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ORIGINAL ARTICLE

The Effect of gender on reference values of nerve conduction studies of upper limb nerves in young Sudanese adults

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ABSTRACT

Background Nerve conduction studies are neurophysiological tests performed to assess nerve dysfunction and provide an objective measure of pathophysiological changes.

Objectives The study was meant to provide reference values for sensory and motor nerve conduction studies parameters of median and ulnar nerves in young Sudanese adults and to explore the effect of gender on these values.

Methods This descriptive study was conducted at the Department of Physiology, Faculty of Medicine; University of Khartoum from July to November 2019. The study recruited 120 healthy young adult Sudanese subjects with a mean age of 20.55 years. Males were 52 (43.3%) whereas females were 68 (56.7%). Bilateral sensory and motor nerve conduction studies of ulnar and median nerves were performed. The statistical package for social sciences was used for analysis.

Results This study will establish normative data for sensory and motor nerve conduction studies parameters of median and ulnar nerves in the evaluation of young Sudanese adult patients with neuromuscular disorders. The study revealed significantly higher conduction velocity of sensory and motor ulnar nerves in female subjects. In addition, sensory amplitudes of ulnar and median nerves were significantly higher in females in contradistinction to motor amplitudes of median and ulnar which were significantly higher in males.

Conclusion Establishing reference values on nerve conduction studies for young Sudanese adults would help local neurophysiology laboratories to evaluate nerve conduction study results accurately. Gender had shown a strong influence on ulnar nerve conduction velocity and on sensory and motor amplitudes of both ulnar and median. This might raise the need for establishing gender-specific reference values.

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INTRODUCTION

Electrodiagnostic testing is frequently performed to diagnose neuromuscular disorders, though a universal standard for nerve conduction studies (NCS) is not available[1,2]. Many neurophysiological laboratories are dependent on reference values derived from textbooks or published literature[3], many of which might not meet up-to-date statistical and methodological standards[2]. As nerve conduction testing is challenging and dependent upon the skill of the neurophysiologists[2], instrumentation, and testing circumstances[1,2], individual laboratories have been encouraged to use their own techniques for performing NCS and develop their own reference data[3]. The median, ulnar are the two most tested nerves in the upper limb.

Nerve conduction velocity may be affected by many factors such as temperature, height, age, gender, and standardized technique[4,5], so control of these factors is essential for appropriate interpretation of NCS results. Many researchers published normative data for the various upper and lower limb nerves so as to use them as baseline values to interpret abnormal results. Accurate interpretation of electrodiagnostic studies requires careful use of standardized technique in electrodes placement, machine setting, and appropriate distance measurement in addition to adequate sample size of healthy subjects. Most of the literature articles are deficient in one or more of the requirements for accurate normative data[5].

Limited studies have been published regarding normative data for upper limb nerves especially in African region[6] and almost none in Sudan. This study was performed to establish normal reference values of NCS parameters for Sudanese young adults' population of the median and ulnar nerves and to find out the effect of gender on the different NCS parameters

METHODS

This descriptive cross-sectional study was performed on under and post-graduate students in the medical campus, University of Khartoum, including faculties of Medicine, Dentistry and Pharmacy. One hundred and twenty healthy adult Sudanese subjects whose age ranged from 18 to 30 years were randomly selected.

All subjects were interviewed using a standardized questionnaire to exclude those with a known history of neuromuscular disorders, any disease or drug that can cause peripheral neuropathy (e.g. diabetes, B12 deficiency, thyroid disease, alcoholism and chemotherapy), radiculopathy and entrapment syndromes. Physical examination was also performed to exclude cases with undiagnosed neuromuscular diseases.

The NCS were performed using Digital Medelec Synergy NCS machine. The procedure was performed while the subject was sitting comfortably on a chair in the upright position. Sensory (antidromic) and motor studies (both proximally and distally along the forearm) were performed bilaterally on the ulnar and median nerves following the standardized techniques in electrode placement, stimulation and recording[7-10]. In this study, the land mark method was used to determine the distance rather than using a standardized fixed distance for electrode placement because of the great variation in limb lengths. Distances between stimulating and recording electrodes in sensory studies and between proximal and distal stimulating sites in motor studies were measured in centimeters using a flexible tape. Skin warming was not needed as environmental temperature remains relatively constant (hot) throughout the year in tropical countries. Room temperature was adjusted at 25 ºC using air cooling system.

The machine settings for motor studies were as follows: Sensitivity (2 mV/division), Low frequency filter (2–3 Hz), High frequency filter (10 kHz), Sweep speed (2 msec/division). For sensory studies: Sensitivity (20 μV/division), Low frequency filter (20 Hz), High frequency filter (2 kHz), Sweep speed (1 msec/division). Recording electrodes consisted of active and reference electrodes while stimulating electrodes consisted of cathode and anode parts. Motor studies stimulation was performed in two points, distal (S1) and proximal (S2) sites to calculate the motor conduction velocity. In general, ground electrode is placed between recording and stimulating electrodes. In this study it was placed on the dorsum of the hand.

Electrode placement of sensory (median and ulnar) nerves

Active recording ring electrode was placed near the second proximal interphalangeal joint and the reference recording ring electrode was put around the second distal interphalangeal joint about 3-4 cm distal to the active electrode. Stimulating electrodes were placed over the median nerve at the mid wrist anteriorly between the tendons of the flexor carpi radialis and the palmaris longus, near the proximal crease with the anode proximal to the cathode.

Active recording ring electrode placement was near the fifth proximal interphalangeal joint slightly distal to the base of the digit and the reference recording ring electrode was put around the fifth distal interphalangeal joint about 3-4 cm distal to the active electrode. Ulnar nerve stimulating electrodes were placed at the wrist near the proximal crease slightly radial to the tendon of flexor carpi ulnaris with the anode proximal to the cathode.

Electrode placement of motor (median and ulnar) nerves

Active recording electrode of the median nerve was placed over abductor policies brevis (APB) muscle (halfway between the midpoint of the distal wrist crease and the first metacarpo-phalangeal (MCP) joint) and the reference electrode over proximal

phalanx of the thumb slightly distal to the first MCP joint. On distal stimulation point (S1), the electrode was placed in mid wrist palmer aspect, between the tendons of the flexor carpi radialis (laterally) and palmaris longus (medially) with the cathode 6.5-8 cm proximal to the active recording electrode and the anode is proximal to the cathode. On proximal stimulation point (S2), the cathode was placed on the elbow just medial to the palpable brachial artery in the antecubital region with the anode proximal to the cathode.

Active recording electrode of the ulnar nerve was placed over the mid portion of abductor digiti minimi (ADM) on the ulnar surface of the hypothenar eminence (halfway between the level of the pisiform bone and the 5th MCP joint) and the reference electrode over the proximal phalanx of the fifth digit slightly distal to the 5th MCP joint. On distal stimulation point 1 (S1), the electrode was placed over the palmar aspect of the wrist just radial to flexor carpi ulnaris tendon with the cathode 7-8 cm proximal to the active recording electrode and the anode proximal to the cathode. On proximal stimulation point (S2), the electrode was placed 3-5 cm distal to the ulnar sulcus (osseous groove in the posterior aspect of the medial epicondyle of the humorous).

Data was analyzed using the statistical package for social sciences (IBM SPSS version 23). Student-t test was used for comparison. Unpaired-t test was used for comparison between the male and the female groups. The study was approved by the Ethics and Research Committee of the Faculty of Medicine of University of Khartoum. All participants were fully informed about the test. They signed an informed consent to volunteer to the research and they had the freedom to withdraw from the study at any time.

RESULTS

This study involved 120 healthy young adults, their mean (±SD) age was 20.6±2.9 years (range 18-30 years), fifty-two (43%) of whom were males and sixty-eight (57%) were females. Their mean (±SD) height was 166.5±9.1 cm and their mean (±SD) body mass index (BMI) was 22.8±.4.8.

The mean distance between stimulating and recording electrodes in sensory studies and between proximal and distal stimulating sites in motor studies was provided with the corresponding mean sensory latency and distal motor latency of median and ulnar nerves (Table 1). Descriptive statistics for NCS parameters were provided in Table 2 including conduction velocity and amplitude of sensory and motor, median and ulnar nerves.

The effect of gender on amplitude and conduction velocity of the studied nerves was illustrated in Table 3. Higher conduction velocities were observed in females, which was extremely significant in sensory ulnar (P=0.005) as well as motor ulnar (P=0.000) nerves, but was not statistically significant in sensory median (P=0.119) and motor median (P=0.223) nerves. In addition, gender had shown significant effect on sensory and motor amplitudes of both median and ulnar nerves. The difference in sensory amplitudes was of extreme statistical significance being higher in females (P=0.000) in both ulnar and median nerves, in contradistinction to motor amplitudes of median (P=0.032) and ulnar (P=0.002) which were noticed to be significantly higher in males.

Table 1. Distance measured and corresponding latencies of sensory and motor median and ulnar nerves.

Nerve	Distance (cm)	Latency (ms)
Sensory Median	14.9±1.4	2.5±0.3
Sensory Ulnar	13.4±1.4	2.2±0.3
Motor Median	21.7±2.2	3.1±0.4*
Motor Ulnar	23.6±2.8	2.4±0.4*

*= distal motor latency

Table 2. Descriptive statistics for NCS parameters of ensory and motor median and ulnar nerves

Values	CV of median sensory nerve (m/s)	CV of ulnar sensory nerve (m/s)	CV of median Motor nerve (m/s)	CV of ulnar motor nerve (m/s)	Amp of median sensory nerve (μV)	Amp of ulnar sensory nerve (μV)	Amp of median motor nerve (mV)	Amp of ulnar motor nerve (mV)
Mean (SD)	60.0 (5.6)	60.9 (7.2)	59.8 (6.5)	62.8 (6.5)	48.7 (19.3)	46.9 (17.9)	8.3 (3.2)	6.7 (2.6)
Minimum-Maximum	36.1-74.3	36.6-88.9	42.9-87.0	50.0-95.5	12.7-126.3	8.4-127.3	0.7-17.9	1.3-13.0
3rd percentile	50.8	50.0	50.7	51.5	15.1	16.6	2.5	2.2

NCS= nerve conduction studies, SD= standard deviation, CV= conduction velocity, Amp= amplitude, m/s= meter per second, μV= micro-volt, mV= milli-volt

Table 3. Effect of gender on conduction velocity and amplitude of sensory and motor median and ulnar nerves.

NCS Parameter	Gender	N	Mean	SD	P- Value
CV of median sensory (m/s)	Male	104	59.38	5.18	0.119
	Female	136	60.50	5.93	
CV of ulnar sensory (m/s)	Male	104	59.38	7.28	0.005
	Female	136	62.03	6.98	
CV of median motor (m/s)	Male	104	59.18	6.07	0.223
	Female	136	60.20	6.83	
CV of ulnar motor (m/s)	Male	104	60.78	5.21	0.000
	Female	136	64.38	7.03	
Amp of median sensory (μV)	Male	104	42.37	15.61	0.000
	Female	136	53.47	20.40	
Amp of ulnar sensory (μV)	Male	104	39.21	13.09	0.000
	Female	136	52.82	18.87	
Amp of median motor (mV)	Male	104	8.78	3.14	0.032
	Female	136	7.90	3.11	
Amp of ulnar motor (mV)	Male	104	7.20	2.73	0.002
	Female	136	6.17	2.32	

NCS= nerve conduction studies, SD= standard deviation, CV= conduction velocity,
Amp= amplitude, m/s= meter per second, μV= micro-volt, mV= milli-volt.

Table 4. Comparison between sensory nerve action potential of both median and ulnar nerves of the current study with other studies.

Sensory NCS	Para-meter	(5)(n=44) +^*(age range = (19-43 years)	(13)(n=50) +^ **(age range =16-56 years)	(14) (n=100) +^ **(age range =20-60 years)	(12), (11) (n=258) +^*(age range =19-79 years)	(15) (n=11,437) +^** age range =2month-89 years)	(10)(n=61-65)+^*(age range = 11/13-74 years)	Current study (n=120) +^* (age range =18-30 years)
Median	Lat	2.5±0.2	2.3±0.3	2.05±0.35	2.7±0.3	1.93±0.22	2.84±0.34	2.5±0.3
(SNAP)	Amp	31.4±8.7^{m}52.4±14.3^{f}	63.3±18.9 ^{m}79.3±28.8 ^{f}	59.32± 16.39 ^{m}68.69± 20.48 ^{f}	41±20 (11) #	49.5±23.1	38.5±15.6 (19) #	42.4±15.6^{m} 53.5±20.4^{f} All subjects= [48.7±19.3] (15.1) #
	CV	61.2±4.3	56.6±7.6	53.43±3.56	-	51.9±4.04	56.2±5.8 (44) #	60.0±5.6
Ulnar	Lat	2.4±0.2	2.0±0.23	1.85±0.25	2.6±0.2	1.94±0.19	2.54±0.29	2.2±0.3
(SNAP)	Amp	27.0±7.8^{m} 52.9±13.9^{f}	54.5±18.4 ^{m} 63.9±16.8 ^{f}	55.51±18.43 ^{m} 64.92±16.84 ^{f}	33±17 (10) #	50.1±19.8	35.0±14.7 (18) #	39.2±13.09 ^{m}52.8±18.87 ^{f}All subjects= [46.9±17.9] (16.6) #
	CV	64.0±6.9	52.3±5.3	55.78±4.13	-	54.2±3.97	54.8±5.3 (44) #	60.9±7.2

+=antidromic, ^=onset latency, ^^=peak latency, *=baseline to peak amplitude, **=peak to peak amplitude, m=male, f=female, #=cut off values.

Table 5. Comparison between motor findings of both median and ulnar nerves of the current study with other studies.

Sensory NCS	Para-meter	(5)(n=44) +^*(age range = (19-43 years)	(13)(n=50) +^ **(age range =16-56 years)	(14) (n=100) +^ **(age range =20-60 years)	(12), (11) (n=258) +^*(age range =19-79 years)	(15) (n=11,437) +^** age range =2month-89 years)	(10)(n=61-65)+^*(age range = 11/13-74 years)	Current study (n=120) +^* (age range =18-30 years)
Median	Lat	2.5±0.2	2.3±0.3	2.05±0.35	2.7±0.3	1.93±0.22	2.84±0.34	2.5±0.3
(SNAP)	Amp	31.4±8.7^{m}52.4±14.3^{f}	63.3±18.9 ^{m}79.3±28.8 ^{f}	59.32± 16.39 ^{m}68.69± 20.48 ^{f}	41±20 (11) #	49.5±23.1	38.5±15.6 (19) #	42.4±15.6^{m} 53.5±20.4^{f} All subjects= [48.7±19.3] (15.1) #
	CV	61.2±4.3	56.6±7.6	53.43±3.56	-	51.9±4.04	56.2±5.8 (44) #	60.0±5.6

Ulnar	Lat	2.4±0.2	2.0±0.23	1.85±0.25	2.6±0.2	1.94±0.19	2.54±0.29	2.2±0.3
(SNAP)	Amp	27.0±7.8[m]	54.5±18.4[m]	55.51±18.43[m]	33±17 (10) #	50.1±19.8	35.0±14.7 (18) #	39.2±13.09 [m]52.8±18.87 [f]All subjects= [46.9±17.9] (16.6) #
		52.9±13.9[f]	63.9±16.8[f]	64.92±16.84[f]				
	CV	64.0±6.9	52.3±5.3	55.78±4.13	-	54.2±3.97	54.8±5.3 (44) #	60.9±7.2

^=onset latency, ^^=peak latency, *=baseline to peak amplitude, **=peak to peak amplitude, #=cut off values

DISCUSSION

The current study included 120 healthy young adults aiming at estimation of reference values of young Sudanese population in order to be used as normative database when evaluating patients with neuromuscular disorders. A comparison was made between the results of this study and the published literature, illustrated in Tables 4 and 5. The large scale internationally recognized Buschbacher study was among few studies that established detailed reference values of NCS reporting both onset and peak latencies as well as baseline and peak amplitudes, together for individual sensory nerve in addition to the other parameters. For the purpose of comparison; the onset latency and baseline to peak amplitude were selected from Buschbacher' findings to be shown in the tables (4 and 5).

Different laboratories prefer different methods (antidromic or orthodromic) for testing different sensory nerves. The velocity correlates with the sensory latency and therefore either the result may be expressed as latency over a standard distance or velocity[9]. Previous studies findings were summarized in separate tables for sensory (Table 4) and motor (Table 5) studies so as to facilitate comparison and decrease confusion between various parameters of NCSs.

Considering latencies of sensory nerve action potential of both median and ulnar nerves, they were in keeping to those of Hennessey[5], Buschbacher[11,12], Shehab[13] and Kimura[10]. Garg's[14] and Hamdan's[15] who reported shorter latencies. Although all sensory studies (listed in Table 4) had used the antidromic technique that made comparison of amplitudes valid, yet there is small variability in latencies reported by different researchers which can be attributed to the different techniques used to determine electrodes placement (landmark vs measurement), the use of different end points for latency measurement (onset vs peak), and the variable body temperature during recording. Measurement to the onset of the action potential for the distal latency is a more representative measure of the fastest nerve conduction fibers than measurement to the peak. Peak latency was used in the past before the development of the sophisticated digital machines which made it much easier to identify the onset latency of sensory potentials[5].

Regarding sensory conduction velocities, they were much similar to that obtained by Hennessey[5] especially for the median nerve but slightly faster than velocities reported by many other researchers[10,13-15]. As conduction velocity indirectly related to latency of the response, all the factors affecting latency would definitely affect the conduction velocity in addition to the accurate measurement of the distance between stimulating and recording electrodes.

As far as sensory amplitudes of median and ulnar nerves are concerned, they were lower than that of Hamdan[15] possibly because he used peak to peak amplitude measurement. On the other hand, they were higher than Bushbacher's[11,12] and Kimura's[10] amplitudes. In case of studies using gender specific amplitudes, our values were lower than reports of Shehab[13] and Garg[14]. Though males' sensory amplitudes of Hennessey showed much lower amplitudes, females' values showed almost typical values to ours[5]. Despite using the same antidromic

technique, the variations in sensory amplitudes could be explained by differences in finger circumference, stimulus intensity, distance between the active and reference recording electrodes, and the use of different measurement points in the recording trace (onset-peak vs peak-peak amplitude) in different studies.

Considering motor studies (Table 5), our distal motor latencies of ulnar and median were comparable to almost all studies provided in the Table 5 especially, Hennessey[5], Shehab[13] and Naseem[4].

With regard to motor conduction velocities, they were very similar to that obtained by Hennessey[5], and Shehab[13], slightly higher than the findings of Kimura[10], Naseem[4], and Bushbacher[16,17]. Compared to the current study, Garg[14] and Hamdan[15] reported lower median and at the same time higher ulnar conduction velocities.

Motor amplitudes of median and ulnar nerves were similar to that reported by Kimura[10] and Naseem[4], but lower than those obtained by other researchers[5,13-17]. Differences between studies' findings could be attributed to technical variations, in addition to differences in study population demographic characteristics (e.g. ethnicity, age, gender distribution, height and BMI…etc.). The present study involved young adults age group compared to a wider age range included in the other studies.

Few studies had expressed cut off (upper or lower limits of normal) values for nerve conduction study parameters as (3rd, 5th, 95th or 97th) percentiles of the distribution[11,12,16-18], which is the preferred method[2], or as mean (±2 SD)[10], instead most other researchers reported them as only mean (±SD) value without determining upper or lower limits of normal values. The current study derived 3rd percentile motor amplitude values for median (2.5 mV) and ulnar (2.2 mV) nerves which were more or less similar to Kimura's values of 3.5 mV and 2.8 mV; respectively[10], but were lower than 5.9 mV and 7.9 mV, respectively as stated by Buschbacher[13,16.17]. On the contrary, this study revealed 3rd percentile values for sensory amplitudes of median (15.1 μV) and ulnar (16.6 μV) nerves which were in the middle between 11 μV for median and 10 μV for ulnar, respectively as reported by Buschbacher[3,11,12] and 19 μV for median and 18 μV for ulnar as reported by Kimura[10]. In addition, this study showed conduction velocity cut off values for median motor as 50.7 m/s and ulnar motor as 51.5 m/s; which were keeping with 49 m/s and 52 m/s reported by Buschbacher[3,16,17)] and 48 m/s and 49 m/s, reported by Kimura[10]. Finally, conduction velocity cut off values for median sensory (50.8 m/s) and ulnar sensory (50 m/s); were higher than 44 m/s reported by Kimura for both sensory median and ulnar nerves[10].

The current study (Table 3) revealed that young females have higher conduction velocities of sensory and motor, ulnar and median nerves but those of median nerve were not statistically significant, compared to the highly significant ulnar values. In addition, it showed that females had significantly higher sensory amplitudes, but significantly lower motor amplitudes than the male subjects.

Our finding that females had higher sensory amplitudes was in agreement with many previous studies[5,13,14,19,20], but the findings that males had higher motor amplitudes was supported only by Thakur et al from Nepal[19]. Young males have larger muscle mass and lower amount of subcutaneous fat than females; that is why recording can be obtained from a larger number of underlying muscle fibers. Gakhar et al reported results similar to the current study, that females have higher sensory amplitudes and conduction velocities in both motor and sensory median and ulnar nerves. It only contradicted ours in their finding that females and not males have higher motor amplitudes[20]. Another study conducted in Sri Lanka showed significant differences between males and females in conduction velocity of only left motor ulnar and right sensory ulnar nerves ($p<0.05$)[21], and in Central India showed significant influence of gender on sensory amplitudes and conduction velocity of ulnar nerve only[22]. The difference in sensory amplitude was attributed to females having digits of smaller circumference, resulting in digital nerves being

closer to the recording ring electrode enclosing the digit[23]. Stetson et al. explained differences in bone mass and subcutaneous tissue to be the main factors contributing to the finger circumference differences[24]. Therefore, the significant difference in sensory amplitudes was concluded to be caused by the influence of finger circumference rather than a direct influence of gender[5].

The strength of this study is the inclusion of large sample size (120) and performance of both sensory and motor NCSs testing the two commonly examined nerves bilaterally. In addition, it had thrown the light to the effect of gender on nerve conduction studies. The reference values were calculated from the analysis of 240 nerves (right and left values) which is a reasonable number to derive reliable reference values. On the other hand, performing the study in specific age group made it difficult to study the effect of age on NCS parameters and provided reference data only for young adults. Further studies in Sudan and other countries in the region and worldwide are needed to establish their own reference values, involving other age groups and to elaborate on the effect of gender and other demographic data on NCS parameters.

CONCLUSION

The study had provided a good base for normative database of the commonly tested upper limb nerves for our young Sudanese population. These reference values were within the range of the published literature. The most important issue, it showed significant influence of gender on the different parameters of nerve conduction studies. This might raise the need for gender specific reference values for accurate evaluation of nerve conduction studies reports in neurophysiology clinics.

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Adherence to anti-seizure medications among Sudanese children and associated factors using Morisky Medication Adherence Scale: facility-based study

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ABSTRACT

Background Adherence to anti-seizure drugs is important and significantly influences the outcome. It is defined as "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen". In this study, we aim to determine the degree of adherence to anti-seizure drugs using special scale and factors associated with non-adherence.

Methods This is a descriptive, cross-sectional study carried out at epilepsy outpatient clinics at Jaafar Ibnauf and Soba University Hospital in Khartoum State, in the period from January 2020 to April 2020. A structured, coded, pre-tested questionnaire was used for data collection and the Morisky tool for assessing medication adherence.

Results The study included 350 participants with a mean age of 8.4 years. About half (n=170, 48.6%) of the participants had high adherence to their medications; 86(24.6%) had medium adherence and 94(26.9%) had low adherence when using Morisky Medication Adherence Scale. Un-availability, un-affordability, and in-accessibility to drugs were the commonest associated factors with low adherence scores. Ensuring the availability and affordability of anti-seizure drugs is highly needed in resource-limited countries.

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INTRODUCTION

Anti-Seizure drugs (ASDs) are the mainstay of therapy in the management of epilepsy and can achieve seizure freedom in 70% of patients if effective treatment guidance is followed[1]. However, epilepsy remains uncontrolled in the majority of patients with epilepsy in developing countries[2] and non-adherence remains the leading cause of treatment failure[3-5]. Adherence to treatment is important for successful epilepsy management; studies reported that the rate of adherence to ASDs ranges from 32% to 62%[6-8]. Many factors including belief about medications, co-morbidity, number of medications, duration of therapy, age, gender, and educational status of caregivers have been reported to affect the rate of medication adherence[9]. Non-adherence to ASDs leads to poor seizure control, frequent hospital admissions, increased healthcare cost, impaired quality of life, and increased risk of mortality[10]. In this study, we used Morisky Medication Adherence Scale (8-item, MMAS-8) to measure adherence to ASDs among epilepsy patients in Khartoum, Sudan and the possible associated factors.

METHODS

This is a descriptive, prospective cross-sectional study, conducted in two main paediatric epilepsy clinics in Khartoum State, namely Jaafar Ibnauf Specialized Hospital for Children and Soba University Hospital. The Neurology outpatient departments (OPD) clinics are carried out as once per week, with a total number of about 30-50 patients per clinic coming from different states of Sudan. The study was conducted from January to April 2020 and all patients (age 2 months to 18 years) with confirmed diagnosis of epilepsy and on ASDs were enrolled. The data was collected using designed questionnaire, which included

seizure profile, epilepsy classification according to The International League Against Epilepsy (ILAE 2017), and factors possibly associated with medication non-adherence. To measure the adherence to ASDs we used the 8-item Morisky Medication Adherence Scale (MMAS-8)[11-12]. Morisky Medication Adherence Scale is a validated assessment tool used to measure non-adherence in a variety of patient populations. It was verified by numerous studies with over 110 versions and over 80 translations. The tool uses a series of short behavioural questions geared in such a way to avoid "yes-saying" bias commonly seen with chronic care patients. Response choices are "Yes" or "No" for items 1 through 7 and item 8 has a five-point Likert response scale. Each "No" response is rated as 1 and each "Yes" response is rated as 0 except for item 5, in which each "Yes" response is rated as 1 and each "No" response is rated as 0. For Item 8, the code (0-4) has to be standardized by dividing the result by 4 to calculate a summated score. Total scores on the MMAS-8 range from 0 to 8, with scores of 8 reflecting high adherence, 7 or 6 reflecting medium adherence, and <6 reflecting low adherence. By understanding, how the patient scored on the scale, clinicians can identify underlying issues that prevent patients from taking their medications correctly. Similar to other self-report methods, the Morisky Medication Adherence Scale can be subject to a lot of confounding factors such as impaired recall.

The Data was analysed using the statistical package for social sciences (SPSS version 24.0). Descriptive statistics was reported as means, standard deviations, frequencies and percentages. Analysis of variance (ANOVA) and Chi squire test were used to assess association between dependent and independent variables; $P < 0.05$ indicated significance. Ethical approval was obtained from Sudan Medial Specialization Board Ethics and Research Committee. Informed written consents were obtained from the parents or caregivers after explaining the aim of the study.

RESULTS

This study included 350 participants with mean (± SD) age of 8.4 ±4.7 years. Male to female ratio was 1.5:1. Two hundred and fifty-seven (73.4%) participants were from urban area and 93 (26.6%) from rural areas. The mean (± SD) age of onset of seizures was 3.73 ±3.73 years and the mean (± SD) duration of the disease was 4.71 ±3.91 years. Three hundred and five (87.1%) participants came from low-income background. Epilepsy was classified using ILAE classification 2017. Ninety-five (27.7%) had focal onset seizures, 251 (71.11%) generalised onset and four (1.1%) had unknown onset seizures. The mean (± SD) duration of ASDs usage was 3.35 ±3.19 years. Two hundred and twenty-three (63.7%) patients were on monotherapy, ninety-four (26.9%) on two ASDs and 33 (9.4%) were on polytherapy. One hundred and seventy (48.6%) patients were on syrup formulae; 150 (30%) on tablets and 75 (21.4%) were on syrup and tablets. One hundred and seventy 170 (48.6%) patients had high adherence to medications on Morisky Scale, 86 (24.6%) had medium and 94 (26.9%) had low adherence (Table 1).

Table 1. Morisky Medication Adherence Scales items response.

		Number	%
Do you sometimes forget to take your medication?	Yes	117	33.4
	No	233	66.6
Are there situation that make you fail to give medication to your child?	Yes	115	32.9
	No	235	67.1
In the past two weeks, are there days the child failed to take medication?	Yes	084	24.0
	No	266	76.0
Do you forget to bring medication when travel or leave home?	Yes	023	6.6
	No	327	93.4
Did you take your medication yesterday?	Yes	319	91.1
	No	031	8.9
When symptoms under control do you stop medication?	Yes	014	4.0
	No	336	96.0
Do you feel hassled about sticking on treatment plan?	Yes	047	13.4
	No	303	86.6

Two hundred and seventy-six (78.9%) of the caregivers reported that they never or rarely had difficulty remembering the ASD medications' time, while, 41 (11.7%) forgot once-in-a-while, 23 (6.6%) sometimes, seven (2.0%) usually and only three (0.9%) forgot to take their medications all the time. Seventy-eight (22.3%) children tended to refuse taking their ASDs. One hundred four (84.6%) of the children took their medications at home and nineteen (15.4%) at school. One hundred and seventy-three (49.4%) caregivers reported that the ASDs were not available, 145 (41.4%) admitted that ASDs were at un-affordable cost and 100 (59.7%) reported that ASDs were not accessible to them.

Almost all participants thought that the time spent with health care givers was enough except two (0.6%) who thought that time was not enough because of the crowded clinics. Three hundred and forty-one (97.4%) thought that they were given all necessary information from their health care givers about ASDs usage and that the information was well understandable.

One hundred and fifteen (32.9%) of the children were given ASDs by their mothers followed by 64 (18.3%) by mother and elderly siblings; 61 (17.4%) given by their parents, 51(18.3%) by child himself, nine (2.6%) by grandmother and mother while 32(9.1%) by others. This was found to be of no statistical significance (p value=0.215)

Table 2. Factors affecting adherence to anti-seizure drugs (ASDs)

Factor	Yes N (%)	No N (%)
Formulation of ASDs Suitable	315(90.0)	035(10.0)
Availability of ASDs	177(50.6)	173(49.4)
Affordability of ASDs	205(58.6)	145(41.4)
Accessibility of ASDs	141(40.3)	209(59.7)
Refusal of taking medication	078(22.3)	272(77.7)
Health insurance	219(62.6)	131(37.4)
Enough time with health care giver	348(99.4)	002(00.6)
Given information by healthcare giver	341(97.4)	009(02.6)
Side effects	305(87.1)	045(12.9)
Understandable	341(97.4)	009(02.6)
Taking medication (school/ home)	School 019(15.4)	Home 104(84.6)
Cost of services for epilepsy treatment	affordable 080(22.9)	Expensive 270(77.2)

One hundred and eighty-seven (53.4%) caregivers thought that epilepsy is both curable and treatable, 109 (31.1%) thought that it is a treatable disease but did not know if it is curable or not and 34 (9.7%) thought that epilepsy is treatable but is not curable while 17 (4.8%) did not know the fate of epilepsy (Table 3).

Table 3. Perception about the fate of epilepsy among the study participants (n=350)

		Number	%
Perception about the fate of epilepsy	Curable	000	00.0
	Treatable	000	00.0
	Curable and treatable	187	53.4
	Treatable not curable	034	09.7
	Treatable, don't know if curable or not	109	31.1
	Don›t know	017	04.8
	Curable, but don›t know if treatable or not	003	00.9

One hundred and twenty-five (64.4%) patients used spiritual methods, 60 (30.9%) spiritual and herbal methods while 8 (4.2%) used herbal medicine.

There was no significant statistical correlation between MMAS-8 scores and age of the patient (p= 0.223), gender (p=0.117), age at onset of the disease (p=0.958), duration of seizure (p=0.143), duration of treatment (p=0.299), educational level of caregivers (p=0.367), gender of caregivers (p=0.072), parental marital status (p=0.453) or perception about epilepsy (p=0.476). There was significant correlation between low MMAS-8 score and low monthly income of the family (p<0.053), un-availability of ASDs (p<0.005), un-affordability of ASDs (p<0.015), and inaccessibility to ASDs (p<0.002). There is also significant correlation between low MMAS-8 score and generalized motor onset seizure type (p<0.005)

DISCUSSION

Anti-seizure drugs (ASDs) regimens can dramatically control seizure manifestation and improve the prognosis for patients with epilepsy. However, it can be difficult to attain best efficacy in practice. One main reason for this is the non-adherence to ASDs regimens. Cramer et al have defined adherence as "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen"[13]. Non-adherence to ASDs may be associated with serious complications of epilepsies such as increased hospitalization, emergency department admission and increases the cost of treatment[14]. Thus, it is important to assess medication adherence and discuss it with patients when treatment appears to fail[15].

Despite the lack of a standard for measuring adherence to medication, both direct and indirect measures are currently used in clinical practice. Direct methods, the most common measures of adherence, involve monitoring metabolite concentration through body fluid and therapeutic drug monitoring. However, in clinical settings, it is often unreliable to measure adherence through plasma concentration because a number of factors can influence the results such as drug interaction, individual drug pharmacokinetics and physiological changes[16]. In addition, assessing plasma concentration is expensive, time intensive and not available at our setting. Thus, health care researchers have begun developing indirect instruments; one self-reported questionnaire, the 8-item Morisky Medication Adherence Scale (MMAS-8)[17] is used to assess adherence in outpatients with chronic disease. It is widely used because it is free to administer, simple, and has a good relationship with other measures of adherence[18]. In this study Morisky scale was calculated and most (n=170, 48.6%) of the participants had high adherence to their medications, 86 (24.6%) had medium adherence and 94 (26.9%) had low adherence. These results are consistent with a study that used the four-item MMAS in Chinese patients with epilepsy[19]. Similarly, Morita et al reported a total adherence of approximately 79.4% in patients with new-onset epilepsy[20] and Kholoud et al from Jordan reflected comparable findings[21].

In this study, there were no statistically significant correlation between adherence scale score and age of the patients, gender, residency, age at onset of seizure or duration of the epilepsy. Similar results were reported from Kenya, Riyadh, Scotland, and Iran[22-25]. However, there is significant correlation between low adherence scale and having generalized motor onset seizures ($p< 0.035$). Noraida et al from Northern Ireland and Eiad et al from Saudi Arabia reported comparable finding[26,27]. In this study, there was also a significant association between low adherence score and un-availability, un-affordability and un-accessibility to ASDs. Badrelddin et al from Sudan and Muhammad Akbar et al from Pakistan observed significant association between availability, affordability and adherence scale[5,23]. Moreover, there was no significant correlation between number of ASDs and adherence scale score, which was in agreement with that reported by Muhammed et al from Bursa and Rose et al from Uganda[28,29]. Ensuring the availability, affordability and accessibility of investigations and ASDs is highly needed in our set up and should to be covered by health insurance.

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Assessment of learning abilities and school performance of epileptic Sudanese children

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ABSTRACT

Objective Patients with epilepsy are at significant risk for cognitive impairment and behavioral abnormalities. The aim of this study was to assess the learning abilities and school performance of epileptic children attending Wad Medani Children Teaching Hospital.

Methods This was a prospective cross-sectional case-control facility-based study. Data were collected from hospital data-base and from school records. A total of 70 patients with epilepsies were recruited as index cases and 70 age and sexmatched non-epileptic patients were included as controls. Both groups underwent comprehensive psychometric assessment. Consensus neurobehavioral diagnoses were made with respect to Diagnostic and Statistical Manual. Stanford Binet Test and Battery Scales were used to assess the intelligent quotient and learning abilities, respectively.

Results The study population were school age (5-16 years) children; 48.6% were less than age 10 years. The male: female ratio was1:1.1 A significant increase in learning difficulties among cases compared to control group in all domains. The overall learning difficulties results showed a statistically significant level of learning difficulties among index cases compared to controls, with P value of < 0.001. Similarly, a significant reduction in intelligent quotient test results among the cases compared to controls.

Conclusions Significant learning disabilities, deterioration in school performance and intelligent quotient were detected in children with epilepsies. All children with epilepsy should be considered vulnerable to learning disabilities.

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INTRODUCTION

Epilepsy is defined as two or more unprovoked seizures occurring in a time frame of longer than 24 hrs[1]. It is a chronic disorder with a cumulative life time incidence of 3%, and annual prevalence of 0.5-1.0%[2]. Children with epilepsy are at risk for academic under-achievement[3]. A significant and continuing disagreement has been associated with the definition of learning disabilities (LD)[4]. The LD has been limited by the Diagnostic and Statistical Manual (DSM-5) to a single diagnosis criterion describing problems of academic skills in general. This includes areas of reading, mathematics, and written expression[5,6]. The National Joint Committee on LD (IDEA)'s defines LD as "a disorder in one or more of the basic psychological processes involved in understanding or in using language, spoken or written. This may manifest as imperfect ability to listen, think, speak, read, write, spell, or do mathematical calculations"[7].

Battery Metrics measures developmental learning, academic learning and the social and emotional behaviour difficulties; based on the teacher, father, or mother's estimate. Measures of developmental learning difficulties consist of five measures: attention, audio recognition, visual perception, cognitive perception and memory. Whereas, measures of academic learning difficulties consist of three measures: reading, writing, listening and mathematics. These nine measures constitute the scale of difficulties of social and emotional behaviour[8]. Stanford Achievement Test–10th edition is the most commonly used comprehensive test. It is a widely accepted standard in the measurement of intelligence[8].

The level of global cognitive function was characterized as within the normal range ("normal" consistent with intelligent quotient (IQ) scores ≥

80), borderline (consistent with IQ scores of 70–79), mildly retarded (consistent with IQ scores of 60–69), moderately or severely retarded (consistent with IQ scores <60), and neurologically devastated-not testable. Based on the manuscript of the scale the scores of the children on the three scales (reading, writing and listening) were as follow: normal skills (0-<21); mild difficulties (21-40); moderate difficulties (41-60); and severe difficulties (> 60).

Learning disabilities association with epilepsy has been ascribed to many psychosocial, medication-related, and epilepsy-related factors. Epilepsies may interfere with LD by various neurophysiological mechanisms including: 1) Disturbance of epileptiform activity continuing processing impedes attention to incoming information, its storage or recovery 2) temporally distant discharges from the learning experience disrupt storage and retrieval of information 3) long-lasting neural tissue damage 4) anti-seizure drugs toxicity and 5) chronic frequent discharges during sleep resulting in disruption of brain function[10]. Subclinical generalized spike wave discharges may be accompanied by transitory cognitive impairment demonstrable by psychological testing during electroencephalogram (EEG) recording[11]. Arzimanoglou A et al, recently reported a good correlation between temporal lobe epilepsy, interictal affective, personality disturbance, well-directed violence and self-destructive behaviour in postictal psychosis[12].

Subclinical EEG discharges may be accompanied by a disruption of educational skills in children, and that ant-seizure drugs (ASDs) suppression of discharges is associated with improvement of cognitive function[13,24]. Frontal lobe epilepsies in children, or in adults are associated with onset of severe behavioural and psychotic disturbances, schizophrenia-like or autism-like syndromes[15].

The efficacy and the presence of cognitive and behavioral side effects of various ASDs had been investigated[16]. Walker M et al, tentatively suggested that drugs such as lamitrogene, carbamazepine (CBZ), oxcarbamazepine, valproate, and felbamate are less often reported as affecting cognitive functions, in contrast to some other drugs such as phenobarbital, phenytoin, and clonazepam, and so there is still a need for evidence-base guidelines in this area, and the effect of many of the new drugs on cognition must be investigated[17].

Age of seizure onset and attention hyperactivity disorder (ADHD) were risk factors for reading and mathematics LD. Writing was the most common domain affected. These variable factors largely suggest that all children with epilepsy should be considered vulnerable to LD[18]. The aim of this study was to assess the learning abilities and school performance of epileptic children attending Wad Medani Children Teaching Hospital.

METHODOLOGY

This was a prospective cross-sectional case-control facility-based study carried out during the period from 1/12/2018 to 1/8/2019. It was conducted in Wad Medani Children Emergency Teaching Hospital, a general children hospital in Gezira State, Sudan with a capacity of 150 beds. There are different referred clinics for different disciplines; one referred clinic per week is assigned for neurology where 35 patients of variable neurological problems were seen. Epilepsy was the commonest disorder and about 15 to 20 new and/or old cases were managed weekly. Only school age children with no obvious cause for the epilepsy i.e. had no structural brain abnormalities explaining epileptic seizures were included as cases. They might conform to the term idiopathic epilepsy (according toThe International League Against Epilepsy (ILAE) Classification 2017). However, further genetic studies were not currently feasible in Sudan for many constraints and logistics reasons. Exclusion included children with symptomatic epilepsies (i.e. disorders with an identifiable cause such as severe head trauma that can cause symptomatic epilepsy), those who recovered completely from idiopathic epilepsies or children who had another disease which might be a confounding factor to poor school performance as well as children whose families refused to join the study.

Four schools (one basic and one secondary) for girls

and similarly for boys were selected purposefully for logistic reasoning. In these schools "the control patients" were healthy (non-epileptic) pupils selected, including senior students from the four classes from basic-school, and senior students from higher schools using systemic random sampling technique. They were age and sexmatched. They were submitted to psychometric tests. In both cases and control groups the number of samples was small due to difficult and lengthy psychometric tests which allowed not more than two to three children to be tested in each setting. Both groups were tested for IQ and learning disabilities.

The data was collected using a pre-designed questionnaire that included the basic data of children such as; demographic data, age, gender …etc. The pupils' academic performance at all classes was obtained from the school registry. The adherence to anti-seizure drugs (ASDs) was checked by Morisky Medication Adherence Scale and this was conducted by researchers. The I.Q. tool used was Stanford-Binet Intelligence Scale, fifth edition (SB5). The test was performed by a trained psychologist. This test measured five weighted factors and consisted of both verbal and nonverbal subtests. The five factors being tested were knowledge, quantitative reasoning, visual-spatial processing, working memory, and reasoning.

The Independent variables included age, gender, father and mother's educational level and diagnosis; while the dependent variables were I.Q, academic score and psychometric test. The study was approved by the Ethics Review Committee of the Sudan Medical Specialization Board and the Council of Paediatrics and Child Health. Permission of the hospital director was granted before starting the study as well as verbal and written consents from the parents. Using the statistical package for social sciences (SPSS version 14.0 Inc. Chicago, IL, USA) all values were expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) and difference between means was assessed by a two-tailed student t-test. $P \leq 0.05$ was considered statistically significant.

RESULTS

A total of 70 cases and 70 controls were studied; 48.6% of the children were less than 10 years of age, and male: female ratio was 1: 1.1. The frequency of repeating a class in school was significantly higher among cases group (41.4%) compared with control group (7.1%) with p value < 0.001. Similar significant differences of the academic score between the two groups before being diagnosed with epilepsy (p value < 0.05) as shown in Table 1.

A significant academic deterioration was found among the cases group before and after epilepsy with p value < 0.001. The proportion of failure cases increased from 17.1% to 34.3% while the proportion of good level was reduced from 45.7% to 27.1%. Concerning some seizures characteristics among the cases group, the study found that more than two thirds (70%) of them had their first seizure attack before age 5 years, and the majority (78.6%) suffered from seizures for 1 to 5 years. However, the vast majority (91.4%) had their last seizure attack one year previously.

Regarding the seizure management, 84.3% of the cases were on regular follow-up: 75.7% were treated with monotherapy and 24.3% with poly-therapy. Most (80%) of them had good compliance with the treatment and 91.4% of them took their medication every 12 hours.

More than four-fifth (88.6%) of the cases under the study had missed a school day because of epilepsy, while 62.9% and 24.2% of them had missed because they had a doctor appointment, or they might have seizure before going to school, respectively. More than half (54.8%) of them had seizures at school and 76.5% went home before the end of classes.

The overall learning difficulties results showed a higher significant level of learning difficulties among the cases compared to controls with P value < 0.001. Similarly, there was a significant reduction in IQ test results among the cases group compared to controls with P value = 0.003 (Table 2). There was no significant association between the learning difficulties with the epilepsy duration (p = 0.399), regularity of follow up (p = 0.4), or treatment

compliance (p = 0.052). However, there was strong correlation between poor academic performance and missing a school day because of epilepsy (p = 0.001), and having seizures at school (p = 0.001, Table 3).

Table 1. The distribution of the study participants according to their academic score (n = 140, 70 cases + 70 controls)

Academic score	Study groups				Total	
	Cases		Controls			
	Freq.	%	Freq.	%	Freq.	%
Fail	12	17.1	03	4.3	27	19.3
Pass	15	21.4	06	8.6	28	20.0
Good	32	45.7	14	20.0	33	23.6
Very good	09	12.9	27	38.6	31	22.1
Excellent	02	2.9	20	28.6	21	15.0
Total	70	100.0	70	100.0	140	100.0

Table 2. Measures of developmental learning difficulties (n = 140, 70 cases + 70 controls)

Measures of developmental learning difficulties	Study groups					P value
	Cases		Controls			
	Freq.	%	Freq.	%		
Attention	Normal*	23	32.9	65	92.9	< 0.001
	Mild*[1]	13	18.6	05	7.1	
	Moderate*[2]	22	31.4	00	0.0	
	Severe*[3]	12	17.1	00	0.0	
Audio recognition	Normal	45	64.3	66	94.3	< 0.001
	Mild	15	21.4	04	5.7	
	Moderate	07	10.0	00	0.0	
	Severe	03	4.3	00	0.0	
Visual perception	Normal	21	30.0	65	92.9	< 0.001
	Mild	11	15.7	05	7.1	
	Moderate	16	22.9	00	0.0	
	Severe	22	31.4	00	0.0	
Cognitive perception	Normal	47	67.1	69	98.6	< 0.001
	Mild	10	14.3	01	1.4	
	Moderate	09	12.9	00	0.0	
	Severe	04	5.7	00	0.0	
Memory	Normal	22	31.4	65	92.9	< 0.001
	Mild	24	34.3	05	7.1	
	Moderate	09	12.9	00	0.0	
	Severe	15	21.4	00	0.0	

*normal= consistent with IQ scores ≥ 80), borderline (consistent with IQ scores of 70–79), *[1]mildly retarded= consistent with IQ scores of 60–69, *[2]moderately or *[3]severely retarded= consistent with IQ scores <60, and neurologically devastated-not testable.

Table 3. Measures of academic learning difficulties among cases (n=70) and controls (n=70)

Measures of academic learning difficulties	Study group					P value
	Cases		Controls			
	Freq.	%	Freq	%		
Reading	Normal*	13	18.6	64	91.4	< 0.001
	Mild*[1]	21	30.0	05	7.1	
	Moderate*[2]	04	5.7	01	1.4	
	Severe*[3]	32	45.7	00	0.0	
Writing	Normal	18	25.7	68	97.1	< 0.001
	Mild	08	11.4	01	1.4	
	Moderate	04	5.7	01	1.4	
	Severe	40	57.1	00	0.0	
Mathematics	Normal	05	7.1	57	81.4	
	Mild	01	1.4	03	4.3	< 0.001
	Moderate	16	22.9	06	8.6	
	Severe	48	68.6	04	5.7	
Social impulse behavior	Normal	50	71.4	70	100.0	< 0.001
	Mild	14	20.0	00	0.0	
	Moderate	02	2.9	00	0.0	
	Severe	04	5.7	00	0.0	

*Based on the manuscript of the scale the scores of the children on the three scales (reading, writing and listening) were as follow: *Normal skills 0-<21, *[1]Mild difficulties 21-40, *[2]Moderate difficulties 41-60 and *[3]Severe difficulties > 60

DISCUSSION

The psychometric testing and IQ assessment are cumbersome tests and time consuming; this is why the number of cases with epilepsy was small in this study despite a considerable number of patients attending the neurology clinics. Nearly two thirds (63.6%) of the study group were in the senior 4 classes of the basic school, while a small proportion (11.4%) of the control group were in the secondary school level. The academic score of the cases group before diagnosed with epilepsy was significantly lower than that of the controls (p value < 0.05). A significant deterioration was found in the academic score among the cases group before and after epilepsy with p value < 0.001. A low overall score increased from 17.1% to 34.3% and the academic performance dropped from 45.7% to 27.1%. In contrast, a West African study by Enugu et al revealed that 13 (26%) of epileptic children had a low overall score, and therefore poor academic performance, compared to 16% of the controls (p value = 0.35)[3]. However, the epileptic children mean score was significantly lower than that of the control group in English language (p value = 0.02), Science (p value = 0.02) and Social studies (p value = 0.02). The overall academic performance of epileptic children without other chronic disorders attending normal schools was not different from that of normal children in the same setting, though they were under-achieving in some subjects[22]. The frequency of repeating a class in school in this study, was significantly higher among the cases (41.4%) compared to the control group (7.1%) with p value < 0.001.

Regarding the seizure management, 91.4% of cases took their drugs every 12 hours and 84.3% of the cases were on regular follow-up. Cases who were on mono-therapy were 75.7% whereas 24.3% were on poly-therapy. The majority (80%) of the cases had good compliance. Not surprisingly, our

study revealed that there was no significant relation between control of epilepsy and specific type of treatment, with impaired learning function. This is supported the study done in 2002 which revealed that ASDs may improve learning by reducing the number of EEG discharges or the frequency of seizures. However, ASDs as a result of its direct side effects: sleepiness, slowed reactions, attention deficit, and so on, may impair learning abilities. The relevance of the clinical observations of each case should be considered[19].

This study showed that more than four-fifth (88.6%) of the cases missed some school days because of epilepsy; this supported Ibekwe R et al study from Nigeria which showed that the mean and standard deviation of the number of days an epileptic child was absent during their study period, was 15.3 ± 13.8 days while that of the controls was 9.4 ± 9.6 days ($x2 = 3.4$, $df = 49$, $p < 0.001$). Their relationship between the rate of absenteeism and overall score among both epileptic children ($x2 = 6.34$, $df = 2$, p. value = 0.18) and the controls ($x2 = 1.43$, $df = 2$, p. value = 0.49) was not significant. School absenteeism was therefore, more common among epileptic children, though there was no observed negative effect of this increased absence on academic performance[20].

In this study there was also a significant increase in learning difficulties in all domains i.e. attention, audio recognition, visual perception, cognitive perception and memory, in addition to academic learning difficulties such as reading, writing, mathematics and social impulse behaviour, among the cases compared to the controls (p value < 0.001 in all). This was in agreement with Marston study which showed that the learning difficulties in general and specific abnormal patterns of cognitive functioning were well documented in children with epilepsy and was most pronounced in those with frequent interictal discharges[21]. Their study showed that epilepsy may interfere with learning abilities in accordance to the review of Cornaggia CM and colleagues[17]. Aarts J et al found that there was no evidence that intermittent cognitive impairment due to the discharges themselves contributes significantly to such neurophysiological abnormalities[13]. However, studies on epilepsies and specific type of learning disabilities were not found on thorough searching of the literature. Singhi PD et al[14] study found a significant reduction in IQ test results based on Malin's Indian modification of the Wechsler Intelligence Scale for Children, among cases compared to the controls with a P value = 0.003. The mean ± SD IQ scores of children with epilepsy (85.6 ± 12) and their siblings (93.2 ± 11) were significantly lower than those of the controls (101.6 ± 9). The IQ scores of the children with epilepsy were also significantly lower than those of their siblings ($p < 0.05$)[14].

Learning disabilities are more common in people with epilepsy than in the general population: One quarter (25%) of epileptic patients are said to have LD[8]. Variable factors in children with epilepsy influence their school performance, such as seizure frequency and absenteeism[17]; effects of anti-seizure medications, hyperactivity/attention deficit; sociability problems and an overprotective attitude by parents and teachers[17]. Our study did not find any significant association between the learning difficulties with the duration of suffering from epilepsy ($p = 0.399$), regularity of follow up ($p = 0.4$), or good treatment compliance ($p = 0.052$). On the other hand, the study found a strong relation between poor academic performance and missing a school day because of epilepsy ($p = 0.001$), having seizures in school ($p = 0.001$), teacher anxiety ($p = 0.001$), and the stigma ($p = 0.001$). Minshew NJ and his colleagues found that undiagnosed severe epileptic conditions, such as some frontal lobe epilepsies with sub-continuous specific EEG activity (including rapid activity lasting between (1 and 1.5 s), are subsequently associated with onset of severe behavioral disturbances (sometimes with psychotic symptoms), or schizophrenia-like or autism-like syndromes. This question occurs not only in children, but also in adults[15].

In conclusion, all children with epilepsy should be considered vulnerable to LD. Adolescent patients need special consideration. It is important to find the reason(s) for a child's poor school performance

and come up with a treatment plan early so that the child can perform up to full potential. The efficacy and the presence of cognitive and behavioural side effects of various ASDs has to be investigated, particularly the effect of many of the new anti-seizure drugs. One of the main limitations of this study is the unavailability of genetic testing that helps in epilepsy diagnosis.

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Pheochromocytoma: Clinical profile and management in children and adolescents, at Gaafer Ibn Auf Children Hospital, Khartoum, Sudan (2015-2020)

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ABSTRACT

Background Pheochromocytomas are rare catecholamines secreting neuroendocrine tumors that arise from the adrenal medulla They are implicated in 0.5–2% of cases of secondary hypertension in paediatrics, Adrenalectomy is the main treatment of pheochromocytoma.

Objectives to describe the clinical characteristics, management and outcome of pheochromocytoma in Sudanese children and adolescents and to raise healthcare professionals' awareness as many cases are likely being missed.

Patients and methods Records of all patients who were diagnosed as having pheochromocytoma in the endocrinology unit at Gaafer Ibn Auf Children Hospital between January 2015 and December 2020 were reviewed, retrospectively. Data including demography, clinical, biochemical, radiological, management and outcome were obtained.

Results A total of eight cases were identified. The most common clinical features were hypertension (100%), headache (87.5%), palpitations (75%), diaphoresis (62.5%) and 62.5% had complications at presentation. The tumors were intra-adrenal and benign in all patients. Three were bilateral with two of them being familial. Adrenalectomy was undertaken in seven patients and there was no use of adjunctive radiotherapy or chemotherapy. No mortality was reported.

Conclusion This is the first report of pheochromocytoma from Sudan; hypertension being the main feature and emphasizing the importance of high index of suspicion allowing early detection and preventing the devastating complications including hypertensive crisis and end organ damage.

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INTRODUCTION

Pheochromocytoma (PCCs) are tumors that arise from the adrenal medulla chromaffin cells secreting catecholamines and represent 80–85% of tumors whereas paragangliomas account for 15–20% of tumors[1]. Catecholamines, synthesized and secreted by PCCs, are mainly norepinephrine (NE) and epinephrine (EPI). These are further metabolized to normetanephrine and metanephrine, respectively[1,2]. Approximately 10% to 20% of the tumors present during childhood, with an incidence of 0.2 to 0.5 cases per million[2,3]. Paediatric PCCs are associated with a gene mutation in 30-70% of cases compared to adults, although sporadic cases can occur[4]. Genetic syndromes most frequently linked with PCC are Von Hippel-Lindau (VHL) disease, multiple endocrine neoplasia (MEN) 2A, 2B, neurofibromatosis (NF) and Type I and PGL-PCC syndromes involving succinate dehydrogenase gene mutations. Therefore, genetic testing is mandatory for all children who present with PCC[5,6].

The clinical manifestations of childhood PCC are quite variable. The average age of paediatric PCCs is 11–13 years at presentation, with a male: female ratio of 2:1. Symptoms and signs are due to catecholamine's excess. PCCs are implicated in 0.5–2% of secondary hypertension in paediatrics[7], which is sustained in contrast to adults who manifest predominantly with paroxysmal hypertension[3]. Diaphoresis, headache, palpitations, anxiety and pallor are the commonest symptoms, whereas nausea, vomiting, weight loss and visual disturbances can also be among presenting symptoms. Furthermore, PCC in children can present with nonspecific symptoms and signs such as behavioral changes and hyperglycemia[7].

The gold standard for diagnosis is through measurement of catecholamine metabolites, the metanephrines (metanephrine and normetanephrine) in plasma and 24-hour urine with sensitivity approaching 100%[7,8]. Once diagnosis is established biochemically, the next step is to perform anatomical imaging by computerized tomography (CT) or magnetic resonance imaging (MRI) of abdomen and pelvis for localization of the tumor, identification of metastatic lesions and for surgical resection. Functional imaging with ^{123}I-MIBG and PET/CT provide a higher specificity than anatomical imaging and is recommended for diagnosis of multi-focal or metastatic disease and for localizing tumor in patient with negative imaging but positive biochemical testing. Adrenalectomy is the primary treatment for PCC and in patients with bilateral PCCs, cortical-sparing surgery should be planned to avoid lifelong steroid replacement[7]. Pre-operative preparation is crucial and patients should be well prepared for at least 7–14 days prior to surgery. The aim is to control arterial blood pressure and restore blood volume to prevent intra-operative hypertensive crisis and mortality. This is accomplished by using α and β blockers. β blockers should never be started prior to α blockers because this may lead to hypertensive crisis, heart failure and death[8,9]. The main intra-operative complication is the hemodynamic instability, hypertension before tumor removal and hypotension after tumor resection. Sodium nitroprusside and nitroglycerine are safe drugs for intra-operative control of hypertension with esmolol as adjunct for intra-operative hypertension and tachycardia control. Post-operative management requires an intensive care. Catecholamine withdrawal will result in hypotension requiring treatment with fluid loading along with vasopressors infusion, and rebound hyperinsulinemia resulting in severe hypoglycemia; thus blood sugar monitoring is mandatory after the surgery[10]. In this series, we aimed to describe the clinical characteristics, management and outcome of PCC in our patients and to highlight difficulties encountered in diagnosis and management. To the best of our knowledge this is first paediatric series to be reported from Sudan.

PATIENTS AND METHODS

This is a retrospective, descriptive hospital-based study. Charts of all patients who were diagnosed as having pheochromocytoma in the paediatric endocrine unit at Gaafar Ibn Auf Children Hospital, between January 2015 and December 2020 were reviewed. This is the main tertiary centre in Khartoum, the capital city of Sudan. The centre gets referrals from all over the country. Data including demographic, clinical, biochemical and radiological findings were obtained in addition to the management and outcome. Catecholeamines assay were done commercially by either Bio Scientia (Germany) or Burg (Saudi Arabia) laboratories. Radionuclear studies (MIBG) or genetic testing were unaffordable or unavailable.

RESULTS

Eight patients who were diagnosed as having PCC were enrolled in this series, from whom two were siblings (Patients 5i and 5ii). The reported consanguinity was 100%. The clinical, biochemical, radiological findings along with treatment and histopathological result are summarized on Table.

The mean age at diagnosis of PCC in this study was 12.8 years (range 6-17years). Male to female ratio was 3:1. The duration of symptoms ranged from one to three months in five patients and it was protracted in three patients, up to 36 months in patient1.

The most common features were hypertension (100%), headache (87.5%), palpitations (75%) and diaphoresis (62.5%). Visual disturbance was also a common symptom (75%). Seizures (37.5%), weight loss and behavioral changes were also among the presenting complaints. Five (62.5%) patients presented with complications namely hypertensive retinopathy (37.5%), left ventricular hypertrophy (25%), hypertrophic obstructive cardiomyopathy (HOCM, 12.5%), and hypertensive encephalopathy with left sided hemiplegia/right central hemisphere atrophy (12.5%). Two were familial (siblings) whose paternal uncle had PCC.

Biochemical and radiological findings

Biochemically, three patients (Patients 1, 2, and 3) exhibited high 24 hours' urine metanephrine level with mean of 6427(3049-9167) µmol/d, that equals to 3.6 × ULN, along with high vanillymandelic acid (VMA) 187.2 µmol/day and 307.8 µmol/day (reference range:<30.3 and <82.2, respectively), that equals to >4 × ULN in two of them. Noremetanephrine level was high in the siblings (24984 µmol/day and 4117µmol / day), that equals to 11 × ULN and 1.8 × ULN, respectively; however, metanephrine level was normal for them. Plasma metanephrines and 24 hour urine VMA for patient 4 and patient 7, respectively were normal and the diagnosis made was based on clinical and radiological findings while biochemical data was missing for Patient 6. No patient was found to have hyperglycemia. At presentation, all patients had CT scan or MRI abdomen for tumor localization. The tumors were localized to the adrenal gland in all patients included in this series. PCCs were bilateral in three patients, two of them were the siblings, right sided in four patients and left sided in one patient. Nuclear scintigraphy with I-labeled metaiodobenzylguanidine (MIBG) and PET/CT scan were not available or affordable. Screening for MEN2 tumors was negative for four patients (Patients 4, 5i, 5ii and 6), demonstrated by normal thyroid ultrasound and serum calcium. Parathyroid hormone (PTH) was normal in Patient 2 and the remaining data was missing for the rest of patients. No patient had stigmata of Von Hippel-Lindau (VHL) disease or neurofibromatosis (NF) Type I.

Management and outcome

Pre-operative management was focused on control of hypertension which was achieved with alpha and beta blockers: doxazosin at a dose of 2-4mg/day and atenolol at a dose of 0.5-1mg/kg/day were used, respectively, in all patients included in this study and two patients required additional nifidipine and lisinopril. All patients underwent adrenalectomy, either by open surgery or laparoscopically as main treatment except patient 4 who had normal level of metanephrines, refused further management to be pursued. No patients received additional therapies (chemotherapy or radiotherapy). Histopathological examination revealed that the tumors were benign PCC for six patients including the siblings while data was missing for patient1. No mortality was reported in this series, three patients were cured based on clinical and radiological evaluation and the remaining patients were lost to follow up.

Table. Clinical, biochemical, radiological and treatment characteristics of the study population(n=8)

PATIENTS	1	2	3	4	5i	5ii	6	7
Age in years	14	15	13	17	13	6	9	15
Sex	Male	Female	Male	Male	Female	Male	Male	Male
duration of symptoms	36m	2m	1m	1m	3m	3m	18m	9m
Family history of PCC	No	No	No	No	Yes	Yes	No	No

Headache	No	Yes	Yes	No	Yes	Yes	Yes	Yes
Hypert-ension	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Palpitations	Yes	Yes	No	Yes	Yes	Yes	No	Yes
Sweating	Yes	No	No	Yes	Yes	Yes	No	Yes
Seizure	No	Yes	Yes	No	No	Yes	No	No
Behavioral changes	No	No	No	No	No	No	Yes	No
eye symptoms	M/D	Yes	Yes	No	Yes	Yes	Yes	Yes
Metan-ephrines	9167µmol /day	3049µmol /day	7064µmol /day	0.5µmol/l	<176. 6µmol/day	387µmol /day	M/D	Not done
Normeta-nephrines	Not done	Not done	Not done	1.83µmol/l	24984µmol /d	4117µmol /day	M/D	Not done
Rt mass*	Rt mass*	Lt mass*	Rt mass*	Rt mass*	Bilateral masses*	Bilateral masses*	Bilateral masses*	Rt mass*
Surgery	Laparo-scopic	Open surgery	Laparos-copic	Not operated	Open surgery	Open surgery	Open surgery	Open surgery
Histopa-thology result	M/D	PCC	PCC	Not operated	PCC	PCC	PCC	PCC
Persistent hypert-ension	No	Yes	Yes	No	No	No	No	No
Complic-ations	HOCM	No	stroke	No	No	Retino-pathy+	Retino-pathy	Retino-pathy+

*Adrenal mass. M/D Missing data, +: Left ventricular hypertrophy, HOCM: Hypertrophic obstructive cardiomyopathy, m: months. PCC: Pheochromocytoma. CT: computerized tomography. MRI: magnetic resonance imaging, Rt: right. Lt: left

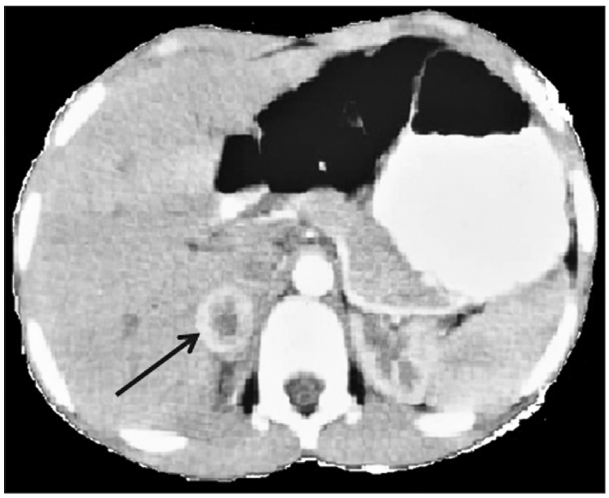

Figure. Computerized tomography scan showing right pheochromocytoma for patient 5ii (arrow).

DISCUSSION

Pediatric PCCs are rare neuroendocrine tumors. The average age of our patients at presentation is consistent with available reports, with the youngest in our cases being 6 years. The M:F ratio of 3:1 is similar to report from Turkey[11]. In our study the mean duration of symptoms was 9.1 months (range of 1-36 months) This is similar to the reported average delay of diagnosis of 36 months[1]. Hypertension was the most frequent feature present in our cases and this is in keeping with the available literature[12,13]. However, Prasanta et al has reported a case of PCC without hypertension in a 14 months old patient[11]. The PCC triad headache, palpitations and diaphoresis were the common presenting

symptoms in our series. This is consistent with the literature, which reports headaches in 55–90%, palpitations in 50–77% and sweating in 40–74% of patients with PCC[12,13]. This triad of symptoms beside hypertension has a sensitivity of 90.9% and a specificity of 93.8% in diagnosis[13]; thus diagnosis can be based on clinical and radiological findings for patients with inconclusive biochemical results. Furthermore, in our study, hypertension persisted in 25% of patients similar to reports from centres in South Africa and Asia, with rates of 10–35%[12,14]. Occasionally patients with PCC present with complications such as a cardiomyopathy, hypertensive crisis, stroke and seizures[7]. In our series, five patients exhibited complications at presentation particularly hypertensive retinopathy, seizure, stroke, left ventricular hypertrophy and hypertrophic obstructive cardiomyopathy (HOCM), The worst complication i.e. left sided hemiplegia with right central hemisphere atrophy, has occurred with the least duration of symptom (one month) mandating early diagnosis and management.

For diagnosis, all patients had 24 hours urine for metanephrines except one who had plasma metanephrines and according to literature both plasma and urine metanephrines are the most sensitive tests[8]. The yielded biochemical results were not > 2 × ULN (diagnostic range however in some literature > 4 × ULN) in all patients and the diagnosis was based on clinical and radiological features for patients with normal to mild elevation of metanephrines. The two siblings manifested high level of normetanephrine with normal metanephrine level questioning the activity of the cytosolic enzyme phenylethanolamine N-methyltransferase (PNMT) which converts norepinephrine to epinephrine[7]. However, half of the adrenal tumors secrete NE whereas the other half secrete EPI[1]. For tumor localization by CT or MRI abdomen and pelvis was performed for all of our patients; fortunately, it localized the tumors accurately as nuclear scintigraphy with I-labeled metaiodobenzylguanidine (MIBG) and PET/CT scan were not available.

Intra-adrenal tumor (PCC) accounted for 100% of our patients which is higher than the figure of 68.6% reported by Abdurraouf et al, and this may be accounted for by small number of patients in our series. Similar to published literature, right sided PCCs predominated in our patients[12]. Furthermore, all our PCCs were benign tumors (100%), unlike figures of 77.1% and 85% reported by Abdurraouf and K Huddle, respectively; however their studies included mainly adult patients and few paediatric patients[12,13]. This is from two centers in South Africa while from the European-American - Pheochromocytoma – Paraganglioma – Registry (EAPPR) 10% of paediatric patients had malignant tumors whereas in adults it varied from 9-23% depending on the gene mutation involved[7]. Genetic testing is mandatory for all paediatric patients since identification of gene mutation is higher in children[5,6]. Our patients deserve genetic testing particularly patients with bilateral PCC and with positive family history. Familial tumors were diagnosed primarily on the basis of the positive family history. However, genetic testing is unavailable at our setting. The benefits of genetic testing reside in early diagnosis of tumors associated with a syndromic disorder (e.g. medullary thyroid carcinoma in MEN2 and renal cell carcinoma in VHL), allowing earlier detection and treatment of family members[1,6,13,15].

The management was focused pre-operatively on blood pressure control since pre-operative management of elevated blood pressure in patients with PCC is crucial to prevent intra-operative hypertensive crisis and mortality. This was achieved with alpha and beta blockers in the majority of our patients with additional antihypertensives in two patients. Patients underwent either open or laparoscopic surgery with smooth intra–and post-operative course high-lightening the essential role of multidisciplinary approach in managing patients with PCC involving expert anaesthetist, surgeon and intensivist.

In this study, no mortality was reported and this is attributed to the benign nature of our PCCs, similar to 100% survival rate for benign disease in previous reports compared to 6% mortality rate of those with

hereditary disease as EAPPR reported[7]. Patient 5ii had PCC in the second adrenal (Figure) one and half years after the first surgery emphasizing the importance of regular annual lifelong follow-up to detect recurrence or metastatic disease as recommended by Endocrine Society Clinical Practice Guideline[9,15]. In our limited resource setting, where measurement of metanephrines is expensive and done abroad follow up is mainly done on clinical and radiological grounds as we are currently doing for our cases who cannot afford.

This study has several limitations including it being a retrospective one, the small number of patients and the lack of some biochemical and genetic tests and patients drop out. However, this is the first series from Sudan, highlighting the essential role of early diagnosis and management in reducing the mortality and morbidity and emphasizing the importance of raising the awareness of healthcare professionals in detecting and refereeing those patients earlier to tertiary care centers for further evaluation and management. Not to mention the importance of multidisciplinary team work.

CONCLUSIONS

Pheochromocytoma has variable clinical presentations with hypertension being the most frequent clinical finding; thus it is imperative to have blood pressure measured for all pediatric patients particularly those with symptoms suggestive of PCC. The triad (headache, palpitation and diaphoresis) cues to PCC and should arouse the suspicion of professionals allowing early diagnosis. Genetic testing is essential and allows earlier screening, treatment and improved outcome. Further studies hopefully with genetic testing and making facilities for diagnosis and follow up are needed.

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Effects of raw *Nigella sativa* seeds on control of lipid profiles among type 2 diabetic patients in a rural hospital in Gezira State, Sudan

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ABSTRACT

Background Diabetes is a common disease in the world and its prevalence rate has increased rapidly. The use of herbal agents as complementary/alternate medicine is prevalent worldwide and is gaining popularity. *Nigella sativa* or "Black seed" is a widely used medicinal plant for treatment of various ailments including diabetes mellitus. This study aimed to evaluate the effect of *Nigella sativa* seeds on lipid profiles level among type 2 diabetic patients in a rural hospital in Gezira State, Sudan.

Patients and methods This is a prospective case-controlled and hospital-based study conducted on 55 type 2 diabetic Sudanese patients aged 35-85 years between January and September 2017. The subjects were randomly selected and assigned into 2 groups: the study group (n =30) who received 2 grams of *Nigella sativa* seeds, daily, by direct chewing for three months, in addition to their standard medications. The control group (n =25) continued on their standard medications for three months. Total cholesterol, high density lipoprotein, low density lipoprotein, triglycerides and body mass index were measured before, and after three months.

Results The fasting glucose levels of the subjects (who were on oral hypoglycemic agents) ranged from 150 to 400 mg/dl. In the study group the initial levels of the total cholesterol, low density lipoprotein cholesterol and triglycerides ± standard deviation were 198.09±50.09, 121.18±32.89 and 138.00±51.73, respectively. These levels had dropped significantly ($P < 0.05$) to 1168.81±49.16, 106.45±36.05 and 122.68±49.53 mg/dl, respectively with significant ($p < 0.05$) increase in high density lipoprotein cholesterol level from 41.4545±6.45 to 52.4545±6.55 mg/dl, after three months of *Nigella sativa* administration. No significant effect on body mass index was observed ($p > 0.05$). In the control group the results of these parameters before and after three months showed no significant change ($P > 0.05$).

Conclusion Direct chewing of *Nigella sativa* seeds for three months significantly reduced the total cholesterol, low density lipoprotein cholesterol and triglycerides with increase in the high density lipoprotein cholesterol among type 2 diabetic patients. Investigation of the effect of the raw of *Nigella sativa* seeds on control of lipid profiles in type 1 diabetic patients is recommended.

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INTRODUCTION

Diabetes mellitus is a common disease in the world and its prevalence rate has increased rapidly[1]. The World Health Organization reported that 422 million people are suffering from diabetes, worldwide[2]. The prevalence in Sudan was about 18.9%[3,4] and it is estimated that 16% of Sudanese adults (aged 20-79 years) suffer from diabetes, with a total of 3 million diagnosed patients and an additional 1.5 million cases undiagnosed[5].

Type 2 diabetes mellitus (T2DM) accounts for 90% of all diabetes mellitus cases It results from the interaction between genetic predisposition and environmental factors[6]. It is characterized by defect in insulin secretion, an action that causes

an elevation in blood glucose levels. It can also be associated with cardiovascular risk factors such as dyslipidemia, hypertension, and obesity. Medical nutrition therapy (MNT) is important in preventing diabetes, managing existing diabetes, and delaying complications. Proper diet is crucial at any stage of management of diabetes including those on medication. The goals of MNT together with medication are to attain and maintain blood lipids levels as close to normal as possible. These goals can be achieved through healthy food choices[7]. A balanced diet consisting of 45–60% energy from carbohydrate, 15–20% energy from protein and 25–35% energy from fat is encouraged. A high fiber diet (20–30g fiber/ day) and limit consumption of sugar-sweetened beverages are also advised[8,5].

The use of herbal drugs as complementary/alternate medicine is prevalent worldwide and is gaining popularity. *Nigella sativa* is a widely used medicinal plant in the form of raw seeds or oil added to medicines and foods. The plant grows to about 20-30 centimeters in height and is commonly known as "Black seed" or "Blessed Seed"[9,5]. It is used to treat various ailments including inflammatory diseases, fungal infections, bacterial and allergic infections[10]. It had been used to treat diabetes mellitus, asthma, respiratory, digestive tract, cardiovascular, kidney and liver diseases[11]. Its use for fatigue, rheumatism, indigestion, dropsy, amenorrhea, dysmenorrhea, as an antiseptic and local anesthetic is also common[12,13]. It has also been recently used as an immune-modulator, antioxidant and for other metabolic conditions (e.g. dyslipidaemia)[5,14,15]. The seeds of Nigella sativa showed richness and diversity in its chemical composition. Carbohydrates, proteins, lipids, volatile and fixed oils are contained in the seeds[16].

Lipid per oxidation in plasma or liver decreased with Nigella suggesting potential in diseases in which free radical damage play a pathogenically role[17,18] suggested that treatment with *Nigella sativa* improved lipid profile of pre-menopausal women[19] and protected the hearts of type 2 diabetic patients from diastolic dysfunction. A polyherbal mixture containing Nigella sativa showed beneficial effects on lipid profile in streptozotocin-induced diabetic rats and it had the potential to be used as a dietary supplement for the management of diabetes[20]. This study aimed to evaluate the effect of raw Nigella sativa seeds on control of blood lipids level in type 2 diabetic patients.

PATIENTS AND METHODS

In this hospital-based study, 55 Type 2 diabetic patients were randomly selected in Mohamed Ahmed Omer Rural Hospital at Dallawat village in Gezira State, Sudan during the period from January to September 2017. (There were 376 diabetic patients in this hospital). They were randomly allocated into two groups: a study group (n=30) and a control group (n=25). They were aged 35-85 years, with a fasting blood glucose (FBG) ranging from 150 to 400 mg/dl, in spite of them taking their usual anti-diabetic medications. They were clinically fit patients and not on insulin therapy. The female patients were not pregnant or lactating. They were directly interviewed and a structured questionnaire was used to collect information on the socio-demographic, anthropometric characteristics, medical history and clinical examination.

Basal and post treatment blood samples were collected after an overnight (12 hours) fasting; 5ml. were taken in a heparin container to assess lipid profile (total cholesterol (TC), high density lipid cholesterol (HDL), low density lipid cholesterol (LDL) and triglycerides (TG)). Salter scale and stadiometre were used for measuring weight and height, respectively. Body mass index (BMI) was calculated in kilograms per the square of the height in meters.

The study group was treated with oral daily dose of two grams of Nigella sativa seeds in addition to their usual anti-diabetic medications for three months. The seeds were cleaned after washing with tap water, dried at room temperature and then packed in envelopes. The control group was asked to continue on their usual anti-diabetic medications for three months. Follow up for the two groups was continued for one month afterwards.

Data were analyzed using the statistical package for social sciences (SPSS v.20.0) and expressed as means with the standard deviation (SD). Chi-square was used to compare between parameters and P value ≤ 0.05 was considered significant. The study was approved by the local health authorities. A written permission was obtained from the hospital administration and informed verbal consents were taken from the participants.

RESULTS

Out of the 55 type 2 diabetic patients enrolled in the study, 59 % (n=32) were females and 41 % (n=23) were males. The mean ±SD age was 52.7 ±13.3 years. Five out of the 30 patients in the study group were excluded due to irregular intake of *Nigella sativa*, three were lost for follows up and 22 continued the study. The initial mean ± SD total cholesterol levels of the study group was 198.09±50.09 mg/dl, which dropped to 168.81±49.16 mg/dl after treatment and this change was significant (P < 0.05). Comparatively, the difference between the initial total cholesterol level and that of the control group after three months was not significant (P > 0.05). The mean ± SD HDL cholesterol level of the study group was initially 41.4545±6.45 mg/dl which increased to 52.4545±6.55 mg/dl after treatment and this change was also statistically significant (P < 0.05). Comparing between the HDL cholesterol levels initially and after three months in the control group, the differences were found to be insignificant (P > 0.05) The mean ± SD LDL cholesterol and TG levels of the study group were initially 121.18±32.89 and 138.00 ±51.73 mg/dl which dropped to 106.45±36.05 and 122.68 ±49.53 mg/dl, respectively, after treatment with *Nigella sativa* for three months and this change was statistically significant (P < 0.05). Compared to similar data of the control group the change was insignificant (P >0.05, see Table)

Table. The levels of TC, HDL, LDL cholesterol and TG of the Study and the control groups before and after three months.

Table. The levels of TC, HDL, LDL cholesterol and TG of the Study and the control groups before and after three months.

	Study group		Control group	
Parameter	Initial	After 3months	Initial	After 3months
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
TC (mg/dl)	98.0950.09±	168.81 ±49.16 **	186.7639.40±	186.6039.55± *
HDL (mg/dl)	41.45 ±6.45	52.456.55± **	39.487.29±	39.527.32± *
LDL (mg/dl)	121.1832.89±	106.4536.05± **	116.2433.71±	116.2033.73± *
TG (mg/dl)	138.00 ±51.73	122.68 ±49.53 **	132.0852.47±	132.0452.46± *

TC=Total Cholesterol HDL= High density lipoprotein LDL= Low density lipoprotein
TG= Triglycerides SD= Standard Deviation **p< 0.05, *p>0.05

The initial mean ±SD BMI level of the study group was 32.87±3.45, which remained 32.87±3.45 after treatment with *Nigella sativa* for three months. Compared to the initial mean ±SD BMI level of the control group which was 33.84±5.42 that changed after three months to 33.45±5.47; the change was also statistically insignificant (P > 0.05).

DISCUSSION

In this hospital-based study we evaluated the effect of raw Nigella sativa seeds on control of blood lipids level in type 2 diabetic patients. The results showed a significant decrease in the levels of total cholesterol, LDL, and TG and increase in HDL after direct chewing of two grams of *Nigella sativa* seed for three months by T2DM patients. These results are in line with those described by Najmi, et al on newly detected patients of metabolic syndrome with poor glycemic control (HbA1C >7 %). Using 500mg of Nigella sativa powder they demonstrated favorable outcomes with improvement LDL levels

confirming its efficacy as add-on therapy in patients with metabolic syndrome[21]. Bamosa.et al had also shown significant reduction in LDL, TG levels when *Nigella sativa* powder was used at a dose of 1g/day[22]. Moreover, Qasim et al had reported significant reduction in TC, TG levels when crushed *Nigella sativa* seed with meals was used at a dose of 2 g/day in diabetics on Day 42 as compared to their base line[23]. Also our findings are in agreement with the reports by Shah et al and Memon et al[24,25] but disagreed with Bilal, who assessed the effects of Nigella sativa oil equivalent to 0.7g *Nigella sativa* / day. This latter study revealed no significant change in total cholesterol, and again disagreed with him when he used Aqueous Extract of *Nigella sativa* (equivalent to 0.7g *Nigella sativa*) and he reported that the changes in HDL cholesterol and LDL cholesterol levels were non-significant[26]. Our study is also consistent with Kaatabi et al who found that *Nigella sativa* seeds in one, two and three g/day for 12 weeks significantly improved the dyslipidemia associated with type 2 diabetes millets[27]. These results were also in line with those described by Sahebkar et al who used *Nigella sativa* powder[28]; Heshmati et al had also shown significant reduction in total cholesterol, LDL, and TG with an increase in HDL levels when *Nigella sativa* oil was used by Iranian type 2 diabetic patients[15].

Many studies have confirmed the results of our study. Ikram and Hussain found that two weeks daily consumption of 100 mg/kg *Nigella sativa* decreased the LDL and TG of alloxan induced diabetic rabbits[29]. Another study by Al-Logmani and Zariin adding 5% *Nigella sativa* oil to the diets of diabetic rats resulted a significant reduction in LDL and TG[30].

Hadi et al found similar results in their randomized double-blind clinical trial which included 43 diabetic type 2 patients. *Nigella sativa* oil 1g/ day was used as adjunctive therapy for 8 weeks[31]. Hosseini et al also confirmed similar results with 70 type 2 diabetic patients treated with *Nigella sativa* 5ml/day for three months[32]. Najmi et al piloted clinical trial on sixty metabolic disorder patients, they were equally divided into two groups: standard group and *Nigella sativa* group. The standard group received Atorvastatin 10 mg/day and metformin 1g/ day while *Nigella sativa* group received adjunctive therapy of *Nigella sativa* 5ml/day for six weeks. Comparison of results of both groups indicated that the *Nigella sativa* group showed a noteworthy reduction in levels of LDL cholesterol, triglycerides than the standard group. The HDL cholesterol level was increased in *Nigella sativa* group[33].

According to experimental studies, the hypolipidaemic effects of medicinal plants may be mediated through different mechanisms such as reducing the intestinal cholesterol absorption, reducing endogenous lipids synthesis, increasing lipoprotein lipase activity, up regulation of LDL receptors, increasing the cholesterol excretion into bile acid, and/or regulating transcription factors of genes involved in lipid metabolism[34]. The exact mechanisms of the lipid-modifying effects of *Nigella sativa* are not yet known, but might be associated with the inhibition of intestinal cholesterol absorption, decreased hepatic cholesterol synthesis, and up-regulation of LDL receptors[32]. This decrease could be as a result of the improvement in glucose profile and insulin output. Similar observations were made in animal and human studies[35,36].

On the other hand, dyslipidemia is an important risk factor responsible for cardiovascular disease in patients with diabetes, so alleviation/elimination of lipid abnormalities is important in the prevention of the complications of diabetes. Thus, keeping the lipid profile of diabetic patients in the normal range can improve their health status, and *Nigella sativa* intake, in combination with anti-diabetics and statins or fibrates, can help diabetic patients to control both dyslipidemia and blood sugar[37].

It is known that insulin plays an important role in lipid metabolism through activation of adipose tissue lipoprotein lipase and inhibition of adipocyte hormone sensitive lipase. Insulin is true antagonist of the growth hormone, glycogen, cortical and catacholamines as it lowers the glucose level in blood whereas the others increases the glucose level[38]. Thus its deficiency manifests as; a) impaired degradation of both chylomicra and low

density lipoprotein particles with resultant increase in their levels and b) through decreased inhibition of hormone-sensitive lipase, there is an increased flux of non-esterified fatty acids to the liver as a potential source of hepatic cell triacylglyceride and of both very low density lipoproteins and ketone bodies leaving the liver. Hence diabetics show high very low density lipoprotein levels and less abnormality in total cholesterol concentrations than in triglyceride concentrations. However, HDL cholesterol levels are reduced but, like the raised LDL levels, they return towards normal with improved glycemic control. LDL levels are usually normal, although they tend to increase with gross hyperglycemia[39].

Another factor may be beta-sit sterol contents of *Nigella sativa,* which is similar to cholesterol chemically but is completely different in its biological function. It interferes with cholesterol absorption hence preventing its rise. It also reduces cholesterol by competitive inhibition of dietary and biliary cholesterol from the intestine[40]. The BMI levels remained unchanged in both groups, as compared to their base line levels, this agreed with all mentioned previous studies except that of Njami et al who reported a decrease in BMI and waist hip ratio[33].

CONCLUSION AND RECOMMENDATION

Our study had shown that chewing Nigella sativa seeds at a dose of 2g/day for three months caused significant reduction in TC, LDL, and TG levels without significant change in BMI among study group compared to the control group. More studies using larger sample size as well as investigating the effect of the raw *Nigella sativa* seeds on control of lipid profile in type 1 diabetic patients is highly recommended.

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Paediatric craniopharyngioma in Sudan: an overview of clinical presentation, related endocrinopathies and outcome

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ABSTRACT

Background/Aims Craniopharyngiomas are rare neuroectodermal tumors arising from the remnants of Rathke's pouch. They occur at any age presenting with hormonal disorders as a result the tumor or its treatment. We report the clinical presentation, related endocrinopathies, treatment and outcome of cases encountered in our center and highlight on barriers faced with diagnosis and management. This is the first report on paediatric craniopharyngioma from Sudan

Patients and methods Records of all children with the diagnosis of craniopharyngioma who were seen in our unit between 2006 and 2020 were reviewed. Clinical and biochemical data were documented; pre-operative and post-operative hormone workups, treatment offered and outcome were identified.

Results Reported patients were 25, males outnumbered females, the youngest age at presentation was 3 months. Headache was the presenting symptom in 68% of patients; 35% had a normal pre-operative hormonal assessment; all patients developed either single or multiple pituitary hormone deficiencies post-operatively while 16 patients were well after surgery.

Conclusion Craniopharyngioma is not uncommon in Sudan, attention should be raised regarding the importance of the multidisciplinary team in managing this disease.

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INTRODUCTION

Craniopharyngioma are rare neuroectodermal benign tumours arising from the remnants of Rathke›s pouch13-. They occur at any age, exhibiting a bimodal distribution. In childhood, most cases arise between 5 and 10 years of age; their close proximity to the pituitary gland, hypothalamus and the on-going development of other neural structures adds to the complexity of the management4. Whether suprasellar and/or intrasellar, their close proximity to vital structures presents with a myriad of symptoms – including headaches, endocrine-related and visual changes2. The symptoms usually develop slowly over time, mirroring the rate of growth of these tumours and is dependent on the location of the tumour and its pressure effects on adjacent structures. The most common initial presentations are related to endocrine symptoms i.e. slow growth, obesity and delayed puberty; headaches and visual impairments are also encountered[5,6].

The management of craniopharyngioma is best achieved using a multi-disciplinary approach including endocrinologists, neuro-ophthalmologists, neurosurgeons and radiotherapists7. There has been a notable improvement in survival rates of childhood craniopharyngioma8. Minimally-invasive approaches such as radiotherapy, and invasive therapies including surgery and intracystic therapy may be utilised in treatment [6,7,9-13].

This is the first report from Sudan aiming to outline diagnosis and management of craniopharyngioma in children and barriers that are faced in limited resource countries.

PATIENTS AND METHODS

Our centre is the main paediatric endocrinology unit in the country. Medical records of all patients who were diagnosed as having craniopharyngioma between January 2006 and August 2020 were reviewed. Data including age, sex, type and duration of symptoms, the time of presentation for medical advice, clinical findings, investigations, pre-operative and post-operative endocrinology assessment, results of investigations and treatment offered were obtained. In addition to the short and long term outcomes for those who reported for follow up. Missing data and verbal consents were obtained through phoning families. Hormonal investigations were done in the endocrinology laboratory in Sudan Childhood Diabetes Center or commercially in private laboratories. Histopathology was done in private laboratories.

Data was analyzed using the statistical package for social science (SPSS v.23) and described as percentage or range. Comparison between variables and the underlying diagnosis were carried out; p value < 0.05 was considered significant. The study was approved by the Ethics Committee of the hospital.

RESULTS

Twenty-five patients with diagnosis of craniopharyngioma were identified; 16 (64%) were males and 9 (36%) were females. The commonest age group (n=11, 44%) was between 5 and 10 years The youngest age at presentation was 3 months, while the eldest one was 23 years old (Table 1).

Table 1. Distribution of patients according to their age (n=25)

Age in years	Frequency	Percentage
<5	5	20
5<10	11	44
10<15	7	28
>15	2	8
Total	25	100

Eight (32%) patients presented first to the ophthalmologists with visual disturbance and were diagnosed as having papilledema while other 8 (32%), 7 (28%) and 2 (8%) sought medical advice from paediatricians, general practitioners and neurologist, respectively. Table 2 shows the time of presentation to endocrinology service after diagnosis and referral. Forty-eight percent of the patients presented to the endocrine clinics at the same time of diagnosis, while 4% presented after 5 years of diagnosis. All cases were referred to endocrinology from neurosurgeons. The presenting symptoms are shown in Table 3; the commonest were headache (68%) and visual disturbances (56%) while 28% had seizures and projectile vomiting.

Table 2. Time of presentation of patients to the endocrine clinic after diagnosis (n=25)

Time of presentation after referral	Number	Percentage
Same time	12	48
3 months	3	12
One year	4	16
5 years	5	20
>5 years	1	4
Total	25	100

Table 3. Symptoms of the patients at presentation (n= 25)

Presenting symptoms	Frequency	Percentage
Headache	17	68
Blindness and visual disturbances	14	56
Seizures	7	28
Projectile vomiting	7	28
Symptoms of diabetes insipidus	3	12
Weakness	2	8
Left eye proptosis	1	4
Secondary amenorrhea	1	4
Gaining weight	2	8

Of all the cases referred from neurosurgery

department; 14 (56%) patients presented before surgery and 19 (76%) after surgery. The results of the hormonal work up of the first group is shown in Table 4. Five (35.7%) patients were normal and 9 (64.3%) had endocrine problems.

Table 4. Pre-operative hormonal assessment of patients referred before surgery (n=14).

Hormone deficiency	Number	percentage
None	5	35.7
Hypothyroidism	4	28.5
Growth hormone deficiency	2	14.2
Permanent diabetes insipidus	2	14.2
Secondary adrenal insufficiency+ Luteinizinghormone insufficiency	1	7.1

All patients who were found to have hormonal deficiency received hormonal replacement treatment before surgery apart from growth hormone. About 20 (80%) patients underwent operations; four (16%) patients did not have surgery because of social issues regarding the cost of the surgery and/or long waiting lists; one (4%) patient was lost to follow up. Radiotherapy was performed for five (20%) patients. The post-operative endocrinological workup showed all patients had a hormonal deficiency post-operatively including those with normal pre-operative hormonal assessment. Post-operative hormone assessments showed that 4 (16 %) patients had a single hormone deficiency while 15 (60%) patients had multiple pituitary hormone deficiencies (MPHD); 6 (24%) patients had no post-operative assessment either lost to follow up or died during or after surgery.

Table 5. Post-operative hormonal findings of the study group (n=19)

Hormone deficiency	Number	Percentage
None	0	0
Hypothyroidism	19	100.0
Growth hormone deficiency	8	42.1
Permanent diabetes insipidus	12	63.1
Secondary adrenal insufficiency	12	63.1
Gonadotropichormones deficiency	6	31.5

The long term outcome of eleven (44%) patients was unknown (lost to follow up). Those who developed hypothalamic obesity, permanent blindness or tumor recurrence were 3 (12%) each; 4 (16%) recovered without complications and another 4 patients died.

DISCUSSION

The commonest age at presentation in this study was similar to that reported before in paediatric age group[1,14]. Craniopharyngioma can be detected at any age, even in the prenatal and neonatal periods[15,16]. The youngest patient in our series was a three-month old in agreement with previous reports[15,16] while the eldest patient reported was 23 years old – although above paediatric age group but many cases with growth disorders are referred to paediatric endocrinology. Two thirds of patients were males, yet no gender difference was reported in many previous studies[17,18].

About 12 (48%) patients were referred to the endocrinology department by neurosurgeons as soon as they were diagnosed prior to surgery but the remaining patients were sent post-operatively as late as 10 years after the operation. However, this has improved recently because of more communication between the neurosurgeons and paediatric endocrinologists and with more availability of diagnostic and treatment facilities as well as increase in number of paediatric endocrinologists.

Craniopharyngioma has a wide range of symptomatology resulting from the tumor compressing vital structures and the associated endocrinopathies. The symptoms depend on the specific location of the tumor and its relationship to other adjacent structures. Headache was found in over two-thirds of our series which is comparable to the findings of previous studies[5,6]. Headache is a

feature of increased intracranial pressure that may sometimes be accompanied by projectile vomiting emphasizing the importance of intracranial masses in children with persistent headache. Visual disturbances are one of the recognized presenting symptoms of patients with craniopharyngioma[19]. Not surprisingly, over one half of patients in this series first sought ophthalmological medical advice. They presented with decreased vision, temporal hemianopia and even total blindness; one patient had left eye proptosis. Neurologicnl presentations e.g. convulsions or focal neurological signs as reported in this series were also documented before[5,6]. However, we did not encounter behavioral problems as reported by others[5,6].

Confirmation of diagnosis of craniopharyngioma needs radio-imaging (e.g. computerized tomography) which might not be available or affordable in many limited resource countries particularly outside the capital cities. All our patients needed to come to the capital city of Khartoum to be accessed by neurosurgeons or for the radio-imaging facilities the cost of which is occasionally not covered by health insurance. Lack of these facilities might mean delayed diagnosis or inability to have post-operative follow up as happened to one third of our patients.

Patients with craniopharyngioma are prone to develop many endocrine disorders due to the mechanical effect of the tumor on the pituitary, hypothalamus and adjacent areas or post-operatively. Symptoms can be very slowly progressive or acute as happens in the peri-operative cases. Therefore, all cases should have endocrine evaluation pre-operatively and post-operatively, hence the importance of collaboration between the neurosurgeons and paediatric endocrinologists. Vasopressin deficiency, or diabetes insipidus (DI), was reported in approximately 14% of patients presenting with symptoms of increased thirst and urination and the diagnosis was confirmed. DI was also reported pre-operatively in 9-38% in previous studies[5.6,20]. Diabetes insipidus is not common but occurs commonly post-operative either transient or persistent. Only two of our cases had it pre-operatively but this increased to 12(63%) post-operatively comparable to published reports[20] .

Adrenocorticotrophic hormone (ACTH) deficiency was the least encountered hormone deficiency found in the pre-operative hormone assessment. It was documented in 7% of patients in this study, which is much less than what has been stated in the study by Muller et al in which the ACTH deficiency was found in 25% of cases. One patient presented with secondary amenorrhea; gonadal effects were also noted previously in 40% of patients[21-24]. Growth hormone deficiency (GHD) was found in 14.2% of patients pre-operatively which much less than that reported elsewhere[5,6,21-24]. Hypothyroidism was present in 28% of patients which was similar to the study performed by Muller et al[21-24].

Twenty (80%) patients underwent total or subtotal tumor resection but the remainder couldn't because of long waiting lists, high cost or lack of post-operative intensive care facilities. Radiotherapy is now becoming a favorable option of treatment either immediately or late; however, deferring radiotherapy is associated with a worse outcome[25-28]. Therefore, the risk of deferring radiotherapy has to be balanced between the increased morbidity relating to multiple recurrences and multiple surgeries[29]. Even in cases of near total resection, recurrence rates are still high, and earlier radiotherapy may improve outcome[30]. Unfortunately, a small percentage of the studied patients had radiotherapy because of the long waiting list and cost. There are only 2 radiotherapy centers in Sudan.

The post-operative hormonal assessment was carried out for 76% of patients. All patients developed either single or multiple pituitary hormones deficiency in the course of their treatment and follow up. All patients were found to be hypothyroid including those who were having hypothyroidism pre-operatively. It is the most common hormone deficient found post-operatively in this study. Hypothyroidism is a recognized post-operative complication for patients treated for craniopharyngioma that may be encountered in up 95% of patients[31]. Diabetes insipidus (DI) is considered as one of the common endocrinopathies encountered post-operatively in

craniopharyngioma patients. Permanent DI was found in 63% of patients. The rate of permanent post-surgical DI ranges between 60-93%[32].

Eight (42%) patients developed GHD post-operatively. This deficiency following treatment for craniopharyngioma is found in about 70–92% of patients. A positive response to growth hormone treatment is seen in most cases. Normal growth in craniopharyngioma patients with proven growth hormone deficiency is also reported in the literature[33-38]. In previous studies post-operative ACTH deficiency was described in up to 90% of cases[39]. In this study post-operative patients with craniopharyngioma ACTH deficiency was reported in 63% of the patients. Post-operatively gonadotropic hormones deficiency was found in 31% of our patients which is comparable to a figure of 30 to 40% reported before[39].

The hypothalamic disturbance in energy management contributes to the development of severe obesity and is exacerbated by factors limiting physical activity such as marked daytime sleepiness, disturbances of circadian rhythms, and neurological deficits[40]. The degree of obesity frequently increases early after treatment and rapid weight gain typically occurs during the first 6–12 months after treatment[41,43]. Hypothalamic obesity was reported previously in up to 50% of patients[44] . In our study 3 patient were obese 2 of them were obese pre-operatively and one patient developed obesity after the operation.

Although the outcome of craniopharyngioma has recently improved with 10-year survival rates reaching up to 93%[8]; in our cases 16% died pre-operatively reflecting the poor intensive care facilities and possibly lack of multidisciplinary team work as these cases were operated on in hospitals where there were no on-site paediatric endocrinologists or trained paediatric intensivist. A considerable number (one third) of patients were lost to follow up.

CONCLUSIONS

This was a retrospective study with limited numbers yet it is the first case report on craniopharyngioma in children from Sudan. However, many cases are possibly missed, under reported or managed by neurosurgeons without referral to paediatric endocrinologists. Nevertheless, this study has shown the difficulties faced in limited resource countries on managing these cases including lack of public and professional awareness, late presentations, lack and cost of investigative facilities, inadequate multidisciplinary team work, cost and long waiting list for surgery, poor intensive care facilities, poor documentation and long term data as many patients are lost to follow with inadequate communication facilities and accessibility in remote areas. All these need to be addressed if we are to improve the diagnosis and management outcome.

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Life style changes among patients with renal transplantation using Basic Human Need Theory at Ibn Sina Specialized Hospital 2021

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ABSTRACT

Background Kidney transplantation is by far the best treatment option available to patients with end stage renal disease. Healthy lifestyle is important because many conditions such as new onset diabetes after transplant, and high blood pressure, can be improved through living a healthy lifestyle. This study aimed to identify those basic human needs that changed in patients who underwent kidney transplantations in the light of theory of basic human need.

Method This is a qualitative hospital-based study, conducted on 60 patients with renal transplant who came for follow up in Ibn Sina Specialized Hospital. The data was collected through structured interview questionnaire and analyzed using the statistical package for social sciences.

Results The study showed that 36(60%) of participants were males, 24(40%) were females and 57(95%) received kidneys from relatives. The appetite of 57(95%) participants increased after renal transplantation; 4(6.7%) got contraceptive counseling after transplant; 36(60%) of patients became socially active and in 27(45%) cases the productivity in work or study improved after transplant. Only 30(50%) of them participated in various form of recreation when compared to pre-transplant.

Conclusion The study identified improvement in the basic human needs of patients undergoing kidney transplantation.

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INTRODUCTION

Worldwide, the number of patients affected by end stage renal disease is increasing sharply, in both developed and developing countries[1]. Among patients with end stage renal disease, many are suitable for kidney transplant[١]. Major progress has been made in kidney transplantation since the first live donor kidney transplant was performed in 1954 in Boston between identical twins[2]. Even though kidney transplantation is by far the best treatment option available to patients with end stage renal disease, kidney transplantation is very successful, with 1-year graft survival rates over 90% for deceased donor transplants and 95% for live donor transplant[2].

An advantage of kidney transplantation when compared with dialysis is that it reverses many of the pathophysiologic changes associated with renal failure[2]. It also eliminates the dependence on dialysis and the accompanying dietary and lifestyle restrictions[٢]. The long term success of a kidney transplant depends on several things including regular follow-up, compliance with transplant team advice, taking daily anti-rejection medications in the proper dose at the proper time and following the recommended schedule for laboratory tests and clinic visits[3]. It is also necessary for the patient to lead a healthy lifestyle such as increase physical activities with regular exercise, eat proper diet, return to normal routine, lose weight as needed to reach and maintain a healthy weight[3].

The Basic Human Need Theory (BHNT) is first described by Maslow who introduced the concept of the hierarchy of needs. This hierarchy suggests that people are motivated to fulfill basic needs

before moving on to other, more advanced needs. Maslow's hierarchy is most often displayed as a pyramid, the lowest levels of the pyramid are made up of the most basic needs, while the most complex needs are at the top of the pyramid. Needs at the bottom of the pyramid are basic physical requirements including the need for food, water, sleep, warmth and sexual reproduction. Once these lower-level needs have been met, people can move on to the next level of needs, which are for safety and security. As people progress up the pyramid, needs become increasingly psychological and social. The need for love, friendship, and intimacy becomes important; further up the pyramid, the need for personal esteem and feelings of accomplishment take priority[4].

However, after transplantation patients take immunosuppressive drugs that put the patient at risk for many complications such as diabetic mellitus, high blood pressure, weight gain, high cholesterol, increased susceptibility to infection and cardiac disease. The life style must be modified to improve quality of the patient life, increase sense of wellbeing, and prevent complications after transplantation. This study aimed to identify those basic human needs that changed in patients who underwent kidney transplantations in the light of the BHNT.

SUBJECTS AND METHODS

This is a qualitative hospital-based study conducted at outpatient clinic in Ibn Sina Specialized Hospital. The target population were patients with renal transplant who came for follow up. The study included 60 patients - transplanted and/or re-transplanted. Patient with cognitive deficit or active psychiatric disease are excluded. The data was collected by interviewing patients and using self-administrated structured questionnaire. Convenient sampling method was adopted. Data were analyzed using the statistical package for social science (SPSS). The ethical clearance was granted by the Ethics Committee of Ibn Sina Specialized Hospital. Informed written consent was obtained from all patients after explaining the nature of study.

RESULTS

In this study, 60 of post-transplant patients were enrolled. Their mean age was 30 years, and the majority (n=36, 60%) were males. Other characteristics are shown on Table 1. The appetite of 95% of the participants increased after renal transplantation; 93.3% of them limited using salt, fat, and sugar (Table 2); 60% of the patients became socially active; in 45% of patients their productivity in work or study improved after transplant and 50% participated in various forms of recreation compared to pre-transplant (Table 3).

Table 1. Demographic characteristics of participants (N=60)

Item	Frequency	(%)
Age in years		
15-39	31	51.7
40-59	25	41.7
60-79	4	6.7
80 +	0	0
Sex		
Male	36	60
Female	24	40
Marital status		
Married	43	71.7
Never married	14	23.3
Widowed	2	3.3
Divorced	1	1.7
Occupation		
Employed	12	20
Unemployed	12	20
House wives	14	23.3
Free workers	22	36.7

Table 2. Distribution of the renal transplant patients according to their physiological needs (N=60)

Item	Frequency	(%)
Nutrition:		
Appetite increase after RT		
Yes	57	95
No	3	5
Limit foods high in sugar, salt and fat		
Yes	56	93.3
No	4	6.7
Increase fruits and vegetables each day		
Yes	55	91.7
No	5	8.3
Increase fluid intake per day		
Yes	56	93.3
No	4	6.7
Oxygenation: Develop fatigue easily		
Yes	9	15
No	51	85
Sexual relation (female patients, N=17)): Get contraceptive counseling after RT		
Yes	4	6.7
No	13	21.7
Get pregnant after RT(N=17)		
Yes	1	1.7
No	16	26.7
Activities and exercise: Have regular exercise program		
Yes	42	70
No	18	30

RT: Renal Transplant

Table 3. The distribution of renal transplant patients according to their social needs, productivity in work or study and participation in various forms of recreation (N=60)

Item	Frequency	(%)
Became socially active		
Yes	36	60
No	24	40
Productivity in work or study improved after RT		
Yes	27	45
No	33	55
Participation in various forms of recreation		
Yes	30	50
No	30	50

RT: Renal Transplant

DISCUSSION

The present study describes the basic human needs of patients who underwent renal transplantation. The majority of the patients were employees and their age ranged between 15 and 39 years; in a similar line with a study done in San Francisco which found that pre-transplantation employment status was the main predictor for post-transplantation employment (OR = 18.6) and was associated with sex, age, education, depression and duration of dialysis[5].

Regarding patient's physiological needs, the appetite of the majority of the patients increased after renal transplantation. Before transplant, loss of appetite was experienced by many patients as a result of kidney disease itself or as complications of uraemic gastropathy which improved dramatically after kidney transplantation. This finding coincides with study done in New Zealand which found that increased appetite, immunosuppressive medications (steroids) and relaxation of dietary restrictions, lead to significant weight gain in kidney transplant recipient, particularly in the first year after transplant[6].

Renal transplant affects dietary style in many ways; including limiting salt, fat, and sugar intake,

increasing intake of fruits and vegetables as well as fluid intake without restriction. These findings were comparable with a study done in Europe which revealed that the amount of proteins, cholesterol, sugar, phosphorus and sodium intake in patients after kidney transplant exceeded the recommended norms for daily intake in the general population; these patients tended to ingest excessive amounts of high energy-dense products[7].

Regarding elimination, the majority of patients in our study had regular bowel habits. This disagrees with a study done in Italy which found that the most common adverse effect in kidney transplant patients was watery afebrile diarrhea, with an incidence reaching 36%. It may be the use of mycophenolate mofetil, which is a part of the standard immunosuppressive protocol in kidney transplantation, that increases the risk of gastrointestinal complications, including diarrhea and gastritis[8].

Only a few patients in this study developed fatigue easily, and this may be related to improvement of hemoglobin level after kidney transplantation. This finding is supported by study done in Italy which found that although fatigue is a frequent and underestimated symptom of kidney transplant recipients; yet a significant lower rate of fatigue is observed in kidney transplant recipient patients compared with Hemodialysis ones[9]. As for the activities and exercise, about half of our patients reported that they were paying more attention to exercise than before. This disagrees with the study done in India which found that only 10.45% of kidney transplant subjects were noncompliant with recommended monitoring activity; this may be mainly due to lack of knowledge and carelessness[10].

The majority of the studied renal transplant married females reported that they were not counseled about contraceptive use after transplantation. This is in line with the study done in Norwegian women which reported that more than one-third (37%) of patients did not receive advice on contraceptive methods from health care personnel in the early post-transplant phase and nearly half of them (45%) did not receive any advice on timing of conception after transplant[11]. The majority of married female patients in this study didn't get pregnant after kidney transplant. Historically, female's kidney transplant recipients were advised not to become pregnant, due to concern for maternal, graft and/or fetal health[12]. Comparatively, a study done in Cairo revealed that pregnancy occurred in 30.8% of RT women at childbearing age. There were associated adverse effects including high blood pressure, elevated creatinine, and development of proteinuria[13]. The guidelines of 2009 allowed pregnancy after one year of RT in case of stable renal function, creatinine clearance >40 ml/min, proteinuria below 1 g/day, and cessation of teratogenic drugs[13].

With regards to patient's self-actualization need, half of patients participated in various forms of recreation and were involved more in their social life. This finding disagrees with the study done in Italy, that revealed only 38% of the renal transplant recipient with high fear of movement had significantly lower total daily physical activities, lower scores on sports and less leisure time physical activities[14].

CONCLUSION

Lifestyle is characterized by identifiable behavioral patterns that can have a marked effect on an individual's health. This study concluded that the positive change in life style after renal transplantation was apparent in physiological needs (nutrition, elimination, activities and exercise), and in social relation and self-actualization needs. However, the life style changed negatively after renal transplant in sexual relation needs.

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Medical Education

Assessment of final year medical students' satisfaction with their clinical education in different departments and its determinant factors, Faculty of Medicine, University of Khartoum, Sudan 2018-2019

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ABSTRACT

Background Assessment of student satisfaction is considered as one of the tools of quality measures in medical education and part of the areas of accreditation in most accrediting bodies. It enlightens the areas which need improvement and development.

Objectives The aim of this study was to evaluate final year medical students' satisfaction towards their clinical education in different departments and the effect of different factors on it.

Methods This was a descriptive cross-sectional study conducted on final year medical students. A pretested questionnaire was completed by the participants after explaining the purpose of the study. Data was analyzed using the statistical package for social sciences.

Results The response rate was 61% (n=223), male to female ratio was 1:4. Holders of the Sudanese secondary education certificate were 78.9% (n=176). Those who were not interested to study medicine on entry were 6.7% but increased to 9.6% at final year. Students were most satisfied with the paediatrics' clinical teaching (92.3%) followed by obstetrics and gynaecology (80.9%), medicine (80.8%) and surgery (64.4%). Student were least satisfied with the group size (except in obstetrics and gynaecology), availability of the course documents, alignment between teaching and assessment methods and chances to give and receive feedback. Students were most satisfied with staff experience, staff attitude towards students and the opportunity to discuss the cases. The majority (78.5%, n=175) of the students were satisfied with their clinical teaching.

Conclusion The students were most satisfied with paediatrics' clinical teaching followed by obstetrics and gynaecology, medicine and surgery. The staff experience and attitude were the most satisfying attribute while group size and unavailability of course documents were the least satisfactory issues.

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INTRODUCTION

For decades, researchers in higher education have assessed student satisfaction for three different justifications. First, most researchers have measured solely the levels of student satisfaction in order to identify the most and the least satisfaction with college programs and services for accountability reporting and self-improvement purposes. Secondly, some researchers have examined student satisfaction to see if satisfaction ratings of college programs and services associate with the satisfaction of the overall college experience. Lastly, few researchers have investigated student satisfaction items related to the occurrence of the educational events such as student retention and attrition[1]

In the era of accountability, quality assurance and accreditation, universities have become major targets of inspection by the governments. One of the

primary objectives of educational institutions is the provision of the highest possible quality education to their customers – both community and students[2]. Moreover, higher education is increasingly recognizing that it is a service industry and is placing greater emphasis on meeting the expectations and needs of students[3]. Rapid social, technological and economic changes mean that educational institutions constantly need to evaluate their programs, structures and processes and strive to ensure that they serve the changing needs of the community and the students[2]. Continuous evaluation of the programs is needed for improving the learning process, having a better outcome and satisfying the customers. Part of the evaluation process is the reflection of the students about their learning experiences. Trainees' satisfaction is an index for evaluating medical education, but only few researches had measured this factor[4]. Good teaching is a necessity. However; good teaching requires financial resources, which might not be available in public institutions especially in developing countries. This is even made worse by the increasing rates of students' enrollment.

Students' satisfaction can be classified into three domains: personal, interpersonal, and organizational[3] Personal domain is considered as an individual's character and it is defined as the specific characteristics that are related to the students (e.g. life satisfaction, self-esteem). Relationship between the student and the clinical tutor is categorized into interpersonal domain. The characteristics of clinical education that might influence satisfaction are categorized as an organizational domain, in which are included: number of teachers and patients, educational methods, and the practical skills that the students learn. It has been shown that autonomy, variety, the availability of learning opportunities, and use of institutionalized methods of orientation increased satisfaction[4].

Clinical teaching - that is teaching and learning involving patients - lies at the core of medical education. At undergraduate level, medical schools do their best to give students contact with patients as earlier in the courses as possible; For postgraduates, "on the job" clinical teaching is the core of their professional development[5] Clinical teaching is a cornerstone part of the medical education as it prepares the students for solving patients' problems in the real life[6]. William Osler, one of the famous medical teachers, stated that 'To study the phenomena of disease without books is to sail an uncharted sea whilst to study books without patients is not to go to sea at all', and: 'Medicine is learned by the bedside and not in the classroom'[7]

In the Sudan, the curricula of medical schools are diverse and are based on different educational philosophies, learning, and teaching strategies. The curricula range from the traditional, to the community-oriented and problem-based or a hybrid of two[8]. In 1954, Kitchener Medical School, was re-named the Faculty of Medicine and became part of the University of Khartoum (U of K). Since that time, the curriculum was a traditional one that showed little changes over the years. However, a new hybrid curriculum was launched in 2008. Recently, the curriculum was reformed in 2017 when professionalism and social accountability principles were emphasized. Despite the traditional system of education adopted earlier, the faculty inherited a rich and successful educational experience in medicine. It has continued to adopt and modify educational strategies and principles in a changing environment without losing sight of the mission and goals[9]. The students have access to all encounters in clinical medicine discipline in number of hospitals and facilities supervised by fulltime and part-time staff members. Four hospitals were owned by the U of K in addition to hospitals belonging to the Ministry of Health. Clinical phase coordinators and the vice dean for academic affairs are responsible for the overall supervision of clinical teaching and also aggregating and interpreting the information in the courses logbook.

METHODS

This is a descriptive, cross-sectional study conducted between August and December 2018. All final year medical students at the Faculty of Medicine, U of K curriculum year 2018-2019 were enrolled The total number of the students was 360 (118

males and 242 females) with male to female ratio 1:2. They all received the questionnaire. Those who responded were 223 with a response rate of 61%. The structured self-administered questionnaire included demographic data, overall clinical teaching satisfaction and satisfaction with different clinical departments. The questions were carefully derived from other similar 'reference' questionnaires in line with the study objectives after making the necessary modifications. Those 'reference' questionnaires included: The Dundee ready education environment measure (DREEM)[10] questionnaire, Modified job satisfaction questionnaire - that was used to evaluate the medical students' satisfaction with clinical education by Ziaee et al[4], Association of American Medical Colleges (2006) Graduation Questionnaire, Student Satisfaction Inventory TM which is distributed by USA Group Noel-Levitz TM and students' outcome survey[11]. Likert Scale was used to assess students' satisfaction on different aspects of clinical teaching with focus on the main clinical departments at the Faculty of Medicine, U of K. The students were asked to indicate their level of agreement with a given statement by way of an ordinal scale: with 3=fully satisfied or fully agree and 1=unsatisfied or don't agree. The data was analyzed using the statistical package for social sciences (SPSS). Parametric test was used to compare means between two independent samples using student t-test. The $p<0.05$ is considered significant.

RESULTS

The respondents were 223 (61%) with male to female ratio of 1:4; 212 (95.1%) were aged between 20-25 years, 10 (4.5%) students more than 25, and only one student was less than 20 years. The majority (n=176, 78.9%) of the students on admission to the university were holders of the local Sudanese secondary school certificate (SSSC), 33(14.8%) Arabian secondary school certificate (ASSC), while 13(5.8%) were holders of International General Certificate of Scientific Education (IGCSE). On admission 15(6.7%) were not interested to study medicine compared to 22(9.9%) of the final year students.

Regarding the overall satisfaction of the student towards the clinical teaching, the majority (n= 175, 78%) of the students were satisfied. Satisfaction with each of the clinical departments, i.e. Paediatrics and Child Health, Obstetrics and Gynaecology as well as Medicine was 92.3% (n=202), 80.9% (n= 178) and 80.8% (n=178), respectively. They were least satisfied with surgery teaching (n=141, 64.4%, Table). This difference was statistically significant ($p<.0.000$)

Table. Students' overall satisfaction towards clinical teaching in different departments (n=223)

Department	Fully satisfied	Partially satisfied	Totally unsatisfied	Means
Medicine	22(10%)	155(70.8%)	42(19.2%)	1.9
Surgery	27(12.1%)	114(52.3%)	77(35.3%)	1.8
Paediatrics	95(43.4%)	107(48.9%)	17(7.8%)	2.5
Obs and Gynae	48(21.8%)	130(59.1%)	42(19.1%)	2.3

Obs and Gynae= obstetrics and gynaecology

When evaluating the effects of different attributes on student satisfaction with clinical teaching of department of medicine it was found that the most satisfying factors were staff experience and attitude towards the students and the most unsatisfying factors were the group size and unavailability of the course documents. Concerning the department of surgery, the most satisfying variables were the chances for clinical examination and attitude towards the students and the most unsatisfying factors were the matching between teaching and assessment methods and unavailability of the course documents. Student satisfaction in department of paediatrics was generally the best; with the satisfaction towards staff experience, attitude and commitment but the least satisfaction was with the group size and unavailability of the course documents. Student's reflection towards the department of ob-

stetrics and gynaecology showed different response with good satisfaction with group size, availability of course documents and chances to discuss the cases, while least satisfying attributes were the chances for giving and receiving feedback (Figure 1).

Comparing the level of satisfaction of all students towards the different variables that affect satisfaction; the experience and attitude of the staff towards the students was the most satisfying variable while the least were the group size and opportunity for the students to give feedback: the differences are statistically significant (p<000, Figure 2).

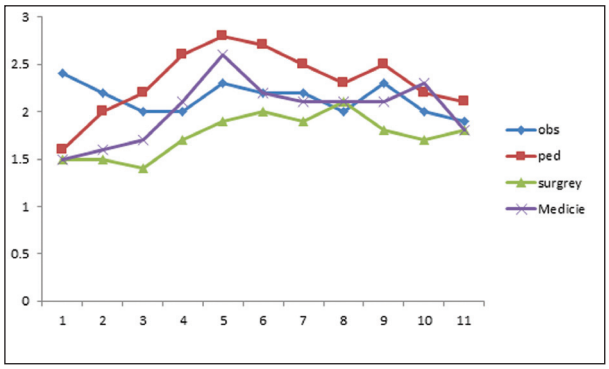


Figure 1. Comparison between satisfactions within different clinical departments

Key for Figures 1 and 2:

1. Group size is optimum
2. Course documents are available
3. Teaching methods are matched with the assessment methods
4. Teaching staff is available and committed
5. Teaching staff is experience
6. Attitude of teaching staff towards students is satisfactory
7. There is a good opportunity to receive guidance in history taking
8. There is a good opportunity to receive guidance in clinical examination
9. There is a good opportunity to discuss the cases
10. There is a good opportunity to receive feedback
11. There is a good opportunity to give feedback

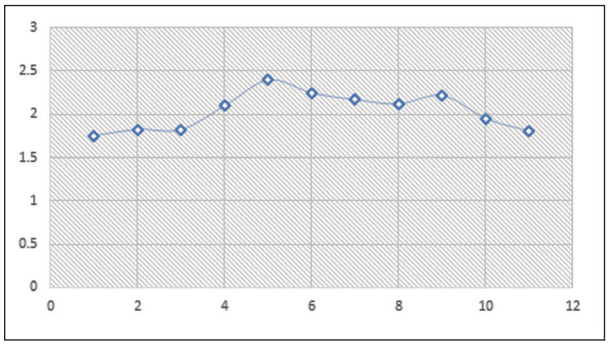
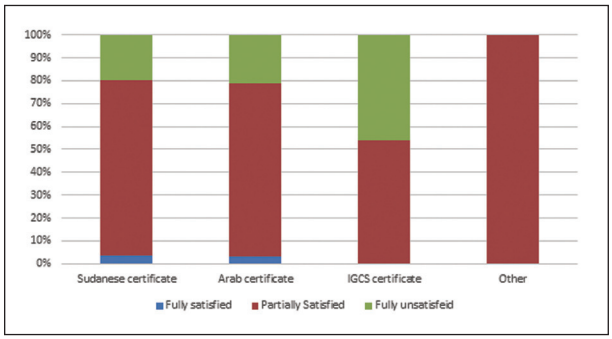


Figure 2. Factors affecting the level of the overall satisfaction (P< 0.000)

When evaluating the relation between types of secondary certificates and overall student's satisfaction, it was found that the student with IGCS were significantly less satisfied than student with SSSC and students with ASSC. Figure 3 shows over 50% of IGCS students were unsatisfied with their clinical teaching. Female students showed better satisfaction than males with mean satisfaction among males and females of 1.73 and 1.83, respectively, but the difference was not statically significant (p= 0.163).



IGCS= International General Certificate of Scientific Education

Figure 3. Relation between types of secondary certificates and satisfaction

DISCUSSION

In this study male to female ratio is 1:4. This was much greater than that reported in other international medical college's satisfactions surveys[12,13] The reason here may be the lower interest to participate in the study among male students as the actual male to female ratio of this patch was 1:2. The response rate of the participants was 61% compared that of 55.7%, 80.51% and 77.86% reported from Ireland, Saudi Kingdom and Pakistan, respective-

ly[12,14]. Most of the participants were between 20-25 years old. They are younger than medical students in Hong Kong and Canada who tend to complete some courses before they enter the medical school [13, 15]

More than half of the class were fully interested to study medicine on entry and 7% weren't interested at all; the interest has decreased in the final year and those who were totally not interested increased to 9%. Influence of parents could be the cause why those who are not interested chose to study medicine. A study in the University of São Paulo to find what is behind the student's choice to study medicine, only 30% studied medicine because they like it and 9% were due to the influence of their parents[16] More research to find the causes of why students decide to study medicine and why the level of their interest declines through the study years is needed.

The students were most satisfied with the paediatrics followed by obstetrics and gynaecology, internal medicine and surgery. Satisfaction with paediatrics clinical teaching was consistently higher in all attributes except in the group size where the satisfaction with obstetrics and gynaecology was the best and it was worst with surgery. The group size in the obstetrics and gynaecology was 10-15 and in the other disciplines it was 20-25 students. Studies have shown that reducing group size could enhance the clinical experience[17]. Students in smaller subgroups feel more obligation and self-confidence to participate and learn more because of their active participation[18]. It has been stated that a group size of 5-8 students is most suitable[17,18]

Students were satisfied with the staff experience, attitude and commitment. Ziaee found that there was no significant association between the students' satisfaction and the instructors' experience in bedside and outpatient teaching[6]. Although subject expertise is important, it is not sufficient. Effective clinical teachers use several distinct forms of knowledge. In a study done in Meharry College it was found that faculty competence and student-faculty relations were significantly associated with the satisfaction of the overall college experience. This discovery suggests that faculty members had played a major role in creating a pleasant environment to facilitate student satisfaction[1]. Students and residents were found to be motivated to engage in clinical reasoning and problem-solving if their preceptor, acting as a role model, provided adequate demonstration and guidance[19, 20]

Almost half of the class thought that they do not have the opportunity to reflect on their clinical experience in surgery and medicine and a little less than half are not satisfied with the frequency of the feedback they receive. This matches what Cantillon advocates about students perception of feedback[21]

As for the overall satisfaction in this study, the students who were partially satisfied (n=596) were much more than those fully satisfied (n=192) or those who were fully dissatisfied (n=178). This is similar to the findings in studies done in Tehran and Pakistan[4,6,22] but different from the finding of Chau-Kaung Chen in Meharry Medical Collage where most of the trainees were satisfied with their clinical experience[1]. When comparing the mean satisfaction of all student towards the different variables it was found that the most satisfying variables were the experience and attitude of the staff towards the students and the least satisfying variables were the group size and opportunity for the students to give feedback.

Judgments of satisfaction or dissatisfaction with educational programs are likely to be influenced by students' entry characteristics[23]. Most of the students who entered the medical school holding the Sudanese certificates were satisfied, followed by those holding the Arabic certificates and lastly by the IGCSE students. There was also no significant difference in the overall satisfaction between male and female students comparable to the results of Daugherty and Zaiee; however, Daugherty found that males were more satisfied with the clinical training during residency[4, 24, 25]

CONCLUSION

Final year medical students in Faculty of Medicine, University of Khartoum were generally satisfied with their clinical teaching and holders of Sudanese

secondary school certificates were more satisfied than holders of other certificates. Female students were more satisfied than males. The students were most satisfied with paediatrics clinical teaching followed by obstetrics and gynaecology, medicine and surgery. The most unsatisfying factors were group size, unavailability of course documents and chances of giving and receiving feedback. The students were mostly satisfied with teaching staff experience, teaching staff attitude and opportunity to discuss clinical cases.

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7. All authors should appear in the list of references i.e. all references are listed in full.
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9. The order of author/s initials, punctuation, title of article, year, journal title – in accepted abbreviated form, volume and page numbers, constitute a full reference citation. The following are examples of commonly used reference sources:

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e.g. Rose ME, Huerbin MB, Melick J, JK et al. Regulation of interstitial excitatory amino acid concentrations after cortical contusion injury. Brain Res 2002; 935: 40-6.

References in books

Author(s) of a book

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Author(s) Title: sub-title. Edition. Place of publication: Publisher; Year

e.g. Guyton AC, Hall JE. Textbook of Medical Physiology. 10th Ed. Philadelphia: Saunders; 1990.

Author(s) of a chapter in a book

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Author(s) of the chapter. Title: sub-title of chapter. In: Author(s) (or editors) of the book. Title: sub-title of book. Place of publication: Publisher; Year; page numbers.

Elmunshid HA. Special senses. In: Sukkar MY, Elmunshid HA, Ardawi MS, editors. Concise Human Physiology 2nd Edn. Oxford: Blackwell Science; 2000.p.401-23.

Reference on-line

Example (from The Michener Institute for Applied Health Sciences, Learning Resource Centre: Irc@ michenere.ca).

Book on the Internet

Foley KM, Gelband H, editors. Improving palliative care for cancer [monograph on the Internet]. Washington: National Academy Press; 2001 [cited 2002 Jul 9]. Available from: http://www.nap.edu/books/o309074029/html/.

Internet homepage/website

Cancer-Pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources, Inc.; c2000-01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: http://www.cancer-pain.org.

For a fuller range of examples of citation from other sources of references, there are innumerable sites on the internet. Please also consult the publications cited in KMJ instructions to authors and the references cited below:-

1. Uniform requirements for manuscripts submitted to biomedical journals: writing and editing for biomedical publication [home-page on the Internet]. Philadelphia, PA: International Committee of Medical Journal Editors; [updated 2003 Nov; cited 2004 Oct 9]. Available from: http://www.icmje.org/.
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