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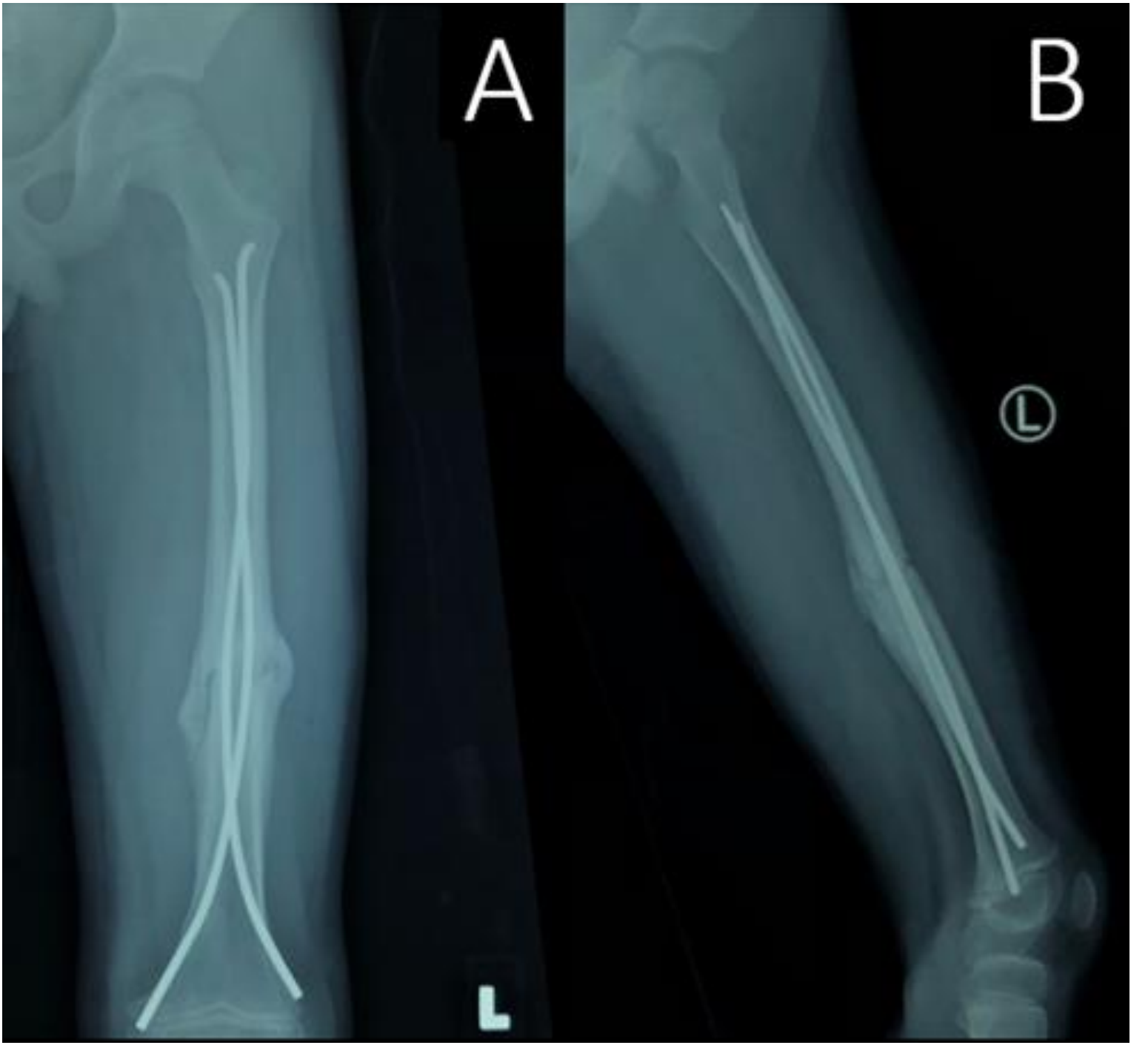

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Research Articles

Case Report Articles

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Frequency of admission to prehospital emergency medical services and satisfaction level of prehospital emergency care during active chemotherapy

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ABSTRACT

Objective: In this study, we aimed to investigate the frequency of admission to prehospital emergency medical services (PEMS) and the satisfaction level of prehospital medical care in cancer patients during the chemotherapy process.

Material and Methods: A total of 218 patients receiving active chemotherapy were included in the study. A personal information form and the 112 Emergency Health Services Patient Satisfaction Scale (EHSPSS) were used to collect data. Sociodemographic characteristics and data on admission to PEMS were compared,

Results: Among the patients, 162 (74.3%) had visited EMS in the previous three months. Ninety-eight (60.5%) patients had visited EMS as outpatients, and 64 (39.5%) patients had arrived via PEMS. The PEMS admission rate of patients who visit EMS from rural areas (71.9%) was significantly higher than that of patients who visit from urban areas ($p < 0.001$). The total satisfaction score was determined to be 89±18.1 points. According to these scores, it could be interpreted that the satisfaction rate of the patients was high. Regarding the dimension scores, the ambulance staff and emergency call center staff scores were high, while the care provided in the venue and ambulance technical equipment scores were above moderate

Conclusion: Patients receiving active chemotherapy frequently visit EMS. Although these patients mostly visited EMS as outpatients, the rate of patients who visited EMS with PEMS was substantial. The PEMS patient satisfaction rate was found to be high among active chemotherapy patients. High patient satisfaction is a prominent patient-centered indicator in measuring the quality of care.

Keywords: prehospital emergency care, cancer, chemotherapy, satisfaction level

INTRODUCTION

In 2020, approximately 19 million new cancer cases were diagnosed worldwide, and 10 million people died due to cancer (1). Estimated cancer patient numbers are expecting to be 28 million in 2040 (1). Chemotherapy plays an important role in cancer treatment, and this role is expanding. Although advances in cancer treatments have provided survival benefits, these treatments have notable side effects and toxicities (2). Neutropenic fever, nausea, vomiting, diarrhea, bleeding, and thromboembolic events are chemotherapy-associated side effects (3). Because of these side effects, patients receiving cancer treatment often visit emergency medical services (2, 4).

The concept of prehospital emergency medical services (PEMS) encompasses many areas of emergency care, including the assessment, management, triage, and transport of patients from the event of an injury or illness to their arrival at an emergency care unit (5). Prehospital emergency medical care is provided by health professionals (doctors, nurses, paramedics, emergency medical technicians) with ambulances in Turkey and the emergency telephone number is 1-1-2. Patients need emergency medical services (EMS) in case of urgent health problems, regardless of their socioeconomic status. Emergency department visits are higher in cancer patients compared to the general population (2, 4).

However, data on cancer patients cared for by PEMS are limited. In this study, we aimed to investigate the frequency of admission to PEMS and the satisfaction level of prehospital medical care in cancer patients during the chemotherapy process.

Research Article

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MATERIAL and METHODS

This cross-sectional study was conducted in the Oncology Department of Necmettin Erbakan University Meram Medical Faculty Hospital, between June and July 2022. Ethics committee approval was obtained for the study (Approval No: 2022/3841). A total of 218 patients receiving active chemotherapy were included in the study. A personal information form and the 112 Emergency Health Services Patient Satisfaction Scale (EHSPSS) were used to collect data. The validity and reliability of this scale in Turkish society have been established (Kaiser-Meyer Olkin=0,636, Cronbach alpha=0.907) (6).

The EHSPSS consists of 26 questions; the minimum total score is 26 points, and the maximum total score is 130 points. Moreover, the EHSPSS is divided into the following four dimensions: ambulance staff (12 questions, minimum 12 points, maximum 60 points), emergency call center staff (3 questions, minimum 3 points, maximum 15 points), care provided in venue (7 questions, minimum 7 points, maximum 35 points), and ambulance technical equipment (4 questions, minimum 4 points, maximum 20 points).

The personal information form included sociodemographic characteristics (age, gender, educational status, urban/rural, comorbidity), cancer type and stage, duration of chemotherapy received (0–3 months, 3–6 months, > 6 months), number of visits to the emergency service, type of admission to the emergency service, the reason for admission to 112 emergency health services, and the number of calls to 112 emergency health services. Sociodemographic characteristics and data on admission to PEMS were compared.

Statistical analysis

The data were analyzed using the IBM SPSS V-20 program. Descriptive statistics were provided as numbers, percentages, and ratios. The chi-square test or Fisher exact test was used to compare categorical variables between groups.

The distribution of the study parameters was performed using the Kolmogorov–Smirnov test. Comparison of homogeneously distributed parameters was performed with an independent sample t-test and ANOVA. Comparison of non-homogeneous parameters was performed with the Mann–Whitney U test. The three groups (duration-of-chemotherapy groups) were compared using a post-hoc Tukey analysis. The significance level was accepted as $p<0.05$.

RESULTS

Two hundred and eighteen patients were included in the study. Of the patients, 106 (48.6%) were female, and 112 (51.4%) were male. The median age was 59.5 (31–85) years. Among the patients, 162 (74.3%) had visited EMS in the previous three months. Ninety-eight (60.5%) patients had visited EMS as outpatients, and 64 (39.5%) patients had arrived via PEMS. The most common reason for admission to EMS was deterioration in general condition (30.9%).

Of the patients admitted to EMS, 53.8% were hospitalized, and 90.5% were received by the oncology service. The sociodemographic characteristics of the patients are presented in **Table 1**.

The PEMS admission rate of patients who visit EMS from rural areas (71.9%) was significantly higher than that of patients who visit from urban areas ($p < 0.001$). The hospitalization rate of patients admitted to EMS via PEMS was significantly higher than that of outpatients ($p < 0.001$) (**Table 2**). There was no significant difference between the gender, education level, comorbidity, cancer stage, chemotherapy duration, or hospitalization service status between the outpatients and those who applied via PEMS ($p > 0.05$ for all) (**Table 2**). There was no significant difference between the outpatients and those admitted via PEMS in terms of gender, educational status, comorbidity, cancer stage, duration of chemotherapy, or hospitalization service status ($p > 0.05$ for all) (**Table 2**).

Table 3 presents the 112 EHSPSS total and dimension scores. The total satisfaction score was determined to be 89±18.1 points. The lowest score was 58, and the highest was 130. According to these scores, it could be interpreted that the satisfaction rate of the patients was high. Regarding the dimension scores, the ambulance and emergency call center staff scores were high, while the care provided in the venue and ambulance technical equipment scores were above moderate (**Table 3**). The emergency call center staff, care provided in venue, ambulance technical equipment, and total scores were significantly higher in the urban group than in the rural group ($p = 0.002$, $p = 0.004$, $p < 0.001$, $p = 0.006$, respectively), but the ambulance staff scores were similar between these two groups ($p = 0.14$).

The emergency call center staff score, care provided in venue score, and total scores were significantly higher in the non-comorbidity group than in the comorbidity group ($p = 0.011$, $p = 0.01$, $p = 0.03$, respectively), but there were no difference in the ambulance technical equipment and ambulance staff scores between these two groups ($p = 0.08$, $p = 0.16$, respectively). The total score and all dimension scores were significantly different between the durations of chemotherapy received (**Table 4**).

The total score and all dimension scores were significantly higher in the 0-3 months chemotherapy received group than in the 3-6 months group ($p<0.05$ for all) (**Table 4**). The total score, ambulance staff score, emergency call center staff score, and ambulance technical equipment score were significantly higher in the 0-3 months chemotherapy received group than in > 6 months group, but there was no difference in the care provided in the venue score between these groups (**Table 4**). Also, there was no difference between the 3-6 months and > 6 months chemotherapy received groups ($p>0.05$ for all).

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Table 1: General characteristics of the study population

Age (year)	Study population 59.5 (31-85)	
Gender (n)	Female (%) Male (%)	106 (48.6) 112 (51.4)
Area (n)	Urban (%) Rural (%)	134 (61.5) 84 (38.5)
Educational status (n)	Literate (%) Illiterate (%)	180 (82.6) 38 (17.4)
Comorbidity (n)	Yes (%) No (%)	108 (49.5) 110 (50.5)
Cancer type (n)	Lung (%) Gastrointestinal (%) Genitourinary (%) Breast (%) Others (%)	34 (15.6) 74 (33.9) 34 (15.6) 56 (25.7) 20 (9.2)
Visiting the emergency medical services in the previous 3 months (n)	Yes (%) No (%)	162 (74.3) 56 (25.7)
Number of admissions to medical emergency service in previous 3 months (n)	3 (1-8)	
Mode of arrival to the medical services (n)	Outpatient (%) Via ambulance (%)	98 (60.5) 64 (39.5)
Number of admissions to prehospital emergency service in previous 3 months (n)	1 (0-6)	
Reason for not calling 112 emergency service (n)	Faster transport than 112 emergency service (%) Good health status of patient (%)	50 (51) 48 (49)
Reason for visit to the emergency services (n)	Nausea-vomiting (%) Fever (%) Loss of consciousness (%) Shortness of breath (%) Pain (%) Deterioration of general condition (%) Oral intake deficiency (%)	6 (3.7) 12 (7.4) 8 (4.9) 31 (19.1) 43 (26.5) 50 (30.9) 12 (7.4)
Intervention of the 112-emergency service (n)	Medication (%) Transporting (%)	4 (6.3) 60 (93.7)
Intervention of the emergency service (n)	Medication (%) Hospitalization (%)	72 (46.2) 84 (53.8)
Hospitalization service (n)	Oncology service (%) Non-oncology service (%)	76 (90.5) 8 (9.5)

Table 2: Comparison of between sociodemographic data and type of admission the emergency services

Features		Mode of arrival to the medical services Outpatient (n)	 Via ambulance (n)	p
Gender (n)	Female (%) Male (%)	50 (%51) 48 (%49)	38 (%69.4) 26 (%40.6)	0.33*
Residency (n)	Urban (%) Rural (%)	72 (%73.5) 26 (%26.5)	18 (%28.1) 46 (%71.9)	**<0.001***
Educational status (n)	Literate (%) Illiterate (%)	81 (%82.7) 17 (%17.3)	47 (%73.4) 17 (%26.4)	0.17*
Comorbidity (n)	Yes (%) No (%)	56 (%57.1) 42 (%42.9)	40 (%62.5) 24 (%37.5)	0.51*
Cancer stage (n)	Stage 2 Stage 3 Stage 4	10 (%10.2) 12 (%12.2) 76 (%77.6)	4 (%6.2) 4 (%6.2) 56 (%87.5)	0.27**
Duration of chemotherapy (n)	0-3 months 3-6 months >6 months	25 (%25.5) 52 (%53.1) 21 (%21.4)	11 (%17.2) 34 (%53.1) 19 (%29.7)	0.3*
Intervention of the emergency service (n)	Medication (%) Hospitalization (%)	67 (%69.8) 29 (%30.2)	5 (%8.3) 55 (%91.7)	**<0.001***
Hospitalization service (n)	Oncology service (%) Non-oncology service (%)	28 (%96.6) 1 (%3.4)	48 (%87.3) 7 (%12.7)	0.25**

*Chi-square test. **Fisher exact test

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Table 3: The overall and sub-dimension satisfaction score of study participant for the prehospital emergency medical services (n = 82).

Sub-dimensions of scale	Score	
	Mean±St.d.	Min-max
Ambulance staff dimension	41.5±8.4	26-60
Emergency call center staff dimension	10.3±2.1	7-15
Care provided in venue dimension	23.5±5.4	16-35
Ambulance technical equipment dimension	13.6±3.2	7-20
Overall satisfaction	89±18.1	58-130

Table 4. Comparison of overall and sub-dimension satisfaction scores and population characteristic

Features			Ambulance staff score	Emergency call center staff score	Care provided in venue score	Ambulance technical equipment score	Overall satisfaction score
Gender	Female		42.1±6.4	10.1±1.8	23.1±4.8	13.3±2.7	88.8±15
	Male		40.6±10.6	10.4±2.5	23.9±6.2	14.1±3.8	89.1±21.5
		p	0.42	0.58	0.52	0.27	0.94
Residency	Urban		44.1±8.5	11.6±2	26.7±4.4	16.6±2.1	99.2±14.9
	Rural		40.7±8.3	9.9±2	22.6±5.3	12.8±3	86.1±18
		p	0.14	**0.002**	**0.004**	**<0.001**	**0.006**
Educational status	Literate		40.4±9.3	10.2±2.3	23.4±5.9	13.5±3.6	87.6±19.9
	Illiterate		43.3±6.5	10.4±1.7	23.6±4.5	13.8±2.5	91.2±14.5
		p	0.14	0.7	0.85	0.66	0.39
Comorbidity	Yes		40.3±6.6	9.8±1.7	22.4±4.6	13.2±3.1	85.9±14.7
	No		43.7±11	11.1±2.6	25.6±6.2	14.3±3.4	94.9±22.4
		p	0.08	**0.011**	**0.01**	0.16	**0.03**
Duration of chemotherapy	0-3 months		48.3±8.4	12.5±2.3	27.5±5.2	16.3±2.2	104.6±16.9
	3-6 months		39.7±8.6	9.6±1	22.4±5.4	13±3.2	84.8±18.5
	>6 months		41.2±7.1	10.2±1.6	23.3±4.9	13.4±3.1	88.2±14.9
	p		**0.007**	**<0.001**	**0.017**	**0.006**	**0.003**
	*p**	0-3/3-6 months	**0.005**	**<0.001**	**0.01**	**0.04**	**0.002**
		0-3/>6 months	**0.03**	**0.004**	0.6	**0.02**	**0.01**
		3-6/>6 months	0.7	0.4	0.7	0.8	0.6

*Post Hoc test: Tukey SD

DISCUSSION

To our knowledge, this is the first study to evaluate the PEMS satisfaction level among cancer patients receiving active chemotherapy. In our study, a high PEMS satisfaction level was detected among cancer patients receiving active chemotherapy. In addition, the study determined that 74% of the patients visited the EMS during the active chemotherapy process, and 39.5% of these patients visited the EMS via PEMS. There are a limited number of published studies on the satisfaction of patients admitted to prehospital emergency care, despite the large number of patients who benefit from this service every year (7). Overall, the rate of satisfaction with prehospital emergency services is high (7). However, there are studies that show contradictory results. In one study, prehospital emergency care for suspected hip fractures was found to be inadequate and unsatisfactory by the patients (8).

In our study, the EHSPSS satisfaction level among cancer patients was high. The scale care provided in the venue sub-dimension score was also high. Another study reported that patients with prehospital emergency problems were mostly satisfied with telephone care assessments (9). Our analysis also reported a high satisfaction rate among emergency call center staff. This satisfaction rate was higher in the urban and non-comorbid groups. Some studies have reported that the most common symptoms of cancer patients who visited the emergency department were pain, respiratory distress, and gastrointestinal problems (10-12). In our study, the most common reasons for admission to the emergency department were deterioration of the general condition, pain, and shortness of breath. It is not uncommon for patients receiving active chemotherapy to have constitutional symptoms, such as anorexia, weakness, and fatigue.

The most common cancer types in patients admitted to the emergency department were breast, lung, and gastrointestinal cancers (13). In our study, the most common cancer types in patients were gastrointestinal, breast, and lung cancers. Chen et al. found the rate of admission among patients brought to the hospital by ambulance to be 22%. (13).

In our study, the rate of admission among patients brought to the emergency department by ambulance was found to be 39.5%. The reason for this high rate could be the easy and widespread accessibility of health services in Turkey. It remains unclear whether the severity of patients' symptoms or the extent of disease is related to the mode of patient transportation to the emergency department. Many studies have shown that patient arrival by ambulance is associated with faster treatment time and shorter hospital stay compared to patients arriving by personal vehicle (14, 15).

A recent study determined that 29.9% of patients who visited EMS were discharged home. (13). In our study, the discharge rate of patients from the emergency room was 46.2%. Considering the use of prehospital emergency health services three months before the death of cancer patients, it was revealed that most of the patients transported by ambulance were hospitalized (10). In our study, the hospitalization rate of patients who received active chemotherapy and were transferred by ambulance was high. Irrespective of whether cancer patients were in the palliative or active chemotherapy period, hospitalization of those transferred by ambulance was higher than outpatients, suggesting that cancer patients' health problems are complex and need significant care.

There are some limitations in our study. Patients who died in the emergency department were not evaluated in this study. There may be a bias in the satisfaction score of patients who presented with unconsciousness since their families received immediate assistance from the medical staff.

CONCLUSION

Patients receiving active chemotherapy frequently visit EMS. Although these patients mostly visited EMS as outpatients, the rate of patients who visited EMS with PEMS was substantial. The PEMS patient satisfaction rate was found to be high among active chemotherapy patients. High patient satisfaction is a prominent patient-centered indicator in measuring the quality of care.

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Conflict of interest: The authors declare no competing interests.

Author Contributions: Design and initiate: **ZK and MZK.** Data collection: **ZK and MZK.** Analysis, literature review and writing: **ZK and MA.** Revision: **MA**

Ethical approval: All procedures performed in studies involving human participants were in accordance with the institutional and/or national research committee's ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. (Approval No: 2022/3841).

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Endotracheal Tube Cuff Inflation Pressure awareness and response to education among anesthesia technicians

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ABSTRACT

Objective: Cuffed endotracheal tubes are used to ensure ventilator compliance and prevent pulmonary aspiration in mechanically ventilated patients. At cuff pressures greater than 40 cmH2O, mucosal irritation, ulceration, hemorrhage, tracheal stenosis, and tracheoesophageal fistula can occur due to increased perfusion pressure of the tracheal mucosa and submucosa. In this study, we compare the awareness of cuff pressure among anesthesia technicians working in the operating room.

Materials and Methods: All anesthesia technicians received a seminar on cuff pressure. An attempt was made to determine the difference between cuff pressures measured before and after the seminar.

Results: A positive correlation was found when the cuff pressure measurement was compared with the first measurement after the training (Cor. Coef.= 0.376). At the first measurement, the mean cuff pressure was 82 cmH20, the lowest pressure was 27, and the highest was 223. At the measurement after completion of the training, the mean pressure was 50, the lowest pressure was 26, and the highest pressure was 105. The difference between the two measurements was statistically significant (p=0.000). Before training, only four technicians (7.40%) inflated below the recommended confidence interval (30 cm H2O), while the remaining 50 technicians (92.6%) inflated above this limit. After training, 11 technicians could inflate below the confidence interval. A statistically significant increase was observed ($p < 0.05$).

Conclusion: Measuring the cuff pressure of the endotracheal tube was essential to avoid possible complications. Educational seminars on this topic and the provision of cuff meters can avoid these problems.

Keywords: cuff pressure, anesthesia, technician, endotracheal tube

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INTRODUCTION

Cuffed endotracheal tubes are used to ensure ventilator compliance and prevent pulmonary aspiration in mechanically ventilated patients. The pressure generated by the inflated cuff is transmitted directly to the tracheal wall around the cuff (1). At cuff pressures greater than 40 cmH2O, mucosal irritation, ulceration, hemorrhage, tracheal stenosis, and tracheoesophageal fistula can occur due to increased perfusion pressure of the tracheal mucosa and submucosa (2).

Most hospitals do not routinely measure endotracheal tube cuff pressure, and cuff palpation has not detected high cuff pressures (3). Measurement of cuff pressure is a simple and reproducible method to evaluate the pressure exerted on the tracheal mucosa. Some suggest that the minimum cuff pressure required to provide an adequate seal and reduce the risk of aspiration is 25 cmH2O (4).

Even when inflated to the minimum occlusion pressure, "low-volume, high-pressure" endotracheal tube cuffs often cause high tracheal pressures and cause clinically significant tracheal ischemia and necrosis. Despite using high-volume, low-pressure cuffs, some patients experience tracheomalacia, tracheal stenosis, and tracheoesophageal fistula with the risk of tracheal ischemia from the cuff (5).

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Cuff pressure measurement is not performed routinely in our country. Many physicians measure cuff pressure only subjectively. First, the swelling and stiffness of the cuff balloon are checked. Some physicians adjuste the pressure to the air leak from the ventilator and the pressure stabilized where the air leak was stopped. However, most physicians do not know how high or low the cuff pressure they set is. In this study, we compare the awareness of cuff pressure among anesthesia technicians working in the operating room of Erzincan Binali Yıldırım University Mengücek Gazi Training and Research Hospital and the pressure they apply after cuff pressure training with previous values.

MATERIAL and METHODS

After obtaining approval from the university ethics committee, all anesthesia technicians were interviewed, and verbal consent was obtained. The technicians were randomized by name. High-volume and low-pressure endotracheal tubes of the same brand and different sizes were used for all intubations, which were selected according to the patient. Patients with emergency surgery and difficult intubation were excluded from the study. Immediately after intubation, the technician inflated the cuff and fixed the tube according to his method. Subsequently, the pressure of the tracheal cannula cuff was measured with a control inflator (VBM medizintechnik. Industriegebiet Wittlensweiler, Farinastrabe 4, D729290, Freudenstadt, Germany). This device measures the cuff pressure on the pilot balloon and allows the pressure to be changed by inflating or deflating the balloon (6). The cuff pressure is measured in cmH2O, with lower and upper ranges of 20 and 30 cmH2O, respectively. The same observer took all measurements during the inspiratory phase of positive pressure ventilation. Patient demographics (including age and sex) were recorded.

After the initial measurement pressures of all anesthesia technicians were recorded, a seminar on cuff pressure was held. The seminar explained what a cuff pressure is, how it is set, what complications are caused by cuff pressures that are too high or too low, and what modern cuff pressure measurements look like. Then, in addition to demographic data, a questionnaire was used asking;

1- How many years he had been working,

2- When he last intubated,

3- How he set the cuff pressure,

4- Whether he was already aware of the cuff pressure,

5- whether he used a cuff pressure monitor and

6- what contribution the seminar made to his awareness of cuff pressure.

After the seminar, the cuff pressures applied by all anesthesia technicians after intubation were measured and recorded.

Statistic: The Statistical Package for Social Sciences (IBM SPSS Statistics) for Windows, version 26, was used for statistical analysis (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test for normality was used for quantitative data. The mean and standard deviation (SD) of the normally distributed data were calculated, and the groups were compared using the paired t test. Frequencies were used to summarize qualitative data, and Pearson's chi-square test was used to assess relationships. A $p < 0.05$ was used to assess the significance of statistical tests.

RESULTS

A total of 54 anesthesia technicians with a mean age of 33.68 ± 8.11 years were included in the study. Twenty-two of them were male, and 32 were female. The seniority was two technicians less than one year, 1-5 years 10, 5-10 years, and over ten years 21 technicians (**Table-1**).

A positive correlation was found when the cuff pressure measurement after training was compared with the first measurement (Cor. Coef.= 0.376). At the first measurement, the mean cuff pressure was 82 cmH20, the lowest pressure was 27, and the highest was 223. At the measurement after completion of the training, the mean pressure was 50, the lowest pressure was 26, and the highest pressure was 105. The difference between the two measurements was statistically significant (p=0.000). This observed difference did not differ by age, gender, or seniority.

Before training, only four technicians (7.40%) inflated below the recommended confidence interval (30 cm H2O), while the remaining 50 technicians (92.6%) inflated above this limit. After training, 11 technicians could inflate below the confidence interval. A statistically significant increase was observed ($p < 0.05$).

Survey questions and technician responses have been shown in **Table 2**.

Compared to the responses in the questionnaire about the cuff measurement method, there was no difference between the groups in terms of cuff inflation pressures. While there was no significant difference in the first measured pressure between technicians who had previously received cuff pressure training and those who had not, there was a significant difference in the pressures measured after training (p=0.013). The inflation pressures did not differ between those who had prior cuff pressure complications and those who did not. Inflation pressures did not differ between those who were frequently intubated and those who were not intubated for a long time. The inflation pressures did not differ between technicians who had previously used a cuff device and those who had not. There was no difference between the first and last inflation pressures between those who reported that their awareness had increased after training and those who reported no difference.

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Table-1. Demographic data

Age		Gender	Frequency	Percent %
Min	18	Male	22	40,7
Max	51	Female	32	59,3
Mean	33,68			
Std. Dev.	8,11			

Professional experience			Last intubation time		
	Freq.	**Percent %**		**Freq.**	**Percent %**
Less than 1 year	2	3,7	0-7 Days	21	38,9
1-5 years	10	18,5	7-15 Days	6	11,1
5-10 years	21	38,9	15-30 Days	9	16,7
over 10 years	21	38,9	Over 30 Days	18	33,3

Table 2. Survey questions and answers

Last intubation time	Freq.	Percent %	How do you set the cuff pressure?	Freq.	Percent %
0-7 Days	21	38,9	**Palpation**	27	50,0
7-15 Days	6	11,1	**Tube specification**	15	27,8
15-30 Days	9	16,7	**Leakage control**	12	22,2
Over 30 Days	18	33,3	**Total**	54	100,0

Have you received cuff pressure before?			If you have a cuff measuring device, do you use it in your routine?		
No	44	81,5	**No**	49	90,7
Yes	10	18,5	**Yes**	5	9,3

Have you had any complications related to cuff pressure after intubation?			Did your awareness of cuff pressure increase after this briefing?		
	Freq	**Perc %**		**Freq.**	**Perc. %**
None	27	50,0	**None**	10	18,5
Sore throat	4	7,4	**Slightly increased**	16	29,6
Horseness	13	24,1	**İncreased a lot**	28	51,9
Bronchospasm	10	18,5			

DISCUSSION

This study aimed to investigate the cuff pressure applied by anesthesia technicians at Erzincan Binali Yıldırım University Mengücek Gazi Training and Research Hospital before and after cuff pressure awareness and cuff pressure training. The cuff pressures measured after training were significantly lower than those before, which was associated with improved cuff pressure safety. This situation was reported by Sayed Siyamdoust et al. (7). This result was similar to the results of his study. However, this study found that the safety of cuff pressure was increased in anesthesiologists after training.

Several factors influence the pressure measurement in the endotracheal tube cuff, including cuff diameter, thickness, compliance, shape, filling substance (air or water for specific procedures), and head and neck posture. Several parameters, such as tube type, cuff shape, and filling material, can affect the pilot balloon's tone and thus the palpation approach's reliability (8). Using a manometer may cause underestimation of the recorded ETT cuff pressure. Because of the internal manometer chamber and pressure equalization, air leaks when the external balloon is connected to the manometer (9). In our study, high-volume, low-pressure endotracheal tubes of the same brand were used in all patients.

The cuff pressure of the endotracheal tube should be maintained between 25 and 30 cm H2O (10). Although the safe perfusion pressure varies from case to case to ensure capillary perfusion, it is defined as 25 cm H2O.

Blood flow in the tracheal mucosa is interrupted at pressures greater than 30 cm H2O and can completely stop at 45 cm H2O (11). In their in vitro work, Seegobin and Hasslet (12) suggested that the cuff pressure should not exceed 30 cm H2O. Inada et al. (13) studied the variation in balloon pressure at different airway pressures. They found that the balloon pressure was less than 34 cm H2O at an airway pressure of 20 cm H2O in men and 25 cm H2O in women. They noted that this pressure corresponds to perfusion pressure but that tracheal ischemia may occur due to other factors, such as hypotension, which lowers perfusion pressure.

Several methods have been developed to ensure proper cuff inflation, including the minimal leakage technique, minimal occlusion volume, inflating the ETT cuff to a minimal pressure level, inflating the cuff with a stethoscope, and the conventional technique of inflating the cuff with an indeterminate volume of air (14). The minimal leakage approach determines how much air is pumped into the cuff based on the amount required to detect a tiny end-inspiratory leak by auscultating the front of the chest (17). In our study, 50% of technicians reported using the palpation method, 27% used the characteristics of the tubes, and 22% used the air leak method. Although this method has been inadequate, the ETT pilot balloon is tested for approximation pressure by palpation.

This method estimates the pressure in the cuff. It has been shown to overinflate the cuff in 30-98% of cases, depending on the type of ETT used and the population studied (15). Saraçoğlu et al. (16) found no significant relationship between anesthesiologist experience and adequacy of ETT cuff pressure when patients were instructed to inflate the cuff to the level they considered appropriate(17)(17)(17) manually. Bulamba et al. (18) suggest using a loss-of-resistance syringe as an alternative to simple palpation. A 7 mL plastic syringe with a luer-slip closure introduces air into the pilot balloon, and the plunger of the loss-of-resistance syringe can be passively withdrawn until it stops.

CONCLUSION

Measuring the cuff pressure of the endotracheal tube was essential to avoid possible complications. In our country, routine cuff pressure measurement is not yet applied in all centers. Measurement with simple manometers is essential to avoid complications. Despite the many intubations in daily anesthesia practice, anesthesia technicians still do not go beyond traditional methods. Educational seminars on this topic and the provision of cuff meters can avoid these problems.

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Impact of serum sodium levels on Helicobacter pylori infection

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ABSTRACT

Objective: Excessive salt consumption could play a role for developing gastric cancer as well as Helicobacter pylori (HP) infection. However, there is no report about the connection between serum sodium levels and HP infection. This study aimed to investigate the relationship between serum sodium disorders and HP infection.

Material and Methods: In this single-center, retrospective, descriptive study, we evaluated the presence of HP infection by enzyme-linked immunosorbent assay (ELISA) among patient with serum sodium disturbances. Patients were divided into two groups as to their serum sodium levels (hypernatremia: Sodium level above 145 mmol/l, and hyponatremia: Sodium level below 135 mmol/l).

Results: In total, 54 patients, half of them were hypernatremic (27), included in the study. At total, 15 (55.6%) patients tested positive for HP immunoglobulin G (Ig G) by ELISA method in hyponatremic patients, 17 (63%) patients tested positive for HP Ig G in hypernatremic patients. There was no difference between groups in terms of HP Ig G seropositivity (p=0.58). Other hand, 9 (33%) patients tested positive for HP Ig A among hyponatremic patients, 19 (70%) patients tested positive for HP Ig A in hypernatremic patients (p=0.029).

Conclusion: According to our results, Hypernatremic patients have high risk for HP infection. Other hand, the presence of HP infection could be a driven-factor in the development of hypernatremia among elderly patients. Larger-scale studies are needed to reveal the relationship between hypernatremia and gastroenteritis.

Keywords: Helicobacter pylori, Hypernatremia, Hyponatremia

INTRODUCTION

Helicobacter pylori (HP) is a gram-negative, spirally-shaped bacterium, impacting over 10% of people globally. It causes a wide range of gastric diseases, including chronic atrophic gastritis, peptic ulcer, mucosa-associated lymphoid tissue lymphoma, and gastric cancer. Thus early diagnosis and screening of HP have potentially toreduce the rates of progression to gastric cancer (1).

Impact of lifestyle and environmental factors on further progression toward gastric cancer due to HP infection are smoking cigarettes, alcohol abuse, salt consumption, and consuming lower quantities of vegetables (2).

Prior studies which examining risk factors associated with HP infection, have demonstrated that high dietary salt intake is a significant risk factor for gastric cancer development. Furthermore, this association was reportedly getting stronger in the presence of HP infection with atrophic gastritis (3, 4).

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Natremia displays the body's hydration status, which is closely regulated by thirst, arginine vasopressin, and the kidneys (5). Hypernatremia is accepted as 145 mmol/l or higher levels of sodium, hyponatremia is accepted as 135 mmol/l or lower levels of sodium in medical textbooks. As an impermeable solute, sodium gives rise to the influx and efflux of water through the cell membranes. In this way, sodium is the main solute to manage water homeostasis (6). The water transport, driven by sodium, gives rise to cell shrinkage in hypernatremia and cell swelling in hyponatremia. The changes of the cell volume may lead to severe symptoms which related with primarily central nervous system, including headache, nausea, vomiting, altered consciousness, seizure even death. Patients with serum sodium disturbances are also under high risk for a wide range of infections, which are associated with higher health costs (7).

Thus, we investigated whether serum sodium disorders are associated with HP infection and whether other laboratory tests are associated with those disturbances in elderly patients.

MATERIAL and METHODS

This is a single-center, retrospective chart review study. We assessed the rate of HP infection by enzyme-linked immunosorbent assay (ELISA) method among patients who had either hypernatremia or hyponatremia. Charts were reviewed from patients who were referred to the internal medicine clinic for treatment of hypernatremia. Demographic data, medical history, laboratory parameters, and HP status were reviewed. Routine laboratory test results and HP tests were obtained during hospitalization. Patients were divided into two groups according to the below and above cut-off values of serum sodium levels. Patients with hypernatremia were defined as having a serum sodium level above 145 mmol/l, and hyponatremia was defined as having a serum sodium level below 135 mmol/l. The primary objective was to assess the rate of HP seropositivity status in hypernatremic and hyponatremic patients by the serum ELISA test. Secondary objectives included HP-associated laboratory parameters in patients with sodium disturbances. We compared the rate of HP infection using by ELISA method.

The data were obtained from the clinical records and were analyzed with student t-test and chi-square test for continuous or categorical variables, respectively. The results are expressed as means with standard deviation, accepted as significant value of $p < 0.05$. SPSS 11.5 statistical program was used. Ethical consent was obtained from Van Yuzuncu Yil University School of Medicine.

RESULTS

At total, 54 patients with sodium disturbances were included for the study. Half of them were hypernatremic and the others were hyponatremic. The mean age of the hypernatremic patients was 79.9±7 years and 15 of them were female. The mean age of the hyponatremic patients was 76,8±6 years and 12 of them were female. There were no significant differences between groups in terms of age and gender (p=0.103 and p=0,414, respectively). In the hypernatremic patients, the mean levels of serum sodium and serum chlorine were higher than those patients with hyponatremia (154±7 versus 121±7 mmol/L and 114±8 versus 89±8 mmol/L all p values below than 0.001, respectively) and the mean potassium level was lower than patients with hyponatremia (3.9±0,6 mmol/L versus 4.7±0,9 mmol/L, p=0.001). Compared to the hyponatremic group, the hypernatremic group had higher levels of liver transaminases, including aspartate aminotransferase and alanine aminotransferase (99±216 U/L versus 85± 256 U/L, p= 0.013 and 66±131 U/L versus 62±181 U/L, p= 0.042, respectively). The overall analysis also showed that levels of serum thyroid stimulating hormone (TSH) and free thyroxine were significantly higher in hyponatremic group compared to hypernatremic counterparts (8.79±24,47 mmol/L versus 1.2±1,49 mmol/L, p=0.013 and 1.3±0,31 mmol/L versus 1.09±0,24 mmol/L, p= 0.019, respectively). Finally, 15 (55.6%) patients tested positive for HP Ig G by ELISA method in hyponatremic patients, 17 (63%) patients tested positive for HP Ig G in hypernatremic patients. There were no significant differences between groups in terms of HP Ig G seropositivity (p=0.58). Otherhand, 9 (33%) patients tested positive for HP Ig A among hyponatremic patients, 19 (70%) patients tested positive for HP Ig A in hypernatremic patients (p=0.029). **Table 1** and **Table 2** has shown the general blood parameters and demographic data of the patients.

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Table 1: Baseline characteristics of the patients.

Variable	n	Hyponatremia Mean ± SD	n	Hypernatremia Mean ± SD	P
Age (years)	27	76,8 ± 6	27	79,9 ± 7	0,103
Hemoglobin (g/dL)	27	10,8 ± 1,9	27	11 ± 1,7	0,972
Hematocrit (%)	27	31,8 ± 5	27	34,4 ± 5,7	0,104
MCV (fL)	27	89 ± 9	27	91,2 ± 7,2	0,164
MCHC (g/dL)	27	34 ± 1,3	27	31,6 ± 1,3	**0,001**
Leukocyte ($x10^9$/L)	27	10,08 ± 5,12	27	11,56 ± 4,41	0,073
Neutrophil ($x10^9$/L)	27	8,25 ± 5,27	27	9,57 ± 4,48	0,130
Lymphocyte ($x10^9$/L)	27	1,09 ± 0,69	27	1,38 ± 1,11	0,478
Thrombocyte ($x10^9$/L)	27	277 ± 153	27	214 ± 113	0,146
Glucose (mg/dL)	27	143 ± 73	27	178 ± 88	**0,035**
Urea (mg/dL)	27	83 ± 60	27	142 ± 78	**0,002**
Creatinine (mg/dL)	27	1,56 ± 1,57	27	1,96 ± 1,63	0,401
AST (u/L)	27	85 ± 256	27	99 ± 216	**0,013**
ALT (u/L)	27	62 ± 181	27	66 ± 131	**0,042**
Albumin (g/L)	27	31,2 ± 8,8	24	29,6 ± 6,8	0,206
ALP (u/L)	25	152 ± 193	21	100 ± 56	0,559
GGT (u/L)	25	116 ± 227	22	62 ± 94	0,932
Sodium (mmol/L)	27	121 ± 7	27	154 ± 7	**0,001**
Potassium (mmol/L)	27	4,7 ± 0,9	27	3,9 ± 0,6	**0,001**
Chlorine (mmol/L)	27	89 ± 8	27	114 ± 8	**0,001**
Calcium (mg/dL)	27	8,8 ± 0,7	27	8,6 ± 0,9	0,143
PT (second)	27	11,15 ± 3,03	27	11,33 ± 3,32	0,646
TSH (mU/L)	22	8,79 ± 24,47	22	1,2 ± 1,49	**0,003**
Free T4 (ng/dL)	23	1,3 ± 0,31	22	1,09 ± 0,24	**0,019**
pH	25	7,37 ± 0,09	25	7,42 ± 0,07	**0,036**

n: Number of patients, SD: Standard deviation, MCV: Mean corpuscular volume, MCHC: Mean erythrocyte hemoglobin concentration, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, GGT: Gama glutamyl transferase, PT: Prothrombin time, TSH: Thyroid stimulating hormone,
T4: Thyroxine

Table 2: Helicobacter pylori status of the patients

Variable		Hyponatremia (n=27)	Hypernatremia (n=27)	P
Gender	Female	12 (44,4)	15 (55,6)	0,414
	Male	15 (55,6)	12 (44,4)	
Dementia	No	25 (92,6)	23 (85,2)	0,386
	Yes	2 (7,4)	4 (14,8)	
HP Ig A	Negative	18 (67)	8 (30)	**0,029**
	Positive	9 (33)	19 (70)	
HP Ig G	Negative	12 (44,4)	10 (37)	0,580
	Positive	15 (55,6)	17 (63)	

n: Number of patients, HP: Helicobacter pylori, Ig: Immunoglobulin

DISCUSSION

This research allowed us to understand the effect of serum sodium levels on the rate of HP infection in routine tertiary care practice and probably was the first in the literature.

Population-based studies demonstrated that, there was a robust link between higher prevalence of gastric cancer and increased salt intake among all genders (8).

In addition, collected data points to high salt consumption as one of the most important habitual key mechanisms underlying HP infection, in a Chinese study conducted by ELISA method to detect HP infection showed that a family history of gastric cancer, consumption of pickled vegetables more than twice a month, and a high monthly salt consumption (more than 500 g/month) were also connected with HP infection (9).

A recent study on higher salt consumption also demonstrated an increased rate of atrophic gastritis and gastric adenocarcinoma among higher salt-consumer subjects compared to those with a normal diet. However, hypernatremia-linked HP infection has not been reported yet (10). Thus, we conducted the current study. Disturbances of serum sodium levels in the hospital setting could cause increased morbidity and mortality even in small ranges (11). Hypernatremia is also a common medical condition among hospitalized elderly patients. The elderly patient population with hypernatremia is frequently experienced with costly complications, including disturbances in mental status, an increased rate of mechanical ventilation, and a higher demand for both of inotropic and vasopressor agents and prolonged intensive care treatment, as well as higher mortality. (12).

Furthermore, an ecological study conducted in aquatic environments during the first years of discovery of HP infection showed that HP strains survived for longer periods in physiological saline (0-15M) than in 0-05M or 0-6M saline solution and optimal pH range for its survival was determined as between pH 5-8 and 6-9 (13). At this perspective, we postulated that most eligible conditions for developing HP infection are both salty and alkaline mediums. We also hypothesized that hypernatremia could be a key factor in supporting the HP infection. A retrospective cohort study involving 51 septic intensive care unit patients also showed that hypernatremia strongly correlated with higher mortality rates (14).

In the current study, we found a strong association between hypernatremia and HP infection, and this contamination may have been due to hypernatremia-related infections. On the other hand, in the presented study, we also found that hypernatremic patients had higher serum TSH levels than hyponatremic patients. It is well-known that hypothyroidism could lead to hyponatremia and some kind of systemic infections (15, 16). In line with classical data revealing hypothyroidism-linked hyponatremia, we found lower TSH levels among patients with hypernatremia. However, we concluded that higher rates of HP Ig A in hypernatremic patients could be seen even in euthyroid status, and hypernatremia was a stronger factor for developing HP infection than hypothyroidism.

Limitations include lack of specific clinical details (e.g. use of proton pump inhibitors and antibiotics before the enrollment of the study) and risk for confounders, including concomitant diseases. Although the presented research was the first in the literature, the overall predictive value could have been limited due to its small sample size.

CONCLUSION

Hypernatremic patients are at high risk for HP infection. This risk has correlated with the prolongation of the hypernatremic status. Otherhand, HP infection could be a driven-factor in developing hypernatremia among elderly patients.

Our results show that hypernatremia is also associated with HP infection, similar to higher dietary salt consumption. More research is needed to explore this unique pathophysiology further.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the institutional and/or national research committee's ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Ganciclovir in the Prevention of Cytomegalovirus Reactivation in Allogeneic Hematopoietic Stem Cell Transplantation: Non-Eliminative Reduction of Viral Load

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ABSTRACT

Objective: Objective: Allogeneic hematopoietic stem cell transplantation (HCT) is used to treat various hematological disorders with a significant risk of treatment-related morbidity and mortality. During long immunosuppressed status, reactivation of cytomegalovirus (CMV) is a challenging complication with its diagnosis, treatment, and toxicity. In our study, we aimed to evaluate the effectiveness of ganciclovir to prophylaxis with valacyclovir in patients who have undergone allogeneic HCT.

Material and Methods: Data of 82 patients were analyzed in a retrospective manner. Patients were grouped as patients receiving valacyclovir alone or ganciclovir plus valacyclovir. CMV-DNA levels were monitored weekly. Reactivation and alterations of viral DNA levels were recorded and compared in both prophylaxis regimes.

Results: Mean age of patients was 44.85 years (19-69 years). The 31 patients were female (37,8%) and 51 were male (62,2%). All recipients were CMV seropositive before allogeneic HCT, and only 2 donors were CMV seronegative (2,4%). Forty-one of the patients received valacyclovir (50%), while 41 received ganciclovir plus valacyclovir (50%). Reactivation was not observed in 32 patients (39%). The 33 of the 41 patients receiving ganciclovir plus valacyclovir and 18 of the 41 patients on valacyclovir alone developed CMV reactivation. Although the inclusion of ganciclovir to valacyclovir was not related with decreased rates of CMV reactivation, the level of CMV DNAemia was relatively lower in patients on ganciclovir plus valacyclovir than in valacyclovir treatment alone.

Conclusion: Inclusion of ganciclovir to valacyclovir in allogeneic HCT patients did not decrease the rate of CMV reactivation, and did not shorten the duration but reduced the degree of CMV DNAemia.

Keywords: Ganciclovir, Cytomegalovirus Reactivation, Allogeneic Hematopoietic Stem Cell Transplantation

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (HCT) is used to treat a variety of hematological malignancies and certain non-malignant hematological disorders. The rate of HCTs worldwide is estimated to exceed 40.000 transplants/year.

Cytomegalovirus (CMV) causes a wide spectrum of involvement with various presentations, mainly depending on the host's immune status. In immunocompetent patients, viral replication is limited with T cell-mediated immunity, resulting in latent infection. DNA of the latent virus is detectable in monocytes and dendritic cells, megakaryocytes, and even myeloid progenitors in the bone marrow (1). The secondary disease may be observed later due to reactivation of the latent infection or, less likely, reinfection with a different strain. Reactivation may be observed in immunocompetent patients and patients under immunosuppression, secondary to certain diseases or treatments (2). Introduction to CMV usually happens in the early years of life with an increased prevalence with age, depending on the socioeconomic status as well as inhabitation [3]. In a population-based study from the United States of America, CMV sero-prevalence is reported as 36% in 6-11 year old individuals while reaching 91% in those aged over 80 years [3,4]. As a common infection, the serious disease is not common in immunocompetent patients but is still a major cause of mortality and morbidity in patients who are immunosuppressed due to solid organ and HCT, HIV infection, and immunomodulating treatments towards T cell immunity.

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The most important risk factor for CMV reactivation in patients who have undergone allogenic HCT is the serologic status of the recipient and the donor, particularly in seropositive recipients, the risk of reactivation is reported as 80%. In contrast, in seronegative recipients with a seropositive donor, the risk of primary infection is reported as 30%. Besides the serologic status of the HCT recipient, corticosteroid treatment, T cell depletion with either purine analogues or Alemtuzumab, development of graft versus host disease (GVHD), and the graft source are also suggested as risk factors (5-7).

Manifestations of CMV disease in immunosuppressed patients include fever, hepatitis, pneumonia, upper and lower gastrointestinal diseases, and central nervous system infections, including retinitis and encephalitis. The diagnosis of CMV disease is challenging in HCT recipients due to the clinical signs and symptoms, which may be confused with graft rejection and infections due to other microorganisms. For this diagnostic challenge, it is suggested that every donor and recipient should be surveyed for CMV seropositivity before HCT with a risk estimation of reactivation and later monitored regularly with polymerase chain reaction (PCR) assay (7).

It is important to clarify the definitions of CMV infection and disease, as CMV infection refers to the demonstration of viral antigens or DNA in blood or anybody fluid with or without signs of invasive involvement, but the definition of CMV disease refers to manifestation of disease-related signs and symptoms with alterations in blood count or invasive disease in tissue samples (8). As isolating CMV by culture techniques is not feasible, a pre-emptive approach with the detection of DNAemia and/or primary infection is recommended with conflicts regarding the thresholds of quantitive-DNA values (8). The first first-line agent for pre-emptive treatment and prophylaxis is intravenous ganciclovir. Ganciclovir and Valganciclovir (its oral prodrug) are reported to reduce the risk of reactivation/primary infection without a favorable effect on overall survival (5, 9). Mechanism of action for all antiviral drugs is generally based on the inhibition of DNA synthesis. Myelosuppression is frequently observed in patients receiving ganciclovir. Novel agents, including Brincidofovir, Maribavir, and Letermovir are currently being under investigation with promising results (7).

With the ongoing concerns on CMV reactivation with its diagnostic and therapeutic challenges, we aimed to investigate our patients who have undergone allogeneic HCT with perspectives including epidemiological projection, the risk factors of reactivation, and the effects of prophylactic antivirals on CMV reactivation.

MATERIAL and METHODS

Patient Cohort:

Eighty-two patients who have undergone allogeneic HCT in the Hematology Department of Bahcesehir University between in 2013-2017 were enrolled in the study in a retrospective manner. Underlying hematological malignancy, age, gender, CMV serology of the patient and the donor, the source of HCT, development of CMV DNAemia and/or infection were recorded from the files (**Table 1**).

Conditioning Treatment:

Patients on allogeneic HCT were prepared to receive either myeloablative conditioning (MAC) or reduced intensity conditioning (RIC) regimen before transplantation. MAC regimens included CY/TBI (cyclophosphamide and total body irradiation), Bu4/Cy (Busulfan and cyclophosphamide) or Flu/Bu4 (Busulfan and Fludarabine) while RIC regimens included Flu/Mel (Fludarabin and Melphalan), Flu/Bu2 or 3 (Fludarabin and Busulfan) or Flu/Cy (Fludarabin and Cyclophosphamide).

Antiviral Prophylaxis:

Starting from day minus 7 till day before HCT, all patients received oral Valacyclovir 500 mg once daily (OD) or oral Valacyclovir 500 mg OD plus intravenous ganciclovir 5mg/kg twice daily for seven days and switched to daily dosing afterward. For all patients, prophylaxis was continued until day plus 100, if reactivation was not observed.

Monitorization:

All patients were also monitored for CMV reactivation weekly starting from day +7. CMV DNAemia was analyzed with Anatolia-Bosphore Quantification Assay (Istanbul, Turkey) using a whole blood sample with a linear interval of 60-13.000.000 IU/mL (1IU/mL=1,2 copies/mL).

When asymptomatic CMV DNAemia is detected with two consecutive increased CMV-DNA levels >1000 IU/mL, treatment is given with ganciclovir 5mg/kg/dose every 12 hours for 14 days and then 5 mg/kg/dose daily or oral Valganciclovir 900 mg twice daily or oral Valacyclovir 1000 mg three times daily until 2 consecutive CMV-DNA PCR negativity.

Statistical Analysis

Statistical analysis was performed with IBM SPSS V.20. Descriptive analysis was performed, and median values were calculated and reported for quantitative variables and the percentage was calculated and reported for categorical variables. Comparisons were performed with chi-square test and Mann-Whitney U test depending upon the parametrical and non-parametrical variables. Logistical regression analysis was performed for all significant correlations 95% CI was used to present the statistically significant level of the results. ROC curve analysis was performed for risk estimation.

Ethical approval was obtained from the local ethical committee. Informed written consent forms were obtained from all patients.

RESULTS

General Features

Mean age of patients was 44,85 years (19-69 years). 31 patients were female (37,8%) while 51 were male (62,2%). Primary disease of patients were acute myeloid Leukemia (AML) or myelodysplastic syndrome (MDS) in 35 patients (42,6%), Acute Lymphoblastic Leukemia (ALL) in 24 patients (29,3%), nonHodgkin's Lymphoma (NHL) in 9 patients (11%), multiple myeloma (MM) in 6 patients (7,3%), Aplastic Anemia in 5 patients (6,1%), and Myelofibrosis in 3 patients (3,7%).

The source of HCT was peripheral blood in 77 patients (93,9%) and bone marrow in 5 patients (6,1%) with matching as sibling full match in 63 patients (76,8%), unrelated full match in 7 patients (8,5%), haploidentical mismatch sibling in 5 patients (6,1%), unrelated mismatch in 7 patients (8,5%). 61 patients received myeloablative conditioning treatment (MAC) (74,4%), while 21 patients received reduced intensity conditioning treatment (RIC) (25,6%). The use of a purine analog is observed in 47 patients (57,3%).

Regarding the risk factors of reactivation, all recipients were CMV seropositive before allogeneic HCT. Only 2 donors were CMV seronegative (2,4%). 41 of the patients received Valacyclovir (50%), while 41 received ganciclovir plus Valacyclovir (50%).

Reactivation was not observed in 32 patients (39%) while in 21 patients, reactivation was observed before engraftment (<30 days) (21%), in 20 patients between days 30-60 (24,4%), in 2 patients between days 60-100 (2,4%) and in 7 patients after days 100 (8,5%). Mean value of first observed CMV-DNA positivity is 1518,95 IU/mL (0-43940) while mean maximum value is 574778,1 IU/mL (0-44830).

With the recognition of reactivation, treatment is commenced with ganciclovir in 37 patients (%45,1), Valganciclovir in 3 patients (3,7%) and Valacyclovir in 12 patients (14,6%). In this Valacyclovir alone group, CMV-DNA levels did not trend to increase and were accepted as probable spontaneous resolution. The timing of CMV-DNA negativity is within 14 days of pre-emptive treatment in 6 patients (7,3%) while in 14-28 days in 25 patients (30,5%) and after 28 days in 14 patients (17,1%).

Regarding survival, 15 patients died (18,3%), all after 100 days, 13 patients due to relapse of the primary hematological malignancy and 2 patients died due to causes which were non-hematological and not transplant related.

Comparisons

As all patients were CMV seropositive before allogeneic HCT, donor seropositivity became a major concern regarding activation and the effectiveness of the prophylactic treatment. However, only 2 of the 41 HCT transplants who were on ganciclovir plus Valacyclovir were CMV seronegative, while all donors of 41 HCT patients who were on Valacyclovir alone were CMV seropositive, which suggested that donor CMV serologic status is not a confounding factor (p=0,247).

Our second concern was the primary hematological cancer and its probable effects on CMV reactivation. But two prophylactic treatment groups were similar regarding the primary hematological cancer (p=0,708).

Likewise, conditioning treatment and prophylaxy groups were compared and 32 of the patients on Valacyclovir alone received MAC while 29 of the patients on ganciclovir plus Valacyclovir received MAC (p=0,307) and a homogeneity was preserved in the comparison. 20 of the Valacyclovir alone patients have received purine analogue treatment while 27 patients of ganciclovir plus Valacyclovir group have received purine analogue (p=0,09).

Regarding prophylaxis and CMV reactivation which was the major question to be answered in our study, 33 of the 41 patients who were receiving ganciclovir plus Valacyclovir developed CMV reactivation while only 18 of the 41 patients who were on Valacyclovir alone developed CMV reactivation (p=0,001).

With the recognition of CMV DNAemia and the commencing of pre-emptive treatment, 12 patients in the ganciclovir plus Valacyclovir group developed a CMV-DNA negativity after 28 days of pre-emptive treatment while in the Valacyclovir alone prophylaxy group, 5 of the 18 CMV reactivated patients reached CMV-DNA negativity within 14 days and 10 reached in 14-28 days, and only 2 patients reached CMV-DNA negativity after 28 days (p=0,019).

As CMV reactivation was observed despite the use of combination antivirals, mean initial CMV-DNA level in Valacyclovir alone was 1.865,15 IU/mL (SD 7.171,924) while in ganciclovir plus Valacyclovir it was 1.172,76 (SD 2.898,508) (p<0,05) and maximum CMV-DNA level in Valacyclovir alone group was 1.099.194,29 IU/mL (SD 7000357.926) while in ganciclovir plus Valacyclovir group it was 50.361,90 IU/mL (139.499,392) (p<0,05). Although the inclusion of ganciclovir to Valacyclovir was not related with decreased rates of CMV reactivation, in the combination prophylaxis group during reactivation, level of CMV DNAemia was relatively lower than Valacyclovir alone group.

The source of HSC, prophylaxis type, and CMV reactivation were compared, and it was observed that 4 of the haploidentical HSC have received ganciclovir plus Valacyclovir and all have developed CMV reactivation while in sibling full match and unrelated full match HSCs, distribution was similar regarding prophylaxis and reactivation (p=0,152). Conditioning treatment have not an impact on CMV reactivation alone (p=0,207). As the distribution of conditioning treatments were similar in respect of antiviral prophylaxis, 25 of 29 patients who were on ganciclovir plus Valacyclovir and have received MAC have developed CMV reactivation, while 8 of the 12 patients who have received ganciclovir plus Valacyclovir and RIC developed CMV reactivation, as the difference was observed in the number of the patients, this difference did not reach to a statistical significance (p=0,614).

Likewise, receiving purine analogue was not related with CMV reactivation (p=0,18) and among patients who are receiving purine analogue therapy, 21 of the 27 patients who have received combination antiviral prophylaxy have developed CMV reactivation while 8 of the 20 patients who have received Valacyclovir alone were observed to develop CMV reactivation. Though a higher percentage of patients on combination antiviral prophylaxis has developed CMV reactivation, the relation did not show statistical significance (p=0,19).

Last of all, prophylaxis with Valacyclovir alone or ganciclovir plus Valacyclovir was not related to post-transplantation survival in respect of CMV activation (p=0,249).

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Table 1. Characteristics of Patients on Prophylaxis with Valacyclovir and Ganciclovir plus Valacyclovir

		Valacyclovir Group (n=41)	Ganciclovir+Valacyclovir Group (n=41)	*p* values
Age (mean/years)		48,2 (23-69) (SD:13,085)	41,51 (19-65) (SD:15,017)	>0,05
Gender (F/M)		16/25	15/26	>0,05
Primary Hematological Disease	**AML-MDS**	19 (46,4%)	16 (39%)	>0,05
	ALL	12(29,3%)	12 (29,3%)	
	NHL	4 (9,8%)	5 (12,2%)	
	MM	1 (2,4%)	5 (12,2 %)	
	AA	3 (7,3%)	2 (4,9%)	
	MF	2 (4,9%)	1 (2,4%)	
Conditioning Regimen	**Myelo-ablative**	32 (78%)	29 (70,7%)	>0,05
	Reduced-intensity	9 (22%)	12 (29,3%)	
CMV Reactivation	**None**	24 (58,5%)	8 (19,5%)	<0,05
	<30 days	4 (9,8%)	17 (41,5%)	
	30-60 days	10 (24,4%)	10 (24,4%)	
	60-100 days	1 (2,4%)	1 (2,4%)	
	>100 days	2 (4,9%)	5 (12,2%)	
Pre-transplantation recipient CMV seropositivity		100%	100%	
Donor CMV seropositivity		100%	95,1%	>0,05
Stem Cell Source	**Peripheral Blood**	39 (95,1%)	38 (92,7%)	>0,05
	Bone Marrow	2 (4,9%)	3 (7,3%)	
Transplantation Type	**Full Match Related**	38 (92,7%)	25 (61%)	>0,05
	Full Match Unrelated	2 (4,9%)	5 (12,2%)	
	Haploidentical	1 (2,4%)	4 (9,7%)	
	Unrelated mismatch	none	7 (17,1%)	
Use of Purine Analogue		20 (48,8%)	27 (65,9%)	>0,05
CMV reactivation and Use of Purine Analogue		8 (40%)	21 (77,7%)	
Pre-emptive therapy	**None**	21 (51,2%)	24 (58,5%)	
	Ganciclovir	13 (31,7%)	3 (7,3%)	
	Valacyclovir	7 (17,1%)	5 (12,2%)	
CMV DNA negativity	**0-14 days**	5 patients	1 patient	<0,05
	14-28 days	10 patients	15 patients	
	>28 days	2 patients	12 patients	
Initial CMV DNAemia (mean-IU/mL)		1865,15 (SD 7171,924)	1172,76 (SD 2898,508)	<0,05
Maximum CMV DNAemia (mean-IU/mL)		1099194,29 (SD 7000357,926)	50361,90 (139499,392)	<0,05

DISCUSSION

In relapsed and/or refractory hematological malignancies, HCT is still an undeniable treatment modality. Immunological properties of graft-host interaction may be modified to form a status of balance-unbalance depending on the status of the disease activity. Graft versus leukemia/lymphoma/myeloma effect may be desired in refractory disease. The immunological interaction of graft and host mainly proceeds on T cell mediated immunity, and the entrance of reactivation of a latent CMV may alter the balance leading to increased rates of GVHD, as well as bacterial or fungal infections and both CMV-related or unrelated mortality (5-7). Primary or secondary prophylaxy, pre-emptive treatment with antivirals, specific and nonspecific immunoglobulins, and adoptive specific T cell transfer therapies are reported with conflicting outcomes (7, 10). In a recent meta-analysis regarding antiviral prophylaxis against CMV in allogeneic HCT patients, ganciclovir and Letermovir have been observed as effective agents in terms of advanced surveillance and the use of pre-emptive therapy (13).

As the prevalence of CMV is related with age, socioeconomic status, and region, rates of CMV positivity have been reported over 90% in immunocompetent patient groups (11,12). In our study, all recipients were CMV IgG positive and only 2 donors were seronegative. This may be a reflection of seropositivity in Turkey. The limitation of the donor spectrum leads to the obligation of laying aside the CMV status of the donor and getting prepared for reactivation. In our study group, this limitation led to an unintended yet homogenous comparison between two prophylaxy groups.

Most of the reactivation was observed during the first 100 days, while on close surveillance (21% <30 days and 24,4% between days 30-60) and regardless of the antiviral agent and mean value of a maximum CMV-DNA positivity as 574.778,1 IU/mL which is a significantly high value of CMV replication. Though the inclusion of ganciclovir did not decrease the rates of CMV reactivation, mean initial and maximum CMV-DNA levels were lower in the combination group (p values <0,05).

With lower CMV-DNA levels, the time to reach CMV negativity with the initiation of pre-emptive therapy was not shortened in the combination group as expected.

Regarding the source of HCT, in haploidentical HCT patients all 4 who have received ganciclovir plus Valacyclovir have developed CMV reactivation, but did not developed for one haploidentical who receiving Valacyclovir. However, in the full match related and unrelated HCT patients, reactivation was similar in both prophylaxis groups. Though the number of haploidentical HCT patients is limited, our observation was in favor of not using ganciclovir plus Valacyclovir for CMV reactivation prophylaxis. In a recent meta-analysis, use of acyclovir was observed to be related with less toxicity but also nonsignificant effectivity in CMV prevention, while ganciclovir as related with increased toxicity, effective to prevent CMV reactivation but ineffective in mortality (13). Our study did not observe a decreased rate of CMV reactivation in a combination antiviral group but only a limitation in CMV viremia.

There were certain limitations of our study. First of all, the retrospective nature of our study has limited the equal distribution of the patients, especially haploidentical HCT patients. Though they were all treated with ganciclovir plus Valacyclovir prophylaxy group due to the concern of CMV reactivation in this sensitive group of patients, all have reactivated. The second major limitation of our study was the lack of evidence of CMV infection, which may be attributed to the prophylactic-pre-emptive approach of our clinic.

CONCLUSION

Inclusion of ganciclovir to Valacyclovir in allogeneic HCT patients did not decrease the rate of CMV reactivation, did not shorten the duration of the CMV-DNAemia and did not affect the overall survival. With the perspective of its cost and possible myelosuppressive effects, it may be wise to monitor CMV-DNA routinely and use ganciclovir as a pre-emptive therapy until better antiviral agents like Letermovir are available.

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Conflict of interest: The authors declare no competing interests.

Author Contributions: OK: Project Design, Data collection, Biochemical Analysis, literature review, **OK:** Manuscript preparation and Revision

Ethical approval: All procedures performed in studies involving human participants were in accordance with the institutional and/or national research committee's ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Surgical Separation of Pygopagus Conjoined twins at Holy Family Hospital Rawalpindi; a Neurological Surgery Perspective and Outcomes: a Case Report

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ABSTRACT

Objective: Objective: Conjoined twins are considered to be the result of aberrant embryogenesis with incomplete embryonic separation. Estimated incidence of Conjoined twins is 1:50,000 pregnancies, and 1:200,000 live births, in new-borns with a female predominance of 3:1.

Conjoined twins are classified into different subtypes according to the site of fusion: Thoracopagus, Omphalopagus, Pygopagus, Ischiopagus, and craniopagus. Even in conjoined twins, Pygopagus has an incidence of 6-19%; subsequently, not many cases have been reported worldwide.

Case: This case report is about 6 months old female Pygopagus conjoined twins who fused at the lumbosacral level with a shared spinal canal. They were successfully separated in Pakistan with great success and had no neurological deficits on consequent follow-ups. An adequate build-up of physiological parameters until twins are old enough to undergo separation with multi-disciplinary management is the cornerstone of the successful management and separation of Pygopagus twins which is only possible in planned elective settings. Whereas emergency separation in the background of concomitant sepsis and sharing of vital organs carries high mortality and raises valid ethical questions regarding which life to prioritize saving and what organs to give to either viable child in case of shared CVS, GIT, and genitourinary systems.

Keywords: Pygopagus Conjoined twins, paediatric, surgery

INTRODUCTION

Conjoined twins, also known as Siamese twins, popularly thought to be a product of erroneous embryogenesis is a rare condition occurring in 1:50000 births but accounting for approximately 60% of cases ending in stillbirth; the true incidence lies between 1:200000 with female predominance [1]. History of conjoined twins goes as far back to caveman drawings, from elevation to divine status by ancient Romans i.e. Janus, to have been feared into culling and killing or put on display for public interest in circuses, at a point they were even revered by churches as saints; most famously is the Biddenden Maids.

Records of attempted separation of twins go back to a millennium in Byzantine; the first successful separation of conjoined twins was reported in the literature by Johannes Fatio a Swiss surgeon who successfully separated Omphalopagus twins, Elizabeth and Catherine Mayerin, in 1689 (After tracking the umbilical vessels to the navel, he applied a ligature to the connecting ensiform cartilage then tightened it over several days until it cut completely through) [1].

With the accepted understanding that conjoined twins are a result of errors in embryogenesis resulting in an abnormal form of monozygotic twinning, two theories are accepted i.e. fusion and fission (Kaufman, 2004; Spencer, 2000a; Spitz, 2005), which state that aberrations occur due to incomplete splitting or cleavage at primitive streak (fission theory) or joining of an embryo at vulnerable sites after complete splitting (fusion) but both have their limitations due to non-conclusive testing and rare phenomenon [2].

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Boer et al proposed that the underlying initial duplication of axial morphogenetic potent primordia could be the starting element in the genesis of ventrally, laterally, and caudally conjoined twins which offers a better explanation and understanding of the formation, etiopathogenesis, and embryogenesis of conjoined twins (3).

Siamese twins are classified based on the site of their attachment site i.e. abdomen (omphalopagus), thorax (thoracopagus), head (craniopagus), sacrum (pygopagus), vertebral column (Rachiopagus), based on site of lateral fusion (parapagus and its subvarieties encompassing varying degrees of thorax and cranium involvement) (4). Pygopagus compromising 6-19% of the conjoined twins poses a unique challenge to neurosurgeons with complex anatomy of the fused spinal cord with variable extent having a common terminal portion of the spine, fused genitourinary system, fused gastrointestinal system (1).

Due to multi-organ system involvement and unique physiology of conjoined twins a multi-disciplinary approach which including Neurosurgery, Paediatrics Surgery, Paediatric medicine, and Obstetrics is required from initial diagnosis on prenatal scans to delivery of baby, survival, and gradual build-up till surgery requires coordinated multi-disciplinary effort and resources, especially in a setting like ours where our health system is already burdened and choked with the inaccessibility of health to all, the lack of trained staff and specialized instruments are a challenge to deal with such delicate tactful cases.

CASE

This case report is about conjoined twins diagnosed at 20 weeks on prenatal scan in a private setup and presented to our setup at 22 weeks. The mother was 30-years-old G5P4A0 who had antenatal care at a local hospital. At the 28th week, the mother developed anaemia and was admitted and treated, an early caesarean section was performed at 37 weeks, the APGAR score at the birth of both twins was 10, and the combined weight was 3500 grams on examination they faced opposite to each other in obvious oblique pattern, and there were no gross musculoskeletal abnormalities noted. However, both were fused at the lumbosacral region with a sacral circumference of 14 cm at the conjoined area. Detailed neurological examination was unremarkable, with normal power in both lower limbs, normal reflexes, and no neurological deficit of any sort.

They had a single common anal opening and a separate vagina. Four separate openings could be identified (two vaginal and two urethral). Assessment of CVS and the respiratory system was unremarkable. They were shifted to a high dependency unit for postnatal care as they were deeply jaundiced, oxygen-dependent, and in sepsis which was being managed accordingly.

They developed abdominal distention with respiratory distress, with scanty stool being passed from a single anal opening. Pelvic divided colostomy was made on the 7th day for both infants with per-operative findings of separate small and large gut until the rectum. They were shifted to CPAP for respiratory distress, breathing settled over time, and free of oxygen dependence.

In subsequent workup, echocardiography showed no abnormality and both CVS functions were in the normal range.

CT angiography of the abdominal aorta showed separate blood supplies with no dependence on each other, and CT Urogram was unremarkable.

- MRI of the Lumbo-Sacral spine showed almost complete fusion of Coccyx with sharing of the common spinal canal, common dural sac, fibers of cauda equina which were fused with spinal canal at the Coccyx

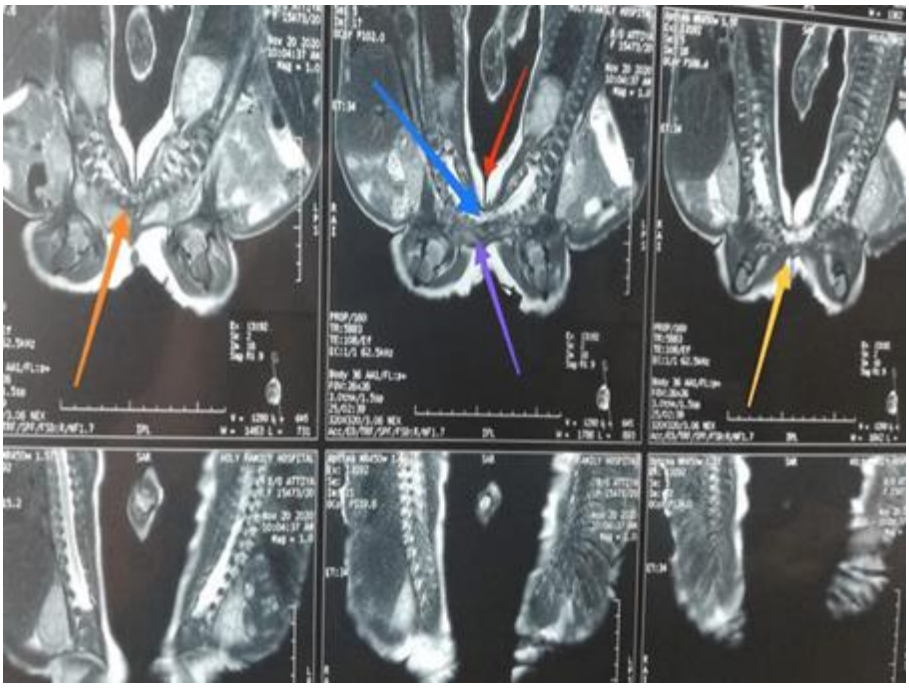

Figure 1: MRI lumbosacral Spine showing complete fusion of Coccyx with common shared spinal canal

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CT Angiography was performed in the second month of life with coronal, sagittal reformats and 3D reconstruction, which showed normal vascular anatomy but vertebral bodies till SV4 with complete non-visualization of SV5 and Coccyx. Multidisciplinary management board comprised paediatric surgery, paediatric medicine, neurosurgery, plastics surgery, anaesthesia department, and it was decided to separate the twins at the 6th month of life. In this study, we will focus on neurosurgical aspects of the separation of conjoined twins.

When they reached the 6th month of age, surgery was planned, and the management team was organized comprising Neurosurgery, Paediatric surgery, and anaesthesia. Twins were operated in Holy Family Hospital. Magnifying loupes were used by neurosurgeons. Pre-operative preparations were done as per standard bowel preparation, and following standard protocol consisting of 4-hour nil per oral pre-op, 2 pints of Blood were arranged and kept in hand. Regarding anaesthesia consideration, two anesthesia teams were ready and involved, and rehearsal by anaesthetic was done pre-operatively. Peripheral lines were placed. Both were labelled as Baby 1 and Baby 2 for convenience, to avoid confusion among management teams, and to have separate identities after separation.

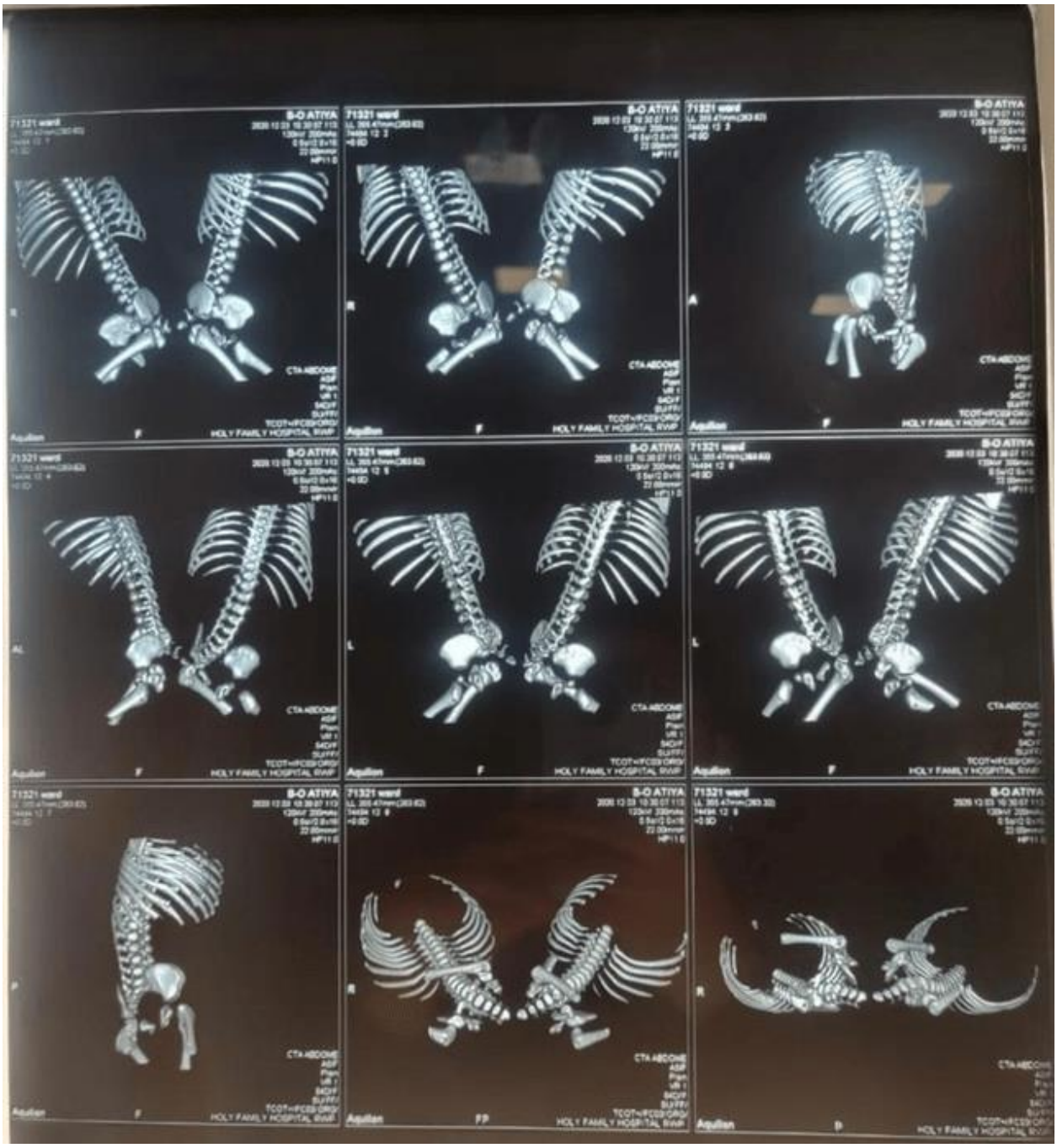

Figure 2: complete non-visualization of 5th sacral vertebrae and Coccyx.

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Figure 3: Incision marking and planning

They were anesthetized separately on separate anaesthetic medicine and machines, The twins were repositioned on the OT table as planned by the neurosurgical team, the skin was prepared and draped, an incision was made, and subcutaneous dissection was done up to the conjoined sacral area where the bone was skeletonized using monopolar cautery under magnification of loupes posterior part of the conjoined dysplastic sacrum was removed to expose the conjoined dural sac.

Dural Sac was carefully exposed to the extent that dural repair would be easily possible. After exposing the dural sac, a linear incision along the longitudinal axis of the sac was given, and CSF flow was observed. Cauda Equina rootlets were observed to be found to be conjoined.

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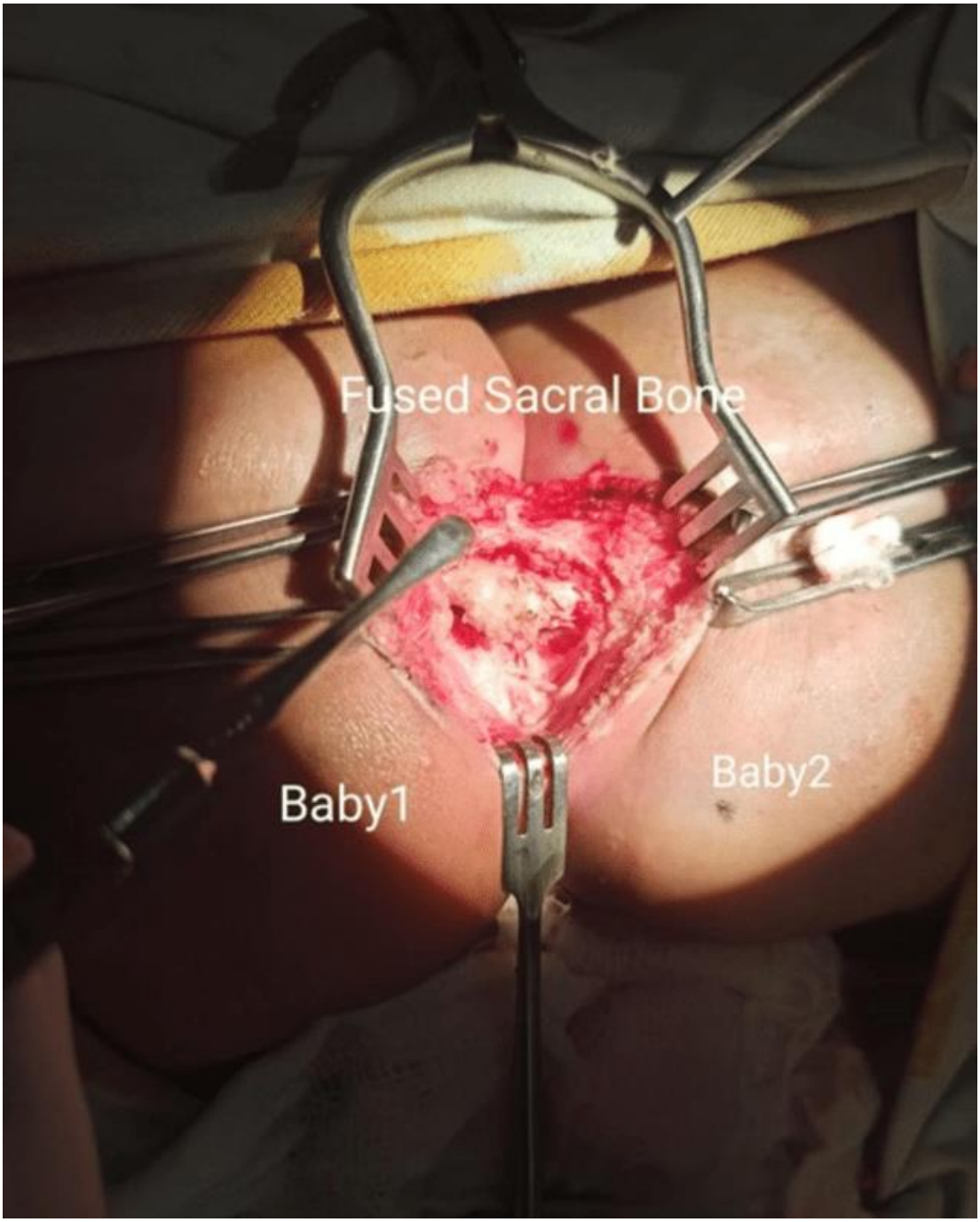

Figure 4: Fused Dysplastic Sacral bone.

We did not have a nerve stimulator or intra-operative neuromonitoring, so we carefully resected the Filum Terminale and Cauda Equina rootlets. After separation and arachnoid dissection, rootlets retracted back into the spinal cord of both babies.

After making sure that rootlets were not attached to the dura, both dural sleeves were closed in a watertight fashion. After that, soft tissue dissection was done, and reaching near the anal canal, babies were handed over to a team of paediatric surgeons who found a common anal opening.

Anoplasty was done at the spot, and the anal canal was reconstructed separately both babies were shifted on separate tables, and by two teams of neurosurgeons and paediatric surgeons, skin flaps were closed in a routine fashion. The wound was closed in reverse order after confirming that there was no CSF leak.

No neurological deficit was observed and normal anal and urethral sphincter tone was examined at follow-up after surgery. Mild CSF leakage in baby 2 was observed which after applying stitches to the skin was stopped within 12 hrs. No further complications were observed on subsequent follow-ups.

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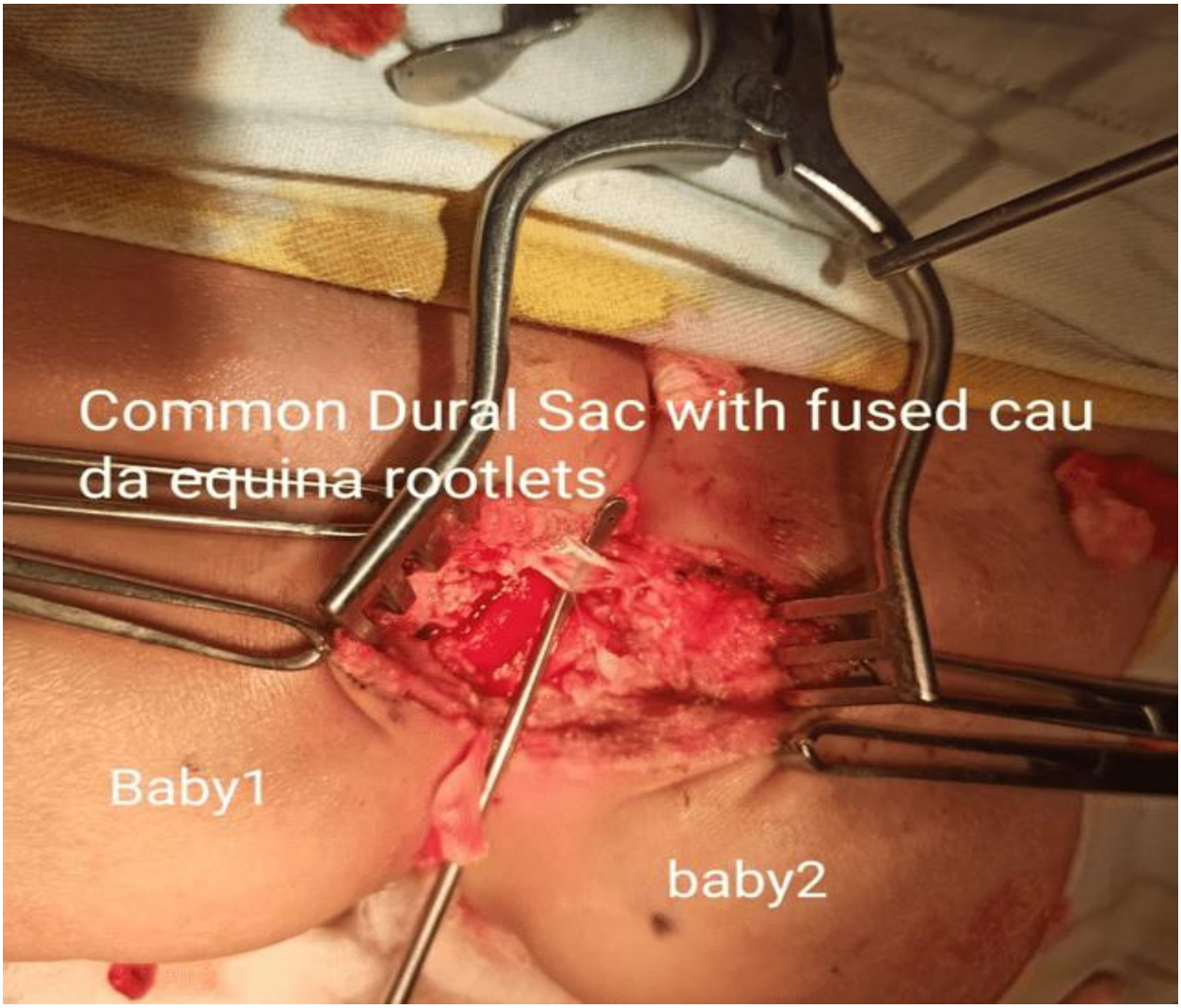

Figure 5: Common Shared Spinal Canal.

DISCUSSION

With the dawn of the scientific age era, Siamese twins are no longer looked at as high mortality or poor prognosis condition, even in the congenital diversity of Siamese twins Pygopagus has a unique presentation as in they are fused at the sacrum and perineum with the union of spine, rectum, urinary tract, and reproductive organs which make up unique physiology and challenging complex anatomy for surgeons and consequently difficult anaesthesia induction, and at the same time they pose a moral dilemma in prioritizing about which of the twins to be saved, and deciding what organs to give particularly in case of the fused anus, urethra, vagina which pose a unique ethical issue for all involved parties hospital authorities, doctors and parents (5). Due to the rarity of the cases and even fewer reported operated cases for Siamese twins, which are 25 cases reported up to date (6), many aspects of Pygopagus from aberrant embryogenesis to surgical management, differ as there is no mutual consensus about definite guidelines, in the modern era our neurosurgical goal is to redefine the anatomy of the spinal canal and vertebral column in a way that prevents neurosurgical deficit, dural CSF leak, prevent infection, pseudomeningocele formation, however in our case, one of the twins developed CSF leak 3rd day postoperatively which is reported in 37 percent of the operated cases of Pygopagus (7,8).

However, it was managed conservatively by applying stitches and giving antibiotics for reduced risk of infection. Neural separation and reconstruction were performed before perineal reconstruction to reduce the risk of post-operative meningitis and avoidance of any possible fecal spillage and contamination; similarly, Prashant Jain et al reported that separation of neural structures before perineal reconstruction carried a better prognosis considering the reduced risk of post-operative meningitis (7).

This was the first successful separation operation of Pygopagus in Pakistan despite having a lack of resources in LMIC countries like ours.

Government and existing health models tend to focus on preventive and curative aspects of communicable diseases, thus focusing less on ‘costly’ and ‘complex’ provision of surgical care; neurosurgery has thus been deprioritized (9).

Pygopagus is an extremely delicate and complicated procedure, and many authors have reported the use of novel devices like three-dimensional solid models (6), intraoperative neuromonitoring, SSEP (somatosensory evoked potential) (10), teleconsultations (11), CAD (computer-aided designs) techniques (12) for 3D

reconstruction of the whole anatomy and allowing rehearsals and planning of the operation.

But in our resource-limited setup, we had no available option of the utilities mentioned above, yet an attempt was taken, and Pakistani Neurosurgeons performed separation, and there was no neurological deficit or complication observed in consequent follow-ups. 33344dsasdf6yu7olöo.şiğĞü

This report emphasizes the need for a multidisciplinary approach as well as delaying the surgery till when the physiological reserves of the twins are well developed I.e. 6 months (1) compared to emergency separation which carries high mortalities 28% mortality vs 85% in elective settings (8), according to a single-center study conducted from 1974 to 2006 in the Philippines on a set of 22 conjoined twins (11 thoracopagus, 5 omphalopagus, 3 ischiopagus, 2 craniopagus, and 1 pygopagus twin) 6 twins were separated on an emergency basis and only 1 twin survived (13) which reached almost 80 percent mortality as reported by Spitz et al. (14), the successful separation and favourable outcomes in elective surgery owes to well-planned multidisciplinary approach, well-planned strategies and better physiologic parameter and optimization of twins for surgery keeping in mind the abysmal factors like intractable acidosis, sepsis, haemorrhage which are the leading cause of mortalities in conjoined twins (13,14).

CONCLUSION

Pygopagus separation may be a technically difficult case demanding excellence and sophistication with a minimum margin of error.

Especially, if the patient has no pre-op neurological deficit, but this is the first of its kind successful reported case in Pakistan owing to its success of well-coordinated multidisciplinary effort at the same time highlighting the lack of resources and basic infrastructure to deal with such complicated cases,

Paediatric neurosurgery should be given priority basis, and units should be established with a specialized workforce and equipped state of the art machinery.

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Acknowledgments: None

Conflict of interest: The authors declare no competing interests.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the institutional and/or national research committee's ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Titanium Elastic Nailing System of Diaphyseal Femur Fracture in a 7 Years Old Child: A Case Report

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ABSTRACT

Objective: Midshaft femur fracture commonly treated conservatively in paediatric patients. However, complications are seen in conservative treatments and lately surgical interventions are being practised tremendously to minimise the complications.

Case Report: A 7 years old boy, sustained a closed fracture midshaft left femur after a motor vehicle accident. Operative management was decided for this patient using Titanium Elastic Nailing System, which revealed a good outcome within 3 months of duration.

Conclusion: Titanium Elastic Nailing System is fixed with minimally invasive techniques in children 6-16 years of age with diaphyseal femoral fractures, which gives a good outcome and minimizes the complications and allows earlier rehabilitation and return to school life by speeding up the fracture healing. However, an experienced surgeon and good surgical technique is desired to minimize the complications that may occur.

Keyword: Paediatric diaphyseal femur fracture, Operative management, Titanium Elastic Nailing

INTRODUCTION

Femoral diaphyseal fractures are the most common types of fractures seen in paediatric injuries (1). Conventionally, the fracture is treated by closed reduction with Bryant's traction, hip spica, and plating for surgical stabilisation (1). Due to spontaneous correction of angulation and the astounding rapid healing power due to age, non-surgical management has been the most favoured method of treatment in paediatric age groups traditionally (1). However, conservative treatments have resulted in complications such as loss of reduction and malunion (1). Moreover, newer understandings have been brought to light as present-day studies have shown that prolonged immobilisation on children by closed reduction such as Bryant's traction and Hip Spica can cause economic and psychosocial disturbances, not only to the children themselves but also to the entire family (2).

In the last two decades, there has been a rise in operative approach to managing femoral diaphyseal fractures in age between 6-16 as good outcomes have been proven in orthopaedic practise (1). Hereby, we are reporting a case of femoral diaphyseal fracture in a 7 years old child who was treated surgically using Titanium Elastic Nailing System (TENS).

CASE

A 7 years old Malay boy was brought to the emergency department, Hospital Tengku Ampuan Rahimah, Klang, by ambulance following a motor vehicle accident. On further history obtained from his parents, the child was seated in the back passenger's seat without fastening his seatbelt while travelling on the highway. Subsequently, the car was hit by a truck from the back and pushed into the drain. Post-trauma, the patient was complaining of intense pain over his left thigh and he was unable to weight bear with his left lower limb. There was no loss of consciousness, or retrograde amnesia. Vital signs were stable upon arrival to the hospital. On examination, noted deformity over the left lower limb. The left lower limb was externally rotated and shortened. There was significant tenderness over the left mid-thigh region. Otherwise, no other injuries or wounds were noted.

Case Report Article

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A plain radiograph was done (**Figure 1**). X-Ray images show a simple transverse fracture midshaft of the left femur. The patient was diagnosed with a closed fracture midshaft left femur, Winquist, and Hansen Classification Type 0.

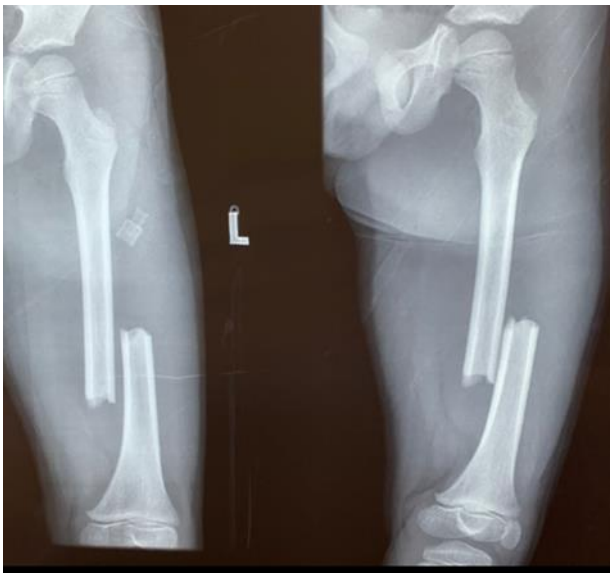

Figure 1: Pre-operative X-Ray images of left femur (Anteroposterior and Lateral View)

The patient was planned for the left femur Titanium Elastic Nailing System. Procedure was done under general anaesthesia. The patient was positioned supine on a radiolucent table. A rolled towel was placed under the distal thigh region with the leg hanging at the edge of the bed. Prophylactic antibiotic was served 30 mins before skin incision. A small skin incision was made over the medial and lateral aspects of the distal thigh. The entry point was made 2.5-3cm proximal to the distal femoral physis medially and laterally using an awl (**Figure 2**).

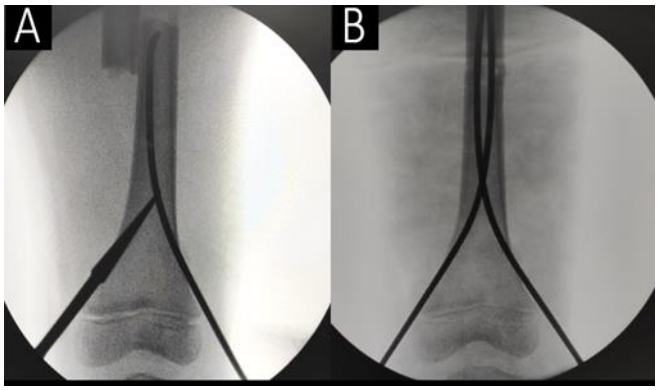

Figure 2: Intraoperative X-Ray images of left femur (Anteroposterior View). A: Pre-reduction image, B: Post reduction image

Two identical nail size 3.0 mm was used, and the nail was prebend 3 times the diameter of the bone at the fracture site. Retrograde nail insertion was done laterally and then medially. Fracture reduced using Kapandji method and subsequently both nails were pushed across the fracture site up to the metaphysis, one towards the lesser trochanter and another nail towards greater trochanter divergently (**Figure3**).

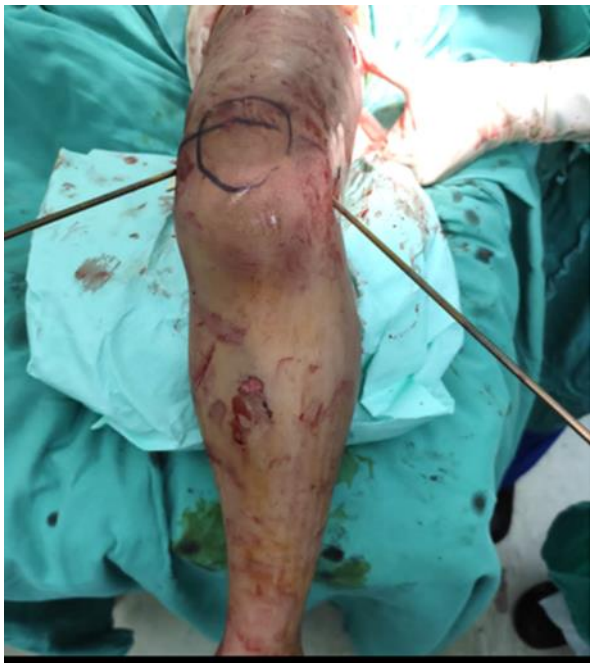

Figure 3: Intra-Operative images of right femur Titanium elastic nail entry point

Postoperatively, distal pulses were palpable, and there was no limb length discrepancy or rotation. Three doses of prophylactic intravenous antibiotics were completed in the ward. Post-operative check x-ray (**Figure 4**) was done, and alignment was acceptable.

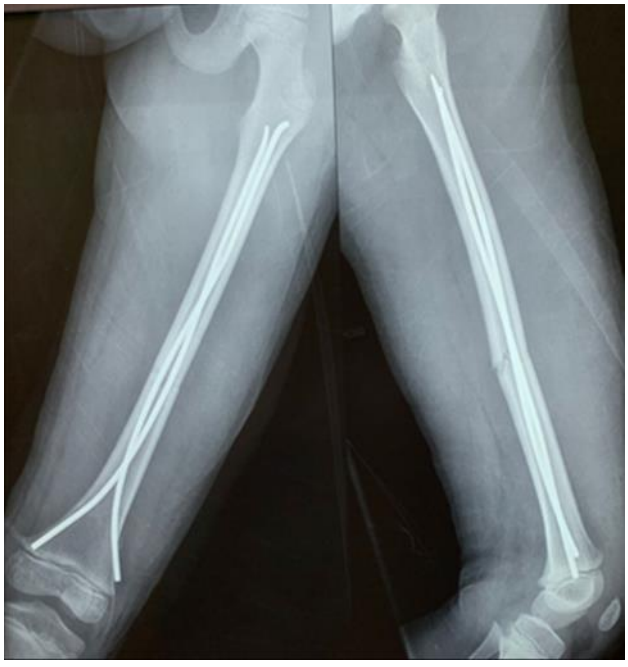

Figure 4: Immediate Post-Operative X-Ray Images of Left Femur (Anteroposterior and Lateral View)

No external immobilization was used, and the patient was started on gradual mobilization. On post-operative Day 2, the patient was well and discharged back home. On 3months follow-up in orthopaedic clinic x-ray (**Figure 5**) showed abundant callus formation. The patient was ambulating without aid (**Figure 6**).

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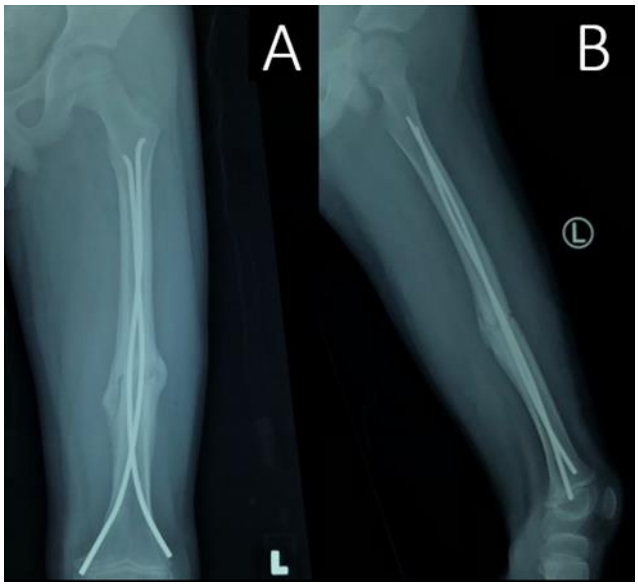

Figure 5: X-Ray left femur post-op 3 months. (A) Antero-posterior view, (B) Lateral view

Figure 6: Full Weight Bearing at Post-Operative 3 Months

DISCUSSION

It's been a constant challenge to the orthopaedic fraternity in choosing the ideal choice of implant or treatment in paediatric diaphyseal femoral fractures (1). Conservative treatment especially in older children noted to have complications such as malunion, joint stiffness and delay in functional recovery (1). Surgeons are looking into more efficient ways of treatment such as simple intramedullary nailing which maintains alignment of fracture and allows early mobilisation (2). TENS is an instrument that is uncomplicated, flexible and obtainable in all sizes (1,2).

It is a stable intramedullary nail or device which provides three-point fixation through the principle of symmetry bracing action of two nails with the same modulus of elasticity (1). This fixation provides rotational, axial, transitional and bending stability by offsetting the distraction and compression forces at the fracture site (1). It can be inserted in retrograde manner without harming the growth plate and this reduces the chance of avascular necrosis of the femoral head (1, 2).

Although there are complications such as limb length discrepancy, site irritation and mal-alignment in an insignificant number of cases, many studies are done which have proven to have remarkable results (1, 2). Transverse, short oblique and minimally comminuted diaphyseal femoral fractures are best to be fixed with TENS as it shows excellent result of outcome in older children (1). Studies revealed usage of TENS in obese children result in varus angulation after a proper pre bend of the nail, this can be avoided by additional plaster stabilization, traction or use of femoral brace (1).

Although, there are some chances for complications to occur, it is most likely due to technical errors made by surgeons such as choosing inappropriate nail diameter size which increases the incidence of varus or valgus angulation and mal-rotation (1, 3). Appropriate selection of nail insertion site and advancement of nail reduces the risk of skin ulceration due to nail protrusion and nail migration as well (1). This indicates that the experience of a surgeon and good surgical technique is the most crucial element in usage of TENS (3).

CONCLUSION

In conclusion, the Titanium Elastic Nailing System is fixed with minimally invasive techniques in children 6-16 years of age in diaphyseal femoral fractures (1). It reduces the risk of shortening and malunion moreover allows earlier rehabilitation and return to school life by speeding up the fracture healing. However, an experienced surgeon and good surgical technique is desired to minimize the complications that may occur.

Author Contributions: ST, ESA, KAHAG: Concept, Data collection and/or processing, Patient examination, and Surgery, Literature review**, ST:** Writing, Revision**.**

Acknowledgments: None

Conflict of interest: The authors declare no competing interests.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the institutional and/or national research committee's ethical standards and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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