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3. Offer opportunities for the publication of service-oriented research and disseminate information aimed at the promotion of health services.

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

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# ORIGINAL ARTICLE

# Effectiveness of educational program on intermittent catheterization compliance among non-compliant mothers of spina bifida children at Cheshire Home, Khartoum State, Sudan

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## ABSTRACT

**Background** Children with spina bifida face many medical problems that challenge surgeons and paediatricians. One of these problems is neurogenic bladder which may lead to renal damage. The management of this problem depends on clean intermittent catheterization, that needs effective compliance. The objective of this study was assess the effectiveness of an educational program on adherence to compliance among non-compliant mothers of spina bifida children.

**Methods** Quasi-experimental study design was conducted, which involved one group pre and post intervention. 36 mothers of spina bifida children who weren't compliant with clean intermittent catheterization were randomly selected. The educational program included: (1) pre intervention questionnaire on knowledge, compliance, satisfaction, and attitude, (2) an educational program on clean intermittent catheterization, (3) follow up every month for the first three months with voiding diary and (4) a second post intervention questionnaires at six months. -

**Results** The knowledge, practice, compliance and satisfaction changed significantly from pre to post intervention at P value < 0.05. There was no change in attitude

**Conclusion** The Education program showed effectiveness of adherence. It is recommended to increase the number of trained nurses on clean intermittent catheterization; this will lessen the burden of travel of mothers and their children and therefore improve compliance

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## INTRODUCTION

Spina bifida is a congenital neural tube defect which occurs either separately or in conjunction with hydrocephalus[1]. It develops in the early stage of pregnancy when one or more vertebrae fail to close normally. There are many types of spina bifida (SB) including spina bifida occulta, meningocoele (MC) and meningomyelocoele (MMC)). Worldwide, the incidence of neural tube defects ranges from1.0 to 10.0 per 1000 births with almost equal frequencies between anencephaly and spina bifida[2]. In the United States, 1500 children are born with spina bifida every year[3]. In Africa, little is known about the incidence of MMC and neural tube defects. The incidence of SB and NTD in Nigeria and south Africa is 4.6/1000 births, while the incidence in Cameron was 1.99/1000 births[4]. In Sudan, the incidence of neural tube defect in Omdurman Maternity Hospital was 3.48/1000 births while another study reported the frequency in newborns admitted to neonatal intensive care units in Soba University Hospital and Omdurman Maternity Hospital was 2.8/1000 births[5,6].

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Children with spina bifida face many medical problems that challenge surgeons and paediatricians. The severity of the problems depends on the site of defect; one of these problems is neurogenic bladder and bowel dysfunction that occurs due to damage of the nerves that control bowel and bladder with subsequent incontinence of stool and urine. This affects the quality of life and 75% of them regard urinary incontinence as a stress factor[7]. Moreover, in children with spina bifida, renal failure maybe a long-term complication and it remains a major cause of death before adulthood due to damage of the kidney as a result of back flow of urine i.e. vesico-ureteric reflux, (VUR)[8]. At the same time, stasis of urine in the bladder may lead to frequent urinary tract infections. Furthermore, constant exposure of skin in the perineal area to stools and urine could cause skin excoriation.

All these problems and others can affect the general condition of the patient, leading to frequent hospitalization, which may be burdensome to the family and hospital. In addition, urine and stool incontinence may prevent child from entering kindergarten and subsequent school, and make the child completely dependent on parents for care.

Clean intermittent catheterization is defined by International Continence Society as the use of clean technique to drain the bladder with subsequent removal of catheter[9,10]. It could be done by patients, caregivers or parents. It is proved that clean intermittent catheterization (CIC) provides continence and improves child quality of life in patients with spina bifida. CIC was first introduced by Lapides et al in 1972 who found that this technique is safe and effective in managing patients with neuropathic or atonic bladder if performed properly on regular intervals[9]. Kaplan and Ellen et al reported that through CIC and medications, 85% of patients were able to stay dry for three to four hours[11].

Clean intermittent catheterization needs compliance and adherence to prevent urinary tract deterioration. World Health Organization (WHO) defines adherence as the extent of which person's behaviors corresponds with agreed recommendations from health care profession[12]. Compliance of patients with chronic diseases is very important for the success of management. Therefore, those who do not adhere or adhere partially develop major medical problems. Pohl et al reported that the frequency of early dropout from CIC among children and adolescents was 20%; therefore, good support, professional instruction on catheterization technique and periodic follow-up are necessary to maintain patient compliance[13].

Few studies explored the factors of non-adherence to CIC. Jai H Seth et al mentioned that the barriers to successful CIC are internal factors which consist of patient-related factors that included the physical factor (practical), and the psychological factor (psychosocial and cultural aspects) which restricted its use. External factors such as the quality of teaching, supervision, follow-up and catheter availability in the community were also involved[8]. A study carried out in Saudi Arabia showed that the success rate of CIC among paediatric patients with neurogenic bladder resulting from MMC ranges from 94% to 100% and that Saudi patients have good acceptance and compliance with CIC procedure; the researcher suggested that for complete success or the maintenance, proper education, teaching and follow-up should be conducted[14].

Moreover SI Afsar et al evaluated the compliance with bladder emptying method at a long-term period among spinal cord injured patients and found that education of patients about catheterization technique and periodic follow-up are necessary to maintain patient compliance[15]reasons for discontinuation and the history of treated UTIs. Results:The most common bladder management method at discharge from inpatient rehabilitation center was clean intermittent catheterization (CIC. The objective of this study was to assess mothers' knowledge, attitude, practice, satisfaction and compliance regarding CIC in a pre- and post-educational program and to identify the relationship between compliance and some factors affecting compliance

## MATERIAL AND METHODS

This study was quasi experimental conducted in Khartoum Cheshire Home; 36 mothers of spina bifida children who were not complying to Clean Intermittent Catheterization were randomly selected; 24 mothers responded to be enrolled and informed verbal consent was obtained from them. The program was composed of four stages. Stage 1 was a pre intervention questionnaire that included assessment of mother's knowledge, attitude, practice and compliance. Stage 2 was an educational program of mothers which was composed of: (a) Theoretical education about clean intermittent catheterization and (b) Hands on practice of clean intermittent catheterization. Stage 3 was follow up for three months with urinary diary. Stage 4 was post intervention questionnaires after 6 months to document post-program assessment of mother's knowledge, attitude, practice and compliance. The data were analyzed using the Statistical Package for Social Sciences (SPSS- ver 20) and P-value of <0.05 was considered significant.

## RESULTS

A total of 36 non-compliant mothers of spina bifida children were approached, 24 mothers responded (response rate of 66%). Children aged between 7-12 years were 54.2% while those whose ages were more than 12 years were 37.5% as shown in Table 1. The majority of participants (79%) lived inside Khartoum. Most of the mothers (85%) were housewives, while (20%) were civil servants; 95.8% of them were married; and 75% of them has studied in schools for 9 -16 years (Table 2).

**Table 1.** Age groups of children of the study group

| Child age group (years) | N | Percent |
|---|---|---|
| Less than 7 | 2 | 8.3 |
| 7 to 12 | 13 | 54.2 |
| More than 12 | 9 | 37.5 |
| Total | 24 | 100.0 |

**Table 2.** Education level of mothers of children of the study group

| Number of school years | N | Percent |
|---|---|---|
| None | 1 | 4.2 |
| 0-8 | 4 | 16.7 |
| 9-12 | 9 | 37.5 |
| 13-16 | 9 | 37.5 |
| >16 | 1 | 4.2 |
| Total | 24 | 100.1 |

In 54.2% of cases the spina bifida were MC, while MMC comprised 41.7% and 4.2% had spina bifida occulta. The site of spina bifida in 50% of cases was lumbo-sacral, in 41.7% it was sacral and in 8.3 % it was lumber as shown in Figure 1.



**Figure 1.** Site of spina bifida
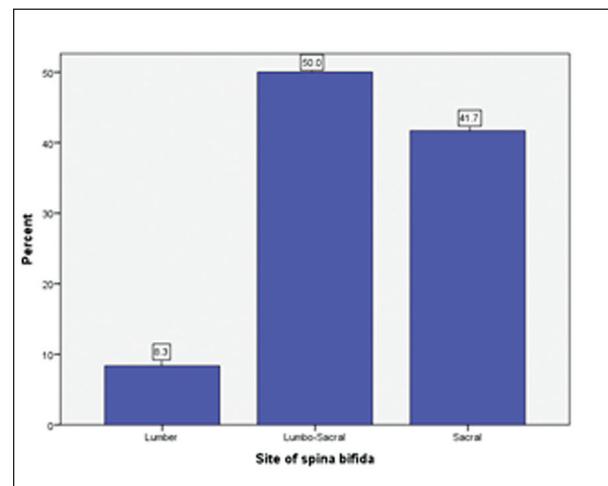
Most children (58.3%) had lower limb paralysis. while 41.7% had no lower limb problem. The majority (54.2%) were on interrupted CIC while 29.2% of them had started and stopped; 16.7% were not on CIC as shown in Figure 2. Most of teaching aid used (75%) was taught through verbal and demonstration while in 16.7% and 8.3% it was verbal and by demonstration, respectively as shown in Figure 3.

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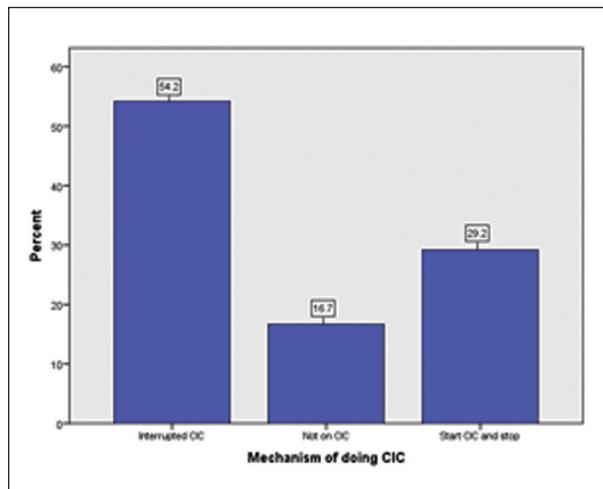
**Figure 2.** Mechanism of doing Clean Intermittent Catheterization (CIC) in children of the study group
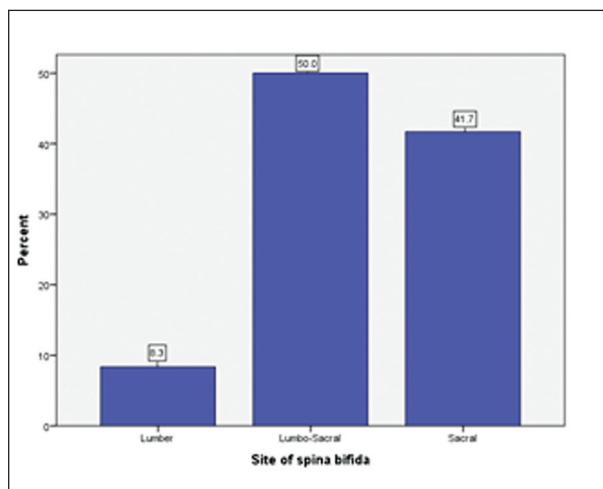


**Figure 3.** Teaching aids used for Clean Intermittent Catheterization (CIC)

Regarding the association between knowledge, attitude, practice, and satisfaction of participants pre and post the program, the P - value is significant for knowledge, practice and satisfaction but insignificant for attitude as shown in Table 3. Also according to the voiding diary, the association of compliance at three-month follow-up and at post program, was again significant (Table 4). There was no correlation between education level of mothers with KAP, satisfaction, and attitude as shown in Table 5. There was no significant association between lower limb problem (walking or paralysis), age of the child, number of children and education of mother with compliance as shown in Table 6.

**Table 3.** Association between knowledge, attitude, practice, satisfaction and quality of life parameters pre and post the program.

| Parameters | Teaching parameters | N | Mean | Standard. Deviation | P value |
|---|---|---|---|---|---|
| Knowledge | Pre | 24 | 16.63 | 7.505 | 0.000 |
| | Post | 24 | 29.29 | 4.389 | |
| Attitude | Pre | 24 | 8 | 0.978 | 0.224 |
| | Post | 24 | 8.29 | 0.624 | |
| Practice | Pre | 24 | 5.88 | 2.675 | 0.000 |
| | Post | 24 | 13.71 | 2.71 | |
| Satisfaction | Pre | 24 | 5.38 | 1.555 | 0.002 |
| | Post | 24 | 6.67 | 1.09 | |

**Table 4.** Association of compliance with time (at three-month follow-up and post program) according to voiding diary

|  | Compliance |  |  | P value |
| --- | --- | --- | --- | --- |
| Time | Non-Compliant | Compliant | Total |  |
| Pre test | 24 | 0 | 24 | Not valid |
| Post test | 5 | 19 | 24 | 0.000 |
| follow up | 6 | 18 | 24 | 0.000 |
| Total | 35 | 37 | 72 |  |

**Table 5.** Correlation between education level of mothers with knowledge, practice, satisfaction, and quality of life parameters.

| Parameter finding |  | Number of school years of mother |
| --- | --- | --- |
| Knowledge | Correlation Coefficient | 0.306 |
|  | Sig. (2-tailed) | 0.146 |
|  | N | 24 |
| ttitude | Correlation Coefficient | 0.188 |
|  | Sig. (2-tailed) | 0.379 |
|  | N | 24 |
| Practice | Correlation Coefficient | 0.207 |
|  | Sig. (2-tailed) | 0.331 |
|  | N | 24 |
| Satisfaction | Correlation Coefficient | -0.198 |
|  | Sig. (2-tailed) | 0.355 |
|  | N | 24 |

Sig= significance.

**Table 6.** Association between compliance with lower limb problems, child age group, number of children and mothers number of school years **.**

|  |  | Compliant |  |  | P value |
| --- | --- | --- | --- | --- | --- |
|  |  | Non-Compliant | Compliant | Total |  |
| Lower limb problems | Paralysis | 2 | 12 | 14 | 0.332 |
|  | Movement | 3 | 7 | 10 |  |
|  | Total | 5 | 19 | 24 |  |
| Child Age group | Less than 7 years | 0 | 2 | 2 | 0.214 |
|  | 7 to 12 years | 2 | 11 | 13 |  |
|  | More than 12 years | 3 | 6 | 9 |  |

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| | | | | | |
|---|---|---|---|---|---|
| | Total | 5 | 19 | 24 | |
| Number of children | 1 to 3 | 1 | 5 | 6 | 0.10 |
| | 4 to 6 | 3 | 9 | 12 | |
| | 7 to 9 | 1 | 5 | 6 | |
| | Total | 5 | 19 | 24 | |
| Mother number of School years | | 0 | 1 | 1 | 0.291 |
| | 1 to 8 years | 0 | 4 | 4 | |
| | 9 to 12 years | 2 | 7 | 9 | |
| | 13 to 16 years | 3 | 6 | 9 | |
| | More than 16 years | 0 | 1 | 1 | |
| | Total | 5 | 19 | 24 | |

## DISCUSSION

Children with spina bifida face many problems; one of these problems is failure of emptying the bladder which was managed through CIC. For CIC to be effective, it needs adherence. The aim of this study was to assess the effectiveness of the education program on adherence of mother's compliance. In this study the majority of patients were aged from 7 to 12 years; it is the same with previous studies reviewed in which the ages of children were above 15 years in one study and from 7 to 12 years in another[16,17]. The majority of the children started CIC early in their life - from 1 to 3 years. Despite teaching the majority of mothers (75%) CIC verbally and through demonstration, the majority of them performed CIC but not at regular intervals, while others did not perform CIC at all. In our study, the barriers of irregular performance of CIC or not performing CIC were ignorance about the frequency in the majority. Other barriers included child going to school, mothers believing that the catheter causes UTI, some doctors advising their patients to perform CIC in three times interval /day, busy mothers, child refusing CIC, fear, pain and urethral stricture. One of these barriers is the same in the study reviewed that found CIC was done in non-school hours and preferred diapers during school hours[17]. Another study addressed these barriers is lack of access to the public toilet (inadequate shelves or countertops

for placing supplies in preparation of CIC), difficult position to insert the catheter, lack of proper training, lack of community support and structural pathway trouble shooting in case of problems[9]. A further study showed that discontinuation of CIC tends to be personal variables (pain, resistant behavior of the child, difficulty in organizing the daily routine, UTI and lack of motivation) rather than demographic and medical characteristics, and significant predictors for non-used CIC were temporary discontinuation of the procedure, daily frequency of CIC and technical difficulties[18]. In this study knowledge, attitude, and practice on CIC pre and post the education program as factors affecting compliance, the mean knowledge changed from to 16.6 to 29.2 (P value = 0.000) while the mean practice changed from 5.8 to 13.7 (P value = 0.000). The attitude did not show any significant difference in pre and post program.

In the literature, there are very few studies addressing the effect of CIC education on compliance. Faure et al in Paediatric Rehabilitation Center reported long-term teaching experience of self-catheterization in boys. They evaluated the study group before CIC (with creatinine assay, VCUG, and urinary tract ultrasonography), then the urology nurse provided therapeutic education and practical instruction

in CIC. The study showed that CIC could be successfully started and continued in older children rather than in younger boys. Compliance of CIC correlated significantly with urinary continence outcome in those with sufficient bladder capacity and the long-term adherence (9.9 years) was 80%; they claimed that their high adherence rate was due to constant involvement of an experienced nurse[19]. In our study the association of compliance in a three-month follow-up and post education is significant (P Value = 0.000), Similarly, Faure et al reported that contacting the patient and requesting him//her to visit the clinic at a regular interval were very important in increasing adherence[16].

## CONCLUSIONS

This study, despite the small sample size of the participants, showed that the education program had made significant effect on knowledge, practice, satisfaction and compliance of the mothers of spina bifida children while the attitude of the mothers did not change

## RECOMMENDATIONS

- Sudan is a large country with different states and there is only one center for CIC in the capital of Sudan, which is difficult for patients to access and this leads to preventing patients from follow up.

- It is important to increase the number of trained nurses on CIC and employ them in hospitals in different states of Sudan to lower the burden of mothers to travel with their children and therefore improve compliance

- Providing continuous emotional and psychological support with education would help the patient to accept CIC.

- Schools should be designed to accept disabled children and should be provided with the facilities needed for CIC

- Urodynamic facilities need to be strengthened

## REFERENCES

1. Emmanuel A Ameh, Stephen W Bickler, Kokila Lakhoo, Benedict C Nwomeh DP. Paeds Surgery Part 1. 1st ed. Ameh E A, Biickler S W, Lakhoo K, Nwomeh B C P, editors. Paediatric Surgery: A Comprehensive Textbook Volume 2. Seatle WA, USA: Global HELP Organization; 2011:p385–388.

2. Liptak GS, El Samra A. Optimizing health care for children with spina bifida. *Dev Disabil Res Rev* 2010;16(1):66–75.

3. National Institute Of Neurological Disorders And Stroke. Spina Bifida Fact Sheet, National Institute of Neurological Disorders and Stroke [Internet]. 13-309. 2013. Available from: https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Spina-Bifida-Fact-Sheet

4. Rabiu TB, Adeleye AO. Prevention of myelomeningocele: African perspectives. *Child's Nerv Syst* 2013;29(9):1533–40.

5. Eltahir A Elsheikh G, Ibrahim SA. Neural tube defects in Omdurman Maternity Hospital, Sudan. *Khartoum Med J* 2009;2(2):185-190

6. Omer IM, Abdullah OM, Mohammed IN, Abbasher LA. Research: Prevalence of neural tube defects Khartoum, Sudan, August 2014-July 2015. *BMC Res Notes* 2016;9(1):1–4

7. Ambartsumyan L, Rodriguez L. Bowel management in children with spina bifida. *J Pediatr Rehabil Med* 2018;11(4):293–301.

8. Dik P, Klijn AJ, van Gool JD, de Jong-de Vos van Steenwijk CCE, de Jong TPVM. Early Start to Therapy Preserves Kidney Function in Spina Bifida Patients. *Eur Urol* 2006;49(5):908–13.

9. Seth JH, Haslam C, Panicker JN. Ensuring patient adherence to clean intermittent self-catheterization. *Patient Prefer Adherence* 2014;8:191–8.

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1966

10. Oakeshott P, Hunt GM. Intermittent self catheterization for patients with urinary incontinence or difficulty emptying the bladder. *Br J Gen Pract* 1992;42(359):253–5.

11. Segal ES, Deatrick JA, Hagelgans NA. The determinants of successful self-catheterization programs in children with myelomeningoceles. *J Pediatr Nurs* 1995;10(2):82–8.

12. Girotti ME, MacCornick S, Perissé H, Batezini NS, Almeida FG. Determining the variables associated to clean intermittent selfcatheterization adherence rate: One-year follow-up study. *Int Braz J Urol* 2011;37(6):766–72.

13. Newman DK, Willson MM. Review of intermittent catheterization and current best practices. *Urol Nurs* 2011;31(1):12–28.

14. Neel KF, Salem MA, Soliman SM, Al-Hazmi H, Gomha AB, Khatab AA. Acceptance and compliance of clean intermittent catherization among Saudi patients. *Saudi Med J* 2008;29(7):1014–7.

15. Afsar SI, Yemisci OU, Cosar SNS, Cetin N. Compliance with clean intermittent catheterization in spinal cord injury patients: A long-term follow-up study. *Spinal Cord* [Internet] 2013;51(8):645–9. Available from: http://dx.doi.org/10.1038/sc.2013.46

16. Lee SR, Lee IS, Oh SJ, Kim SH, Chin YR. Adherence to the clean intermittent catheterization following a customized intensive education program for patients with emptying failure. *J Korean Acad Community Heal Nurs* 2018;29(4):467–75.

17. Mathew G. Study to assess compliance and selected factors affecting compliance to clean intermittent catheterization (CIC) in childern with spina bifida [Internet]. RGUHS; 2006. Available from: http://hdl.handle.net/123456789/3211%0D%0A

18. Faleiros F, Pelosi G, Warschausky S, Tate D, Käppler C, Thomas E. Factors influencing the use of intermittent bladder catheterization by individuals with spina Bifida in Brazil and Germany. *Rehabil Nurs* 2018;43(1):46–51.

19. Faure A, Peycelon M, Lallemant P, Audry G, Forin V. Pros and cons of transurethral self-catheterization in boys: A long-term teaching experience in a paediatric rehabilitation centre. *Urol J* 2016;13(2):2622–8.

# Female student's knowledge attitude and practice towards breast cancer: Risk factors and clinical examination in University of Medical Sciences and Technology, Khartoum, Sudan 2022.

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## ABSTRACT

**Background** Breast cancer is a worldwide disease resulting in many deaths. African women including Sudanese are more likely than women in the developed world to be diagnosed at later stages of the disease, with consequent drastic reduction of survival rates. This study intended to assess female student's knowledge attitude and practice towards breast cancer risk factors and clinical examination.

**Methodology** A descriptive cross-sectional study was conducted on female students at University of Medical Sciences and Technology. A convenient sampling technique using self-administered questionnaire to collect information on knowledge, attitude, and practice was adopted. The data were analysed using statistical package for social sciences; chi-square and goodness of fitness significant tests were used for analysis of categorical variables. The total scores were categorized into good, fair and poor (bad). 70% cut-off point out of the total expected score for each was taken as good. P-value of <0.05 was considered statistically significant.

**Results** This study involved 306 female students; the mean knowledge score was good (71.8%) with the fourth and third year's students having the maximum mean score. The overall attitude score was good (70%) while the practice score was poor (41%). There was a significant correlation between age (p< 0.000), academic level (p< 0.000) and knowledge; hence age (p< 0.002) and marital status (p< 0.012) are significantly related to practice.

**Conclusion** The study threw a spotlight on the need for establishing educational programs to raise awareness regarding regular breast cancer screening behavior.

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## INTRODUCTION

Breast cancer is one of the most common diseases affecting women worldwide with most cases occurring in the developed countries, where age-standardized rates are three times higher than in developing countries. In 2018, 18.1 million people around the world had cancer and 9.6 million died from the disease. By 2040, those figures will nearly double, with the greatest increase in low- and middle-income countries (L/MIC), where more than two thirds of the world's cancers will occur. Cancer is the cause of about 30% of all premature deaths from non-communicable diseases (NCDs) among adults aged 30-69 years. The most

frequently diagnosed cancer is lung cancer (11.6%), followed by female breast (11.6%) and colorectal cancers (10.2%). It is also reported by the World Health Organization (WHO) as one of the leading causes of death. Approximately one million cases of breast cancer are diagnosed every year[1]; it is also the leading cause of death due to cancer in women between the ages of 15 and 54 years. Every thirteen minutes a woman dies from breast cancer, and every three minutes a new case of breast cancer is diagnosed[2].

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Cancer in Sudan is a relatively unknown health problem with most public health efforts directed toward tropical and infectious diseases but cancer incidence has been growing at an average annual rate of 0.061 over the previous five decades (1967–2010) and is likely to continue to grow. According to Globocan estimates, the top most common cancers in both sexes are breast, non-Hodgkin lymphoma, leukaemia, oesophageal, and colorectal[3].

There are numerous risk factors associated with breast cancer. Being a woman is the main risk factor that increases probability of developing breast cancer. The incidence of breast cancer and its death rates generally increase with age[4]. Women with family history of breast cancer in a first degree relative are at increased risk and those with a history of breast cancer are at increased risk for developing a second breast cancer[5]. Recent studies have shown that about 5% to 10% of breast cancer cases are hereditary as a result of gene mutations. The most common mutations are those of the BRCA1 and BRCA2 genes[6]. Having one first-degree relative (mother, sister, or daughter) with breast cancer approximately doubles a woman's risk. Other familial associations include presence of both breast and ovarian cancer in the family, particularly in a single person; presence of other gland-related cancers in the family, such as pancreatic, colon, and thyroid cancer. Women who started menstruation early or went through menopause late have a slightly higher risk of breast cancer[7]. Obesity increases the risk of postmenopausal to breast cancer, use of hormonal replacement therapy (HRT) with combined oestrogen and progesterone increases the risk of developing breast cancer.

Delaying childbirth or remaining childless increases the risk of developing breast cancer. Women who haven't had a full-term pregnancy or have their first child after age 30 years have a higher risk of breast cancer compared to women who gave birth before that age. The higher parities and earlier age at first pregnancy of women in many developing countries might account for lower incidence of breast cancer as compared to developed countries.

Recent studies have shown alcohol consumption increase the risk of breast cancer.  In a summary analysis of epidemiologic studies, breast cancer in two thirds of women who drink daily have increased risk between 40 and 70 percent. Another study also found the same result specially the post-menopausal women. In addition, the risk of developing breast cancer is higher among those who consume alcohol before the first full-term pregnancy. In a case–control study, after the old age in the first childbirth, alcohol consumption, with a 4.2-fold increase, was one of the main risk factors for breast cancer. In a population-based case–control study, there was a correlation between alcohol consumption and invasive lobular carcinoma[8].

Both passive and active tobacco smoking have been associated with an increased risk of breast cancer, especially among premenopausal women. This risk is associated with early initiation, longer duration, and/or higher pack-years of smoking[9].

Early breast cancer is usually symptomless. But some symptoms develop as cancer advances. Breast lump is the main symptoms of the breast cancer. The lump is usually painless, firm to hard with irregular borders. Not every lump is cancerous; sometimes some lumps or swelling in the breast tissue may be due to hormonal changes or benign in nature. Besides presence of others symptoms e.g. lump in the armpit, change in the size or shape of the breast, change in the colour or feel of the skin of the breast, nipple, or areola dimpled, puckered, or scaly, retraction, "orange peel" appearance, redness, breast pain, enlargement, or discomfort on one side only as well as any breast lump, pain, tenderness, or other change in a man[10].

The methods most recommended for early detection of breast cancer are mammography, clinical breast examination (CBE) and breast self-examination (BSE). Mammography is a radiologic diagnostic procedure that is used to detect any pathological changes in the breast and is highly recommended for accurate diagnosis of breast cancer; while most of the studies concentrated on mammogram

images, however, mammogram images sometimes have a risk of false detection that may cause danger to the patient's health. It is crucial to find substitute methods which are easier to implement and work with different data sets, cheaper and safer[11]. At the moment, the only evidence-based method of early detection is mammographic screening[12].

Mammography is a costly screening tool, generates controversy in terms of its impact and adverse effects, and its uptake remains low among some populations[13]. However, in a study done in Nigeria, mammogram was found not to be routinely performed due to low level of awareness, ignorance, illiteracy, costliness, high technology equipment and expertise requirements. Mammogram is also less sensitive, with high false negative results among young age group below 40 where BC is widely reported.

Although CBE and BSE are not efficient enough for early diagnosis of breast cancer, there is evidence that most of early BC were self-discovered, and that, the majority of self-detected cases were by BSE performers. In Sudan breast cancer was the most common malignancy in women at Gezira State. Unfortunately, 80-85% of these women presented at a late stage[14].

The American Cancer Society guidelines for early detection of breast cancer recommend yearly mammogram starting at the age of forty, clinical breast examination (CBE) about every three years for women in their twenties and thirties, and every year for women at age forty and over. The guidelines also recommend Breast Self-Examination (BSE) for women starting their twenties. BSE is a simple, free of cost, easy to perform and non-invasive adjuvant screening method for the detection of early breast cancer. Its purpose is to make women familiar with both the appearance and feel of their breasts as early as possible. However, it appears that many women either perform it incorrectly or not at all[15]. Women need to examine their breasts monthly; the best time for a BSE is a week after menstruation. It is a cost effective method of breast cancer screening

in limited resource countries. BSE is a formalized practice that a woman is taught to examine her own breast regularly - usually monthly after the age of 20. During the breast self-examination (BSE), a woman systematically inspects and palpates each breast using her contralateral hand with her ipsilateral arm raised above her head.  She performs the examination both in lying and standing position. Usually it is better to examine the breast in front of a mirror so that she can inspect any sort of asymmetry or dimpling[15]. Monthly examination of breasts conducted by women following the five major steps of breast self-examination which include: examining both the breasts for size, shape, colour and contour while looking in front of the mirror with their arms straight, on the hips, and over the head, to palpate or feel the breast both in standing and lying position using the three finger pads. Clinical breast examination (CBE) about every three years for women in their twenties and thirties, and every year for women at age forty and over is also recommwended[15].

Women in low resource countries (including Sudanese) are more likely to be diagnosed at late stages of the disease, with consequent drastic reduction of survival rates. Attention needs to be drawn to the growing problem of breast cancer in the Sudan. In order to achieve this, the university students, in addition to having their perspective on BC improved, are in the best position to play a well-informed evidence-based role to educate and raise women awareness on BC in health care institutions. Dissemination of BSE screening modality as an accessible and affordable tool empowers women and makes them more "breast aware", which may in turn motivate them to fight for an earlier diagnosis of breast cancer. This study was done to assess female student's knowledge, attitude and practice towards breast cancer risk factors and clinical examination.

## SUBJECTS AND METHODS

This was a cross-sectional institutional based study, performed in the University of Medical Science and Technology (UMST) in Khartoum City, Sudan. The study targeted all female students from various

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colleges of the university. The sample size was calculated according to the formula: $n=z^2pq/d^2$, n= sample size, Z= the z value corresponding to 95% confidence interval in the normal distribution curve =1.96, p= prevalence = average density margin of error=0.05, q = is complementary to p=1-0.5=0.5. Taking the p value of 0.5 within the 95% confidence interval = $(1.96)^2(0.5)^2/(0.05)^2$= 3.84. Therefore, n =n/1+n/N=1501/1+1501/385=1501/385= 310. Convenient sampling method was used to include 310 female students. Using self-administered structured questionnaire, after testing its validity and reliability. It is divided into four parts; demographic data: three questions, history of disease: three questions, knowledge: nine questions, attitude: six questions and three questions of practice. Basic scoring was done by giving good knowledge to full answer, fair knowledge for more than half answer and poor knowledge for less than half answer. The data was analysed using statistical package for social sciences (SPSS); P < 0.05 was considered significant.

## Ethical considerations

Ethical clearance was obtained from the University Deanship of Scientific Research. Informed verbal consent was obtained from eligible female students prior to enrolment in the study.

## RESULTS

The total number of the students enrolled in the study was 310; four of them were excluded due to record incompleteness. As shown in Table 1, the age range of the majority (n=168, 55.1%) was 20 – 24 years; most of the respondents (n=73, 24.4%) were from third academic year, followed by fourth year (n= 60, 20.1%), and mature students (n=52, 17.4%). The least were from the first years (n=39, 12.7%). The overwhelming majority (n=279, 91.1%) of the respondents were single. The bulk (n=220, 70.3%) of the respondents reported no family history of breast cancer while 60 (19.2%) of them gave family history of breast cancer among their first and second degree relatives. The vast majority (n=263, 84.6%) reported having no breast problems during the time of the study.

The majority of the respondents (n=267, 87.4%), (n=188, 62%), (n= 179, 58%) and (n=164, 53.5%) believe that the risk of BC increases with having a relative with BC, increasing age, smoking, and alcohol consumption, respectively as shown in Table 2.

Table 3 shows that the majority of the respondents correctly identified the presenting symptoms and signs including breast lump (n=250, 81.8%), breast discharge (n=211, 68.9%), pain (n=206, 67.3%), change in breast shape (n=250, 81.6%) size (n=224, 73.2%) or nipple discoloration (n=218, 71.2%).

With regards to knowledge about BC diagnostic modalities, 67.3% (n=306), 77.1% (n=236), 84% (n=257) and 74.3% (n=227) of the respondents knew that fine needle aspiration, BSE, CBE, and mammography, respectively, are the methods of diagnosis (Table 4). However, when asked about when to start mammography examination, only 52 (16.9%) knew the correct answer while 143 (46.4%) did not know; overall 23% scored good, 71.3% fair and 6% scored poor.

The majority (n=220, 72 %) agreed to immediately seek medical advice upon feeling a lump in the breast. However, 93 (30.1%) of the respondents believed that it was possible for one to self-identify BC whereas158 (52%) admitted that, they will be fear stricken upon hearing news of having BC detected in their breasts; not surprisingly, 75% (n=230) never had clinical breast examination. Nevertheless, 239 (78 %) of the respondents believed that it was useful to perform breast self-examination (Table 5). In contrast when asked directly if they practice BSE, 170 (55.5%) admitted their total ignorance about BSE practice. but 92 (30.5%) respondents reported to be performing BSE and correctly (Table 6).

**Table1.** Distribution of respondents according to demographic background (n=306):

| Characteristic | | Frequency | % | P-value |
|---|---|---|---|---|
| Age (years) | 15-19 | 87 | 28.5 | .000 |
| | 20-24 | 168 | 55.1 | |
| | 25-29 | 27 | 8.9 | |
| | 30-39 | 20 | 6.6 | |
| | >39 | 4 | 1.3 | |
| Academic year | 1st | 39 | 12.7 | .000 |
| | 2nd | 44 | 14.7 | |
| | 3 rd | 73 | 24.4 | |
| | 4th | 60 | 20.1 | |
| | 5th | 38 | 12.7 | |
| | Mature | 52 | 17.4 | |
| Marital Status | Single | 279 | 91.1 | .000 |
| | Married | 23 | 8.1 | |
| | Divorced | 2 | 0.7 | |
| | Widowed | 2 | 0.7 | |
| Do you have any family history of breast cancer? | No | 220 | 70.3 | .000 |
| | Not sure | 26 | 8.4 | |
| | Yes | 60 | 19.2 | |
| If yes, degree of relationship | 1st degree relation | 13 | 23.0 | .000 |
| | 2nd degree relation | 47 | 77.0 | |
| Do you have any breast problem? | No | 263 | 84.6 | .000 |
| | Not sure | 32 | 10.4 | |
| | Yes | 11 | 3.5 | |

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**Table 2.** Knowledge about risk factors associated with breast cancer (n = 306).وة

| Variable | | Frequency | % | P-value |
|---|---|---|---|---|
| Increase with age | No | 55 | 18.0 | .000 |
| | Not sure | 63 | 20.0 | |
| | Yes | 188 | 62.0 | |
| Positive family history | No | 23 | 7.4 | |
| | Not sure | 16 | 5.2 | .000 |
| | Yes | 267 | 87.4 | |
| High fat diet | No | 71 | 23.3 | .002 |
| | Not sure | 133 | 43.4 | |
| | Yes | 102 | 33.3 | |
| Smoking | No | 51 | 16.9 | .000 |
| | Not sure | 76 | 25.1 | |
| | Yes | 179 | 58.0 | |
| Race/ethnicity | No | 78 | 25.4 | .034 |
| | Not sure | 128 | 42.0 | |
| | Yes | 100 | 32.6 | |
| Working class women | No | 159 | 51.9 | .000 |
| | Not sure | 98 | 32.0 | |
| | Yes | 49 | 16.1 | |
| Alcohol consumption | No | 53 | 17.5 | .000 |
| | Not sure | 89 | 29.5 | |
| | Yes | 164 | 53.5 | |
| First child at late age | No | 87 | 28.4 | .136 |
| | Not sure | 125 | 41.0 | |
| | Yes | 94 | 31.0 | |
| Early onset of menarche | No | 84 | 27.4 | .000 |
| | Not sure | 146 | 48.4 | |
| | Yes | 76 | 24.2 | |
| | No | 84 | 27.4 | .008 |
| | Not sure | 139 | 45.4 | |
| Late menopause | Yes | 83 | 27.2 | |
| Stress | No | 99 | 32.5 | .400 |
| | Not sure | 89 | 29.0 | |
| | Yes | 118 | 38.5 | |

**Table 3.** Knowledge about presenting symptoms and signs of breast cancer (n = 306).

| Symptoms and signs of BC identification | | Frequency | % | P-value |
|---|---|---|---|---|
| Lump in the breast | No | 22 | 7.1 | .000 |
| | Not sure | 34 | 11.1 | |
| | Yes | 250 | 81.8 | |
| Discharge from the beast | No | 27 | 9.0 | .000 |
| | Not sure | 68 | 22.1 | |
| | Yes | 211 | 68.9 | |
| Pain or soreness in the breast | No | 52 | 17.0 | .000 |
| | Not sure | 48 | 15.7 | |
| | Yes | 206 | 67.3 | |
| Change in the size of the breast | No | 31 | 10.1 | .000 |
| | Not sure | 51 | 16.7 | |
| | Yes | 224 | 73.2 | |
| Discoloration /dimpling of the breast | No | 20 | 6.6 | .000 |
| | Not sure | 68 | 22.2 | |
| | Yes | 218 | 71.2 | |
| Ulceration of the breast | No | 37 | 12.0 | .000 |
| | Not sure | 89 | 29.0 | |
| | Yes | 180 | 59.0 | |
| Weight loss | No | 67 | 22.0 | .000 |
| | Not sure | 76 | 24.8 | |
| | Yes | 163 | 53.2 | |
| Changes in the shape of the breast | No | 21 | 7.0 | .000 |
| | Not sure | 35 | 11.4 | |
| | Yes | 250 | 81.6 | |
| Inversion/pulling in of nipple | No | 31 | 10.0 | .000 |
| | Not sure | 91 | 30.0 | |
| | Yes | 184 | 60.0 | |
| Swelling or enlargement of the breast | No | 22 | 7.1 | .000 |
| | Not sure | 60 | 19.7 | |
| | Yes | 224 | 73.2 | |
| Lump under armpit | No | 29 | 9.6 | .000 |
| | Not sure | 80 | 26.1 | |
| | Yes | 197 | 64.3 | |
| Scaling/dry skin in nipple region | No | 30 | 9.9 | .000 |
| | Not sure | 123 | 40.1 | |
| | Yes | 153 | 50.0 | |

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Table 4. Knowledge about diagnostic modalities of breast cancer

| Variable | | Frequency | % | P-value |
|---|---|---|---|---|
| Pathological examination of breast tissue by using Fine Needle Aspiration Cytology (FNAC) | No | 18 | 6.0 | .000 |
| | Not sure | 82 | 26.7 | |
| | Yes | 206 | 67.3 | |
| Self-Breast Examination (SBE) | No | 25 | 8.2 | .000 |
| | Not sure | 45 | 14.7 | |
| | Yes | 236 | 77.1 | |
| Clinical Breast Examination by doctor | No | 20 | 6.6 | .000 |
| | Not sure | 29 | 9.4 | |
| | Yes | 257 | 84.0 | |
| Mammography | No | 14 | 4.5 | .000 |
| | Not sure | 65 | 21.2 | |
| | Yes | 227 | 74.3 | |
| | No | 37 | 12.3 | .000 |
| | Not sure | 94 | 30.3 | |
| | Yes | 176 | 57.5 | |
| Stress | No | 99 | 32.5 | .400 |
| | Not sure | 89 | 29.0 | |
| | Yes | 118 | 38.5 | |

**Table 5.** Attitude towards breast cancer (n = 306).

| Probing question | | Frequency | % | P-value |
|---|---|---|---|---|
| If_you_develop_breast_lump_how soon_ will_you_go_to_see_a_doctor | Wrong answer- | 86 | 28.0 | .000 |
| | Correct answer | 220 | 72.0 | |
| Can you identify breast cancer by yourself? | Disagree | 86 | 28.0 | .007 |
| | Unsure | 127 | 41.7 | |
| | Agree | 93 | 30.1 | |
| Are you afraid that you›ll detect breast cancer? | Disagree | 53 | 17.0 | .000 |
| | Unsure | 95 | 31.0 | |
| | Agree | 158 | 52.0 | |
| Screening for breast abnormality using BSE is important and useful | Disagree | 21 | 7.0 | .000 |
| | Unsure | 46 | 15.0 | |
| | Agree | 239 | 78.0 | |
| Have you ever had your breast examined by a doctor? (Clinical Breast examination) | No | 230 | 75.0 | .000 |
| | Not sure | 21 | 7.0 | |
| | Yes | 55 | 18.0 | |
| (If doctor exam Yes) what was the frequency of examination? | Once | 44 | 80.1 | .000 |
| | 2 - 5times | 8 | 14.5 | |
| | >5 times | 3 | 5.4 | |

BSF= Breast Self-Examination

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**Table 6.** Breast Self-Examination (BSE) practice experience (n = 306).

| Probing questions | | Frequency | % | P-value |
|---|---|---|---|---|
| Do you practice Breast Self-Examination (BSE)? | No I don't | 170 | 55.5 | .000 |
| | Yes but inappropriate | 44 | 14.0 | |
| | Yes I do | 92 | 30.5 | |
| If yes, how often? | Wrong answer | 178 | 58.0 | .547 |
| | Correct answer | 128 | 42.0 | |
| At what age have you started practicing BSE? | Wrong answer | 120 | 39.6 | .011 |
| | Correct answer | 186 | 60.4 | |

## DISCUSSION

With the rising incidence of breast cancer, and also in view of limited national breast screening program in the Sudan, it becomes important to assess female student's knowledge attitude and practice towards breast cancer risk factors and clinical examination in various age groups.

The vast majority of the students involved in the present study were aged 15 – 39 years – a suitable age to motivate them and instill in them a positive attitude of practicing BSE regularly. Besides, being females of high level of education; some of them belong to specialties of health care provision; they are expected to be potential agents that can disseminate information to patients as well as families and friends in the general population. Moreover, half of the respondents were between 20 – 24 years of age and from the middle academic year classes (3rd and 4th); this makes them a suitable target for the study, if awareness on breast health is to be addressed.

The majority (n=279, 91.1%) of the respondents were single. Such group of young adults is expected to benefit from the outcome of this study in improving their awareness of the modifiable risk factors, and understanding the simple ways of early identification of BC.

Although over two-thirds of the respondents gave no family history of BC but 60 (19.2%) of them had a family history of BC of whom 47 (77%) were of second degree relatives which was

significant (p<0.000). Therefore, a family history of BC constitutes a risk factor and is doubled on having a first degree relative. This has to be viewed from the stand point of the culture of marriage consanguinity, a common practice in Sudan that needs to be avoided.

The bulk of the respondents reported having no breast problems while 11 (3.5%) admitted having problems. The nature of these problems was not explored. However, it is clear that some women are so tolerant to breast diseases so that some of these conditions could be BC in making. If anything, poor breast health awareness could be behind this silence to early reporting.

Most of the respondents surveyed, seemed to have heard of breast cancer. Their knowledge of increased risk factors of BC is significantly related to aging (p<0.000), having a relative with BC (p<0.000), smoking (p<0.000), and alcohol consumption (p<0.000, Table2). However, a good number of them hesitated to answer questions considering things like fatty diet, race and ethnicity, first child at late age, and early onset of menarche. The responses were reserved with the level of knowledge score dropping to below 50%. Similar responses were obtained in a prospective cross-sectional KAP study conducted among non-medical students in Ain Shams University, Egypt[16]. Modifiable risk factors including smoking, exposure to radiation, alcohol consumption, and obesity associated with uncontrolled intake of fatty meals, lend their importance to being soft targets

that can be manipulated, thereby reducing the level of risks exposure. Such strategy is the role that breast awareness campaigns could play.

Looking at the level of knowledge with regards to warning symptoms and signs of BC, the respondents showed fair degree of knowledge ability. Four fifth of them would - correctly identify breast lump, and over two-thirds would correctly identify breast discharge, sore breast or change in nipple or size of breast. –

With regards to knowledge about BC diagnostic methods, i.e. FNAC, BSE, CBE and mammography, the level was good. However, the level of knowledge was observed to decline when the respondents were put to test. For example, when asked about the age at which BSE should start and whether they were able to perform BSE, only half knew the answer, with 60% of them correctly knew that it should be performed monthly for women under the age 40. Moreover, the overall response for how often to go for CBE or when to start mammography examination was not satisfactory (scoring good, fair and poor) - marking an important area for advocacy.

The vast majority of the respondents expressed their willingness to immediately seek medical advice upon feeling a lump in the breast. However, about one-third believed that it was possible for one to self-identify BC, while half of them admitted that, they will be fear stricken upon hearing news of having BC detected in their breast. This may partly explain why three quarters of the respondents never had clinical breast examination Nevertheless, the method of performing breast self-examination was believed to be useful for most of the respondents. This showed that the level of concern about screening for breast cancer is expectedly high among the respondents considering their status as women in a high learning institution, where the level of awareness is understood to be high. The fact that three quarters of the respondents never experienced clinical breast examination by a doctor is not surprising in view of the cultural influence on such young females in a conservative community such as Sudanese, who would not allow their breasts to be

exposed unduly; however, it is left to be desired for these young educators to positively influence their pattern of thoughts and beliefs.

With regards to BSE practice, only one third of the respondents reported to be performing it correctly, while over half of them admitted their total ignorance about BSE practice. This is sharply contrasting with the high level of knowledge about BSE; where more than three-quarters of them believed that BSE was a useful screening tool and about one third claimed that they were able to perform BSE, but still the overall practice aspect of the study was undoubtedly found to be poor (41%) as compared to knowledge and attitude. Our study bears similarity to a cross-sectional study conducted on a sample of 200 female medical students drawn from three Sudanese universities of Bahri, Alzaeem Alazhari, and Alnilain. The aim was to assess KAP regarding BSE among them; 87% of the students were aware of BSE and 64.5% were regularly performing BSE but Only 46.5% knew how to perform it correctly[16]. Other comparable studies include those of Taif University College of Medicine and Lagos University[16,18]. Their figures were better than those in our study but the conclusions were the same i.e. poor practice. This poor practice reflects the fact that, adequate health education is essential to facilitate early detection of breast cancer using cheap and easily accessible interventions such BSE and CBE.

This study also showed that age (p< 0.000), and academic level (p< 0.000) significantly influenced the knowledge level among the study group. Conversely, marital status had no effect on knowledge level. Strikingly enough, none of the variables influenced attitude towards BC, and BSE. Finally, age (p-value = 0.002 within 95 CI), and marital status (p-value = 0.012 within 95 CI) influenced practice of BSE. Our findings are partially supported by a Nigerian community-based study, in which the level of education was found to be significantly influencing the level of knowledge of BC, which correspond to academic level in our study. The age in contrast, had no influence on knowledge in the Nigerian study[19].

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## CONCLUSION

Though, this study was carried out on medical and non-medical groups of UMST female students, the knowledge and attitude was fair, while the practice of BSE was quite low. As health behaviours acquired early in life have an influence on future health, there is a good opportunity to shape the behaviour of these students at this young age through creation of educational programs aimed at raising their breast health awareness.

### Acknowledgements

## REFERENCES

1. Cancer-Pain.org [homepage on the Internet]. WHO report on cancer - World Health Organization [updated 2020 cited 2021decr30]. Available at http://apps.who.int/iris. ... cancer control, through prevention, diagnosis, treatment. *Cancer* 2013;119

2. Ferlay J, Soerjomataram I, Ervik M, et al. Globocan 2012 v1. 0. Cancer incidence and mortality worldwide: IARC Cancer Base No. 11. Lyon, IARC, 2013.

3. Elamin A, Ibrahim ME, Abuidris D, Mohamed KE, Mohammed SI. Part I: Cancer in Sudan: burden, distribution, and trends breast, gynaecological, and prostate cancers. *Cancer Medicine* 2015;4(3):447-56.

4. Donnelly TT, Al Khater AH, Al-Bader SB, et al. Arab women's breast cancer screening practices: a literature review. *Asian Pacific Journal of Cancer Prevention* 2013;14(8):4519-28.

5. Nemenqani DM, Abdelmaqsoud SH, Al-Malki AH, Oraija AA, Al-Otaibi EM. Knowledge, attitude and practice of breast self-examination and breast cancer among female medical students in Taif, Saudi Arabia. *Open Journal of Preventive Medicine* 2014 Jan 29;2014.

6. Oeffinger KC, Fontham ET, Etzioni R, et al. Breast cancer screening for women at average risk: 2015 Guideline Update from the American Cancer Society. *JAMA* 2015;314(15):1599-614.

7. Southey MC, Goldgar DE, Winqvist R, et al. PALB2, CHEK2 and ATM rare variants and cancer risk: data from Cogs. *Journal of Medical Genetics* 2016;53(12):800-11.

8. Momenimovahed Z, Salehiniya H. Epidemiological characteristics of and risk factors for breast cancer in the world. *Breast Cancer: Targets and Therapy* 2019; 11:151.

9. Seo BR, Bhardwaj P, Choi S, et al. Obesity-dependent changes in interstitial ECM mechanics promote breast tumorigenesis. *Science Translational Medicine* 2015;7(301):301ra130.

10. Tazhibi M, Feizi A. Awareness levels about breast cancer risk factors, early warning signs, and screening and therapeutic approaches among Iranian adult women: a large population based study using latent class analysis. *Bio Med Research International* 2014 Sep 11;2014.

11. Tahmooresi M, Afshar A, Rad BB, Nowshath KB, Bamiah MA. Early detection of breast cancer using machine learning techniques. *Journal of Telecommunication, Electronic and Computer Engineering* 2018;10(3-2):21-7.

12. Yip CH. Challenges in the early detection of breast cancer in resource-poor settings. *Breast Cancer Management* 2016;5(4):161-9.

13. Granado MN, Guell C, Hambleton IR, Hennis AJ, Rose AM. Exploring breast cancer screening barriers among Barbadian women: a focus group study of mammography in a resource-constrained setting. *Critical Public Health* 2014;24(4):429-44.

14. Zaroug SM. Knowledge, Attitude and practice of Women 20 Years Old and Above on Breast Cancer and Breast Self-examination in Fadasi

Alamrab, Great Wad Medani Locality, Gezira State, Sudan (2015). Doctoral Dissertation, University of Gezira, Medani, Sudan.

15. Sambanje MN, Mafuvadze B. Breast cancer knowledge and awareness among university students in Angola. *Pan African Medical Journal* 2012;11(1):70

16. Smith RA, Manassaram-Baptiste D, Brooks D, et al. Cancer screening in the United States, 2015: a review of current American cancer society guidelines and current issues in cancer screening. *CA: Cancer Journal for Clinicians* 2015;65(1):30-54.

17. Donnelly TT, Al Khater AH, Al-Bader SB, et al. Arab women's breast cancer screening practices: a literature review. *Asian Pacific Journal of Cancer Prevention* 2013;14(8):4519-28.

18. Nemenqani DM, Abdelmaqsoud SH, Al-Malki AH, Oraija AA, Al-Otaibi EM. Knowledge, attitude and practice of breast self-examination and breast cancer among female medical students in Taif, Saudi Arabia. *Open Journal of Preventive Medicine* 2014 Jan 29;2014.

19. Adogu P, Omosivwe O, Ilika A, Egenti N. The effectiveness of health education on knowledge attitude and practice of breast self-examination among secondary school girls in Nnewi North Local Government Area, Anambra State, Nigeria. *Br J Med Health Res* 2015; 2:1-4.

# Review article

## Emerging resistance of praziquantel and the use of combinational therapy in schistosomiasis: Sudan

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Schistosomiasis is one of the neglected tropical disease with the highest endemicity, worldwide[1]. Despite advances in the treatment and prevention, schistosomiasis is currently a major public health problem in Sudan, with social and economic implications. About 5.8 million people (around 15% of the Sudan population) are estimated to require treatment for schistosoma; the majority of those infected are children, mostly residing in rural communities with limited access to running water, toilets or latrines for domestic use. This makes water sources places for defecation and urination[2].

Epidemics of bilharziasis were reported in different pump irrigation farms in Sudan; as in Dongola Province in northern Sudan and Kurdofan Province in Western Sudan[3]. Blue Nile Province and Darfur Province were also declared endemic by the Annual Report of Sudan Medical Services[4]. *S. haematobium*, in specific, was found to be endemic in two regions in South Darfur, in White Nile Province, in the Rahad Irrigation Scheme and in Gedaref state[5,6,7]. Although Khartoum Province, Central Sudan, is considered to be mostly of urbanized communities, yet some areas along the White Nile were found to be highly infected with urinary schistosomiasis[8].

Different Control programs were established towards the reduction of Schistosomiasis medical burden and infection; starting with the London Khartoum Bilharzia Project in year 1970, The Blue Nile Health Project 1979–1990 and The National Control Programme from year 2000 to date[8,10,11]. According to the reports reviewed, these projects have reduced overall prevalence in endemic areas but without eliminating disease transmission[7,12,13].

## THE EMERGING RESISTANCE OF PRAZIQUANTEL

While praziquantel **(**PZQ) has been used for over 30 years the exact mechanism of action of the drug remains unknown. PZQ appears to exert multiple effects on schistosomes, mainly damaging the tegument and causing muscle contraction[14]. As outlined in several reviews, the relationship between PZQ and Ca+2 influxes suggests that the sites of ction are Ca2+ ion channels in the membrane of tegument and muscle cells[15].

The mainstay protocol for treatment of Schistosomiasis in Sudan is the single dose of 60 mg/kg. praziquantel[7]. A repeated standard dose of 60 mg/kg achieved satisfactory efficacy compared to a single dose against the most common parasite species[16]. Praziquantel though it has a strong curative effect, but never reaches 100% efficacy, where drug resistance has emerged as an issue with continued single-drug use of praziquantel (PZQ)

against schistosomiasis[17]. The definitive evidence of clinical resistance to PZQ has not yet been reported, but field studies show reduced efficacy of PZQ in some settings and the ability to induce resistance in laboratory-maintained isolates[18]. While it has proven difficult to find and maintain PZQ resistant *Schistosoma spp.* in field isolates, resistance has been successfully generated in the laboratory especially in the asexual stages of the agents[19,20]. We have found valuable and provoking initial studies, but it is difficult to find a study which tailors all factors of speculated resistance in one accommodated setting.

However, tabulations in efficacy are discussed if due to failure of treatment, resistance, or loss of tolerance. This is especially true for schistosomiasis because of the variable susceptibility of different stages of maturation where sexually immature, juvenile schistosomes are refractory to PZQ action, in addition to strain's rates of maturation, and sexes of the parasite, and correlations to host immunity[21].

Resistance to PZQ is defined as the genetically transmitted loss of susceptibility in worm populations that were previously susceptible to PZQ[22]. Resistance in some areas may also be `clonal' where it's introduced by an out-comer and spread explosively[23]. Or it could be attributed to lack of previous immunologic exposure to schistosomes in studied populations[18]. The factors contributing to the development of resistance to PZQ in schistosomiasis could be drug-related, host-related, parasite-related, or environmentally-related. High parasitic loads, fast reinfection, the presence of immature worms, the use of low quality drugs, differences in evaluation, and cure criteria, or actual drug resistance are all examples of why PZQ efficacy could be affected overtime[20,22]. Host factors are also invaluably regarded, such as age-relation, gender-relation, immune problems, history of exposure, pre-treatment intensity and water contact patterns[23,24].

The factor of host's immune system is of major importance in this discussion. In some reports, low cure rates were considered to be due to an immature immune mechanism at the time of treatment[23]. It has been shown that the effectiveness of Praziquantel is impaired in immune-deficient animals, but the same study showed that the activity can be restored if antibody specific for certain surface antigens is administered to such animals[25].

The host-parasite relationship was studied in our population which notified the diverse outcomes of schistosoma infections being majorly affected by the balance of different immune responses directed against the egg, larval and adult stages of the parasite[26]. **A** study conducted with chronically infected irrigation canal cleaners, who were occupationally hyper-exposed to *S. mansoni***,** suggested that epidemiological factors and immune responses to schistosomes depend on the actual infection status (patent versus pre-patent/low egg producing) where man can develop partial immunity to a schistosoma infection[27]. One of the studies done on Sudanese isolates of urinary bilharziasis concludes genetic crossing occurring between adult worms where heterogeneity of an infection was thought to strongly influence development of new variants of the parasite[7]. Since damage from schistosoma infections is inherently linked to reactions of the immune system to parasite eggs deposited in tissue; the diversity of heterogeneous versus homogeneous infections may play a role in the pathology of our diseased population, and therefore, the drug effect and resistance.

## Possible pathways of resistance

In some biological systems, drug resistance results from the acquisition of a new activity in resistant organisms, in the resistance of *Schistosoma spp.,* there may be one or more mutations in a single gene, or epigenetic change may lead to a change may alter the toxicity and/or half-life of a drug[19,20]. Drug resistance through increased drug efflux is an important phenomenon in which multidrug transporters of detoxified compounds by cellular enzymes such as glutathione-S-transferase (in addition to its function in the transport of immune-modulators) is altered in worms exposed to PZQ were expressed at higher levels in worms from isolates with reduced praziquantel susceptibility[28].

Resistance could be associated to juvenile stages of the parasite that would have not yet switched on bio-transforming activities which are present in the adult PZQ-sensitive stage[23,29]. Although, it is speculated that resistance not being widespread is perhaps due its biological cost[20]. The selective pressure exerted by PZQ leads to decreased genetic variability in Schistosoma and increased endogamy[22,30]. The decrease in the genetic diversity of these populations upon chemotherapy can be interpreted as the selection of less sensitive parasites[20,31]. As it was indicated that PZQ resistance has shown to come with a fitness trade-off, as it is conceivable that in an endemic situation a resistant phenotype may be selected for under frequent drug pressure[20]. Which may provide an account for the absence of sustained PZQ resistance where there is a large refugee of drug sensitive schistosomes[19,32].

Yet, there is some natural variation in the parasite sensitivity to PZQ where resistant or tolerant adult worms could likely be a subset of the natural variation, rather than a result of selection[30]. Determining the inheritance basis of schistosome resistance to PZQ is also valid to predicting the spread of resistance; with accounts for known limitations such as inheritance traits, reduced penetrance and polygenic and epistatic factors[29].

## The use of combinational regimens

Sudan is known highly endemic for both malaria and schistosomiasis[5]. Where areas of co-endemicity could present many arguments to the use of such combinational regimen - antimalarial and antischistosomal drugs in one affected population[33]. It is likely that immunological interactions occurring between these infections in humans who might be repeatedly infected with schistosomiasis and malaria, would have implications in the modulation of human immunological responses, and the response to the type of number of treatment regimens tried in the process of curing infection. For instance, one of the studies in the Sudanese population was done to detect cross-reactivity between *Schistosoma mansoni* and *Plasmodium falciparum*; serological responses among individuals were examined in

areas where both schistosomiasis and malaria are endemic[33].

Single-celled malaria plasmodia and schistosome worms are phylogenetically very distant from each other, and one might think that the damage caused by the artemisinins to both these organisms would be due to different principles. A derivative of antimalarial artemisinin is found chemoprophylactic to PZQ affecting refractory young developmental stages of schistosome parasites[23]. Therefore, artemisinin derivates are a true transmission-blocking drugs as they target stages before egg production starts contributing to disease elimination. The mechanism is yet not determined, but haemoglobin digestion by both parasites in host erythrocytes and interference with the formation of haemozoin is considered[17].

When compared to monotherapy, it was found that most worms die shortly post-treatment and the tegument of the parasites is significantly more disrupted with artemether (AM) and Praziquantel management, which suggested not only additive but also even synergistic effects[37]. This combinational regimen has successfully been applied in interventions in Egypt, China and in comprehensive meta-analysis studies and animal models studies[17,23,25]. However one report of a randomized, double-blind, placebo-controlled trial for evaluating combined chemotherapy for schistosomiasis japonica in China; found no improved efficacy in dual AM and PZQ chemotherapy compared to PZQ alone[34].

Successful results were indicated out of a small study in eastern Sudan in treating uncomplicated *Plasmodium falciparum* malaria with co-infections with *Schistosoma mansoni*[35]. Thus we highlight that developed or developing resistance to antimalarial drugs could affect the outcomes of combinational therapy of this regimen. International studies have debated on the efficacy of this regimen on schistosomiasis; whilst Borrmann et al. has reported a poor efficacy among infected schoolchildren in Gabon[36]. On the other hand, Inyang-Etoh et al. observed that treatment of urinary schistosomiasis

with the combination was safe and more effective than treatment with either drug alone[37].

An artemisinin/PZQ combination would be complimentary, and potentially additive, as it would kill two schistosome life cycle stages and thus confer a transmission-blocking modality to current chemotherapy. In this literature review, we present an augmenting argument to support the use of combination regimen of antimalarial drug, artemether along with praziquantel, as shown to be an efficient methodology treatment.

## REFERENCES

1. Othman A, El Ridi R. Schistosomiasis. In: Bruschi F, editor. Helminth Infections and Their Impact on Global Public Health [Internet]. Vienna: Springer Vienna; 2014. p. 49–92. Available from: https://doi.org/10.1007/978-3-7091-1782-8_3

2. Health and well-being profile of the Eastern Mediterranean Region: an overview of the health situation in the Region and its countries in 2019. Cairo: WHO Regional Office for the Eastern Mediterranean; 2020. Licence: CC BY-NC-SA 3.0 IGO.

3. Osman, M. Shazali and Heeh. Irrigation Practices and Development in the Sudan. *Sudan Notes Rec* 2016;55(1974):96–110.

4. Annual Report of Sudan Medical Services (1927) URL: http://www.who.int/schistosomiasis/epidemiology/en/sudan.pdf (accessed 2nd February 2016).

5. Deribe K, Eldaw A, Hadziabduli S, Kailie E, Omer MD, Mohammed AE, et al. High prevalence of urinary schistosomiasis in two communities in South Darfur: implication for interventions. *Parasit Vectors* [Internet]. 2011;4(1):14. Available from: https://doi.org/10.1186/1756-3305-4-14

6. Ahmed ES, Daffalla A, Christensen NO, Madsen H. Patterns of infection and transmission of human *Schistosomiasis mansoni* and *Schistosomiasis haematobium* in White Nile Province, Sudan. *Ann Trop Med Parasitol* 1996;90(2):173–80.

7. Mutamad A, Kardaman M, Mounkaila N, Abubaker H, Homeida M. The Transmission Patterns of Shistosomiasis in Khartoum State, Sudan. 2016;4.

8. Ismail Haha, Hong ST, Babiker Ateb, Hassan Rmae, Sulaiman Maz, Jeong HG, et al. Prevalence, risk factors, and clinical manifestations of schistosomiasis among school children in the White Nile River basin, Sudan. *Parasit Vectors* [Internet]. 2014;7(1):478. Available from: https://doi.org/10.1186/s13071-014-0478-6

9. Grimes JET, Croll D, Harrison WE, Utzinger J, Freeman MC, Templeton MR. The roles of water, sanitation and hygiene in reducing schistosomiasis: a review. *Parasit Vectors* [Internet]. 2015;8(1):156. Available from: https://doi.org/10.1186/s13071-015-0766-9

10. el Gaddal AA. The Blue Nile Health Project: a comprehensive approach to the prevention and control of water-associated diseases in irrigated schemes of the Sudan. *J Trop Med Hyg* 1985;88(2):47–56.

11. World Health Organization. Regional Office for the Eastern Mediterranean. (2010). Country cooperation strategy for WHO and Sudan: 2008–2013. World Health Organization. Regional Office for the Eastern Mediterranean. https://apps.who.int/iris/handle/10665.

12. Lee H, Jeong H, Kong W, Lee SH, Cho H, Nam HS, et al. Reduction of urogenital schistosomiasis with an integrated control project in Sudan. *PLoS Negl Trop Dis* 2015;9:e3423.

13. Cha S, Elhag MS, Lee YH, Cho DS, Ismail Haha, Hong ST. Epidemiological findings

and policy implications from the nationwide schistosomiasis and intestinal helminthiasis survey in Sudan. *Parasit Vectors* [Internet]. 2019;12(1):429. Available from: https://doi.org/10.1186/s13071-019-3689-z

14. Chienwichai P, Ampawong S, Adisakwattana P, Thiangtrongjit T, Limpanont Y, Chusongsang P, et al. Effect of Praziquantel on Schistosoma mekongi Proteome and Phosphoproteome. Pathog (Basel, Switzerland). 2020 May;9(6).

15. Chan JD, Zarowiecki M, Marchant JS. Ca$^{2+}$ channels and praziquantel: a view from the free world. *Parasitol Int* 2013;62(6):619–28.

16. 16. Jin Y, Cha S, Lee J, Elhag MS, Hong ST, Lee YH. Parasitological observation in schoolchildren with urogenital schistosomiasis following treatment with three different brands of praziquantel. *J Korean Med Sci* 2020;35(46):e394.

17. Bergquist R, Elmorshedy H. Artemether and praziquantel: origin, mode of action, impact, and suggested application for effective control of human schistosomiasis. *Trop Med Infect Dis* 2018;3(4):125.

18. Black CL, Steinauer ML, Mwinzi PNM, Evan Secor W, Karanja DMS, Colley DG. Impact of intense, longitudinal retreatment with praziquantel on cure rates of *schistosomiasis mansoni* in a cohort of occupationally exposed adults in western Kenya. *Trop Med Int Health* 2009;14(4):450–7.

19. Sanchez MC, Cupit PM, Bu L, Cunningham C. Transcriptomic analysis of reduced sensitivity to praziquantel in *Schistosoma mansoni*. *Mol Biochem Parasitol* 2019;228:6–15.

20. Coeli R, Baba EH, Araujo N, Coelho PMZ, Oliveira G. Praziquantel treatment decreases *Schistosoma mansoni* genetic diversity in experimental infections. *PLoS Negl Trop Dis* [Internet]. 2013 Dec 19;7(12):e2596. Available from: https://doi.org/10.1371/journal.pntd.0002596

21. Greenberg RM. New approaches for understanding mechanisms of drug resistance in schistosomes. *Parasitology* 2013;140(12):1534–46.

22. Pinto-Almeida A, Mendes T, Armada A, Belo S, Carrilho E, Viveiros M, et al. The Role of Efflux Pumps in *Schistosoma mansoni* Praziquantel Resistant Phenotype. *PLoS One* 2015;10(10):e0140147.

23. Mahmoud MR, Botros SS. Artemether as adjuvant therapy to praziquantel in murine Egyptian schistosomiasis mansoni. *J Parasitol* 2005;91(1):175–8.

24. Ismail M, Botros S, Metwally A, William S, Farghally A, Tao LF, et al. Resistance to praziquantel: direct evidence from *Schistosoma mansoni* isolated from Egyptian villagers. *Am J Trop Med Hyg* 1999;60(6):932–5.

25. Brindley PJ, Sher A. The chemotherapeutic effect of praziquantel against *Schistosoma mansoni* is dependent on host antibody response. *J Immunol* 1987;139(1):215–20.

26. Elfaki TEM, Arndts K, Wiszniewsky A, Ritter M, Goreish IA, Atti El Mekki Meya, et al. Multivariable regression analysis in *Schistosoma mansoni*-infected individuals in the Sudan reveals unique immunoepidemiological profiles in uninfected, egg+ and non-egg+ infected individuals. *PLoS Negl Trop Dis* 2016;10(5):e0004629.

27. Satti MZ, Lind P, Vennervald BJ, Sulaiman SM, Daffalla AA, Ghalib HW. Specific immunoglobulin measurements related to exposure and resistance to *Schistosoma mansoni* infection in Sudanese canal cleaners. *Clin Exp Immunol* 1996;106(1):45–54.

28. Kasinathan RS, Morgan WM, Greenberg RM. *Schistosoma mansoni* express higher levels of multidrug resistance-associated protein 1 (SmMRP1) in juvenile worms and in response to praziquantel. *Mol Biochem Parasitol* 2010;173(1):25–31.

29. 29. Liang YS, Dai JR, Zhu YC, Coles GC, Doenhoff MJ. Genetic analysis of praziquantel resistance in *Schistosoma mansoni. Southeast Asian J Trop Med Public He*alth [Internet] 2003;34(2):274-280. Available from: http://europepmc.org/abstract/MED/12971549

30. 30. Faust CL, Crotti M, Moses A, Oguttu D, Wamboko A, Adriko M, et al. Two-year longitudinal survey reveals high genetic diversity of *Schistosoma mansoni* with adult worms surviving praziquantel treatment at the start of mass drug administration in Uganda. *Parasit Vectors* [Internet] 2019;12(1):607. Available from: https://doi.org/10.1186/s13071-019-3860-6

31. 31. Barbosa LM, Reis EA, Dos Santos CRA, Costa JM, Carmo TM, Aminu PT, et al. Repeated praziquantel treatments remodel the genetic and spatial landscape of schistosomiasis risk and transmission. *Int J Parasitol* 2016;46(5–6):343–50.

32. 32. Almeida GT, Lage RCG, Anderson L, Venancio TM, Nakaya HI, Miyasato PA, et al. Synergy of omeprazole and praziquantel in vitro treatment against *Schistosoma manso*ni adult worms. *PLoS Negl Trop Dis* 2015;9(9):e0004086.

33. 33. Naus CWA, Booth M, Jones FM, Kemijumbi J, Vennervald BJ, Kariuki CH, et al. The relationship between age, sex, egg-count and specific antibody responses against *Schistosoma mansoni* antigens in a Ugandan fishing community. *Trop Med Int Health* 2003;8(6):561–8.

34. 34. Hou XY, McManus DP, Gray DJ, Balen J, Luo X-S, He Y-K, et al. A randomized, double-blind, placebo-controlled trial of safety and efficacy of combined praziquantel and artemether treatment for acute *schistosomiasis japonica* in China. *Bull World Health Organ* 2008;86(10):788–95.

35. Mahgoub HM, Mohamed AA, Magzoub M, Gasim GI, Eldein WN, Ahmed AA, et al. *Schistosoma mansoni* infection as a predictor of severe anaemia in schoolchildren in eastern Sudan. *J Helminthol* 2010;84(2):132–5.

36. Dejon-Agobé JC, Edoa JR, Honkpehedji YJ, Zinsou JF, Adégbitè BR, Ngwese MM, et al. *Schistosoma haematobium* infection morbidity, praziquantel effectiveness and reinfection rate among children and young adults in Gabon. *Parasit Vectors* [Internet]. 2019;12(1):577. Available from: https://doi.org/10.1186/s13071-019-3836-6

37. Kramer C V, Zhang F, Sinclair D, Olliaro PL. Drugs for treating urinary schistosomiasis. Cochrane database Syst Rev. 2014 Aug;2014(8):CD000053

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