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## PENGANTAR EDITOR



Salam sehat,

**A**lhamdulillah edisi ke dua volume ke dua Jambura Medical and Health Science Journal kembali dapat diterbitkan. Sebagaimana pada edisi sebelumnya, maka jurnal terbitan Fakultas Kedokteran (FK) UNG pada edisi kali ini menampilkan 4 *Original Article* yang ditulis oleh akademisi dari berbagai instansi di Indonesia. Selanjutnya ada 1 *Review Article* yang ditulis oleh sejawat Universitas Hasanuddin. Terakhir ada 1 *Case Report* yg ditulis oleh sejawat dari Ponorogo, Jawa Timur. Hal ini menunjukkan JMHSJ juga diminati oleh para peneliti, akademisi, hingga praktisi dari berbagai penjuru Indonesia.

Topik yang diangkat pun bervariasi mulai dari *non-specific neck pain*, potensi antibakteri alga merah, sikap kesiapsiagaan bencana, fungsi paru pengemudi bentor, kemoterapi keganasan palpebral, hingga torsio testis. Semoga kedepan akan lebih banyak tulisan dari berbagai disiplin ilmu kedokteran yang diangkat dalam JMHSJ dari berbagai penjuru instansi. Hal ini diharapkan dapat menjadi indikator baiknya kualitas pengelolaan jurnal yang sebentar lagi akan diakreditasi pada indeksasi nasional (SINTA). Selamat membaca.

Gorontalo, 31 Agustus 2023

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## The Correlation Between Working Posture and Work Duration and Non-Specific Neck Pain Symptoms in Computer User Employees

Andi Siti Irfa Fidia Mustafah<sup>1\*</sup>, Nurhikmawaty Hasbiah<sup>1</sup>, Andi Rahmaniar<sup>3</sup>  
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### ABSTRACT

**Introduction:** Longer work processes with non-ergonomic working postures by employees who use computers can certainly cause musculoskeletal tension. One of the musculoskeletal disorders (MSDs) associated with computer use is complaints of non-specific neck pain caused by a non-ergonomic posture of the neck muscles over a long period, which causes muscle tension. This study aims to determine the relationship between working posture and duration of work using a computer on non-specific neck pain complaints among Hasanuddin University Rectorate employees.

**Method:** A cross-sectional research design was carried out on 121 administrative employees aged >22 years who met the inclusion and exclusion criteria. Assessment of working posture uses the Baseline Risk Identification of Ergonomic Factor (BRIEF) questionnaire, and for non-specific neck pain complaints using the Nordic Body Map (NBM) questionnaire. The Spearman's rho correlation test analyzes the relationship between variables.

**Results:** 49 out of 121 respondents had a high-risk working posture for non-specific neck pain, and 59 out of 121 had a long working duration. Working posture is positively correlated with symptoms of non-specific neck pain ( $p = 0.001$ ;  $r = 0.598$ ). In contrast, work duration did not correlate with symptoms of non-specific neck pain ( $p = 0.063$ ;  $r = 0.169$ ).

**Conclusion:** High-risk working postures can predict the incidence of non-specific neck pain in office administration employees. This can be a consideration for office leaders to pay attention to the working posture of their employees.

**Key words:** Duration, non-specific neck pain, working posture



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## **Introduction**

In the workplace, interactions that cannot be avoided between humans, work tools, and the work environment always involve the human senses, either directly or indirectly. Some jobs that use repetitive movements and static conditions for extended periods can cause musculoskeletal disorders (MSDs) due to stretching and muscle tension in the neck area. This condition usually affects administrative workers who work in front of a computer for a long time.<sup>1</sup> Neck pain is one of the most common musculoskeletal disorders (MSDs) worldwide and has the risk of causing disability.<sup>2</sup>

One of the MSDs associated with computer use is neck muscle fatigue caused by non-ergonomic postures of the neck muscles for a long time, resulting in muscle tension.<sup>3</sup> A non-ergonomic posture can cause a part of the body to move away from its natural position, i.e. the movement of the worker's arms that are too raised, the back position is too bent, the neck position looks up or down, and other non-ergonomic positions. The farther the body's position from the centre of gravity of the body, the higher the risk of complaints of muscle fatigue.<sup>4</sup>

According to the International Association for the Study of Pain (IASP), neck pain is localized from the superior to the nuchal line to the first thoracic spinous process.<sup>5</sup> The pain is often described as burning, stabbing and continuous and can be worsened by movement, constant stimulation and stress.<sup>6</sup> Blanpied et al. stated that around 70% of the population has experienced neck pain during their lifetime, and the incidence of neck pain will continue to increase. The results of an epidemiological study show that neck pain is highest in groups working in offices and in front of computers.<sup>7</sup> The prevalence of neck pain in office workers in Turkey reaches 84% .<sup>8</sup>

Hasanuddin University is one of the higher education institutions in Makassar City. Administrative employees in the rectorate building work to support administrative process activities centred in the rectorate building. Almost all administrative employees in the rectorate building use computers in their work processes. A study by Situmorang revealed that computer use exceeding 4 hours was significantly associated with complaints of non-specific neck pain.<sup>3</sup> This study analyses the relationship between working posture and work duration during computer use on non-specific neck pain complaints among Hasanuddin University Rectorate employees.

## **Methods**

This quantitative study with a cross-sectional approach aims to determine the

relationship between working posture and work duration during computer use on complaints of non-specific neck pain among Hasanuddin University Rectorate Employees. The population in this study were employees of the Hasanuddin University Makassar Rectorate, totalling 165 employees who were more than 21 years old. The research was conducted in March-April 2022. A minimum sample was 121 according to the normogram Harry King calculation for alpha 5%. A simple random sampling was conducted to obtain the sample. This research has received ethical approval from the Health Research Ethics Committee, Faculty of Public Health, Hasanuddin University 3806/UN4.14.1/TP.01.02/2022.

The data obtained was primary data by measuring working posture using the Baseline Risk Identification of Ergonomic Factor (BRIEF) questionnaire and for complaints of non-specific neck pain using the Nordic Body Map (NBM) questionnaire. The work duration was classified into long (2-4 hours) and very long (more than 4 hours) according to the average daily work hours.

The data was analyzed using the SPSS 25 computerized program (IBM, USA). To determine whether the data is normally distributed or not, the Kolmogorov-Smirnov normality test is carried out. Data is said to be normally distributed if  $p > 0.05$ . Bivariate analysis was carried out with a non-parametric correlation test, namely Spearman's rho test, to determine the relationship between working posture, work duration, and complaints of non-specific neck pain.

## Results

Table 1 shows the characteristics of the respondents. In this study, the dominant age group was 33-42 years (43 people, 34.7%). Most of the respondents in this study were female (72 people, 59.5%). Most respondents were employees who had worked >4 years in the administration department of the rectorate (92 people, 72%).

**Table 1.** Characteristics of Study Participants

Characteristics	Total (n)	Percentage (%)
<b>Age (years)</b>		
23-32	33	27.3
33-42	42	34.7
43-52	33	27.3
53-62	13	10.7
<b>Gender</b>		
Male	49	40.5
Female	72	59.5
<b>Work Experience</b>		
Short-term ( 0 – 1 years)	3	2.5
Medium (2 – 4 years)	26	21.5
Long-term (>4 years)	92	72.0

Table 2 shows the distribution of working postures based on respondent characteristics. The age range of 33-42 years was the most dominant among respondents, whereas in the high-risk working posture category, the predominant age was 43-52 years (22 people, 18.2%). For the low-risk category, the highest value was 6 (5%) respondents aged 22-32. In the medium-risk category, the highest value was the age range 33-42, with 20 (16.5%) respondents. The female gender was mainly found in all working posture categories, including high-risk, medium-risk, and low-risk. Meanwhile, the work experience more than 4 years dominate the total number of respondents, and working postures in the high-risk category occupy the highest number (58 people, 47.9%).

**Table 2.** Distribution of working posture based on age, gender and work experience

Characteristics	Classification of Working posture (N=165)			Total (n)
	Low-Risk (%)	Medium-Risk (%)	High-Risk (%)	
<b>Age (years)</b>				
23-32	6 (5)	14 (11.6)	13 (10.7)	33 (27.3)
33-42	1 (0.8)	20 (16.5)	21 (17.4)	42 (34.7)
43-52	2 (1.7)	9 (7.4)	22 (18.2)	33 (27.3)
53-62	0	0	13 (10.7)	13 (10.7)
<b>Gender</b>				
Male	4 (3.3)	15 (12.4)	30 (24.8)	49 (40.5)
Female	5 (4.1)	28 (23.1)	39 (32.2)	72 (59.5)
<b>Work Experience</b>				
Short-term (0 – 1 years)	0	3 (2.5)	0	3 (2.5)
Medium (2 – 4 years)	6 (5)	9 (7.4)	11 (9.1)	26 (21.5)
Long-term (>4 years)	3 (2.5)	31 (25.6)	58 (47.9)	92 (76)

Table 3 shows the distribution of work duration based on respondent characteristics. Employees aged 33-42 years dominated the total number of respondents in the category of long working duration, which occupied the highest number with 34 (19.8%) respondents. Females were primarily found in both work duration categories, including long and very long work duration. The respondents with long-term work periods dominate the total number of respondents, and the long work duration occupies the highest number with 92 (76%) respondents.

Table 4 shows the incidence of non-specific neck pain complaints from respondents based on working posture and work duration. Most employees in the low-risk, medium-risk, and high-risk categories had non-specific neck pain complaints in the no-pain (6 people, 66.7%), moderate pain (19 people, 44.2%), and painful category (49

people, 71%), respectively. Most employees with long and very long work durations complained of non-specific neck pain in the painful category.

**Table 3.** Distribution of work duration based on age, gender and work experience

Characteristics	Classification of Work Duration		
	Long (%)	Very Long (%)	Total N (%)
<b>Age (years)</b>			
23-32	14 (11.6)	19 (15.7)	33 (27.3)
33-42	24 (19.8)	18 (14.9)	42 (34.7)
43-52	24 (19.8)	9 (7.4)	33 (27.3)
53-62	8 (6.6)	5 (4.1)	13 (10.7)
<b>Gender</b>			
Male	28 (23.1)	21 (17.4)	49 (40.5)
Female	42 (34.7)	30 (24.8)	72 (59.5)
<b>Work Experience</b>			
Short-term (0 – 1 years)	1 (0.8)	2 (1.7)	3 (2.5)
Medium (2 – 4 years)	13 (10.7)	13 (10.7)	26 (21.5)
Long-term (>4 years)	56 (46.3)	36 (29.8)	92 (76)

**Table 4.** The distribution of non-specific neck pain complaints from respondents based on working posture and work duration

Characteristics	Classification of non-specific neck pain		
	No Pain n (%)	Moderate Pain n (%)	Painful n (%)
<b>Working posture Category</b>			
Low-risk	6 (66.7)	3 (33.3)	0
Moderate-risk	14 (32.6)	19 (44.2)	10 (23.3)
High-risk	3 (4.3)	17 (24.6)	49 (71)
<b>Work Duration Category</b>			
Long	12 (9.9)	24 (19.8)	34 (28.1)
Very Long	11 (9.1)	15 (12.4)	25 (20.7)

Table 5 shows the correlation test results between working posture and work duration with complaints of non-specific neck pain. A positive correlation exists between working posture and complaints of non-specific neck pain ( $p = 0.001$ ;  $r = 0.598$ ). The higher the risk of working posture, the more severe the degree of non-specific neck pain complaints. Even though there is a positive correlation between work duration and complaints of non-specific neck pain, this correlation is insignificant ( $p > 0.05$ ,  $r = 0.169$ ).

**Table 5.** Correlation Test Results Between Working Posture and Working Duration with Non-specific Neck Pain Complaints

Variables	Non Specific Neck Pain Category		
	n	Correlation Coefficient (r)	p value
Working Posture	121	0.598	0.000
Work Duration	121	0.169	0.063



## **Discussion**

The sample in this study were employees aged 21-60 years. Those aged >60 years predominantly experience a decline in physiology, thus triggering an imbalance in muscle protein synthesis (MPS) and muscle protein breakdown (MPB).<sup>9</sup> In this study, the age group of 33-42 years dominated the total number of respondents, namely 34 (19.8%). Previous study also revealed that workers are between 30 and 45 years old. This age is considered very productive for workers because if the age is under 20, the average individual still needs more skill maturity and educational process.<sup>10</sup>

In this study, the number of respondents was dominated by female respondents. Based on research, there is also a gender factor in assessing a person's level of participation and productivity at work. Jobs basically cannot be differentiated based on gender. But in general, men are more productive in jobs that require physical strength. However, in certain circumstances, women's productivity can sometimes be higher than men's because women are more thorough, patient and diligent.<sup>11</sup>

Based on the results of this research, it was found that working posture using a computer was related to complaints of non-specific neck pain among Hasanuddin University rectorate employees. Most employees with low-risk work postures had non-specific neck pain complaints in the no-pain category. In contrast, most employees with high-risk work postures had non-specific neck pain complaints in the painful category. Respondents felt that complaints of neck pain were handled both while working and after working for relatively long periods, and the lack of movement resulted in subjective complaints of neck pain. The results of this study are similar to that of Affanatu's study, which states that respondents have poor posture and need to apply several good ergonomic principles.<sup>12</sup> The principle of body ergonomics aims to maintain normal body posture so that it is not harmful to body health. It can be concluded that in this study, incorrect posture is the main and most prominent risk factor that causes neck pain in college students.

Poor work posture from most respondents can be due to several things, such as flexed head posture, which often causes changes in the cervical spine, curvature, ligaments, tendons and muscles in the neck area, which in turn causes changes in posture and pain in the neck. In addition, workplace designs that are less ergonomic or have an imbalance in the body when using chairs and work desks with high duration and frequency of computer use also cause complaints of neck pain. As in previous studies, there was a significant relationship with static bending posture for a long time, particularly in bending forward posture (flexi neck), leaning too much to the right or left, which caused many students to complain of pain in their

necks with a static posture. This mechanism causes the muscles to contract longer so that blood flow to muscle tissue will be limited.<sup>13,14</sup>

Work duration was not correlated with complaints of non-specific neck pain in the present study. These results are in line with one of the previous studies conducted by Situmorang, which stated that there was no significant relationship between the duration of computer use and neck pain complaints in respondents. From the results of the respondent's analysis, the duration of computer use did not significantly affect neck pain complaints. However, a history of previous neck pain complaints and the influence of activities outside working hours were the highest factors causing musculoskeletal complaints, namely neck pain. The task load with the time limit that the respondent has is also the reason the respondent spends a prolonged duration while using the computer.<sup>3</sup> This long duration of work can lead to an accumulation of musculoskeletal complaints, especially for respondents with the wrong work posture, which can increase the occurrence of non-specific neck pain complaints. Even though computer use is prolonged, coupled with correct posture and routine stretching or resting for 10-15 minutes after 2 hours of work, it can function in relaxing muscles, thereby reducing the risk of neck pain complaints.<sup>15</sup>

In contrast to the research conducted by Kenwa et al., which states that there was a weak significant correlation between the long duration of smartphone use and an increase in the neck pain scale, using a smartphone for 7 hours or more increases the risk by 2.8 times to be affected. Moderate to severe neck pain. Generally, the longer the duration of exposure to a risk factor, the greater the risk level. It should be noted that the combined causative factors, including the risk of occurrence of complaints, will increase workers' exposure to several risk factors simultaneously in carrying out their work. The complaints may include pain and spasms in the muscles of the user's neck, arms and eyes. This complaint, if left continuously, will become chronic neck pain. If this is the case, the best way is to stop work and rest.<sup>16</sup>

This study has limitations in analyzing the effect of sample characteristics on non-specific neck pain complaints, such as age, gender, and years of service. These factors may have contributed to the dependent variable in this study. Filling out the BRIEF questionnaire might cause bias during data collection related to the possibility that respondents did not display their usual work posture.

## **Conclusion**

Based on the research results that have been done, it is concluded that there showed high acceptance and satisfaction of the digital illustrator in practical skills. The learners expressed high perceived usefulness, ease of use, and intention to use the digital illustrator in

learning practical histology skills. The learners also found the materials relevant, effective, enjoyable, and exciting and would recommend them to their fellow students for use. The expressed high acceptance of and satisfaction with the video-based instructional materials was, to a large extent, also uniform among the respondents of the three study centers. Thus, irrespective of location, the learners generally appeared optimistic about their experiences using the digital illustrator to learn histology practicals in medical faculty.

### **Conflicts of Interest**

Nothing to declare

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## Potential of Red Algae *Eucheuma spinosum* as Antibacterial to *Pseudomonas aeruginosa*

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### ABSTRACT

**Introduction:** *Eucheuma spinosum* is one of Indonesia's potential marine resources that can be used as an antimicrobial. The red algae *E. spinosum* contains many secondary metabolites which can inhibit the growth of bacteria. This research aimed to determine the optimum inhibitory power of the red algae extract *E. spinosum* using n-hexane, ethyl acetate, and methanol solvents in inhibiting the growth of *Pseudomonas aeruginosa* bacteria.

**Method:** The extraction process uses the maceration method with n-hexane, ethyl acetate, and methanol as solvents. Antibacterial testing was carried out using the paper disk diffusion method with soaking for 1 hour and incubating for 24 hours. The extract with the largest clear zone diameter was then tested further using Gas Chromatography-Mass Spectrometry (GCMS) to investigate the compound content in the sample.

**Results:** The solvent that produced the largest inhibition zone diameter was ethyl acetate extract, namely 16.1 mm at a concentration of 4%. Analysis of the compounds contained in the ethyl acetate extract using GCMS showed the presence of hexadecanoic acid which is a terpenoid group.

**Conclusion:** The optimum concentration of red algae *E. spinosum* extract to inhibit the growth of *Pseudomonas aeruginosa* was 16.1 mm in 4% ethyl acetate solvent.

**Key words:** Antibacterial, *Eucheuma spinosum*, *Pseudomonas aeruginosa*



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## Introduction

Indonesia is a country whose vast territory is surrounded by ocean and is the country with the largest number of islands in the world. The huge potential of marine biota has made scientists and antibiotic producers in several countries interested in developing it as a potential antibiotic. This is due to the lack of maximum utilization of marine biota while the need for new types of antibiotics is increasingly urgent because the current antibiotics being marketed are decreasing in their effect on some bacteria which are increasingly becoming resistant to these antibiotics. One of the marine biota that can be utilized is red algae (*Eucheuma spinosum*).<sup>1</sup>

*E. spinosum* belongs to the Rhodophyceae group which is capable of producing carrageenan in large quantities.<sup>2</sup> This type of algae is used for traditional medicine because it does not cause side effects on health.<sup>3</sup> The ability of red algae *E. spinosum* to produce bioactive secondary metabolites are very likely due to extreme environmental conditions such as high salinity or used to defend itself from predators. Red algae *E. spinosum* contains bioactive compounds such as flavonoids, alkaloids, steroids, and triterpenoids which can treat various diseases in humans but are toxic to all bacteria.<sup>4,5</sup>

Bioactive compounds can inhibit the growth of bacteria due to inhibition of protein synthesis because they accumulate and cause changes in the components that make up the bacterial cell, which ultimately results in toxic effects on the bacteria.<sup>6</sup> Inhibition of bacterial growth can be seen by the size of the diameter of the inhibition zone produced on the paper disc which is then measured using a caliper or ruler to determine antibacterial effectiveness. The diameter of the inhibition zone is the diameter where there is no growth around the disc paper minus the diameter of the disc paper. The inhibitory activity against bacterial growth increases with the concentration extract.<sup>7</sup>

Cultivation is carried out in places where the current conditions are relatively calm so that productivity can be increased. Based on the background above, this research aims to determine the inhibitory power of the red algae *Eucheuma spinosum* extract against *Pseudomonas aeruginosa* bacteria.

## Methods

This research was conducted from January 25 to April 13, 2023 at the Biochemistry Laboratory and Analytical Chemistry Laboratory of Science and Technology at Universitas Islam Negeri Alauddin Makassar. The materials used are samples of red algae (*E. spinosum*), *Pseudomonas aeruginosa* bacteria, dimethyl sulfoxide (DMSO), methanol (CH<sub>3</sub>OH), n-

hexane, ethyl acetate, physiological sodium chloride (NaCl), Nutrient Agar (NA), Nutrient Broth (NB) and Oxoid disc paper.

### ***Preparation and Extraction of Red Algae (*E. spinosum*) Samples***

20 kg of red algae *E. spinosum* was washed with water and then sliced into small pieces. After that, let it air dry and grind it using a grinder to get the red algae powder *E. spinosum*. The weight of the dry red algae sample obtained was 273 gr. The samples were put into 3 different containers and then macerated using each solvent n-hexane, ethyl acetate, and methanol. Each container is then evaporated using a rotary evaporator. The thick extract obtained was diluted to various concentrations of 2%, 4%, and 6% using DMSO solvent.

### ***Making Nutrient Agar (NA) and Nutrient Broth (NB) Media***

The tools used were sterilized in an oven at 170°C for ± 1 hour while the media was sterilized in an autoclave at 121°C for 15 minutes. Weigh 2.5 g of NA, then dissolve it in 100 mL of warm H<sub>2</sub>O, then put all the ingredients in an Erlenmeyer and sterilize in an autoclave for 15 minutes at 121°C and 1 atm pressure. Weigh 0.8 grams of NB in a beaker then dissolve it in 100 mL of warm distilled water. Sterilize in an autoclave at 121°C for 15 minutes and 1 atm pressure.

### ***Bacterial Rejuvenation Test***

The test bacteria used is *Pseudomonas aeruginosa*. Rejuvenation of bacteria is carried out by taking 1 cycle of pure culture and then transferring it to a petri dish containing NA. Incubation for 24 hours at 37°C.

### ***Preparation of Bacterial Suspension***

The bacterial culture resulting from rejuvenation was taken 1 cycle on NA media. Suspend it in NB media. Incubation for 24 hours at 37°C. Bacterial growth is characterized by turbidity in the suspended media.

### ***Making Antibacterial Positive and Negative Control Solutions***

A positive control was made by weighing 1 gram of amoxicillin and then diluting it in 2 mL of physiological NaCl then homogenizing. Negative control was made from 2 mL of distilled water

### ***Inhibitory Power Test of Red Algae *E. spinosum* Extract***

A total of 15 mL of agar media was poured into a sterile petri dish. Take 100 µL of the bacterial culture in the suspension and pour it into a sterile petri dish and then homogenize it with agar media. Each extract at various concentrations of 2%, 4%, and 6% (w/v) and 100 µL of the control solution were dropped onto sterile disc paper and left for 30 minutes. Place the dry paper discs regularly on the agar medium containing the test bacteria

and then label them. Incubate the petri dish containing the media and paper discs for 24 hours at 37°C. The inhibitory power of the extract was determined by subtracting the diameter of the inhibition zone formed from the diameter of the paper disc (6 mm).

### Compound Analysis using Gas Chromatography-Mass Spectrometry (GCMS)

1 µL of red algae extract *E. spinosum* was injected into GCMS. Identify the graph peaks at each retention time from the initial peak to the final peak and match them with the reference in the GCMS program by selecting a similar search.

### Results

The measurement of the diameter of the inhibition zone in the study used *Pseudomonas aeruginosa*, which is a pathogenic bacteria. The incubation process for 24 and 48 hours used the solvents n-hexane (Figure 1), ethyl acetate (Figure 2), and methanol (Figure 3). Figure 1 shows that at a concentration of 2% the initial diameter of 4.00 mm increased to 6.8 mm; concentration of 4% initial diameter of 4.3 mm increased to 6.2 mm; while at a concentration of 6% the initial diameter of 4.3 mm increased to 6.5 mm.

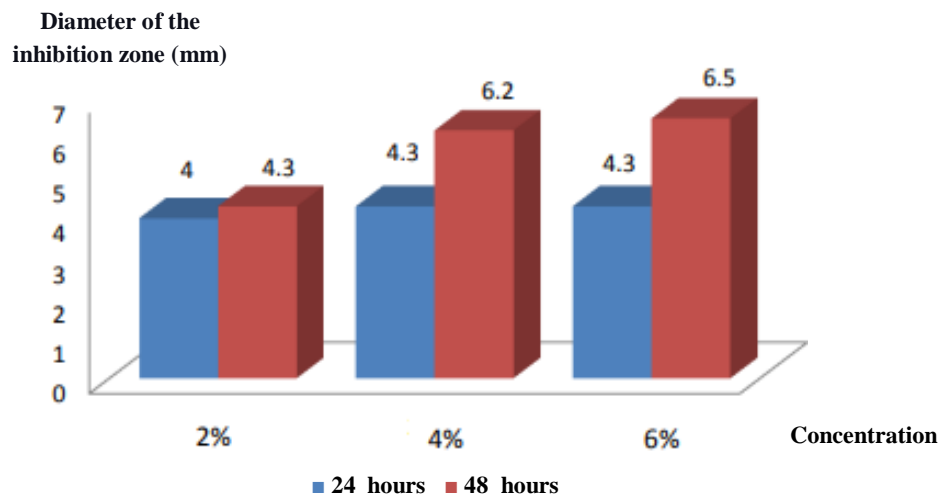


Figure 1. Diameter of the inhibition zone of n-hexane extract

Figure 2 shows the diameter of the inhibition zone of *E. spinosum* ethyl acetate extract produced with an incubation period of 24 and 48 hours. The largest diameter of the inhibition zone was at a concentration of 4%, namely 16.1 mm. Figure 3 shows the results of the inhibition zone diameter of the methanol extract of *E. spinosum* which was produced at a concentration of 2%, the initial diameter of 6.3 mm decreased to 4.7 mm, at a concentration of 4%, the initial concentration of 6.7 mm decreased to 4.1 mm and the concentration of 6. % initial diameter of 6.3 mm reduced to 4.6 mm.



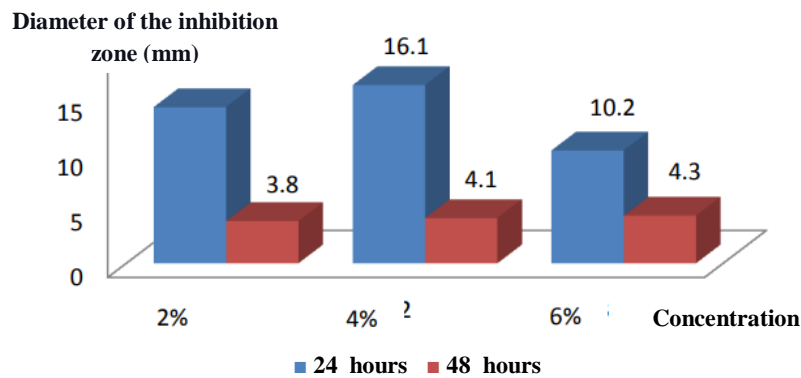


Figure 2. Diameter of the Inhibitory Zone of Ethyl Acetate Extract

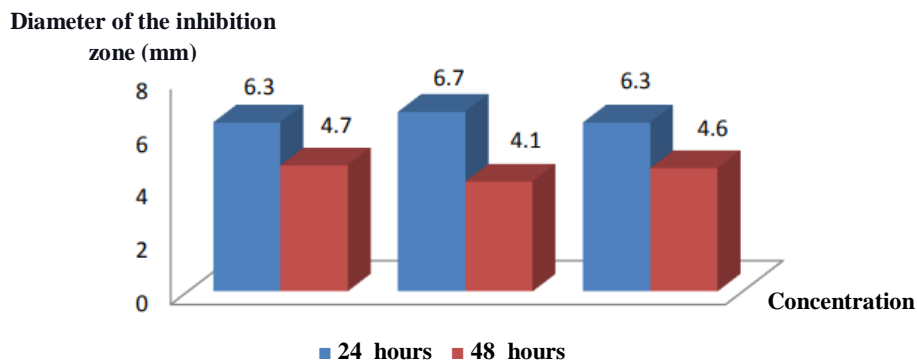


Figure 3. Diameter of the Inhibitory Zone of Methanol Extract

Analysis with GCMS can be divided into two groups, namely: qualitative and quantitative. Both analyses use a mass spectrometer as a detector. The mass spectrum of the results of the analysis of the mass spectroscopy system is an illustration of the type and number of molecular fragments formed from a chemical component (each peak on the chromatogram). The chemical content of the red algae *E. spinosum* was analyzed using KGSM as shown in Figure 4. The chromatogram results showed that the 7th peak had the highest percent area, namely 31.40% with a retention time of 20.23. The mass spectrum in Figure 5 shows the presence of molecular ion peaks, namely 256, 43, 60, 85, 15, 143, and a basic peak of 73, and is indicated as a hexadecanoic acid compound.

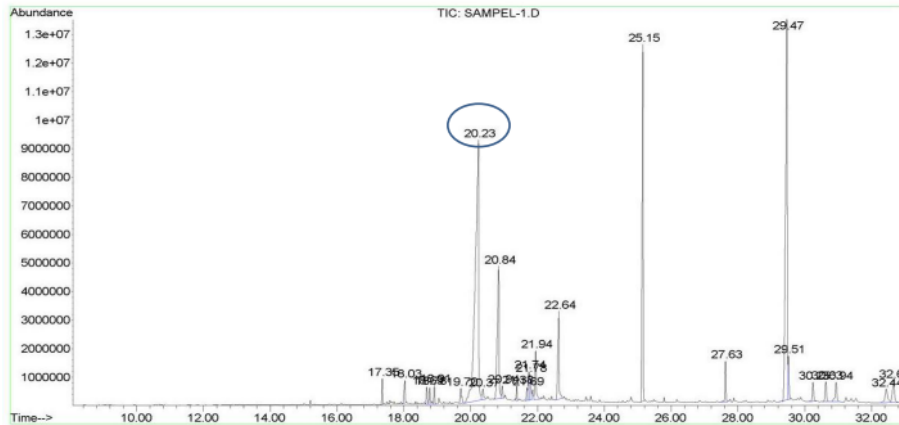


Figure 4. GCMS chromatogram of Ethyl Acetate Extract of Red Algae *E. spinosum*

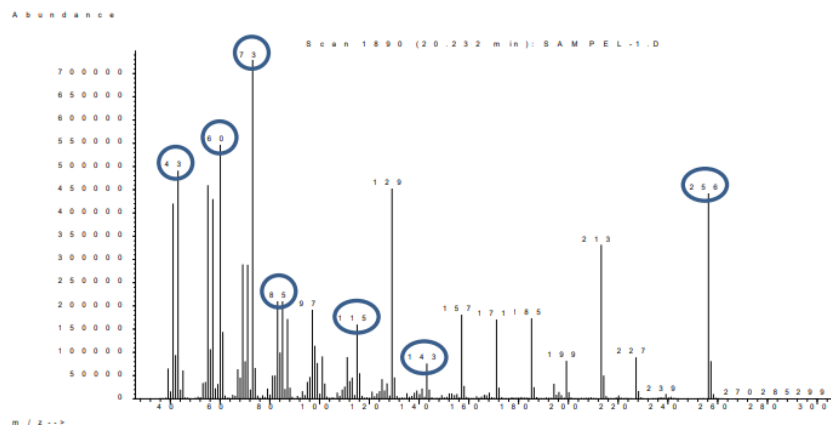


Figure 5. Mass spectrum of hexadecanoic acid at a retention time of 20.23

## Discussion

Red algae contain secondary metabolites with different polarities, namely non-polar, semi-polar and non-polar, so solvents with different polarities are also used to extract these compounds, such as n-hexane, ethyl acetate and methanol. The method used to extract these compounds is the maceration method.<sup>9</sup>

The maceration extraction method extracts a sample using an organic solvent with several simple stirs. The maceration method does not use heating so that the natural material samples used do not decompose or become damaged.<sup>10</sup> The nonpolar solvent used is n-hexane. The n-hexane solvent can attract nonpolar compounds found in the red algae *E. spinosum* extract, namely terpenoids.<sup>11</sup> The semi-polar solvent used is ethyl acetate. Ethyl acetate solvent can extract active antibacterial compounds. Ethyl acetate can attract semi-polar active compounds in the red algae *E. spinosum*, namely tannins. Tannins have antibacterial properties related to their ability to inactivate microbial cell adhesion, inactivate

enzymes, and interfere with protein transport in the inner layer of cells.<sup>12</sup> Meanwhile, the polar solvent used is methanol. Methanol can dissolve almost all organic compounds in polar and nonpolar compound samples. Methanol is volatile, so it is easily released from the extract. Red algae samples also contain polar secondary metabolite compounds, namely flavonoids. Flavonoids are a chemical compound in the red algae *E. spinosum*, which is bacteriostatic.<sup>9</sup> The thick extract obtained in each solvent was diluted at concentrations of 2%, 4% and 6% using DMSO.

According to the data above, a concentration of 2% makes the initial diameter 4.00 mm increased to 6.8 mm; at a concentration of 4%, the initial diameter of 4.3 mm increased to 6.2 mm; while at a concentration of 6%, the initial diameter of 4.3 mm increased to 6.5 mm. This is because at this concentration the extract is bacteriostatic against the test bacteria. An antimicrobial is bactericidal if the diameter of the inhibition zone increases at 48 hours of incubation, this is because the compound can kill and increase the physiological activity of the bacteria, even though the administration of the compound is stopped.<sup>11</sup> The size of the inhibition area is influenced by several factors, namely the growth rate of microorganisms, the ability and rate of diffusion of active ingredients in the medium, the sensitivity of microorganisms to the active substance, and the thickness of the viscosity of the medium.<sup>13</sup>

The 4% ethyl acetate extract has the optimum level of polarity. A compound that has an optimum level of polarity has maximum antibacterial activity because the interaction of antibacterial compounds with bacteria requires a balance (HLB: Hydrophilic Lipophilic Balance). Ethyl acetate extract at concentrations of 2% and 6% had an inhibition zone diameter of 14.1 mm and 10.2 mm smaller than 4%. This shows that higher concentrations will not always increase the inhibition zone formed. The diameter of the inhibition zone is not always directly proportional to the concentration of the extract.<sup>15</sup>

The chromatogram of the ethyl acetate extract of the red algae *E. spinosum* shows 25 peaks. However, there was one peak with a relatively high abundance that was analyzed by the mass spectrometer, namely at a retention time of 20.23 with an area percent (abundance) of 31.40%. Retention time shows how long it takes for a compound to move through the column to the detector. Hexadecanoic acid is a carboxylic acid derivative compound and is a saturated fatty acid composed of 16 carbon atoms ( $C_{16}H_{32}O_2$ ). The mechanism of action of hexadecanoic acid in inhibiting bacterial growth is that it can absorb nutrients in bacteria and can inhibit water and inhibit the enzyme systems of some bacteria.<sup>15</sup> The compound analysis carried out still focused on n-hexane, ethyl acetate, and methanol extracts so the chromatogram results showed many peaks.

## Conclusion

The optimum concentration of red algae *E. spinosum* extract to inhibit the growth of *Pseudomonas aeruginosa* bacteria was 16.1 mm in 4% ethyl acetate solvent.

## Conflicts of Interest

Nothing to declare

## Funding sources

Nothing to declare

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## The Relationship between Disaster Knowledge and Disaster Preparedness Attitudes in Medical Students of Universitas Negeri Gorontalo

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### ABSTRACT

**Introduction:** The incidence of natural disasters worldwide is increasing and unpredictable. As one of the high-risk disaster countries, good knowledge and disaster preparedness in Indonesia residence are needed to reduce the risk of a disaster. As agents of change, students should have competent skills in disaster situations. This study aims to determine the relationship between disaster knowledge and disaster preparedness attitudes among medical students at Universitas Negeri Gorontalo (UNG).

**Method:** This research is a descriptive study with a cross-sectional design and uses a total sampling technique on active UNG medical students during the research period. The research was conducted at the UNG Faculty of Medicine from September to November 2022. The research instrument used a questionnaire that had been used in previous studies. The independent variable is disaster knowledge, while the dependent variable is disaster preparedness attitudes. Bivariate analysis was carried out using the chi-square test to determine the relationship between the two variables.

**Results:** Of the 208 respondents, most have a high level of disaster knowledge of 81.7%. The description of disaster preparedness attitudes shows that most respondents have a good attitude towards disaster preparedness, namely 52.4%. There is no significant relationship between disaster knowledge and preparedness attitudes (p-value 0.160).

**Conclusion:** There is no relationship between disaster knowledge and disaster preparedness attitudes among UNG medical students. It is hoped that the institution will continue to develop disaster education so that students can have better disaster knowledge and be able to deal with disaster situations.

**Key words:** Attitude, disaster, knowledge, preparedness



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## **Introduction**

Disasters in various parts of the world are currently increasing.<sup>1</sup> Indonesia is a country that is prone to disasters. According to the Indonesian Disaster Information Data (DIBI), compiled by the National Disaster Management Agency (BNPB), in 2021, 2,032 disaster events were recorded, both natural and non-natural disasters. Whereas in 2022 until the middle of this year, there have been recorded as many as 1,814 disasters.<sup>2</sup> Disasters have the potential to occur in unpredictable circumstances and times. Disasters can impact damage in all areas, including the economic, social, and environmental sectors.<sup>3,4</sup>

Disaster management essentially seeks to reduce and prevent people from disasters and overcome vulnerabilities. The disaster management cycle is divided into three stages, namely the pre-disaster stage, the stage when a disaster occurs, and the post-disaster stage. The magnitude of the potential for disaster events can be minimized by preparedness from groups who are vulnerable to disasters.<sup>5</sup> Preparedness is a series of activities in an effort to anticipate disasters and provide an adequate response to the possible impacts of the threat of disasters.<sup>6</sup>

Disasters have the potential to occur in unpredictable circumstances and times. Disasters can impact damage in all areas, including the economic, social, and environmental sectors. Educational environments such as universities are not immune to areas that can be affected by a disaster. Gorontalo State University, which is one of the largest universities in Gorontalo, also has great potential for disasters to occur so that the community, in this case students, is a group that is vulnerable to disasters, so disaster management is needed to reduce the risk of a disaster occurring.

The Faculty of Medicine, State University of Gorontalo (UNG) is one of the medical education institutions in Indonesia that has excellence in disaster emergency medicine. As a group that is vulnerable to disasters, medical students at Gorontalo State University are required to have good knowledge and attitudes in dealing with a disaster. Many factors can affect student knowledge, including good education and individual experience in dealing with disasters. Research from Abhinav Sinha et al., which involved 375 medical students from Netaji Subash Chandra Bose Medical College, Jabalpur, India, showed that the knowledge and attitudes of respondents towards disaster preparedness were still lacking.<sup>7,8</sup>

The existence of a disaster management curriculum at the UNG Faculty of Medicine cannot guarantee that medical students have good knowledge and attitudes about disasters which are needed as capital when these students become doctors and also support the achievement of the vision and mission of the UNG Faculty of Medicine. Based on this,

research is needed related to the relationship between disaster knowledge and disaster preparedness attitudes. So, the aim of this research is to see the relationship between disaster knowledge and disaster preparedness attitudes among medical students at Gorontalo State University.

## **Methods**

This research is a descriptive study with a cross-sectional research design. The research was conducted at the UNG Faculty of Medicine in September-November 2022 using a total sampling technique with a sample of 208 medical students. The independent variable in this research is disaster knowledge where students' knowledge measured is related to disasters and disaster risk, which includes the understanding of disasters, environmental vulnerability, and the vulnerability of public facilities to disaster emergencies. The dependent variable in this research is disaster preparedness attitudes, which measure student responses regarding preparedness in facing disasters, including attitudes and concern for disaster risks.

The instrument in this research uses a questionnaire that has been used previously by Fadhil Alwan 2019, and tested for validity and reliability. This questionnaire has a validity value of  $r$  calculated  $> r$  table, that is, the calculated  $r$ -value ranges from 0.269 – 0.680 with an  $r$  table value of 0.2709, making this questionnaire can be said to be valid and the reliability value with Cronbach's alpha on this questionnaire is 0.611.<sup>9</sup>

Univariate analysis of disaster knowledge is categorized as high knowledge if the score is  $\geq 60\%$  and low knowledge if the score is  $<60\%$ , while univariate analysis related to disaster preparedness attitudes is categorized as good attitude if  $\geq$  mean and poor attitude if  $<$  mean. Bivariate analysis was performed using the chi-square test to determine the relationship between disaster knowledge and disaster preparedness attitudes. If the  $p$ -value is less than 0.05, it can be concluded that there is a significant relationship between these variables, whereas on the contrary, if the  $p$ -value is more than 0.05, it can be concluded that there is no significant relationship between these variables.

## **Results**

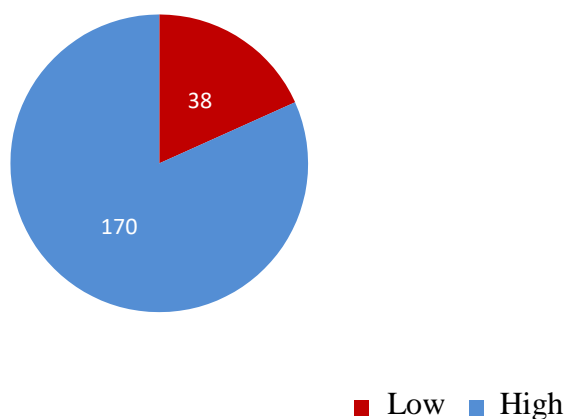
Based on the research results, the subjects obtained from this study amounted to 208 respondents. Based on Table 1, regarding the frequency distribution of research respondent data which includes age and gender, it shows that most gender was female (72.1%), while based on age, most respondents were 20 years old (26.4%). The youngest respondent was 16 years old (0.05%) and the oldest respondent was 22 years old (5.3%). Based on the analysis of Figure 1, it shows that most respondents had a high level of knowledge about disasters, namely 170 people with a percentage of 81.7%.



**Table 1.** Data on Respondent Characteristics

Characteristics	N	%
<b>Gender</b>		
Male	58	27.9
Female	150	72.1
<b>Age</b>		
16	1	0.05
17	13	6.2
18	45	21.6
19	46	22.1
20	55	26.4
21	37	17.8
22	11	5.3

Disaster Knowledge



**Figure 1.** Distribution of Respondents' Level of Knowledge about Disasters

Table 2 shows the level of disaster knowledge by class of students. The highest level of knowledge was the class of 2019 (91.8%), and the lowest level of knowledge was the class of 2022 (71.2%).

**Table 2.** Level of Disaster Knowledge by Class of Students

Class	Disaster Knowledge				Total
	Low		High		
	N	%	N	%	
<b>2019</b>	4	8.2	45	91.8	49
<b>2020</b>	8	17.0	39	83.0	47
<b>2021</b>	9	17.0	44	83.0	53
<b>2022</b>	17	28.8	42	71.2	59
<b>Total</b>					<b>208</b>

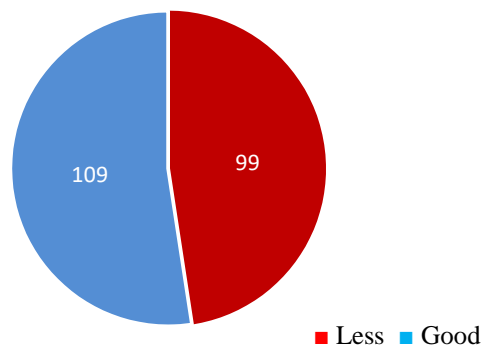
Table 3 shows knowledge level of Disaster Medical Assistance Team (MAT). Regarding the level of disaster knowledge of medical students who are members of the Cutaneous Medical Assistance Team (Tim Bantuan Medis, TBM), it was shown that most

TBM members have a high level of knowledge (90.7%). Their proportion was higher than the students who do not incorporate in TBM membership (78.6%). Based on the analysis of Figure 2, it was found that the majority of respondents had a good attitude towards disaster risk, namely 109 people with a percentage of 52.4%.

**Table 3.** Knowledge Level of Disaster Medical Assistance Team (MAT)

Member	Disaster Knowledge				Total
	Low		High		
	N	%	N	%	
<b>TBM</b>	5	9.3	49	90.7	54
<b>Non TBM</b>	33	21.4	121	78.6	154
<b>Total</b>					<b>208</b>

Disaster Preparedness Attitude



**Figure 2.** Distribution of Respondents' Attitudes towards Disaster Preparedness

Table 4 shows the disaster preparedness attitudes based on class of students. The best attitude was the class of 2019 (57.1%). In contrast, the lacking attitude was the class of 2022 (47.5%).

**Table 4.** Disaster Preparedness Attitudes Based on Force

Class of	Preparedness attitude				Total
	Less		Good		
	N	%	N	%	
<b>2019</b>	21	42.9	28	57.1	49
<b>2020</b>	21	44.7	26	55.3	47
<b>2021</b>	26	49.1	27	50.9	53
<b>2022</b>	31	52.5	28	47.5	59
<b>Total</b>					<b>208</b>

Table 5 shows the disaster preparedness attitudes based on MAT participation. Most of TBM members had good and better attitudes when compared to students who were not members of the TBM.

**Table 5.** Disaster Preparedness Attitude of the Medical Assistance Team (MAT)

Member	Preparedness Attitude				Total
	Less		Good		
	N	%	N	%	
<b>TBM</b>	24	44.4	30	55.6	54
<b>Non TBM</b>	75	48.7	79	51.3	154
<b>Total</b>					<b>208</b>

Table 6 shows the relationship between disaster knowledge and disaster preparedness attitudes. From the table, a p-value of 0.160 was obtained, which means that the value was greater than 0.05 (H0 was accepted). This illustrates no significant relationship between knowledge about disasters and attitudes toward disaster preparedness.

**Table 6.** The relationship between disaster knowledge and disaster preparedness attitudes

Disaster Knowledge	Preparedness Attitude			Total	p-value
	Less	Good			
<b>Low</b>	22 10.6%	16 7.7%	38 18.3%	0.160	
<b>High</b>	77 37.0%	93 44.7%	170 81.7%		
<b>Total</b>	99 47.6%	109 52.4%	208 100%		

## Discussion

The results of univariate analysis regarding the description of the level of disaster knowledge among UNG medical students show that the majority have a high level of expertise. This is supported by various aspects, including because the UNG Faculty of Medicine has a superior vision in disaster emergency medicine so that students are exposed to emergencies and disasters from the start of college. The curriculum regarding emergency education and disaster management provided at the UNG Faculty of Medicine significantly influences medical students' high level of knowledge. Apart from that, to support understanding regarding emergencies and disaster management, the UNG Faculty of Medicine has a student organization, the Cutaneous Medical Assistance Team (TBM). This organization operates in medical emergencies and non-emergencies, which has a role in training and developing each member's knowledge and skills, especially in emergencies. The process of emergency education and disaster education, which is often exposed to medical students, significantly influences their disaster knowledge level.

Disaster Management is an indicator that shows the best results regarding student knowledge. Disaster management attempts to reduce and prevent communities from disasters and overcome vulnerabilities. These results show that the curriculum regarding disaster

management provided at the UNG Faculty of Medicine has had a significant influence on the high level of knowledge of medical students, especially in disaster management.<sup>8</sup>

The description of the level of disaster knowledge by TBM Cutaneus members shows that their understanding of disasters is very high compared to students who are not members of TBM Cutaneus. In running the organization, TBM has exceptional staff, namely Education and Training Staff, who play a role in training and developing the knowledge and skills of all TBM members, especially in emergencies. At that time, there were 54 TBM members, or around 19% of all active medical students. The education and training system by TBM members is carried out in stages, gradually and continuously, which is standardization. TBM members' abilities include knowledge and skills for emergency and non-medical emergencies. Students who are members of TBM Cutaneus also have much experience directly involved in disaster simulation activities and social service when a disaster occurs. The experience of attending training and being directly involved in disaster activities influences their cognitive abilities so that their knowledge level is excellent. The results of this study align with research conducted by Hoffman et al. in 2017, where it was stated that experience can increase one's awareness.<sup>10</sup>

The results of univariate analysis regarding the description of disaster preparedness attitudes among UNG medical students show that most students have good disaster preparedness attitudes. This is because students are often directly involved in disaster activities by the Faculty of Medicine and other student organizations such as TBM. All TBM members are active in disaster activities. Disaster simulation activities carried out in the disaster management and disaster response social service blocks, which are often participated in by Medical Faculty students, bring a tendency to act in a good direction.

The description of the disaster preparedness attitude of each class shows that the best attitude is possessed by the class of 2019. It was because all medical students of the type of 2019 have passed the disaster management and emergency block courses. In the disaster management course, students are also involved in disaster simulation activities besides getting disaster knowledge education. Apart from that, students from the class of 2019 have often participated in disaster response social service activities since the beginning of their studies, whether carried out by the Faculty of Medicine or in collaboration with other agencies. This involvement encourages a good attitude towards disaster preparedness in the class of 2019.

The description of the attitude of disaster preparedness by TBM Cutaneus members shows that most TBM members have a good perspective of preparedness. This good attitude

arose because all TBM members were required to receive training on emergencies and be directly involved in disaster emergency response activities. This factor triggers TBM members to tend to act in a good direction because of their experiences.

Based on the results of statistical tests related to the relationship between disaster knowledge and disaster preparedness attitudes, it was found that there was no significant relationship between the level of disaster knowledge and disaster preparedness attitudes. This research is in line with research conducted by Fadhil in 2020 which stated that there was no significant relationship between knowledge of disaster preparedness for Andalas University Medical Professional students.<sup>9</sup>

Researchers assume that knowledge of disasters is one of the factors that influences disaster preparedness attitudes in this research. Knowledge obtained from various sources of information can be stored in natural form (explicit knowledge) and described in actions or attitudes. However, researchers also assume that medical students' high level of knowledge will not necessarily provide a good attitude toward disaster preparedness because many factors, including personal experience, can influence a person's perspective. Individual experiences greatly influence how a person behaves towards something because attitudes are usually driven by direct involvement, or the person has experienced something similar.<sup>10</sup> This is in line because not all medical students have experienced disaster situations, such as being directly involved in disaster activities or living in disaster-prone areas, even though they have relatively high knowledge of disasters. In research conducted by Azwar in 2012, it was stated that a person's attitude can be influenced by personal experience, the influence of other people, and the influence of the environment and culture around them.<sup>11</sup>

Researchers also assume that there is no significant relationship between disaster knowledge and disaster preparedness attitudes due to the different perceptions of each medical student. In responding to the same situation, each person's perception will differ. Still, it will vary depending on how someone assesses the situation based on cognitive and affective factors and their tendencies to act. According to Yayat, factors directly related to knowledge are cognitive factors that can be obtained from the information received and then digested by the brain to produce a situation that is judged true or not by the person who receives it.<sup>12</sup>

However, a person's response is not only influenced by cognitive factors. There are affective factors and also tendencies to act. This affective factor is a person's tendency towards sensitivity in receiving and responding to something that exists.<sup>10</sup> Even though medical students already know something they are experiencing, they cannot guarantee that

medical students will act or react to it. This difference in perception causes various variations between the knowledge possessed by medical students and the attitude of these medical students.

However, the results of research conducted by Rana Rofifah in 2019 showed the opposite result, where knowledge greatly influences attitudes towards disaster preparedness.<sup>13</sup> A person's attitude directly involves their knowledge, influencing feelings and emotions, which can trigger a response or tendency to act.<sup>14</sup> Based on this, knowledge can be the initial influence in directing an attitude or action. Good knowledge and supported by previous experience can form a good attitude in dealing with a disaster. With good knowledge and attitudes, good preparedness aspects can also be realized.<sup>12,15</sup>

The limitation of this research is that the further factors other than knowledge and attitudes had not been measured. Those factors could influence the research results. Apart from that, in the data collection process, the answers given by respondents in the questionnaire may not show the actual opinions of the respondents due to differences in thinking, differences in understanding, and also the honesty factor of the respondents.

### **Conclusion**

The level of disaster knowledge and disaster preparedness attitudes of students in the Medical Study Program at the UNG Faculty of Medicine is classified as good, and there is no significant relationship between disaster knowledge and disaster preparedness attitudes in students of the UNG Medical Study Program. Furthermore, institutions can continue developing a curriculum regarding disaster management so that the disaster management learning process at the Faculty of Medicine can improve.

### **Conflicts of Interest**

Nothing to declare

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## Overview of Characteristics for Impaired Lung Function in Bendor Drivers in Gorontalo City in 2023

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### ABSTRACT

**Introduction:** Impaired lung function is a functional disorder of the lungs that causes a slowing of airflow during respiration. Bendor drivers are a profession with a risk of decreasing lung function due to work activities that are always on the road and exposed to motor vehicle pollution. Exposure to cigarette smoke in active and passive smokers is also significant in causing several other respiratory diseases, such as chronic obstructive pulmonary disease (COPD). The purpose of this study was to describe the risk factors for impaired lung function in Bendor drivers in Gorontalo City in 2023.

**Method:** The research was conducted in June 2023 on eligible Bendor drivers accidentally found in Gorontalo City. The research instrument used a questionnaire, stress perception scale (SPS), and spirometry.

**Results:** The results obtained are the distribution of risk factors for impaired lung function in Bendor drivers in Gorontalo City in 2023, based on length of work found more work more than five years (63.33%), more work more than 8 hours a day (75%), had smoking habits with a smoking duration of more than ten years (58.3%) and smoked more than ten cigarettes a day (62.5%) and had a severe perception of stress (66.6%).

**Conclusion:** Bendor drivers are one of the contributing factors in impaired lung function. There is a relationship between the risk factors for smoking, length of work, duration of exposure to pollution, and perception of stress with lung function in Bendor drivers in Gorontalo City.

**Key words:** Bendor drivers, lung function, smoking, stress perception



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## **Introduction**

Impaired lung function is when the lungs cannot expand elastically, or there is interference with the airways both structurally and functionally, which causes a slowdown in airflow during respiration. Types of lung function disorders can be Restrictive, Obstructive, and Mixed.<sup>1,2</sup> Extrinsic or intrinsic factors can cause impaired lung function. Extrinsic factors that can interfere with lung function are inhalation of irritants such as gas, dust, and vapor.<sup>3</sup> Smoking habits can also accelerate the decline in lung function.<sup>4</sup> The World Health Organization (WHO) mentions chronic obstructive pulmonary disease (COPD) as the third most common cause of death globally, with smoking as the main factor. More than 90% of COPD deaths occur in low and lower-middle countries.<sup>5,6</sup> Apart from that, air pollution is another factor, such as motor vehicle fumes, street dust, industrial exhaust gases, coal briquettes, and volcanic ash from volcanic eruptions, forest fire smoke, mosquito coil smoke, firewood smoke, stove smoke, workplace pollution, chemicals, dust/irritating substances, and toxic gases.<sup>7</sup>

Indonesia, as a country in Asia that is developing into a newly industrialized country, also faces air pollution problems, most often caused by motor vehicle exhaust and factory fumes.<sup>8</sup> Disturbances commonly known as the result of Motor vehicle emissions are respiratory tract disorders, headaches, eye irritation, asthma exacerbation attacks, respiratory infections, impaired lung function, and heart disease.<sup>9</sup> Psychological factors are also thought to affect lung function.<sup>10</sup> Bentor drivers in Gorontalo City are a profession with a risk of decreasing lung function due to work activities that are always on the highway and exposed to motor vehicle pollution. This study aims to describe the prevalence and associated characteristics of abnormal lung function in the Bentor drivers in Gorontalo City.

## **Methods**

This quantitative research was conducted at Gorontalo City in June 2023. The population in this study were Bentor drivers in Gorontalo City. Thirty eligible people were observed based on the purposive sampling technique. The inclusion criteria were male, aged  $\geq 18$  years, and fulfilling the requirement for the spirometry examination. Exclusion criteria in this study were Bentor drivers who were not willing or in sick condition, were too full, and had suffered from severe respiratory or mental illness. The variables in this study are the length of work, length of exposure to pollution, smoking habits, and perceptions of stress.

The data source in this study used primary data, namely data from the results of interviews with respondents through questionnaires and the consequences of pulmonary function examination using spirometry. Lung functions were classified into two categories.

Normal lung function category is determined if the forced vital capacity (FVC) is more than 80% predictive value and forced expiratory value in the first second (FEV1) or forced vital capacity is more than 75%. The abnormal lung function category is determined if the restricted defects (FVC less than 80% and FEV1 more than 75% predictive value), the obstructive defects (FVC is more than 80% and FEV1 is less than 75% predictive value), or the mixed defects (FVC is less than 80% and FEV1 is less than 75% predictive value) were found. In addition, stress perception was measured according to the Perceived Stress Scale questionnaire and classified the finding into two categories: normal results (total score between 13 and 19) or severe stress (total score more than 20).

The data analysis technique in this research was carried out using univariate analysis. Univariate analysis aims to explain or describe the characteristics of each research variable. In this study, the variables are smoking habits, length of work, length of exposure, perception of stress and lung function of bento drivers in the city Gorontalo. The data obtained in this study were processed using the Microsoft Excel program.

## Results

Based on the research conducted, the distribution of respondents based on the age variable is shown in Table 1. It shows that the ages of 21-25 years and 26-30 years are the most age with seven people (23.3%), followed by the 41-45 years age group with five people (16.7%), and the lowest was in the age group 46-50 years and >50 years with two people (6.7%).

**Table 1.** Distribution of Bendor Drivers Based on Age

Age	Frequency	Percentage (%)
21-25 years	7	23.3
26-30 years	7	23.3
31-35 years	4	13.3
36-40 years	3	10
41-45 years	5	16.7
46-50 years	2	6.7
> 50 years	2	6.7
<b>Total</b>	<b>30</b>	<b>100</b>

The description of the distribution of respondents based on the length of work and daily workhours is shown in Table 2. It shows that 19 people (63.33%) worked more than five years as Bendor drivers and 11 (36.67%) worked less than five years as Bendor drivers. Based on the daily work hours, the distribution of Bendor drivers who work less than 8 hours

a day is six people (20%) and 24 people (80%) who work more than 8 hours a day.

**Table 2.** Distribution of Bantor Drivers based on length of work and daily workhours

Characteristics	Frequency	Percentage (%)
<b>Length of Work</b>		
≤ 5 years	11	36.67
> 5 years	19	63.33
<b>Daily Workhours</b>		
≤ 8 hours	6	20.0
> 8 hours	24	80.0
<b>Total</b>	<b>30</b>	<b>100</b>

Table 3 shows smoking behavior in the sample. Based on the length of smoking variable, the distribution of Bantor drivers who smoked for less than ten years was 13 people (43.3%), and Bantor drivers who smoked for more than ten years were 17 people (56.7%). Based on the number of cigarettes per day, the distribution of Bantor drivers who smoked less than ten cigarettes was 12 people (40%), and those who smoked more than 10 were 18 people (60%).

**Table 3.** Distribution of smoking behavior in Bantor drivers

Characteristics	Frequency	Percentage (%)
<b>Length of Smoking</b>		
≤ 10 years	13	43.3
> 10 years	17	56.7
<b>Number of Smoke</b>		
≤ 10 cigarette	12	40.0
> 10 cigarette	18	60.0
<b>Total</b>	<b>30</b>	<b>100</b>

Table 4 shows the distribution of Bantor drivers based on perceived stress. Nine people (30%) had normal stress perceptions and 21 (70%) had severe stress perceptions. Table 5 shows lung function distribution based on the characteristics of Bantor drivers in Gorontalo City. Based on lung function variables, the distribution of Bantor drivers with normal and abnormal lung function was six (20%) and 24 people (80%), respectively. Of the 24 abnormal lung function people, 15 (62.5%) worked for over five years. Moreover, 18 people (75%) worked more than 8 hours. In addition, 14 people (58.3%) had smoked for over ten years. Fifteen people (62.5%) smoked more than ten cigarettes a day. However, 16 people (66.7%) got the perception of severe stress.

**Table 4.** Distribution of Bentor Drivers based on Perceived Stress

Perceived Stress	Frequency	Percentage (%)
Normal	9	30
Severe	21	70
<b>Total</b>	<b>30</b>	<b>100</b>

**Tabel 5.** Distribution of Characteristics of Bentor Drivers based on Lung Function

Characteristics	Frequency	Percentage (%)
<b>Lung function (N=30)</b>		
Normal	6	20.0
Abnormal	24	80.0
<b>Length of Work (N=24)</b>		
< 5 years	9	37.5
≥ 5 years	15	62.5
<b>Daily Workhours (N=24)</b>		
≤ 8 hours	6	25.0
> 8 hours	18	75.0
<b>Length of Smoking (N=24)</b>		
≤ 10 years	10	41.7
> 10 years	14	58.3
<b>Number of Smoke (N=24)</b>		
≤ 10 cigarette	9	37.4
> 10 cigarette	15	62.5
<b>Perceived Stress (N=24)</b>		
Normal	8	33.3
Severe	16	66.7

## Discussion

The present study revealed that 80% of Bentor drivers had abnormal lung function. A similar result was found in the village officials in Denpasar Timur, Indonesia. Most of the sample study (76.6%) had abnormal lung function, including 57.4% had restrictive lung dysfunction, 10.6% had obstructive lung dysfunction, and 8.5% had mixed lung dysfunction. Length of work and history of smoking habits were also found not to be associated with impaired lung function in the study.<sup>3</sup>

The study's results found 11 respondents who worked for less than five years (36.67%) and 19 who worked more than 5 years (63.33%). In this study, 24 respondents (80%) had impaired lung function. Of the 24 people, nine (36.67%) had worked for less than five years, and 15 (63.33%) had worked more than five years. This research aligns with the investigation of Wiwin Prasiwi and Sri Darnoto (2015), who examined the relationship between age and years of work and lung function capacity at SUPELTAS (traffic control



volunteers) in Surakarta. There was a relationship between years of work and lung function capacity at SUPELTAS Surakarta. The longer a person's working period coupled with a dusty and polluted work environment, the greater the risk of decreased lung capacity function. Someone who works > 5 years has a greater chance of experiencing impaired lung function than someone who works < 5 years.<sup>11</sup>

Research on Marble Craftsmen conducted by Alia et al. (2022) through the results of a contingency correlation shows a positive value between length of work and impaired lung function, which indicates that the more extended the work period, the higher the risk of workers suffering from poor lung function, although the relationship is weak. Because the length of service does not always determine whether workers experience poor lung function.<sup>12</sup>

This research is different from Pradnyana and Muliarta (2015) on traditional stakeholders in East Denpasar District, which states that exposure to smoke only sometimes causes interference with lung function. There was no significant relationship based on the length of work for impaired lung function.<sup>3</sup>

The study found that six people (20%) worked less than 8 hours daily, and 24 (80%) worked more than 8 hours daily. In this study, 24 respondents (80%) had impaired lung function, and 6 (20%) had normal lung function. Of the 24 people, 6 (25%) worked less than 8 hours daily, and 18 (75%) worked more than 8 hours. Exposure time is expressed as the time a person spends at work. The length of time a person works in general is 8 hours per day. Most Bentor drivers in Gorontalo City work more than 8 hours daily (80%). This has a three times greater risk of developing lung function disorders because the longer a person is exposed to dust, smoke, and vehicle pollution, the greater the possibility of respiratory problems. This is in line with research on fish-smoking workers in Bandarharjo Semarang by Annisa et al. (2018), which illustrates that workers who work 8 hours a day are more at risk of experiencing respiratory and health complaints. This is likely a significant risk of developing lung function disorders because the longer workers are exposed to dust, the greater the possibility of respiratory problems.<sup>13</sup>

This study found that respondents who smoked for less than ten years were 13 people (43.3%), and respondents who smoked for more than ten years were 17 people (56%). Based on the number of cigarettes smoked in one day, 12 respondents (40%) smoked less than ten cigarettes daily, and 18 respondents (60%) smoked more than ten cigarettes daily. Of the 24 people with impaired lung function, 10 (41.7%) had smoked for less than ten years, and 14 (58.3%) had smoked for more than ten years. Based on the number of cigarettes smoked in

one day, nine people (37.5%) smoked less than ten cigarettes daily, and 15 people (62.5%) smoked more than ten cigarettes daily. This research is in line with research on male employees at the Rectorate Building at the University of Lampung by Nisa et al. (2015), which showed that there was a significant relationship between smoking duration and the interpretation value of the FEV1/FVC ratio. Smoking duration affects the ratio of forced expiratory volume in one second and forced vital capacity in male Rectorate of the University of Lampung employees. Daily cigarette consumption affects the ratio of one-second forced expiratory volume and forced vital capacity at the Rectorate of the University of Lampung. The daily consumption of 1-10 cigarettes is the dominant factor in reducing the FEV1/FVC ratio.<sup>4</sup>

This research aligns with the theory that smoking can cause changes in the anatomy and physiology of the respiratory system. Inhaled cigarette smoke causes increased fluid secretion in the bronchial tree and swelling or metaplasia of the epithelial layer. The nicotine content in cigarettes will constrict the terminal bronchioles, resulting in resistance to airflow into and out of the lungs. Nicotine can also damage the cilia on epithelial cells, so a lot of debris collects in the airway. Continuous smoking habits can cause a decrease in lung function.<sup>14,15</sup>

Most of the respondents had severe stress perceptions. Of the 24 people with abnormal lung function, 8 (33.3%) had normal stress perceptions, and 16 (66.6%) had severe stress perceptions. This is in line with research conducted by Arunima (2019). In that study, workers with high-stress perception scores of 20 or more showed decreased FEV1 and FVC values. Most workers with a high perception of stress may have poor lung function test results. Increased levels of perceived stress can even affect lung function in young, healthy individuals.

## **Conclusion**

This study had 24 (80%) Bendor drivers with impaired lung function. Based on the length of work, it was found that Bendor drivers with impaired lung function had worked more than five years (63.33%). This shows that the longer a person's working period combined with a dusty and polluted work environment, the greater the risk of decreased lung function. Based on the length of exposure, it was found that Bendor drivers with impaired lung function worked more than 8 hours a day (75%). This shows that the longer a person is exposed to dust, smoke, and vehicle pollution, the greater the possibility of respiratory problems. Based on smoking habits, Bendor drivers with impaired lung function have smoking habits for more than ten years (58.3%) and smoke more than ten cigarettes a day

(62.5%). This shows that continuous smoking habits can cause a decrease in lung function because nicotine can lead to constriction of terminal bronchioles and damage to cilia on epithelial cells. The majority of Bentor drivers with impaired lung function have a perception of severe stress (66.6%), indicating that increased levels of perceived stress can even affect lung function.

### **Conflicts of Interest**

Nil

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## Periocular Chemotherapy in Palpebral Malignancies: A Review

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### ABSTRACT

**Background:** Palpebral malignancy is still a significant health problem and consists of sebaceous gland carcinoma (SGC), basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and malignant melanoma (MM). Although total resection using the Moh micrograph method is standard therapy for these cases, periocular chemotherapy may be an alternative therapy in patients where surgery cannot be performed.

**Content:** Periocular chemotherapy in lid malignancy is recommended in cases that are inhibited or contraindicated for surgery, with obscure tumor margins, with markers of tumor invasion of vascular, lymphatic, nerve, or other orbital structures, signs of relapse after surgery, local pagetoid involvement, sizeable tumor size, and also presented an appearance of diffuse and multifocal tumor on histopathological examination. Choices of local chemotherapeutic agents based on the variety of palpebral malignancy, namely: (1) imiquimod for BCC; (2) mitomycin-C for SGC; (3) cisplatin, doxorubicin, bleomycin, peplomycin, methotrexate, and 5-fluorouracil for SCC; and (4) Imiquimod for MM. Topical chemotherapy is given to patients using an iodontoherapy method or ophthalmic cream.. More often than not, topical chemotherapy possessed a few side effects that are mild and tolerable and disappear on their own after treatment has finished.

**Conclusion:** Local/periocular chemotherapy for palpebral malignancy is an alternative adjuvant therapy that can be considered, especially in cases where surgery is not possible.

**Key words:** Malignancy, chemotherapy, palpebral, periocular



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## **Introduction**

The palpebra is an accessory visual anatomy with anterior and posterior lamellae that branch along the mucocutaneous margin of the lids and serve primarily as an orbital region protector. The lid's skin is the thinnest on the human body and lacks subcutaneous fat; it is covered in all other skin structures, including hair follicles and accessory glands like eccrine and apocrine glands.<sup>1</sup> Anywhere in these layers—the upper and lower lids, bulbar conjunctiva, fornix, and limbus—can have a lid tumor.<sup>1</sup> The most prevalent type of cancer in Europe and America is basal cell carcinoma (BCC), which accounts for 80–95% of cases. A small percentage of the palpebral malignancies in this area are squamous cell carcinomas (SCC) (5%), sebaceous gland carcinomas (SGC) (1-3%), malignant melanomas (1%), and other cancers (1%). Although BCC is infrequent (11-65%) in Asian populations, SCC (5-48%) and SGC (7-56%) are more common there than in the West.<sup>2</sup>

Wide excision biopsy via frozen surgery or more commonly known as Moh micrographic control surgery is the advised treatment modality for any kind of malignant palpebral tumors. In case of SGC, the advised modality would be conjunctival map biopsy. Further treatment in the form of topical chemotherapy, cryotherapy, and radiation should be utilized if the tumor has undefined margins or if the bulbar conjunctiva is still involved.<sup>1</sup> In general, local or periocular chemotherapy is adjunctive therapy in palpebral malignancies with partial response outcomes.<sup>3</sup> Periocular chemotherapy is administered with carboplatin, cisplatin, mitomycin-C, imiquimod, vismodegib, and other chemotherapeutic agents. Chemotherapy is often given in cases of bilateral retinoblastoma with a poor prognosis or contraindications to systemic chemotherapy. However, apart from retinoblastoma, chemotherapy can be given in cases of basal and epithelial cell malignancies in the eyelids.<sup>4,5</sup> Therefore, we will discuss periocular chemotherapy in palpebral malignancies in this article.

## **Classification of Palpebral Malignancy**

The tissue or cells from which an eyelid tumor develops determine whether it is benign or malignant. The majority of eyelid malignancies originate in the epidermal layer, from which epithelial and melanocytic cancers can be separated. About 85% of all eyelid malignancies are benign epithelial lesions, basal cell carcinoma (BCC), cystic lesions, and melanocytic lesions. Less frequent cancers include squamous cell carcinoma (SCC), melanoma, stromal tumors, and adnexal cancers. Other types of eyelid tumors include choristomas, hamartomas, and lymphoid tumors.<sup>3,6-8</sup>



Sebaceous gland carcinoma (SGC), basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and malignant melanoma are the most common types of eyelid malignancies in Asia, in contrast to Western populations like those in America and Europe where basal cell carcinoma and squamous cell carcinoma are the most common types of cancer. Each type of palpebral malignancy has its own response to the therapy given. In BCC, the main therapy recommended is surgery, especially in the early stages. Topical immunotherapy can be considered in advanced stages or local metastases and cases where surgery is not possible.<sup>4</sup> The preferred course of treatment for palpebral SGC is wide excisional biopsy under frozen surgery or Moh's micrographic surgical control, followed by lid reconstruction. Cryotherapy and topical chemotherapy are also beneficial when the pagetoid is localised.<sup>2</sup> The same principles of therapy are also applied in cases of SCC and malignant melanoma<sup>5,6</sup>

### **Periocular Chemotherapy in Basal Cell Carcinoma**

BCC is the most common skin malignancy, accounting for 85-95% of all malignant mole epithelial cells in non-Asian countries. Most often, the lower straps and inner frame are damaged. BCC mostly affects adults and is rare in children - children who are not predisposed. Prolonged exposure to UV light is the main risk factor.<sup>7</sup> BCC typically manifests as a single injury. Other types, such shallow BCC, are more frequently found elsewhere and are less common within the eyelid. BCC on the eyelid usually causes little pain and also results in lash loss. Clinically, the more prevalent type of nodular BCC manifests as a raised, hard, pearly nodule with irregularly spaced telangiectatic vessels. The nodule may develop an ulcer in the middle as its size increases. BCC with amelanotic pigmentation is comparable to nodular or nodulo-ulcerative BCC. A pale, indurated plaque with hazy or ill-defined edges represents the type that infiltrates. However, when the BCC is found within the inward canthus and is of the infiltrative type, local invasion into adjacent tissues, particularly the orbit, may take place. Rarely does BCC metastatically spread. An intraocular attack is uncommon.<sup>7</sup>

Most solitary BCCs with distinct margins are histopathologically associated with the nodular type variety and the morphea or sclerosing types, which match to the clinical infiltration categorization. Solitary types have oval nuclei, minimal cytoplasm, and projecting outer palisades on their epithelial cell lobules. Adnexal characteristics, known as keratolytic, cystic, or adenoid type, help identify solid BCCs. The properties of elongated basaloid strands embedded in solid fibrous stroma are used to explain the morphea patterns. The

aggressiveness of this form of BCCs causes remarkable infiltration into the nearby dermis, and at a later stage, into the orbital structures and paranasal sinuses, as well as occasionally intraocularly. The epidermis may be diffusely and multicentrically involved in the superficial type, stretching into the surface dermis. Histologically, it might be challenging to differentiate between BCCs and adnexal malignancies like sebaceous carcinoma and trichoepithelioma. An intriguing variant of BCC known as basosquamous carcinoma has morphological characteristics that are in between those of BCC and squamous cell carcinoma.<sup>7</sup>

Currently, it is believed that the pathophysiology of BCC is caused by disruption of the Hedgehog (Hh) pathway. Contrary to the underlying oncogenic mutation, the hedgehog pathway was demonstrated to be uncontrollably activated. The Hh pathway is essential for regulating cell division, proliferation, apoptosis, and self-regeneration in the growing embryo. After the embryonic stage, the Hh pathway is dormant in all normal cells, with the exception of hair, skin, and stem cells. A mutation in Ptch that causes ongoing Smo activation is the most frequent modification seen in BCC, followed by changes in p53 and cyclin-dependent kinase inhibitor 2A (CDKN2A). When used in BCC chemotherapy, vismodegib had both a full and partial response, according to reports. Vismodegib, a particular Hh pathway inhibitor, binds to Smo and blocks the activation of Hh target genes, hence blocking the Hh pathway.<sup>10</sup>

Therapeutic modalities generally used in managing palpebral BCC are summarized in Table 1. Surgical therapy is the main choice in this case but can be combined with radiotherapy if the tumor margins are unclear. In BCC patients who cannot undergo surgery or radiotherapy, periocular chemotherapy using vismodegib or imiquimod can be considered.<sup>4</sup>

**Table 1.** Therapeutic options for palpebral or periocular BCC.<sup>11</sup>

Therapy Options	Indications
MMS	The most effective therapy option for eliminating BCC on the palpebra
Exanteration	significant invasion of the orbit or bulbus
Radiotherapy	Exenteration of high-risk histological subtypes (morphotic/infiltrative, micronodular, or basosquamous) with perineural invasion may occur in conjunction with, when margins are uncertain, or after.
Vismodegib	For individuals who cannot tolerate surgery or radiation therapy, or who have locally advanced illness that recurs after surgery or metastatic disease.
IMQ	Periocular BCC topical immunotherapy, particularly for nodular periocular BCC.

BCC, basal cell carcinoma; MMS, Mohs micrographic surgery; IMQ, imiquimod.

### ***Vismodegib***

The majority of BCCs are treated surgically, however there is no established cure for advanced or metastatic BCC. Vismodegib, an inhibitor of the hedgehog pathway, has been used often to treat periocular and orbital BCC and lessen tumor burden. Patients with advanced-stage or metastatic BCC who are unable to undergo surgery or radiotherapy, who have additional local conditions that could return after surgery or metastatic disease, or for whom surgery could result in additional issues like loss of vision, diplopia, or the loss of structure in the eye or orbit, are advised to use this specific oral treatment. Vismodegib also treats the untreatable basal cell nevus syndrome (Gorlin syndrome), which manifests as many skin lesions on the face and periocular region. The suggested daily dosage is 150 mg. Similar to BCC, the pathophysiology of basal cell nevus syndrome involves disrupted hedgehog signaling. Since the hedgehog signal transduction system is essential for cell proliferation, alterations in the hedgehog signaling pathway could convert conjunctival intraepithelial neoplasia into an aggressive squamous cell carcinoma. In patients with basal cell nevus syndrome, vismodegib specifically blocks the G protein-coupled receptor protein, which stimulates the hedgehog pathway, to halt the evolution of BCC and lower tumor burden.<sup>11</sup>

The initial histological description of vismodegib's effects on BCC in a patient is provided by Kahana et al. After 5 months of vismodegib treatment, the residual squamous cells not only showed degenerative cytology but also failed to stain nuclear for the marker Ki-67 in surgical specimens. Muscle spasms, alopecia, dysgeusia, dysosmia, weight loss, fatigue, nausea, decreased appetite, diarrhea, keratoacanthoma, and squamous cell carcinoma are a few of the side effects of vismodegib. Generally speaking, vismodegib is well tolerated and has little adverse effects. However, some individuals stopping their treatment because of these various adverse effects. To adequately assess therapy risks and develop treatment criteria, more research will be needed.<sup>11</sup>

### ***Imiquimod (IMQ)***

Even while surgical excision remains the gold standard for treating periocular nodular basal cell carcinoma (PNBCC) and is associated to the most effective cure rate, local immunotherapy may be an alternative for patients who cannot undergo surgery. IMQ is an immune modulator that increases both innate and adaptive immunity while inducing death in tumor cells. In numerous trials, the usage of IMQ in 5% cream for nodular BCC has been documented. Depending on the patient's condition, it is often taken once daily, five times weekly, for eight to sixteen weeks. Conjunctival irritation, conjunctivitis, keratitis, foreign body sensation, weeping, poor vision, ectropion, and discomfort when blinking are common

periocular BCC symptoms that normally diminish after therapy. A clinical trial involving 19 patients evaluated the efficacy of topical immunotherapy with 5% IMQ emulsion in treating PNBCC. The histologic clearance rate was 89.5% at 3 months and 84.2% after 39.5 months. After three years, lesions larger than 10 mm receive histological clearance. Another study with 15 PNBCC patients found that after three months of IMQ treatment, all patients experienced histological remission, and after 24 months of follow-up, clinical remission. A smaller study found that 83% of those with PNBCC lesions got treatment, had clinical and histological improvement, and were symptom-free for a median of 11.7 months. In order to treat PNBCC, Garcia-Martin et al. looked at the effectiveness, aesthetic outcomes, and tolerance with 5% IMQ cream and radiation. All 15 patients in the IMQ group experienced complete clinical remission at the 24-month follow-up. Another 12 patients in the radiation group were in clinical remission at final assessment at 24 months after having therapy two or three times a week for five weeks at a dose of 300 cGy per session and a total given dose of 4,000–7,000 cGy. The cosmetic and function of the eyelid treating with IMQ were superior, despite the fact that the radiation group's treatment was more tolerable.<sup>11</sup>

### **Periocular Chemotherapy in Sebaceous Gland Carcinoma**

About 5% of these tumors are sebaceous gland carcinomas (SGC), a highly malignant tumor that is the second most frequent malignant eyelid tumor among Caucasians. However, it is equally prevalent as palpebral BCC in Asian nations including Japan, China, and India. This very malignant tumor, with a mortality rate of 30%, is capable of a highly aggressive local invasion, as well as metastasis to nearby lymph nodes and distant organs. But in recent years, more efficient administration has allowed the death rate to drop to 10%. SGC often affects older people, more frequently affecting women and the superior eyelid. Younger people who have had radiation to the periocular area may develop SGC.<sup>7</sup>

Clinically, a solitary nodule or a widespread disease may both be present with palpebral SGC. The solitary nodule, which is more prevalent, manifests as a hard, painless subcutaneous lesion that develops from the Zeis gland, settles on the tarsus, or shows up at the lid border. Even though SGC resembles chalazion, it causes eyelash loss as opposed to chalazion. In addition to extensive lid thickness, SGC can affect the fornix and bulbar conjunctiva. The patient may initially be identified as having conjunctivitis or persistent unilateral blepharitis because SGC has a tendency to penetrate the overlaying epithelium. The SGC caruncle appears to be a distorted yellow mass.<sup>7</sup>

SGC can be categorized histopathologically according to the level of cell differentiation. Neoplastic cells with sebaceous differentiation, displaying vacuolated foamy

cytoplasm, can be found in well-differentiated malignancies. The majority of cancerous cells in tumors with intermediate sebaceous differentiation have hyperchromatic nuclei, large nucleoli, and basophilic cytoplasm. The anaplastic tumor's poorly differentiated tumor has hyperchromatic, frequently abnormal cells, prominent pleomorphism, and strong mitotic activity. Necrosis can be seen in the tumor's center in the comedocarcinoma SGC pattern. The Oil Red O lipid stain is used to establish the diagnosis. Traditional Oil Red O staining can be substituted with immunostaining using human milk fat globulin 1 to identify SGC from BCC and SCC.<sup>7</sup>

The conjunctival epithelium and palpebral epidermis frequently show intraepithelial spread in SGC. This process is known as "pagetoid spreading." Additionally, the orbit, paranasal sinuses, and brain cavity may all be directly impacted by this invasion. Perineural infiltration and lymphatic invasion may be present in SGC with poor differentiation. Although recent medical advances have decreased mortality to less than 10%, the disease still has a mortality rate of roughly 30% and can spread to nearby lymph nodes as well as distant organs.<sup>7</sup>

Initially, the SGC therapy is frequently insufficient. Depending on the tumor's stage at the time of presentation, a number of treatments are possible, including radiation, chemotherapy, radical neck dissection, local excision, and orbital exenteration. In the beginning, wide excision is needed. A thorough examination of the patient is necessary before performing a surgical excision in order to look for any signs of pagetoid spread or multicentric origin with double eyelid eversion, as well as for any conjunctival modifications like telangiectasia, papillary changes, or malignancies. In addition to surgically removing the lid lesion, a conjunctival punch biopsy should be carried out.<sup>12</sup>

Wide excisional biopsy under freezing surgery or Moh micrographic surgical control followed by lid repair are the approved treatments for palpebral SGC. In situations where the pagetoid is localized, cryotherapy and topical chemotherapy are also beneficial. In situations of diffuse eyelid SGC, systemic chemotherapy is helpful. When a tumor has diffuse orbital and/or pagetoid involvement and is highly advanced, orbital exenteration is the advised course of treatment.<sup>13</sup> An alternate therapy for palpebral SGC is neoadjuvant chemotherapy. In enormous tumor size cases, neoadjuvant chemotherapy performed before the main operation can dramatically reduce the tumor size. This neoadjuvant therapy should be based on the findings of the histology examination. Adjuvant cryotherapy is a possibility if a map biopsy shows intraepithelial invasion in up to one quadrant. However, there are other treatment options for diffuse and multifocal involvement, including orbital exenteration,

plaque brachytherapy, surgical excision, and topical mitomycin-C. People with orbital extension and those who have lymphovascular invasion as evidenced by histopathology might wish to think about using adjuvant chemotherapy in coordination with an oncologist..<sup>13,14</sup>

In the study by Shields et al. (2004), In six (10%) cases, topical chemotherapy utilizing mitomycin C was the main course of therapy. In these situations, the initial tumor has typically been removed in its entirety from a different location, the remaining tumor is histopathologically contained to the epithelium, and based on the clinical results, no additional surgical excision is required. After the initial therapy, some patients receive ongoing care. Due to their small numbers and complexity, these types of therapies are challenging to analytically examine. Topical chemotherapy utilizing mitomycin C may be an advantageous adjuvant therapy if there is any question regarding the neoplasm's residual involvement of the bulbar conjunctiva.<sup>15</sup>

Studies on the use of topical mitomycin-C 0.04% in the treatment of sebaceous gland cancer revealed significant reductions in the invasion of the pagetoid layer of the conjunctiva. In vivo, mitomycin converts into tri- and bifunctional alkylating agents. DNA synthesis and function are impeded via binding to DNA, which leads to in cross-linking. A general cell cycle phase inhibitor is mitomycin. The chemotherapeutic medication mitomycin has been around in use for many years. It is an antibiotic with anticancer properties that has been demonstrated. The synthesis of deoxyribonucleic acid (DNA) is specifically inhibited by mitomycin. The amount of mitomycin-induced cross-linking correlates with levels of guanine and cytosine. At high levels of medication, cellular RNA and protein output may also be inhibited. The proliferation of B cells, T cells, macrophages, interferon-gamma, TNF $\alpha$ , and IL-2 production have all been demonstrated to be inhibited by mitomycin in vitro..<sup>16,17</sup>

### **Periocular Chemotherapy in Squamous Cell Carcinoma**

The squamous cell layer of the skin epithelium gives rise to squamous cell carcinoma of the lids, an aggressive malignancy that primarily affects elderly Caucasian persons. Exposure to UV radiation is the most frequent risk factor. The areas most frequently impacted are the inner canthus and inferior palpebral border. In comparison to BCC, it happens more commonly in the superior eyelid and outer canthus. SCC of the eyelid makes up just around 5% of all eyelid malignancies in comparison to BCC. Although these tumors are capable of developing on their own, they frequently do so in response to radiation therapy or pre-existing lesions such actinic keratosis, xeroderma pigmentosum, or carcinoma in situ (Bowen's disease). Clinically, SCC typically presents as a wavy-margin plaque or nodule that



is indurated but painless, frequently with core ulceration. There may be additional manifestations of these tumors, such as papillomatous lesions. The majority of eyelid SCCs have fairly favourable prognoses; nevertheless, advanced and untreated cases frequently return locally and have the potential to migrate to nearby tissues, including the orbit and lacrimal drainage system as well as the intracranial cavity. In contrast to BCC, eyelid SCC has a greater propensity to metastasize to distant organs, such as the preauricular and submandibular lymph nodes. High TNM and ACC staging have been linked to local recurrence and metastasis.<sup>7</sup>

The stage of tumor differentiation determines the histological appearance of SCC. Tumors with a high degree of differentiation are characterized by polygonal cells with a profusion of acidophilic cytoplasm, hyperchromatic nuclei of various sizes and staining characteristics, dyskeratotic cells, and plainly distinguishable intercellular bridges. Pleomorphism with anaplastic cells, aberrant mitotic features, little to no keratinization evidence, and loss of intercellular bridges are characteristics of poorly formed SCC. Adenoid and spindle SCC are the two types of SCC. A form of SCC known as keratoacanthoma has just been found.<sup>7</sup>

UV light is the primary risk factor that initiates the pathophysiology of SCC. The most frequent genetic abnormalities in actinic keratosis, in situ squamous cell carcinoma, and invasive squamous cell carcinoma are p53 gene mutations. The three main causes of therapeutic UV exposure, ionizing radiation, and tanning bed use are the risk factors for developing squamous cell cancer. The p53 protein stops mutant cells from functioning or DNA replication. When the p53 gene is altered, the p53 protein is rendered inactive, which results in the formation of cells with DNA damage, such as those seen in squamous cell carcinoma.<sup>18,19</sup>

One other therapy also showed that chemotherapy using cisplatin and doxorubicin administered systemically and/or locally (iontophoresis) showed good resolution without any signs of therapeutic toxicity. For this investigation, the provided dose must still be altered.<sup>3</sup> The patient in a prior study with invasive Three cycles of intravenous chemotherapy (cisplatin 150 mg and 5-FU 1000 mg daily for three days during each cycle) were administered to SCC cases, with each cycle being repeated three weeks apart. With each treatment session, the orbital tumor's size is reduced. All hematological indicators were constant during the treatment cycles, and no major side effects materialized.<sup>20</sup>

Deoxyribonucleotide (FdUMP) and the folate cofactor N5-10-methylenetetrahydrofolate are thought to form a covalently bonded complex with thymidylate

synthase (TS) as fluorouracil's main mechanism of action. This hinders the conversion of uracil into thymidylate, prevents the production of DNA and RNA, and results in cell death. RNA can become fragmented when fluorouracil replaces the uridine triphosphate (UTP), which prevents both protein synthesis and RNA processing.<sup>21</sup>

Cisplatin, on the other hand, is an alkylating agent that functions in three different ways. In order to cause DNA repair enzymes to attempt to remove the alkylated base, it first binds an alkyl group to a DNA base. This slows down the target DNA's ability to produce DNA and translate it into RNA. DNA atoms are bound together by structures called cross-links, which prevent DNA from being separated for synthesis or transcription. The second creates cross-links. The third is the product of mutations brought on by nucleotide pair errors.<sup>22</sup>

In periocular SCC with microscopic stratum or perineural infiltration and/or swollen lymph nodes in unresectable, large, or multiple lesions or when the patient opposes surgery/surgical contraindications, chemotherapy may be utilized as an adjuvant therapy. Specifically, 5-fluorouracil, doxorubicin, bleomycin, peplomycin, methotrexate, and cisplatin.<sup>5</sup>

### **Periocular Chemotherapy in Malignant Melanoma**

Malignant melanocyte proliferation leads to cutaneous malignant melanoma (CMM). The cancer whose incidence has significantly increased in recent years is CMM. The chance of acquiring CMM throughout the course of one's lifetime in the United States was estimated to be 1 in 55 for males and 1 in 82 for women between 1998 and 2000. Although CMM only accounts for 5% of malignant skin tumors, it is accountable for more than 65% of skin cancer-related fatalities. 20% of cases of CMM occur in the head and neck area. 66% of these instances had facial injuries, while 3% involved eyelid injuries.<sup>6</sup>

At the time of diagnosis, histologic features and clinical criteria are used to determine the majority of CMM subtypes. The radial growth phase and the vertical growth phase are the two stages of melanomas' development. The melanoma initially forms a flat, black lesion on the skin during the radial growth phase by spreading laterally in two dimensions. The melanoma's spread into the epidermis past the three epidermal rete ridges is known as the radial growth phase, in contrast to the lesion's dermal (invasive) component. The largest melanocytic nest in the dermis must, however, be larger than the largest junctional/epidermal nest for the vertical growth phase to exist, or there must be signs of mitosis in the dermal

melanocytes. Although amelanotic melanoma can develop in the periocular and eyelid regions and present a diagnostic challenge, most melanomas are pigmented. It causes a delay in diagnosis.<sup>6</sup>

The structure of the eyelash adnexa can be used to identify malignant lentigo, which also has an aberrant pattern of melanocytes in the basal layer of the epidermis.<sup>23,24</sup> Studies have revealed that BRAF mutations were present in 40–60% of all melanoma cases. The serine/threonine protein kinase, a part of the RAS-RAF-MEK-ERK kinase pathway that encourages cell growth and proliferation, is encoded by the proto-oncogene BRAF. In response to growth signals, BRAF commonly forms homo- or heterodimers with other RAF kinases. However, BRAF mutations can lead to unchecked cell growth until malignancies develop.

BRAF mutations were found in 60–70% of melanoma lesions and metastatic vertical growth, according to another study, raising the possibility that these oncogenic alterations play a role in the formation of cancer. This gene is then targeted for therapy in malignant melanoma.<sup>25–27</sup>

In addition to BRAF activation, NRAS, which shares the same activation pathway as BRAF, is one of the molecules that is known to contribute to the development of malignant melanoma. Then come mutations in p53, CDK4 / CDKN2A, c-KIT, MC1R, and Cadherin, which affect melanoma cells' ability to proliferate and remain alive. BRAF activation is currently the primary target of melanoma treatment.<sup>28</sup>

Depending on the clinical stage at the time of diagnosis, CMM is treated surgically. Treatment of main lesions and close-by lymph nodes should be considered when evaluating CMM. CMM of the palpebral and periocular region requires collaborative diagnosis and treatment, as with all malignant eye tumors, to provide patients with the best care available.<sup>6</sup>

In administering additional therapy of periocular chemotherapy, imiquimod has an important role. An immune response modulator called imiquimod increases cell-mediated immunity. The Food and Drug Administration (FDA) has given the topical 5% imiquimod its approval to treat superficial basal cell carcinoma. However, in situ melanoma has also been successfully treated with it. Surface malignant lentigo of the palpebral skin with diffuse involvement of considerable portions of the palpebral skin may be treated with topical imiquimod. Surgery to remove malignant lentigo that has frequently returned is not recommended due to the size of the lesion or the challenges of attaining negative surgical margins on older individuals with extensive sun damage.<sup>6</sup>

Recently, the imiquimod 5% immune modulator has been successfully used to treat

malignant lentigo. This may affect future LMM events. Borucki and Metze published case reports showing imiquimod's efficacy in the treatment of LMM; nevertheless, more research is required to determine its function in the management of MFIs and MMs.<sup>29</sup>

The FDA has given the drugs dacarbazine and temozolomide permission to be used. Drugs that introduce alkyl groups into guanine bases, such as dacarbazine and its analog temozolomide, damage DNA damage can cause apoptosis and other processes that result in cell death. Following ingestion, dacarbazine undergoes hepatic demethylation to produce 3-methyl-(triazine-1-yl)imidazole-4-carboxamide (MTIC), which is further transformed into diazomethane and its active metabolite. The "standard of care" in the treatment of metastatic melanoma is dacarbazine, the gold standard. Usually, dacarbazine has a 10–20% response rate and three–6 month cancer-free intervals. Leukopenia, anemia, and nausea—all indications of bone marrow suppression—as well as vomiting and nausea are among dacarbazine's most frequent side effects. When taking temozolomide, antiemetics can be used to treat nausea and vomiting. Temozolomide (TMZ), an analog of dacarbazine and a derivative of triazene, was found similar with dacarbazine in a phase III trial comprising 305 patients.<sup>13,30</sup>

## **Conclusion**

The most common type of palpebral malignancy, particularly among Asian populations, is sebaceous gland carcinoma (SGC), which is followed by basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and malignant melanoma (MM). Another therapeutic approach that has the potential to result in a partial remission of the tumor is local chemotherapy. This therapy is indicated in cases of surgical rejection/contraindications, unclear tumor boundaries, signs of tumor invasion into the vascular, lymphatic, nerve, or other orbital structures, chances of recurrence after surgery, local pagetoid involvement, large tumor size, and if there are diffuse and multifocal tumor features on histopathological examination. Choice of local chemotherapeutic agents based on the type of palpebral malignancy, namely: (1) imiquimod for BCC; (2) mitomycin-C for SGC; (3) bleomycin, peplomycin, doxorubicin, cisplatin, 5-fluorouracil, and methotrexate for SCC; and (4) Imiquimod for MM. Giving topical chemotherapy can use the iodontoherapy method or ophthalmic cream. In general, topical chemotherapy has side effects that are mild and tolerable and go away on their own after treatment is finished. Thus, local/periocular chemotherapy for lid malignancy is an alternative adjuvant therapy that can be considered.

### Conflicts of Interest

Nothing to declare

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Nothing to declare

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## Delayed Management of Pediatric Testicular Torsion with Absence of Severe Pain: An Evidence-Based Case Report

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### ABSTRACT

Testicular torsion is a surgical emergency. To protect the affected gonad, early diagnosis and surgical therapy are essential. The pediatrician's difficulty in communicating his complaints is one of the potential patient-specific causes for a delayed diagnosis related to any of these symptoms. We describe a case of unilateral testicular torsion in a 13-year-old child who had complained of swelling but hadn't experienced intense scrotal discomfort in six days. His right testicle was completely shattered. When the right testicle was discovered to have a 360-degree torsion and to be detorted but not viable in the operating room, it had an orchidectomy, and the left testis underwent an orchidopexy. Three internet databases—PubMed, Google Scholar, and Science Direct—were used to search the literature. An English journal that discusses pediatric testicular torsion has inclusion criteria. There is insufficient research on testicular torsion that manifests with painless symptoms. Treatment could be postponed if this phenomenon isn't considered appropriately.

**Keywords :** Delayed management, painless, pediatrics, testicular torsion



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## **Introduction**

Scrotal issues account for at least 0.5% of all emergency room visits, making them relatively prevalent. Testicular torsion, a time-dependent diagnosis that is a true urologic emergency, can result in testicular loss; early examination can assist with urologic care to prevent this.<sup>1</sup> Since testicular viability substantially decreases six hours following the onset of symptoms, early diagnosis is crucial. Young people are most frequently affected by testicular torsion; however, older persons are rarely affected. Surgery is the only feasible course available in this case.<sup>2</sup>

The vast majority of cases, which often result from a processus vaginalis abnormality at birth, affect people who are younger (less than 25 years old). The initial manifestation could have been spontaneous, brought on by an effort, or, less frequently, by trauma. Testicular torsion accounts for about one-fourth of scrotal issues seen in emergency rooms.<sup>3</sup> The twisted spermatic cord and blood supply cause testicular torsion. Because it is frequently securely related to the posterolateral portion of the testis, the spermatic cord is immobile inside the tunica vaginalis. If the point of attachment of the tunica vaginalis is high, the spermatic cord may internally twist and result in intravaginal torsion. The bell clapper deformity, bilateral in at least 40% of cases, is the name attributed to this condition.<sup>4</sup>

Surgery is required immediately for testicular torsion. Early identification and surgical intervention are crucial for the gonad that is ill to be preserved.<sup>5</sup> The pediatrician may have trouble communicating his issues, which could be a patient-specific reason for a delayed recognition of any of these signs. Although 4-10% of torsions are detected after a testicular trauma, most torsions cannot be attributed to a specific incident.<sup>6</sup> Testicular ischemia and venous congestion result from the testicle interrupting venous blood flow as it coils around the spermatic cord. The testicle will become painful, swollen, and even erythematous. As the testicle rotates, the arterial blood supply is cut off, leading to acute ischemia and necrosis of the testis.<sup>7</sup> It is generally accepted that testicular torsion is characterized by one or more of the symptoms or clinical signs listed below, including sudden, severe, persistent, unilateral scrotal pain, vegetative symptoms like nausea and emesis, visible displacement of the testicle, either in rotation or height, swelling and/or tenderness of the scrotal sac, and decline of cremasteric reflex.<sup>8</sup>

Although the majority of patients do not arrive at the emergency room promptly, these symptoms are typically presented to the primary care physician.<sup>9</sup> Fear, shame among pubescent children, decreased pain sensitivity, or limited communication skills, particularly

among very young or neurological patients, are potential patient-specific reasons for delayed presentation with any of these symptoms. Lack of clinical experience, inadequate health system infrastructure, and incorrect identification of the illnesses by the examining health experts are external causes for delayed diagnosis or treatment. The differential diagnosis accounts for tumor markers, duplex sonography, urine analysis, blood analysis, and more diagnostic tests.<sup>10</sup> To prevent testicular necrosis, detorsion of the testicle should be accomplished within 6 to 8 hours.<sup>11</sup> One explanation for this could suggest that older kids can express their symptoms more easily. Although 4-10% of torsions are detected after a testicular trauma, most torsions cannot be attributed to a specific incident.<sup>12</sup>

Ultrasound can be difficult to diagnose with tumor torsion, particularly in young patients. For instance, 40% of newborn testicles may not show any color flow Doppler. Consult with a urologic surgeon right away if the clinical issue is significant. Any treatment delay could cause testicular necrosis and loss. Six hours after the first signs of pain are the normal cutoff for surgical intervention and testicular salvage. Therefore, prompt consultation with a urologist following the presentation may be crucial even without confirming tests.<sup>13</sup> Manual detorsion should be used if rapid urological intervention is not available. Before determining whether pain relief has occurred, the aberrant testicle should be rotated 180 degrees (open book) from medial to lateral. If the pain worsens, oppositely rotating the testicle may be considered. The restoration of blood flow can also be monitored at the bedside using ultrasound serially. The testicle may twist 180 degrees, so it can be tried again if manual detorsion doesn't work.<sup>14</sup>

The outcome of testicular torsion depends on the patient's arrival time at the emergency department (ED) as well as how quickly the diagnosis is made and treatment is initiated. Delays in diagnosis and treatment always bring on testicular atrophy. Orchiectomy is required in about 20–40% of cases of testicular torsion. African Americans and younger males are substantially more likely to lose a testis. If therapy is attempted within the first six hours of the onset of symptoms, the salvage rate is over 100%; however, if more than 12 to 24 hours pass, it quickly drops to less than 50%. More importantly, when the testis is healed using orchiopexy, future torsion is also possible.<sup>15</sup>

## Case

A 13-year-old boy complained to the emergency room with a swollen and painless scrotum for six days. The patient had already gone to the paramedics on the third day for a checkup. Antibiotics had been administered to the patient. The patient is currently

enrolled in school, there is no history of prior massages, and daily activities are unremarkable. There was no past medical history, trauma, or disease. No complaints of fever, nausea, emesis, or other vegetative symptoms existed. The right scrotum was swollen and showed a minor redness. Still, according to the physical examination findings, there was no noticeably elevated local temperature, which also revealed edema in the scrotum and mild pain (three points on the visual analog scale). Figure 1 illustrates the clinical examination results, which showed that the right testicle was larger and slightly raised relative to the left testicle.



**Figure 1.** Initial clinical presentation of the case showed an enlarged and slightly elevated right testicle compared to the left testicle.

Orchitis was diagnosed in the emergency room, and test findings revealed a 14,000 L rise in leukocytes. He had full torsion of the right testicle, as shown in Figure 2, following scrotal ultrasonography. An orchidectomy was performed on the right testicle and an orchidopexy on the left testis, as shown in Figure 3, after the right testicle was discovered to have a 360° torsion and to be detorted but not viable in the operating room. The patient received outpatient treatment in the form of antibiotics and painkillers for two days following surgery, and no fever was present. The patient was then instructed to visit urologists five days later for control.



**Figure 2.** Testicular ultrasound of the case showed complete torsion of the right testicle.



**Figure 3.** Intraoperation finding of the case.

## Discussion

An operational and clinical diagnosis of testicular torsion is made. According to the literature and medical and surgical textbooks, it is characterized by abrupt, acute, unremitting pain that frequently results in vegetative symptoms. This combination of symptoms should cause the patient to look for medical attention. This is not always the case, as our case presentation makes very evident. There was no reason to believe that the patient was in serious pain. He was only mildly to moderately uncomfortable even accounting for interpersonal variations in pain perception. More than the pain, the scrotal edema was his main concern. The patient-specific causes for delayed presentation with any of these symptoms, particularly among very young patients, may include fear, pubertal children's shame, diminished pain sensitivity, or weak communication skills. External factors contributing to delayed diagnosis or treatment include inadequate health system infrastructure, insufficient clinical experience, or a misinterpretation of the illness by the

examining health professionals.

There is a limited report on painless testicular torsion. A similar example without considerable discomfort was presented in the case report by Kapp et al. They describe a case of unilateral testicular torsion in a 14-year-old kid who did not experience excruciating pain at the time of presentation. Even though the gonad wasn't brought to the emergency room (ER) right away, it could still be saved. While this phenomenon may not always go unreported, it is uncommon.<sup>6</sup> In contrast, one of the testicles in our case could not be preserved, and an orchidectomy was ultimately necessary.

In retrospective research, 50 patients with torsion testis were observed when they arrived at the hospital. 90% of patients had an orchidectomy because their testicles were gangrenous. This demonstrates how conducting an orchidectomy, like in this case report, will increase if cases of testicular torsion are handled slowly. An increase in testicular examination of 14% ( $p=0.032$ ) was observed in Cheng et al.'s observational study between before and after intervention periods. Examination quality improved after the intervention, rising from an average of 0.85 documented domains to 2.29 ( $p < 0.001$ ). Because the patient arrived at the ER after hours and the history and physical examination results were vague, the diagnosis was delayed in this case, resulting in testicular torsion and a patient misdiagnosis.<sup>16</sup>

The case's main strength is discovering a rare instance of testicular torsion without painful symptoms. Naturally, we as clinicians must be vigilant while treating patients who may have testicular torsion, even if there is no pain. These uncommon examples teach medical professionals in the emergency room how to conduct an accurate anamnesis, physical examination, and determination of supporting examinations. This case report's limitation is the paucity of literature on testicular torsion without painful symptoms, which results in a relatively constrained discussion. Although cases like this have never been reported, testicular torsion without pain appears rare, even though cases like this may be discovered frequently. More testicular torsion cases, particularly those that are painless, are desired to be published in cases similar to this one. This may be an introduction to discuss a wider range of related topics.

### **Conclusion**

Underestimating the risk of painless testicular torsion can cause treatment delays. Continuous education targeted at improving awareness of testicular torsion in the emergency room and reducing the chance of missed or delayed diagnosis will improve the quality of clinical examinations.

### **Conflict of interest**

Nothing to declare

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