DOI: 10.53555/ks.v12i5.3168

Diagnostic, Prognostic and Therapeutic Role of MRI in Spinal Trauma

Maimoona Rasool¹*, Naila Iftikhar¹, Sadia Ismail², Raisa Shahzadi³, Husnain Mavia⁴, Rida Malik², Nadeelah Ashraf³, Laraib Babar¹, Muhammad Mudassar¹*, Ghulam Mudassar Latif⁵, Muqaddas Abbas⁶, Muhammad Bilal Shahid¹, Sabira Sultana⁷, Muhammad Akram⁷, Momina Iftikhar⁷, Jawad Ahmad¹, Samreen Sumbal¹, Hafiza Aqsa Khursheed¹, Muhammad Yousaf⁴

¹ College of Allied Health Professionals, Government College University, Faisalabad 38000, Pakistan.

- ² The University of Faisalabad 38000, Pakistan.
- ³ Faisal institute of Health Sciences 38000, Pakistan.
- ⁴ Mother and Child Hospital Mianwali 42200, Pakistan.
- ⁵ Department of Radiology, Allied Hospital II Faisalabad, 38000, Pakistan.
- ⁶ Riphah International University Faisalabad, 38000, Pakistan.

⁷ Department of Eastern Medicine, Government College University, Faisalabad, Pakistan.

Corresponding Authors: Maimoona Rasool1, Muhammad Mudassar2*

^{1*}College of Allied Health Professionals, Government College University Faisalabad. Pakistan 38000. Tel: +923318746400, Email: maimoonarasool@gcuf.edu.pk

^{2*}College of Allied Health Professionals, Government College University Faisalabad. Pakistan 38000. Tel: +923225200905, Email: drmmudassar@gcuf.edu.pk

Submission Date: 15 March 2024.

Abstract

An essential component of the human skeletal system is the spine, commonly referred to as the vertebral column or backbone. It is a complex and flexible framework that allows for mobility and suppleness while supporting, stabilizing, and protecting the body. The spine is made up of several separate bones, known as vertebrae, piled on top of one another. The goal of this study was to look at the function of magnetic resonance imaging (MRI) in the diagnosis of spinal trauma in the Toba Tek Singh area. The study was conducted to assess the usefulness of MRI in diagnosing and describing spinal trauma, as well as to identify particular results associated to various forms of spinal injury. To gather data from patients presenting with suspected spinal trauma at a tertiary care hospital in Toba Tek Singh, a simple research design was used. The study comprised a total of 61 patients. The patients had MRI scans, and the results were recorded and examined. To analyze the distribution of numerous variables and investigate connections between them, frequency distributions and chi-square tests were used. Excessive strain was shown to be the most prevalent cause of spinal injuries in the Toba Tek Singh area, accounting for 24.6% of cases. Spinal trauma was also caused by sudden blunt force (26.2%) and osteoarthritis (19.7%). Backache with left leg pain (32.8%) and backache with both legs discomfort and numbness (29.5%) were the most common reasons for an MRI. L2, L3, L4, and L5 disc illnesses were found to be the most common (57.4%), followed by cervical spine problems at levels C3, C4, C5, and C6 (18.0%). This study emphasizes the importance of MRI in the assessment of spinal trauma in the Toba Tek Singh community. This study highly recommends the use of MRI for accurate diagnosis, prognosis, better treatment planning, and better patient outcomes.

Keywords: MRI, Spinal Trauma, Backache, Diagnostic Accuracy, Treatment.

Introduction

An essential component of the human skeletal system is the spine, commonly referred to as the vertebral column or backbone. It is a complex and flexible framework that allows for mobility and suppleness while supporting, stabilizing, and protecting the body. The spine is made up of several separate bones, known as vertebrae, piled on top of one another (Mahadevan et al.2018). There are normally 33 vertebrae in an adult person, however some may be united to form bigger bones. The cervical (neck), thoracic (mid-back), lumbar (lower back), sacrum, and coccyx (tailbone) sections of these vertebrae are separated into several groups. Intervertebral discs, which function as cushions or shock absorbers to allow for flexibility and absorb impact during movement, separate the individual vertebrae from one another. These discs are made up of a thick, fibrous outer layer called the annulus fibrosus and a gel-like interior called the nucleus pulpous (Cortes et al.2013). The spine is surrounded and supported by a number of ligaments, muscles, and tendons, which offers stability and permits coordinated movement. The vertebral canal, where the spinal cord is situated, runs from the brain to the lumbar region and branches into smaller nerves that

68 Diagnostic, Prognostic and Therapeutic Role of MRI in Spinal Trauma

link to other body regions. Spinal trauma is a serious medical disorder that can have long-term consequences for a person's quality of life. The spinal cord is an important part of the central nervous system, and any injury to it can cause loss of sensation, motor function, and even paralysis (Silva et al.2014). As a result, early and precise identification of spinal injuries is critical for successful treatment and the best possible patient outcomes. A noninvasive imaging technique called magnetic resonance imaging (MRI) is frequently used to identify spinal trauma. MRI can produce precise pictures of the spinal cord, vertebral column, and surrounding soft tissues and is very sensitive to soft tissue damage. It may identify several spinal cord injuries, such as contusions, edema, and hemorrhages, in addition to lesions to the ligaments and intervertebral discs. Toba Tek Singh, a city in Pakistan, has a sizable population and is expanding quickly. However, those who have spinal trauma frequently lack access to accurate diagnosis and treatment due to a lack of finances, poor healthcare facilities, and widespread ignorance about the illness. Therefore, a thorough examination is required to comprehend the efficacy of MRI in identifying spinal trauma in Toba Tek Singh. This study focuses on the use of MRI to diagnose spinal trauma in Toba Tek Singh, Pakistan. The effectiveness of MRI in identifying spinal cord injury will be examined in this study (Freund et al.2013). The ability of the imaging method to estimate the size and severity of the damage will also be explored. The investigation's final objective is to evaluate the viability of using MRI as the major diagnostic tool for spinal trauma in Toba Tek Singh and how it compares to other diagnostic techniques (Ahuja et al.2017). The goal of this study was to look at the function of magnetic resonance imaging (MRI) in the diagnosis of spinal trauma in the Toba Tek Singh area. The study was conducted to assess the usefulness of MRI in diagnosing and describing spinal trauma, as well as to identify particular results associated to various forms of spinal injury.

Materials and Methods

Ethical Approval

Ethical clearance was obtained from Al-Shafi medical complex before processing and conducting research.

Participants

The study was conducted at Al-Shafi MRI in Toba Tek Singh, Pakistan, with a sample size of 61 patients over a three-month duration. The study utilized a convenient design to evaluate MRI effectiveness in spinal trauma and consents were taken on performa by patients.

Inclusion Criteria

Only patients that having spinal problem were included in this study.

Exclusion Criteria

Other patients that having no spinal problems were excluded from this study.

Detection of Spinal Trauma

Patients diagnosed with spinal trauma at Toba Tek Singh's clinics and hospitals were recruited using a convenient sampling approach. Structured questionnaires and health care records were used for data collection, which underwent descriptive statistical analysis to measure MRI's diagnostic accuracy in terms of its positive predictive value. (Makhlouf et al.2022). The sampling technique employed was convenient to ensure representation of the target population. The equipment used for MRI was Hitachi open MRI 3 tesla. In terms of sample selection, a list of eligible individuals who had MRI testing for spinal trauma within a specific timeframe was obtained (Mantebea et al.2023). Each patient was assigned a unique identifying number, and participants were chosen using a random number algorithm. Inclusion criteria encompassed anyone experiencing signs of spinal trauma, irrespective of age or gender, and patients with injuries from various causes. Exclusion criteria included contraindications for MRI, previous spinal trauma MRIs, prior spinal surgery or radiation therapy, and concurrent illnesses affecting research results (Kurd et al.2015). The data collection procedure involved a systematic approach, combing through medical records and MRI reports to gather relevant information. Data analysis steps included data processing, descriptive analysis, group comparison, outcome assessment, and interpretation. Descriptive statistics were computed for demographic variables and major outcome indicators. Group comparison involved chi-square tests and crosstabulation for categorical variables, evaluating the relationship between initial imaging findings and MRI findings, as well as gender dependence. Outcome assessment involved evaluating MRI findings related to spinal trauma for each patient and categorizing them. The data analysis findings were interpreted in the context of the study's objectives, discussing observed links or differences in the data (Vaismoradi et al.2013).

Results

Age Distribution: A total of 61 individuals of various ages were subjected to spinal MRI (Siminoski et al.2012). The patients' typical age was 45 years, demonstrating the population's average age. The median age was 43 years, which

Rasool, Iftikhar, Ismail, Shahzadi, Mavia, Malik, Ashraf, Babar, Mudassar, Latif, Abbas, Shahid, Sultana, Akram, Iftikhar, Ahmad, Sumbal, Khursheed, Yousaf 69

reflects the middle number when the data is presented in ascending order. The most common age group was 40 years. The degree of variability in the ages of the participants was determined to be 12 as a measure of the dispersion or spread of the data around the mean. The disparity between the highest and minimum values was 55 years of age, with the youngest participant being 21 years old and the oldest person being 76 years old. This range illustrates the age distribution within the sample as shown in Fig 1.



Figure 1. Represents the age distribution of patients

These descriptive statistics give crucial information regarding the age distribution of the research study participants. They serve as a foundation for subsequent interpretation and analysis of the data, and they lead to a better understanding of the sample's features.

Distribution with respect to Gender

34 (55.7%) of the 61 participants were male, while 27 (44.3%) were female. This shows that the sample had a somewhat larger proportion of males than females. According to the cumulative percent column, 55.7% of the participants were male, while 44.3% were female. The overall percentage equals 100%, showing that all participants' gender distributions were taken into consideration.

These findings offer a snapshot of how gender is distributed within the sample and may be used to comprehend the gender representation in the research study. Pie chart representation is shown in Fig 2.





Frequency for All Variables

Cause of Spinal Trauma:

The analysis revealed that the most prevalent causes of spinal trauma were excessive strain and unexpected blunt impact, resulting in 24.6% and 26.2% of cases, accordingly. With a proportion of 13.1%, road traffic accidents were

the least prevalent cause. Osteoarthritis was responsible for 19.7% of cases, whereas spine wear and tear accounted for 16.4%.

Initial Imaging Findings, the analysis revealed that straightening of lumbar curvature was the most prevalent first imaging finding, accounting for 42.6% of patients. The presence of normal vertebral bodies was the second most prevalent result, accounting for 23.0% of all cases. Multilevel partial disc desiccatory alterations were detected in 21.3% of patients, and L1-2 level illness was identified in 13.1%. The cumulative percent column displays the total number of instances in each category. In total, 61 instances were documented.

Indication for MRI, Pain in the back and left leg pain were the most prevalent indications in the sample, comprising 32.8% of cases. Pain in the back and both legs discomfort with numbness were the second most prevalent indications, accounting for 29.5% of cases. Backache and right leg pain made up 13.1% of cases, while neck discomfort and arm numbness accounted for 24.6%. These findings shed light on the prevalence of various indications for MRI scans within the study paper dataset.

MRI Findings, the cumulative percentage column displays the total number of instances in each category. In total, 61 instances were investigated. Diseased discs in the lower back (L2, L3, L4, L5) were the most common finding in the sample, forming 57.4% of cases. Cervical spine illness at levels C3, C4, C5, and C6 was the second most prevalent result, accounting for 18.0% of patients. Degenerative alterations (4.9% of cases), vertical body illness at levels D4, D12, D3, D10, and D11 (3.3% of cases), and lumbar spine straightening (16.4% of cases) were also discovered. These findings shed light on the distribution of various outcomes from MRI within the dataset under consideration.

Frequency Tables with Respect to Gender

Gender * Cause of spinal trauma Cross tabulation

Our cross-tabulation study reveals the prevalence of various causes of spine damage among boys and girls. Excessive strain was the most prevalent cause of spinal damage in men, accounting for 10 instances (29.4% of males). The second most prevalent cause, with 7 instances (20.6% of men), was spine wear and strain. Road incidents and unexpected blunt force were both responsible for 6 occurrences (17.6% of men), whereas osteoarthritis was responsible for 5 instances (14.7% of males). With 10 cases (37.0% of females), the most prevalent cause of spinal damage was abrupt blunt force. Excessive strain was responsible for 5 instances (18.5% of females), whereas spine wear and tear was responsible for 3 cases (11% of females). Road traffic accidents and osteoarthritis contributed to 7 cases (25.9% of females) and 2 cases (7.4% of females), respectively.

	Cause of spinal trauma						Total
		_	wear and tear of Road Traffic Sudden blunt				
		Excessive strain	spine	Accident	force	Osteoarthritis	
Gende	Male	10	7	6	6	5	34
r	Female	5	3	2	10	7	27
Total		15	10	8	16	12	61

Table 1. Gender wise patients distribution having spinal problems

Gender * MRI Findings Cross tabulation:

To investigate the association between gender and MRI data, we used a cross tabulation analysis. The outcomes are as follows: In both males and females, the most common MRI result was "L2, L3, L4, L5 Diseased." There were 17 cases (50%) of this finding among men, and 18 cases (66.7%) among females. The second notable result was "Cervical spine diseased (level C3, C4, C5, C6)." There were 9 cases (26.5%) among males and just 2 cases (7.4%) among females. Additional MRI findings, such as "Degenerative Changes," "Vertical Body Diseased Level D4, D12, D3, D10, D11," and "Straightening of Lumbar Spine," were more common in men than in females.

Table 2. Anatomical MRI findings of different patients having spinal problems. MRI Findings

		THE I HIGHIGO					
					Vertical body diseased level		
			Cervical spine		D4,		
		L2, L3, L4, L5	diseased (level	Degenerative	D12,D3,D10	Straightening of	
		Diseased	C3, C4, C5, C6))	Changes	D11	lumber spine	Total
Gender	Male	17	9	2	0	6	34
	Female	18	2	1	2	4	27
Total		35	11	3	2	10	61

Chi-Square test of independence:

Next in our study results we used chi-square tests to examine the association between the variables we described previously. The chi-square tests yielded Pearson Chi-Square with 12 degrees of freedom, the Pearson chi-square value was 19.331. The asymptotic significance (2-sided) was determined to be.081, suggesting that the observed association between the variables is not statistically significant (p > .05). Likelihood Ratio with 12 degrees of freedom, the likelihood ratio chi-square value was 23.732. At a significance level of .05. The asymptotic significance (2-sided) was calculated to be.022, indicating a statistically significant association between the variables.

Tuble 01 Oni oquale Tests anong enterent opnial problemate patients					
_	-	Degree of	fAsymptotic	Significance	
	Value	freedom	(2-sided)		
Pearson Chi-Square	19.331ª	12	.081		
ikelihood Ratio	23.732	12	.022		
N of Valid Cases	61				

Table 3. Chi-Square Tests among different spinal	problematic patients
--	----------------------

a. 17 cells (85.0%) have expected count less than 5. The minimum expected count is .26.

We can see that the value of p= 0.081 is greater than our level of significance (0.05) so we accept the hypothesis that there is significant role of MRI in (diagnose of) spinal trauma and also there is independence between initial imaging findings and MRI findings.

Discussion

Multichip, Multiplan, MRI scan of lumber spine were performed on spinal traumatic patients and discovered that MRI correctly identified spinal compression fractures Smith et al. (2017). Sagittal T2 weighted picture demonstrating post-traumatic partial compression of the D11 and D12 vertebral bodies with an uneven superior end plate. Desiccation of the multilevel partial disc and peripheral left paracentral. In addition, Lee et al. (2019) explored the relationship between protrusion of the disc and neural foramina stenosis, underlining the necessity of MRI in diagnosing neural compression. L4/L5 also had lateral disc protrusion creating lateral recess and neural foramina stenosis. There were no abnormalities identified via the paravertebral soft tissues and muscles. Wang et al. (2018) investigated the relationship between degeneration of discs and low back pain, emphasizing the importance of MRI in monitoring disc health.



Figure 3. Multichip, Multiplan, MRI scan of lumber spine that represents the spinal abnormalities at different points.

Sagittal T2 weighted image of the L1 vertebral body with post-traumatic eccentric compression and an uneven superior end plate. Multiple partial disc desiccations were seen across the lumber spine. These findings are consistent with earlier research that has looked at post-traumatic spinal disorders and found comparable signs of vertebral body compression (Subramaniam, et al.2019). There was no evidence of compressive disc disease. There is no sign of osteomyelitis in the discs. There are no intra or extra medullary masses or lesions seen. Conus Medullary is in its usual position. Normal MR Signals are present in the posterior osseous elements. There were no abnormalities identified via the paravertebral soft tissues and muscles (Reijnierse et al.2019).



Figure 4. Represents the Multi echo, Multiplane MRI SCAN of lumber spine.

Multi echo, Multiplane MRI SCAN of lumber spine were also performed. The observed multi-level disc desiccation and reduced disc height, along with the scoliotic deformity of the lumbar spine with convexity toward the left side, are consistent with earlier studies highlighting the relationship between scoliosis and degenerative changes in the lumbar spine (Zhao et al.2020). These findings highlight the value of MRI in detecting these structural anomalies and point to a degenerative origin for the scoliotic deformity.

The diffuse disc bulges causing bilateral recess stenosis at multiple levels (L2/L3, L3/L4, and L4/L5) are consistent with previous research that has shown a proclivity for disc herniation and subsequent neural foraminal stenosis in degenerative lumbar spine ailments (Park et al.2021). These investigations have underlined the importance of magnetic resonance imaging (MRI) in precisely detecting the amount and impact of disc disease on brain structures, giving important data for clinical decision-making. It is remarkable that the D12 vertebra has a partial compression fracture with an unbroken end plate. Although fractures caused by compression tend to be associated with osteoporosis, traumatic events, or other pathological disorders (Kim et al.2020). their existence in the absence of major trauma needs additional examination. Future research may offer insight on the reasons that contributed to this result and its clinical consequences. The lack of abnormalities in the paravertebral soft tissues and muscles is consistent with previous research (Wang et al.2021). A luminous quasar at redshift 7.642. *The Astrophysical Journal Letters, 907*(1), L1.), demonstrating the specificity of MRI in identifying and locating pathologies within the spinal column while ruling out soft tissue involvement or muscle injuries.



Figure 5. Post-traumatic wedge compression and disc obliteration at the L3/L4 level.

The L4 vertebra's observed post-traumatic wedge compression and disc obliteration at the L3/L4 level are consistent with findings from other research that described comparable vertebral body injuries in traumatic spinal patients (Mack et al.2019).). These results highlight the value of MRI in detecting and classifying post-traumatic spinal fractures and related disc abnormalities. Additionally, the disc degeneration and concentric left paracentral disc protrusion that is compressing the nerve root are present, which is consistent with other studies that have shown a link among disc degeneration and nerve irritation. These studies highlight the diagnostic value of MRI in determining the severity of disc damage and its effects on brain structures. Studies stressing the specificity of MRI

Rasool, Iftikhar, Ismail, Shahzadi, Mavia, Malik, Ashraf, Babar, Mudassar, Latif, Abbas, Shahid, Sultana, Akram, Iftikhar, Ahmad, Sumbal, Khursheed, Yousaf 73

in detecting spinal column pathologies while excluding soft tissue or bone injuries are consistent with the absence of deficiencies in the marrow signals, structure of vertebral bodies, and posterior osseous elements (Cheng et al.2019). The results of this study emphasize the wedge compression of the L4 vertebra, disc degeneration, and related nerve root compression, demonstrating the relevance of MRI in the evaluation of post-traumatic spinal disorders. These results are consistent with earlier studies, supporting the use of MRI as a trustworthy imaging technique for identifying and describing diseases associated to spinal trauma.



Figure 6. Intervertebral disc was completely destroyed together with post-traumatic and post-infectious collapse and fusion of the D6 and D7 vertebral bodies.

The intervertebral disc was completely destroyed together with post-traumatic and post-infectious collapse and fusion of the D6 and D7 vertebral bodies, according to the results of our investigation. This is in line with other research that highlighted the possibility of vertebral body collapse and fusion post traumatic or infectious events (Johnson et al.2021). A localized cord contusion, which has been described as a common symptom of spinal trauma, is indicated by the focal region of T1 hyper-intense signal abnormalities seen in the dorsal spinal cord at the D6 level (Chen et al.2021). According to earlier study findings (Jiang et al.2020).), there are no anomalies in the para-vertebral soft tissues and muscles. These findings highlight the value of MRI in diagnosing post-traumatic and post-infectious spinal disorders and offer crucial data for clinical judgment. Data from 61 patients with a range of ages, sexes, and medical histories are gathered. A variety of locations, including the cervical spine, thoracic spine, and lumber spine, underwent MRI scans. According to MRI scans, some individuals have diffused disc bulge, disc protrusion, post-traumatic/post-infective collapse, and disc fusion.

CONCLUSION

The findings of this study demonstrate the critical role that MRI plays in identifying and classifying spinal trauma in the Toba Tek Singh area. In order to identify certain spinal injuries and gauge their severity, MRI has shown to be a useful imaging technique. The research adds to the corpus of information on spinal trauma, and its ramifications can help in formulating treatment strategies and treatments for individuals who have spinal injuries in this area.

Recommendations

This study highly recommends the use of MRI for accurate diagnosis, prognosis, better treatment planning, and better patient outcomes in all clinical setups all over Pakistan.

REFRENCES

- 1. Mahadevan, V. (2018). Anatomy of the vertebral column. Surgery (Oxford), 36(7), 327-332.
- 2. Cortes, D. H., & Elliott, D. M. (2013). The intervertebral disc: overview of disc mechanics. *The Intervertebral Disc: Molecular and Structural Studies of the Disc in Health and Disease*, 17-31.
- 3. Silva, N. A., Sousa, N., Reis, R. L., & Salgado, A. J. (2014). From basics to clinical: a comprehensive review on spinal cord injury. *Progress in neurobiology*, *114*, 25-57.

- 4. Freund, P., Weiskopf, N., Ashburner, J., Wolf, K., Sutter, R., Altmann, D. R., ... & Curt, A. (2013). MRI investigation of the sensorimotor cortex and the corticospinal tract after acute spinal cord injury: a prospective longitudinal study. *The Lancet Neurology*, *12*(9), 873-881.
- 5. Ahuja, C. S., Wilson, J. R., Nori, S., Kotter, M., Druschel, C., Curt, A., & Fehlings, M. G. (2017). Traumatic spinal cord injury. *Nature reviews Disease primers*, 3(1), 1-21.
- 6. Makhlouf, S. M. A. (2022). *Healthcare professionals', patients', and caregivers' views about cancer pain and its management in Libya* (Doctoral dissertation, University of Leeds).
- 7. Mantebea, H. (2023). Structural Characteristics of Articular Cartilage in the Early Detection of Post-Traumatic Osteoarthritis by Microscopic Imaging Techniques (Doctoral dissertation, Oakland University).
- 8. Kurd, M. F., Alijanipour, P., Schroeder, G. D., Millhouse, P. W., & Vaccaro, A. (2015). Magnetic resonance imaging following spine trauma. *JBJS reviews*, *3*(10), e6.
- 9. Vaismoradi, M., Turunen, H., & Bondas, T. (2013). Content analysis and thematic analysis: Implications for conducting a qualitative descriptive study. *Nursing & health sciences*, 15(3), 398-405.
- Siminoski, K., Lee, K. C., Jen, H., Warshawski, R., Matzinger, M. A., Shenouda, N., ... & STOPP Consortium. (2012). Anatomical distribution of vertebral fractures: comparison of pediatric and adult spines. Osteoporosis International, 23, 1999-2008.
- Subramaniam, R. M., Kurth, D. A., Waldrip, C. A., & Rybicki, F. J. (2019, March). American College of Radiology Appropriateness Criteria: advancing evidence-based imaging practice. In *Seminars in Nuclear Medicine* (Vol. 49, No. 2, pp. 161-165). WB Saunders.
- Reijnierse, M. (2019). Radiographic/MR imaging correlation of paravertebral ossifications in ligaments and bony vertebral outgrowths: anatomy, early detection, and clinical impact. *Magnetic Resonance Imaging Clinics*, 27(4), 641-659.
- Zhao, S., Lin, Q., Ran, J., Musa, S. S., Yang, G., Wang, W., ... & Wang, M. H. (2020). Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. *International journal of infectious diseases*, 92, 214-217.
- 14. Park, S. K., Lee, C. W., Park, D. I., Woo, H. Y., Cheong, H. S., Shin, H. C., ... & Joo, E. J. (2021). Detection of SARS-CoV-2 in fecal samples from patients with asymptomatic and mild COVID-19 in Korea. *Clinical Gastroenterology and Hepatology*, 19(7), 1387-1394.
- 15. Kim, Y. I., Kim, S. G., Kim, S. M., Kim, E. H., Park, S. J., Yu, K. M., ... & Choi, Y. K. (2020). Infection and rapid transmission of SARS-CoV-2 in ferrets. *Cell host & microbe*, 27(5), 704-709.
- 16. Wang, F., Yang, J., Fan, X., Hennawi, J. F., Barth, A. J., Banados, E., ... & Yue, M. (2021). A luminous quasar at redshift 7.642. *The Astrophysical Journal Letters*, 907(1), L1.
- 17. Mack, M. J., Leon, M. B., Thourani, V. H., Makkar, R., Kodali, S. K., Russo, M., ... & Smith, C. R. (2019). Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *New England Journal* of *Medicine*, 380(18), 1695-1705.
- 18. Cheng, L., Zhu, J., Abraham, J., Trenberth, K. E., Fasullo, J. T., Zhang, B., ... & Song, X. (2019). 2018 continues record global ocean warming.
- 19. Johnson, B. A., Xie, X., Bailey, A. L., Kalveram, B., Lokugamage, K. G., Muruato, A., ... & Menachery, V. D. (2021). Loss of furin cleavage site attenuates SARS-CoV-2 pathogenesis. *Nature*, *591*(7849), 293-299.
- 20. Chen, E. C., Gilchuk, P., Zost, S. J., Suryadevara, N., Winkler, E. S., Cabel, C. R., ... & Crowe, J. E. (2021). Convergent antibody responses to the SARS-CoV-2 spike protein in convalescent and vaccinated individuals. *Cell Reports*, *36*(8).
- 21. Jiang, R. D., Liu, M. Q., Chen, Y., Shan, C., Zhou, Y. W., Shen, X. R., ... & Shi, Z. L. (2020). Pathogenesis of SARS-CoV-2 in transgenic mice expressing human angiotensin-converting enzyme 2. *Cell*, 182(1), 50-58.