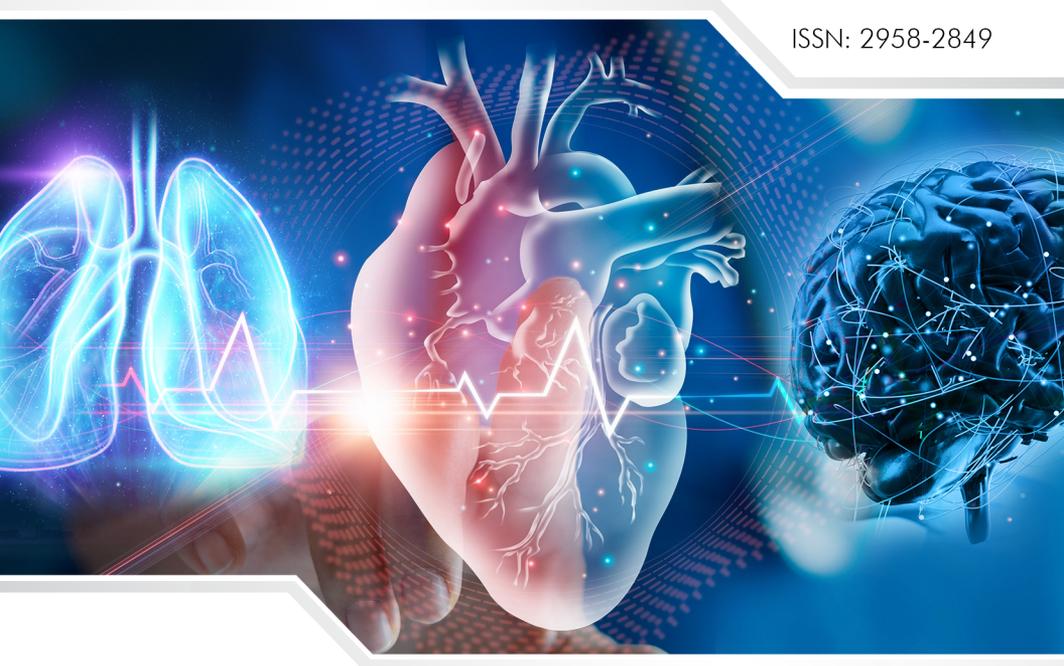


SOMALIA TURKIYE MEDICAL JOURNAL

(STMJ)

ISSN: 2958-2849



✉ info@stmedj.com

🌐 www.stmedj.com

SCALP Block Model in Sprague-Dawley Rats: In Vivo Experimental Study and Model Identification

Caghan Tonge

Department of Neurosurgery, Etlik City Hospital, University of Health Sciences, Ankara, Turkiye.

Corresponding Author Caghan Tonge **Email:** caghtonge@gmail.com

Received January 19th, 2023

Accepted February 20th, 2023

Abstract **Introduction:** The SCALP block is an important regional anesthesia method. In this study, we analyzed the SCALP block model for the first time in a rat model. **Materials and Methods:** In this study, 16 rats were divided into four different groups. Six nerve blocks were planned in both halves of the skull for the SCALP block, and three entry points were determined for each. Bupivacaine (Marcaine, AstraZeneca) 0.5 mg/kg was injected in the "low-dose" group, 1 mg/kg in the "medium-dose" group, 2 mg/kg in the "high-dose" group, and 4 mg/kg in the "very high-dose" group. A midline fronto-occipital incision was made, and a craniectomy was performed. At 0, 30, 60, 90, and 120 minutes after the surgical procedure, the rats were evaluated using the Rat Grimace Scale, and their pain scores were evaluated. At the end of 2 hours, the rats were sacrificed, blood samples were taken, and methemoglobin levels were studied. Finally, a comparative analysis was performed between the four groups. **Results:** In 30, 60, 90, and 120 minutes after surgery, the differences between the grimace scores between low-dose and medium-dose and high-dose and low-dose groups were statistically significant ($p < 0.001$). There was no significant difference between the high-dose and very high-dose groups regarding the grimace scale ($p > 0.05$). Methemoglobin levels were statistically significantly higher after SCALP block with a very high dose of bupivacaine than blockade with a high dose of bupivacaine ($p < 0.001$). Therefore, very high-dose bupivacaine injection was not superior to high-dose bupivacaine injection in pain control. In addition, very high doses of bupivacaine injection can be associated with increased morbidity and mortality due to increased methemoglobin levels. **Conclusion:** In this SCALP block technique described in rats, a 2 mg/kg bupivacaine injection can be considered an appropriate dosage for both safety and efficacy.

Keywords SCALP block; Sprague-Dawley rats; Regional anesthesia; Model

Introduction

Regional anesthesia is a safe anesthetic method that can bypass the systemic side effects and complications of general anesthetic agents (1). Following the emergence of regional anesthesia techniques, significant improvements have been experienced in durations, postoperative outcomes, and remission processes of several surgeries. Many studies are showing that SCALP block, which is a type of regional anesthesia, is an alternative option in patients with heart failure, lung diseases, and metabolic syndrome where the administration of systemic anesthetic agents is at high risk, as well as reducing the need for opioids in the postoperative period in patients (1,2). Patel et al. published a case series showing that SCALP block significantly reduced postoperative opioid use (1). Another case-control study by Festa et al. demonstrated the efficacy of SCALP block in postoperative pain control in patients with craniosynostosis (2).

Procedures requiring craniotomy constitute an essential part of neurosurgery practice (3-5). One of the significant steps of the rehabilitation process after craniotomy is pain control. Postoperative pain may cause hypertension and tissue edema through sympathetic discharge. This condition adversely affects wound healing through tissue edema and increases the risk of intracranial hemorrhage in the surgical site in the postoperative period (3-5). In this respect, proper pain control is essential in ensuring postoperative patient comfort and improving surgical outcomes.

Animal research has become one of the critical components of scientific progress recently. Experimental animal models in vivo studies help investigate problems that may be encountered in the clinic. In many models, such as the experimental traumatic subarachnoid hemorrhage model and experimental spinal cord ischemia-reperfusion model, rats, rabbits, and mice are used as subjects (6, 7). However, the literature has previously described no method for SCALP block in rats. This study aimed to prepare a protocol to create a model of SCALP block in rats.

Materials and Methods

This experiment was carried out in Ankara NeSa Animal Research Laboratory. The Ankara NeSa Animal Research Laboratory Ethics Committee reviewed the research protocol, and the ethics committee approval was obtained (10.01.2023/003). In addition, all animals received care as per "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Institute of Health.

Rats were divided into four equal groups: Low-dose, medium-dose, high-dose, and very high-dose, with four rats in each group.

Animal Care

The animals were kept at room temperature between 18-21 degrees Celcius. The rats were injected intramuscularly with xylazine 5 mg/kg (Rompun, Bayer) as a muscle relaxant and allowed to breathe spontaneously.

The SCALP Block Technique

The supraorbital, supratrochlear, posterior auricular, temporal, zygomatic, major, and minor occipital nerves are targeted in this technique. For targeting, three separate injection points were determined for both halves of the skull. For the first injection point, the end of the orbital rim was determined at 3 mm posterior to the mid-pupillary line. Next, the supraorbital and supratrochlear nerve blockade was targeted by entering a 30G insulin injector at a 45-degree angle (Figure 1). The second injection point was determined as the junction of the posterior zygomatic arch 2 mm anterior and inferior to the ear tragus. Next, the posterior auricular, temporal, and zygomatic nerves were blocked by an oblique entry with a 30G insulin injector (Figure 1). The third injection point was determined as the junction of the occipital protuberance, 4 mm lateral to the mid-sagittal line posteriorly. Finally, the minor and major

occipital nerve blocks were targeted by entering with a 30G insulin injector at a 45-degree angle (Figure 1). No sedation was performed during the procedure.

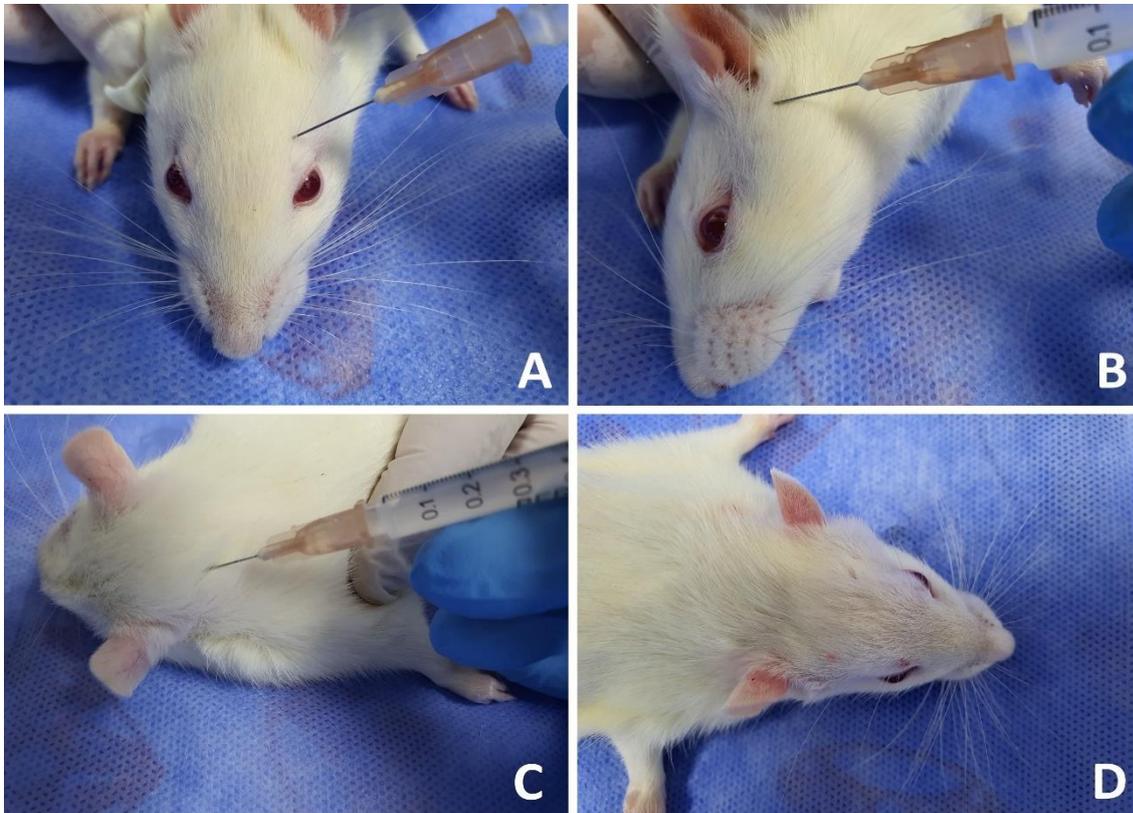


Figure 1. Injection points for SCALP block model. A: The first entry point. The end of the orbital rim was determined at 3 mm posterior to the mid-pupillary line and targeted by entering a 30G insulin injector at a 45-degree angle. B: The second entry point. The junction of the posterior zygomatic arch 2 mm anterior and inferior to the ear tragus was entered obliquely with a 30G insulin injector. C: The third entry point. The junction of the occipital protuberance, 4 mm lateral to the midsagittal line posteriorly, was targeted by entering with a 30G insulin injector at a 45-degree angle. D: Prone position after SCALP block.

Surgical Technique

A 6-point SCALP block protocol was performed on each animal in four groups. For the block, 0.5 mg/kg bupivacaine (Marcaine, AstraZeneca) was administered in the low-dose group, 1 mg/kg in the medium-dose group, 2 mg/kg in the high-dose group, and 4 mg/kg in the very high-dose group.

After bilateral SCALP block with a 6-point injection protocol and intramuscular injection of xylazine, animals were placed in the prone position (Figure 1). After the scalp was shaved, the skin was dissected by a linear incision in the fronto-occipital plane (Figure 2). After the periosteum was scraped, fronto-occipital craniectomy was performed (Figure 2). Subsequently, the subcutaneous layer and skin were sutured and closed (Figure 2). After closure, the rats were placed in cages and recorded with a camera. Pain scores of the rats were performed using the Rat Grimace Scale (RGS) at 0, 30, 60, 90, and 120 minutes postoperatively (6). At the end of the second hour, the rats were sacrificed by intracardiac puncture and aspiration, and blood samples were collected.

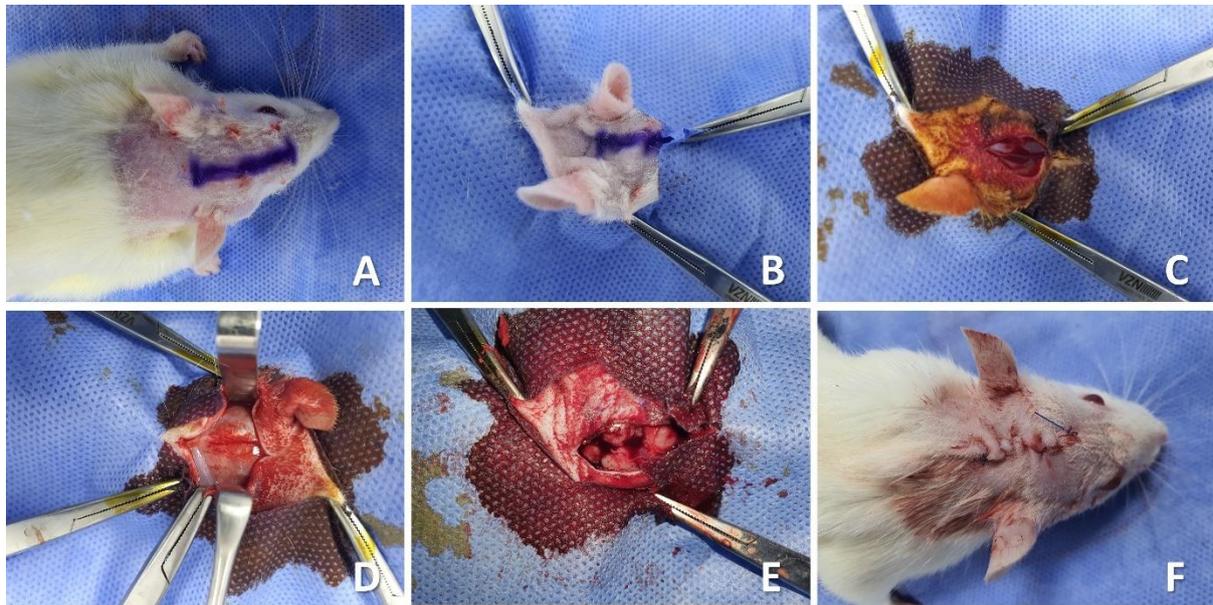


Figure 2. Surgical procedures. A: Shaving the scalp B: Preparing surgical area by draping C: Linear incision in the fronto-occipital plane D: Removal of the periosteum E: Craniectomy procedure F: Primary closure of the skin

Biochemical Evaluation

Blood gas and methemoglobin levels were studied to evaluate bupivacaine's toxicity.

Statistical Analysis

Data collected in groups were analyzed using IBM SPSS Statistics Version 25. The one-way ANOVA test was used to determine parametric differences between groups. In addition,

descriptive analysis for one numeric variable was used to create plots. Data were presented as means and standard deviations. The confidence interval (CI) was computed as 95%, and the difference was considered significant when the p-value was lower than 0,05.

Results

Sixteen Sprague-Dawley weighing 250-350 grams male rats were used. Each group included four rats. In the very high-dose group, 2 of the rats died 30 minutes after completion of the surgical procedure, and their blood samples were taken immediately after death.

The comparative analysis found a statistically significant difference between the low-dose group and the other three groups in terms of the 0-minute, 30-minute, 60-minute, 90-minute, and 120-minute RGS scores ($p < 0.001$). A statistically significant difference was found in the comparison of the medium-dose group with the high-dose and very high-dose groups ($p < 0.001$). When blood methemoglobin levels were compared, a statistically significant difference was observed between low-dose, medium-dose, high-dose, and very high-dose groups ($p < 0.001$) (Figure 3). Since deaths were detected in the very high-dose group, 4 mg/kg was considered a lethal dose in the SCALP block.

In 30, 60, 90, and 120 minutes after surgery, RGS scores were significantly between the low-dose and medium-dose, medium-dose and high-dose, and low-dose and high-dose groups ($p < 0.001$) (Figure 3). However, there was no significant difference between the high-dose and very high-dose groups in terms of RGS scores ($p > 0.05$) (Figure 3). From this point of view, it can be suggested that the performance of SCALP block with very high-dose bupivacaine does not contribute to the improvement in the pain scale compared with blockade using high-dose bupivacaine. In addition, methemoglobin levels were significantly higher after SCALP block with very high-dose bupivacaine compared to blockade with high-dose bupivacaine ($p = 0.002$) (Figure 4).

Thus, it can be suggested that very high doses of bupivacaine used for SCALP block may increase the risk of morbidity and mortality due to increased methemoglobin levels.

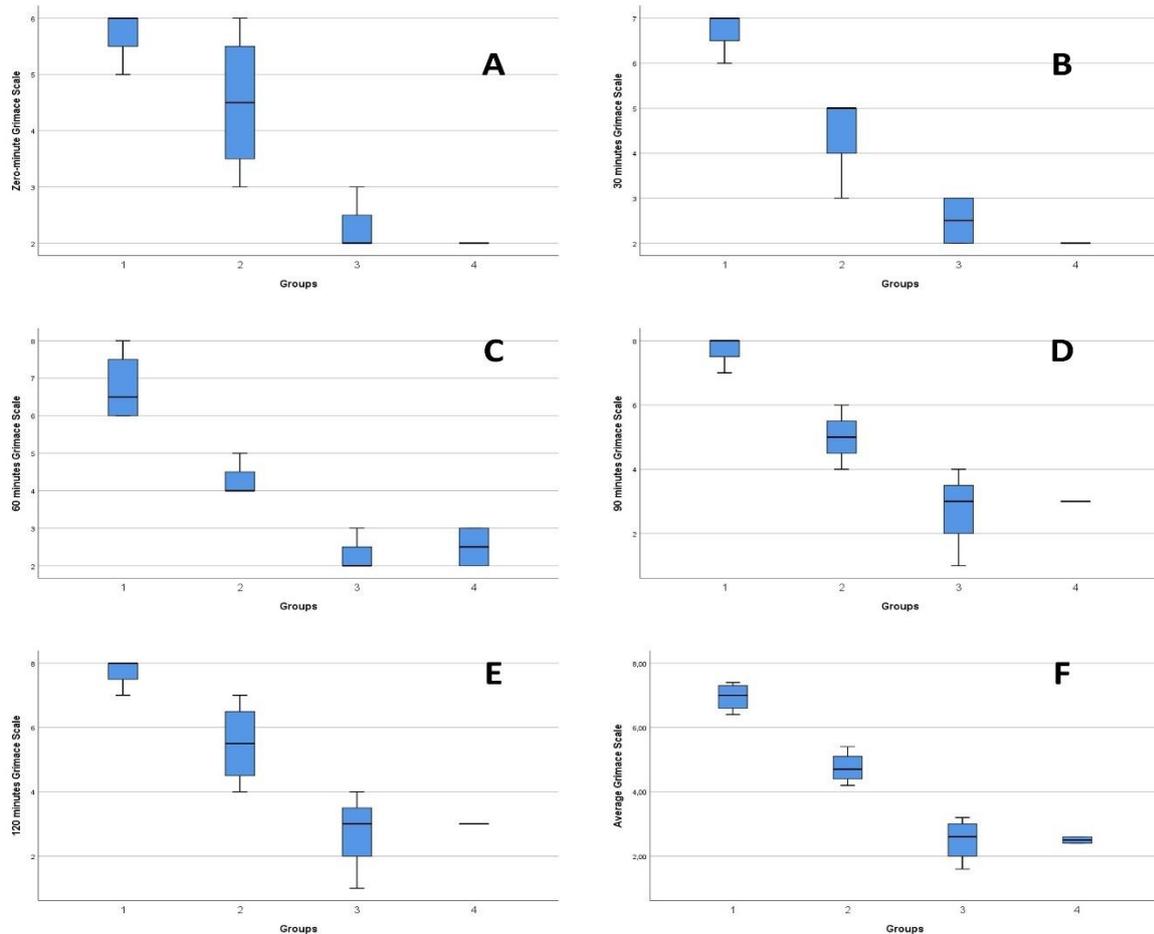


Figure 3. Rat grimace scales (RGS) in groups A: 0-minute RGS scores B: 30-minute RGS scores C: 60-minute RGS scores D: 90-minute RGS scores E: 120-minute RGS scores F: Mean RGS scores in groups

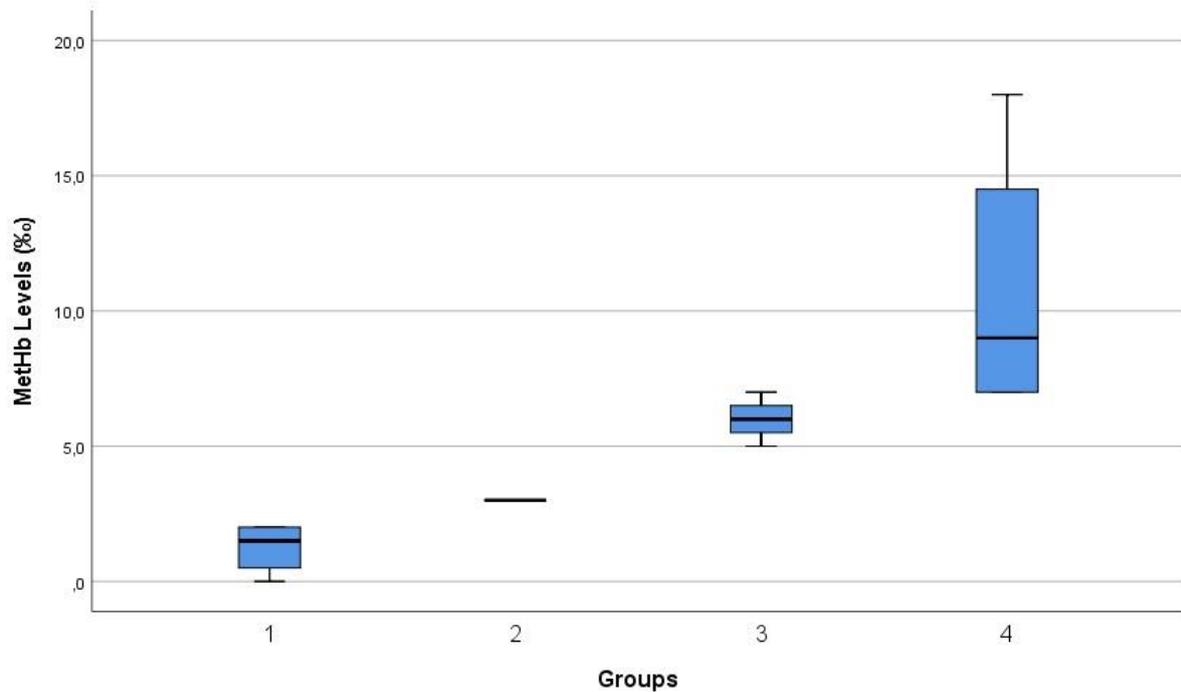


Figure 4. Methemoglobin levels in groups.

Discussion

Numerous studies have been conducted on modeling in animal research in recent decades. Drug research, biochemical markers, and imaging techniques could represent samples through these models (7, 8). These improvements offer the opportunity to research many fields. On top of that, these standardizations were carried to the top with monoclonal experimental animals (9, 10). This study was planned to define the SCALP block model in Sprague-Dawley rats, species that can mimic human physiology significantly.

There are similar studies in the literature which used sedation and muscle relaxants (11-15). On the other hand, some studies used local anesthesia in line with ours (16-19).

Local anesthetic injections to 6 different points in each half of the skull and SCALP block are widely used for many procedures (20). Various studies have been conducted on SCALP block's postoperative pain control and neuroprotective and anti-inflammatory effects (21,22). Chen et al. evaluated the effects of SCALP block on postoperative pain control and the effects of

SCALP block in a meta-analysis including 12 studies (21). These studies showed that SCALP block maintained intraoperative hemodynamic stability (22).

The rat grimace scale is developed to assess pain severity in rats (6,23). Apart from this, different tests such as swallowing analysis, cage monitoring, and nesting have also been defined in rodents (24). In our study, we used the RGS to evaluate the rats in 30-minute periods and assess the pain scale through components such as orbital tightening, nose/cheek flattening, and ear and whisker changes. There are also studies on the use of RGS in anesthesia (25). In their study, Miller et al. used this scale to evaluate general anesthetic agents' effects (25). The SCALP block model described in our study also has the potential to allow the evaluation of local and systemic effects of anesthetic agents in future studies that can be performed by applying the model.

Local anesthetics can act as indirect oxidizers in iron metabolism (26). Therefore, they cause the development of methemoglobin by oxidizing the iron in hemoglobin. Although they are used in local applications, their systemic absorption and side-effect profiles are well-defined (27-30). One of the significant complications of SCALP block is methemoglobinemia. Methemoglobinemia should be considered in clinical situations with low oxygen saturation despite adequate ventilation after local anesthetic admission (26). A blood gas study is sufficient for diagnosing methemoglobinemia; most of the current blood gas devices can analyze the methemoglobin levels. Hence, we analyzed blood gas after the SCALP block to evaluate the presence of methemoglobinemia.

This study had some limitations. First, although the RGS evaluation is a standardized scoring system, the subjectivity of the assessor may affect results. Also, two rats in the very high-dose group died within 30 minutes after the completion of the procedure. Finally, the study did not include long-term results and provided minimal information on whether the SCALP block contributed to late-term postoperative pain control.

Conclusion

The model of SCALP block in rats was defined for the first time in this study, and this article is a pioneer for future studies. However, further work is needed to develop and refine this model.

Conflicts of interest

The authors declare no conflict of interest.

Funding

This study is unfunded.

Ethical approval

The Ankara NeSa Animal Research Laboratory Ethics Committee reviewed the research protocol, and the ethics committee approval was obtained (10.01.2023/003).

References

1. Patel KS, Sun MZ, Willis SL, et al. Selective scalp block decreases short-term postoperative pain scores and opioid use after craniotomy: A case series. *J Clin Neurosci* 2021;93:183-187.
2. Festa R, Tosi F, Pusateri A, et al. The scalp block for postoperative pain control in craniosynostosis surgery: a case-control study. *Childs Nerv Syst* 2020;36:3063-3070.
3. Mordhorst C, Latz B, Kerz T, et al. Prospective assessment of postoperative pain after craniotomy. *J Neurosurg Anesthesiol* 2010;22:202-206.
4. Goobie SM, Haas T. Bleeding management for pediatric craniotomies and craniofacial surgery. *Paediatr Anaesth* 2014;24:678-689.
5. Nesvick CL, Oushy S, Daniels DJ, Ahn ES. Safety of immediate use of nonsteroidal antiinflammatory drugs after pediatric craniotomy for tumor. *J Neurosurg Pediatr* 2020;26:327-333.
6. Sotocinal SG, Sorge RE, Zaloum A, et al. The Rat Grimace Scale: a partially automated method for quantifying pain in the laboratory rat via facial expressions. *Mol Pain* 2011;7:55.

7. Pearlstein RA, Wan H, Aravamuthan V. Toward in vivo relevant drug design. *Drug Discov Today* 2021;26:637-650.
8. Gonzalez-Gualda E, Baker AG, Fruk L, Munoz-Espin D. A guide to assessing cellular senescence in vitro and in vivo. *FEBS J* 2021;288:56-80.
9. Sulzer D, Edwards RH. The physiological role of alpha-synuclein and its relationship to Parkinson's Disease. *J Neurochem* 2019;150:475-486.
10. Heysieattalab S, Lee KH, Liu Y, et al. Impaired cerebellar plasticity and eye-blink conditioning in calpain-1 knock-out mice. *Neurobiol Learn Mem* 2020;170:106995.
11. Chauvette S, Soltani S, Seigneur J, Timofeev I. In vivo models of cortical acquired epilepsy. *J Neurosci Methods* 2016;260:185-201.
12. Mitsunaga Junior JK, Gragnani A, Ramos ML, Ferreira LM. Rat an experimental model for burns: a systematic review. *Acta Cir Bras* 2012;27:417-423.
13. Bosch L, de Haan JJ, Bastemeijer M, et al. The transverse aortic constriction heart failure animal model: a systematic review and meta-analysis. *Heart Fail Rev* 2021;26:1515-1524.
14. Stokes EL, Flecknell PA, Richardson CA. Reported analgesic and anaesthetic administration to rodents undergoing experimental surgical procedures. *Lab Anim* 2009;43:149-154.
15. Richardson CA, Flecknell PA. Anaesthesia and postoperative analgesia following experimental surgery in laboratory rodents: are we making progress? *Altern Lab Anim* 2005;33:119-127.
16. Kondamudi PK, Tirumalasetty PP, Malayandi R, Mutalik S, Pillai R. Lidocaine Transdermal Patch: Pharmacokinetic Modeling and In Vitro-In Vivo Correlation (IVIVC). *AAPS PharmSciTech* 2016;17:588-596.
17. Jiang J, Wu H, Zou Z. In vitro and in vivo evaluation of a novel lidocaine-loaded cubosomal gel for prolonged local anesthesia. *J Biomater Appl* 2022;37:315-323.
18. Zhang H, Zhao Z, Chen W, Lv M, Cheng J, Sun Z. In vitro and in vivo studies of micro-depots using tailored microemulsion for sustained local anaesthesia. *Pharm Dev Technol* 2020;25:874-881.
19. van der Wal SE, van den Heuvel SA, Radema SA, et al. The in vitro mechanisms and in vivo efficacy of intravenous lidocaine on the neuroinflammatory response in acute and chronic pain. *Eur J Pain* 2016;20:655-674.

20. Osborn I, Sebeo J. "Scalp block" during craniotomy: a classic technique revisited. *J Neurosurg Anesthesiol* 2010;22:187-194.
21. Chen Y, Ni J, Li X, Zhou J, Chen G. Scalp block for postoperative pain after craniotomy: A meta-analysis of randomized control trials. *Front Surg* 2022;9:1018511.
22. Luo M, Zhao X, Tu M, et al. The effectiveness of scalp nerve block on hemodynamic response in craniotomy: a systematic review and meta-analysis of randomized trials. *Minerva Anesthesiol* 2022.
23. Mota-Rojas D, Olmos-Hernandez A, Verduzco-Mendoza A, et al. The Utility of Grimace Scales for Practical Pain Assessment in Laboratory Animals. *Animals (Basel)* 2020;10.
24. Tappe-Theodor A, King T, Morgan MM. Pros and Cons of Clinically Relevant Methods to Assess Pain in Rodents. *Neurosci Biobehav Rev* 2019;100:335-343.
25. Miller AL, Golledge HD, Leach MC. The Influence of Isoflurane Anaesthesia on the Rat Grimace Scale. *PLoS One* 2016;11:e0166652.
26. Golembiewski J. Local anesthetics. *J Perianesth Nurs* 2013;28:409-412.
27. Barletta M, Reed R. Local Anesthetics: Pharmacology and Special Preparations. *Vet Clin North Am Small Anim Pract* 2019;49:1109-1125.
28. Cherobin A, Tavares GT. Safety of local anesthetics. *An Bras Dermatol* 2020;95:82-90.
29. On'Gele MO, Weintraub S, Qi V, et al. Local Anesthetics, Local Anesthetic Systemic Toxicity (LAST), and Liposomal Bupivacaine. *Clin Sports Med* 2022;41:303-315.
30. Dickerson DM, Apfelbaum JL. Local anesthetic systemic toxicity. *Aesthet Surg J* 2014;34:1111-1119.

Dynamic Plasma Thiol/Disulfide Balance In Experimental Pancreatitis Model In Rats

Seyit Murat Aydin¹, Omer Parlak²

¹Ankara Training and Research Hospital General Surgery, Ankara

²Yıldırım Beyazıt University General Surgery, Ankara

Corresponding Author Seyit Murat Aydin **Email:** drseyitmurat@gmail.com

Received January 4th, 2023

Accepted April 1st, 2023

Abstract **Introduction:** Dynamic thiol-disulfide balance has critical roles in regulating antioxidant protection and detoxification. Thiol/disulfite levels, which can be easily measured in blood, were investigated in various proliferative and inflammatory diseases. It was observed that the changes in this balance were correlated with oxidant parameters. In previous studies, it has been shown that oxidative stress increases significantly in acute pancreatitis, and it has been shown that these levels are related to the severity of the disease. Owing to acute pancreatitis is a severe inflammatory condition; the thiol/disulfide balance may correlate with the severity of this disease. Our study investigated thiol/disulfide levels in the experimental pancreatitis model.

Materials and Methods: In our study, 16 Wistar-Albino male rats were used and divided into two groups as experimental and control groups, each group being eight rats. In the experimental group, we generated acute pancreatitis with Cerulein. Amylase, lipase, and thiol/disulfide balance were determined from inferior vena cava blood sampling with median laparotomy. **Results:** Amylase and lipase levels were found to be significantly different in the experimental group compared with the control group, but there was no significant difference in the plasma thiol/disulfide balance. **Conclusion:** The study results showed that the plasma thiol/disulfide level did not reveal the severity of acute pancreatitis. In previous studies, thiol/disulfide levels increased in oxidative stress, but this did not happen in our study. The fact that our study was conducted with a small group may have caused this situation. There is a need for more comprehensive studies to investigate in more detail the plasma thiol/disulfide balance.

Keywords Thiol/disulfide; Acute pancreatitis; Rats.

Introduction

Acute pancreatitis is inflammation of the pancreas. It is a common and non-bacterial disease characterized by the development of widespread inflammation as a result of autodigestion of the pancreas and surrounding tissue by digestive enzymes normally inactive in the pancreas, activated due to an etiological factor (1). Although it is most commonly due to gallstones, it

can also develop due to alcohol, various drugs, and excess blood lipids. Acute pancreatitis is a condition that can range from mild to mortal (2). In previous studies, it has been shown that oxidative stress increases significantly in acute pancreatitis, and it has been shown that these levels are related to the severity of the disease. However, all the methods used are complicated and lengthy methods in clinical practice. With a new method developed by Erel et al., thiol/disulfite levels, which can be easily measured in blood, were investigated in various proliferative and inflammatory diseases, and it was observed that the changes in this balance were correlated with oxidant parameters (3). A sulfhydryl group is formed when a hydrogen atom and a sulfur atom come together. Thiols are a class of organic compounds that have such sulfhydryl groups attached to a carbon atom, also known as mercaptans. When oxidation occurs, a covalent disulfide bond, called the SS bond, is formed with thiols. Oxidation of cysteine residues under oxidative stress results in mixed reversible disulfides between thiol proteins. These disulfide bonds can be reduced to thiol groups for a dynamic hemostasis. This thiol/disulfide balance plays essential roles in antioxidant protection, detoxification, enzymatic activity, regulation of transcription factors, apoptosis and cellular signaling pathways (4, 5). Owing to acute pancreatitis is a severe inflammatory condition, the thiol/disulfide balance may correlate with the severity of this disease. Our study aimed to observe thiol/disulfide balance in acute pancreatitis after induction with cerulein in rats.

Materials and Methods

Ankara Training and Research Hospital Animal Experiments Local Ethics Committee approval was obtained for this experimental study (Date: 04.06.2015, Number: 374). The study was carried out in Ankara Training and Research Hospital Experimental Animals Laboratory. 16 Wistar-Albino male rats weighing between 300-350 grams were used in the study. A total of 16 rats were divided into two groups as, experimental and control groups, each group being eight rats. Rats were held in 12-hour light and 12-hour dark cycles under suitable conditions, with four animals per cage. The rats were fed with standard feed, and their water needs were supplied with tap water. 50mcg/kg Cerulein (Sigma & Aldrich Chemie, GmbH, C-9026) was injected intraperitoneally into the rats in the experimental group. The rats in the control group were injected with 1cc normal saline intraperitoneally. After the procedure, rats were administered general anesthesia with 50 mg/kg ketamine(Ketalar vial, Parke-Davis, Eczacıbaşı Pharmaceuticals Marketing Co.. İstanbul-Turkey) and 10 mg/kg xylazine hydrochloride (Rompun vial, Bayer, Leverkusen, Germany) intramuscularly at the 30th hour. During the study, the rats were allowed to breathe

spontaneously. After the depth of anesthesia was controlled, the rats were placed under a heating lamp and placed on a heating pad in order to keep their body temperature at approximately 37 °C. A median laparotomy was performed and blood sampling was performed from the inferior vena cava. The blood samples were centrifuged at 2500 rpm for 15 minutes, and the serum samples taken were analyzed by the Roche-Hitachi-Cobas C501 autoanalyzer for amylase, lipase, AST, ALT, total bilirubin, direct bilirubin and thiol/disulfide levels (Table 1).

Statistical Analysis

There was no death in the experimental and control group animals throughout the study. The conformity of the laboratory variables in our study to the normal distribution was evaluated with the Shapiro-Wilks test. Interquartile range of the variables determined not to be normally distributed was used. The mean standard deviation values of the normally distributed variables were given. Mann-Whitney U test was used to determine whether there was a significant difference between the group variable (experimental-control) and ALP, AST and lipase variables in the study. Independent Sample T test was used to determine whether there was a significant difference between Amylase, AST, Direct bilirubin, Total bilirubin, Total thiol, Native thiol, and Disulfide variables. Boxplots and error bar graphs of the relevant variables were prepared. IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0 Armonk, NY: IBM Corp.) was used for statistical analysis and calculations. Statistical significance level was accepted as $p < 0.05$.

Results

In general, the average amylase value of the rats was 1874 ± 308.05 , while the minimum amylase value was 1407 and the maximum amylase value was 2428. In our study, the amylase average of the animals in the control group was found to be 1725 ± 265.37 , and the amylase average of the animals in the experimental group was 2023 ± 286.59 . The amylase average of the animals in the experimental group was higher than those in the control group. The amylase variable in the experimental and control groups showed a statistically significant difference ($p = 0.049$) (Table 2, Figure 1). While the lipase median of the rats in the experimental group was 5.50 (IQR=1), the lipase median of the rats in the control group was 4.00 (IQR=1). The lipase median of the rats in the experimental group was higher than the rats in the control group. The lipase variable showed a statistically significant difference between the experimental and control groups ($p = 0.005$) (Table 3, Figure 2).

Table 1. General descriptive statistics of variables

Parameters	Median (IQR)	Min; Max
	Mean \pm SD	
ALP	106.00 (52)	61; 382
ALT	54.50 (13)	35; 156
LIPASE	5.00 (2)	4; 7
AMYLASE	1874.19 \pm 308.05	1407; 2428
AST	118.06 \pm 19.28	92; 159
DBIL	0.06 \pm 0.02	0.01; 0.12
TBIL	0.02 \pm 0.01	0.01; 0.05
TOTAL THIOL	215.12 \pm 26.45	163.0; 269.8
NATİV THIOL	162.98 \pm 19.78	126; 206
DISULFIDE	26.07 \pm 5.79	17.75; 34.65
SS/SH	16.06 \pm 3.37	10.35; 22.35
SS/TSH	12.06 \pm 1.95	8.57; 15.44
SH/TSH	75.87 \pm 3.91	69.10; 82.84

SS/SH: Native thiol disulfite ratio, SS/TSH: Total thiol disulfite ratio, SH/TSH Native thiol Total thiol ratio

Table 2. Comparison of Amylase, AST, D.BIL, T.BIL, T.THIOI, N.THIOI, DISULFIDE, SS/SH and SS/TSH variables on a group basis

Parameters	Control group	Experimental group	t	p
	Mean \pm SD	Mean \pm SD		
AMYLASE	1725.12 \pm 265.37	2023.25 \pm 286.59	2.159	0.049
AST	125.25 \pm 20.99	110.88 \pm 15.42	1.561	0.141
DBIL	0.06 \pm 0.05	0.06 \pm 0.01	0.262	0.798
TBIL	0.02 \pm 0.01	0.02 \pm 0.01	0.000	1.000
TOTAL THIOL	213.76 \pm 32.56	216.48 \pm 20.85	0.199	0.845
NATİV THIOL	162.80 \pm 25.17	163.15 \pm 14.32	0.034	0.973
DISULFIDE	25.48 \pm 6.40	26.66 \pm 5.48	0.398	0.696
SS/SH	15.76 \pm 3.59	16.36 \pm 3.36	0.347	0.734
SS/TSH	11.88 \pm 2.15	12.24 \pm 1.87	0.363	0.722

SS/SH: Native thiol disulfite ratio, SS/TSH: Total thiol disulfite ratio, SH/TSH Native thiol Total thiol ratio

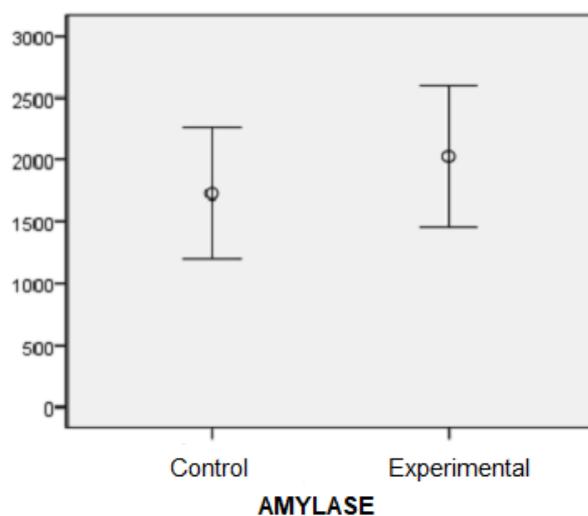


Figure 1. Comparison of amylase variable on a group basis

Table 3. Comparison of ALP, ALT, and LIPASE variables on a group basis

Parameters	Control group Median (IQR)	Experimental group Median (IQR)	Z	p
ALP	115.50 (52)	83.00 (48)	1.420	0.156
ALT	58.50 (23)	49.50 (10)	1.210	0.234
LIPASE	4.00 (1)	5.50 (1)	2.907	0.005

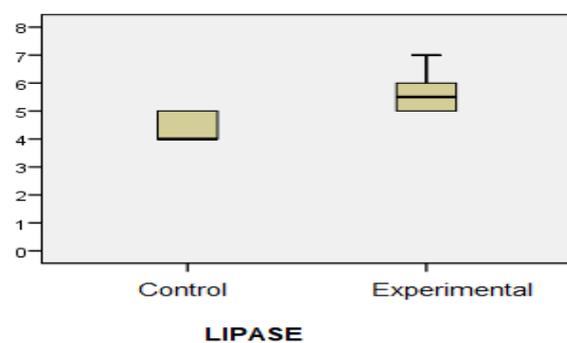


Figure 2. Comparison of lipase variable on a group basis

The disulfide of the animals in the experimental group in the study was 26.66 ± 5.48 , the disulfide of the animals in the control group was 25.48 ± 6.40 . The disulfide mean of the animals in the experimental group was higher than that of the control group, but no

statistically significant difference was found ($p=0.696$). While the total thiol average of the animals in the experimental group was 216.48 ± 20.85 , the total thiol average of the animals in the control group was 213.76 ± 32.56 . Total thiol mean of the experimental group is higher than that of the control group, but no statistically significant difference was found ($p=0.845$). The mean of native thiol of the animals in the experimental group was 163.15 ± 14.32 , and the mean of native thiol of the animals in the control group was 162.80 ± 25.17 . The native thiol average of the experimental group animals is higher than the control group animals, but no statistically significant difference was found ($p=0.973$). The average native thiol/disulfide ratio of the experimental group animals was 16.36 ± 3.36 , and the average of the native thiol/disulfide ratio of the control group animals was 15.76 ± 3.59 . The native thiol/disulfide ratio of the experimental group was higher than the control group, but no statistically significant difference was found ($p=0.734$). The mean total thiol/disulfide ratio of the animals in the experimental group was 12.24 ± 1.87 , the average of the total thiol/disulfide ratio of the animals in the control group was 11.88 ± 2.15 . The mean total thiol/disulfide ratio of the experimental group was higher than the average of the total thiol/disulfide ratio of the control group, but no statistically significant difference was found ($p=0.722$) (Table 2).

Discussion

Experimentally, pancreatitis was first developed by Claude Bernard in 1856 by administering olive oil to the canine pancreatic duct (6). After this study, many researchers about acute pancreatitis understand the pathophysiology and biology of the disease; conducted studies for new diagnosis and treatment options. Acute pancreatitis continues to be an important problem in surgical practice. It is believed that acinar cell damage occurs as a result of activation of zymogens in acinar cells at the beginning of acute pancreatitis (7). The main cause of acinar cell damage is reactive oxygen products formed as a result of inflammation. After acinar cell damage, endothelial damage, microvascular circulation disorder in the tissue, increased capillary permeability and edema occurs (8). The increase in reactive oxygen products results in an increase in oxidative stress. Under normal conditions, reactive oxygen products are neutralized by antioxidant mechanisms, but excessive and uncontrolled reactive oxygen products cause cell damage and dysfunction (9). The balance between generation and elimination of reactive oxygen products is achieved by redox sensitive signals that provide thiol and disulfide in proteins in cells under suitable conditions. In tandem with thiol oxidation due to inflammation causes an increase in reactive oxygen products and thus the progression of oxidative stress (10). Dynamic thiol-disulfide balance has critical roles in the

regulation of antioxidant protection, detoxification, signal transduction, apoptosis, enzyme activity, transcription factors, and cellular signaling mechanisms. In addition, researchers are continuing to diagnose many diseases day by day by looking at the dynamic thiol-disulfide balance. There is also evidence showing that abnormal thiol/disulfide homeostasis plays a role in the pathogenesis of various diseases including diabetes, cardiovascular diseases, cancer, rheumatoid arthritis, chronic kidney disease, acquired immunodeficiency syndrome (AIDS), Parkinson's disease, Alzheimer's disease, Friedreich ataxia (FRDA), multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS). Therefore, the determination of dynamic thiol-disulfide balance can provide valuable information about various normal or abnormal biochemical processes (3). Disruption of oxidative and antioxidative balance plays an important role in the development of acute pancreatitis (11). The resulting oxidative stress is critical in the disease's severity and the development of complications that may arise (12).

Conclusion

Our study investigated the newly developed plasma thiol/disulfide balance, which shows oxidative stress in an experimental pancreatitis model. When the experimental group in which pancreatitis was induced by giving Cerulein and the control group were compared, no statistically significant difference was found between the two groups in terms of plasma thiol/disulfide balance. The fact that our study was conducted with a small group may have caused this situation. This topic should be investigated in acute pancreatitis cases with more comprehensive studies to be done.

Conflicts of interest

Authors declare no conflict of interest

Funding

This study is unfunded.

Ethical approval

Ankara Training and Research Hospital Animal Experiments Local Ethics Committee approval was obtained for this experimental study (Date: 04.06.2015, Number: 374).

References

1. Robins SL, Kumar V. Robbins Basic Pathology 7th ed. 2003.
2. Bradley EL. A clinically based classification system for acute pancreatitis: summary of the International Symposium on Acute Pancreatitis. *Arch Surg* 1993;128:586-590.
3. Erel O, Neselioglu S. A novel and automated assay for thiol/disulphide homeostasis. *Clin Biochem* 2014;47:326-332.
4. Koseoglu H, Alisik M, Basaran M, et al. Dynamic thiol/disulphide homeostasis in acute pancreatitis. *Turk J Gastroenterol* 2018;29:348.
5. Sen CK, Packer L. Thiol homeostasis and supplements in physical exercise. *Am J Clin Nutr* 2000;72:653S-669S.
6. Guyton AC. Textbook of Medical Physiology. 11th ed. 2006.
7. Saluja AK, Steer ML. Acute Pancreatitis-New Approaches for the Management of Acute Pancreatitis-Pathophysiology of Pancreatitis. Role of Cytokines and Other Mediators of Inflammation. *Digestion* 1999;60:27-33.
8. Mentis A. Üst gastrointestinal sistem hastalıkları 6. uzmanlık sonrası eğitim kursu kitapçığı. 2001;35-40.
9. Baser H, Can U, Karasoy D, Ay AS, Baser S, Yerlikaya FH, Ecirli S. Evaluation of oxidant/anti-oxidants status in patients with mild acute-pancreatitis. *Acta Gastroenterolog Belg* 2016;79:23.
10. Moreno ML, Escobar J, Finamor I, Martínez-Ruiz A, Sastre J. Disulfide stress and its targets in acute pancreatitis. *Inflam Allergy Drug Targets* 2014;13:312-322.
11. Dziurkowska-Marek A, Marek TA, Nowak A, Kacperk-Hartleb T, Sierka E, Nowakowska-Dulawa E. The dynamics of the oxidant-antioxidant balance in the early phase of human acute biliary pancreatitis. *Pancreatology* 2004;4:215-222.
12. Abu Zidan FM, Bonham MJ, Windsor JA. Severity of acute pancreatitis: a multivariate analysis of oxidative stress markers and modified Glasgow criteria. *Br J Surg* 2000;87:1019-1023.

Knowledge, Attitude, and Practices of Pregnant Women Towards Antenatal Care in Tertiary Care Hospital Somalia: A Prospective Study

Abdikarim Ali Omar¹, Ahmed Issak Hussein¹, Rahma Yusuf Haji Mohamud², Mohamed Omar Hirsi¹

¹Department of Obstetrics and Gynecology, Somalia Turkiye Training and Research Hospital, Mogadishu, Somalia.

²Department of Education Coordinatorship, Somalia Turkiye Training and Research Hospital, Mogadishu, Somalia.

Corresponding Author Abdikarim Ali Omar

Email: drtimirali@gmail.com

Received January 22nd, 2023

Accepted March 20th, 2023

Abstract Introduction: All women, regardless of their pregnancies, deserve high-quality maternal services during pregnancy, delivery, and afterward. This study aims to evaluate the knowledge and attitude of pregnant women toward antenatal care. **Materials and Methods:** A prospective study was carried out among pregnant women attending at obstetrics outpatient department of Mogadishu Somali Turkish Training and Research Hospital. The sample was obtained using random sampling methods. In addition, information was gathered using a structured interview schedule between August and October 2022. **Results:** The majority (63.3%) of respondents were aged between 20 and 24, while 21% were between the ages of 25 and 29, and 8% were between the ages of 30 and 34. One hundred sixty-five pregnant women had primary school education, 31% had secondary education, 15% had a university education, and 11% were illiterate. Only 252 (63.3%) correctly identified the first prenatal check-up within three months. **Conclusion:** According to the findings, most of the study's participants had a high level of knowledge and good practices, and most had a favorable opinion about ANC. The Federal Ministry of Health's public health department should strengthen national health education programs to promote antenatal care.

Keywords Antenatal care; Health care; Prenatal care; Somalia.

Introduction

Antenatal care (ANC) is one strategy to reduce maternal mortality, which makes it easier to identify and manage risk factors early in pregnancy. The timely and frequent use of a package ANC enables the provision of essential services, such as the detection and treatment of infections and the detection and treatment of obstetric complications like preeclampsia (1).

Antenatal care is a time to encourage healthy behaviors, including breastfeeding, early postnatal care, and planning for the best pregnancy spacing, as well as the utilization of competent attendance at delivery (2).

Prenatal care is an important safety net for good parenting and childbirth, where the potential mother and her fetus's health may be monitored. The care a woman receives to protect the health of both the mother and the unborn child is known as ANC. Prenatal care is a clinically valuable and affordable safety net for healthy parenting, including antenatal care, a successful strategy to reduce adverse perinatal outcomes such as preterm birth, intrauterine growth restriction, and low birth weight (3).

More than 200 million women become pregnant each year around the globe. In many underdeveloped nations, complications during pregnancy or delivery account for 25–33% of all fatalities of reproductive age. Nearly 90% of these fatalities occur in Asia and Sub-Saharan Africa, with 10% in other developing nations and fewer than 1% in other parts of the world (4).

A healthy pregnancy diet and lifestyle are crucial for the growth of a healthy baby and may improve the child's health in the long run. Unfortunately, nearly 90% of maternal deaths occur in underdeveloped nations, and more than 500,000 women pass away every year from conditions connected to pregnancy and delivery in these countries (5). The extraordinarily high figures in developing countries have been linked to the latter's use of outdated obstetric services, so maternal and infant morbidity and death rates in developed countries have been

reported to be much lower. Studies in developing nations have revealed that the availability, quality, and cost of services, as well as the social structure, health attitudes, and individual characteristics of consumers, all influence the use of healthcare services. In addition to other socioeconomic variables, inadequate prenatal and other health service access and usage continue to contribute to the high maternal death rate (6).

To ensure their health and the well-being of their babies in the womb, all women, whether or not their pregnancies are complicated, need high-quality maternal services throughout pregnancy, delivery, and the postpartum period. The women in need must have access to high-quality maternal health care that is inexpensive, efficient, suitable, and acceptable. Approximately 63% of pregnant women are in Africa, 65% of pregnant women in Asia, and 73% of pregnant women in Latin America. Contrarily, in developed nations, maternal healthcare is almost universal (7)

This study identifies or evaluates the knowledge and attitude toward antenatal care. Women are allowed to determine when to visit for antenatal care and what to do at each stage of pregnancy (8).

Materials and Methods

A prospective study was conducted among pregnant women attending the obstetrics outpatient department at Somalia Turkiye Training and Research Hospital. The sample was obtained using random sampling methods. Information was gathered using a structured interview schedule between August and October 2022. Questions about socioeconomic factors, mother antenatal knowledge, and attitude toward attending prenatal clinics were included. Data collected from the women were analyzed using SPSS version 22. The variables were measured with the respondents' knowledge, measured with a three-Likert scale with the options: "correct", "incorrect", and "I do not know". The respondents' attitudes were measured with a two-Likert scale, with the options including agree and disagree.

The data were analyzed using descriptive statistical analysis such as frequency counts and percentages.

Each response received a score: 2 for the correct and 0 for the incorrect or "I do not know" answer. A percentage was calculated from each participant's total score.

Those who obtained a score of greater than 96% were considered "knowledgeable" (a high level of knowledge). Those between 60 and 90 percent were assessed to have an average degree of knowledge, while those with less than 40 percent were considered "unknowledgeable" (a low level of knowledge). The questionnaire also collected information on the women's sources of ANC knowledge.

The maximum score was 95, and the lowest score was 18. Therefore, these numbers represent the range of possible scores. The percentage of attitude was determined as follows: those with scores greater than 95% were classified as having a "positive attitude," and those with scores below 40% were classified as having a "negative attitude."

Results

The majority of respondents, 252 (63.3%) aged 25 to 29, while 84 (21%) were between the ages of 25 and 29, and 32 (8%) were aged 30 and 34.

One hundred sixty-five pregnant women had primary school education, 31% had secondary education, 15% had a university education, and 11% were illiterate. However, the second to fourth deliveries was 195 (55%).

Most of the respondents (222, 55.5%) had one abortion, while 120 (30.0%) women had no prior history of abortion, and only 58 (14.4%) had two or more. One hundred and 86 (53%) of all respondents gave birth in hospitals. One hundred eight women gave birth at home; in contrast, only 56 (22.9%) had previously given birth in private clinics (Table 1).

Table 1. Socio-demographic characteristics of pregnancy

Variable	Frequency	Percent
Age		
<20	9	23%
20-24	252	63%
25-29	84	21%
30-34	32	8%
>35	23	5%
Education		
Illiterate	45	11%
Primary school	165	41%
Secondary school	130	32%
University	60	15%
Occupation		
Labor worker	80	20%
Non-labor worker	320	80%
Location		
Urban	355	88%
Rural	45	11%
Parity		
1	95	27%
2-4	195	55%
5-7	50	14%
>8	30	2.9%
Normal previous delivery		
N of vaginal delivery	252	72%
Caesarean section	98	28%
Place of delivery		
Public hospital	56	16%
Private	186	53%
Home	108	30%

Abortion		
0	120	30%
1	222	55.5%
2-4	58	14.4%
Annual income		
50-100	62	15.5%
101-300	178	44.5%
301-500	120	30%
501-900	40	10%

Table 2. Distribution of expectant mothers according to their knowledge of antenatal care

	Correct (%)	Incorrect (%)	I do not know (%)
Does the first prenatal check-up have to be performed during the first three months?	252 (63%)	120 (30%)	28 (7%)
The newborn needs exclusive breastfeeding for the first six months.	168 (42%)	178 (44%)	54 (13%)
Is daily fetal movement counting necessary during the last three months' stages of pregnancy?	360 (90%)	20 (5%)	20 (5%)
Does taking more food with vegetables during pregnancy help prevent anemia?	385 (96.3%)	9 (1.5%)	6 (1.3%)
Does a pregnant woman require a vitamin supplements?	208 (52%)	152 (38%)	40 (10%)
Is medication intake without a physician's prescription safe for the fetus?	38 (9.5%)	340(65.5%)	22 (4.2%)
Do pregnant women need dental care?	160 (40%)	180 (456%)	60 (15%)

Does a pregnant woman require any vaccinations?	252 (63%)	48 (12%)	100 (48%)
---	-----------	----------	-----------

Most individuals responded correctly when asked whether having a daily fetal movement count during the last three months of pregnancy was necessary.

They also had an excellent understanding of maternal vaccination; 256 (95.8%) knew the importance of vaccination, while 48 (12%) did not.

Three hundred and 85 (96.5%) knew they should eat more vegetables during pregnancy to help prevent anemia; only 252 (63.3%) could accurately determine that the first prenatal check-up had to be performed during the first three months (Table 2).

According to the findings of general attitudes toward the program, most pregnant women (96.0%) demonstrated a good attitude toward ANC. Our participants needed to attend antenatal care. Regarding mothers taking vaccination, only 18 (4%) agreed, while 382 (9%) disagreed. They were aware, as acknowledged, but some of them did not take the vaccination.

Three hundred and 70 (92.5%) of the participants were aware of the effects of smoking, while 30 (7.5%) had no idea of the detrimental effects of smoking on their fetuses (Table 3).

In addition, 252 women aged 20–24 who had one to four or more antenatal care visits had a statistically significant higher knowledge score (89%), while 27 women (10.7%) did not attend antenatal care. Among 84 women aged 25-29 years, 71 (84%) went to antenatal care more than five times, whereas 55 mothers over 30 years (17%) were less likely to go to antenatal care ($p < 0.001$).

Table 3. Distribution of the expectant mothers according to their attitudes on prenatal care Attitudes

	Agree	Disagree
The pregnancy mother needs antenatal care.	320 (95%)	20 (5%)
Have you ever taken a vaccine during pregnancy?	18 (4%)	382 (95%)
I believe that the smoking of the pregnant mother affects the unborn child.	370 (92,5%)	30 (7.5%)
Is there any importance of routine screening tests for pregnancy	389 (97.3%)	11 (2.8%)
Does regular monitoring facilitate delivery?	18 (45 %)	220 (55%)
Are you going to the hospital when you know you are pregnant?	261 (65.3%)	139 (34.8%)
Does the pregnant mother need an ultrasound?	271 (67%)	129 (32.3%)

Ninety-five percent of women with one child attended antenatal care; 59 women (62%) attended antenatal care 1 to 4 times, while 36 women (37%) did not.

One hundred ninety-five women in the study had 2 to 4 children, 179 (91%) attended antenatal care one to four times, 16 (8.2%) attended antenatal care > 5 times, and 60 women (1.2%) had five or more children, were > 5 times less likely to attend ANC (p<0.005).

The majority of respondents had a history of one abortion-related significantly higher ANC. Two hundred twenty-two pregnant women attended ANC, with 154 (69%) attending previous pregnancies 1 to 4 times for antenatal care and 68 (30.6%) attending antenatal care. While the mother has a history of abortion two to four times, ANC (10.7%) has been less likely to attend antenatal care (p<0.001).

Forty-five of the women who came to ANC were illiterate. Forty-five (80%) had not attended ANC in their previous pregnancy, while nine women (20%) came 1 to 4 times to ANC;

compared to 130 pregnant women who attended primary school, 130 (100%) received ANC and only came ANC 1 to 4 times in the previous pregnancy. While 99 (60%) of the 165 pregnant women graduated from high school, 66 (40%) attended ANC more than five times. Of the other 60 pregnant women who graduated from university, 60 (100%) had good antenatal care visits ($p < 0.001$) (Table 4).

Table 4. Cross tabulate Antenatal Care for Pregnant Women of Different Demographics, Parity, and Socioeconomic

	0	1-4	>5	p-value
Age				
<20	9	0	0	p<0.001
20-24	27	225	0	
25-29	0	13	71	
30-34	0	0	32	
>35	0	0	13	
Parity				
1	36	59	0	p<0.005
2-4	0	179	16	
5-7	0	0	50	
>8	0	0	10	
Abortion				
0	36	84	0	p<0.001
1	0	154	68	
2-4	0	0	58	

Education				
Illiterate	36	9	0	p<0.001
primary school	0	139	0	
secondary school	0	99	66	
University	0	0	60	
Occupation				
Labor worker	36	44	0	
Non-labor worker	0	194	126	
Annual income				
50-100	36	26	0	p<0.001
101-300	0	178	0	
301-500	0	34	86	
501-900	0	0	40	

Discussion

A pregnant woman should get special care from her family and the community since pregnancy is a significant occurrence. In addition, other studies have shown the importance of knowledge and awareness among pregnant women as factors influencing the acceptability and utilization of health care (9). Similarly, having the correct information and attitude ensures that Somalian women continue receiving ANC.

The current study found that most pregnant women (95.3%) had good knowledge of ANC. Regarding immunization, the tetanus toxoid vaccine is beneficial in preventing the potentially fatal illness known as tetanus neonatorum. However, a neurotoxin may be produced due to tetanus infection and cause titanic muscular spasms. Therefore, the mother must get two tetanus shots during the first pregnancy and one additional dose for each subsequent pregnancy (10).

Our study also showed that they had an excellent understanding of maternal vaccination; 256 (95.8%) knew the importance of vaccination. Regarding mothers taking vaccination, only

18(4%) agreed, while 382(9%) disagreed. Two hundred twenty-two pregnant women came to ANC, 154 (69%) attended previous pregnancy 1 to 4 times, while 68 women with zero abortions attended > 5 times, While the mothers who had a history of three to five abortions attended only two to four times to ANC (10.7%) ($p < 0.001$).

The WHO also emphasized the importance of antenatal care (ANC) throughout pregnancy and recommended that women visit the antenatal clinic at least four times. These appointments would allow medical professionals to detect problems, such as anemia and chronic constipation, as early as possible. In addition, they will assist the mother in gaining the necessary knowledge about pregnancy, delivery, and puerperium (11).

Healthy eating is essential during pregnancy; maternal nutritional needs change to meet the demands of pregnancy. In addition, healthy eating can help ensure adequate nutrients are available for both the pregnant mother and the fetus; similarly, a study about nutritional practices for breastfeeding and pregnancy conducted in Guatemala shows that the baby's health will be improved by eating vegetables, grains, and milk throughout pregnancy. It should also be considered that sociocultural attitudes might impact maternal health, and different people have different eating habits and behaviors (12).

According to the findings of general attitudes toward the program, most pregnant women (96.0%) demonstrated a good attitude toward ANC. Of our participants, 320(95%) showed the importance of attending antenatal care.

Conclusion

According to the results, most of the study's participants had a high level of knowledge and good practices, and most had a favorable opinion of ANC. However, health education programs must be undertaken to raise women's knowledge of ANC in Somalia to achieve a high level of awareness.

Conflicts of interest

Authors have no financial or personal conflicts of interest.

Funding

This study is unfunded.

Ethical approval

Ethical approval was obtained from the ethical committee of Somalia Turkiye Training and Research Hospital. Written and informed consent was taken from the patient for participation.

References

1. Umer A, Zinsstag J, Schelling E, et al. Antenatal care and skilled delivery service utilisation in Somali pastoral communities of eastern Ethiopia. *Trop Med Int Health* 2020;25:328-337.
2. Onasoga OA, Afolayan JA, Oladimeij BD. Factors influencing utilization of antenatal care services among pregnant women in Ife Central Lga, Osun State Nigeria National Hospital Abuja, Nigeria. *Adv Appl Sci Res* 2012, 3:1309-1315
3. Paredes I, Hidalgo L, Chedraui P, et al. Factors associated with inadequate prenatal care in Ecuadorian women. *Int J Gynecol Obstet* 2005;88:168-172.
4. Ibrahim HK, El Borgy MD, Mohammed HO. Knowledge, attitude, and practices of pregnant women towards antenatal care in primary healthcare centers in Benghazi, Libya. *J Egypt Public Health Assoc* 2014;89:119-126.
5. Ogunba BO, Abiodun OB. Knowledge and attitude of women and its influence on antenatal care attendance in Southwestern Nigeria. *J Nutr Health Sci* 2017;4:207.
6. Varma GR, Kusuma YS, Babu BV. Antenatal care service utilization in tribal and rural areas in a South Indian district: an evaluation through mixed methods approach. *J Egypt Public Health Assoc* 2011;86:11-15.
7. Ekholuenetale M, Nzopotam CI, Barrow A, Onikan A. Women's enlightenment and early antenatal care initiation are determining factors for the use of eight or more antenatal visits in Benin: further analysis of the Demographic and Health Survey. *J Egypt Public Health Assoc* 2020;95:1-2.
8. Ahrned M, Schytt E, Andersson E, et al. Antenatal care for Somali-born women in

- Sweden: Perspectives from mothers, fathers and midwives. *Midwifery* 2019;74:107-115.
9. Akhtar S, Hussain M, Majeed I, Afzal M. Knowledge Attitude and Practice Regarding Antenatal Care among Pregnant Women in Rural Area of Lahore. *Int J Soc Sci Manage* 2018;5:155–162.
 10. Ciceklioglu M, Soyer MT, Ocek ZA. Factors associated with the utilization and content of prenatal care in a western urban district of Turkey. *Int J Qual Health Care* 2005;17:533–539.
 11. Kiah FK, Zuhriyah L, Indrawan IW. Knowledge, Attitude, and Utilization of Antenatal Care in Kupang City, East Nusa Tenggara, Indonesia. *EAS Journal of Nursing and Midwifery* 2020;2:52-55.
 12. Pallikadavath S, Foss M, Stones RW. Antenatal care: Provision and inequality in rural north India. *Soc Sci Med* 2004;59:1147–1158.

Does Percutaneous Nephrolithotomy Cause a Local Decrease in Renal Parenchymal Thickness?

Mehmet Altan¹, Ahmet Emin Dogan¹, Berk Yasin Ekenci¹, Ahmed Muhammad Bashir², Hasan Nedim Goksel Goktug¹

¹Department of Urology, Diskapi Training and Research Hospital, University of Health Sciences, Ankara, Turkiye.

²Department of Internal Medicine, Somalia Turkiye Training and Research Hospital, Mogadishu, Somalia.

Corresponding Author Mehmet Altan **Email:** memetaltann@gmail.com

Received January 4th, 2023

Accepted April 1st, 2023

Abstract **Introduction:** This study aimed to investigate the effects of PCNL on the renal parenchymal thickness.

Materials and Methods: Adult (≥ 18 years) patients who underwent percutaneous nephrolithotomy (PNL) in Health Sciences University Diskapi Training and Research Hospital between May 2016 and May 2021 constituted the target population of this descriptive study. Patient data were retrospectively reviewed. All patients had preoperative and postoperative sixth-month abdominopelvic computerized tomography (CT) scan images and preoperative and postoperative day 1 blood workup results. Stone surface areas (SSA) and stone densities were measured using preoperative CT scans. The renal parenchymal thickness (RPT) was calculated on preoperative and postoperative CT images. Preoperative and postoperative RPT values were compared. **Results:** 358 patients (232 men and 126 women) were included. Thirty-two (8.9%) patients had 2 PNL surgeries. Median SSA and stone density were calculated as 566.5 (100-2237) mm² and 937.5 (304-1474) Hounsfield Units. The mean duration of hospital stay was 4.2 \pm 2.1 days. Our analysis revealed a significant reduction in RPT ($p < 0.001$). While the median RPT reduction was 2.5 (0-8) mm in patients who underwent PNL once, it was five (1-12) mm in patients who underwent PNL twice ($p < 0.05$). Correlation analysis revealed no correlation between RPT reduction and duration of hospital stay. **Conclusion:** A significant decrease in RPT was detected after PNL. No correlation was found between the decrease in renal parenchyma thickness and the length of hospital stay.

Keywords Computed tomography; Percutaneous nephrolithotomy; Renal parenchymal thickness; Renal stone

Introduction

The incidence of urinary tract stone disease depends on geographical, climatic, ethnic, dietary, and genetic factors (1). The prevalence of urinary tract stones ranges from 1% to 20%. Urinary tract stone disease is a common health problem with a recurrence rate of 51% within ten years, depending on its etiology (2).

The decision regarding the treatment method is given based on stone composition, localization, and burden (3). Treatment strategies include conservative methods, medical therapy, extracorporeal shock wave lithotripsy (ESWL), flexible or rigid ureterorenoscopy, percutaneous nephrolithotomy (PNL), and open/laparoscopic surgery.

The PNL procedure is the preferred treatment modality in cases with a high stone burden since it can lead to a stone-free rate of as high as 95% with relatively low retreatment rates and short hospitalization and convalescence periods (4,5). Also, it is recommended as the standard treatment method for all renal stones larger than two cm and lower pole stones larger than one cm by both the American Association of Urology (AUA) and European Association of Urology (EAU) guidelines (6). It was reported that bleeding requiring transfusion, urinary extravasation, septicemia, colon injury, and pleural injury are the most common complications of this procedure (7). Although there are sufficient clinical studies and data regarding PNL outcomes, little is known about the effects of the PNL procedure on the renal parenchyma.

Protection of the renal parenchyma is essential for saving the glomerular function and glomerular filtration rate (GFR). Since there is a risk of renal parenchymal loss with the PNL procedure, the clinicians need to know the factors related to this risk.

This study aimed to investigate the effects of PNL on renal parenchymal thickness (RPT) with the guidance of computed tomography (CT) scan. Pre-PCNL and post-PCNL renal parenchymal thicknesses of the kidneys were measured and compared for this analysis.

Materials and Methods

Adult (≥ 18 years) patients who underwent PNL in Health Sciences University Diskapi Training and Research Hospital Department of Urology between May 2016 and May 2021 constituted the target population of this study. It was approved by the Ethical Review Committee of the same institution (01.11.2021-123/09). Data of the patients were retrospectively reviewed. Patients who did not have a preoperative CT scan and a postoperative follow-up CT scan and those with incomplete data were excluded. Also, those with a solitary kidney, renal ectopia, or any other congenital renal abnormality were excluded.

In our routine practice, preoperative abdominopelvic CT scans are performed one month before PNL surgery, while postoperative CT scans are performed six months after the procedure. Therefore, all patients had preoperative and postoperative abdominopelvic CT scans.

All CT scans were performed using the same machine with GOM software (ZEISS Group Company, Braunschweig, Germany). An experienced radiologist reviewed the CT images, and coronal or sagittal reformatted CT images were also evaluated to supplement the axial images when found necessary by the radiologist. Attenuation value measurements were calculated as Hounsfield units using bone window settings with appropriate magnification. Stone densities were recorded in Hounsfield Units. The renal parenchymal thickness was measured preoperatively at the planned calyx of puncture and postoperatively at the puncture site indicated in the operative note using soft-tissue window settings in the axial CT images (Figure 1). These

values were measured and recorded in milliliters. Stone surface areas were measured using an arithmetic calculation formula.

All PCNL surgeries were performed in a standard aseptic manner and the prone position under general anesthesia. Tract dilatation was performed with Amplatz dilators in all patients.

An 18F nephrostomy catheter was routinely left in place after completing the procedure. The nephrostomy catheter was removed on the second or third postoperative day unless there was a complication associated with drainage. *Success* was defined as stone-free status or the presence of residual fragments smaller than four millimeters.

All patients underwent preoperative routine laboratory workup at our institution. Complete blood counts of all patients were checked the day before and the day after surgery. All data, including the duration of hospital stay, were collected from electronic patient folders. In addition, the preoperative and postoperative RPT measurements were compared.

Categorical variables were expressed as counts and percentages. Kolmogorov Smirnov test was used to evaluate the normality of continuous variables. Variables with non-normal distribution were expressed as median (i.e., interquartile range) and analyzed using Wilcoxon and Spearman correlation tests. A p-value <0.05 was considered to be statistically significant. The Statistical Package for Social Sciences (SPSS) version 22.0 for Windows (SPSS Inc. Chicago, USA) software package was used to analyze the study data.

Results

After applying inclusion and exclusion criteria, 358 patients were included in this cohort. Among these patients, 232 (64.80%) were men, while 126 were women (35.19%) (Table 1). Thirty-two (8.9%) of these patients had two PNL surgeries. Median stone surface areas were calculated as 566.5 (100-2237) mm², and median stone densities (Hounsfield Unit-HU) were calculated as

937.5 (304-1474). The mean duration of post-surgical hospital stay was 4.2±2.1 days. While the median parenchyma reduction was 2.5 (0-8) mm in patients who underwent PNL once, it was found as five (1-12) mm in patients who underwent PNL twice.

Table 1. Demographic data and descriptive characteristics of the patients

Male / Female, n (%)	232 (64%) / 126 (36%)
Number of patients who underwent PNL once, n(%)	326 (91.1%)
Number of patients who underwent PNL twice, n(%)	32 (8.9%)
Stone size (mm ²), (min-max)	566.5 (100-2237)
Stone density (HU), (min-max)	937.5 (304-1474)
Postoperative hospital stay (Day), (mean±SD)	4.2±2.1
Renal parenchyma thickness reduction after the first PNL (mm), (min-max)	2.5 (0-8)
Renal parenchyma thickness reduction after the second PNL (mm), (min-max)	5 (1-12)

PNL: Percutaneous nephrolithotomy, HU: Hounsfield unit, SD: Standard deviation

While the median RPT of the patients in our study was 23.5 (10-36) mm before the PNL operation, the median RPT of the patients who had one PNL operation was 21 (8-30) mm. Some patients in our study (n=32) underwent two PNL operations from the same kidney and with the same calyx access. Before the second PNL procedure, the median RPT of the patients who underwent PNL operation for the second time was measured as 20 (7-29) mm. After the second PNL procedure, the median RPT of the patients who underwent PNL operation for the second time was measured as 18.5 (8-27) mm. Our comparative analysis revealed a significant reduction in RPT after PNL operations (p< 0.001) (Table 2).

Table 2. Parenchymal thicknesses before and after PNL surgeries

	n=358	Before PNL	After the PNL	p	n=32	Before the second PNL	After the second PNL	p
Parenchymal thickness of kidneys (mm), (min-max)		23.5 (10-36)	21 (8-30)	<0.001*		20 (7-29)	18.5 (8-27)	<0.001*

*Wilcoxon test, PNL: Percutaneous nephrolithotomy

There was no statistically significant relationship between RPT reduction, stone density, stone size, and postoperative hospital stay ($p=0.211, 0.733, 0.814, \text{ and } 0.659$) (Table 3).

Table 3. Relationship between renal parenchymal thickness reduction and perioperative data

	Value	p
Stone density (HU), (min-max)	937.5 (304-1474)	0.733*
Stone size (mm ²), (min-max)	566.5 (100-2237)	0.814*
Postoperative hospital stay (Day), (mean±SD)	4.2±2.1	0.659*

*Spearman correlation test, SD: Standard deviation

Discussion

Ideal surgical treatment of urinary system stone disease aims to remove the stones with minor damage to the kidney (8). Among several surgical treatment modalities, PNL is especially preferred in patients with a relatively high stone burden. This procedure has advantages such as a relatively short hospital stay, low treatment cost, short convalescence period with favorable cosmetic results. Despite these advantages, there are insufficient data and only a few clinical studies on the effects of PNL on renal function. It is widely accepted that CT is an optimal imaging modality for assessing the renal parenchyma after PNL (8). In our study, the median preoperative RPT was significantly higher than the median postoperative RPT.

The complication rate of PNL is reported to be in the range of 3% to 18% in the literature (9). Bleeding requiring transfusion is one of the most severe surgical complications of this procedure. It was reported that the factors responsible for renal hemorrhage were the duration of the PNL procedure, stone size, stone location, and the RPT (9). Al-Nahas et al. stated that increased RPT and increased kidney size may increase the risk of bleeding due to the potential damage in the

renal tissue and vascular structures during both percutaneous access and dilatation of the access tract (10).

Currently, imaging methods such as ultrasound (US) and CT are used for the morphological assessment of the renal parenchyma (11).

In the literature, there are studies regarding the effect of PNL on kidney functions and renal parenchyma (12,13). However, these studies have relatively small sample sizes. In one of these studies, Handa et al. showed that PNL damaged the kidney tissue and led to renal functional impairment (12). However, these studies have relatively small sample sizes. In one of these studies, Handa et al. showed that PNL damaged the kidney tissue and led to renal functional impairment (12).

On the other hand, Holman et al. reported that PNL did not damage the kidney even in the early postoperative period and improved kidney function (13). However, the effect of surgical trauma caused by PNL on the renal parenchyma should be considered. It was previously suggested that the number of PNL procedures performed on the kidney was correlated with the severity of renal parenchymal damage, and the decrease in RPT was more significant in these patients (12,13). In our study, the comparison of the preoperative and postoperative CT images revealed a statistically significant difference regarding RPT, both in patients who underwent PNL once or twice.

In the studies with large patient series from the normal patient population, a very high correlation was observed between CT and Tc-99m DMSA scintigraphy regarding kidney size and RPT measurements (14). Therefore, in our study, CT was used for these measurements.

Only a few studies in the literature evaluated the association between stone density and post-PNL reduction in RPT (15). Our study did not find a statistically significant correlation between stone

density and reduction in the RPT after PNL. Therefore, we suggest that the decrease in RPT after PNL is due to renal parenchymal injury. Although it can be proposed that the amount of renal parenchyma loss could be directly correlated with intraoperative blood loss, we did not find a significant hemoglobin drop in our patients (data not shown).

In many studies, stone size was associated with renal parenchymal damage and PNL success (16). However, in our study, there was no statistically significant correlation between the stone size and post-PNL reduction in RPT.

There are only a few studies in the literature on the relationship between the decrease in RPT and the length of hospital stay (15). Karalar et al. found no statistically significant correlation between RPT and length of hospital stay. Also there was no correlation between the decrease in RPT and the length of hospital stay.

This study has some weaknesses which need to be considered while evaluating its findings. First, it is a retrospective study that can be affected by all weaknesses stemming from its retrospective design. Second, data such as the number of punctures and duration of surgery were not included. Third, estimated glomerular filtration rates of the patients were not analyzed since these data were incomplete in our database.

Conclusion

Despite these weaknesses, we conclude that PNL can lead to a significant decrease in RPT. However, no correlation was found between the decrease in RPT and the length of hospital stay. Our study should be supported by prospective clinical trials, which include data regarding the changes in ipsilateral renal function such as eGFR.

Conflicts of interest

The authors declare no conflicts of interest.

Funding

This study is unfunded.

Ethical approval

This study has been approved by Ankara Diskapi Training and Research Hospital Ethical Review Committee (01.11.2021-123/09)

References

1. Sorokin I, Mamoulakis C, Miyazawa K, Rodgers A, Talati J, Lotan Y. Epidemiology of stone disease across the world. *World J Urol* 2017; 35:1301-1320.
2. Sánchez-Martín FM, Millán Rodríguez F, Esquena Fernández S, et. al. Incidencia y prevalencia de la urolitiasis en España: Revisión de los datos originales disponibles hasta la actualidad. *Actas urológicas españolas* 2007;31:511-520.
3. Gorbachinsky I, Wood K, Colaco M, et al. Evaluation of renal function after percutaneous nephrolithotomy—does the number of percutaneous access tracts matter? *J Urol* 2016 1;196:131-136.
4. Awan AS, Mithani S, Yousuf F, et. al Percutaneous Nephrolithotomy in a Previously Operated Kidney. *J Coll Physicians Surg Pak* 2020; 30:1201-1205.
5. de la Rosette J, Assimos D, Desai M, Gutierrez J, Lingeman J, Scarpa R, et al. The Clinical Research Office of the Endourological Society Percutaneous Nephrolithotomy Global Study: indications, complications, and outcomes in 5803 patients. *J Endourol* 2011; 25:11-17.
6. Türk C, Petřík A, Sarica K, et al. EAU Guidelines on Interventional Treatment for Urolithiasis. *Eur Urol* 2016; 69:475-482.

7. Kyriazis I, Panagopoulos V, Kallidonis P, Özsoy M, Vasilas M, Liatsikos E. Complications in percutaneous nephrolithotomy. *World J Urol* 2015; 33:1069-1077.
8. Assimos D, Krambeck A, Miller NL, et al. Surgical Management of Stones: American Urological Association/Endourological Society Guideline, PART I. *J Urol* 2016;196:1153-1160.
9. Seitz C, Desai M, Häcker A, et al. Incidence, prevention, and management of complications following percutaneous nephrolitholapaxy. *Eur Urol* 2012; 61:146-158.
10. El-Nahas AR, Shokeir AA, El-Assmy AM, et al. Post-percutaneous nephrolithotomy extensive hemorrhage: a study of risk factors. *J Urol* 2007;177:576-579.
11. Dhar M, Denstedt JD. Imaging in diagnosis, treatment, and follow-up of stone patients. *Adv Chronic Kidney Dis* 2009;16:39-47.
12. Handa RK, Matlaga BR, Connors BA, et al. Acute effects of percutaneous tract dilation on renal function and structure. *J Endourol* 2006;20:1030-1040.
13. Holman E, Salah MA, Tóth C. Comparison of 150 simultaneous bilateral and 300 unilateral percutaneous nephrolithotomies. *J Endourol* 2002;16:33-36.
14. Wadhwa P, Aron M, Bal CS, Dhanpatty B, Gupta NP. Critical prospective appraisal of renal morphology and function in children undergoing shockwave lithotripsy and percutaneous nephrolithotomy. *J Endourol* 2007;21:961-966.
15. Karalar M, Tuzel E, Keles I, Okur N, Sarici H, Ates M. Effects of Parenchymal Thickness and Stone Density Values on Percutaneous Nephrolithotomy Outcomes. *Med Sci Monit* 2016;22:4363-4368.

16. Gücük A, Üyetürk U, Öztürk U, Kemahli E, Yıldız M, Metin A. Does the Hounsfield unit value determined by computed tomography predict the outcome of percutaneous nephrolithotomy? *J Endourol* 2012 1;26:792-796.

Extrasosseous Primary Ewing's Sarcoma of the Lungs Mistakenly Diagnosed and Managed as Hemothorax: An Extremely Aggressive and Fatal Rare Tumor with an Unusual Site

Ahmed Adam Osman¹, Ibrahim Mohamed Hirsi², Mohamed Osman Dahir¹, Ahmed Abdirahman Hussein³, Ahmed Muhammad Bashir³

¹Department of Radiology, Somalia Turkiye Training and Research Hospital, Mogadishu, Somalia.

²Department of Pediatrics, Somalia Turkiye Training and Research Hospital, Mogadishu, Somalia.

³Department of Internal Medicine, Somalia Turkiye Training and Research Hospital, Mogadishu, Somalia.

Corresponding Author Ahmed Muhammad Bashir **Email:** ambashir@hotmail.com
Received February 23rd, 2023
Accepted March 31st, 2023

Abstract Extrasosseous Ewing's sarcoma of the lungs is a rare soft tissue tumor of children and adolescents usually found in the extremities. In this case report, we present a 4-year-old male child with primary Ewing Sarcoma of the lungs who presented with shortness of breath, cough, left-side chest pain, and hemoptysis for two months. We reviewed clinical, radiological, and pathological findings for this rare malignancy.

Keywords Extrasosseous Ewing's sarcoma; Lungs; Tumor; Computed tomography.

Introduction

Ewing's sarcomas are rare neuroectodermal tumors that primarily arise from the bone and are the second most common primary bone tumor (1). James Ewing first described this tumor in 1921 as an endothelioma of bone (2). Extrasosseous Ewing's sarcomas are sporadic neuroectodermal tumors, and Hammer et al. reported the first case in 1989 (3). Herein, we report a primary extraskelatal Ewing's sarcoma affecting the lungs diagnosed at a tertiary care

hospital in Mogadishu, Somalia. Considering the disease's clinical, radiological, and pathological features, the role of an integrated approach has been highlighted.

Case Report

A 4-year-old child complained of shortness of breath, cough, left-side chest pain, and hemoptysis for two months before admission to Somalia Turkiye Training and Research Hospital. On respiratory examination, air entry of the right lung site was markedly decreased on auscultation, and the percussion was dull on the left hemithorax. Other systemic examinations were unremarkable. Over the previous year, the family reported visiting up to 5 hospitals due to similar complaints. The last hospital that referred the patient to our hospital performed a chest X-ray, detected a massive left-sided pleural effusion, and planned to insert a chest tube. After the chest tube insertion, the patient's condition worsened, and they referred him to our hospital. Blood tests and a chest x-ray were performed when the patient reached our hospital. His blood investigations were unremarkable, but the chest x-ray demonstrated a completely homogenous opacification in the left hemithorax with an extensive mediastinal shift towards the right side. In addition, a chest tube was detected between the seventh and eighth intercostal space on the left side. The tube was twisted and oriented upward due to a solid mass lesion (Figure 1). We admitted the patient for further evaluation and removed the chest tube. A thoracic ultrasound was performed to rule out effusion, and unexpectedly this scan demonstrated a large hypoechoic heterogeneous solid mass. It was hypervascular in color Doppler examination, and multiple areas of cystic degeneration were present in the left hemithorax (Figure 2).

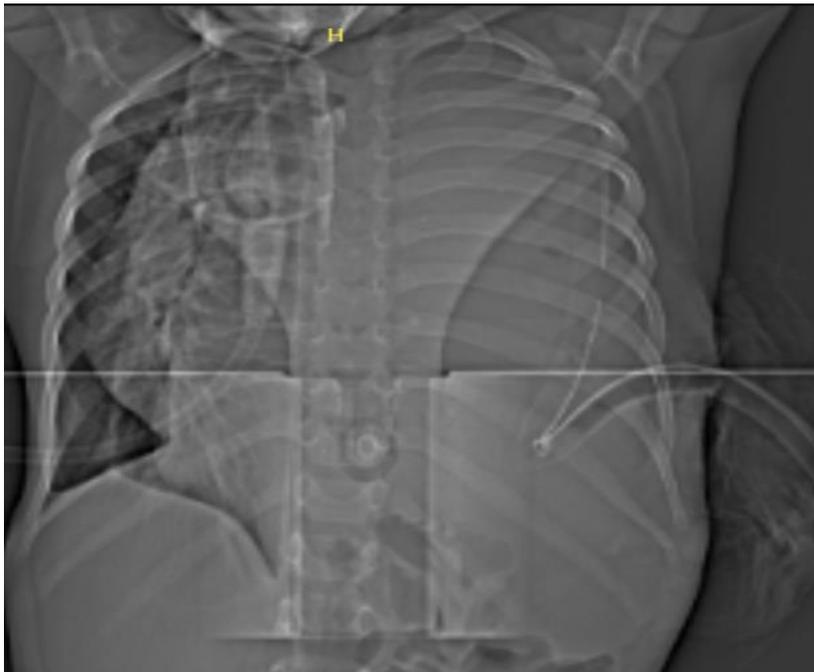


Figure 1. Frontal chest X-ray showing complete opacification of the left hemithorax, a chest tube that twisted and oriented upward.

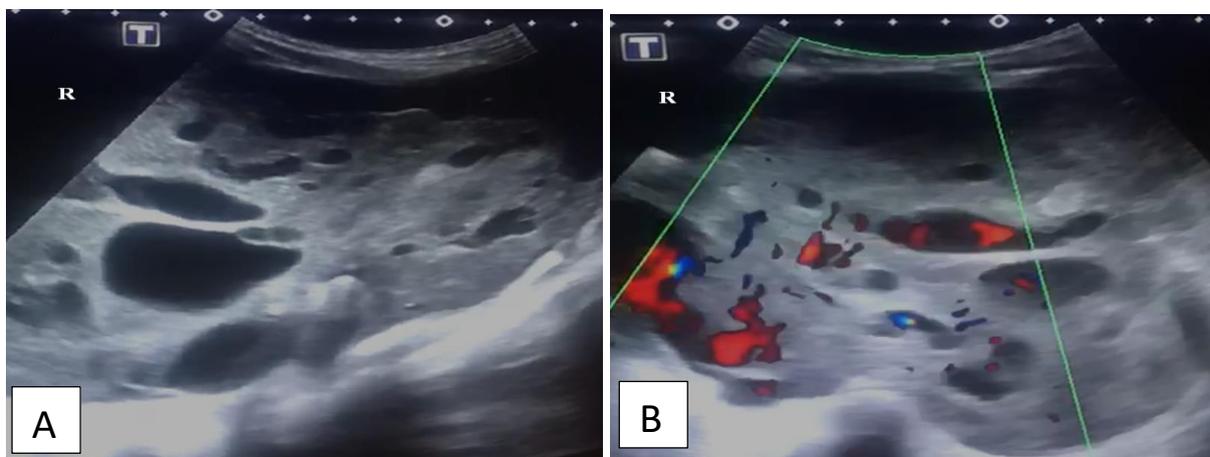


Figure 2. **A**-Chest ultrasound shows a large hypoechoic area containing multiple cystic changes in solid mass lesions. **B**-Chest Doppler ultrasound revealed a large hypoechoic solid lesion that is highly vascular in some areas.

A thoracic contrast-enhanced computerized tomography (CT) scan was performed to characterize the lesion further. This scan revealed a large heterogeneous, contrast-enhanced mass with multiple cysts and hypodense areas involving the entire left hemithorax. Also, the mediastinum shifted to the right side due to compression. No calcification was detected within the mass (Figure 3). Subsequently, a whole-body CT scan was performed, and no distant metastasis was detected. A tru-cut biopsy was performed, which revealed Ewing sarcoma of

the chest wall. The patient was referred to the oncology department. However, he died due to disease progression and respiratory failure soon after referral.

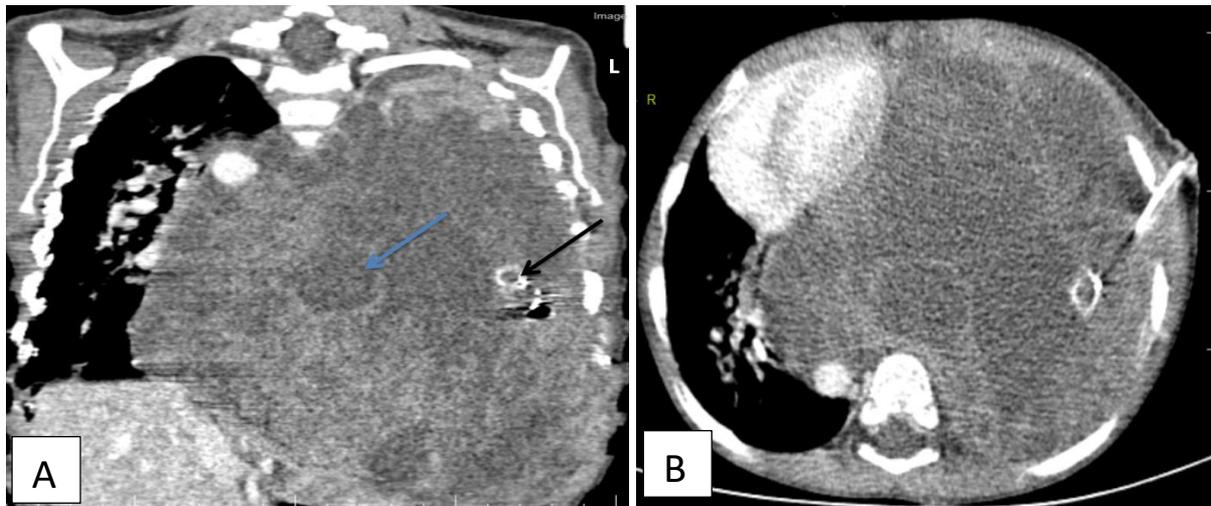


Figure 3. A-Coronal computerized tomography scan of the chest showing complete opacification at the left hemithorax heterogeneously enhanced with hypodense necrotic areas (blue arrow) and marked mass effect with a right-sided mediastinal shift. The black arrow shows the twisted chest tube. B- An axial section showing the right-sided mediastinal shift with markedly reduced right lung volume.

Discussion

Extrasosseous Ewing's sarcomas (EES) is a sporadic neuroectodermal tumor initially described by Hammer et al. in 1989(3). Our case was a 4-year-old child. However, it is usually diagnosed in the second decade of life (1). This finding indicates a possible early presentation in our study (1).

Although the diagnosis of EES is primarily based on histology, clinical and radiological features also have a significant role in the diagnostic management of EES and its differential diagnosis from other sarcomas (4). A computerized tomography scan helps describe the tumor's extent and confirm that the soft tissue mass is extrasosseous. In the present case, an enhanced thoracic CT scan revealed a heterogeneously enhanced mass with multiple cystic necrosis areas involving the entire left hemithorax associated with a right-sided mediastinal shift due to compression. No calcification was detected within the tumor. Also, a whole-body CT scan was performed, which excluded distant metastasis.

Typically, EES is an aggressive tumor with a high risk for local recurrences and metastases (5). Therefore, the treatment of choice is an early surgical intervention with intensive chemotherapy and radiation therapy to eliminate a potential residual microscopic disease. Our patient had no distant metastasis but died due to local disease-related complications.

Conclusion

Primary EES is a scarce soft tissue neuroectodermal tumor. Due to its rarity and aggressive character, there are no guidelines for managing this disease. In addition, since it is rare, it may be overlooked during the differential diagnosis stage of patients with malignant tumors. Although there is a high risk of distant metastasis, patients may also die due to the aggressiveness of the local disease and erroneous interventions. Therefore, performed needed combined modality treatment. Also, primary EES should be considered in the differential diagnosis of children and young adults presenting with primary pulmonary mass.

Informed consent

The child's parents provided permission (written and informed consent) to publish this case report.

References

1. Bernstein M, Kovar H, Paulussen M, Randall RL, Schuck A, Teot LA, Juergens H. Ewing's sarcoma family of tumors: current management. *The oncologist* 2006;11:503-519.
2. Ewing J. Diffuse endothelioma of bone. *CA Cancer J Clin* 1972;22:95-98.
3. Hammar S, Bockus D, Remington F, Cooper L. The unusual spectrum of neuroendocrine lung neoplasms. *Ultrastructural Path* 1989;13:515-560.
4. Lai M, Sheu R, Chen C, Liu G. Extraosseous Ewing's Sarcoma: A case report with MR manifestations. *Chin J Radiol* 2000;25:251-254.
5. Siddiqui MA, Akhtar J, ShAMEEM M, Baneen U, Zaheer S, ShAhID M. Giant extraosseous Ewing sarcoma of the lung in a young adolescent female—A case report. *Acta Orth. Belg* 2011;77:270.