pneumonia findings in lung imaging, stillbirth, maternal death, 1st and 5th minute APGAR scores of newborns, RT-PCR results in swab samples taken from newborns within the first 24 hours were obtained by examining patient files in an electronic environment. The pregnant patients with COVID-19 who were taken into custody were examined by dividing them into two categories as the mild disease group and the severe and critical disease group. The data used in the study were analyzed comparatively between these two groups. In this study, the severity scale defined by Wu and McGoogan [9] was used as a reference. In this definition, the mild disease group was defined as patients with asymptomatic or mild symptoms, the severe disease group was defined as patients with tachypnea (respiratory rate 30/min), hypoxia (SPO_2 93 and below in room air or PaO_2/FiO_2 <300 mmHg), patients with more than 50% lung involvement in imaging, and the critical disease group was defined as patients with respiratory failure, septic shock, or multiorgan failure. Among the patients, asymptomatic patients and those with oxygen saturation over 93% and showing mild signs of disease without the need for oxygen support were in the mild disease group, those with severe dyspnea symptoms and oxygen saturation was 93% and below, those who received oxygen support with mechanisms such as a nasal cannula, mask with reservoir, high flow oxygen, continious positive airway pressure, bilevel positive airvay pressure, and patients who received mechanical ventilation and respiratory support were evaluated in the severe and critical disease group.

Statistical Analysis

The Statistical Package for the Social Sciences 23.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum were appropriate). The Shapiro-Wilk test was used to determine whether the parameters in the study showed normal distribution, and the chi-square and Fisher's exact tests were used to compare the categorical expressions. The Mann-Whitney U test was used for the parameters that did not show normal distribution and the logistic regression test was used for the mortality findings of the patients. The statistical significance level was taken as 0.05 in all tests.

Results

It was found that 273 (90%) of the 303 pregnant patients who were diagnosed with COVID-19 included in the study had mild disease and 30 (10%) had severe and critical disease findings. The mean age of the pregnant women was 29.0±6.2 years. The mean age of the pregnant women in the severe and critical disease group was found to be significantly higher than that of the pregnant women in the mild disease group (p=0.010; p<0.05) (Table 1).

The mean gestational week of the patients who were included in the study was 33.8±6.6. It was found that the pregnant women in the severe and critical disease group had a lower gestational week than the pregnant women in the mild disease group, and this difference was significant (p=0.004; p<0.05) (Table 2).

It was found that 205 (68.3%) of the patients who were included in the study gave birth. When the patients who gave birth were examined in terms of preterm birth, delivery types, and first- and fifth- minute APGAR scores of newborns, the rate of preterm birth was found to be significantly higher in pregnant women in the severe and critically ill group than in the mild disease group (p<0.001). The frequency of cesarean delivery was significantly higher in the severe and critical disease group than in the mild disease group (p=0.001; p<0.05) (Table 3).

When the patients who were included in the study were examined in terms of laboratory findings, Troponin, Procalcitonin, Ferritin, CRP, AST, ALT, and LDH values were significantly higher in pregnant women in the severe and critical disease group when compared to the pregnant women in the mild disease group, and the lymphocyte count was

Table 1. Demographic characteristics of patients

	Mild illness (number of patients=273)	Severe and critical illness (number of patients=30)	Total (number of patients=303)	p[a]
	Mean ± standard deviation	Mean ± standard deviation	Mean ± standard deviation	
Age	28.7±6.2	31.8±5.7	29.0±6.2	**0.010***[, a]
BMI	28.9±4.7	30.0±0.4	29.0±4.8	0.245[a]
Body mass index grup	**Number of patients (%)**	**Number of patients (%)**	**Number of patients (%)**	
18.5≤ weak	1 (0.4)	-	1 (0.3)	0.419[b]
25-30 normal	162 (61.4)	18 (60)	180 (61.2)	
30-34.9 slightly fat	76 (28.8)	7 (23.3)	83 (28.2)	
35-39.9 fat	17 (6.4)	2 (6.7)	19 (6.5)	
40≥ morbidly obese	8 (3.0)	3 (10)	11 (3.7)	
Chronic diseases	**Number of patients (%)**	**Number of patients (%)**	**Number of patients (%)**	
Diabetes mellitus	5 (1.8)	-	5 (1.7)	0.455[b]
Hypertension	16 (5.9)	3 (10)	19 (6.3)	0.375[b]
Hypothyroidism	1 (0.4)	-	1 (0.3)	0.740[b]
Asthma	4 (1.5)	-	4 (1.3)	0.505[b]
Cardiovascular disease	2 (0.7)	-	2 (0.7)	0.638[b]

*p<0.05, [a]Mann Whitney U test, [b]Chi-square test, BMI: Body mass index

Table 2. Pregnancy characteristics of the patients

	Mild illness (number of patients=273)	Severe and critical illness (number of patients=30)	Total (number of patients=303)	p[a]
	Mean ± standard deviation	Mean ± standard deviation	Mean ± standard deviation	
Gestational week	34.1±6.7	30.4±5.2	33.8±6.6	**0.004****
Trimester	**Number of patients (%)**	**Number of patients (%)**	**Number of patients (%)**	
1. Trimester[+]	7 (2.6)	-	7 (2.3)	0.460
2. Trimester[++]	31 (11.0)	5 (16.7)	35 (11.6)	
3. Trimester[+++]	236 (86.4)	25 (83.3)	261 (86.1)	
Multiparity presence	**Number of patients (%)**	**Number of patients (%)**	**Number of patients (%)**	
Nullipar	54 (19.8)	4 (13.3)	58 (19.1)	0.394
Multipar	219 (80.2)	26 (86.7)	245 (80.9)	

**p<0.001, [a]Mann-Whitney U test, [+]0-14, [++]14-28, [+++]28 above

significantly lower (p=0.002; p=0.002; p<0.001; p=0.001; p<0.001; p<0.001; p<0.001; p=0.030, respectively) (Table 4).

Discussion

It is considered that COVID-19, which first emerged in China in December 2019 and turned into a serious pandemic all over the world, will cause various clinical differences in pregnant patients when compared to the normal population, with the effect of physiological and immunological adaptation mechanisms brought by pregnancy. The diagnosed patients follow a clinical course ranging from asymptomatic to severe disease requiring respiratory support and even death.

In this study, the mean age of the pregnant women was 29.0±6.2 years. The mean age of the pregnant women was

Table 3. Pregnancy outcomes and examination of newborns

	Mild illness (number of patients=273)	Severe and critical illness (number of patients=30)	Total (number of patients=303)	p[a]
Patients giving birth	185 (68.5)	20 (66.7)	205 (68.3)	0.836[b]
Preterm/term[+]				
Preterm	62 (33.5)	17 (85)	79 (38.5)	**<0.001**[**, b]
Term	123 (66.5)	3 (15)	126 (61.5)	
Type of birth				
C/S	115 (62.2)	20 (100)	135 (65.9)	**0.001**[**, b]
Vaginal birth	70 (37.8)	-	70 (34.1)	
1. Minute APGAR (mean ± standard deviation)	7.97±0.5	7.58±1.1	7.91±0.6	0.092[a]
5. MinuteAPGAR (mean ± standard deviation)	9.39±0.6	9.05±1.2	9.34±0.7	0.476[a]

**p<0.001, [a]Independent Student's t-test, [b]Chi-square test, [+]Less than 37 weeks, C/S: Cesarean section

Table 4. Laboratory findings

	Mild illness (number of patients=273)	Severe and critical illness (number of patients=30)	Total (number of patients=303)	p[a]
	Mean ± standard deviation	Mean ± standard deviation	Mean ± standard deviation	
Troponin	4.87±6.7	8.0±9.2	5.2±7.0	**0.002****
Procalcitonin	0.16±1.2	3.42±12.5	0.49±4.2	**0.002****
Urea	14.9±5.7	16.0±9.8	15.1±6.2	0.504
Creatinine	0.45±0.1	0.43±0.1	0.44±0.1	0.200
Ferritin	51.9±109.6	113.3±177.5	58.1±19.2	**<0.001****
C-reactive protein	34.8±43.8	72.9±84.5	38.6±50.5	**0.001****
Sodium	137.2±7.9	137.1±3.7	137.2±7.6	0.270
Potassium	4.02±0.4	3.90±0.4	4.0±0.4	0.094
Aspartate transferaminase	32.3±26.2	57.1±56.9	34.8±31.4	**<0.001****
Alanine transferaminase	21.4±23.7	47.7±60.0	24.0±30.2	**<0.001****
Lactate dehydrogenase	257.9±109.6	366.9±33.6	268.9±116.8	**<0.001****
Leukocyte	9127.3±3730.9	9680.0±3696.5	9182.0±3725.1	0.374
Neutrophil	6999.6±3352.5	7866.7±3451.9	7085.5±3366.7	0.108
Lymphocyte	1399.7±728.8	1146.7±616.3	1374.6±721.5	**0.030***
Monocyte	620.9±322.6	580±346.8	616.8±324.7	0.215
INR	1.30±5.8	0.93±0.05	1.26±5.5	0.194
Fibrinogen	482.7±334.1	471.7±144.6	481.6±320.1	0.579
D-dimer	2789.5±6295.2	2128.7±1737.3	2723±5996.8	0.289
Hemoglobin	11.2±1.6	11.5±1.3	11.2±1.5	0.534
Thrombocyte	226.7±157.9	254.2±130.6	229.4±155.5	0.294

*p<0.05, **p<0.00, [a]Mann-Whitney U test, INR: International normalized ratio

found to be significantly higher in the severe and critical disease groups than in the mild disease group. In a review that included 62 studies conducted by Lassi et al. [10], COVID-19 was examined in 2 categories as severe and non-severe, and it was found that 85.6% of pregnant women had non-severe COVID-19 and the remaining 14.4% had severe COVID-19. The study reported that pregnant women with severe COVID-19 were approximately 3.7 years older and had a higher risk of severe COVID-19 among women in a higher age group (>35 years) [10]. In another review of 33 studies including 385 patients, 95.6% of patients had mild disease, 3.6% had severe disease, and 0.8% had critical disease [11].

In the non-pregnant population, obesity was associated with severe COVID-19 disease, and several case series and cohort studies involving pregnant patients showed increased severity of COVID-19 in pregnant women with high BMI scores and obesity [12]. No significant differences were detected between the mild disease and severe and critical disease groups in terms of BMI scores. In a study that was conducted with pregnant patients in Italy, the mean BMI score of the patients was found to be 22.8, the mean BMI score of women with severe disease was found to be 30, and it was reported that the BMI of patients with severe disease was significantly higher than those with mild disease [13]. In a case series study conducted by Andrikopoulou et al. [14] in New York, mild disease was detected in 52% and severe disease in 47%, and it was found that there was no significant difference between the two groups regarding age and obesity.

In most previous studies, BMI scores were calculated by considering the weight of the patients before pregnancy or in the early gestational weeks, and the data on the weight of the patients in our study were obtained at the time of hospitalization. We think that the reason why our study was incompatible with the data given in the literature that BMI increases the severity of the disease was because of this.

It was reported in many previous studies that severe COVID-19 is more common in adults over 60 years of age, immunocompromised patients, and those with chronic diseases such as diabetes, hypertension, and chronic lung disease [15]. No significant differences were detected between the groups in terms of chronic disease findings. In a meta-analysis of pregnant patients with COVID-19, severe COVID-19 was associated with increased maternal age, high BMI scores, any pre-existing maternal disease, chronic hypertension, preeclampsia, gestational diabetes, and pregestational diabetes [2]. In a case series study conducted with 158 pregnant women by Andrikopoulou et al. [14], it was found that pregnant patients with moderate or severe disease had an underlying chronic disease and were diagnosed with asthma. The data obtained in our study regarding comorbidities do not match the literature data. The reason for this may be some hereditary differences because of ethnic origin as well as a lack of data because of deficiencies in the anamnesis of the patients.

In the present study, it was found that the pregnant women in the severe and critical disease group had a lower gestational week than the pregnant women in the mild disease group. In all studies conducted so far, there were not enough data on first- and early second-trimester pregnant patients, many data were obtained from patients in the third trimester. For this reason, according to the data in the literature, the data on whether gestational week affects the severity of the disease is not yet sufficient to comment on this issue.

The pregnancies of 3 (1%) of the 303 patients who were included in the current study resulted in abortion. Although there are some studies reporting data showing that the rate of miscarriage increased in other previous coronavirus (SARS, MERS) outbreaks, there was no evidence in the literature showing that COVID-19 increased the risk of miscarriage [16]. Among the patients who gave birth, 135 (65.9%) were delivered by cesarean section and 70 (34.1%) were delivered by normal vaginal delivery (NVD). Twenty patients who underwent cesarean section were in the severe and critical disease group, and none of the patients who gave birth with NVD had severe or critical disease findings. It was found that cesarean delivery rates differed according to the country where the study was conducted. In a systematic review conducted by Huntley et al. [17], the cesarean section rate was reported as 42.9% in Italy, 44.4% in the USA, and 92.2% in China. In the study, it was suggested that the difference in these rates was caused by the acceptance of COVID-19 as an independent cesarean indication in the data from China [17]. High cesarean rates may be caused by one of the following factors: concerns that pregnancy may increase the severity of the disease, fetal or neonatal transmission may increase with NVD, fetal distress may occur because of systemic inflammatory response in the mother, and thoughts such as reducing transmission to healthcare personnel. However, the role of cesarean section in reducing these risks has not been proven. In a study conducted by Khoury et al. [18] in New York in 5 centers, the rate of cesarean section was reported to be 52.4% in pregnant women with severe COVID-19 and 91.7% in critically ill patients, and a significant increase was reported between COVID-19 severity and cesarean rates. In a meta-analysis conducted by Lassi et al. [10], 48.4% of the patients gave birth with cesarean section, and the risk of cesarean section was found to be 1.39 times higher in severe cases.

It was found that the rate of preterm birth in the severe and critical disease groups was significantly higher than in the mild disease group. In the study conducted by Metz et al. [19], 1.219 pregnant COVID-19 patients were evaluated, and it was reported that the risk of preterm birth increased in severe

and critically ill patients when compared to asymptomatic patients.

Only 1 (0.3%) of the patients who were included in this study had positive RT-PCR results in their babies. This patient was admitted to the clinic with the diagnosis of PROM at 29 weeks of gestation, tocolysis was applied to the patient for 1 day, but the delivery could not be prevented, and the patient delivered by NVD. Based on these findings, although it is considered that RT-PCR positivity in the baby may have occurred with ascending transmission rather than vertical transmission, vertical transmission could not be excluded. There are many articles in the literature arguing that there is no vertical transition, as well as many publications containing data on vertical transition [20-22].

It was also found that troponin, procalcitonin, ferritin, CRP, ALT, AST, and LDH values in the blood samples taken at the time of hospitalization of the pregnant women who were included in the study were significantly higher in the severe and critical disease group than in the mild disease group. However, lymphocytopenia was also found to be significantly higher in the severe and critically ill group than in the mild disease group. Although the mean D-dimer values were above the upper reference value in all patient groups, no significant differences were detected between the groups. In a cohort that examined inflammatory biomarkers in pregnant patients with COVID-19, it was reported that especially lymphocytopenia and high CRP levels were associated with disease severity and mortality, and lymphopenia was associated with the possibility of receiving oxygen support. It was also reported in the same study that although D-dimer values were above the upper reference value, they were not associated with oxygen demand and did not cause any significant changes in the clinical course [23]. In a study by Zhou et al. [24] with patients in the normal population, high D-dimer values were reported to be associated with poor prognosis. It was concluded in another systematic review that D-dimer elevation is associated with mortality, as in many similar studies [25]. Pregnancy increases the risk of thromboembolism, and D-dimer values increase physiologically, especially in the third trimester. For this reason, the prognostic role of D-dimer in pregnant women with COVID-19 is controversial, and the data obtained from the publications so far do not provide sufficient evidence that high D-dimer affects the prognosis negatively in pregnant women with COVID-19 [26].

Study Limitations

The limitations of the current study were that only hospitalized pregnant patients were evaluated and outpatients were not included in the study, and insufficient data on the clinical prognosis of COVID-19 at early weeks of gestation were not presented because of the low number of first- and second-trimester patients.

Conclusion

The present study will contribute to many issues regarding the clinical course of the disease and maternal and fetal outcomes based on the data on pregnant patients with COVID-19, which has become a serious healthcare concern all over the world. We tried to contribute to the literature in terms of minimizing maternal and fetal complications by showing how it affects maternal and perinatal outcomes. We believe that further studies are needed to determine the negative impacts and unidentified aspects of COVID-19 on maternal and newborn health with prospective studies to be conducted with larger patient populations.

Ethics

Ethics Committee Approval: This study was approved by University of Health Sciences Turkey, Adana City Training and Research Hospital, Clinical Research Ethics Committee (date: 04.11.2021, meeting number: 92, decision no: 1628).

Informed Consent: Since all information was obtained from the hospital automation system, informed consent was not required from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ş.E.B., N.Y., E.B., Design: Ş.E.B., N.Y., E.B., Data Collection or Processing: Ş.E.B., N.Y., H.E.S., A.R.Ş., E.B., E.G., A.G., A.A., R.A.O., Analysis or Interpretation: Ş.E.B., N.Y., H.E.S., A.R.Ş., E.B., E.G., A.G., A.A., R.A.O., Literature Search: Ş.E.B., N.Y., H.E.S., A.R.Ş., E.B., E.G., A.G., A.A., R.A.O., Writing: Ş.E.B., N.Y., H.E.S., A.R.Ş., E.B., E.G., A.G., A.A., R.A.O.

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References

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507-13.
2. Khailany RA, Safdar M, Ozaslan M. Genomic characterization of a novel SARS-CoV-2. Gene Rep. 2020;19:100682.
3. Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infect Dis Poverty. 2020;9:29.
4. WHO coronavirus (COVID-19) Dashboard. WHO coronavirus (COVID-19) dashboard with vaccination data. Available from: https://covid19.who.int/
5. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020;370:m3320.

6. Di Mascio D, Khalil A, Saccone G, Rizzo G, Buca D, Liberati M, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. Am J Obstet Gynecol MFM. 2020;2:100107.

7. Berhan Y. COVID-19, a disease of enigma: why pregnant women are less vulnerable? Ethiop J Health Sci. 2020;30:315-8.

8. Pregnant and Recently Pregnant People, Available from: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnant-people.html

9. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323:1239-42.

10. Lassi ZS, Ana A, Das JK, Salam RA, Padhani ZA, Irfan O, et al. A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity. J Glob Health. 2021;11:05018.

11. Elshafeey F, Magdi R, Hindi N, Elshebiny M, Farrag N, Mahdy S, et al. A systematic scoping review of COVID-19 during pregnancy and childbirth. Int J Gynaecol Obstet. 2020;150:47-52.

12. McCartney SA, Kachikis A, Huebner EM, Walker CL, Chandrasekaran S, Adams Waldorf KM. Obesity as a contributor to immunopathology in pregnant and non-pregnant adults with COVID-19. Am J Reprod Immunol. 2020;84:e13320.

13. Savasi VM, Parisi F, Patanè L, Ferrazzi E, Frigerio L, Pellegrino A, et al. Clinical findings and disease severity in hospitalized pregnant women with coronavirus disease 2019 (COVID-19). Obstet Gynecol. 2020;136:252-58.

14. Andrikopoulou M, Madden N, Wen T, Aubey JJ, Aziz A, Baptiste CD, et al. Symptoms and critical illness among obstetric patients with coronavirus disease 2019 (COVID-19) infection. Obstet Gynecol. 2020; 136:291-9.

15. Choi HM, Moon SY, Yang HI, Kim KS. Understanding viral infection mechanisms and patient symptoms for the development of COVID-19 therapeutics. Int J Mol Sci. 2021;22:1737.

16. Woodworth KR, Olsen EO, Neelam V, Lewis EL, Galang RR, Oduyebo T, et al. Birth and infant outcomes following laboratory-confirmed SARS-CoV-2 infection in pregnancy - SET-NET, 16 Jurisdictions, March 29-October 14, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1635-40.

17. Huntley BJF, Huntley ES, Di Mascio D, Chen T, Berghella V, Chauhan SP. Rates of maternal and perinatal mortality and vertical transmission in pregnancies complicated by severe acute respiratory syndrome coronavirus 2 (SARS-Co-V-2) infection: a systematic review. Obstet Gynecol. 2020;136:303-12.

18. Khoury R, Bernstein PS, Debolt C, Stone J, Sutton DM, Simpson LL, et al. Characteristics and outcomes of 241 births to women with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection at five new york city medical centers. Obstet Gynecol. 2020;136:273-82.

19. Metz TD, Clifton RG, Hughes BL, Sandoval G, Saade GR, Grobman WA, et al. Disease severity and perinatal outcomes of pregnant patients with coronavirus disease 2019 (COVID-19). Obstet Gynecol. 2021;137:571-80.

20. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet. 2020;395:809-15. Erratum in: Lancet. 2020;395:1038. Erratum in: Lancet. 2020;395:1038.

21. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, Xia S, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Transl Pediatr. 2020;9:51-60.

22. Api O, Sen C, Debska M, Saccone G, D'Antonio F, Volpe N, et al. Clinical management of coronavirus disease 2019 (COVID-19) in pregnancy: recommendations of WAPM-World Association of Perinatal Medicine. J Perinat Med. 2020;48:857-66.

23. Lombardi A, Duiella S, Li Piani L, Comelli A, Ceriotti F, Oggioni M, et al. Inflammatory biomarkers in pregnant women with COVID-19: a retrospective cohort study. Sci Rep. 2021;11:13350.

24. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395:1054-62. Erratum in: Lancet. 2020;395:1038. Erratum in: Lancet. 2020;395:1038.

25. Rostami M, Mansouritorghabeh H. D-dimer level in COVID-19 infection: a systematic review. Expert Rev Hematol. 2020;13:1265-75.

26. Goodacre S, Horspool K, Nelson-Piercy C, Knight M, Shephard N, Lecky F, et al. The DiPEP study: an observational study of the diagnostic accuracy of clinical assessment, D-dimer and chest x-ray for suspected pulmonary embolism in pregnancy and postpartum. BJOG. 2019;126:383-92.

ORIGINAL RESEARCH

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An Evaluation of the Effect of the COVID-19 Pandemic Lockdown on Hanging Cases

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Abstract

Objective: To investigate whether the coronavirus disease-2019 (COVID-19) lockdown influenced the rate of hanging in all age groups. To identify the prognosis, risk factors, and injury patterns of hanging cases. To compare the difference between rates of survival and fatal hanging cases.

Materials and Methods: A retrospective patient review was carried out. This study was conducted in the Emergency Department (ED) of University of Health Sciences Turkey, Bursa Yüksek İhtisas Training and Research Hospital, Bursa, Turkey, between 1 January, 2018 and 30 September, 2022. Survivors and patients who had died were compared in terms of injury patterns and epidemiologic data. Cases admitted to the ED during the COVID-19 lockdown were also documented. A total of 34 hanging cases were reviewed.

Results: This study enrolled 5 men (14.7%) and 29 women (85.3%) with an average age of 33 (32.6-38.4) years. Ten of them died as a consequence of hanging. The findings indicate that the ligature mark most commonly occurs on the anterior side of the neck (n=28, 82.4%).

Conclusion: Additionally, more than half of the patients needed intubation (n=20, 58.8%). Half of the cases that presented on the lockdown days died.

Keywords: Emergency department, forensic sciences, hanging, suicide, the COVID-19 pandemic

Introduction

Every 40 seconds someone dies by suicide. Hanging is one of three common suicide methods worldwide, along with the usage of pesticide poisoning and gunshots [1]. In our country, 1.627 people died by suicidal hanging in 2019. Hanging is the leading suicide method, with a rate of 47.8% among other suicide methods [2]. The term "hanging" refers to an act with the intention of killing oneself by suspension from a ligature point with the usage of a ligature which around the neck [3]. Near-hanging cases are those patients who were unsuccessful in hanging themselves and were brought alive to the hospital [3]. Near-hanging is also a significant cause of morbidity.

The influence of the lockdown and curfew during the coronavirus disease-2019 (COVID-19) period on hanging cases has not been fully investigated. After the first COVID-19 case emerged in China on 1 December, 2019, the infection began to spread around the world and developed into a pandemic. The pandemic lockdown measures involving the curfews were declared as of 21 March, 2020 in Turkey and worldwide. The pandemic lockdown lasted until 17 May, 2021 in our country. Along with the curfew, individuals under the age of 20 and older than the age of than 65 were completely prohibited from leaving their homes [4].

The goal of this study was to reveal the effects of the COVID-19 pandemic lockdown period and its restrictions on hanging cases in all age groups. It also aims to show the differences in specifications between the surviving and fatal hanging cases. Our goal is to show the epidemiologic data, injury patterns, symptoms, and consequences of hanging cases using regional data.

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Materials and Methods

Our study was approved by the Ethics Committee of the University of Health Sciences Turkey, Bursa Yüksek İhtisas Training and Research Hospital (no: 2011-KAEK-25 2022/10-06). A review was performed of the cohort of 34 patients who suffered from hanging injuries and were admitted to the emergency department of the tertiary hospital in Bursa city in Turkey between 1 January, 2018 and 30 September, 2022. The patient information, including the medical status and epidemiological information, with regard to age, sex, Glasgow Coma scale (GCS), injury patterns, locations of the ligature marks (LMs), and history of chronic disease (CD) or psychiatric disease (PD), was obtained by reviewing the medical records of the patients. Superficial skin lesions were also documented and cross-referenced with specific body parts. Evidence of prior suicides and intubation interventions was also documented.

Statistical Analysis

As statistical analysis, in the data evaluation, frequency tables and percentages, minimum and maximum values and median values were presented. The chi-square and Fisher's exact tests were performed when required. In addition, the Kolmogorov-Smirnov and Shapiro-Wilk normality tests were used for selecting the Student's t-test or Mann-Whitney U analysis. SPSS 15.0 for Windows software package program was used for statistical analysis, and a p value below 0.05 was accepted as statistically significant.

Results

Thirty-four hanging cases were included in our cohort. Ten of them had died as a consequence of hanging. Four of the patients had CD. Five of the cases had a PD; three cases suffered from depression and two of them had post-traumatic stress disorder (PTSD). Of the patients, 29 were women (Table 1), which shows a high female dominance. The median age was found to be 33 years. Three cases presented with radiological findings. Three cases had made a prior suicide attempt. Most of the patients presented with skin lesions (n=28, 82.4%). Two cases sustained cervical vertebrae injury. Six cases did not present with any LMs on their necks. LMs most commonly occurred on the anterior side of the neck (n=28, 82.4%) (Graph 1). More than half of the patients needed intubation (n=20, 58.8%).

No statistical association was found between the period before and during the curfew of the COVID-19 lockdown period due to the low number of admissions during the curfew. The specifications of the patients are shown in Table 2.

There was no significant association found between fatal cases and survivors, according to the parameters of our study. Nevertheless, survivors tended to be older than those who died (Table 3). One third of the female cases died, while one fifth of the male cases died. Two-thirds of the cases with PD died. Skin lesions were seen in twice as many survivors as in victims of death. None of the patients had bone fractures, ecchymosis, or

Table 1. Epidemiologic data of the cases

Parameter	Numbers
Gender male/female n/(%)	5 (14.7)/29 (85.3)
Age (year)*	33 (32.6-38.4)
Glasgow Coma score	9 (7.6-9.8)
CT or MR finding yes/no	3 (8.8)/21 (61.8)
Chronic disease yes/no	4 (11.8)/30 (88.2)
Psychiatric disease yes/no	5 (14.7)/29 (85.3)
Depression yes/no	3 (8.8)/31 (91.2)
Post traumatic stress disorder yes/no	1 (2.9)/33 (97.1)
Suicide before yes/no	3 (8.8)/31 (91.2)
Skin lesion yes/no	28 (82.4)/6 (17.6)
Abrasion yes/no	28 (82.4)/6 (17.6)
Facial petechiae yes/no	3 (8.8)/31 (91.2)
Cervical vertebral injury yes/no	2 (8.3)/22 (91.7)
Dislocation yes/no	2 (8.3)/22 (91.7)
Ligature mark on the neck yes/no	28 (82.4)/6 (17.6)
Location of the ligature mark on the neck (anterior/lateral/posterior)**	28 (82.4)/12 (35.3)/2 (5.9)
The patients needs for intubation yes/no	20 (58.8)/14 (41.2)

*Continuous data were expressed as median (25-75 percentile), **Some cases have ligature marks on the neck on multiple sides, CT: Computed tomography, MR: Magnetic resonance

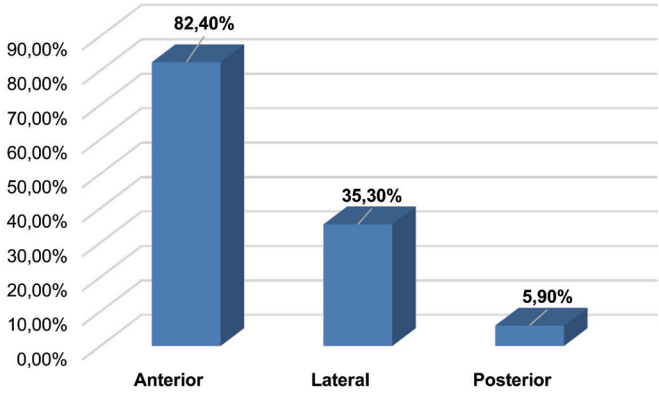
Table 2. The Specifications of the hanging cases during the COVID-19 pandemic

Variables	Case-1	Case-2	Case-3	Case-4
Age	18	31	25	28
Sex	Female	Male	Male	Male
Prognosis	In ward	Reject the treatment	Ex	Ex
GCS	12	15	3	3
Abrasion	Yes	None	Yes	Yes
Location of LM*	Anterior	Posterior	Anterior and lateral	Anterior
Hypoxia	Yes	None	Yes	Yes

*Some cases have ligature marks on the neck on multiple sides, COVID-19: Coronavirus disease-2019, GCS: Glasgow Coma scale, LM: Ligature mark

vessel tears in the cervical structures. Neither did any patients sustain subcutaneous emphysema or cervicospinal damage. None of the cases showed any of the following: Gastrointestinal findings, urinary incontinence, stroke findings, neurological deficits, cough, stridor, dysphagia, headache, or hemoptysis.

During the lockdown curfew, the following patients were admitted: A 26-year-old man who had a PD was admitted. He died as a result of hanging. A 28-year-old man with a diagnosis of depression died as consequence of hanging. A 40-year-old woman who suffered from PTSD was admitted during the curfew days. Although she had many findings, such as a low score on the GCS, aphonia, history of suicide, and loss of conciousness, there was no ligature mark. A 39-year-old man with a CD presented. After the treatment, he was discharged.



Graph 1. Distribution of the cases in terms of locations of the ligature mark on the neck

Discussion

Many studies have reported that most of the hanging cases were of adult age and male [5-9]. In a study exploring ten near-hanging cases, it was found that the mean GCS score was 9.5/15, which was slightly less than our results (11.1/15) [9]. In another study, conducted in the United States of America and consisting of 655 hanging cases, it was stated that the most significant prognostic factor was a GCS score below 15 [5]. Incredibly, it was suggested that any leakage of GCS points increases the mortality rate from 1.5% to 29% [5]. Bordia et al. [10] revealed that a GCS score of 15 excluded brain damage in hanging cases.

Somewhat similar to our results (n=3, 14.7%), Buitendag et al. [6] stated that the prevalence of PD as an illness comorbid with hanging was (n=17; 11.2%) [6]. Although Buitendag et al. [6] reported that 59% of their cohort had abrasions on the neck, our findings indicate higher numbers (n=28, 82.4%). However, in another study, LMs were found in 163 cases (38.4%) [11].

Similar to our results, in a study conducted in Australia exploring 72 near-hanging cases, it was suggested that neither spinal injury nor neurological deficits were found in cases who made a full recovery [7]. Compatible with our findings (n=4, 9%), in the same study, it was reported that the mortality rate of near-hanging cases was n=3, 8.8%. [7]. In studies by Ganesan et al. [8] and Hanna [12] (n=12, 15.6%) and (n=5, 38.4%) respectively of the subjects had made prior suicide attempts.

As in our study (n=28, 82.4%), Sharma et al. [13] revealed that most of the hanging cases (n=53, 80%) had LMs on the neck. In a study including 102 hanging cases, it was revealed that the most of the ligature knots were typically located on the posterior side of the neck (n=54, 52.9%) [14]. While our results

Table 3. The comparison of the cases according to their life status

Variables	Ex (n=10)	Near-hanging (n=24)	p
Age (year)	30.2±2.5	37.7±3.3	0.167
Gender male/female n/(%)	1 (20.0)/9 (31.0)	4 (80.0)/20 (69.0)	1.0
Glasgow Coma score		11.1±1.0	-
CT or MR finding yes/no	0 (0.0)/0.0	3 (100.0)/21 (100.0)	0.000
Chronic disease yes/no	2 (50.0)/8 (26.7)	2 (50.0)/22 (73.3)	0.564
Psychiatric disease yes/no	3 (60.0)/7 (24.1)	2 (40.0)/22 (75.9)	0.138
Depression yes/no	1 (33.3)/9 (29.0)	2 (66.7)/22 (71.0)	1.000
Post traumatic stress disorder yes/no	0 (0.0)/10 (30.3)	1 (100.0)/23 (69.7)	1.000
Suicide before yes/no	1 (33.3)/9 (29.0)	2 (66.7)/22 (71.0)	1.000
Skin lesion yes/no	10 (35.7)/0 (0.0)	18 (64.3)/6 (100.0)	0.148
Abrasion yes/no	10 (35.7)/0 (0.0)	18 (64.3)/6 (100.0)	0.148
Facial petechiae yes/no	0 (0.0)/10 (29.4)	3 (100.0)/21 (67.7)	0.539
Cervical vertebra injury yes/no	-	2 (100.0)/22 (100.0)	-
Dislocation yes/no	-	2 (100.0)/22 (100.0)	-

CT: Computed tomography, MR: Magnetic resonance

did not look at knot location, the most common location of LMs is found on the anterior. Contrary to our results (n=3, 8.8%); Kurtulus et al. [14] indicated that facial petechiae were observed in 46 (45.1%) subjects. A possible reason for the big difference was that their study was conducted only on dead subjects, whereas our cohort involves both survivors and deaths.

Incompatible with our findings (n=10, 4.1%), in a study that investigated 13 near-hanging cases, it was reported that five patients (38%) needed intubation [12]. In another study involving hanging cases admitted over the course of eight years, it was reported that 28 patients (68.2%) needed intubation [15].

In a study that evaluated suicide attempts during the COVID-19 pandemic, it was stated that a three fold decrease (6% vs. 2%) in hanging admissions was observed during the pandemic [16]. Despite there not being any observed statistical difference before and after the curfew between the number of hanging cases, an upward trend was seen in hanging cases after the lockdown in the UK [17].

Study Limitations

Neither trauma score nor injury severity score was included in our study. Nevertheless, GCS was achieved. Possibly, these scores are recorded in the more accessible patient files. Blood ethanol or drug levels could not be determined. These are the limits of our study.

Conclusion

The COVID-19 pandemic was a significant event that affected the behaviors of individuals. It may have triggered stressful events in all societies. Hanging is one of the most common suicide methods worldwide. In our study, we evaluated the regional data of hanging cases, the trend of hanging cases during the lockdown and the injury patterns of hanging cases were evaluated completely.

Ethics

Ethics Committee Approval: Our study was approved by the Ethics Committee of the University of Health Sciences Turkey, Bursa Yüksek İhtisas Training and Research Hospital (no: 2011-KAEK-25 2022/10-06).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.K., A.Z., M.Y., M.Ş., Design: S.K., A.Z., M.Y., Data Collection or Processing: A.Z., M.Y., M.Ş., Analysis or Interpretation: S.K., M.Y., M.Ş., Literature Search: S.K., M.Y., Writing: S.K., M.Y., M.Ş.

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References

1. https://www.who.int/news/item/09-09-2019-suicide-one-person-dies-every-40-seconds Accesed 10 January 2023.
2. https://data.tuik.gov.tr/Bulten/Index?p=Olum-ve-Olum-Nedeni-Istatistikleri-2019-33710 Accesed 10 January 2023.
3. Sabrinskas R, Hamilton B, Daniel C, Oliffe J. Suicide by hanging: a scoping review. Int J Ment Health Nurs. 2022;31:278-94.
4. https://www.icisleri.gov.tr/65-yas-ve-ustu-ile-kronik-rahatsizligi-olanlara-sokaga-cikma-yasagi-genelgesi# Accesed 18 January 2023.
5. Martin MJ, Weng J, Demetriades D, Salim A. Patterns of injury and functional outcome after hanging: analysis of the National Trauma Data Bank. Am J Surg. 2005;190:836-40.
6. Buitendag JJP, Ras A, Kong VY, Weale RD, Blodgett J, Bruce JL, et al. Hanging-related injury in Pietermaritzburg, South Africa. S Afr Med J. 2020;110:400-2.
7. Davidson JA. Presentation of near-hanging to an emergency department in the Northern Territory. Emerg Med (Fremantle). 2003;15:28-31.
8. Ganesan P, Jegaraj MKA, Kumar S, Yadav B, Selva B, Tharmaraj RGA. Profile and Outcome of Near-hanging Patients Presenting to Emergency Department in a Tertiary Care Hospital in South India - A Retrospective Descriptive Study. Indian J Psychol Med. 2018;40:205-9.
9. Atreya A, Kanchan T. Clinico-epidemiological study of near-hanging cases - an investigation from Nepal. J Forensic Leg Med. 2015;33:35-8.
10. Bordia R, Freeman C, Kou HH, Culhane J. Do we need neuroimaging in every case of near-hanging?: experience from a level 1 trauma center and analysis of the National Trauma Data Bank. Emerg Radiol. 2022;29:49-57.
11. Williamson F, Collins S, Dehn A, Doig S. Vascular injury is an infrequent finding following non-fatal strangulation in two Australian trauma centres. Emerg Med Australas. 2022;34:223-9.
12. Hanna SJ. A study of 13 cases of near-hanging presenting to an Accident and Emergency Department. Injury. 2004;35:253-6.
13. Sharma BR, Harish D, Sharma A, Sharma S, Singh H. Injuries to neck structures in deaths due to constriction of neck, with a special reference to hanging. J Forensic Leg Med. 2008;15:298-305.
14. Kurtulus A, Yonguc GN, Boz B, Acar K. Anatomopathological findings in hangings: a retrospective autopsy study. Med Sci Law. 2013;53:80-4.
15. Kao CL, Hsu IL. Predictors of functional outcome after hanging injury. Chin J Traumatol. 2018;21:84-7.
16. Lee I, Choi J, Kim KS, Suh J, Kim JH, Kim S. Suicide attempts presenting to the emergency department before and during the COVID-19 pandemic: a comparative study. Clin Exp Emerg Med. 2022;9:120-7.
17. McClelland G, Shaw G, Thompson L, Wilson N, Grayling M. Impact of the COVID-19 lockdown on hangings attended by emergency medical services. Resuscitation. 2020;157:89-90.

ORIGINAL RESEARCH

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Association of Whole Blood Viscosity and Severe Extracranial Carotid Artery Stenosis

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Abstract

Objective: Carotid artery stenosis (CAS) is not only an important risk factor for cerebrovascular events but also can indicate generalized atherosclerosis. Hemorheological parameters are altered in CAS and chronic cerebrovascular disorders as well, but it is controversial whether hemorheological parameters could be markers of stenosis or atherosclerosis.

Materials and Methods: We studied 154 patients with extracranial internal carotid artery stenting for symptomatic or asymptomatic severe CAS. Hematocrit total protein values of the patients included in the study were calculated using the De-Simone constant formula, low shear stress (LSR) and high shear stress (HSR).

Results: No statistically significant difference was found between the whole blood viscosities (LSR, HSR) of asymptomatic and symptomatic patients with carotid artery stenting (p=0.234, p=0.165).

Conclusion: Although hemorheological parameters are impaired in both CAS and chronic cerebrovascular disorders, the severity of stenosis cannot be detected based on hemorheological parameters. Our investigation suggests that the alteration of hemorheological parameters could indicate carotid atherosclerosis.

Keywords: Carotid artery stenosis, hematocrit, viscosity, carotid artery stenting

Introduction

The relationship between age, gender, blood pressure, total cholesterol, low-density lipoproteins and high-density lipoproteins, triglyceride levels, smoking, fibrinogen concentration, whole blood viscosity (WBV), and cerebrovascular diseases has been reported [1-5]. Blood viscosity level in patients with small artery occlusion was higher than in other stroke subtypes with large artery atherosclerosis or cardioembolism [6,7]. Flow resistance is proportional to blood viscosity and inversely proportional to vessel diameter; thus, flow resistance is markedly increased in narrow vessels such as stenotic lesions or small perforating arteries [6,8]. This is only a hypothesis, and whether blood viscosity affects large arteries other than small vessels has not been proven. In addition, there are few studies showing that WBV can also correlate with the degree of carotid artery stenosis (CAS) in both symptomatic and asymptomatic patients [9-11].

CAS that is defined by a stenosis of ≥70 (high-grade) CAS in the region of the bifurcation of the extracranial internal carotid artery, is a major risk factor for ischemic stroke [12].

It is not clear whether alterations in blood rheology are the late consequences of cerebrovascular events or markers of carotid atherosclerosis. Several studies have investigated the connection between hemorheological parameters and stenosis of carotid arteries, but their methods of hemorheological measurements and patient classification according to stenosis were different. In this study, we decided to compare the acute clinically significant stenosis with non-significant stenosis.

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Materials and Methods

A total of 154 consecutive patients with severe extracranial internal CAS who underwent endovascular carotid artery stenting between January 2018 and December 2021 were included in this study. The severity of the stenosis (≥70%) was detected by Doppler ultrasonography and/or computed tomography angiogram and was confirmed by the American Symptomatic Carotid Endarterectomy Trial formula. Both symptomatic (acute stroke or tia) and asymptomatic patients were evaluated.

The inclusion criteria were; age between 18 and 80 years, having no history of coronary and peripheral artery diseases, no history of malignancy, rheumatological diseases, and alcohol. Other patients were excluded from the study.

Ethics committee approval was obtained from the Ethics Committee of Samsun University, Samsun Training and Research Hospital with dated 26.05.2021 and decision number 2021/10/15. Informed consent was obtained from all patients included in the study.

Calculation of Whole Blood Viscosity

Hematocrit and total protein values were calculated using the De-Simone constant formula, low shear stress (LSR) and high shear stress (HSR) [5].

For HSR calculation: (0.12 × HCT) + 0.17 (TP - 2.07)

For LSR calculation: (1.89 × HCT) + 3.76 (TP - 78.42)

Statistical Analysis

Statistical analysis was performed with IBM SPSS statistical software version 26. Data are expressed as mean standard deviation. Differences between categorical variables were investigated with the chi-square test. Difference among groups for variables that were considered a normal distribution with Shapiro-Wilk test was evaluated by One-Way ANOVA and Dunnett post-hoc tests. Non-parametric Mann-Whitney U test was used for non-normal distribution variables. Significance level was defined as $p<0.05$.

Results

One hundred fifty four patients were included in the study; 43 (27.9%) were female and 111 (72.1%) were male. The mean age was 67.8±9 years. According to DSA, patients with stenosis of 70% or more were divided into two groups; symptomatic and asymptomatic. Seventy eight (50.6%) of patients constituted the symptomatic patient group. Demographic characteristics and biochemical parameters (albumin, total protein, etc.) are shown in Table 1. There was no statistically significant difference in demographic and biochemical data between symptomatic and asymptomatic patients (p=0.791).

According to their smoking habits, they were divided into two groups as current smokers and non-smokers. The smoker ratio was 29.9 %.

Comorbidities such as diabetes mellitus (DM) and hypertension (HT) are shown in Table 2. Stenting was applied to the right internal carotid in 83 (53.9%) patients. Re-stroke was seen in 11 (7.1%) of all patients within the last 6 months (Table 2).

WBV was not statistically significant between the symptomatic and asymptomatic groups (Table 3). The effect of gender on LSR (p=0.097), HSR (p=0.084), and stenosis grade (p=0.912) was not statistically significant. The effects of DM and HT on LSR (p=0.106), HSR (p=0.063), and the degree of stenosis (p=0.272) were not statistically significant. Both group LSR (p=0.774), HSR (p=0.903), and degree of stenosis (p=0.927) did not differ between smokers and non-smokers. The side of the carotid artery stenting on LSR (p=0.772), HSR (p=0.901), and stenosis grade (p=0.165) was not statistically significant.

Table 1. Demographic data

	Total	Minimum	Maximum	Mean	Standard deviation
Degree of carotid artery stenosis	154	70.0	99.0	84.8	10.5
Age	154	48.0	82.0	67.8	9.0
Haematocrit	154	23.2	49.4	38.4	4.9
Total protein	154	3.5	8.6	6.7	0.7
Albumin	154	1.8	5.1	3.8	0.5
LDL	154	24.0	211.0	107.0	43.7
HDL	154	14.0	120.0	42.1	11.9
Triglyceride	154	37.0	799.0	173.2	126.6
Total cholesterol	154	73.0	363.0	178.4	55.09
Total	154				

LDL: Low-density lipoprotein, HDL: High-density lipoproteins

Table 2. Risk factors and stroke recurrence

Risk factors	Yes	No	Total
Smoking	46 (29.9%)	108 (70.1%)	154
Hypertension	154 (100%)	0	154
Diabetes mellitus	58 (37.7%)	96 (62.3%)	154
Re-stroke after carotid stenting	11 (7.1%)	143 (92.9%)	154

Table 3. LSR and HSR rates in the both groups

	Symptomatic group	Asymptomatic group	p value
WBV at LSR (0.5/s-1)	46.5±13.4	45.3±10.4	0.234
WBV at HSR (208/s-1)	16.5±0.7	15.1±0.9	0.165

WBV: Whole blood viscosity, HSR: High shear stress

There was no statistical difference between LSR (p=0.464), HSR (p=0.413), and stenosis grade (p=0.726) values in patients who had and did not have a stroke after stenting.

Discussion

Our study is the first to investigate WBV in asymptomatic and symptomatic severe CAS. Previous investigations showed increased hematocrit levels, WBV, and plasma viscosity in stenosis in patients with chronic cerebrovascular diseases, but in acute stroke, no differences were found in hematocrit and WBV [11,13,14]. Only plasma viscosity was higher in patients with severe CAS [11]. Our results in our study were similar to those in the literature.

Prior findings suggested that red blood cell deformability and WBV may be potential markers of atherosclerotic plaque formation in patients after three months of acute stroke [15]. There are several studies claiming that WBV and hematocrit levels may predict intima-media thickness (IMT), early phase atherosclerosis, and the progression of stenosis [14-17]. The studies found a correlation between hematocrit and IMT [17], between WBV and early phase atherosclerosis [14,17].

Studies showed an association between active or ex-smokers and hemorheological disturbances such as increased hematocrit, WBV, fibrinogen, deteriorated red blood cell aggregation, and deformability [14,17-19]. Our results suggest that active smoking is a relevant factor, but past history smoking does not play a significant role in hemorheology [19].

Our study results show no statistical association between WBV and severe CAS, but cerebrovascular events themselves play a remarkable role.

Multicentre and prospective studies are needed in large populations to better characterize the relationship between severe CAS and WBV.

Study Limitations

The modest sample size, retrospective, non-randomized, and single-center study are important methodological shortcomings. WBV was not validated by accurate measurement of viscosity using a viscometer. The extrapolation formula that we used in our study has been validated and used in several other studies, but direct comparison of estimated and directly measured WBV in this patient population may strengthen our results and serve precision. In addition, other hemorheological factors that may affect blood viscosity, such as platelet and erythrocyte aggregability and rigidity, were not evaluated.

Conclusion

To our knowledge, this is the first study to evaluate the relationship between WBV and stenosis in patients with severe CAS. Results of our study showed that increased WBV, LSR, and HSR were not significantly clear in patients with symptomatic and asymptomatic stenosis.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the Ethics Committee of Samsun University, Samsun Training and Research Hospital with dated 26.05.2021 and decision number 2021/10/15.

Informed Consent: Informed consent was obtained from all patients included in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.B.B., Concept: Ç.K.A., Design: A.B.B., Data Collection or Processing: A.B.B., Analysis or Interpretation: Ç.K.A., Literature Search: A.B.B., Writing: A.B.B.

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References

1. Lowe GD, Drummond MM, Forbes CD, Barbenel JC. The effects of age and cigarette-smoking on blood and plasma viscosity in men. Scott Med J. 1980;25:13-7.
2. Levenson J, Simon AC, Cambien FA, Beretti C. Cigarette smoking and hypertension. Factors independently associated with blood hyperviscosity and arterial rigidity. Arteriosclerosis. 1987;7:572-7.
3. Koenig W, Sund M, Ernst E, Mraz W, Hombach V, Keil U. Association between rheology and components of lipoproteins in human blood. Results from the MONICA project. Circulation. 1992;85:2197-204.
4. Bonithon-Kopp C, Levenson J, Scarabin PY, Guillanneuf MT, Kirzin JM, Malmejac A, et al. Longitudinal associations between plasma viscosity and cardiovascular risk factors in a middle-aged French population. Atherosclerosis. 1993;104:173-82.

5. de Simone G, Devereux RB, Chien S, Alderman MH, Atlas SA, Laragh JH. Relation of blood viscosity to demographic and physiologic variables and to cardiovascular risk factors in apparently normal adults. Circulation. 1990;81:107-17.

6. Furukawa K, Abumiya T, Sakai K, Hirano M, Osanai T, Shichinohe H, et al. Increased blood viscosity in ischemic stroke patients with small artery occlusion measured by an electromagnetic spinning sphere viscometer. J Stroke Cerebrovasc Dis. 2016;25:2762-9.

7. Grotemeyer KC, Kaiser R, Grotemeyer KH, Husstedt IW. Association of elevated plasma viscosity with small vessel occlusion in ischemic cerebral disease. Thromb Res. 2014;133:96-100.

8. Goldstein LJ, Rypins EB. Blood vessel modeling. Int J Biomed Comput. 1991;29:23-9.

9. Assayag EB, Bova I, Kesler A, Berliner S, Shapira I, Bornstein NM. Erythrocyte aggregation as an early biomarker in patients with asymptomatic carotid stenosis. Dis Markers. 2008;24:33-9.

10. Harrison MJ, Pollock S, Kendall BE, Marshall J. Effect of haematocrit on carotid stenosis and cerebral infarction. Lancet. 1981;2:114-5.

11. Levenson J, Gariepy J, Del-Pino M, Salomon J, Denarie N, Simon A. Association of plasma viscosity and carotid thickening in a French working cohort. Am J Hypertens. 2000;13:753-8.

12. Touzé E. Treatment of carotid stenosis. Curr Vasc Pharmacol. 2012;10:734-8.

13. Li RY, Cao ZG, Li Y, Wang RT. Increased whole blood viscosity is associated with silent cerebral infarction. Clin Hemorheol Microcirc. 2015;59:301-307.

14. Szapary L, Horvath B, Marton Z, Alexy T, Demeter N, Szots M, et al. Hemorheological disturbances in patients with chronic cerebrovascular diseases. Clin Hemorheol Microcirc. 2004;31:1-9.

15. Magyar MT, Szikszai Z, Balla J, Valikovics A, Kappelmayer J, Imre S, et al. Early-onset carotid atherosclerosis is associated with increased intima-media thickness and elevated serum levels of inflammatory markers. Stroke. 2003;34:58-63.

16. Grotta JC, Yatsu FM, Pettigrew LC, Rhoades H, Bratina P, Vital D, et al. Prediction of carotid stenosis progression by lipid and hematologic measurements. Neurology. 1989;39:1325-1331.

17. Lee AJ, Mowbray PI, Lowe GD, Rumley A, Fowkes FG, Allan PL. Blood viscosity and elevated carotid intima-media thickness in men and women: the Edinburgh Artery Study. Circulation. 1998;97:1467-73.

18. Ergun DD, Karis D, Alkan FA, Cakmak G, Yenigun M, Ercan M. Effects of cigarette smoking on hemorheologic parameters, plasma osmolality and lung function. Clin Hemorheol Microcirc. 2016;63:313-24.

19. Kannel WB, D'Agostino RB, Belanger AJ. Fibrinogen, cigarette smoking, and risk of cardiovascular disease: insights from the Framingham Study. Am Heart J. 1987;113:1006-10.

REVIEW

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Optimizing Patient Care in the Emergency Department: Insights from Automated Alert Systems and Triage Strategies

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Abstract

Over the past three decades, various scoring systems have emerged in clinical practice, but evidence primarily originates from ward contexts, yielding conflicting data on their impact, including mortality and referrals. Although early intervention benefits emergency department (ED) patients, the effectiveness of early warning systems remains uncertain due to insufficient evidence. This systematic review aims to comprehensively analyze current literature, exploring the integration of automated alerts and novel triage methods in the ED. Thorough database searches (e.g., MEDLINE/PubMed, Cochrane Library) identified relevant articles meeting specific criteria: adults (≥18 years), randomized controlled trials, observational, and comparative studies. Inclusion focused on English-language, human-participant studies; exclusions involved pediatric, case, non-English studies, and abstract-only content. Initially, 260 studies underwent screening based on titles and abstracts, with 218 papers excluded. Subsequently, 42 papers underwent full-text assessment, eliminating articles not meeting the criteria. Ultimately, only four studies were deemed suitable for final data collection and inclusion in the review. The integration of technology-assisted decision support, combined triage approaches, and standardized assessment tools shows promise in enhancing patient outcomes and optimizing resource utilization. Nonetheless, the studies' limitations highlight the importance of robust research methods and a considerate implementation process. Advancing emergency care necessitates a harmonious balance between innovation and evidence-based practice to ensure the highest quality of patient well-being.

Keywords: Early warning score, mortality, triage methods, vital signs

Introduction

Physiological scoring systems such as the early warning score (EWS) play a vital role in quantifying the degree of deviation of physiological parameters from their normal values by consolidating them into a single numerical measure. These scores are extensively used in emergency departments (EDs) and general wards to promptly detect critically ill and deteriorating patients, facilitating early intervention and escalation of care [1].

Over the past three decades, several different scoring systems have been developed and implemented in clinical practice [2]. However, most of the supporting evidence comes from the ward setting, leading to conflicting data on the effectiveness of these scores in improving patient care, such as reduced mortality rates or increased referrals/admissions to intensive care facilities. Despite the benefits of early care for many conditions in the ED [3-5], the benefit of EWS in this setting remains uncertain due to a lack of sufficient evidence. One of the reasons for the limited evidence could be that most EWS were originally developed based on ward data sets, which might not fully capture the unique challenges of the ED environment. ED patients often present with acute and rapidly resolved physiological disturbances (e.g., supraventricular tachycardia), making the application of ward-based scoring systems challenging [6,7]. For example, diseases that are normally mild can suddenly become very aggressive and potentially fatal for patients [8]. Recognizing these patients early in the ED is crucial. Therefore, EWS systems are of great importance in EDs.

In response to these concerns, the UK-based Royal College of Physicians developed the national early warning score (NEWS)

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and its updated version, NEWS2, to enhance the detection of patients at risk for deterioration, thereby triggering timely escalation of care [9,10]. Both NEWS and NEWS2 have demonstrated superior performance over other EWS in predicting mortality and clinical deterioration, leading to widespread adoption in hospitals and EDs in the UK and beyond [11,12].

However, EWS have faced criticism for their failure to consider chronic hypoxia in their scoring systems, particularly in patients with chronic pulmonary diseases. Current scoring systems often trigger similar scores for decreased oxygen saturations (SpO_2) regardless of patient age or disease chronicity, potentially resulting in higher scores for patients with chronic lung conditions. National guidelines for patients with chronic lung disease recommend lower SpO_2 target levels (88-92%) during oxygen therapy, which fall below the trigger thresholds of most EWS, including NEWS [11]. This could lead to an overestimation of physiological disturbance in patients with chronic lung disease.

To address these concerns, the NEWS2 was introduced in 2017, incorporating a new SpO_2 scoring scale specifically tailored to patients with or at risk of chronic lung disease and type II respiratory failure [9]. Some studies have indicated that a NEWS2 score ≥5 effectively identifies patients at a higher risk of death, potentially benefiting from intensive care unit (ICU) admission (sensitivity for in-hospital mortality: 84.5%, and for ICU admission: 83.4%) [13].

However, despite being an updated version of NEWS, some studies have reported lower success rates for NEWS2 in discriminating adverse outcomes, such as inpatient mortality, unanticipated ICU admission, or cardiac arrest within the first 24 hours of admission, when compared to NEWS [14].

Given these uncertainties, this systematic review aims to comprehensively assess and synthesize the current body of literature surrounding the integration of automated alert systems and innovative triage strategies in EDs.

Methods

This systematic review adheres to the recommendations provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines [15]. The primary objective of this review is to comprehensively analyze and consolidate existing literature on the incorporation of automated alert systems and inventive triage strategies within the ED. To achieve this goal, the study question was framed using the population, exposure (intervention), control group, and outcome framework, ensuring a predetermined and well-defined methodology for the investigation [16].

Search Strategy

A comprehensive literature search was conducted across multiple electronic databases, including MEDLINE/PubMed, PubMed Central, Google Scholar, and the Cochrane Library, to identify relevant articles for this study. The search terms encompassed EWSs "in conjunction with terms related to the" ED acute medical unit in adult populations. Additionally, extensive searches were performed in reference lists and relevant journals to ensure the inclusion of all pertinent papers. Two independent reviewers executed the search and selected articles for further assessment. Furthermore, the references of the initially retrieved papers were manually examined to uncover any additional research that might have been overlooked during the initial search.

Inclusion and Exclusion Criteria

We included studies that met the following inclusion criteria: adult patients aged 18 years and above, randomized controlled trials, observational studies, and comparative studies. Only studies involving human participants and published in the English language were considered for inclusion.

However, the review excluded studies that fell under the following criteria: pediatric populations, individual case studies, studies presented in the form of letters, responses to letters or comments, articles published in languages other than English, and studies with only abstracts available and lacking full-text content.

Risk-of-Bias Assessment

In this systematic review, we utilized the "risk of bias in non-randomised studies-of interventions (ROBINS-I)" tool to assess the ROBINS included in our analysis [17]. Two independent reviewers conducted the evaluation of each study, and any discrepancies were resolved through discussion or consultation with a third reviewer when necessary.

For each included study, the reviewers assessed bias across the various domains outlined in the ROBINS-I tool. They carefully examined the study design, participant selection methods, intervention classification, deviations from intended interventions, outcome measurement procedures, and potential selective reporting of results. Each domain was evaluated to determine the level of bias in the study.

Following the assessments, an overall judgment of the risk of bias for each study was assigned based on the findings from individual domains.

Results

Following the initial search across PubMed, Google Scholar, and the Cochrane Library, a substantial pool of 2.937 studies was identified. However, an automated screening tool flagged 2.615 studies as ineligible based on predefined criteria.

A total of 260 studies underwent the initial title and the abstract screening process, and of these, 218 papers were excluded from further consideration. The remaining 42 papers underwent full-text evaluation, where articles that did not align with the topic or meet the exclusion criteria were removed. Only 4 studies emerged as suitable candidates for the final data collection and inclusion in the review (Figure 1, Table 1) [18-21].

Discussion

The synthesis of the reviewed studies offers a comprehensive exploration into the intricate landscape of optimizing patient care within the ED by integrating automated alert systems and innovative triage strategies. These studies collectively unravel multifaceted insights that underscore the potential benefits, operational challenges, and ethical considerations associated with these transformative approaches. By delving into the intricacies of patient assessment, monitoring, and timely interventions, these studies contribute to the evolving paradigm of emergency care.

In the midst of the hectic and unpredictable clinical atmosphere of the ED, an automated EWS becomes a vital ally and safety net, providing crucial assistance to patients in these dynamic and bustling healthcare hubs [22-25].

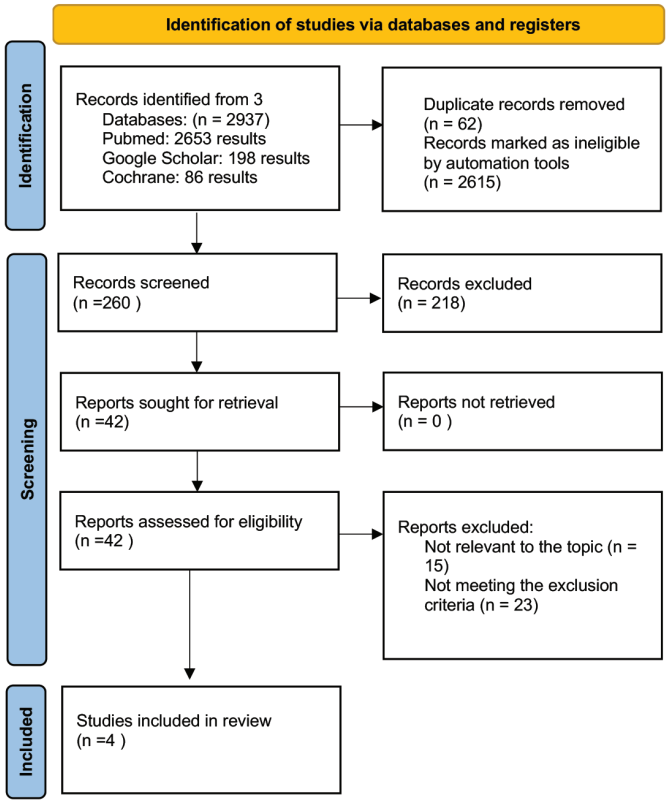

Figure 1. PRISMA diagram

PRISMA: Preferred reporting items for systematic reviews and meta-analyses

Writing a clinical trial varies with respect to the audience it is intended for [26]. This consideration is essential in ensuring effective communication and tailored dissemination of study results to different stakeholders.

In Alam et al. [18] study, correlations between NEWS and patient outcomes were significant across various time points, encompassing 30-day mortality, hospital admission, and length of stay. Although bearing a moderate level of bias and operational challenges, the study's findings indicate that NEWS holds potential value in the ED-distinct from its role as a triage system-by offering continuous monitoring throughout patients' ED and hospital stay. While the study design is commendable, limitations in sample size and operational aspects warrant consideration.

The concept of leveraging technology-driven solutions, as observed in studies examining automated alert systems, introduces a promising avenue for proactive patient management. The integration of an automated decision support system coupled with the NEWS, as demonstrated in Howard et al. [21] showcases tangible improvements in patient outcomes, such as reduced adjusted hospital mortality and length of stay. This finding aligns with emerging evidence that underscores the role of EWSs in identifying patients at risk of decompensation. However, the presence of moderate bias in the study warrants a measured interpretation of the results and prompts a critical assessment of potential confounders that may influence the observed outcomes.

Triage is a crucial step in emergency care, evaluating the urgency of a patient's clinical state. Various triage scales facilitate this evaluation [27-31]. Although generally displaying moderate to good validity [32], these scales may encounter challenges in terms of interrater reliability [27]. Additionally, while effective for prioritization, they might not serve as continuous monitoring tools in the ED [33]. This drawback could potentially result in undetected patient deterioration, especially during extended waiting periods.

The interplay between different triage strategies, notably the combination of the manchester triage system and the EWS, in McCabe et al. [19] study elucidates the potential to address the challenges posed by overcrowded EDs. While the study suggests positive effects on patient categorization and waiting times, the underlying operational complexities and the presence of serious bias necessitate caution in extrapolating the findings. This study underscores the intricate balance between appropriate prioritization, efficient resource utilization, and the need for a experienced clinical staff.

Direct comparisons between traditional triage scales and EWSs, as conducted in the Schinkel et al. [20] study, highlight the potential superiority of EWS in recognizing patients in need of urgent care. The robust performance of the modified

Table 1. Individual studies and their outcomes

Author	Aims	Study design, setting, and sample	Main results	Conclusions
Alam et al. [18]	To explore the performance of the NEWS in an ED with regard to predicting adverse outcomes	Study design: prospective observational. Patients: ED attendees with ESI 2 and 3 (excluding resuscitation room). Intervention: NEWS recorded at T0, T1, and T2 (arrival, 1 hour after arrival, transfer to ward/ICU). Outcomes: hospital admission, ICU admission, length of stay, 30-day mortality	Complete data was able to be collected for 274 patients on arrival at the ED. NEWS was significantly correlated with patient outcomes, including 30 day mortality, hospital admission, and length of stay at all-time points	The NEWS measured at different time points was a good predictor of patient outcomes and can be of additional value in the ED to longitudinally monitor patients throughout their stay in the ED and in the hospital
McCabe et al. [19]	To determine the effect of the EWS in conjunction with the MTS on the accuracy of the MTS and waiting times for patients in the ED	A retrospective cohort chart review of all adult patients who presented to the ED in one large hospital in Ireland (n=10,048) at three time points between 1st September 2015-30th September 2016; 3 months prior to EWS introduction, implementation month and 9 months post implementation	Patients were significantly more likely to be categorised as an MTS category 2 (rather than 3-5) after the EWS was introduced ($p<0.001$). Waiting times between triage and clinician review ($p<0.05$) increased as did total time in the ED ($p>0.001$). A similar finding was observed for patients with an MTS of 3-5	Although positive in terms of patient outcomes, the effective and sustained combined use of the MTS and EWS requires increased bed capacity and experienced clinical staff to ensure that the ED journey time reduced rather than increased
Schinkel et al. [20]	To compare the ability of currently used triage scales and EWS scores to recognise patients in need of urgent care in the ED	A retrospective, single-centre study on all patients who presented to the ED of a Dutch level 1 trauma centre, between 1 September 2018 and 24 June 2020 and for whom a NTS score as well as a MEWS was recorded. The performance of these scores was assessed using surrogate markers	MEWS score had a significantly better AUC than the NTS for predicting the need for hospital admission (0.65 vs. 0.60; $p<0.001$) or 30-day all-cause mortality (0.70 vs 0.60; $p<0.001$). Furthermore, when non-urgent MEWS scores co-occur with urgent NTS scores, the MEWS score seems to more accurately capture the urgency level that is warranted	EWSs could potentially be used to replace the current emergency triage systems
Howard et al. [21]	To study the effectiveness of a early warning score based decision support system to detect and intervene on clinical decompensation in the ED by evaluating reductions in hospital mortality and LOS	If and when a vital sign(s) deviation occurred to the point that an overall NEWS score of "5" was reached, an electronic text alert was sent the pagers of both the charge nurse and ED physician, prompting the performance of a rapid clinical assessment	The control group consisted of 11 150 admissions (across a period of 12 months) and the intervention group consisted of 8.363 admissions (across a period of 9 months). The reduction in O/E LOS was significant, and although the reduction in adjusted O/E mortality did not quite reach a p value of 0.05 ($p=0.09$) the effect size was large ($d=0.87$) indicating a substantial difference	Using an automated decision support surveillance and alert system to trigger alerts for ED patients reduced both adjusted hospital mortality and hospital length of stay

NEWS: National early warning score, ED: Emergency department, ICU: Intensive care unit, MTS: Manchester triage system, NTS: Netherlands triage system, MEWS: Modified early warning score, AUC: Area under the curve, LOS: Length of stay

EWS in predicting the need for hospital admission and 30-day all-cause mortality challenges the conventional reliance on patient complaints as the basis for triage decisions. This study contributes to the growing body of literature advocating for standardized assessment tools that can enhance the accuracy and efficiency of patient prioritization. However, the presence of serious bias underscores the importance of future investigations with rigorous designs and methodological robustness.

Among these insightful findings, it is imperative to acknowledge the limitations that underpin the studies. Operational

challenges, inherent biases, and relatively low patient numbers underscore the complexities of conducting research in a dynamic and fast-paced ED environment. While these studies provide valuable glimpses into the potential benefits of integrated approaches, they also emphasize the need for comprehensive evaluation and contextual understanding.

In conclusion, the amalgamation of these studies paints a nuanced portrait of optimizing patient care within the ED by merging automated alert systems and innovative triage strategies. The integration of technology-assisted decision support, combined triage methodologies, and standardized assessment tools holds promise for enhancing patient outcomes and streamlining resource allocation. However, the studies' limitations underscore the necessity of robust research methodologies and a thoughtful approach to implementation. The evolution of emergency care necessitates a concerted effort to balance innovation with evidence-based practicewhile striving to ensure the highest quality of care for patients in their most vulnerable moments.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.H.A., S.A., Design: B.H.A., S.A., Data Collection or Processing: B.H.A., S.A., Analysis or Interpretation: B.H.A., S.A., Literature Search: B.H.A., S.A., Writing: B.H.A., S.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Prytherch DR, Smith GB, Schmidt PE, Featherstone PI. ViEWS--towards a national early warning score for detecting adult inpatient deterioration. Resuscitation. 2010;81:932-7.
2. Lee A, Bishop G, Hillman KM, Daffurn K. The Medical Emergency Team. Anaesth Intensive Care. 1995;23:183-6.
3. Seymour CW, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, et al. Time to treatment and mortality during mandated emergency care for sepsis. N Engl J Med. 2017;376:2235-44.
4. Ferrer R, Martin-Loeches I, Phillips G, Osborn TM, Townsend S, Dellinger RP, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. Critical Care Medicine. 2014;42:1749-55.
5. Soar J, Nolan JP, Böttiger BW, Perkins GD, Lott C, Carli P, et al. European Resuscitation Council Guidelines for Resuscitation 2015: section 3. Adult advanced life support. Resuscitation. 2015;95:100-47.
6. Rees JE, Mann C. Use of the patient at risk scores in the emergency department: a preliminary study. Emerg Med J. 2004;21:698-9.
7. Bruijns SR, Wallis LA, Burch VC. A prospective evaluation of the Cape triage score in the emergency department of an urban public hospital in South Africa. Emerg Med J. 2008;25:398-402.
8. Yigit Y, Haddad M, Elmoheen A, Shogaa MR, Tawel R, Mohamed YK, et al. Can COVID-19 Cause flare-ups of acute hepatitis B? An atypical presentation of COVID-19 with acute hepatitis B. Case Rep Infect Dis. 2021;2021:8818678.
9. Royal College of Physicians (London). National Early Warning Score (NEWS) 2: standardising the assessment of acute-illness severity in the NHS - Updated report of a working party, 2017. Available from: URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6542226/
10. Royal College of Physicians (London). National Early Warning Score (NEWS Standardising the assessment of acute illness severity in the NHS - Report of a working party. London: Royal College of Physicians (London), 2012.
11. Nannan Panday RS, Minderhoud TC, Alam N, Nanayakkara PWB. Prognostic value of early warning scores in the emergency department (ED) and acute medical unit (AMU): a narrative review. Eur J Intern Med. 2017;45:20-31.
12. Smith GB, Prytherch DR, Meredith P, Schmidt PE, Featherstone PI. The ability of the national early warning score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. Resuscitation. 2013;84:465-70.
13. Fernando SM, Fox-Robichaud AE, Rochwerg B, Cardinal P, Seely AJE, Perry JJ, et al. Prognostic accuracy of the hamilton early warning score (HEWS) and the national early warning score 2 (NEWS2) among hospitalized patients assessed by a rapid response team. Crit Care. 2019;23:60.
14. Pimentel MAF, Redfern OC, Gerry S, Collins GS, Malycha J, Prytherch D, et al. A comparison of the ability of the national early warning score and the national early warning score 2 to identify patients at risk of in-hospital mortality: a multi-centre database study. Resuscitation. 2019;134:147-56.
15. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
16. Morgan RL, Whaley P, Thayer KA, Schünemann HJ. Identifying the PECO: a framework for formulating good questions to explore the association of environmental and other exposures with health outcomes. Environ Int. 2018;121:1027-31.
17. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355:i4919.
18. Alam N, Vegting IL, Houben E, van Berkel B, Vaughan L, Kramer MH, et al. Exploring the performance of the national early warning score (NEWS) in a European emergency department. Resuscitation. 2015;90:111-5.
19. McCabe C, O'Brien M, Quirke MB. The introduction of the early warning score in the emergency department: a retrospective cohort study. Int Emerg Nurs. 2019;45:31-5.
20. Schinkel M, Bergsma L, Veldhuis LI, Ridderikhof ML, Holleman F. Comparing complaint-based triage scales and early warning scores for emergency department triage. Emerg Med J. 2022;39:691-6.
21. Howard C, Amspoker AB, Morgan CK, Kuo D, Esquivel A, Rosen T, et al. Implementation of automated early warning decision support to detect acute decompensation in the emergency department improves hospital mortality. BMJ Open Qual. 2022;11:e001653.
22. Bashir K, Arshad W, Azad AM, Alfalahi S, Kodumayil A, Elmoheen A. Acceptability and feasibility of mini clinical evaluation exercise (Mini-CEX) in the busy emergency department. Open Access Emerg Med. 2021;13:481-6.
23. Courtney DM, Neumar RW, Venkatesh AK, Kaji AH, Cairns CB, Lavonas E, et al. Unique characteristics of emergency care research: scope, populations, and infrastructure. Acad Emerg Med. 2009;16:990-4.
24. Roland D, Coats TJ. An early warning? Universal risk scoring in emergency medicine. Emerg Med J. 2011;28:263.
25. Yigit Y, Yilmaz S, Ozbek AE, Karakayali O, Cetin B, Halhalli HC. Can platelet indices reduce negative appendectomy rates? Cureus. 2019;11:e4293.

26. Bhatti JA, Janjua NZ, Akhtar U, Azad A. Writing the introduction and methods of a controlled trial. J Pak Med Assoc. 2014;64:720-2.

27. Mélot C. To score or not to score during triage in the emergency department? Intensive Care Med. 2015;41:1135-7.

28. Mirhaghi A, Heydari A, Mazlom R, Ebrahimi M. The reliability of the Canadian triage and acuity scale: meta-analysis. N Am J Med Sci. 2015;7:299-305.

29. Parenti N, Reggiani ML, Iannone P, Percudani D, Dowding D. A systematic review on the validity and reliability of an emergency department triage scale, the Manchester Triage System. Int J Nurs Stud. 2014;51:1062-9.

30. Gottschalk SB, Wood D, DeVries S, Wallis LA, Bruijns S; Cape Triage Group. The cape triage score: a new triage system South Africa. Proposal from the Cape Triage Group. Emerg Med J. 2006;23:149-53.

31. Widgren BR, Jourak M. Medical emergency triage and treatment system (METTS): a new protocol in primary triage and secondary priority decision in emergency medicine. J Emerg Med. 2011;40:623-8.

32. Zachariasse JM, Seiger N, Rood PP, Alves CF, Freitas P, Smit FJ, et al. Validity of the manchester triage system in emergency care: a prospective observational study. PLoS One. 2017;12:e0170811.

33. Jo S, Jeong T, Jin YH, Lee JB, Yoon J, Park B. ED crowding is associated with inpatient mortality among critically ill patients admitted via the ED: post hoc analysis from a retrospective study. Am J Emerg Med. 2015;33:1725-31.

CASE REPORT

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A Rare Case of Orbital Cellulitis with Zona Zoster

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Abstract

Orbital and preseptal cellulitis is very important diagnoses. These diseases are often caused by bacteria. Early diagnosis and treatment are important for complications. In our cases, 71-years old female patients had swelling lesions around the left eye. There was no rhinosinusitis or bacterial infection sign. On the computed tomography image, soft tissue was edema. The findings showed zone zoster infections around the eye. Zona zoster around orbital tissue is a rare condition. Untreated cases will have lost vision and intracranial complications. Therefore, these cases must be diagnosed early and treated with antiviral agents.

Keywords: Preseptal cellulitis, varicella, emergency department

Introduction

Zona zoster is a viral disease, that stays latent in the ganglion. The adult population prevalence is 1.2-3.4 persons per 1000. The elderly population prevalence is 3.9-11.8 persons per 1.000 [1,2]. Near of eye Zona zoster infection is expanded on the trigeminal nerve divisions. In these cases, it observed keratitis, uveitis, and optic neuritis. The other condition is preseptal cellulitis near the eye [2]. It is screened on physical examination; pain, eye movement, ptosis, and computed tomographic imaging are the important diagnostic tests [3]. The preseptal cellulitis is from Gram-negative *Cocci*; *Staphylococcus aureus*, *Streptococcus pneumoniae* etc. [4]. In our case report, we presented viral preseptal cellulitis from varicella zoster.

Case Report

Seventy one-years old female patient came to the emergency department (ED) with swelling in the left eye. Different types of rash lesions and swelling on the scalp and orbital zone were observed. In the patient medical history, it was hypertension and diabetes mellitus. Therefore, she takes aspirin, sitagliptin, metformin, and lansoprazole daily. Vital signs were screened in ED. Arterial blood pressure was 173/112 mmHg and peripheral oxygen saturation was 99%. Heartbeats were calculated at 112/min and body temperature was 36 degree celsius. Blood biochemical investigation displayed creatinine 0.9 mg/dL, C-reactive protein 13.3 mg/L (references value: 0-5 mg/L), and white blood cells 6.700/mm^3.

On first physical examination in ED, the patient consciousness was clear, cooperation was normal, and Glasgow Coma score was 15/15. The respiratory was regular and spontaneous. The right eye was clear and eye movements were normal. The left eye had swelling lesions, but movements and vision were normal (Figure 1). Then after these findings, it was planned computed tomography (CT). The right maxillary sinuses had edema. Around the left eye, the soft tissue had edema (Figure 2). After CT, the otolaryngology department consulted the patient. In examinations by the otolaryngology specialist, there was no pathological sign of sinusitis to complication of cellulitis. The second time, consulted by the ophthalmology department, the patient was examined by the specialist. On biomicroscopic examination, the right eye was clear, and the left eye's cornea had punctate epitheliopathy. There was no vitritis. All examination findings and CT imaging were screened and diagnosed around the left eye lesions from varicella-zoster infections. It was suggested that ganciclovir gel and hyaluronic acid eye drops, were called to the outpatient clinic.

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Discussion

Orbital cellulitis was usually caused by sinusitis. In the past reviews, orbital cellulitis was observed with 89-95% rhinosinusitis [5,6]. Orbital cellulitis cases must be recognized and early treated. Untreated cases will present with loss of vision and intracranial complications [4]. Around of eyes, preseptal cellulitis cases were around of eyebrows, occurred by mucormycosis, and occurred on sino-orbital osteoma [7-9]. Zona zoster of orbital zone cases presented with myositis, preoptic neuritis, and dacryocystitis [10]. Trigeminal neurotic cases were limited. These cases were usually detected in the division of V1 and V2 of the trigeminal nervous [11]. Our cases were shown on the trigeminal nerve branches of V1 and V2. The infection lesions were observed around the left eye. The left eye cornea has been damaged. The early diagnoses and treatment were very important for this case.

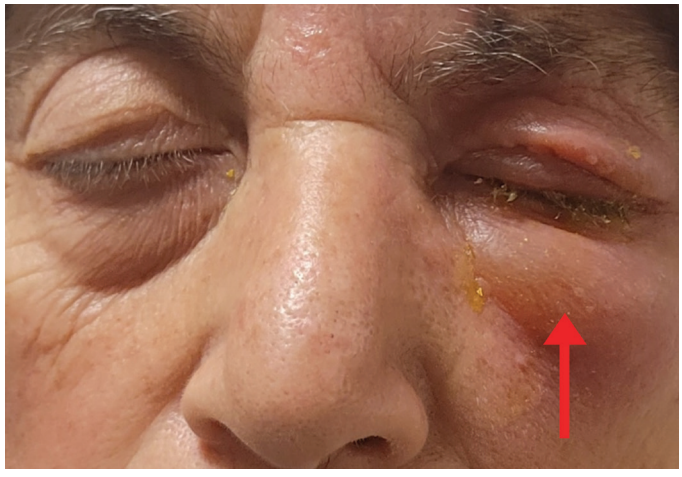

Figure 1. The left eye had swelling lesions (arrow)

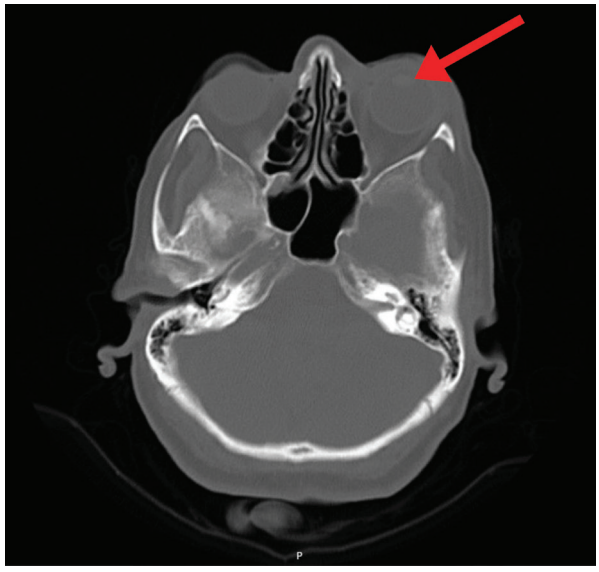

Figure 2. Edematous image in the left eye and soft tissue in the patient's computed tomography (arrow)

Most varicella-related complications are in the pediatric age group, and neurological and infectious complications have been reported. Although many sporadic cases exist, the causative agent has often been reported as group A beta hemolytic *Streptococcus*. Less so are hemophilus influenza type B and other pathogens. In general, medical treatment is sufficient, and surgical drainage may be required in selected cases [12]. In our case, preseptal cellulitis was one of the possible cutaneous complications of varicella zoster virus infection.

Conclusion

Although bacterial agents often cause orbital cellulitis in the ED, we wanted to draw attention to a viral orbital cellulitis case as in our case. Emergency physicians should keep in mind that varicella-zoster infections may also cause eye symptoms in patients with orbital cellulitis.

Ethics

Informed Consent: Informed consent was obtained from the patient in this case report.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.S., Concept: Ö.Z., F.S., C.B., Design: Ö.Z., F.S., C.B., Data Collection or Processing: Ö.Z., F.S., C.B., Analysis or Interpretation: Ö.Z., F.S., C.B., Literature Search: Ö.Z., F.S., C.B., Writing: Ö.Z., F.S., C.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Heineman TC, Cunningham A, Levin M. Understanding the immunology of Shingrix, a recombinant glycoprotein E adjuvanted herpes zoster vaccine. Curr Opin Immunol. 2019;59:42-8.
2. van Oorschot D, Vroling H, Bunge E, Diaz-Decaro J, Curran D, Yawn B. A systematic literature review of herpes zoster incidence worldwide. Hum Vaccin Immunother. 2021;17:1714-32.
3. Hamed-Azzam S, AlHashash I, Briscoe D, Rose GE, Verity DH. Common orbital infections ~ state of the art ~ part I. J Ophthalmic Vis Res. 2018;13:175-82.
4. Brambilla L, Maronese CA, Tourlaki A, Veraldi S. Herpes zoster following COVID-19: a report of three cases. Eur J Dermatol. 2020;30:754-6.
5. Botting AM, McIntosh D, Mahadevan M. Paediatric pre- and post-septal peri-orbital infections are different diseases. A retrospective review of 262 cases. Int J Pediatr Otorhinolaryngol. 2008;72:377-83.
6. Seltz LB, Smith J, Durairaj VD, Enzenauer R, Todd J. Microbiology and antibiotic management of orbital cellulitis. Pediatrics. 2011;127:566-72.
7. Ferreri A, Roszkowska A, Fabiani C, Polimeni G, Ferreri G, Aragona P. A Preseptal cellulitis following to foruncle on the eyebrow: a case report. Invest Ophthalmol Vis Sci. 2009;50:4834.

8. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. Cureus. 2020;12:e10726.

9. Bagheri A, Feizi M, Jafari R, Kanavi MR, Raad N. Orbital cellulitis secondary to giant sino-orbital osteoma: A case report. Cancer Rep (Hoboken). 2021;4:e1296.

10. Bak E, Kim N, Khwarg SI, Choung HK. Case Series: herpes zoster ophthalmicus with acute orbital inflammation. Optom Vis Sci. 2018;95:405-10.

11. Pelloni LS, Pelloni R, Borradori L. Herpes zoster of the trigeminal nerve with multi-dermatomal involvement: a case report of an unusual presentation. BMC Dermatol. 2020;20:12.

12. Qualickuz Zanan NH, Zahedi FD, Husain S. Varicella zoster causing preseptal cellulitis - uncommon but possible. Malays Fam Physician. 2017;12:37-9.

CASE REPORT

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Intracranial Subdural Hematoma: A Rare Complication Following Spinal Anesthesia for C/S Surgery

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Abstract

Intracranial subdural hematoma is an uncommon complication of spinal dura mater penetration with few reported cases in the medical literature. This condition is initially misdiagnosed as post-dural punction headache, a common occurence, and treated as such after the procedure. The incidence of postoperative complications is relatively low. The most common complication is headache, which typically begins 24-48 hours after dural puncture, varies in place, and subsides within the first 5 days. Approximately one-third of people undergoing dural puncture report headache. Subdural hematoma should be suspected, particularly if there is no change in posture and the headache lasts longer than expected. It has been reported that the incidence of cerebral subdural hematoma after lumbar puncture is about 1:500,000 and 1:1,000.000. This uncommon consequence, which is rarely reported in the medical literature, is a life-threatening illness for which early identification and treatment are crucial.

Keywords: Spinal anesthesia, subdural hematoma, headache, C/S surgery, emergency medicine

Introduction

Currently, spinal anesthesia is used safely for cesarean deliveries [1]. Advantages include not requiring general anesthesia and permitting patients to remain awake during surgery [2]. It is gaining prominence as a superior alternative to general anesthesia, particularly for obstetric procedures and delivery [1,2]. The incidence of postoperative complications is relatively low. The most common complication is headache, which typically begins 24-48 hours after dural puncture, varies in place, and subsides within the first 5 days [3,4]. Approximately one-third of people undergoing dural puncture report headache [5]. Subdural hematoma should be suspected, particularly if there is no change in posture and the headache lasts longer than expected. It has been reported that the incidence of cerebral subdural hematoma after lumbar puncture is about 1:500,000 and 1:1,000.000 [6]. This uncommon consequence, which is rarely reported in the medical literature, is a life-threatening illness for which early identification and treatment are crucial [4-7]. In this case, we present an extremely rare complication of subdural hematoma in a patient who underwent a cesarean section with spinal anesthesia, had no risk factors for bleeding in the postpartum months, and presented to the emergency department with a headache that did not respond to analgesic treatment and with very superficial neurological deficits. The patient's consent was obtained prior to the publication of the case report.

Case Report

A 30-year-old woman with a headache was admitted to our emergency department. A month ago, the patient received spinal anesthesia for a cesarean section. The headache subsided around one week following the anaesthetic, but returned three weeks later. In the initial week, medications alleviated the headache, but later headaches did not respond to analgesics. There were no head injuries throughout this time. In the initial medical history of pain, no recognized disease history is present. No known history of substance abuse. At the time of admission, the patient's vital signs were as follows: Arterial blood pressure:

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100/60 mmHg, respiration rate: 16/min, and pulse: 94/min. The patient was conscious, cooperative, oriented, and occasionally totally oriented during the medical examination. The patient's meningeal irritation findings were normal. With the exception of the interference scar in the lumbar area, the neurological examination revealed no aberrant results, and all other examinations of the patient were normal. In the patient's history, it was noted that the patient's right arm and leg were occasionally weak, although this weakness was not permanent. On the basis of these findings, it was determined that the patient should undergo central imaging; non-contrast brain computed tomography (CT) was consistent with acute subdural hemorrhage in the chronic floor measuring 20x73 mm in the thickest part of the vertex left lateral and minimal right shift (about 3 mm) in the midline structures (Figure 1). Magnetic resonance imaging (MRI) was also used to locate the subdural hemorrhagic region of the brain, as seen in Figure 2. In addition, laboratory analyses of the patient's total blood count, biochemistry parameters, and coagulation parameters revealed no disease (international normalized ratio, activated partial thromboplastin clotting time). The neurosurgeon who examined the patient advised drainage and the insertion of burr holes as treatments for the subdural hematoma.

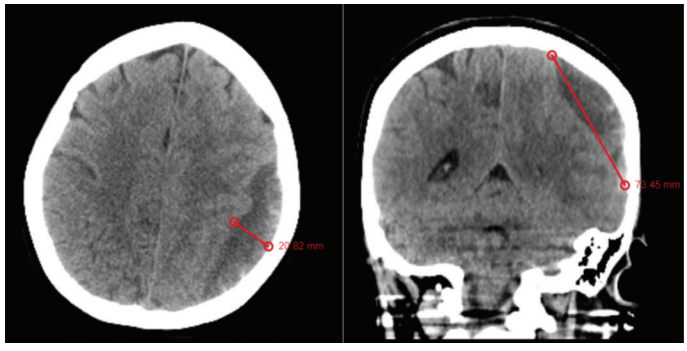

Figure 1. Imaging with a CT scan of the patient

CT: Computed tomography

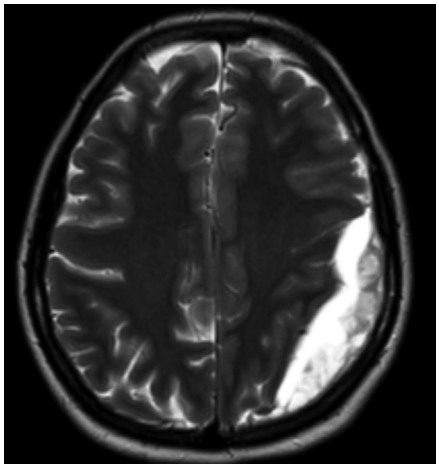

Figure 2. Imaging with a MRI scan of the patient

MRI: Magnetic resonance imaging

The patient declined the proposed treatment and checked out of the hospital. In the first week and first month of the application, information about patient's general condition was acquired through phone call. The patient received medical treatment from the neurosurgery clinic with the drugs which contain deksametazon and levetirasetam.

Discussion

Subdural hematoma is caused by head trauma, coagulation issues, certain medications, iatrogenic causes, dehydration, and lumbar puncture [4-7]. When short-term anesthetic is required for surgical procedures, epidural anesthesia is preferred [2]. Furthermore, general anesthesia has a 1.7-fold higher maternal death rate than regional anaesthetic [8], and general anesthesia increases postoperative hospital stay [9]. An extremely rare but dangerous consequence of spinal anesthesia is subdural hematoma following spinal or epidural anesthesia [10]. As a pathophysiological mechanism, it is hypothesized that the short-term cerebrospinal fluid (CSF) imbalance that occurs during epidural anesthesia creates strain in the vein walls, which may result in subdural bleeding [5,6]. In addition, leakage of CSF decreases intraspinal and intracranial pressure [7]. These changes result in the caudal displacement of the brain and stretching of pain-sensitive tissues and veins [6].

As previously stated, a variety of therapeutic options are available, including observation, blood patch, burr hole drainage, craniectomy, or a combination together. Subdural hematomas may spontaneously resolve [10]. The decision should be based on the neurological condition of the patient and the extent of the hematoma [11]. Among all strokes, ischemic stroke comprises 75-80%, and hemorrhagic stroke comprises 20-25% [12]. It is unknown what the actual incidence of postpartum subdural hematoma is because most affected patients are likely to be treated without further investigation [13]. Any patient with neurological symptoms, a subdural hematoma larger than 10 millimeters, or a midline displacement greater than 5 millimeters must receive surgical evacuation [7,13]. In this case study, the subdural hematoma was greater than 10 millimeters in size, and there was limited midline movement of approximately 3 millimeters. In this case, the extent of the subdural hematoma necessitated surgical intervention. The patient declined the proposed surgical treatment and checked out of the hospital. The neurosurgical outpatient clinic monitored the patient's stable vital signs.

According to our case, when patients arrive with a novel type of headache, this appears to be a rare but significant condition that demands physicians' careful attention. If the headache changes in nature, does not respond to treatment, or there are neurological symptoms such as nausea/vomiting and blurred vision, a subdural hematoma should be examined. Immediately, a CT scan or MRI should be conducted.

Conclusion

After spinal anesthesia during the postpartum period, headaches are extremely prevalent. Headaches may be symptoms of dural puncture headache or cerebral subdural hematoma, both of which are exceedingly rare but lethal complications. After spinal anesthesia, intracranial subdural hematoma should be considered in the differential diagnosis of headaches.

Ethics

Informed Consent: The patient's consent was obtained prior to the publication of the case report.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: K.Ş., B.Ç., A.A., R.G., Data Collection or Processing: K.Ş., B.Ç., A.A., R.G., Literature Search: K.Ş., B.Ç., A.A., R.G., Writing: K.Ş., B.Ç., A.A., R.G.

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References

1. Evans RW, Armon C, Frohman EM, Goodin DS. Assessment: prevention of post-lumbar puncture headaches: report of the therapeutics and technology assessment subcommittee of the american academy of neurology. Neurology. 2000;55:909-14.
2. Weng MH, Chou HC, Liaw JJ. Women's sense of control during labour and birth with epidural analgesia: a qualitative descriptive study. Midwifery. 2022;116:103496.
3. Martins LB, Bisinotto FMB, Dezena RA, Meirelles R. Intracranial rebleeding post spinal anesthesia in pregnant patient with undiagnosed chronic subdural hematoma: case report. Braz J Anesthesiol. 2022;72:522-4.
4. Lim G, Zorn JM, Dong YJ, DeRenzo JS, Waters JH. Subdural hematoma associated with labor epidural analgesia: a case series. Reg Anesth Pain Med. 2016;41:628-31.
5. Szeto V, Kosirog J, Eilbert W. Intracranial subdural hematoma after epidural anesthesia: a case report and review of the literature. Int J Emerg Med. 2018;11:36.
6. Zeidan A, Farhat O, Maaliki H, Baraka A. Does postdural puncture headache left untreated lead to subdural hematoma? Case report and review of the literature. Middle East J Anaesthesiol. 2006;15:50-8.
7. Halalmeh DR, Sandio A, Adrian M, Moisi MD. Intracranial subdural hematoma versus postdural puncture headache following epidural anesthesia: a case report. Cureus. 2022;14:e21824.
8. Hawkins JL, Chang J, Palmer SK, Gibbs CP, Callaghan WM. Anesthesia-related maternal mortality in the United States: 1979-2002. Obstet Gynecol. 2011;117:69-74.
9. Havas F, Orhan Sungur M, Yenigün Y, Karadeniz M, Kılıç M, Özkan Seyhan T. Spinal anesthesia for elective cesarean section is associated with shorter hospital stay compared to general anesthesia. Agri. 2013;25:55-63.
10. Joudi N, Ansari J. Postpartum headaches after epidural or spinal anesthesia. Curr Opin Obstet Gynecol. 2021;33:94-9.
11. Vallejo MC, Zakowski MI. Post-dural puncture headache diagnosis and management. Best Pract Res Clin Anaesthesiol. 2022;36:179-89.
12. Hakkoymaz H, Gungor EO, Gedik MS, Inanc Y. A Retrospective evaluation of acute ischemic stroke patients presenting to the emergency department. EJMI. 2020;4:221-7.
13. De Lipsis L, Belmonte R, Cusano M, Giannetti MA, Muccio CF, Mancinelli M. Subdural hematoma as a consequence of labor epidural analgesia. Asian J Neurosurg. 2018;13:931-4.

CASE REPORT

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Purple Urine Bag Syndrome: A Case Report

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Abstract

Purple urine bag syndrome (PUBS) is characterized by the urinary drainage bag turning purple, which is a disease of people with chronic catheterized urinary tract infections, often in the elderly with constipation. Recognizing PUBS is an important indicator for a quick and accurate diagnosis that emergency physicians should be aware of. Management involves reassurance, antibiotics, and regular changing of catheters. The prognosis is generally good, but PUBS is associated with high morbidity and mortality due to the background of patients. We present the clinical case of a 82-year-old male patient with chronically catheterized prostate cancer, who presented with purple- urine.

Keywords: Catheter, purple urine bag, urine discoloration

Introduction

Purple urine bag syndrome (PUBS) is a rare syndrome in emergency services, characterized by purple staining of the urinary bladder after urinary tract catheterization. In the literature, PUBS was first described by Buist [1] in 1978 with the development of purple urinary bladder in a patient following long-term urinary catheterization.

Normal urine is clear and light yellow in color. Dehydration, food coloring consumption, certain foods such as beets, certain drugs such as rifampin, phenytoin, hydroxycobalamin, propofol, amitriptyline, metabolism disorders such as hemoglobinuria, myoglobinuria, chyluria, urinary tract infections, and alkaptonuria can change the color of urine. As can be seen, it can also be the first finding of an important clinical case.

Female gender, advanced age, increased tryptophan content in the diet, increased urinary alkalinity, constipation, chronic persistent urinary catheterization, urinary tract infections, and kidney failure are risk factors associated with PUBS. Although *Pseudomonas aeruginosa, Proteus mirabilis, Providencia* spp., *Escherichia coli, Klebsiella pneumoniae, Morganelli morganii, Citrobacter* spp., methicillin-resistant *Staphylococcus aureus*, group B *streptococci*, and *Enterococcus* spp. are the most common bacterial species that can be considered to cause PUBS [2].

During constipation, the tryptophan taken from the bacteria colonizing the intestine is converted to indole. Indole is sulfated in the liver and excreted in the urine as indoxyl sulfate. Bacteria in the urinary catheter convert indole sulfate to indoxyl through sulfatase and phosphatase enzymes. As a result of the oxidation of indoxyl, blue (indigo) and red (indirubin) colors are formed. Alkaline urine accelerates the oxidation of indoxyl. A purple color is formed when the synthetic components of the urinary catheter bag containing indigo and indirubin and polyvinyl chloride come into contact [3].

In this report, a case with chronic constipation who was diagnosed with PUBS while being followed up with a urinary catheter for a long-time and the related literature review is presented.

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Case Report

An 82-year-old male patient presented to the emergency department (ED) with complaints of deterioration in general condition, decreased oral intake, malaise, fatigue, and fever. In his history, he stated that his complaints had been for about 10 days and had increased for 2-3 days. He stated that he had been constipated for 2 days and had occasional constipation. It was learned in his history that he had been followed up for hypertension and prostate cancer for 10 years. For this reason, it was learned that he had long-term urinary catheterization and frequent urinary tract infections. There was no feature in his family history. He has used amlodipine for hypertension. Vital signs of the patient on admission to the ED; were fever: 37.2 °C, blood pressure: 142/83 mmHg, pulse: 82/min, and sO_2: 93%, respiratory rate: 10/min. On physical examination, the oral mucosa was dry, and the prostate was palpable on rectal examination. Other system findings were normal. Laboratory findings were leukocytes: 11,700/mm^3 (4,000-10,000/mm^3), haemoglobin: 10.9 g/dL (12.00-14.00 g/dL), platelet: 339.000/mm^3 (100.000-400.000/mm^3), C-reactive protein: 1.489 mg/L (0-0.5 mg/L), creatinine: 0.8 mg/dL (0.75-1.25 mg/dL), blood urea nitrogen was 30 mg/dL (8.9-20.6 mg/dL). It was observed that the urine coming from the patient's urinary catheter stained the urinary bladder of the patient purple (Figure 1) and it was thought that he might have a urinary tract infection. In the sent complete urinalysis: 33 erythrocytes and 207 leukocytes were detected. Urine pH was measured as 7.5. The urine culture and antibiogram were taken from the patient. The patient was administered 2 grams of ceftriaxone intravenously. No feature was found in the abdominal imaging. Our patient was transferred to infectious diseases for further examination and treatment.

Figure 1. Purple discoloration of urine bag

There was no complication, and the patient was discharged three days after hospitalization.

Discussion

PUBS is a clinical syndrome that should be kept in mind because of the underlying pathological factors and urinary tract infection being an important cause of morbidity and mortality. Early diagnosis and initiation of treatment in patients with high comorbidity who had urinary tract infections, as in our patient, are of great importance for the patient's mortality. In a study conducted by Sabanis et al. [4], case reports and clinical studies in the literature between 1978-2017 were discussed. Evidence of urinary tract infection was found in all patients in their study. Hygiene measures and maintaining the general well-being of catheterized patients are essential in the prevention of this syndrome. It is also necessary to strengthen antibiotic management in the context of an individualized approach. Primary and secondary health clinicians involved in geriatric care should be highly aware of the syndrome, which may indicate serious underlying comorbidities [4].

In the urine culture of the patients; several bacterial strains associated with PUBS have been reported, including *Pseudomonas aeruginosa, Proteus mirabilis, Providencia* spp., *Escherichia coli, Klebsiella pneumoniae, Morganelli morganii, Citrobacter* spp., methicillin-resistant *Staphylococcus aureus*, group B streptococci, and *Enterococcus* spp. Our urine culture results were similar to previous reports and revealed that it was *Escherichia coli* [5,6].

Another risk factor that triggered the development of PUBS in our patient was constipation. It is thought that it accelerates the development of PUBS because there is more time for bacterial deamination in the gastrointestinal flora [5]. In a study by Su et al. [7], constipation was found in 84.6% of 13 patients who developed PUBS.

Because of the risk factors, it is important to manage PUBS appropriately. Sanitation measures should be taken, including urinary tract infections, constipation, and urinary catheter replacement. Removal of an unnecessarily placed urinary catheter should be considered in the prevention of catheter-related urinary tract infections. Antibiotic use should be kept in mind according to the current condition of the patient. Non-plastic catheter bags are another alternative. It is essential to inform the patient, their relatives, and the clinical team dealing with the patient about the nature of the condition and its usual clinical course. In general, it is important to manage PUBS patients on a case-by-case basis [2].

Conclusion

PUBS is a disease that every emergency physician can easily diagnose and manage comfortably. Management includes

finding the underlying cause, identifying risk factors, treating urinary tract infections and constipation, and replacing the urinary catheter regularly. It is an important point that the clinician should not forget that PUBS is associated with high morbidity and mortality due to the history of the patient.

Ethics

Informed Consent: Written informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.T., Concept: M.K., A.Ö., D.T., Design: R.A., N.M.H., H.A., Data Collection or Processing: M.K., A.Ö., Analysis or Interpretation: R.A., N.M.H., H.A., Literature Search: R.A., N.M.H., D.T., Writing: M.K., A.Ö., H.A.

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References

1. Buist NR. Purple urine bags. Lancet. 1978;1:883-4.
2. Kalsi DS, Ward J, Lee R, Handa A. Purple urine bag syndrome: a rare spot diagnosis. Dis Markers. 2017;2017:9131872.
3. Popoola M, Hillier M. Purple urine bag syndrome as the primary presenting feature of a urinary tract infection. Cureus. 2022;14:e23970.
4. Sabanis N, Paschou E, Papanikolaou P, Zagkotsis G. Purple urine bag syndrome: more than eyes can see. Curr Urol. 2019;13:125-32.
5. Khan F, Chaudhry MA, Qureshi N, Cowley B. Purple urine bag syndrome: an alarming hue? A brief review of the literature. Int J Nephrol. 2011;2011:419213.
6. Lin CH, Huang HT, Chien CC, Tzeng DS, Lung FW. Purple urine bag syndrome in nursing homes: ten elderly case reports and a literature review. Clin Interv Aging. 2008;3:729-34.
7. Su FH, Chung SY, Chen MH, Sheng ML, Chen CH, Chen YJ, et al. Case analysis of purple urine-bag syndrome at a long-term care service in a community hospital. Chang Gung Med J. 2005;28:636-42.