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RESEARCH ARTICLE

Accuracy of Magnetic Resonance Spectroscopy in Discrimination of Neoplastic and Non-Neoplastic Brain Lesions

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Abstract: ***Background***: Differentiation of brain lesions by conventional MRI alone is not enough. The introduction of sophisticated imaging methods, such as MR Spectroscopy (MRS), will contribute to accurate differentiation.

Objective: To determine the diagnostic accuracy of MRS in differentiating neoplasm and non-neoplastic brain lesion.

Methodology: This is a cross-sectional descriptive study conducted at Khartoum State from the period of 2015 to 2017. Thirty cases with brain lesions were included in the study investigated with MRS (Single-voxel spectroscopy) and conventional MRI. A comparison of MRS findings and histopathologic analysis was performed. The ratios of Cho/Cr and Cho/NAA were analyzed and compared between neoplastic and non-neoplastic brain masses. Data were analyzed using SPSS version 23.

Results: Out of the 30 patients affected with brain lesions, there were 16 females and 14 males with a mean age of 44 +- 18 years. The ratios of Cho/Cr and Cho/NAA were higher in gliomas, astrocytoma, and meningioma than non-neoplastic lesions. Kappa statistical value (K) showed a good agreement between MRS and histopathological analysis (K= 0.60). The diagnostic accuracy of MRS was 100%, with 82.60% sensitivity, 85.71% specificity, 95% PPV, and 60% NPV.

Conclusion: MRS has high diagnostic accuracy in differentiating neoplasm from non-neoplastic brain tumors. The elevation ratios of Choline-to- N-acetyl aspartate and choline-to- creatine can help neurosurgeons and clinicians differentiate benign from malignant masses.

Keywords: Brain lesions, accuracy, MRS, Cho/Cr, Cho/NAA ratio, PPV, NPV.

1. INTRODUCTION

Diagnosis of brain lesions and other focal intracranial lesions based on imaging methods alone is still facing a challenging problem. Accurate diagnosis is fundamentally vital for clinical management in patients with brain tumors [1]. When accessible, most tumors are surgically resected; there is a balance between removing tumor tissue and maintaining the vital brain functions [2, 3].

Conventional MR imaging provides high resolution for anatomic information and has been considered as a primary first step in the diagnosis of suspected brain lesions [4, 5]. There are many advances, such as the development of diffusion-weighted MR imaging that have significantly improved the diagnostic accuracy and capability of MR imaging. Despite this advance, the accurate characterization of malignancy and benignancy of brain lesions with MR imaging alone remains deficient in many cases [6].

Proton MR Spectroscopy is a noninvasive imaging technique, which determines the metabolite profile of the brain [7, 8]. It is safe and available in most MRI centers. It provides useful information on spectral analysis of the metabolic composition of brain lesions within a region of tissue. By comparing the relative concentration ratios of these metabolites, neurosurgeons and clinicians can judge factors such as neurotoxins, neuronal viability, and membrane turnover within the area of interest and, thereby, determine the likely underlying pathology [9].

Discriminating neoplastic from non-neoplastic brain lesions is extremely necessary since a misdiagnosis can lead to a severe effect on neurosurgery and exposure to toxic chemotherapy or radiotherapy, which may cause damage to

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brain tissue. This study aims to describe the value of MRS for characterizing brain lesions in comparison to histopathological analysis. Moreover, to determine accuracy in discrimination between neoplastic and non-plastic lesions.

2. MATERIALS AND METHODS

In a cross-sectional descriptive study, we determined the usefulness of MRS in the diagnosis of brain lesions. The study was conducted in the medical imaging department, Royal Care International Hospital (RCIH), Khartoum, Sudan, from the period of 2015 to 2017. The study was approved by the local ethics committee of Al-ribat National University, Khartoum Sudan. The participants were selected using a convenient non-probability sampling method. All patients with brain lesions were investigated using MRI, proton MRS, and stereotactic biopsy. MRS findings were assessed for the distribution patterns of pathologic spectra such as signal intensity ratios of NAA/Cho and Cho/Cr across the lesion and neighboring surrounding tissue.

The datasheet was designed to include demographic data, findings of the MRI and MRS, and histopathological findings. All patients underwent MRI and MRS.

2.1. MRS and MRI Procedures

The patients were examined using a Toshiba Excelart Vantage MRI machine. It is of 1.5 tesla equipped with an ultra-short and ultra-wide-bore system, adjustable lighting, and ventilation features.

All patients underwent the standard protocol of brain MRI. The sequences were performed using standard imaging head coil in supine positioning. Routine brain MRI was maintained in three orthogonal planes, including at least T2, T1, and FLuid-Attenuated Inversion Recovery (FLAIR) weighted images with selected parameters including Echo Time (TE) and Repetition Time (TR). T1-weighted images were obtained in at least two planes after administration of intravenous gadolinium contrast medium. Proton MRS was applied and all spectroscopic images were performed. Spectra were recorded from multiple areas and then map out the spatial distribution of metabolites within the brain lesions. Post-contrast imaging was performed to localize the selected lesion, and then voxel was placed on the area of interest. After water suppression, the Point Resolved Spectroscopy (PRESS) technique was applied for localization.

The findings in both MRS and MRI were analyzed by experienced certified Radiologists who were unaware of the histopathological results. Stereotactic biopsy was done at the department of neurosurgery. The results were matched with the histopathologic findings of brain lesions taken by stereotactic biopsy. The histopathology was taken as a standard gold reference. The result of pathologic tissue diagnosis was the "gold standard" reference in all cases.

2.2. Statistical Analysis

The data analysis was performed using SPSS version 23, statistical software (SPSS Inc., Chicago, Illinois). The mean values for each metabolite with their standard deviations (S-D) based on their relation (cause) with the Cho, Cr, and NAA were calculated. The results were put into tables from which we obtained comparisons of MRS findings with the histopathologic analysis. Statistical analysis of the different spectra was done using the *chi*-square test.

Continuous variables were presented as mean ± SD. Categorical data were expressed as percent frequencies, and differences between qualitative variables were compared using the *chi*-square test. P-values > 0.05 were considered as significant.

3. RESULTS

A total of 30 patients were examined using MRI and MRS for the evaluation of brain lesions. The incident was higher in females than males exhibiting 'female': male' ratio of 1.14: 1. The mean age of the patients is 44± 18 years, and half of the participants are in the age group of 41-60 years old (50%), as shown in Table **1**.

Table 1. Sociodemographic characteristics of the study sample.

Factors	Frequency (%)
Gender	
Males	14
Females	16
Age groups	
10-20 years	5
21-40 years	6
41-60 years	15
61-79 years	4

The MRS findings reveal that glioma was the most common brain mass (26.67%), while astrocytoma is the least frequent one (6.66%) as shown in Fig. (**1**).

Comparison of MRS findings with histopathological analysis in differentiation of malignant and benign brain lesions is shown in Fig. (**2**) . The measure of agreement between MRS and the histopathological analysis was acceptable (K = 0.6) with significant difference (p-value = 0.003) as shown in Fig. (**2**). Thus, the sensitivity of MRS is 82.60%, and the specificity is 85.71% (Table **2**). The strongest point that the accuracy of MRS is 100%.

There is a significant association between spectral analysis and MRS findings (p-value = 0.003), as demonstrated in Table **3**. The malignant brain lesions such as gliomas, astrocytoma, and other malignant masses reveal high Cho/Cr and Cho/NAA peaks on MRS. Abscesses showed high peaks of amino-acids and acetate. The cases **1** to **4** demonstrated MRS analysis associated with brain masses taken from the study sample.

4. DISCUSSION

MRS is an advanced technique that mainly produces a noninvasive spectral analysis of the metabolism of the tissue assessing the relative concentrations of their metabolites. Thus, the anatomical information provided by conventional MRI is combined with the biochemical data provided by the MRS. Despite MRS, the biopsy is still the "gold standard" to determine the definitive diagnosis of a brain lesion. The MRS would help in some instances to avoid taking unnecessary biopsies (in non-neoplastic lesions). The study aims to describe the value of MR spectroscopy for characterizing brain lesions, and to determine the diagnostic accuracy for differentiating neoplastic from non-neoplastic lesions.

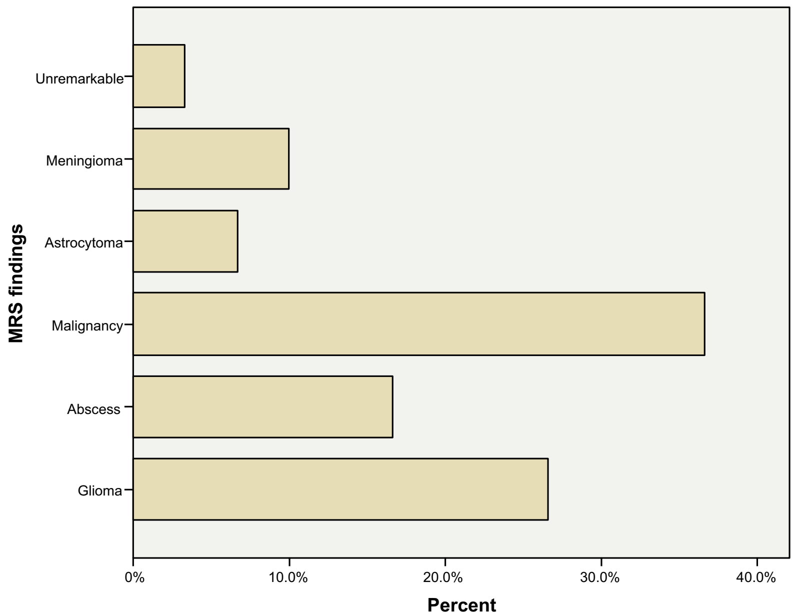


Fig. (1). Distribution of MRS findings of brain lesions. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

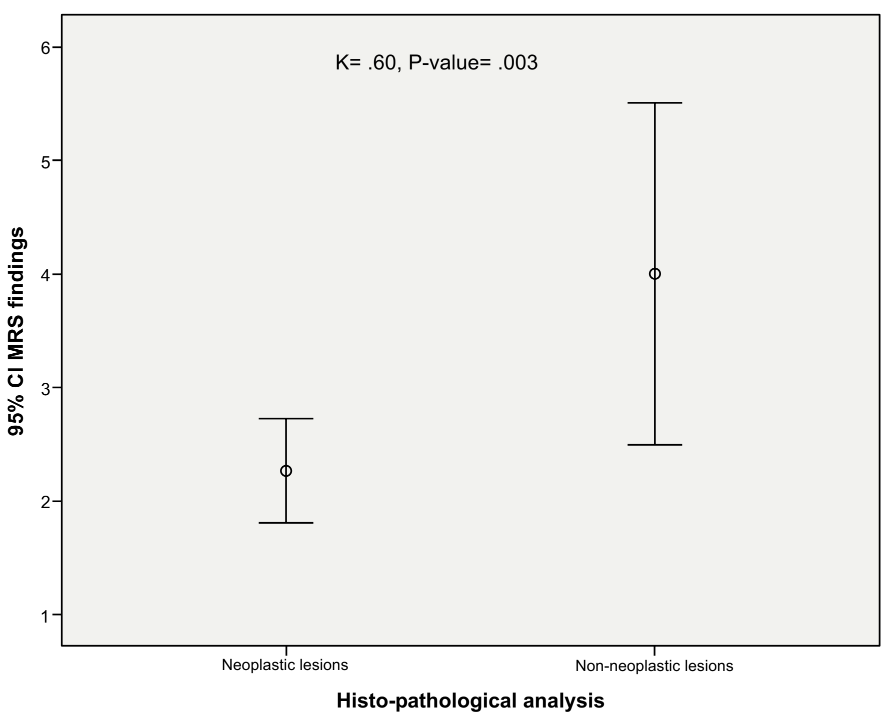


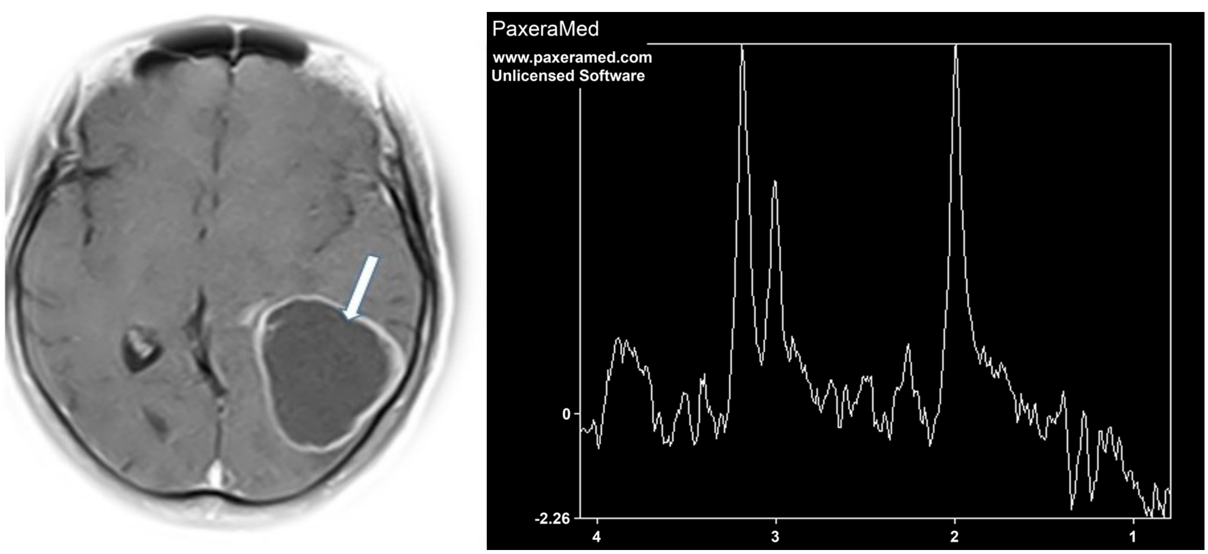
Fig. (2). Comparison of MRS findings with histopathological analysis in differentiation of malignant and benign brain lesions. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

Table 2. Performance of MRS in differential diagnosis of brain lesions compared to histopathology.

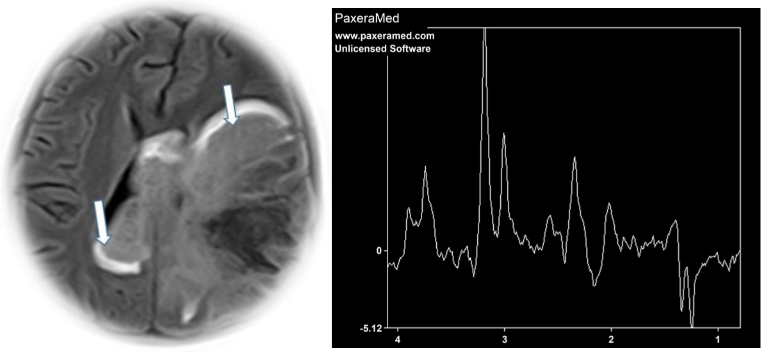
Test Performance	Values
Sensitivity	82.60%
Specificity	85.71%
Accuracy	100%
PPV	95%
NPV	60%

Table 3. Association of spectral analysis with diagnosed brain lesions.

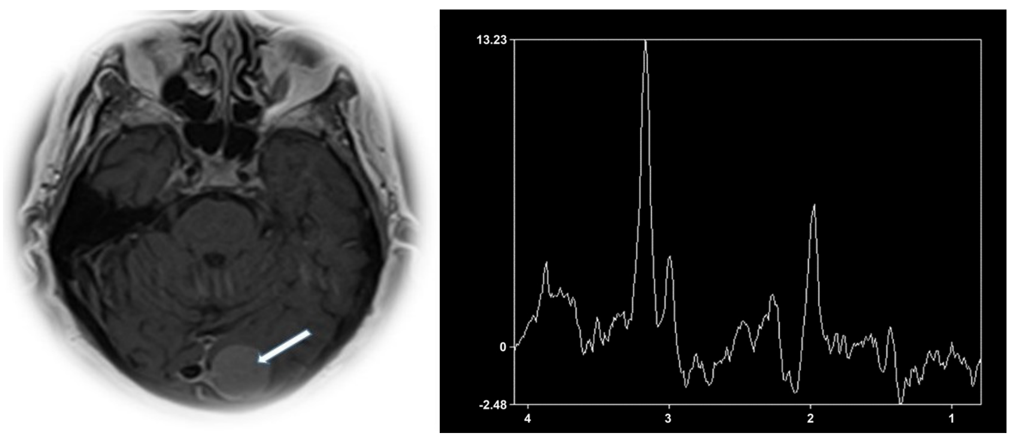
Spectral Analysis	MRS Findings							Total
	Astrocytoma	Malignancy	High Grade Glioma	Unremarkable	Meningioma	Glioma	Abscess	
High Cho/Cr and Cho/NAA ratios	2 (6.66%)	3 (10%)	0	0	0	7 (23.33%)	0	12 (40%)
Increase Cho/Cr peaks with NAA remains unchanged	0	7 (23.33%)	0	0	0	0	0	7(23.33%)
Increase Cho with reduction of NAA and Cr with increase Lactate	0	0	1 (3.33%)	0	0	0	0	1 (3.33%)
Normal Curves	0	0	0	1(3.33%)	0	0	0	1(3.33%)
Raised Cho, Low Cr and NAA	0	0	0	0	2(6.66%)	0	0	2 (6.66%)
Significant elevation of both Lipid and Lactate peaks, and reduced NAA peak	0	1(3.33)	0	0	1(3.33)	0	0	2 (6.66)
Presence of acetate, lactate, and amino-acids	0	0	0	0	0	0	5 (16.66%)	5 (16.6%)
Total	2(6.66%)	11 (36.67%)	1(3.33%)	1(3.33%)	3 (10%)	7 (23.33%)	5(16.66%)	30 (100%)
P-value	0.003							



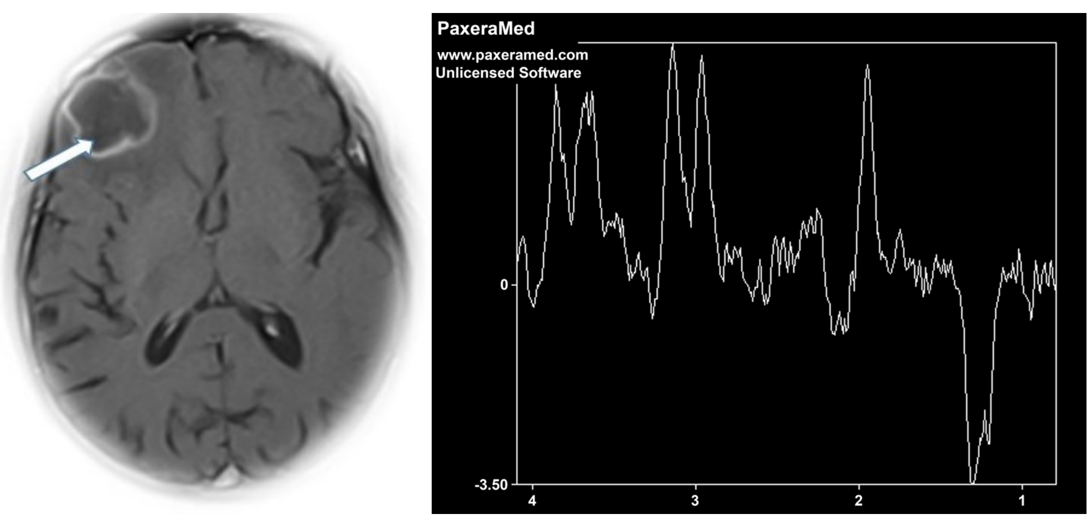
Case 1. MRS image of a 54-years-old female, shows high Cho/Cr, and Cho/NAA peaks with necrotic area reveal high lipid/lactate peak. Overall features are suggestive of neoplastic cyst-astrocytoma. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).



Case 2. MRS image of a 13-years-old female, shows a significant increase in choline with a reduction of NAA and Cr associated with increase lactate. Features are suggestive of high-grade glioma. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).



Case 3. MRS image of a 52-years-old female, shows enhancing of the left extra occipital lesion. It was observed fixed elevation of the creatine peak rather than choline with slightly reduced NAA. No critical changes in lactate or lipid peaks, Overall features are consistent with meningioma rather than malignant process. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).



Case 4. MRS image of a 52-years-old female, shows enhancing of the left extra occipital lesion. It was observed fixed elevation of the creatine peak rather than choline with slightly reduced NAA. No critical changes in lactate or lipid peaks. Overall features are consistent with meningioma rather than malignant process. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

In the current study, the average age of patients with brain lesions was 43.90± 18.027 years. There were 53.33% (16/30) males and 46.67% (14/30) female. In agreement with previous studies, Rahman *et al.* study [10] reported 40% females and 60% males with a mean age of 37 ± 13.24 years.

Surur *et al.* reported [11] 57.9% of women and 42.1% men were aged between 12 and 81 years (average =35 years).

It was found that nearly all neoplastic brain masses have often increased Cho levels and decreased NAA signals, hence leading to elevated Cho/NAA ratios. In this study, the high ratios of Cho/NAA and Cho/NAA were clearly shown on gliomas, astrocytoma, and other malignant tumors. Significant elevation of both Lipid and lactate peaks and Cho was noted in meningioma and malignancy. It was observed that increase Cho with reduction of NAA and Cr with increase lactate were shown in high-grade glioma. Similarly, our findings were consistent with previous studies, which reported that MRS revealed a significant elevation in Cho/NAA and Cho/Cr ratios in brain tumors ($P < 0.01$) [12]. Kousi *et al*. [13] reported that Cho/Cr and Cho/NAA ratios elevated significantly in gliomas, and they were used to differentiate grades of gliomas. Literature reports showed increased Cho/-NAA and Cho/Cr ratios in the tumor area compared to the normal parenchyma, and this increase was attributed to a decrease in NAA due to neuronal loss and rise in Cho due to destruction of the cell membrane [14].

It was found that abscesses have presented decreased ratios of Cho/Cr and Cho/NAA and Lactate peaks on MRS compared to neoplastic lesions. There were different spectra of metabolites in brain abscess regarding MRS. Similar to our findings, Alshafey *et al*. [15] reported elevated amino acids, lactate, and acetate peaks in pyogenic brain abscesses. On the other hand, Lai *et al*. [16] reported the presence of lactate and cytosolic amino acids in 18 of 21 cases of brain abscesses on MRS. Amino acids and acetate arise from bacterial metabolism, were visualized in the MRS spectra of the abscess, whereas they are not present in the spectra of neoplasms, as shown in Table **3**. Therefore, MRS can differentiate abscesses from brain tumors by indicating the changes in metabolite concentrations, thus distinguishing between neoplastic lesions and non-neoplastic ones.

The performance of MRS in the present study showed sensitivity (82.60%), specificity (85.71%), and accuracy (100%) in differentiating neoplastic from non-neoplastic brain lesions using MRS. These results were comparable to the previous studies, which reported sensitivities of (96.8%), specificity (95.3%), and accuracy (96%) [17]. Another study reported a sensitivity of 93.02%, a specificity of 70%, and diagnostic accuracy of 88.67% for spectroscopy [18]. In this study, PPV and NPV were 95% and 60%; while one study had found 95.45% PPV and 83.3% NPV [10]. Kappa statistics (K) showed a good agreement between MRS findings and histopathological analysis (K= 0.60). Importantly, the diagnostic accuracy of MRS in our study was very high (100%), while Aydın *et al*. [19] reported an accuracy of 77% of MRS, and they reported diagnostic accuracy of 100% when MRS combined with diffuse weighted imaging (DWI) or perfusion MR (MRP). The strength of this study that MRS performed diagnostic accuracy of 100% without a combination of DWI or MRP.

CONCLUSION

MRS proved to be a reliable and accurate method to determine whether a brain lesion is a neoplasm or non-neoplastic mass. MRS predicted 100% diagnostic sensitivity. Gliomas, astrocytoma, and malignant lesions showed high ratios of Cho/NAA and Cho/Cr, while abscesses displayed amino-acids and acetate peaks. Characterization of brain masses improves diagnosis and management and very beneficial for neurosurgeons and clinicians.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the local ethics committee of Al-ribat National University, Khartoum, Sudan (Approval no. NRU-2017-12).

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures were followed in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained from all participants.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declare none.

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