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4. Encourage the development of medical and allied sciences research.

CONTENTS

Original articles

Case report

Performance of GeneXpert test compared to conventional methods in diagnosis of childhood tuberculosis in Khartoum, Sudan

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ABSTRACT

Background Despite advanced technology, diagnosis of Childhood Mycobacterium Tuberculosis (MTB) remains a challenge. Recently GeneXpert test (GXT) came out as a breakthrough in diagnosis of childhood TB. This study aims to compare GXT diagnostic performance to the conventional methods and to investigate its correlation with the clinical features.

Methods A total of 104 patients were enrolled in a cross-sectional facility-based study. The enrollment was based on World Health Organization (WHO) criteria for TB suspect for pulmonary and extra-pulmonary diseases. A pre-coded questionnaire was completed and the relevant investigations including sputum, gastric, pleural aspirate and ascitic fluid were done.

Results GeneXpert test was positive in 17 of 78 pulmonary and 7 of 26 extra-pulmonary samples. GXT significantly outperformed presence of acid alcohol fast bacillus (AAFB, $P < 0.001$). It detected MTB in 22.7 % compared to 14.5 % by Ziehl-Neelsen stain for AAFB in the sputum and 21.2 % compared to 6 % in the gastric aspirate. Tuberculin skin test (TST) outperformed GXT by 8 % in case detection with no significant correlation between them ($P = 0.74$); GXT was positive in 24.5% of patients with significantly high scoring system but the relation between the two was not significant ($P = 0.16$). All cases ($n = 24$) with positive GXT showed abnormal features in the CXR ($P < 0.03$). GXT had no correlation neither with most of the presenting complaints nor with history or timing of contact ($P > 0.05$). Pallor was the only sign that showed a correlation with the GXT ($P < 0.001$).

Conclusion GXT performed better than Ziehl-Neelsen stain in diagnosis of MTB in both sputum and gastric aspirate of suspected cases. TST outperformed GXT in case detection. GXT showed significant association with abnormal radiological finding but not with the clinical presentation. The need for more studies cannot be overemphasized.

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INTRODUCTION:

Worldwide, tuberculosis (TB) is the single most common cause of death among infectious diseases.[1] The majority of cases are reported from developing countries.[2] The great difference between number of patients notified to WHO and the combined estimate incidence in 2014 indicates that so many cases were not detected.[3,4] In Sudan, the burden of childhood TB represents 15% of all notified cases.[5]

The diagnosis of childhood TB remains a challenge because of the nonspecific presentation, similar to many childhood illnesses; difficulty of expectoration in younger children to obtain the gold standard result, low mycobacterial load of diagnostic samples and moreover, confirmation using culture rarely exceed 40%. Furthermore, Acid Alcohol Fast Bacilli smear microscopy (AAFB) is limited by its low sensitivity of less

than 15% in young children, despite advances on its performance together with the inability to differentiate between mycobacterium tuberculosis (MTB) and other mycobacteria.[6-8]

A positive Tuberculin Skin Test (TST) in a child can be caused by non-tuberculous mycobacterium. However, a history of contact with a TB patient suggests that positive results may be due to MTB infection.6 False-negative results may be attributed to immune-suppression or malnutrition. Moreover, around 20% of patients with active TB were reported to have normal TST.[6,9] The Sudan National Tuberculosis Program (NTP) has adopted one of the WHO recommended scoring system (Table 1) trying to overcome the diagnostic difficulties and identify children in need of treatment in a rational approach.[10] However, because of its low specificity, this scoring system is not recommended especially where chest X-ray (CXR) facility is available. But is still in use for community workers.[6,11-14]

GeneXpert test (GXT), is a nucleic acid amplification test that uses fully automated and integrated computer-based technique.[15] It simultaneously detects MTB and rifampicin drug resistance with as few as 131 Colony Forming Unit/ml of MTB vs 10,000 for AAFB.[7,16] It provides accurate results in two hours with minimal bio-safety requirements.[16] Its limitations include cartridges shelf life of only 18 months, need for very stable electricity supply, annual recalibration of the instruments and the high cost.[17] GXT can be used for most body fluids specimens with few exceptions like whole blood.18 It also demonstrated poor sensitivity.[19]

Moreover, GXT cannot be used for treatment monitoring, as it detects both live and dead bacteria.[20] In 2013, WHO had recommended GXT as an initial diagnostic measure in children for both pulmonary and extra-pulmonary TB.[18] GXT is highly specific, (specificity more than 95%) even in extra-pulmonary specimens.[21-23] However, its sensitivity is variable. It is higher in smear positive pulmonary TB, as high as 100%, and lower in smear negative pulmonary and extra-pulmonary samples ranging from 72-80% and 77-83%, respectively.[21-24] The new strategy to approach suspected TB patients ignores the scoring system and TST.[11] This study aimed to investigate the correlation between the GXT and the TB clinical presentation as well as its diagnostic performance compared to conventional methods, namely AAFB, TST and scoring system.

MATERIALS AND METHODS

The study populations were 104 children, aged 2 months to 17 years, who presented to the paediatric pulmonology clinic and to the in-patient wards at Jaffar Ibn Auf Specialized Hospital for Children over a one-year period from March 2016 to March 2017. Sample size was determined by Steven Thompson equation ($n= [N P (1-P)] / [(N-1) (q^2/z^2) +P (1-P)]$, z = Statistical certainty = 1.96. , N = Number of new cases per year. p = 0.5, (1-P) = 95% q = Design margin of error = 0.05).

The enrollment was inclusive and based on WHO case definitions for a) clinically diagnosed TB and/or b) presumptive TB.[25] Clinically diagnosed TB is a case with suggestive histology or radiological abnormalities without bacteriological confirmation. The presumptive TB cases included those having a persistent cough of 2 weeks or more and one of the followings: household TB contact, unexplained weight loss or failure to gain weight, and unexplained fever for 2 weeks or more.

It was an analytical, cross-sectional, facility-based study. Participants were interviewed at the study area and all relevant demographic data, history and physical findings were documented. Every patient was given a score according to Sudan NTP scoring system (Table 1). Erythrocyte sedimentation rate (ESR), TST and CXR were done. TST was performed and interpreted by well-trained personnel. Indurations of > 9 mm were considered

positive. The CXRs were evaluated by a senior pediatricians and confirmed by a radiologist as TB. Sputum was collected by expectoration (or early morning gastric lavage in under-5 children). Extra-pulmonary samples which needed invasive procedures i.e. pleural, pericardial or ascitic aspirate were performed at hospital after taking consent and guarding for all precautions. About 2-3 ml of different samples were collected in sterile plastic containers and were tested for AAFB and GXT at Sudan National Laboratory.

Data were collected using a pre-coded questionnaire. The Statistical Package for Social Sciences (SPSS) version 20 was used for analysis. A comparison between the variables and the results of GXT had been carried out using cross-tabulation and Chi square test. P value of < 0.05 was considered significant.

RESULTS

The proportion of cases between the ages of 5-15 years was 54% while those under 5 years were 39.4%; 56.7 % were males, with male: female ratio of 1.3:1.0 Out of 104 samples tested, 55 were sputum, 33 gastric aspirates, 9 pleural aspirates, 6 peritoneal aspirates and 1 sample was a pericardial fluid. GXT were positive in 24 samples from 24 patients (13 sputum, 7 gastric aspirate, 3 pleural aspirates, 1 of peritoneal aspirates) with no correlation between the GXT and the type of the specimen sample taken ($p = 0.928$, Table 2).

The main presenting complaints of most of the patients were unexplained fever (93.3 %), weight loss (92.3 %) and cough for more than 2 weeks (86.5 %). There was no significant correlation between GXT and any of the presenting symptoms. Among those having history of contact, the majority (86.3 %) did so within the past year of their presentation. No correlation between GXT and history or timing of contact was found. The only physical finding that had a significant correlation with the GXT was the pallor ($P < 0.01$). The correlation of GXT with status of BCG vaccination was insignificant ($P = 0.18$). Most of patients (n=57/71, 80%) with TST of < 5 mm and all cases (n=3) with TST of 5−9 mm were malnourished. However, there was a significant correlation between TST and history of contact with TB case ($P < 0.001$).

Out of the 104 patients who participated in the study 98 scored 5 or more according to Sudan NTP scoring system but no significant correlation with positive GXT test was found ($p=0.16$). There was a significant association between the GXT and AAFB in detection of MTB ($P < 0.001$) in spite of the small number of samples. The majority of participants had abnormal CXR findings. No one with normal CXR had a positive GXT and all cases (24/104) with positive GXT had abnormal CXR signs ($P < 0.02$, Table 3).

Table 1. Sudan National Tuberculosis Program Scoring System[10]

Criterion	Score points in children <= 5 years	Score points in children > 5 years
History of contact	2	2
Skin test	2	2
Cough	2	1
Weight loss	3	3
Fever	1	2
Total	>5	>5

Table 2. Correlation between the GXT and type of the specimen sample (n=104)

	GXT* - ve n	GXT* + ve n	Spearman Correlation	P value
Sputum	42	13	-0.04	0.928
GA** washout	26	7		
Pleural effusion	6	3		
Peritoneal aspirate	5	1		
Pericardial aspirate	1	0		

*GXT= GeneXpert Test, **GA=Gastric aspirate

Table 3. Correlation between GXT with BCG vaccination status, NTP scoring system and other investigations (n=104)

Test		GTX* -ve n	GTX * +ve n	P value
BCG vaccination	given	68	19	0.49
	Not given	12	5	
NTP** score	5	74	24	0.16
	< 5	6	0	
AAFB ***	Positive	1	9	0.00001
	Negative	70	10	
	Not Done	9	5	
TST****	<5	55	16	0.95
(mm)	5-9	3	0	
	10-14	4	2	
	15-19	9	3	
	>20	9	3	
ESR*****	0-49	18	4	0.74
	50-99	39	10	
	>100	23	10	
CXR******	Normal	8	0	0.029
	Hilar/peritracheal gland	29	3	
	Pleural effusion	15	3	
	Miliary mottling	3	1	
	Persisting consolidation	20	12	
	Cavitation	4	4	
	Middle lobe syndrome	1	1	

*GXT= GeneXpert test. **NPT = National Tuberculosis Program. ***AAFB = Acid Alcohol Fast Bacillus, ****TST = Tuberculin Skin Test, *****ESR = Erythrocyte Sedimentation Rate (mm/first hour) ******CXR = Chest X-ray

DISCUSSION

The diagnosis of childhood TB presents a major challenge as its symptoms are similar to many other diseases. However, TB is characterized by a progressive clinical course if not treated.[26] A South African study in under 13-years-old concluded that the use of well-defined symptoms approach had a significant value in the diagnosis. Persistent fever and chronic cough for > 2 weeks were reported in 100% and 93.8% of their study participants, compared to similar figures in this study i.e. 93.3% and 86.5%, respectively.[26] In Sudan, a recent study of 197 suspected TB patients under 15-years-old had shown that all participants had cough for > 2 weeks and weight loss. More than 60% of them were either confirmed with culture, had a history of close contact with CXR showing suggestive findings or had a history of close contact and TST-positive.[27] These evidences reflect the significance of these symptoms in diagnosing childhood TB. Though, the current study showed no significant correlation between GXT and any of the clinical findings.

A positive history of contact has a great impact in the diagnosis, particularly in endemic areas due to high case density and diagnostic delay.[28] In Sudan, a history of contact was reported in 31% of a recent study group compared to 42% (n = 44/104) in this study.27 Closeness and timing of contact has a role on the risk of acquiring TB and over 90% of patients in this study had a close contact.[2] History of contact in most cases is usually within the last year of their presentation similar to what had been shown in the current study (86.3%).[29] However, GXT failed to show a correlation neither with history (P = 0.06) nor with timing (P = 0.30) of contact. This is unlike the study from Uganda that reported significant correlation which might be due to its larger number of participants (n=235).[30] A TST of ≥ 5 mm had a significant correlation with a history of contact (P = 0.0013). TST outperformed GXT in detection of cases in both groups, those with history of contact (50% vs 31.8%) and others with no history of contact (18.3% vs 16.7%). Although there was no significant difference between TST and the GXT in diagnosing childhood TB (P= 0.74), TST succeeded to detect 8.7% additional cases bearing in mind that the TST was done on symptomatic patients (not as a screening tool).

There was no significant correlation between GXT and presence or absence of BCG scar (P= 0.18), a finding that agreed with the finding of the study from Uganda (P= 0.4).30 It was not surprising to find insignificant correlation with the BCG vaccine in this study. since the vaccine is known to prevent only the severe types of TB i.e. tuberculous meningitis, disseminated and miliary TB. [31]

The overall detection rate (positive GXT) among both pulmonary and extra-pulmonary samples was 23.1 % (24/104) which is higher than that (15.6%) reported by Giang et al in 2015.[32] This might be due to the larger number of samples (n=302) tested in the latter study. In the present study, one-fifth of the cases with suspected pulmonary TB had positive GXT, this was higher than that reported from South Africa (13%) and Uganda (14%) whose sample size was much larger than ours.30 Again, the larger sample size might be the contributing factor for a lower detection in the latter studies. GXT identified 26.9 % of extra-pulmonary samples, compared to 21.8 % of pulmonary samples. This may be due to the fewer extra-pulmonary samples that had been tested in this study. Among the 90 specimens tested for both AAFB and GXT, 10 were positive for AAFB and 19 were GXT positive indicating that GXT significantly outperformed ZN microscopy by 10 % (P < 0.001). This finding is comparable to the study from Pakistan in which out of the 10 cases with sputum positive for AAFB, 9 were also positive for GXT, while 10 cases were found to be positive for GXT out of 80 cases negative for AAFB indicating a significant correlation between the two tests.[21] This was in contradistinction to the study from India, where GXT was found to be positive in 62.5 % of

smear negative cases.[33]

The performance of GXT in detection of MTB in sputum and gastric aspirate samples was approximately equivocal, i.e. 23.6 % and 21.2 %, respectively. This findings is comparable to meta-analysis results done by WHO in 2014.20 In comparison to AAFB, GXT succeeded to detect additional 9 % in the sputum and 15 % in gastric wash out samples. About 74 (94.2 %) of the participants in this study had a score of ≥ 5 of the Sudan NTP scoring system. Among them, all patients with positive GXT (n=24/24) and the majority of cases positive for AAFB (n=9/10) scored >5 on Sudan NTP. This support the belief that Sudan NTP scoring system is likely to over diagnose childhood TB.

Although the CXR and ESR are non-specific tools for diagnosis of tuberculosis, the majority of patients' CXRs (n = 96, 92.3 %) showed abnormal findings and a similarly large proportion of patients (n= 82, 78.8 %) had a high ESR greater than 50 mm/first hour. All the cases (n= 24) who were GXT positive showed some CXR changes indicating a significant correlation between the two tests ($P < 0.03$). Therefore, both CXR findings and high ESR might support the diagnosis of childhood TB.

The limited number of extra-pulmonary samples in this study was due to either technical problems (as the GXT machine needed stable electricity supply), patients' unwilling to be subjected to another biopsy (after having the first one previously taken for histopathology) or a contraindication of lumbar puncture.

CONCLUSION

GXT performed better than Ziehl-Neelsen stain in diagnosis of MTB in both sputum and gastric aspirate of suspected pulmonary and extra-pulmonary cases. TST outperformed GXT in case detection. All cases who were GXT positive showed abnormal features in the CXR indicating a significant association between the two. Out of all the presenting features studied, GXT showed positive correlation with pallor.

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Praziquantel in the treatment of Schistosoma haematobium in children: A double-blind, randomised controlled trial using two regimens.

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ABSTRACT

Objectives This is a randomised controlled trial (RCT) with two parallel arms. The objective was to compare the efficacy and side effects of two different doses of Praziquantel (PZQ) namely 40 mg/kg.b.wt. (Milligrams per kilogram body weight) vs 60 mg/kg.b.wt. in the treatment of urinary *Schistosoma haematobium* in children

Methods The participants were primary school children from two villages namely Elkeriab and Tayba Elkababish in the East Nile locality, Khartoum State, Sudan. They were all tested positive for *Schistosoma haematobium* ova in the urine. The infected children were randomly assigned to two groups: group A who received PZQ 40 mg/kg.b.wt. and group B who received 60 mg/kg.b.wt. of PZQ. The outcome measures were cure rate (CR), egg reduction rate (ERR) and improvement in other urine parameters

Results A total of 1205 primary school children were screened and there were 105 cases who tested positive for *S. haematobium* in the urine. These cases were randomised into two groups: group A were 52 and group B were 53 children. The CR for group A was 88%, and for group B was 100% ($p < 0.01$). There was also a significant difference in the improvement of macrohaematuria ($p < 0.01$) and microhaematuria ($p < 0.01$) with better responses in group B. Two children in group B, vomited once, but no other side effect was noted.

Conclusion The higher dose of PZQ had better efficacy in the treatment of *S. haematobium* infection in children, with no significant side effects.

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INTRODUCTION

Schistosomiasis is a parasitic disease prevalent in tropical and subtropical regions; caused by trematodes of the subclass Digenea, super family *Schistosomatoidea* and genus *Schistosoma*. More than 15 species of *Schistosoma* have been reported in humans, but the major agents causing human infections are *S.mansoni, S.haematobium* and *S.japonicum*[1]

Schistosomiasis is the most prevalent water-based disease from a global public perspective. It is ranked second only to malaria among the parasitic diseases with regard to the number of people infected and those at risk.[1] According to World Health Organization (WHO) Schistosomiasis is endemic in 76 countries and about 95% of the cases are in Sub Sahara Africa.[2] In 2018, the WHO estimated that 229 million people were infected with Schistosoma and globally, there are 200,000 deaths per year attributed to Schistosoma infection.[3] There is a significant association between poverty and schistosomiasis; infection is higher in countries with limited health resources.[3,4] and tends to affect school-aged children, adolescent and young adults.[3]

In Sudan, schistosomiasis has become a significant public health and socio-economic issue with a reported prevalence rate of S.*haematobium* between

0-20%.[2,5,6] It is estimated that around five million people require treatment, most of whom are children. It mainly affects poor, rural and agricultural communities, where inadequate hygiene and contact with snail-infested water make the residents vulnerable to infection.[3] According to the WHO, the number of people treated from the disease in Sudan in 2011 was 2,281,000 out of 5,820,000 who were in need of treatment.[6] However, this number has increased, after the spread of the disease to other regions that were not previously considered habitat of the disease such as Khartoum state, Northern Kurdufan and Southern Darfur states. This was due to the expansion in water resource development and increased population movement.[3]

The WHO recommends preventive chemotherapy (PC) consisting of periodic administration of Praziquantel for schistosomiasis as a short-term measure for the control of morbidity associated with Schistosomiasis.[8,9] This PC is required for 52 countries to a total of 219.9 million people; 60 % of whom are school-age children. The goal of the WHO is to treat at least 75% of school-age children in all Schistosomiasis endemic countries by 2020.[10]

Urinary Schistosomiasis may cause serious complications, especially among children and early diagnosis and management are essential. PZQ is the drug of choice for the treatment of this infection. A dose of 40 mg/kg.b.wt. has been shown to cure 37-93% of cases.[11] and data on the use of different treatment doses for *S. haematobium* infection in children is meagre.

Praziquantel is an effective anti-helminthic drug. The first clinical trial on the use of PZQ was conducted by Davies *et al* in collaboration with WHO and showed good results.[12] It was introduced in Sudan in the 1980s to treat patients infected with urinary and/or intestinal Schistosomiasis in the Gezira region and proved to be effictive.[13,14] The dose recommended by the WHO for the treatment of urinary Schistosomiasis is 40 mg/kg.b.wt[15] The standard treatment dose of PZQ for *S. mansoni* and *S. haematobium* is 40 mg/kg.b.wt. However the dose of PZQ could be increased to 60 mg/kg.b.wt in patients with high egg count or at risk of rapid reinfection.[16]

A systemic review of RCTs found no benefit of a double dosing regimen, in which patients infected with *S. haematobium* were retreated 2-8 weeks after an initial dose of PZQ, which was in contrast to the treatment of *S.mansoni* infection in which a significant improvement was accomplished by repeating the dose of PZQ.[11]

The objectives of this study was to compare the efficacy and side effects of two different doses of PZQ (40 mg/kg.b.wt. vs. 60 mg/kg.b.wt) in the treatment of *S.haematobium.* Our hypothesis was that a higher dose of PZQ of 60 mg/kg.b.wt. is better for eradication of *S.haematobium* infection and does not expose the children to additional side effects of PZQ.

MATERIALS AND METHODS

The target population was school children from the three primary schools in the villages of Elkeriab and Tayba Elkababish in the East Nile locality of Khartoum State. The villages are situated within the Elselit irrigation scheme; they had safe water supply and the general hygiene and sanitary conditions were reasonable. Elisilat scheme was established in 1980 and is irrigated by surface canals coming from the Blue Nile River. Since 1990 the area had become endemic with *S. haematobium.*[18]

This study was a single center, randomised controlled trial (RCT), double blind study with two parallel groups conducted from January 2017 to April 2017. All the school children (n =1205) were screened for *S.haematobium* ova in the urine. A local laboratory was established in the area to avoid sample transportation. The terminal part of the urine was collected from the children between 9-10 a.m. during the morning break and the samples were tested immediately each day.

Out of 1205 children who were screened, urine samples of 105 (8.7%) children tested positive for *S. haematobium* on wet film preparation. The

prevalence of infection was 5.6% (39/699) among the 5-9 year-old and 13.1% (66/506) among the 10-14 year-old school children. (Chi-square was 39.6187, p <0.01) These samples were further tested for microhaematuria, macrohaematuria, egg count using filtration technique and egg viability using water dilution (slide test method).[19,20] Polycarbonate (Nuclepore) membrane filter with a pore size of 13 μm. was used. Urine sediment was examined by high magnification power microscopy for microhaematuria counting the maximum number of Red Blood Cells (RBCs) per high power field (HPF) as normal (when < 5 RBCs), Mild (5-9 RBCs), Moderate (10-20 RBCs) and Severe if RBCs were more than 20/HPF. For macrohaematuria a reagent strip of Sangur-Test (Boehringer, Mannheim, Germany) test was performed; the result was expressed in cross system as 0= normal, + = mild, ++ = moderate , +++ and more = severe.

The 105 positive cases were randomised into two parallel groups A and B (Figure 1). The randomisation scheme was computer-generated, with allocation concealment by opaque, sequentially numbered, sealed envelopes. The random allocation sequence was generated by a member of the team who was not involved in the clinical trial. The children and their parents were blinded to the group allocation, and the research assistant who was examining the urine sample was also blinded to the group allocation.

All the children who tested positive were weighed, before group allocation and the two different doses were calculated according to body weight. After the randomisation the corresponding dose was given according to the allocation group. The doctor who administered the medication was not involved in the first or subsequent urine testing. Group A was composed of 52 children; they were given a single dose of 40 mg/kg.b.wt of PZQ. Group B, n = 53 children were given a single dose of 60 mg/kg.b.wt of PZQ. Once the participants were enrolled, the doctor who was administering the PZQ would open the sequentially numbered, opaque envelope to determine the child's group allocation. The assessor who was assessing the study outcome, i.e. the researcher performing the urine examination and the data analyst were both blinded to the group allocation. All the doses were given and witnessed by a member of the team. All of the children were seen and interviewed for three days after treatment to check for any adverse drug reactions. Urine samples from all the children were examined weekly for eggs count, egg viability as well as haematuria quantification (using microscopy) and urine strips for macrohaematuria.

The primary outcomes of the study were the a) cure rate i.e. the percentage of children with *S. haematobium* ova in their urine before treatment who became ova-negative after treatment,[17] and b) disappearance of macroscopic and microscopic haematuria by week six. The secondary outcomes were the reported side effects of PZQ during the study period. Analysis was performed using Statistical Package for Social Studies (SPSS) version 22. The two groups were compared using a t-test, and $p < 0.05$ was considered significant.

Arrangements were made to obtain permission from the local, educational and school authorities. The trial was explained to the teachers, parents and children, and a letter was sent to the parents giving information about the trial and asking for consent.

RESULTS

A total of 1205 children were screened for *S. haematobium* ova, by urine examination; 105 children (8.7%) were found to have evidence of infection. Males were 16.7% (103/616) and females were 0.3% (2/589) with a significant gender difference, $p < 0.01$. The prevalence in Tayba Elkababish School children was 15% (60/375) while in Elkeriab School it was 5.4% (45/830). Out of the 52 children in group A,27 ,(75%) 39 11.5%) 6 ,(28.8%) 15 ,(40.3%) 21 ,(51.9%)), and 6 (11.5%) had a positive egg hatching test at one, two, three, four, five, and six weeks after treatment, respectively, while out of the 53 children in group B, the number of positive cases were 24 (45.2%), 14 (26.4%), and 1 (1.8%) after one, two, and three weeks, respectively, but no positive hatching test

was found in the following weeks and this was also statistically significant (p< 0.01). The cure rates for group A and group B were 88%, and 100%, respectively These results showed group B responded significantly better compared to group A (p <0.01).

The egg reduction rates (ERR) for group A and B was 89.6% and 100%, respectively. Here if we used the arithmetic mean, as recommended by the WHO, because it proved to be better than the geometric mean,[21,22] there would be no statistically significant difference in the average egg count between the two groups (p = 0.3, Table 1).

The response of macrohaematuria and microhaematuria to the different doses of PRQ was also statistically significant, favoring group B with p <0.01 and p <0.01, respectively (Tables 2 and 3). Each of two children in group B vomited once within 24 hours after the dose of PZQ, but no other side effect was documented, indicating no significant difference in the side effects between the two groups.

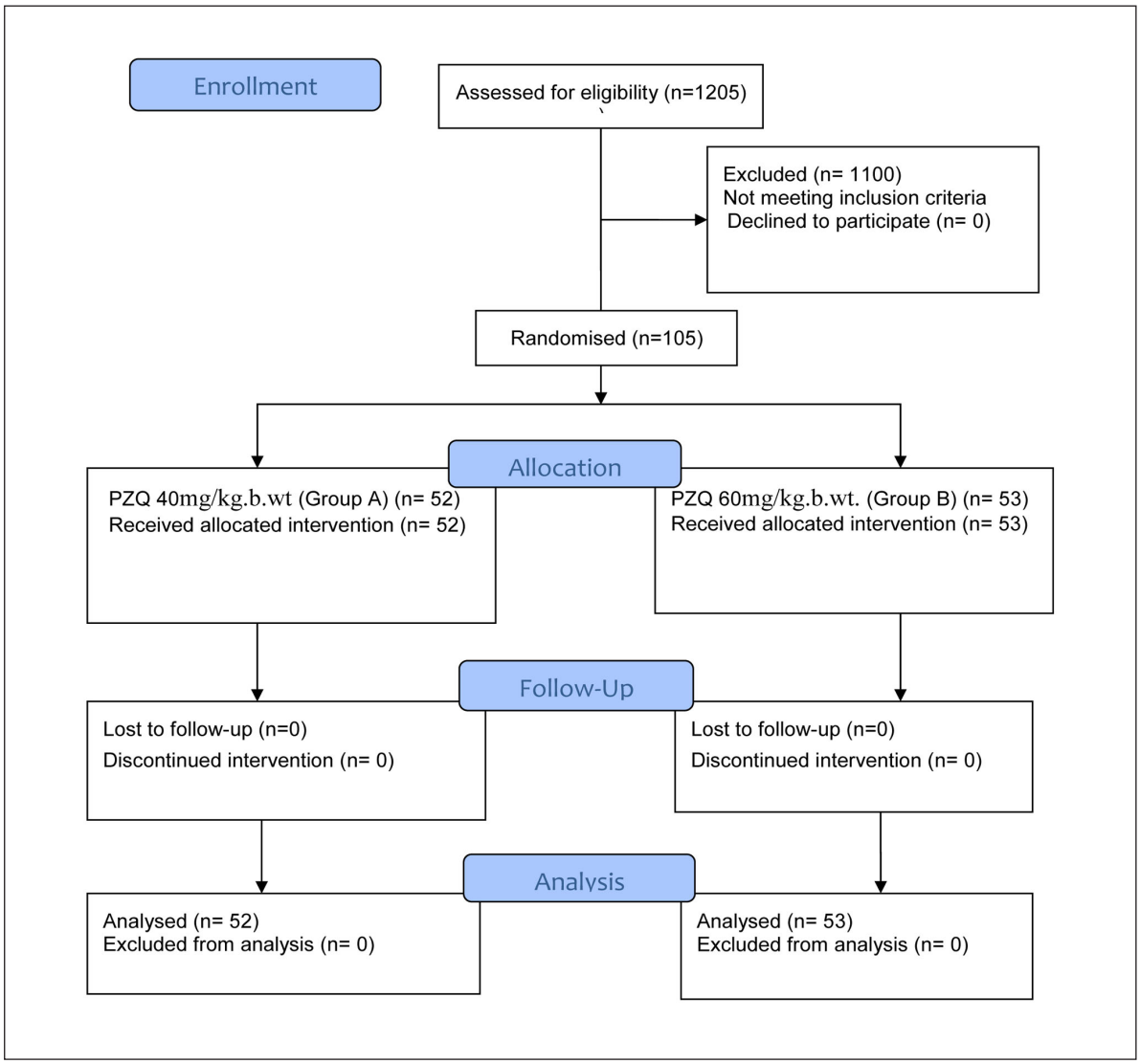

Figure 1. Flow Diagram of the randomized controlled trial

Table 1. Arithmetic mean of egg count of the two treatment groups

Time of treatment	Group A	Group B	SD
Week zero	7.7	7.5	0.14
Week one	5.9	5.0	0.63
Week two	4.4	4.0	0.28
Week three	3.2	2.5	0.49
Week four	2.3	1.0	0.91
Week five	1.3	0	0.91
Week six	0.8	0	0.56

SD= standard deviation.
(The t-value is 0.56217. p= 0.3)

Table 2. Response of macrohaematuria among the two treatment groups

Time of treatment	Group A	Group B
Week zero	Severe	Severe
Week one	Moderate	Moderate
Week two	Moderate	Mild
Week three	Moderate	Mild
Week four	Mild	Normal
Week five	Mild	Normal
Week six	Mild	Normal

0= normal, + = mild, ++ = moderate, +++ and more = severe. (The chi-square = 39.1239, p< 0.01)

Table 3. Response of microhaematuria among the two treatment groups

Time of treatment	Group A	Group B
Week zero	Severe	Severe
Week one	Severe	Moderate
Week two	Moderate	Mild
Week three	Moderate	Mild
Week four	Mild	Normal
Week five	Mild	Normal
Week six	Mild	Normal

Normal < 5 RBCs, Mild = 59- RBCs,
Moderate =1020- RBCs, severe > 20 RBCs.
(The chi-square = 78.2986, p< 0.01)

DISCUSSION

The prevalence of *S. haematobium* infection of nearly 10% among school children living nearby scheme irrigation is expected. The great predominance of males over females (103/2) is no surprise since boys tend to swim and fish in water-infested canals. As reported by others, culturally and socially girls do not usually swim in the canals in public[2] and they had minimal contact with infested water as both villages had safe water for domestic use. The prevalence in Tayba Elkababish School was significantly higher compared to that of Elkeriab School is because Tayba Elkababish village is nearer to irrigation canals and children from the school usually go swimming after the school day especially during summer time.

The infection was highest among the 10-12 year-old group who were more active and adventurous than the youngest children who were also the newcomers to the school. Although there was a significant difference in the prevalence across the age groups, but there was no parasitic load difference between the age groups. Interestingly all the children tested positive gave no history of having haematuria, although many of them had severe macroscopic haematuria (Table 2). We believe the number of symptomatic children might be higher and the children tend to hide their symptoms to avoid being prevented from swimming in the canals

Praziquantel remains the effective and the drug of choice against *S. haematobium.*[23] There is currently no evidence for the development of resistance of S. haematobium to PZQ.[24] However, drug failure was reported and this was caused by the inactivity of PZQ against immature worms.[25] In areas of constant reinfection, PZQ might effectively kill adult worms, but immature worms would then develop and present as adults, implying drug failure. In such settings, repeated PZQ treatment 3-6 weeks apart kills initially resistant juvenile worms and improves the treatment effect of the drug. While a systematic review of RCTs failed to show any benefit of repeated PZQ doses, 3-6 weeks apart, for the treatment of *S. haematobium*, the same study showed a benefit of this approach for *S. mansoni* infection.[11]

Two previous studies from Sudan using a dose of 40 mg/kg.b.wt. showed a cure rate of 58% and 83% in six weeks.[18,26] In this study the cure rate group B was 100% compared to 88 % for group A. There was a significant difference between the two groups egg hatching; in group B there was no single viable egg from week four onward. This is not in agreement with a study by Ouldabdallahi *et al* conducted in Mauritania comparing the efficacy and side effects of PZQ at the doses of 40 mg/kg.b.wt and 60 mg/kg.b.wt and reported no difference in the efficacy of the two doses against *S. haematobium*.[27] On the hand, a study by Belizario et al conducted in Philippines found that a single dose of 60 mg/kg.b.wt. had better efficacy than a 40 mg/kg.b.wt dose in the treatment of *S. haematobium* and *S. mansoni*.[28] Similarly a systematic review of PZQ doses found that a dose of 60 mg/kg.b.wt. was slightly more effective than the standard dose of 40 mg/kg.b.wt.[29]

Side effects of PZQ have been reported to occur in 30-60% of cases; they are usually mild and disappear within 24 hours of drug administration. The most commonly reported side effects are headache, nausea, anorexia, vomiting, abdominal pain, epigastric pain, diarrhea with or without blood and/or mucus, lassitude, fever, myalgia, dizziness, sleeplessness, sleepiness and a skin rash with edema.[16,30] The severity and frequency of the side effects are related to the intensity of the infection as measured by the pre-treatment egg count. In this study, only two children in group B reported mild symptoms of nausea and vomiting, which resolved without treatment in less than 24 hours.

Praziquantel is the corner stone in the prevention and treatment of schistosomiasis, but this has to be supplemented by other measures if we aim to eradicate the disease. These include having access to safe water, improved sanitation, hygiene education, and snail control.[3,31] In our study we only tested for *S. haematobium* ova in the urine, we are sure that the prevalence of the infection would have been higher if we tested stools for *S. mansoni* ova as well. So we think all the school children and adults are at high risk. Together with farmers, irrigation workers children should receive preventive chemotherapy once every two years.[8] The finding for our study suggested that PZQ at a dose of 60 mg/kg.b.wt. gave a 100% cure rate and a 100% ERR. Systemic review of mass drug administration found that school based treatment outcome was similar to community based treatment, and there was evidence in moderate to high risk communities that school based treatment, reduces infection prevalence in adults and in new children entering school.[31]

A meta-analysis of PZQ treatment for schistosomiasis showed that the odds of long term morbidity is markedly reduced when greater post-treatment reductions in parasite burden are achieved i.e. as reflected by a higher Egg Reduction Rate . This suggests that repeated or more effective anti-parasite drug treatment will be a valuable tool for greater reduction of schistosoma-related patient morbidities in affected areas.[32] Therefore getting 100% cure rate and 100% ERR with this higher dose of PZQ will give a big boost for the reduction in the disease burden in the community, complemented by other non-drug based intervention.

The limitation of this study is that it has a relatively short follow up period of six weeks that does not reveal the long term differences and. risk of reinfection between the two groups

CONCLUSION

Praziquantel remains a very effective drug for the treatment of schistosomiasis in Sudan. A dose of 60 mg/kg.b.wt. of PZQ was more effective in clearing *S. haematobium* infection, with a cure rate of 100% in four weeks, compared to a dose of 40 mg/kg.b.wt. of PZQ, with a cure rate of 88.5% in six weeks. There was a significant difference in the ERR, response of microhaematuria, macrohaematuria and egg viability between the two groups. The dose of 60 mg/kg.b.wt. was well tolerated with no significant side effects.

RECOMMENDATION

A single dose of PZQ at 60 mg/kg.b.wt. is effective for treatment of children with urinary

schistosomiasis, the same dose should be considered for the preventive chemotherapy.

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Preparedness of Sudanese medical students for COVID-19 challenge: Knowledge, perceptions, and readiness to participate in the campaign against the disease

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ABSTRACT

Background COVID-19 pandemic threatens nations particularly; those with preexisting problems. The exponential spread of the virus stretches health systems capacity to the limit of failing to meet the health care demands of populations. This makes the recruitment of medical students to provide some of these needs a plausible option. Decades of mismanagement have compromised the Sudanese Health Care System. Having at least one medical school/state provides a valuable opportunity to face disasters. This study aims to evaluate medical students' knowledge, perceptions, and preparedness to participate in efforts against COVID-19.

Methods This is a cross-sectional descriptive study, which included a convenient sample of 347 Sudanese medical students. A self-administered online questionnaire was used to collect data on the students' knowledge, perceptions and preparedness in efforts against COVID-19.

Results The response rate was 99%. Students, especially seniors, possessed adequate knowledge, but they had doubts regarding their practical capacity to respond to COVID-19. Within the various activities students were interested in working in areas other than directly caring for COVID patients; 47% of the students felt that their current training did not prepare them to combat the pandemic; 87% of the participants suggested adding disaster medicine component to their curricula.

Conclusion Medical students can be recruited to expand the capacity of the health care system during COVID-19 pandemic by providing certain types of health care services. Medical curricula need strengthening with contextualized disaster medicine components.

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INTRODUCTION

On December 31, China reported to The World Health Organization (WHO) pneumonia of unknown origin that appeared in the city of Wuhan. The WHO —soon recognised what was later identified as Coronavirus Disease 2019 (COVID-19) as a Public Health Emergency of International Concern. On March 11, the disease was declared as a pandemic.[1] The new virus, COVID-19 belongs to Coronaviruses, a family which infects humans and animals. In humans, these viruses cause mainly respiratory illness; they spread through droplets of saliva or nasal discharge of the infected individuals while other routes of transmission are still being investigated.[2]

The majority of infected people may experience no, mild or moderate respiratory symptoms that require no specific treatment. However, for individuals with pre-existing conditions that weaken their immunity, the disease might be associated with high morbidity and mortality, and they may need assisted ventilation at specialised centres.[2]

The main problem with this disease is the exponential spread pattern that threatens to exceed the capacity of health systems. Thus, the principal strategy to avoid catastrophic situations is to prevent the spread or slow it down through public health measures such as reliable health education, social distancing,

practicing respiratory etiquette and increasing personal hygiene. Currently, there is no definitive treatment or vaccine for the virus, but the on-going research may come up with satisfactory results.

The disease had spread over 216 countries and territories, resulting in a high Global Risk Level according to WHO Classification. On the 2nd of July 2020, the confirmed cases were 10,514,028 and the number of deaths was 512,311.[1] This implies that the whole world is confronting a disaster.- a disaster means "the destructive effects of natural or man-made forces that overwhelm the ability of the community to meet the demand for health care."[3]

COVID-19 is a natural biological disaster, which is threatening the world and requires global coordination and practical measures to overcome.[4] The disease represents extraordinary challenges to all countries in many facets, e.g. the needed resources, economy, possible human rights violations, social disruption and other humanitarian crisis.[5]

Students' involvement during times of disasters is well recognised. It aims at expanding the human resources capacity at times of need.[6] The first documented formal participation was in the 1918 influenza epidemic when Pennsylvania University in the USA closed classes and recruited senior years students to work at hospitals and care for the sick due to diminished numbers of doctors and nurses during the First World War.[7] Similar incidences of students' involvement occurred in Copenhagen polio epidemic in 1952, the Samoa tsunami in 2009 and the Haitian earthquake in 2010.[8] After participating in different disaster management situations, students reported a sense of increased commitment to the profession, high motivation to become physicians and enhanced skills and preparedness for future practice. Others reported that the majority of students were willing to participate during such conditions, but only a few of them felt prepared to do so. If only specific measures to decrease the level of students' anxiety e.g. to be assigned duties relevant to their abilities, training, working in team and ensuring safety, this would make the best use of their involvement.[9]

In Sudan, the first case of COVID-19 was discovered in March 13, 2020. The government had immediately declared a state of a public health emergency. Many preventive measures were implemented to control the spread of the disease, including closing down of ports, schools and universities; banning of gatherings and later partial curfew. Moreover, with the help of the WHO, a countrywide preparedness and response plan was set.[10] The vulnerable socio-political situation in the country has forced the government to take extreme measures to limit the disease spread.[11] By July. 2020, the official count was 10,527 confirmed cases and 668 deaths.[12]

At the forefront against the disease is the Sudanese Health Service System (HSS), which is one of the oldest in the region similar to Sudanese medical education.[13,14] However, the negligence and mismanagement during the last three decades had significantly reduced the quality and efficiency of both systems. Nevertheless, there are 66 medical schools in the country with at least one school in each State.[15] This situation can provide an opportunity to support the overloaded health system with extra-human recourses in the event of a disaster. It is therefore likely that medical students will officially be encouraged to join the front against COVID-19 and applications were launched requesting health professionals including final year medical students to volunteer to work at hospitals.[16] With this background, this study was set to infer the preparedness, knowledge and perceptions of Sudanese medical students to respond to COVID-19 and to assess their readiness and willingness to participate with health professionals in the efforts against COVID-19.

MATERIAL AND METHODS

This is a cross-sectional web-based descriptive study, conducted to estimate Sudanese medical students' knowledge, perceptions and readiness (defined as willingness) to participate in the efforts against

COVID-19. These will be considered as indicators of their preparedness to respond to the pandemic. The study hypothesis is that Sudanese medical students are willing to participate in the campaign against COVID-19. The target population included medical students of two of the students' organizations: the Students Network Organization-Sudan (SNO), and the Medical Students International Network-Sudan (Med SIN-SUDAN).[17,18] These two organisations were chosen because of their large membership (1500 students) that comprises students from all over the country. Moreover, the study was conducted during the lockdown. While Internet services were not available for every medical student, most of the members of these organisations did have access to the Internet. They could also be reached through Net-Based Applications (e.g. Facebook, WhatsApp, Telegram, etc.).

The sample size was 350 students - calculated using a web-based application with a margin of error of 5% (confidence level 95%).[19] A convenient sample was invited through a link to the questionnaire sent to students' groups in social media (Facebook, WhatsApp and Telegram).

A pre-designed self-administered questionnaire was used after validation. The questions were generated from the literature, and adapted to suit the local context.[20-22] The first version of the questionnaire included 26 questions. For validation, a pilot study that included 12 students was conducted, and ten medical experts reviewed the collected data. Based on their feedback, five questions were omitted, one more question added, two questions edited, and an Arabic translation was added after consultation and re-testing. The final questionnaire of 22 questions and the informed consent document were combined using Google Forms, and the link was sent through the different Web-based Applications.

The Google Forms document was organised as follows: Section One consisted of the consent form, Section Two included the demographic data (four questions), Section Three for knowledge and perceptions of disaster medicine (nine questions) and Section Four for the knowledge and perceptions on COVID-19 and readiness to contribute to efforts fighting the pandemic (nine questions).[23]

For analysis the study population was subdivided into Junior Students (JS: from years one, two and three) and Senior Students (SS: from years four, five and six). Descriptive statistical tests were used, and for some parameters, group comparison was performed. Chi-square test was applied and $p < 0.05$ was considered significant.

RESULTS

There were 346 responders with a response rate of 99%. The participants were enrolled from 43 medical schools, (25 public medical schools and 18 private schools, representing 58% and 43% of the total number of medical schools, respectively) located in 11 state.[15] Females comprised 73% of the students in the study; 54% of the students were in the age group 17-20 years, and 67% of them were junior students (Figure 1).

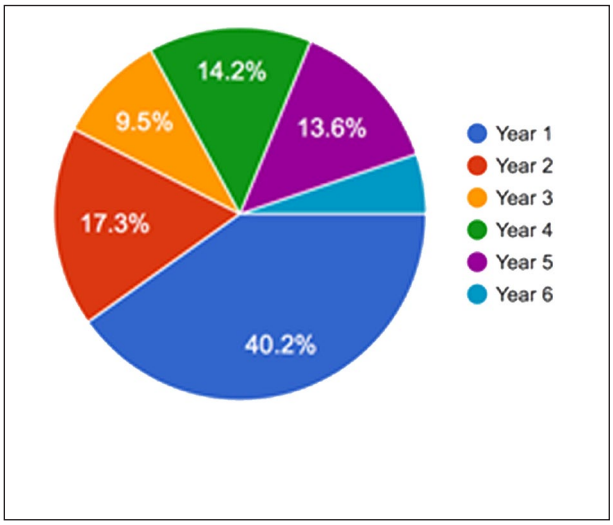

Figure 1: Academic levels of the students in the study

Students' knowledge and perceptions of Disaster Medicine

In this study, 77% of the students had no previous education in disaster medicine. Only one-third of the 33% who had prior education received it formally in their universities. Likewise, 84% had no practical experience in disaster management and the remaining 16% of the students gained

their experience through working with voluntary youth groups or NGOs. Regarding the perceived knowledge and capacity to respond to disasters, the participants were asked to rate their knowledge referring to aetiology, signs and symptoms and management of different types of disasters, such as epidemics, outbreaks, natural disasters, chemical and nuclear incidents. Around two-thirds of students thought they had adequate knowledge (satisfactory, good and very good) and that they were capable of responding to them. Almost half of the students thought they were knowledgeable and able to respond to natural disasters. Less than one-third had the knowledge and capability to deal with chemical incidents. And for the nuclear incidents, only 18% of the students thought they had the required knowledge, and 15% thought they could respond to them.

In the area of epidemics and outbreaks, 76% of the senior students thought their knowledge was adequate (Satisfactory and above). Whereas only 56% of the junior students believed they had adequate knowledge. This difference is statistically significant, $p<0.005$. Regarding the capacity to respond to disasters, 72% of the senior students believed that they could respond (satisfactory and above) compared to 59% of the junior students. This difference is also statistically significant, $p<0.005$.

Regarding the students' knowledge and perceptions on disasters in Sudan, 88% of participants agreed to various degrees that Sudan is prone to disasters and they showed that they were familiar with most of the disasters experienced by Sudan. For the different types of disasters, from a list of 15 types in which only nine were correct, more than 50% of participants were able to select at least seven correct disasters. These included internal conflicts, meningitis, famine, non-communicable diseases, floods, dengue fever and chikungunya virus disease. Two local disasters were less recognised by the students, namely the drought (recognized by 47%) and Rift Valley Fever (by 35%) of the students. The idea of integrating a basic course in disaster medicine within undergraduate curricula was strongly recommended by 78% of the participants.

Students' knowledge, perceptions and readiness to participate in COVID-19 management

As for COVID-19, 62% of the participants had attended formal discussions on the topic. For reliable sources of information about the pandemic, students used different media. From the most preferred to the least, these sources were; social media, news media, the government websites, friends and families. Regarding the students' knowledge and perception of the disease, 63% correctly answered most of the questions. However, one-third of the students did not know basic facts e.g. the virus mode of transmission, and 70% of the participants thought that COVID-19 is fatal.

Currently 78% of the participants were not involved in the efforts against the pandemic. Regarding participants' willingness to be involved in the various health care activities, it was found that 58% were willing to be involved, 37% were indecisive, and 5% were not interested. Concerning the students' willingness to get involved in specific tasks during the COVID-19 pandemic crisis, 24% of them were willing to work in hospitals and isolation centres, whereas 38% of them were disinterested and the remaining participants showed some degree of interest. In this area, significant difference ($p < 0.02$) was noted between the senior (57% willing to work in hospitals) and the junior groups (64% willing to work in hospitals).

Almost two-thirds of the students were willing to work for health education to raise community awareness and to provide health care services to special vulnerable groups, and 55% of them were willing to provide service and support to patients with long-standing diseases. The students' knowledge of the concepts, processes, and measures taken during COVID-19 outbreaks was generally good. 72% of participants had adequate knowledge of isolation and quarantine procedures for persons exposed to infectious agents. 62% of participants had adequate knowledge on the selection of the appropriate personal protective equipment and decontamination processes when caring for patients; 67.5% of the participants had adequate Knowledge on disease reporting strategy to the Ministry of Health.

Regarding the students' decision-making capacity to join the campaign against COVID-19, the study revealed that 68% of participants could decide for themselves, whereas parents take this decision for 26% of them.

Almost half of the participants (47%) thought that their current training in medical schools does not prepare them to deal with COVID-19, 32% were unsure of that while 21% thought it does.

DISCUSSION

Across the globe, the COVID-19 pandemic has taken different population by surprise and forced them to slow down and modify their regular schedules, Sudanese people are no exception. An additional factor had caused further derangement and disruption of life style is the political instability in Sudan. Since December 2018, the majority of higher education institutions were closed for almost one year. Towards the end of 2019 educational institutions resumed their activities for less than five months before the pandemic imposed another lockdown.

In this study, the majority of participants were junior medical students, mostly in the first year of their programme. This may be explained by their desire to be part of the medical community, the long periods away from regular training and education made them more eager to see themselves as doctors and hence had participated in the study. This may also explain the finding that junior students were more motivated to work in hospitals. The higher participation of female students in this study is no surprise as 64-88% of the students at health/medical higher institutions are females.[24]

The study indicated that participants had limited formal training and experience in disaster medicine. Students expressed the need for having such training in their undergraduate education. The Association of American Medical Colleges issued comparable recommendations - to integrate the disaster response training in undergraduate medical curricula so as to support medical students training in this area.[25] Other studies from Sudan, Qatar, Yemen, Saudi Arabia, Pakistan, Germany, Belgium, and The Netherlands had also published similar recommendations.[6,20,21,25-30]

The study revealed that students' knowledge of disease epidemics and outbreaks is relatively better than that of other types of disasters. This finding reflects the traditional orientation of curricula that lack proper inclusion of all types of disasters and focuses on the biomedical component.[9] Although the students' knowledge of local disasters was satisfactory, yet; this observation needs further analysis to verify whether there are variations between universities in different parts of the country in this area. Ideally, socially accountable curricula would ensure better context relevance so as to graduate doctors who are capable of responding to their community needs and challenges.[31]

Pressured by a lot of unmet needs of their societies, Sudanese youth groups had substituted the government in providing social services to the deprived communities and during natural disasters.[32] The finding that participants were not involved in the campaign against COVID-19 was not expected, especially when we consider the pattern of activism in this generation. This observation requires further study; nevertheless, it may be explained by some of the study findings e.g. the students' misconceptions and knowledge, lack of disease transmission and infectivity. The fear of transmitting the disease to their families might be a restricting factor - most of these students live with their families. For the senior group, the long period of absence from formal education might have negatively affected their motivation but this needs further analysis.

Based on the findings in this study, Medical students can be recruited to provide health services other than working with COVID-19 patients. These include community health education, and this task is crucial in Sudan were the norms and traditions significantly compromise the official measures to prevent the disease spread. In this context, most of the conventional preventive measures, i.e. the lockdown and curfew were not properly

implemented be by a large population sector due to their low socioeconomic status and health education level. For this sector, context-sensitive messages might be the only tool at hand, and students can take this responsibility. Such experience will enhance the students' abilities to understand their community and to develop them into socially accountable practitioners. This suggestion is highly recommended by the National Programme of Accreditation on Basic Medical Education.[33]

Information on COVID-19 is accumulating by the day, and it is transmitted through the different information sources both validated and non-validated. The collected data in this study had shown that students have a knowledge gap on the pandemic. This can be bridged through exploiting students' most preferred sources of information as found in this study, to transmit the relevant messages.

Involvement of students in campaigns against disasters is beneficial for both the health care system; as it expends its human resource capacity and the students who would gain authentic experiences that would boost their learning.[34] The potential gains for students as professionals or as human beings are unique and unparalleled by any other type of education or exposure. This notion was expressed brilliantly by one of the fresh graduates who volunteered in a Call Centre for Coronavirus to provide information to the public callers during this pandemic. She wrote about her experience the following: "With every phone call I receive, I understand a little more about my country, its people's mentalities, and what they are suffering from the most. I truly believe that the customers who have called have taught me and will continue to teach me much more than I could ever teach them." [35]

CONCLUSIONS

This study revealed that medical students could be recruited to the front against COVID-19 to cover some of the vital health care needs relevant to their training level. Moreover, it affirmed the need for integrating disaster medicine components within undergraduate medical curricula. Preparedness for disasters requires proper attention to the local context and most importantly, to authentic community consultations that will inform the choice of the most relevant response strategies. The limitations of this study were the sample size and type which were attributed to the country's lockdown during the study period. Further studies are certainly needed.

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Ethical considerations

Ethical clearance for the study was obtained from the National Research Ethics Review Committee, the Health Research Council and the Federal Ministry of Health. Each participant gave informed consent.

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Indications and outcome of continuous positive airway pressure in three neonatal intensive care units in Khartoum State, Sudan.

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ABSTRACT

Background Nasal continuous positive airway pressure (CPAP) is a non invasive form of respiratory assistance that has been used to support spontaneously breathing infants with lung disease for nearly 45 years**.**

Objectives To study the indications and outcome of CPAP in three neonatal intensive care units (NICUs) in Khartoum State.

Methods This is hospital based cross sectional study of 100 newborns conducted during the period from November 2015 to July 2016. Data was collected via a questionnaire and analysed using Statistical Package for Social Sciences.

Results One hundred newborns were included in the study. Males were 59(59%) and females were 41(41%). Thirty (30%) newborns were delivered with birth weight (B Wt) of 1000-<1500 grams (g), 29 (29%) had B Wt of 1500-< 2500*g,* and 33(33%) had B Wt of 2500-3500g. Almost all the study newborns, n=99(99%) were put on Bubble CPAP and only 1(1%) on ventilator CPAP. The indications for CPAP were respiratory distress syndrome (RDS) in 54(54%) cases, transient tachypnea of the newborn (TTN) in 7(7%), meconium aspiration syndrome (MAS) in 11(11%), sepsis in 10(10%), congenital heart disease in 11(11%) and recurrent apnea in 7(7%) cases; 55(55%) cases were put on CPAP after more than 24 hours of age. and 55(55%) newborns were weaned from CPCP gradually while 45(45%) cases were weaned suddenly. Marked improvement occurred in 71(71%) cases, 4(4%) deteriorated after CPAP but recovered after ventilation and death was the outcome of 24(24%) of the study newborns.

Conclusion The most common indication for using CPAP was RDS: majority of cases improved and death was the outcome of 24(24%) cases of whom 15 (62.5%) were preterm. No major complications were reported. .

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BACKGROUND

Nasal continuous positive airway pressure (CPAP) is a noninvasive method for applying a constant distending pressure level (above atmospheric) during inhalation and exhalation to support spontaneously breathing newborn infants with lung disease. Continuous positive airway pressure was first described by Gregory in 1971 for treatment of neonatal respiratory distress syndrome (RDS). It has become a recognized method to improve both pulmonary and extra pulmonary outcomes by avoiding prolonged mechanical ventilation in premature infants.[1] By applying nasal prongs to neonates and blowing air at certain pressures through the prongs, one can generate a positive airway pressure in the neonate's lungs. The physiological effects of this include improving

oxygenation, maintaining lung volume, lowering upper airway resistance and reducing obstructive apnoea. Therefore, it can effectively be used in many neonatal respiratory conditions, including the prevention of extubation failure, prevention of apnoea of prematurity and as an alternative to intubation and mechanical ventilation in neonates with respiratory distress syndrome.[1,2]

There are many devices available, including single and double (binasal) prongs in the short (nasal) and long (nasopharyngeal) forms. A meta-analysis of randomized controlled trials, provided evidence that short binasal prongs are more effective at preventing re-intubation after extubation than other devices.[1] A randomized controlled trial reported better results where short binasal prongs were used when compared with a single nasopharyngeal prong.[1]

METHODS

This is a cross sectional hospital based study conducted in three main neonatal intensive care units (NICUs) in Khartoum State, namely Soba University Hospital NICU, Omdurman Maternity Hospital NICU and Gaafar Ibn Auf Referral Hospital NICU, from November 2015 to July 2016.

Soba University Hospital (SUH) is located along the Blue Nile River, 15 kilometers (km) south of Khartoum, and is the largest training site for the students of the Faculty of Medicine, University of Khartoum. The obstetric department at SUH is one of the main referral centers for high risk pregnancies in Sudan. The NICU accommodates for 25 babies, all are inborn. The turnover is in the range of 800-1000 babies per year.

Omdurman Maternity Hospital (OMH) is located along the River Nile 10 km north of the centre of Khartoum. It is the first specialized hospital in the Sudan (opened 1957). It provides maternity and newborn care to Omdurman and its urban and periurban areas covering a population of about 6 millions. The NICU accommodates for 75 babies; 95% of the babies are inborn. The turnover is about 5000 babies per year.

Gaafar Ibn Auf Children's Referral Hospital (GIARH) is located in the center of Khartoum to receive referrals from all over the country. It accommodates all paediatric specialties but there is no delivery suite and the babies in the NICU are all out born. The capacity of the NICU is for 16 babies and the turnover is about 500 newborns per year.

Sampling was total coverage and all newborns who were connected to CPAP daring the study period were included. All the 3 NICUs use Bubble CPAP and they adopt similar guidelines as regards to CPAP policy. The data was collected using questionnaires and analysis was done using the statistical package for social sciences (SPSS). P value of <0.05 was considered significant.

Ethical approval was granted from all bodies concerned. Written agreements from hospital administrations and the treating doctors were obtained and informed verbal consent was also obtained from parents and / or care givers after explanation of the study objectives.

RESULTS

One hundred newborns were included in the study. Males were 59(59%) and females were 41(41%). Sixty three (63%), 19(19%) and 18(18%) newborns were enrolled from OMH, SUH and GIARH, respectively. The entire study sample (n=99, 99%) were put on Bubble CPAP except one case (1%) who was put on ventilator CPAP. Forty five (45%) of the cases were connected to the CPAP within the first 24 hours (hrs): 9 within less than 4 hrs, 10 between 4-11 hrs and 26 within 12-24 hrs. while 55 (55%) of them started CPAP after >24 hrs.

Eight (8%) newborns were delivered with birth weight less than 1000 grams (g); 30(30%) were at 1000-<1500 g; 29 (29%) were at 1500-< 2500 g and 33(33%) had birth weight of 2500-3500 g. The Apgar score at five minutes in 81(81%) cases was >6 and 19(19%) scored 2-6. Twenty-three (23%) of them required active resuscitation at birth. Singleton was the outcome of pregnancy in 86(86%) and 14(14%) newborns were product of multiple birth.

The pre CPAP fraction of inspired oxygen (FiO2) of 81(81%) newborns was <50% and was >50% in 19(19%). Pre CPAP oxygen flow was 2 litres/minute (l/m) for 81(81%) cases and 3-5 l/m for 19(19%) of them. The pre CPAP oxygen saturation (SpO2) was 88% for 55(55%) and >88% in 45(45%) cases. The reported pre CPAP heart rate was normal (100-160 beats/m) in 71(71%), >160 beats/m) in 26(26%) and <100 beats/m in 3(3%) of the newborns. The reported pre CPAP respiratory rate was >60 breaths/m in 80(80%), 30-60 breaths/m in 16(16%) and <30 breaths/m in 4(4%) cases (Table 1).

Table 1. Parameters of the study newborns before CPAP initiation

Parameter	Value	N	%
Pre CPAP FiO2	< 50%	81	81.0
	> 50%	19	19.0
Total		100	100.0
Pre CPAP oxygen flow	2 litres/min	81	81.0
	3-5 litres/min	19	19.0
Total		100	100.0
Pre CPAP SpO2	Abnormal < 88%	55	55.0
	Normal => 88%	45	45.0
Total		100	100.0
Pre CPAP heart rate (beats/minute)	Low (< 100)	3	3.0
	Normal (100-160)	71	71.0
	High (> 160)	26	26.0
Total		100	100.0
Pre CPAP Respiratory rate (breaths/ minute)	Low (< 30)	4	4.0
	Normal (30-60)	16	16.0
	High (> 60)	80	80.0
Total		100	100.0

CPAP: Continuous Positive Airway Pressure
FiO2: Fraction of inspired Oxygen
SpO2: Oxygen Saturation

The main indications for CPAP were RDS in 54(54%) cases, meconium aspiration syndrome (MAS) in 11(11%), congenital heart disease in 11(11%) and sepsis in 10% (Table 2).

Table 2. Indications for CPAP in the study group

Indications for CPAP	N	%
RDS	54	54
TTN	7	7
MAS	11	11
Sepsis	10	10
Congenital heart disease	11	11
Recurrent apnea	7	7
Total	100	100

CPAP: Continuous Positive Airway Pressure

RDS: Respiratory Distress Syndrome

TTN: Transient Tachypnea of the Newborn

MAS: Meconium Aspiration Syndrome

The complications of CPAP reported in this study included abdominal distention in 4(4%) of the newborns, nasal septum erosion in 5(5%) and nasal septum necrosis was reported in 5(5%) cases.

The outcome of the study included marked improvement in 71(71%) of the newborns, 4(4%) deteriorated but recovered after ventilation while 24(24%) of the newborns died. All cases with TTN as an indication for CPAP showed marked improvement, followed by sepsis in 8(80%) out of 10, CHD 8(72.7%) out of 11, RDS 35(64.8%) out of 54, MAS 7(63.6%) out of 11 and recurrent apnea in 4(57.1%) out of 7 of the study cases. The outcome of the cases in relation to gestational age is shown in Table 3. Out of the 76 living newborns, 44(55.3%) were weaned gradually and 34(44.7%) of them were weaned suddenly.

The mothers of 14(25.9%) cases out of the 54(100%) preterm newborns included in the study, received antenatal steroid but 4 (28.6%) of them failed CPAP. While in 40 (74.1%) preterm newborns whose mothers did not receive antenatal steroids the CPAP failure rate was 35% (n=14) and the difference was significant ($p<0.04$).

Table 3. Outcome of CPAP in relation to gestational age of the study newborns*

Gestational Age	Outcome	N	% (within group)	% of total sample
24-28 weeks	Marked improvement	6	50.0	6.0
	Deteriorated and ventilated	2	16.7	2.0
	Death	4	33.3	4.0
	Total	12	100.0	12.0
29-32 weeks	Marked improvement	14	63.6	14.0
	Death	7	31.8	7.0
	Total	22	100.0	22.0
33-36 weeks	Marked improvement	14	70.0	14.0
	Slight improvement	1	5.0	1.0
	Deteriorated and ventilated	1	5.0	1.0
	Death	4	20.0	4.0
	Total	20	100.0	20.0
37-42 weeks	Marked improvement	36	78.3	36.0
	Deteriorated and ventilated	1	2.2	1.0
	Death	9	19.6	9.0
	Total	46	100.0	46.0

CPAP: Continuous Positive Airway Pressure *Chi Squire = 16.18, P < 0.03

DISCUSSION

In the one hundred study cases, the male: female ratio was 1.43: 1.00, which is comparable to the study done by Jeena et al, where the reported male: female ratio was 1.34: 1.00. [4] About two thirds of the study sample were enrolled from OMH as it had the highest turnover compared to SUH and GIARH.

CPAP was initiated in more than half (55%) of the newborns after the first 24 hours of age. The majority of these cases (n=32) had RDS. The reason for delay in initiation of CPAP was either due to shortage of machines which were occupied most of the time and /or late referral.

The most common indication for CPAP in this study was RDS (54%), which is comparable to the Study by Mathaiet *al.* where RDS was the indication in 60% of their cases.[5] However, in a study from Brazil, RDS was the indication in 32%.[6] The other indications for CPAP in this study were congenital heart disease (11%), meconium aspiration syndrome (11%), congenital pneumonia (10%), TTN (7%) and recurrent apnea (7%). These are different from other studies where the main indications were weaning from ventilator, apnea and pneumonia.[6] These differences are mainly due to lack of ventilators in our situation as well as sampling differences.

Regarding the starting pressure, the majority of babies were put on pressure of 6 centimeters of water (cmH_2O), based on the hospitals protocols, while in few cases the pressure was decided on individual basis according to the clinical conditions.

Needless to mention that introduction of CPAP markedly decreased the need for intubation and possibly mechanical ventilation; the outcome improves with increased gestational age, increased birth weight and early initiation of CPAP.

The success rate of CPAP in this study was 71%, comparable to other studies by Shoemaker et al and Jeenaet al who reported success rates of 50% and 74%, repectively.[4,7] Regarding gestational age, the success rates in this study significantly increased with increase in gestational age ($p<0.03$) (Table 3), in agreement with a study from South Africa by Yee et al.[7] Also the success rate in this study significantly increased with the increased birth weight ($p<0.03$), and marked improvement was reported in newborns with normal birth weight, This is comparable to the study done in Brazil by Rego and Martinez.[6]

Failure rate among our study cases who received early CPAP was 22.2% and was significant ($P<0.02$), male gender and fraction of inspired O2 >0.25 were significantly associated with early CPAP failure (2 out of 9 newborns) and this was less than that reported from the study conducted in Netherland by De Jaegere et al who reported that the failure rate in early CPAP was 34%, but also male gender and fraction of inspired O2 >0.25 contributed to higher failure rate.[8]

The main complications were skin abrasion in form of nasal septum necrosis / nasal septum erosion and abdominal distention (10% and 4%, respectively) which were less than the finding in a study conducted by Mathai et al. in India who reported the complications in 30% and 26%, respectively.[4] Pneumothorax as a complication of CPAP was not observed in this series, which is in agreement with a study done in South Africa.[9]

CPAP didn't provide adequate respiratory support for 29 newborns (five of whom improved with mechanical ventilation). It is noteworthy that 15(62.5%) out of the 24 cases who expired were preterm and 11 (50%) of them were <32 weeks gestation with RDS being the main contributing factor for mortality Similarly in a study by Jeena et al CPAP did not provide adequate respiratory support for 22 out of 85 preterm and the mortality rate was 25%.[4]

We observed that apnea and late initiation of CPAP, had higher incidence of failure of 29%, and this is in congruent with a study from India by Matthau et al who found that apnea and late CPAP initiation also had a higher incidence of failure rate of 30%.[5] Moreover, in this study there were 23(23%) newborns who received active resuscitation at birth

($p<0.03$). Furthermore, the 14(25.9%) preterm newborns whose mothers did not receive antenatal steroids had a significantly higher incidence of failure rate ($p<0.04$) compared to those whose mothers received antenatal steroids. However, some of the cases whose mothers received antenatal steroid also failed CPAP and that was probably related to the late administration of steroids and / or not receiving the optimal doses.

CONCLUSION

Most of the newborns, who received CPAP in this study, were preterm. The indications for CPAP were RDS, TTN, MAS, sepsis, congenital heart disease and recurrent apnea. Marked improvement was the outcome of the majority while one quarter of them had died mainly of prematurity and RDS and partly due to lack of surfactant and ventilator support. No major complication was reported in this series

RECOMMENDATIONS

CPAP should be initiated as early as possible for newborns with respiratory distress to improve the outcome. CPAP is a simple and cheap modality of respiratory support which can be delivered to babies in resource-limited countries. In Sudan CPAP can be introduced to all units in the States. Needles to mention that availing surfactant and ventilator support would further reduce the mortality. -

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Effects of raw *Nigella Sativa* seeds on control of blood glucose among type 2 diabetic patients in a rural hospital in Gezira State, Sudan

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ABSTRACT

Background The use of herbal agents as complementary/alternate medicine is prevalent worldwide and is gaining popularity. *Nigella sativa (N.sativa)* or "Black seed" is widely used medicinal plant for treatment of various ailments including diabetes mellitus.

Objective This study aimed to evaluate the effect of *Nigella sativa* seeds on blood glucose level among type 2 diabetic patients in a rural hospital in Gezira State, Sudan.

Patients and methods This is a prospective case-controlled 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 (g) of *N.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. Fasting levels of blood glucose (FBG), blood glucose level 2 hours postprandial (2hr PG), and glycosylated haemoglobin (HbA1c), were measured before, and after three months,

Results The FBG level of the subjects ranged from 150 to 400 mg/dl and they were all on oral hypoglycaemic agents. In the study group the initial levels of the fasting blood glucose ±SD, 2 hours postprandial ±SD and glycosylated haemoglobin ±SD were 229.18±66.17 mg/dl, 313.09±61.14 mg/dl, and 10.40%±2.27%, respectively. These levels had decreased significantly to 198.36±54.03 mg/dl, 262.81±59.96 mg/dl, and 9.16%±1.81%, respectively after three months of *Nigella sativa* administration ($P < 0.05$). No significant effect on body mass index (BMI) 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 FBG level, 2hr PG level and HbA1c among type 2 diabetic patients. Investigation of the effect of the raw of *Nigella sativa* on control of blood glucose in type 1 diabetic patients is recommended.

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INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycaemia, disturbed carbohydrate, fat and protein metabolism caused by defective insulin secretion, action, or both.[1-4] Type 2 Diabetes (T2DM) or non-insulin dependent diabetes mellitus (NIDDM) results from the body cells resistance to insulin which may be combined with relatively reduced insulin secretion. It is the commonest type of diabetes mellitus and is a major public health concern.[4-8] It is estimated that 65% of the world's population will be diabetic by 2025.[5] In 2014, the Middle East and North Africa had the

highest age-adjusted global prevalence of diabetes of about 11%. The prevalence in Sudan was about 18%.[9] and it is estimated that 16% of Sudanese adults (20-79 years) suffer from diabetes, with a total of 3 million diagnosed patients and additional 1.5 million cases undiagnosed.[10,11]

The criteria for the diagnosis of diabetes mellitus are: FBG ≥ 126 mg/dl (7.0 mmol/l), 2hr PG ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test, HbA1c ≥6.5% (48 mmol/mol) or in a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis, a random plasma glucose ≥200 mg/dl (11.1 mmol/l).[12] The risk factors include obesity, physical inactivity, pre-diabetes, poor nutrition, family history of diabetes, past history of gestational diabetes and advancing age.[13] The main symptoms of T2DM are polyuria, polydipsia, fatigue, stomach cramps or constipation, and skin infections.[13,14] The long-term complications of T2DM include atherosclerosis, stroke, heart disease, chronic kidney disease, retinopathy, neuropathy, sexual dysfunction, loss of bladder control and leg ulcers[3,14-17] Management of T2DM should be based on the initial assessment; it involves lifestyle modification, medications and patient education to encourage self-care and empowerment.[18]

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 glucose and blood pressure levels as close to normal as possible. These goals can be achieved through healthy food choices.[19] 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.[12]

The use of herbal drugs as complementary/alternate medicine is prevalent worldwide and is gaining popularity. *Nigella sativa* is widely used medicinal plant in the form of raw seeds or oil added to medicines and foods. The plant grows to about 20-30 centimetres in height and is commonly known as "Black seed" or "Blessed Seed".[20] It is used to treat various ailments including inflammatory diseases, fungal infections, bacterial and allergic infections.[21] It had been used to treat diabetes mellitus, asthma, respiratory, digestive tract, cardiovascular, kidney and liver diseases.[22] Its use for fatigue, rheumatism, indigestion, dropsy, amenorrhea, dysmenorrheal, as antiseptic and local anesthetic is also common.[23-25] It is also recently used as an immune-modulator, anti-antioxidant and for other metabolic conditions (e.g. dyslipidemia).[26,27] The seeds of *N. sativa* showed richness and diversity in its chemical composition. Carbohydrates, proteins, lipids, volatile and fixed oils are contained in the seeds.[28]

The hypoglycaemic and anti-diabetic effect of *N. sativa* has been reported by numerous scientific studies. It has been demonstrated that *N. sativa* seed ethanol extract (NSE) exhibits a remarkable ability to concomitantly increase insulin secretion, induce proliferation of pancreatic Beta cells, and stimulate glucose uptake in skeletal muscles and fat cells.[20,29] This study aims at evaluating the effect of raw *N. sativa* seeds on control of blood glucose 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 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.

Blood samples were collected after an overnight (12 hours) fasting; (2.5 ml in a fluoride oxalate container for FBG, 2.5 ml. in an EDTA {Ethyline Diamine Tetra-acetic Acid} container for haematological variables and 2.5ml in fluoride oxalate container for 2hr PG). Salter scale and stadiometer 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* 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 analysed 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 % were female, 41 % 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 *N. sativa,* three were lost for follow up and 22 continued the study.

The initial mean ± SD fasting blood glucose levels of the study group was 229.18 ±66.17 mg/dl, which changed to 198.3636±54.03 mg/dl after daily chewing of *N sativa* for three months and this change was significant ($P < 0.05$). Comparatively, the difference between the initial FBG level and that after three months of the control group was not significant ($P > 0.05$). The mean ± SD 2hr PG levels level of the study group initially was 313.09±61.14 mg/dl which changed to 262.8159.96± mg/dl after treatment for three months with *N. sativa* and this change was also statistically significant ($P < 0.05$), Comparing between the 2hr PG levels initially and after three months in the control group, the differences was found to be insignificant ($P > 0.05$) as seen in Table 1.

The mean ± SD HbA1c levels of the study group was initially 10.40% ±2.27% which changed to 9.16%±1.81% after treatment with *N. sativa* for 3 months and this change was significant ($P < 0.05$) Comparatively the initial HbA1c levels of the control group were not statistically significant from the levels at three months ($P > 0.05$, Table 1).

Table 1. The levels of fasting blood glucose, 2hrs postprandial blood glucose and HbA1c of the Study and the control groups before and after three months

	Study group Control group		Control group	
Parameter	Initial Mean ± SD	After 3months Mean ± SD	Initial Mean ± SD	After 3 months Mean ± SD
FBG (mg/dl)	229.18 ±66.17	198.36±54.03**	214.5665.05±216.00	62.01±*
2hr PG (mg/dl)	313.09± 61.14	262.81±59.96**	299.7270.04±296.04	72.27±*
HbA1c (%)	10.40±2.27	9.16±1.81**	13.79 ±17.39	13.79 ±17.39*

FBG= Fasting blood glucose. 2hr PG= 2 hours postprandial glucose. HbA1c=Haemoglobin A1c
**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 *N. 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 statistically insignificant (P > 0.05) as seen in Table 2.

Table 2..The levels of body mass index (BMI) of the study group and the control group

	BMI		
	Initial Mean ± SD	after 3months Mean ± SD	p-value
Study group	32.87±3.45	32.87±3.44	>0.05
Control group	33.84±5.42	33.45±5.47	>0.05

DISCUSSION

The results showed a significant decrease in the levels of glucose parameters (FBG, 2hr PG and HbA1c) after direct chewing of two grams of *N. sativa* seed for three months by T2DM patients. These results were in line with those described by Bilal [30] who used *N. sativa* powder at a dose of 0.7 gm/day and *N. sativa* oil equivalent to 0.7 gm of *N.* sativa / day Similarly, previous studies had reported significant reduction in FBG levels when *N. sativa* powder was used at a dose of 2g m/ day.[31-36] Hosseini et al had also shown significant reduction in FBG levels when *Nigella sativa* was consumed at 100mg/kg/day for 4 weeks in diabetic rats.[8] Moreover, Khalid et al had reported significant reduction in FBG levels when oral *N. sativa* was used at a dose of 4 gm twice / day for 2 day in Sudanese non-diabetic adult.[20] Furthermore, Moustafa et al reported a significant reduction in FBG levels when *N. sativa* oil was used at a dose of 1350 mg per day in newly diagnosed type 2 diabetic patients.[37]

Our finding of significant reduction of 2hr PG level is in agreement with the reports by Najmi and Bamosa.[31,32] Our study also demonstrated that the *N. sativa* has significantly reduced HbA1c which is consistent with Bamosa et al. who found that *N. sativa* seeds in one, two and three g/day significantly improved glycaemic control.[32,34,35] It is also in line with Hosseini and Al-Jamal who reported significant reduction in HbA1c when *N. sativa* oil used at a dose of 0.5ml /kg IP for one month in diabetic rats.[8,38] However it is in disagreement with Moustafa et al who found no significant chnges.[37]

The efficacy of *N. sativa* is related to numerous active components which had been isolated from the seeds and the oil including thymoquinone, thymohydroquinone, dithymoquinone, thymol, carvacrol, nigellimine-N-oxide, nigellicine, nigellidine, and alpha-hederin, as well as flavonoids.[20] The anti-inflammatory, antioxidant and antihistamine properties of *N.sativa* oil has various pharmacological effects such as reduction of inflammatory cytokines, reduction of glucose, lipid and blood pressure.[8,39] The anti-inflammatory and antioxidant properties *N. sativa* could improve insulin secretion (i.e maintain the activity of pancreatic beta cells) and reduce insulin resistance resulting in control of blood glucose and diabetes.[39] Thymoquinone can reduce the expression of gluconeogenic enzymes (glucose 6-phosphatase and fructose 1,6-biphosphatase) and the production of hepatic glucose. Furthermore, *N. sativa* prevents gluconeogenesis by activating the protein kinases activated by adenosine monophosphate (AMPK) in liver and muscles.[27]

The hypoglycaemic effect of *N. sativa* can be achieved by various mechanisms including inhibiting glucose absorption from intestine, increasing insulin secretion from the pancreas, inhibiting glucose production from hepatocytes, enhancing glucose uptake into the peripheral tissue

via the glucose transporters or by simulating the action of the new incretin peptide analogs.

The changes in BMI levels remained statistically insignificant in both groups and this is in agreement with most of the previously mentioned studies except that of Najmi et al who reported a decrease in BMI and waist hip ratio.[31]

CONCLUSION

Our study had shown that chewing *Nigella sativa* seeds at a dose of 2g / day for three months caused significant reduction in FBG, 2hr PG, and HbA1c blood levels without significant change in BMI among study group compared to the control group. Because of the small sample size (due to the high costing of the blood investigations), this study therefore represents a marginal degree of significance.

RECOMMENDATIONS

More studies using larger sample size as well as investigating the effect of the raw of *N. sativa* seeds on control of blood glucose in type 1 diabetic patients is highly recommended.

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Barriers to transparency and safety reporting tools facing fourth year nursing students in clinical settings in governmental universities in Khartoum State.

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ABSTRACT

Background Improving the safety of care for patients has been a priority for nurse educators as unsafe and low quality services leads to diminished health outcomes and /or harm. Students' perspectives can provide insight into the role of nursing education in empowering students to provide safe care during their programme and as future practitioners. This study aimed to evaluate nursing students' perception of barriers to transparency and safety reporting tools that is facing fourth year nursing students' in clinical settings.

Methodology This is a descriptive cross-sectional study conducted in Khartoum State in five governmental universities; total coverage sampling method was used; 470 nursing students in the 4th year 2017-2018 were included; data was collected using self administered questionnaire. Statistical Package for Social Sciences was used for analysis.

Results Among 519 nursing students enrolled, a total of 470 students responded. A 5-point Likert scale was used; 391(83.2%) of respondents reported that they did not complete a hospital incident report when an error was made and 401(85.3%) reported that they had never completed nursing school specific error report; 362(77%) replied that they never reported near miss-errors; 270(57.4%) revealed that they never reported errors that made potential harm to the patient, although more than half (283(60.2%) perceived that they were concerned about errors; while 138(29.4%) of respondents revealed that they were sometimes concerned about errors. 152(32.2%) of respondents perceived but that clinical instructors never supported them when errors were committed; on the other hand, 109(23.2%) of respondents reported that clinical instructors sometimes supported them when errors were committed. The authors asked hospital and faculty authorities and found that no tool was available for the nurse students to report errors.

Conclusion The study concluded that barriers exist for the nursing student to report errors and near-miss errors.

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INTRODUCTION

There are five main challenges to incident reporting identified. These included poor processing of incident reporting, inadequate engagement of doctors with insufficient subsequent visible action, scarce institutional support in form of weak incident reporting systems and too little usage of information technology. In order to save our patients from mistakes, transparency, safety reporting tools and strong reporting system must be in place. Moreover, the healthcare earn benefits by learning from mistakes and errors which in turn mitigates the contributing factors and in so doing prevents future errors and ultimately makes patients' care safer.[1]

A cross-sectional study which included 2319 nurses and 386 physicians from three Canadian provinces was conducted in order to identify and understand factors influencing fear of repercussions for reporting and discussing medical errors among nurses and physicians. Nurses' responses showed that fear from managers' or supervisors'

disciplinary actions are limiting career advancement opportunities. Hence, we need a supportive safety leadership to reduce fear of reporting errors for both nurses and physicians which in turn increases transparency.[2]

Another study that explored the problem of low level of reporting and the root causes of medication errors in a nursing home of residents with diabetes showed that there is a lot of medication errors made by nurses due to the lack of transparency related to blame culture and the poor reporting by nursing home i.e. the National Health Service (NHS) staff had placed the residents in danger. [3]

A systematic review done to explore barriers to nurses' reporting of medication errors and near-misses in hospital settings revealed organizational barriers such as culture, the reporting system and management behaviour, in addition to personal and professional barriers such as accountability, fear and characteristics of nurses. The study concluded that to overcome reporting barriers we need to create and adopt a non-blaming, non-punitive and non-fearful learning culture at organizational levels with efficient reporting systems and supportive management behaviour [4]

Movement from a culture of blame and shame to trust "Just Culture" by encouraging, rewards for reporting errors would create an open and fair working environment.[5] Requirements to develop a highly reliable organization include adopting trust and fairness culture, fair treatment to employees when reporting safety incidents and escalating system difficulties.[6] Behaviour of leaders that enables change, encourages open reporting, active questioning and frequent sharing of concerns and/or insights is highly needed.

Non-punitive reporting is defined as the communication of faults, mistakes, errors or weak links without the fear of punishment or legal action to be taken against the individual who caused the error. So we need to adopt a non-punitive reporting system that encourages individuals to report errors and mistakes without having to fear. [1] The perception of students is an influential factor in determining safety in clinical settings. For any educational value in clinical settings, students must follow educationally sound behaviors such as participation, interaction, communication, feedback and transparency that our conscious has urged. However, more transparency in risk reduction processes in health care institutions and organizations is highly desirable.

SUBJECTS AND METHODS

This is cross-sectional study conducted in the faculties of nursing sciences of five governmental universities, namely Alzaiem Alazhari, Bahry, Al-Néelain, Khartoum and Omdurman Islamic University. Table1 shows the number of nurses enrolled from each university.

Table 1. The number of nurses enrolled from different universities

University	Number of students (in 4th year) from nursing faculties
University of Alzaiem Alazhari.	94
University of Bahry.	168
University of Al-Néelain.	118
University of Khartoum.	107
Omdurman Islamic University	142
Total	629

The sample was inclusive for all the 4th years students (2017-2018, n=519). Forth year students were selected because they were semi-graduate and they had rotated in most departments of clinical practice. They had seen in-patients, attended out-patient clinics, community, mental health sites and kindergartens.

Data were collected using a pre-tested self administered survey.[8] The students based their responses on their clinical experience. Safety reporting tools using a 5-point Likert scale was adopted. The data were analyzed using the Statistical Package for Social Sciences (SPSS); P value <0.05 is considered significant.

Ethical approval was obtained through the deans of the five faculties of nursing sciences. Recruitment was voluntary; the study objectives were explained to each participant and written consents were obtained.

RESULTS

In this descriptive survey a total of 519 of nursing students were enrolled from the five governmental universities. Completed questionnaires were received from 470 respondents with a response rate of 90.5%. The majority of the remainder students submitted incomplete questionnaires but there were also few refusals.

Using a 5-point Likert safety reporting tools scale, 391(83.2%) respondents reported that they did not complete a hospital incident report when an error was made and 401(85.3%) reported that they never completed nursing school specific error report; 362(77%) replied that they had never reported near-miss errors; also 270(57.4%) revealed that they never reported errors that they witnessed/made. The authors asked hospital and faculty authorities and found that no tool was available for the nurse students to report potential harm to patients. More than half (n=283, 60.2%) participants perceived that they were concerned about errors while 138(29.4%) of respondents reported that they were sometimes concerned about errors; in addition 152(32.2%) of respondents perceived that clinical instructors never supported them when errors were committed. On the other hand 109(23.2%) of respondents reported that clinical instructors sometimes supported them when errors were committed (Table 2**).**

Table 2. Nurses' perception regarding safety reporting tools (n=470).

Safety	Never n (%)	Rarely n (%)	Sometimes n (%)	Most of the time. n (%)	Always n (%)	Mean	SD
Did your clinical instructor discuss patient safety including the use of reporting tools?	232 (49.4)	69 (14.7)	57 (12.1)	45 (9.6)	67 (14.3)	2.246	1.491
When an error is made, a hospital incident report is completed?	391 (83.2)	36 (7.7)	22 (4.7)	11 (2.3)	10 (2.1)	1.32	0.84
When an error is made, a nursing school specific error report is Completed?	401 (85.3)	27 (5.7)	20 (4.3)	22 (4.7)	0 (0)	1.28	0.75
Near miss events are reported.	362 (77)	46 (9.8)	31 (6.6)	19 (4)	12 (2.6)	1.45	0.96
How often do you report error that made potential harm to the patient?	270 (57.4)	51 (10.9)	49 (10.4)	43 (9.1)	57 (12.1)	2.07	1.46
Students are concerned about errors.	50 (10.9)	29 (6.2)	34 (7.2)	74 (15.7)	283 (60.2)	4.08	1.36
Nurses are concerned about errors.	130 (27.7)	72 (15.3)	138 (29.4)	81 (17.2)	48 (10.2)	2.73	1.92
Clinical instructors support students when errors are committed.	152 (32.2)	83 (17.7)	109 (23.2)	68 (14.5)	58 (12.3)	2.56	1.38

SD: Standard deviation

Among the 470 respondents, majority (n=283, 60.2%) of them stressed that they were concerned about errors but they did not complete a hospital incident report when an error was made while a minority (n=138, 29.4%) reported that they were sometimes concerned about errors.

DISCUSSION

Nurses must protect the client when safety is affected and should always seek to promote patient safety. In addition, ethical practice requires that nurses should report and document an incident report in order to save the client. However, patient's safety needs to be approached from a system perspective rather than from an individual perspective which means to move from a culture of blame and shame and not to punish the nurses to the culture of safety and trust. [7]

Fourth year nursing student's education is expected to provide a high quality education, with the objective of ensuring that the nurse must be able to provide safe patient care. ⁻Barriers for reporting errors and near-miss events for nursing students identified by this study included unavailability of reporting tools or incidents report specific for the nursing students. Clinical instructor and clinical nurse never discuss the use of error reporting tools. The clinical nurses were not free to speak out if they saw something that may negatively affect the patient due to fear of punishment or fear of being awarded low grade. This finding is comparable with a study done in San Francisco, which demonstrated that barriers of reporting errors were fear of failing, blame, embarrassment, and guilt. In addition, another issue that affected the student was the occasional pressure of not reporting errors from the clinical nurse, thus nursing student had conflicting messages: one from the clinical nurse not to report errors and one from the clinical instructor to report errors. These conflicting messages from two people in power serve to confuse the nursing student. [8] This finding is supported by studies which stressed that the goal of a reporting system is to identify and remove the root causes of fear, increase student's knowledge about threats to safety in the clinical settings and may guide educators to promote the development of safe service practitioners while preserving patient safety.[9]

Furthermore, under reporting of incidents leads to adverse events and small database with insufficient data for analysis while adopting culture of trust and safety encourages reporting and offers large database for analysis. The reporters are not at the risk of blame, shame or legal litigation which positively influences the staff willingness to report these incidents without any fear; the reporters may even be rewarded because of their efforts for doing no harm. [9]

It is expected that the results of this study would guide and help nurses' leaders, educators and policy makers in clinical settings and faculties of nursing to create a blame-free, safe environment for our nursing students that encourages transparency. We do need supportive nursing leaders to open communication between nursing students, faculties, nursing staff including clinical instructors and clinical (hospital) nurses to transmit transparency and safety issues that must be introduced as early as the beginning of students' educational training and then continued through to the end.

CONCLUSIONS

This study revealed that barriers exist for the nursing student to report errors and near-miss errors. There is a need for creating a reporting system which is one example of increasing transparency and safety in faculties of nursing and health professions. In addition to adopting a policy for reporting and follow-up of students' errors and near-misses. This necessitates development of reporting tools and implementation of educational programs that improves the competencies of supervisors of nursing students ⁻

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Case Report

Scrotal cystocele in a sliding left inguino-scrotal hernia: A case report and review of literature

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ABSTRACT

Scrotal cystocele is a rare condition defined as massive inguino-scrotal herniation of the bladder; it may involve herniation of small part or diverticulum of bladder into scrotum. A 70-year-old male was admitted from the outpatient clinic complaining of left scrotal pain for seven hours duration. The pain was of acute onset, localized to lower abdomen, and aggravated by walking. On examination the patient looked unwell but vitally stable. There was a large tender ingiuno-scrotal hernia involving the left scrotum; the left testis was impalpable and the abdomen was soft. The diagnoses of obstructed inguino-scrotal hernia was made and intra-operatively a large indirect inguino-scrotal hernia was identified; hernial sac was opened containing segment of small bowel which became viable after decompression and hot path. On trying to remove the sac, there was a hollow organ that leaked fluid. By inserting a finger, the prostate was identified and a urinary bladder was verified using a Foley catheter. Urinary bladder and hernia were repaired and the patient was discharged in good condition. This was a rare case of left indirect cystocele. In the absence of diagnostic imaging, insertion of a Foley catheter pre-operatively is highly recommended.

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INTRODUCTION

Sliding inguinal hernia is defined as protrusion of retroperitoneal organ through the inguinal canal with or without peritoneal sac. It accounts for 1-4% of all inguinal hernias. It can involve the urinary bladder, caecum, sigmoid colon, appendix, ureter, ovaries and fallopian tube as common sliding organs. Sliding hernia has three types: Type 1, which is protrusion of a retroperitoneal organ by forming part of the sac's wall and this is the commonest type. Type 2 when the meso-appendix and sigmoid mesentery form part of the sac's wall; and type 3 when the retroperitoneal organ herniates without a sac and this is the rare type. Sliding hernia can be misdiagnosed because it is a rare condition. It can also be associated with iatrogenic bladder injury.[1] Globally, it affects 3-8% of the population. It represents 80-83% of all hernias (50% indirect inguinal, 25% direct inguinal and 5% femoral); 75%-85% of cases are males.[2,3] Sliding inguinal hernias account for 1-4% of all inguinal cases; it is usually associated with obese, 50 to 70 years old males. Most of inguinal bladder herniation are direct and occur at the right side.[4]. It is one of the commonest diseases that face the general surgeon. It's usually associated with men and account for 70-78% of all abdominal wall hernias and 96% of all groin hernias while femoral hernia accounts for 4%.[5,6].

Scrotal cystocele is a rare condition defined as massive inguino-scrotal herniation of the bladder; it may involve herniation of small part or diverticulum of the bladder into the scrotum. Sometimes it can involve herniation of the urinary bladder into the inguinal, femoral and obturator canals, and perineum. It is first described by Levine

in 1951. It occurs in 3-8% of the population and 1-3% of all inguinal hernias while a large scrotal cystocele accounts for less than 1% of cases, and is diagnosed preoperatively in less than 7% of cases. It is usually associated with men above 50 years of age; the incidence can increase reaching 10% in association with obese men older than 50 years. Inguinal herniation of the bladder is classified into 3 types according to their relation to the peritoneum: a) para-peritoneal hernias where bladder remains extra-peritoneal and is medial to the peritoneal herniation, b) intra-peritoneal hernia where bladder is covered completely with peritoneum in the hernial sac and c) extra-peritoneal hernias where the bladder herniates without peritoneum.[2,3,7-13]

It is also reported that inguinal herniation of the bladder occurs in 1-5% or 1-4% of all inguinal hernias. It can result from increased intra-vesical pressure for a long period that can lead to secondary bladder diverticulum and hernia.[6,12,14,15] Association of bladder stone with inguinal herniation of the bladder is a very rare condition.[6] Inguinal herniation of the bladder is a very rare condition which can present with recurrent episodes of urinary tract infection (UTI).[16,17] It is usually associated with obese males, aged over 50 years and occurs in right-sided hernias. Approximately 120 cases have been reported until 2018.[18,19] Many causes can lead to herniation of the bladder including: urinary tract obstruction; in males the commonest cause for bladder outlet obstruction is benign prostatic hyperplasia, chronic bladder distension, loss of bladder tone, peritonitis, protrusion of peri-vesical fat, obesity, pelvic mass, and previous hernia operation.[2,9,14]. The risk factors of inguinal herniation of the bladder include obesity, male gender particularly between 50-70 years of age and its frequency increase to about 10% if body mass index is >30 Kg/m^2, previous pelvic injuries and previous abdominal wall surgery.[6,13] Patients are always asymptomatic but can present with features of urinary tract obstruction in rare cases. They can present with inguinal or scrotal swelling, flank pain, dysuria**,** haematuria**,** infection, calculi, hydronephrosis, vesicoureteral reflux and acute renal failure. Also, they can present with voiding symptoms such as painful voiding or double stroke voiding or manipulated voiding. Emptying of a scrotal cystocele with voiding is an important diagnostic feature in a patient with incarcerated bladder diverticula but it is usually diagnosed during surgery or as a result of intra-operative bladder injury[2-4,8,9,11,13,18]. Scrotal cystocele is usually asymptomatic but pressure on the groin to innate micturition is the most diagnostic symptoms.[7,19] One of the differential diagnoses of the scrotal cystocele is bone metastasis[7] Scrotal cystocele can result in life- threatening complications such as: infarction and perforation of the bladder, obstructive uropathy with consecutive renal failure, epididymitis, UTI and malignancy.[9,18] The diagnosis is usually made during surgery, but early diagnosis through history and radiological imaging can help to reduce the risk of complications during the surgery. Diagnosis is usually made by Ultrasonography, voiding cysto-urethrography, and magnetic resonance imaging.[2-4,7,9,11,12,15,17,20] Most of the cases are usually diagnosed intra-operatively but less than 7% are diagnosed pre-operatively.[18] Surgical repair is the only treatment of choice.[6,13,18,19]

Case report:

A 70-year-old male, not known to be hypertensive or diabetic was admitted to Outpatient Clinic at Elhassaheisa Teaching Hospital, Gezira State, Sudan in April 2020 complaining of left scrotal pain for seven hours duration. The pain was severe, of acute onset, localized to the lower abdomen, colicky in nature, aggravated by walking and relived by rest. He had normal bowel habits with malena. The left inguino-scrotal swelling started one month previously and increased in size gradually, associated with small amount of urine, increased frequency, urgency, nocturia and weak urine stream. He had history of appendicectomy 36 years previously. On examination, the patient looked unwell, febrile, not pale, vitally stable and fully conscious. The ingiuno-scrotal hernia was large, involving the left scrotum, tender and the left testis was impalpable; the abdomen was soft. Laboratory findings were as follow: Hb: 11.9 g/l,

leukocytes: 8.5 ×10*3µl, urine showed 12-14 pus cell/HPF, blood Urea 45mmol/l, serum creatinine 1.1mmol/l, random blood glucose; 100mg/l, viral screening (for HIV, HBV, and HCV) was negative. The patient was diagnosed as obstructed inguino-scrotal hernia. Due to unavailability of sonography in our hospital and the urgency of the situation; we proceeded to operation under spinal anesthesia.

Operative findings, tips and tricks in management: Through a left inguinal incision, a large indirect inguino-scrotal hernia was identified; hernial sac when opened was found to contain a segment of small bowel which became viable after decompression and hot path, then returned to intra abdominal cavity. Through long dissection to remove the sac by cutting it, a fluid came out and a hollow organ was identified in the sac, from which fluid leaked out. By inserting a finger, the prostate was identified. In order to verify that this is a urinary bladder a Foley catheter was inserted through the penile urethra which appeared in the injured urinary bladder (Figures 1 and 2). Urinary bladder was repaired in double layer and the hernia was also repaired through darns method. The patient received antibiotics and discharged in a good condition. Follow up for 15 days revealed no recurrence of hernia or any other complication.

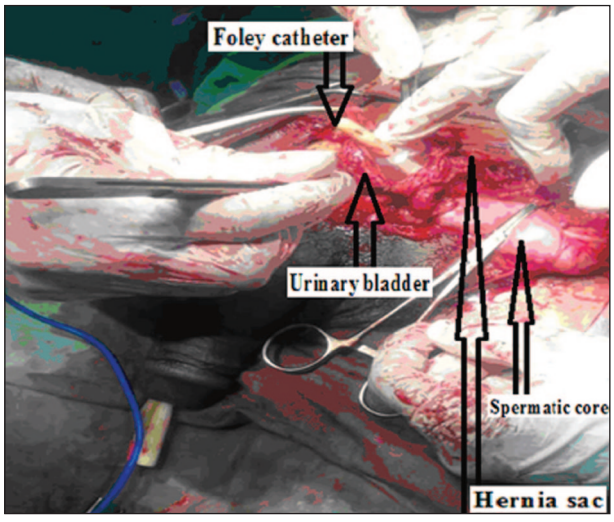

Figure 1. Injured urinary bladder in a case of left inguino-scrotal swelling

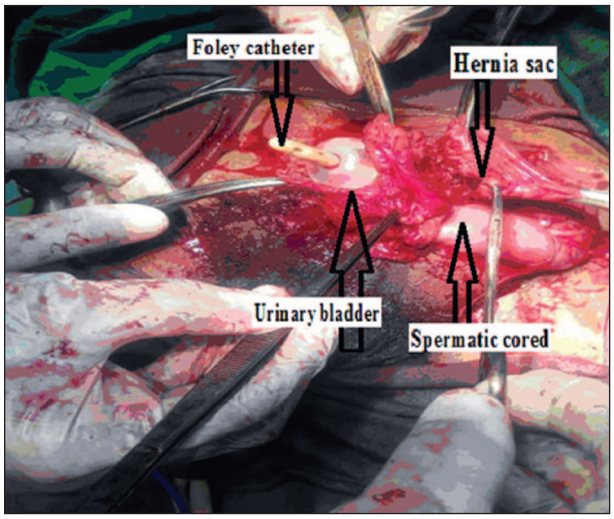

Figure 2. A Foley catheter inserted through the penile urethra which appeared in the injured urinary bladder in a case of left inguino-scrotal swelling

DISCUSSION AND CONCLUSION

We report a case of a 70-year-old male with extraperitoneal hernia where the bladder herniated without peritoneum. This is consistent with many international findings[2,3,7-13]. The associated risk factors were male gender, age of 70 years and previous abdominal wall surgery. This is similar to two other studies world wide.[6,13] This case was diagnosed and treated intra-operatively as in other studies.[2-4,7,9,11,12,15,17,20,]

Unlike most of inguinal urinary bladder herniation which are direct and occur on the right side,[4] this case was indirect and occurred on the left side. In the absence of ultrasonography, voiding cysto-urethrography, and magnetic resonance imaging, as the situation in our rural hospital, we recommend that in such similar situations it is better to introduce Foley catheter pre-operatively so as not to damage the urinary bladder.

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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.

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