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RESEARCH

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Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) values of optic nerve head in Papilledema

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Abstract

Background: Papilledema is optic disc pathology characterized by swelling of the optic disc occurring secondary to elevated intracranial pressure (ICP), and it was proposed that elevated ICP is transferred along the subarachnoid space to the optic nerve (ON) leading to metabolic process interruptions and MRI changes within ON head. This study aimed to rule out if DWI and ADC map can be used as a diagnostic tool for detection of papilledema and if ADC values can be helpful in papilledema grading.

Result: ADC value was significantly lower in papilledema cases group (A) in comparison with control group (B).

Conclusion: Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) map can be utilized as a diagnostic tool for diagnosis of papilledema, and ADC values can be helpful in diagnosis of papilledema grade.

Keywords: Diffusion-weighted imaging (DWI), Optic nerve (ON), Apparent diffusion coefficient (ADC)

Background

Papilledema is an optic disc pathology characterized by swelling of the optic disc occurring secondary to elevated ICP; it was proposed that elevated ICP is transferred along the subarachnoid space to the optic nerve (ON) leading to metabolic process interruption with consequent edema, ischemia and sometimes visual loss [1]. Elevated ICP is frequently happening due to intracranial space occupying lesions, intracranial inflammations, hydrocephalus, venous sinus thrombosis and idiopathic intracranial hypertension (HTN) (pseudotumor cerebri) [2]

Several MRI signs were described as indicators of elevated ICP as optic nerve sheath (ONS) expansion, ON tortuousness, convexity of posterior sclerotic coat, intra-ocular protrusion of ON papilla and partially empty sella [1]. MRI can, at times, be the first detector of papilledema, predominantly in those cases with headache in whom a fundoscopic test hasn't yet been accomplished or hasn't been able to diagnose papilledema [3].

Diffusion-weighted imaging (DWI) is an MRI method that depends on movements of water molecules in the tissues. ONH hyper-intensity that is detected on DWI can be a possible sign of papilledema with 100% specificity; but, the sensitivity of this sign is low as the absence of this sign doesn't exclude papilledema.

ADC mapping is an MRI sequence that can display diffusion more precisely than conventional DWI, by removing the T2 weighting that is otherwise characteristic to conventional DWI [4]. ADC imaging does so by getting multi-conventional DWIs with dissimilar quantities of DWI weighting, and the variation in signal is proportional to the diffusion rate. In contrast to DWI scans, the standard grayscale of ADC scans is to denote a smaller scale of diffusion as darker [5].

This study aimed to rule out if DWI and ADC map can be used as a diagnostic tool for diagnosis of papilledema and if ADC values can be helpful in papilledema grading.

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Patients and methods

This study was a cohort study including 95 cases. The cases were divided into 2 groups. Group (A) included 48 patients diagnosed as papilledema by fundal examination and MRI brain was requested to clarify the cause. Group (B) included 47 patients as control who came to do brain MRI examination for other causes than papilledema.

The study started from January 2020 to November 2021. The age of the enrolled population ranged between 21 and 60 years.

Inclusion criteria for group (A)

Fundoscopy showing papilledema.

Inclusion criteria for group (B)

All MRI of the brain was done during the study period for patients who came for other reasons than visual impairment and papilledema and with normal fundal examination.

Exclusion criteria for both groups

Patients with absolute contraindications to MRI, e.g., aortic stent grafts, coronary artery stents, and temporary pacemaker, were excluded.

Fundal examination report was obtained for all patient and papilledema grading was obtained for all patient in group A according to the fundal examination (Table 1) [6]

MRI Brain examination protocol

Brain MR imaging for studied 95 patients (cases and control groups) was done on MR machine Siemens (Sempra) closed 1.5 Tesla with basic brain sequences used in brain MRI protocol including T2W sagittal coronal and axial sequences ((TE) = 103 ms and (TR) = 4.5 s), T1W axial sequence (TE) = 13 ms and (TR) = 430 ms, axial FLAIR ((TE) = 82 ms and (TR) = 9.0 s), and additional sequence T1 with contrast (Gadolinium based contrast agents) was used in 10 cases.

DWI and ADC map with b-values of 50 mm^2/s and 1000 mm^2/s by readout-segmented, multiple-shot EPI sequence [rs-EPI]. ADC value was obtained at the ADC map as a circular or elliptical region of interest (ROI) was located at the zone of hypo-intensity at ONH analogous to the zone of hyper-intensity in the $b = 1000$ images. In case of non-visualized hyperintensity of ONH on DWI isotropic trace images at $b = 1000$, the ROI was located at the ONH casing at minimum 50 to 66% of the ONH. Commonly, the mean area of the ROI was around 4 to 7 mm^2.

Statistical analysis

IBM SPSS-22 program (Inc, Chicago, IL, USA) has been used to perform statistical analysis. Data have been examined for normal distribution via the Shapiro–Wilk testing. Qualitative data have been presented as frequency and relative percentage. Quantitative data have been presented as mean ± SD (Standard deviation). Non-dependent sample t-testing has been utilized in comparison among the two groups of normal distribution variables (parametric data) and Mann–Whitney testing. $p < 0.05$ has significance.

Table 1 Papilledema grading system (Frisen scale)

Papilledema grading system (Frisen scale)
Grade 0: Normal optic disc blurring of nasal, superior and inferior poles in inverse proportion to disc diameter. Radial nerve fiber layer (NFL) without NFL tortuosity Rare obscuration of a major blood vessel, usually on the upper pole
Grade 1-Very Early Papilledema: Obscuration of the nasal border of the disc. No elevation of the disc borders. Disruption of the normal radial NFL arrangement with Grayish opacity accentuating nerve fiber layer bundles. Normal temporal disc margin. Subtle grayish halo with temporal gap (best seen with indirect ophthalmoscopy) Concentric or radial retrochoroidal folds
Grade 2-Early Papilledema: Obscuration of all borders. Elevation of the nasal border. Complete peripapillary halo
Grade 3-Moderate Papilledema: Obscurations of all borders. Increased diameter of optic nerve head. Obscuration of one or more segments of major blood vessels Leaving the disc. Peripapillary halo-irregular outer fringe with finger-like extensions
Grade 4-Marked Papilledema: Elevation of the entire nerve head. Obscuration of all borders. Peripapillary halo. Total obscuration on the disc of a segment of a major blood vessel
Grade 5-Severe Papilledema: Dome-shaped protrusions representing anterior expansion of the optic nerve head. Peripapillary halo is narrow and smoothly demarcated Total obscuration of a segment of a major blood vessel may or may not be present. Obliteration of the optic cup

[6]

Table 2 Demographic distribution of the studied patients group (A) and group (B)

	Group (A) (*n* = 48)	**Group (B) (*n* = 47)**
Age (years)	21–60	20–55
Mean ± SD	37.77 ± 11.68	31.56 ± 10.89
Sex		
Female	19 (39.6%)	25(53.2%)
Male	29 (60.4%)	22(46.8%)

Table 3 Causes of papilledema in group (A)

	Group (A) (*n* = 48)	
	N	**%**
Idiopathic Intracranial hypertension	19	39.6
Tumor	15	31.3
Hemorrhage	7	14.6
Cerebral venous sinus thrombosis	5	10.4
Drug-induced raised ICP	1	2.1
Meningitis	1	2.1

Table 4 Papilledema laterality among group (A)

	Group (A) (*n* = 48)	
	N	**%**
Unilateral	2	4.2
Bilateral	46	95.8

Table 5 Papilledema grades among papilledema patients group (A)

	Papilledema patients (*n* = 48)	
	N	**%**
Grade I	24	50.0
Grade II	22	45.8
Grade III	1	2.1
Grade IV	1	2.1

Table 6 ADC value between the two groups

	Group (A) (*n* = 48 patient)	**Group (B) (*n* = 47 patients)**	***t***	***p***
ADC value Mean ± SD	1511.82 ± 177.1	2208.94 ± 729.15	6.5	.001

Table 7 ADC value of ONH among group (A) patients and papilledema grades

Group (A) (*n* = 48)	**ADC value Mean ± SD**
Grade I (*n* = 24)	1572.57 ± 162.86
Grade II (*n* = 22)	1488.92 ± 125.87
Grade III (*n* = 1)	1125.8 ± 0.00
Grade IV (*n* = 1)	966.6 ± 0.00

Results

This study was a cohort study conducted on 95 patients. The cases were divided into two groups: group (A) including 48 patients as cases diagnosed by fundal examination as papilledema and group (B) including 47 patients as control who came to do brain MRI examination for other causes than papilledema with normal fundal examination.

In this study 60.4% of the papilledema patients group (A) were males and 39.6% were females with mean age of 37.77 ± 11.68 years and 53.2% of group (B) were females and 46.8% were males with mean age of 31.56 ± 10.89 (Table 2).

This work revealed that the commonest cause of papilledema in group (A) was idiopathic intracranial hypertension (39.6%) and brain tumors (31.3%) (Table 3).

Also this study showed that the majority of patients (95.8%) in group (A) had bilateral papilledema (Table 4).

This study showed that the most common papilledema grade in patients group (A) were grade I (50%) and grade II (45.8%) (Table 5).

ADC values of the ONH were significantly lower in papilledema cases group (A) in comparison with control group (B) (Table 6).

ADC value also found to be gradually decreased with higher papilledema grades among group (A) cases (Table 7).

In our study 44 of 48 papilledema patients diagnosed by fundoscopy among group (A) showed changes in DWI (Table 8).

In this study the DWI sensitivity was 89.8%, specificity was 100%, NPV was 90.38%, and PPV was 100% with accuracy of 94.79% for evaluating papilledema (Table 9).

ADC value was a significant diagnostic tool at cut off 1682.07 with sensitivity of 95.2% and specificity of 93% (Fig. 1).

Table 8 Association of DWI with fundoscopy in evaluation of papilledema in group (A)

DWI	Fundoscopy				Total	*p*
	Papilledema (*n* = 48)		Normal (*n* = 47)			
	N	%	*N*	%		
DWI changes	44	91.7	0	–	44 (46.3%)	.001
No DWI changes	4	8.3	47	100%	51 (53.7%)	
Total	48	100	47	100%	95	

Table 9 Diagnostic value of DWI in evaluation of papilledema

Statistic	Value (%)	95% CI
Sensitivity	89.8	77.77–96.6%
Specificity	100	92.45–100%
Positive predictive value (PPV)	100	–
Negative predictive value (NPV)	90.38	80.38–95.57%
Accuracy	94.79	88.26–98.29%

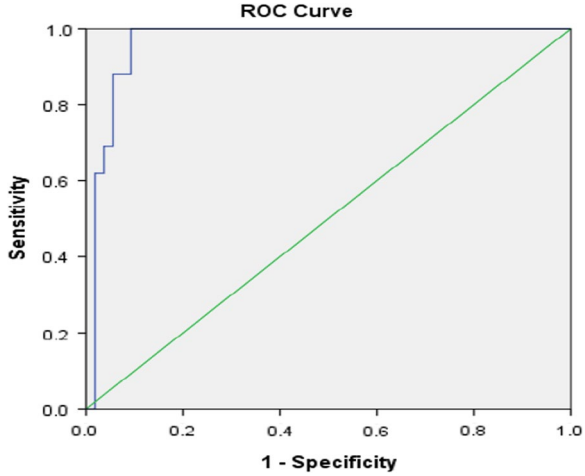

Fig. 1 ROC curve for ADC value as a diagnostic tool for papilledema

Case presentation

Case (1)

In female patient 48 years old with known idiopathic intracranial hypertension, the fundoscopy revealed bilateral grade III papilledema. Bilateral optic nerve head hyperintensity was seen in DWI (a), flattening of the posterior sclera (b) and bilateral optic nerve head hypointensity were seen on ADC map (c), right ONH ADC value = 1203.4 mm^2/s grade III; Left ONH ADC value = 1183.2 mm^2/s grade III (d) as shown in Fig. 2a–d

Case (2)

Male patient 60 years old with fundoscopy shows right grade II papilledema, right sided cerebral marginally enhanced lesion at coronal T1 with contrast (brain abscess) (a), DWI showed restricted diffusion and hyperintensity of right ONH (b), in ADC map there was hypointensity of right ONH (c), right ONH ADC value = 1340.3 mm^2/s and left ONH ADC value = 2107.8 mm^2/s (d) as shown in Fig. 3a–d.

Discussion

Regarding demographic distribution of the studied patients' group (A) cases and group (B) controls, we found that 60.4% of the papilledema patients' groups (A) were males and 39.6% were females with mean age of 37.77 ± 11.68 years and 53.2% of group (B) were females and 46.8% were males with mean age of 31.56 ± 10.89.

In the study by Salvay et al. [4], they investigated association between severity of papilledema and DWI in idiopathic intracranial HTN, and in the included forty-two patients there were 97.6% females and 2.4% males with a mean age of 31.2 ± 10.0 years.

Regarding brain edema distribution among the studied patients group (A), our results revealed that the majority showed no brain edema (52.1%), while 22.9% of the patients presented with grade I brain edema and 25% of the patients presented with grade II brain edema.

Regarding the frequency of papilledema, furthermore we found that the majority of patients had bilateral papilledema (95.8%). We also found that the majority of patients had papilledema grade I (50%) and grade II (45.8%).

The study by Ray et al. [5] revealed that all 32 cases were revealed to have two-sided papilledema with a total of 64 eyes. 20 had IIH, while 4 cases had intracranial cancers and 4 cases had meningitis, 3 had cerebral venous sinus thrombosis, and one had medication-made elevated ICP. 18 of the eyes had papilledema of grade-I, while grade-II, -III, and -IV papilledema was detected in 26, 12, and 8 eye. No cases of papilledema of grade-V were found in their study. The similar papilledema grade in the two eyes was detected in 18 cases, and dissimilar grades in the two eyes have been

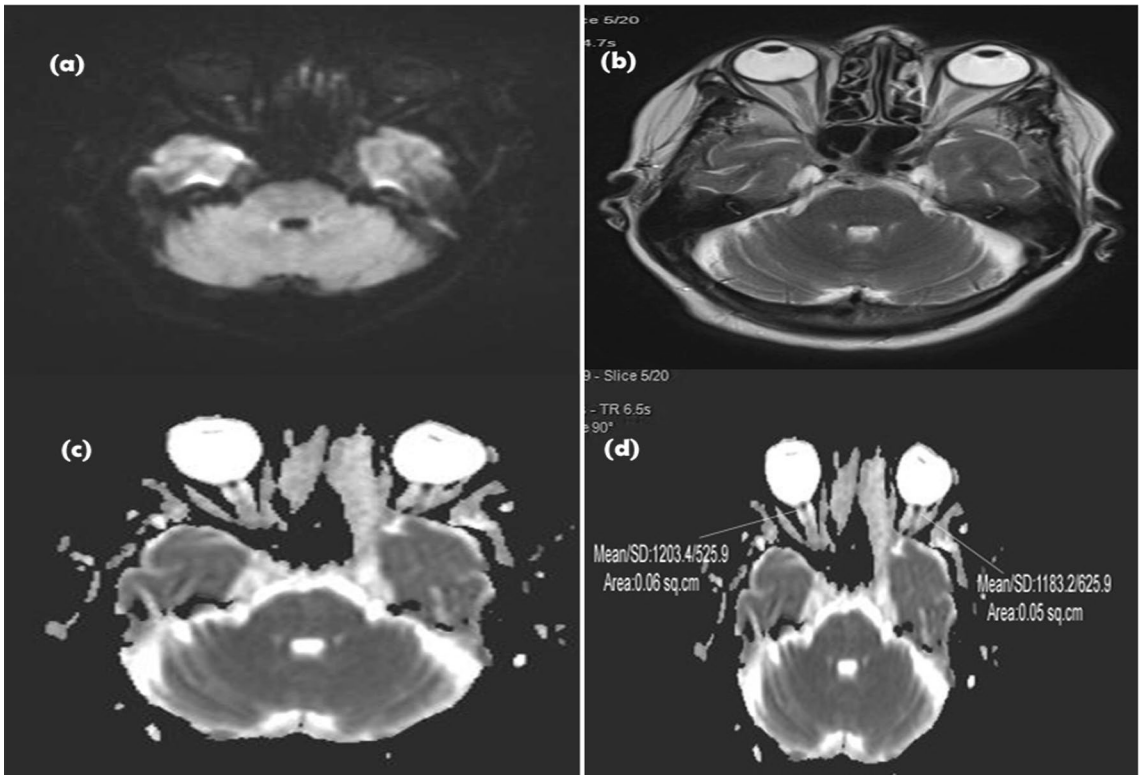

Fig. 2 **a**, **b**, **c**, **d**: Case (1)

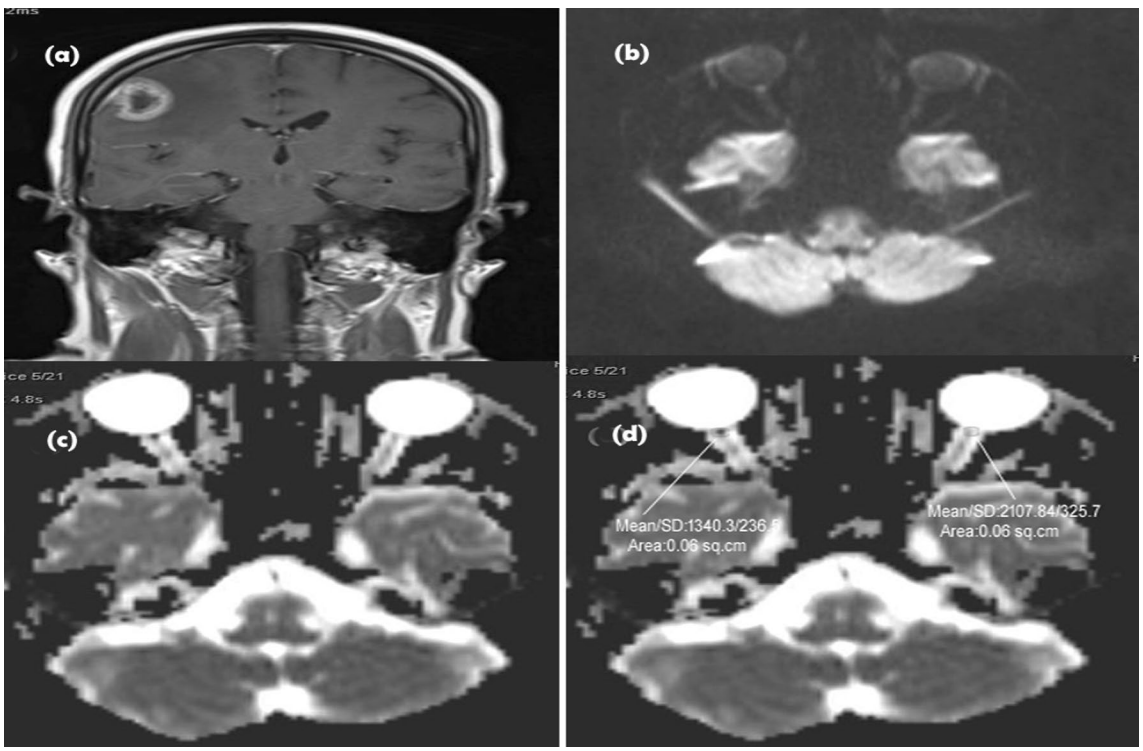

Fig. 3 **a**, **b**, **c**, **d**: Case (2)

detected in 14 cases. They also found that the grade papilledema didn't differ by more than single grade between the two eyes and cases who had dissimilar grades papilledema had grade II or III.

Regarding the correlation of ADC value between the two groups, we found that ADC value was significantly lower in papilledema cases in comparison with control group.

In agreement with our results, the findings by Ray et al. [5] revealed that there was a significant association between the mean ADC value of ONH with clinical papilledema grade and among patients and controls.

Also, in agreement with our results Yilmaz et al. [7] revealed that there was a significant change detected in the ADC values among the patients and controls. ADC values of ONH significantly reduced in the cases in comparison with the controls ($p < 0.05$).

Our findings of the mean ADC values showed that ADC value gradually decreased with higher papilledema grades.

In agreement with our results, the report by Ray et al. [5] showed that ADC value gradually decreased with higher papilledema grades.

We also found a significant change among the groups regarding ONH hyperintensity.

In agreement with our findings, the results by Ray et al. [5] revealed that there was a significant change ($p = 0.001$) detected among the patients and controls for the existence of ONH hyper-intensity on DWI.

As well, the report by Salvay et al. [4] revealed that a significant association was found amid DWI hyper-intensity of the ONH at diagnosing and the papilledema grade at following-up ($p < 0.05$).

In line with our findings, the study by Viets et al. [8] reported that Hyper-intensity of the ON heads on DWI was significantly correlated with papilledema ($p < 0.05$).

In the studied patients group (A), 44 out of 48 patients' showed DWI changes and only 4 patients did not show DWI changes.

By means of ROC curve analysis, we found that the DWI sensitivity was 89.8%, specificity was 100%, NPV was 90% and PPV was 100% with accuracy of 95% for evaluating papilledema. Also, we found that ADC value was a significant diagnostic tool at cutoff 1682.07 with sensitivity of 95.2% and specificity of 93%.

The study by Viets et al. [8] was the first who assessed the existence of ONH hyper-intensity in papilledema patients. They revealed that ONH hyper-intensity on DWI to had high specificity (100%) as radiological signs of papilledema, while it has low sensitivity (26.3% and 42.1% for 2 viewers). They reported that the existence of hyper-intensity on DWI at the ON head looks to be a dependable imaging indicator for papilledema. These signs look to have perfect specificity, particularly when the hyper-intensity is bi-lateral and/or prominent.

Ray et al. [5] showed that ONH hyper-intensity was revealed to have high sensitivity (87.5% for both) and specificity (97.1% and 98.6% for 2 viewers) signs of papilledema. A mean cutoff ONH ADC value was revealed to have highly sensitive (96.8%) and specific (95.3%) to discriminate patients and controls.

Ray et al. [5] also reported that the ADC value of ONH may be utilized as a non-direct quantitative measure of elevated ICP in a suitable clinical basis. Furthermore, a mean cutoff ADC value of ONH (1844.5×10^{-6} mm^2/s) was described in their report that can aid to discriminate between patient and control with highly sensitivity, specificity and PPV and NPV, but, the comparatively high PPV wants to be interpreted with attention, as in the general populace, the prevalence of papilledema is very lower than that in their research (50%).

As well, Wan et al. [9] reported that DWI has a 77–83% sensitivity, 80–84% specificity, and diagnosing accuracy of 80–83% when utilized to assess optic neuritis.

Conclusion

DWI and ADC map can be used as a diagnostic tool for diagnosis of papilledema, and ADC values can be helpful in diagnosis of papilledema grade.

Abbreviations

ICP: Intracranial pressure; ON: Optic nerve; ADC: Apparent diffusion coefficient; DWI: Diffusion-weighted imaging; CBC: Complete blood picture; Hb %: Hemoglobin concentration; WBCs: White blood cells; RBCs: Red blood cells; TR: Repetition time; TE: Echo time; FLAIR: Fluid-attenuated inversion recovery; rs-EPI: Readout-segmented, multiple-shot EPI sequence.

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Author contributions

We confirm that all of us as we are the authors accept the manuscript for submission. All authors read and approved the final manuscript. We hope to publish this manuscript in the journal for presenting this manuscript to the research community.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Written informed agreement was obtained from all the cases. The study was accepted by the Ethics Committee of Faculty of Medicine, Menoufia University.

Consent for publication

I confirm that all authors accept the manuscript for submission.

Competing interests
The authors declare that they have no competing interests.

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