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1. Provide a forum for scientific and clinical medicine publications.
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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.
5. Provide opportunities for development of expertise in medical and allied sciences education.
6. Act as a platform for the expression of professional and scientific opinion and exchange of information.
7. Provide a forum for the exchange of ideas and experiences in the field of education and training in the medical and health professions.

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Leading article

Quality management in higher education institutions (HEI)

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Introduction

The need for quality management in education goes back to the 1880s when it was realized that standards need to be put in place to ensure that educational institutions graduate competent degree holders (who have been trained in accredited programs) This is now seen necessary to standardize higher education to meet the expectation of society & to respond to cross-border employment ^(1, 2)

Quality assurance models were adopted by HEIs, mainly relying on industrial models which were not entirely suitable for HEI due to the complexity of the product/s & processes involved in higher education ⁽³⁾

This paper focuses attention on the day-to-day requirements for a feasible and practical model of quality management in institutions of higher learning. It is a fact that many universities & colleges today have established such units, but the variation in their conceptual framework, structure and functionality vary from the very sophisticated, high power, expensive model, to the rudimentary & often inadequate units of quality management.

It is important that financial, physical & human resources should be made available. If these are not met, the implementation of quality assurance will be difficult or impossible. The proposed model is formulated in as simple terms as possible; pointing out the main components, processes & guidelines.

For this model of quality management to succeed, it is important to ensure leadership commitment at the highest level. The focus on delivery of education and services should be clear and made known to all levels of stakeholders.

Principles for Quality enhancement

- Responsibility: The university takes & maintains a consistent approach to quality and standards.
- Professionalism: The university conducts all business with commitment to objective professional practices
- Commitment: The university is committed to the principles and practices of quality enhancement
- Students' participation: The university values students' involvement in quality enhancement processes.
- Social accountability: The university is committed to its role of social responsibility & community development.

The above principles of Quality Enhancement & Quality Assurance are guided by the following:

1. Regular processes according to a time frame.
2. Objectivity to be enhanced by internal and external assessments.
3. Inclusive participation of staff & students.

4. Comprehensive evaluation of educational programs.
5. Clarity and objectivity of evaluation instruments.

Mission:

“The Quality Management Administration aims at providing a system of comprehensive and inclusive information gathering upon which continued & enlightened quality enhancement decisions are made.”

The above mission statement of QMA can be modified by the institutions according to their own philosophy, vision & perceived goals. It proposes that the main purpose of the unit or administration is quality enhancement through regular monitoring and feedback.

The scope of quality assurance in a HEI:

The following are the main areas that any quality management unit should attend to (table 1) Each of the specified areas includes sub-areas which can be included in the units assessment procedures. It is important to concede, at this juncture, that different quality assurance agencies adopt different framework for the scope of its evaluation.

Table 1: main areas for quality assurance.

-
- Educational programs
 - Research & Graduate Studies
 - Resources
 - Governance
 - Services
-

However, the main areas suggested here are intended to guide the activities, plans & schedules adopted by the unit and are by no means exclusive of others. It is proposed that these areas are to be the main framework for the unit's activities. Each of the main areas will be represented by several subareas or parameters as seen fit by the institution. In

this regard, there are many models that can be used to enrich the unit's scope of evaluation, its methods and channels of communication for quality enhancement.

Documentation: Documentation is an essential requirement for periodic evaluation and preparing for external assessment and accreditation. QMA should make sure that various departments and units maintain rigorous documentation; preferably in both hard and soft forms.

Structure:

The Quality management Administration (or whatever name the institution chooses) should fit in the appropriate position of its organizational structure. If it is a university, then the main unit is part of the university organization chart. In this case, it will be useful for the university to design a common framework for subunits flexible enough to meet the requirements of various university faculties, centres & institutes. If, however, it is a college or specialized institution, the organogram would be simple and fitting within the college or the institute's setup.

1. For instance, in a university the top leadership should be committed & involved. Therefore, a central Quality Management Administration (QMA) body near the top of the organogram should be established with subunits in various subsidiaries of the university (fig.1) In general, QMA acts as the main advisory body to the top academic and administrative management. For this purpose special statutory regulations should be in place.

Internal structure: The QMA internal structure

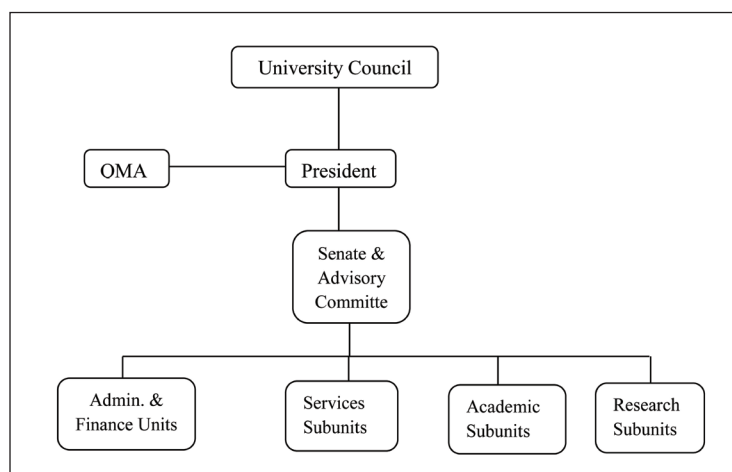


Fig. 1 the Quality Management Administration (QMA) fits near the top pyramid of the university organogram.

should consist of qualified leadership and the supporting staff required for the job.

i. Quality management Committee QMC: This is the internal management body for QMA. Its role would be to lay down programs according to university vision and policies. The committee will also oversee the implementation of the QA procedures according to agreed schedules.

ii. Quality Assurance officer (QMO): This is the leader of the QMA responsible for implementation of all quality assurance policies & procedures. He, or she, should possess the qualifications, personality and ,if possible, experience in quality management.

iii. Supporting staff: Two categories are proposed. For practical purposes the first consists of the full-time staff whose job is to collect data according to schedules or *ad hoc* requirements. The second category includes data entry and analysis staff. The number & qualifications is left to the discretion of the university or college administration. However, it must be pointed out that the minimum requirements should be a BSc or BA with good computer competence. It goes without saying that in all cases appropriate training is a must.

iv. Resources: The above section dealt with the structure of QMA & the human resources.

Now, we deal with essential physical resources. Suitable office accommodation should be provided for the QMO & his staff. Office equipment includes: computers, internet connections (if possible), high capacity digital storage, printers and standard office furniture for the above equipment and personnel. Filing systems must be put in place from the start so that documents can be stored, accessed and used for reporting and decision making.

v. Training: training on quality assurance principles and procedures should be undertaken by competent trainers. The training should not only aim at knowledge; but also attitudes, especially commitment to the need for regular monitoring and feedback. This area of activity of QMA is not only for those involved in the processes but should also target all academic and administrative staff. The objective being to increase awareness and concern on all matters related to quality enhancement.

Processes & Methods:

The choice of processes & methods depends upon the scope and selected parameters. The following is a proposed list divided into two sections: essential and advanced. It will be described taking care of the five main areas of quality management: (academic, research, resources, administrative & services).

To peruse its quality assurance function QMA may adopt the following processes and methods:

Timing	Regular	Periodic	Annual	External
Areas	Courses/modules Skills training Prog. implementation	Program review Graduates programs Research Resources	Courses/Modules HR Administration Finance	Examinations Institutional evaluation
Methods	Students and staff feedback Attendance Schedules maintained	Program evaluation Admin & financial review	Program reports HR reports Admin & financial reports	External examiners M of Higher Educ. Professional bodies International Bodies

Table 1: For each of the above the responsible persons use specified and approved data collection instruments in the time frame set by the Quality Management Administration (QMA). For external evaluation and self-studies parameters adopted by national or international accreditation bodies are used. All assessed parameters should have supporting documents.

Essential subareas.

Educational Programs:

- Program documents
- Course /module documents
- Curriculum committee
- Qualified staff/students ratio
- Students selection regulations
- Methods of instruction
- Examinations regulations
- Educational resources
- External relations
- Community based training
- etc

Research & Graduate Studies:

- Research committee regulations
- Ethical review committee
- Research policy
- Research facilities
- Research support

- Academic staff development
- Graduate studies regulations
- Graduate degree programs
- Publications
- External relations
- Publications.

Resources:

- Academic staff
- Supportive staff
- Lecture rooms
- Scientific laboratories & workshops
- Computer labs
- Skills labs & museums
- Libraries
- etc,

Governance:

- University, college organization chart
- All senior posts & supporting jobs filled with qualified staff
- Appointments, promotion & admin committees
- Financial and accounting regulations & procedures
- International relations services
- Students services (health counseling, sports, catering etc.)
- Computers and informatics service
- Liaison and information services
- Security
- Maintenance dept.
- Transport services

Advanced subareas:

We will not attempt to define these parameters, because there are so many experiences locally and abroad. Each institution can draw upon the literature according to their needs and resources, (-)

Quality Enhancement Framework

A policy of maintaining and improving the quality of programs & academic standards of all awarded degrees should be adopted. Guiding principles are stipulated as follows(table 2):

Table 2 : Guidelines of feedback mechanisms for quality Enhancement

	Internal review	Quality Enhancement	Students Involvement	Social Accountability	External Review
Methods	QA Monitoring and self-assessment	Regular & periodic feedback	Student feedback Students representation	Sensitivity groups Participation of stakeholders	National & international evaluation systems
Standards	Using national & international standards	National higher education standards International good practice	Students community participation International students participation	Inputs from stake holders. Institutional participation in comm. development	National & international accreditation standards

Data gathering tools:

Teaching & learning: This section will focus on data related to the delivery of course material. The importance of this aspect of quality assurance cannot be overemphasized in any educational institution. All learning experiences should have feedback from both students & teachers. The feedback should be

regular and its analysis & dissemination to the parties concerned done in time for remedial action. It goes without saying that some of the feedback may be used immediately; but some may need time e.g revision of a course, training of teachers, or acquisition of new resources.

In all cases, the feedback is used either for

immediate action or for medium- or long-term improvement. A case-in-point is the semester organization of courses. A mid-semester test and filling a feedback form on course material, delivery, resources etc, will be useful; or for remedial action in the short-term as well as for future development.

Ideally, all courses should have a schedule of learning experiences with dates, titles, methods, and the teacher/facilitators responsible for the sessions. Monitoring the delivery of such schedules needs to be arranged so that immediate feedback is possible. Medium- & long-term decisions can also be made based on the collected data. Special forms can be designed for this purpose for easy analysis & reporting .

Program evaluation: As previously stated, this is one of the periodic activities. It is usually based on cumulative experiences during implementation. But it can be undertaken as a comprehensive review. In this case, each component of the educational program needs to be assessed. The evaluation results can be used to report strengths, weaknesses, opportunities and challenges. With an eye on international trends, aspects of program development can be proposed and decisions made.

Student assessment: One of the most important sources of feedback on teaching and learning are the results of students' assessment. Overall performance of classes can be a good indicator. However, it must be emphasized that the methods of assessment and the examination plans (blue prints) are well conceived and evaluated as to allow minimally acceptable performance to be attainable (criterion- referenced rather than norm- referenced standard setting).

Another source of feedback is the external examiner's report. Care should be taken in selecting examiners with relevant experience & reliable reporting. Examiners' reports can also be used to obtain views on the curriculum & discovering the strengths & weaknesses of the program. For this purpose, a special form for

the examiner's report should be designed to get the best of this important method of external assessment.

Table No 2. Tools for data gathering for the area of teaching and learning

-
1. Course module assessment
 2. Course implementation form
 3. Examination results analysis
 4. Exams. item analysis
 5. External examiners report
 6. Program evaluation forms
-

Educational Resources:

These consist of a long list of needs: some essential & some complementary and lend themselves to achievement of excellence. Specifications for each are usually stipulated in rules, regulations of the institution & standards set by higher education authorities and professional bodies.

The QMA should keep records of the above resources & facilities for each program & their utilization. Such records will be useful for internal review, external evaluation & accreditation.

Governance & Finance:

Institutional evaluation or international and accreditation systems at national or international levels have set standards for this area. Therefore, it goes without saying that QMA must keep records and carry-out periodic monitoring of the administrative and financial bodies & their performance. The scope & methods, however, will vary according to the governance policies and arrangements of each institution. Therefore, there is room for selecting parameters based on the above considerations.

Development & Renewal: This is an area of governance and finance indicative of updating and development. Ideally, development should be guided by strategic planning. A unit for strategic planning or, at least, a working

arrangement using existing bodies of the university, should be responsible for strategic medium- and long-term planning with periodic review of progress and decision-making. Continued development and renewal is usually measured over a period of 4 or 5 year for a program or project to be adequately assessed. The evaluation of development and renewal by QMA is best done by keeping regular records & reports on renewals and developments in each of the main areas of the national and international accreditation systems.

It is not difficult to renew and develop in the area of teaching and learning. Innovative methods can be introduced or modified to suit the situation. A lot can be done to promote the effectiveness of teaching and learning without additional resources. This only needs commitment and an open mind to change.

Conclusion:

For an institution of higher education to maintain and enhance the quality of its activity. There is a need for establishment of a unit vested with the authority of monitoring and evaluation, in the structure of various institutions and their internal culture. The mandate proposed in this paper has been left as flexible as possible. Reference to national and international standards has been made wherever details of evaluation are impossible to summarize in this context. It is hoped that the outline of the QMA will be found useful by those who want to establish or develop an existing unit.

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Original Article

Cyclophosphamide versus cyclosporine in children with frequent-relapsing and steroid-dependent nephrotic syndrome in Khartoum State, Sudan

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Abstract:

Background: in children with frequent-relapsing and steroid-dependent (FR/SD) nephrotic syndrome (NS) remission can be achieved with either cyclophosphamide (CPM) or cyclosporine (CSA). Our objective was to compare the efficacy and safety of these agents.

Methodology: Records of all children with FR/SD NS who received CPM or CSA at the Pediatric Renal Unit, Soba Hospital, Khartoum, during the period 2005–2015 were retrospectively reviewed. Main outcomes were: remission rate, relapse rate, and renal outcome.

Results: We studied 82 children with FR/SD NS treated with CPM (59.8%) or CSA (40.2%). Males were 69.5% and females 30.5%. The mean admission age was 5 ± 3.10 years. At 6 months, 77.6% children on CPM and 60.3% on CSA were in complete remission (CR), ($P=0.012$) whereas 22.4% versus 39.4% relapsed respectively ($P=0.012$). At 12 months, 57.5% on CPM and 72.7% on CSA were in CR, ($P=0.013$) whereas 42.5% versus 27.3% relapsed respectively, ($P=0.013$). At 24 months, 16.6% on CPM and 29% on CSA were in CR, ($P=0.030$) whereas 83.4% versus 71% relapsed respectively, ($P=0.030$). The mean number of relapses per 24 months were 1.7 ± 0.86 in CPM group versus 2.2 ± 0.85 in CSA group, ($P=0.72$). Mild complications were recorded in 12.4% of patients on CPM group versus 33.3% on CSA, ($P=0.031$). At the latest follow-up, there was no significant change from basal levels of TWBC, mean serum creatinine, GFR, or BMI, ($P>0.05$ for all parameters).

Conclusion: In children with FR/SD NS, both CPM and CSA were effective and safe in achieving remission with less risk of serious side-effects. However, long-term remission was less stable with both agents.

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Introduction:

About 70% of all children with steroid-sensitive NS (SSNS) will relapse; of whom 60% relapse frequently or become steroid-dependent⁽¹⁻³⁾. Treatment of such children is difficult since prolonged steroid therapy may cause serious side-effects as well as increasing the risk of mortality⁽⁴⁾. A Cochrane meta-analysis showed that in children with SSNS, CPM and chlorambucil reduced the rate of relapse

as compared to treatment with prednisone alone with no significant difference in relapse rate between the two drugs. No difference in efficacy (maintenance of remission) was found between intravenous CPM and oral CPM. CSA was found to be as effective as CPM and chlorambucil. The main concern about CPM is gonadal toxicity, but limitation of treatment to 8 weeks/course (2.5 mg/kg/day) minimizes this

side-effect without greatly increasing the rate of relapse⁽⁵⁾. Limitations of using CSA were the relapse rate and nephrotoxicity⁽⁶⁾. Therefore, it is uncertain which one of the two agents is better for children with FR/SD NS. The objective of this study was to compare the efficacy and safety of CPM and CSA in FR/SD NS.

Patients & Methods:

We retrospectively reviewed the records of all children (age >1-18 years) with FR/SD NS who were treated with oral CPM or CSA and followed-up at the Pediatrics Nephrology Unit, Soba University hospital, Khartoum, in the period between January 2005 to February 2015. We excluded all cases with incomplete records and those with follow-up period <6 months. NS, remission, relapse, FR, and SD were defined according to the International Study of Kidney Disease in Children (ISKDC)^(7, 8). NS: proteinuria >40 mg/hr/m² or urine albumin/creatinine ratio (UACR) >0.2 gm/mmol and hypoalbuminemia <25 g/L ± edema. Steroid-responsive: complete remission (CR) with steroid treatment. CR: proteinuria <4 mg/hr/m² or negative or trace (<30 mg) on Albustix for 3 consecutive days. Partial remission (PR): persistence of urine dipstick proteinuria of 30-100 mg/dl with normalization of serum albumin. Sustained remission: no relapse for at least 6 months. Relapse is: proteinuria ≥40 mg/hr/m² or Albustix +++ for 3 consecutive days after being in remission. Frequent relapse (FR) is 2 or more relapses within 6 months of initial response or 4 or more relapses within one year. Steroid-dependent (SD) is 2 consecutive relapses during steroid therapy or relapse within 14 days after stopping therapy.

Age, gender, height, weight and blood pressure, urine dipstick test for albumin, urine UPCr, hemoglobin, blood urea, serum creatinine, serum calcium and phosphorous and histological patterns were recorded. Treatment protocols and responses, complications, and outcome were also recorded. Renal impairment was defined as serum creatinine above the upper limit of normal for age. Estimated glomerular filtration rate (eGFR) was calculated from

the Schwartz formula⁽⁹⁾. CKD was defined as GFR < 60 ml/min/1.73m² for ≥ 3 months and CKD5 requiring RRT as GFR <15 ml/min/1.73 m²^(10, 11). Hypertension was defined as blood pressure above 95th percentile for age⁽¹²⁾. Following induction of CR with prednisolone, CPM or CSA was started. Oral CPM was used in a dose of 2-2.5 mg/kg/day for 8-12 weeks in maximum cumulative dose of 168/mg/kg¹³. Steroid therapy was tapered and stopped over the next 8 weeks. CSA was given at a dose of 4-5 mg/kg daily for 12 months and gradually tapered and stopped⁽¹⁴⁾. Prednisone is then gradually reduced by 0.15-0.25 mg/kg every 4 weeks to a maintenance dose of 0.25-0.5 mg/kg continued for six or more months. Trough (12-hour) CSA levels were kept between 100-150 ng/ml. Indications for renal biopsy were: significant persistent hypertension, gross haematuria, and renal impairment. Main outcomes measures were: remission rate, relapses rate, complications and renal outcome.

Statistics:

Data was organized into master sheet using the Statistical Package for Social Sciences (SPSS) version 19. Data was presented using frequencies and percentages for categorical variables and means ± standard deviation (SD) for numerical continuous variables. Variables were compared using independent t-test for independent variables. For all statistical analysis P value less than 0.05 was as considered as statistically significant.

Ethical approval:

Ethical clearance was obtained from the Ethical Committee in Sudan Medical Specialization Board and Soba Hospital Research Committees.

Results:

We studied 82 children: 75 (91.4%) with SD NS and 7 (8.6%) with FR NS were included in the study. Males were 57 (69.5%) and females 25 (30.5%). Male to female ratio was 2.3:1. The mean age at admission was 5 ± 3.10 (range 1.2 -16) years. Oral CPM was used for 49 patients (59.8%) and CSA for 33 (40.2%).

Characteristics of CPM and CSA treated groups at initiation of treatment are shown in table 1. There was no statistically significant difference between the two groups except for the mean follow-up period which was significantly longer in CSA group ($P=0.013$). Renal biopsy findings were available in 36 patients (43.9%), showing no predominance of MCD, Table 2. CR, PR and relapse rates at 6, 12, and 24 months in CPM and CSA groups were compared and shown in Table 3. At 6 months: CR rate was significantly higher ($P=0.012$) and the relapse rate was significantly lower in CPM group than CSA group ($P=0.012$). Among the 11 cases who relapsed on CPM, eight had nephrotic proteinuria and three had significant non-nephrotic proteinuria. Among the 13 who relapsed on CSA, three had nephrotic proteinuria and ten had significant non-nephrotic proteinuria. At 12 months: 40 patients on CPM and 33 on CSA presented to follow-up. The CR rate was significantly higher ($P=0.013$) and the relapse was significantly lower ($P=0.013$) in CSA group than CPM group. At 24 months: 30 patients on CPM and 31 on CSA presented to follow-up. The CR rate was significantly lower ($P=0.030$) and

the relapse rate was significantly higher ($P=0.030$) in CPM than in CSA-treated patients. Variables such as age, gender, initial levels of serum albumin, serum cholesterol and serum creatinine, pattern of relapses (FR versus SD) and renal histopathology were not significantly correlated with rates of CR in CPM compared to CSA group ($P=0.328, 0.286, 0.897, 0.112, 0.717, 0.834$ and 0.336 respectively). The mean number of relapses per 24 months in CPM group was 1.7 ± 0.86 and in CSA 2.2 ± 0.85 with no statistically significant difference ($P=0.72$). The renal outcome measures at latest follow-up, as measured by serum creatinine and GFR, did not change from the baseline levels ($P>0.05$ for all parameters) as shown in table 4. Mild complications of treatment were more observed in CSA-treated (33.3%) than CPM-treated (14.2%) patients ($P=0.013$), Table 5. The mean TWBC and BMI did not change significantly from basal levels with either CPM or CSA treatment ($P>0.05$ each).

Table 1: Characteristics (demographic, clinical and biochemical) of the study groups at the start of treatment

Patients characteristics	CPM group (n =49)	CSA group (n =33)	P- value
Male : Female ratio	3.5 : 1	1.4 :1	0.086
Mean age (years)	5 ± 3.05	5 ± 3.23	0.955
Mean Body Mass Index (BMI)	15.89 ± 2.71	16.82 ± 3.09	0.276
SDNS	46(93.9%)	29 (87.9%)	0.340
FRNS	3 (6.1%)	4 (12.1%)	0.340
Serum creatinine	0.58 ± 0.46	0.73 ± 0.39	0.797
Mean GFR (ml/min/1.73m ²)	99.70 ± 40.31	130.01 ± 118.34	0.581
Mean S. albumin (gm/L)	2.48 ± 0.878	2.31 ± 0.60	0.425
Mean S. cholesterol (mg/dl)	342.06 ± 186.00	258.63 ± 68.92	0.169
Hypertension	11(22.4%)	8 (24.2%)	0.850
Mean follow-up (months)	$39.53 \pm 28.79(7-132)$	$56.72 \pm 31.51(15-132)$	0.013*

* P value is statistically significant

Table 2. Renal biopsy findings in the study group, (n = 36)

Histopathology lesion	CPM Group	CSA group	Total
Minimal change disease (MCD)	7 (43.8%)	5 (25.0%)	12
Focal segmental glomerulosclerosis (FSGS)	1 (6.20%)	9 (45.0%)	10
Mesangial proliferative glomerulonephritis (MesPGN)	8 (50.0%)	6 (30.0%)	14
Total	16	20	36

Table 3. Complete remission, partial remission and relapse rates at 6, 12 and 24 months (CMP versus CSA group)

Period of follow up	CPM group	CSA group	P value
At 6 months			
Complete remission	38/49 (77.6%)	20/33 (60.6%)	0.012
Relapse	11/49 (22.4%)	13/33 (39.4%)	
Nephrotic protienuria	8/49 (16.3%)	3/33 (9.1%)	0.012
Significant non-nephrotic protienuria	3/49 (6.1%)	10/33 (30.3%)	
At 12 months			
Complete remission	23/40 (57.5%)	24/33 (72.7%)	0.013
Relapse	17/40 (42.5%)	9/33 (27.3%)	0.013
At 24 months			
Complete remission	5/30 (16.6%)	9/31 (29%)	0.030*
Relapse	25/30 (83.4%)	22/33 (71%)	0.030

* P value is statistically significant

Table 4. The mean TWBC, serum creatinine, GFR and BMI of the study groups (basal versus latest follow up)

Treatment group	Parameter	Basal	Latest follow up	P value
Cyclophosphamide	Mean TWBC	9.93 ³ ±4.15	11.08 ³ ±4.31	0.060
	Mean serum creatinine (mg/dl)	0.58 ±0.46	0.61±0.32	0.782
	Mean GFR (ml/min/1.73m ²)	99.70 ±40.31	90.66±56.89	0.055
	BMI	15.89±2.71	17.10±1.14	0.657
Cyclosporine A	Mean TWBC	11.08 ³ ±4.31	5.53 ³ ±2.19	0.063
	Mean serum creatinine (mg/dl)	0.73±0.39	0.92±1.14	0.797
	GFR(ml/min/1.73m ²)	90.66±56.89	94.79±33.25	0.052
	Hypertension	8 (24.2%)	3 (9.4%)	0.001
	BMI	16.82±3.09	17.19±3.11	0.645

Table 5. Types and frequency of complications in CPM and CSA treated groups

Complications	CPM group n=49	CSA group n=33
Cushinoid appearance	1 (2.0%)	3 (9.0%)
Gingival hyperplasia	0 (0.0%)	2 (6.1%)
Hypertrichosis	0 (0.0%)	2 (6.1%)
Hemorrhagic cystitis	1(2.0%)	0 (0.0%)
Infection	2 (4.1%)	2 (0.0%)
Stunting of growth	3 (6.1%)	2 (6.1%)
Total	7 (14.3)	11 (33.3%)

P= 0.031

Discussion:

In children with frequent-relapsing (FR) and steroid-dependent (SD) nephrotic syndrome (NS) remission can be achieved, and relapse rate can be reduced, with steroid sparing-drugs. These agents are usually prescribed for children who develop adverse side effects from steroid treatment. They in-

clude Cyclophosphamide (CPM), Levamisole, and Cyclosporine (CSA). CPM and Levamisole have been commonly used as first line therapy and CSA as second line for those who continued to follow FR/SD course after the initial therapy. However, many studies showed different results regarding the efficacy and safety of CPM versus CSA (3, 14-19). In Sudan published data comparing these agents in nephrotic children is lacking. We, therefore, conducted this study to compare the efficacy and safety of CPM and CSA in treatment of a population of Sudanese children with SD/FR NS. The demographic, biochemical and clinical parameters of the two groups were well-matched at the initiation of treatment. Our data showed that both CPM and CSA were effective in achieving CR remission (77.6% and 60.3% respectively) in children with SD/FR NS up to 6 months of the start of treatment. At 12 months: the CR was still maintained in 57.5% of CPM group and 77.7% of CSA group. However, at 24 months both drugs had disappointing long-term efficacy as only 29% of CSA- and 16.6% of CPM-treated groups were in CR and the majority relapsed. Studies comparing CPM and CSA showed variable remission rates (17-19). In this study, CPM-achieved CR rate of 77.6% at six months was similar to Rahman et al report (80%) (17). Poniceili et al reported a lower CR rate (64%) at nine months (18). In our study, CPM-achieved CR dropped to 57.5% at 12

months and 16.6% at 24 months. These findings suggest failure of CPM to maintain stable long-term remission. Similar disappointing long-term efficacy with CPM had been reported in other studies^(3, 15) despite the use of a higher cumulative dose of CPM (>170 mg/kg)⁽¹⁵⁾. In contrast, other studies showed better long-term efficacy of CPM treatment with 68-60% of treated children having stable remission at 24 months^(18, 20). These variations in response to CPM could be related to duration of treatment of CPM (8 versus 12 weeks). However, we used CPM in a dose of 2/kg for 8-12 weeks at a cumulative dose of 168 mg/kg as in these studies⁽¹⁸⁾. APN also suggested the benefit of treatment CPM for 12 weeks⁽²¹⁾. Different studies used CSA with different treatment durations: 9, 12 and 24 months^(18, 19, 22) respectively. In general, long-term CSA therapy is recommended. In our study, we tapered CSA after 12 months and, therefore, we achieved a higher rate of remission up to 12 months (72.7%); but that dropped after tapering to 29% at 24 months. Similar higher short-term efficacy, but disappointing, long-term efficacy with CSA: 70% CR at 9 months and 20% at 24 months was reported in Ponticelli study⁽¹⁸⁾. In that study, CSA was tapered after 9 months. However, in studies using long-term CSA therapy, remissions at 12 and 24 months were achieved in 60% and 40% of the children, respectively⁽²²⁾. Other similar studies reported stable remission rate (54%) at two years⁽²³⁾. In this study, there was no significant change in the mean serum creatinine, GFR when basal and latest follow-up values were compared in both treatment groups ($P > 0.005$ for both parameters). The prevalence of hypertension initially reported in CSA-treated group had significantly dropped ($P = 0.001$) on latest follow-up. After two years 36.8% of CPM group and 51.5% of CSA group were shifted to other steroid-sparing agents.

In this study, tolerance to both drugs was generally good. Only mild complications were recorded which were more common in CSA than CPM group. Side effects, like hypertrichosis and gum hypertrophy seen in few patients on CSA, disappeared after drug tapering. Most of the previous studies revealed that these CSA-related complications can be reversed after completion of CSA therapy. However, Hino et al. reported CSA nephrotoxicity in 15% of their patients with SDNS⁽²⁴⁾. Long-term toxicity

of CPM was gonadal toxicity with subsequent risk of infertility mainly in boys. However, results of many reports varied markedly and were sometimes contradicting. Oligo/azospermia may occur with a cumulative CPM dose of 150- 250 mg/kg⁽²⁵⁻²⁷⁾ but azospermia was reversible in some patients in some studies⁽²⁸⁾. There was no definite sperm count that can predict fertile and infertile males⁽²⁹⁾ and no correlation was found between the cumulative dosage of CPM and the risk for sperm abnormalities in other reports⁽³⁰⁾. Few studies in girls and women with FR childhood NS reported a risk for gonadal damage as some menstruating women developed transient amenorrhea with CPM treatment⁽³¹⁾. Other studies reported pregnancies after cumulative doses of 182–525 mg/kg CPM⁽³²⁻³⁴⁾. In a meta-analysis of cytotoxic treatment (CPM versus Chlorampucil) for FR NS in children⁽³⁵⁾, it was concluded that cytotoxic therapy is effective in reducing the need for corticosteroids in many children with SSNS; but the long-term efficacy is still limited and, hence, firm guidelines could not be developed. Repeated courses of cytotoxic therapy should be avoided because of serious side effects. Gonadal toxicity and the risk of malignancies are inbuilt and only partly dose-dependent risks. CPM appears to be the drug of choice and is considered to be safer than Chlorampucil⁽³⁵⁾.

In conclusion: our study demonstrated that both CPM and CSA are effective in achieving remission up to 12 months in children with FR/SD NS. However, long-term remission was less stable with both drugs with the majority of patients being in relapse and needing other therapy. Both drugs were safe and well-tolerated, with no serious side-effects on short-term. Since CPM is safe, cheap, easy to administer and does not require blood level monitoring, we recommend its use as initial therapy for children with SD/FR NS. CSA is reserved for those who continue to relapse after CPM treatment.

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Disclosure:

The authors declare that the research protocol has been approved by Sudan Medical Specialization Board Research Committee and Soba Hospital Research Committees and an informed consent was then obtained. They also declare that the results of this study have not been published before except as abstracts.

Authors contribution:

The authors declare that they all had significant contribution to the study and they all agree with contents of the study.

Conflict of interest:

Authors declared no conflict of interest.

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Voided and washed urine cytology in diagnosis of bladder cancer. Dose it make differences?

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المخلص:

أهداف البحث: لدراسة القيمة التشخيصية لمرضى يعتقد لديهم ورم في المثانة من خلال دراسة عينات أخذت عبر غسيل المثانة والتبول العادي.

طرق البحث: تمت دراسته مستقبليه وصفيه مقطعيه لعدد (٨٦) مريض بمستشفى مدني لأمراض وجراحة الكلي. تم جمع عينات عشوائية من التبول العادي من ٨٦ مريض يعتقد إصابتهم بسرطان المثانة وذلك قبل مسحة الخلايا وغسيل المثانة في الوقت الذي سبق استئصال ورم المثانة. تم الفحص المجهرى لكل من غسيل المثانة والتبول العادي، واعتبر الإختبار المجهرى موجب إذا كانت الخلايا سرطانية أو شبيه لها.

النتائج: تراوحت أعمار المرضى في هذه الدراسة بين ال ٢٥ وال ٩٥ سنة، ٦٢ منهم (٧٢,١٪) زكور بنسبة ٢,٥ الي ١. بالنسبة الي الفحص النسيجي، ٩٠,٣٪ منهم يعانون من سرطان الخلايا الإنتقالي، ٦٤,٥٪ يعانون من سرطان الظهارة البولية عالي الدرجة (من ٢ الي ٣)، و ٤١,٩٪ مصابين بورم المثانة الدرجة الثالثة. الحساسيه للاختبار كانت (٩٣,٥٪) والنوعيه ١٠٠٪ للعينتين على حد سواء لكن الجودة في مسحة الخلايا كانت (٧٩,١٪) في عينات غسيل المثانة و(٣٠,٢٪) في عينات التبول العادي.

الاستنتاجات: وضحت هذه الدراسة الأفضلية لعينات غسيل المثانة عن عينات تجميع التبول العادي، وذلك اعتمادا علي جودة مسحة الخلايا مع وضوح الخلايا وحفظها النوعي عند الفحص المجهرى، وأوصت الدراسة بإستخدام غسيل المثانة علي الرغم من عدم راحة المريض والتكلفة المادية عند أخذ العينة.

Abstract:

Objectives: To evaluate the diagnostic value of voided and washed urine cytology in diagnosis of bladder cancer.

Methodology: This is a prospective, cross-sectional, descriptive hospital- based study conducted at Gezira Hospital for Renal Diseases and Surgery (GHRDS). Random voided urine samples from 86 patients with suspected bladder cancer were collected before cystoscopy and bladder washing at the time of transurethral resection of bladder tumor (TURBT). Each urine and bladder washing were examined microscopically, and the test is considered positive if cells are malignant or suspicious.

Results: The study patients age ranged between 25- 95 years and 62 (72.1%) of the patients were male with a ratio of 2.5:1. According to the histological finding: 90.3% of study cases were having transitional cell carcinoma (TCC); 64.5% were having high grade urothelial cancers (2 or 3), and

41.9 were diagnosed as having bladder tumor grade 3. The sensitivity of both voided and washed urine cytology in the study was 93.5%; specificity 100%; and positive predictive value was 100%. More than 79% of bladder wash-out specimens had an excellent quality with more cellularity and preservation of cells observed in cytological smears, while only 30.2% of voided urine had an excellent quality.

Conclusion: We have demonstrated the superiority of bladder washing over voided urine cytology in terms of excellent quality with more cellularity and preservation of cells in the cytological smears, and recommend its routine use in spite of patient discomfort and the additional cost.

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Introduction:

Urine cytology was popularized by George Papanicolaou in the 1940s as a way to detect and follow-up patients with bladder cancer (BC) ⁽¹⁾. The current standard of care for the primary detection and follow-up of non-muscle-invasive bladder cancer (NMIBC) consists of urethro-cystoscopy (UCS), which is invasive and uncomfortable.

Cytopathological examination of urine is a routine, non-invasive, diagnostic procedure to detect cancers of the urinary tract. Many urine-based tests have been developed, and in general, these tests have a higher sensitivity than cytology, but a lower specificity. Furthermore, urine cytology enables direct microscopic examination of individual urothelial cells and it has shown clinical cost-efficacy when compared with novel tests such as: bladder tumor antigen (BTA), nuclear matrix protein 22 (NMP22) and fluorescence in-situ hybridization (FISH) ⁽²⁾.

The accuracy of urine cytology depends on several factors that are mainly related to: histologic grade of the tumor, the pre-treatment or post-treatment status, the nature of specimen and sampling ⁽³⁾. There are six types of urinary specimens for cytologic analysis, the most common is voided urine. Bladder washing samples are also very frequent samples sent for cyto-pathological examination.

A most common sample from the urinary tract is spontaneous-voided urine. In collecting true voided urine, one should avoid the first morning

specimen and collect the second morning voided sample, since the overnight urine shows different degree of degenerated urothelial cells being exposed to low acid-base balance (pH) of urine throughout the night, and hypertonic environment complicating both morphologic and marker analysis ⁽⁴⁾. True voided urine has the so-called funnel effect: it samples the entire urinary tract system from renal pelvis to ureters, bladder, and urethra. Considering the fact that urothelial cancer is often a field disease, the funnel effect ensures detection of lesions in the entire urinary tract, especially high-grade lesions ⁽⁴⁾.

The bladder washing sample is obtained during or prior to cystoscopy by irrigating the bladder with 5 to 10 pulses of 50 mL of sterile normal saline, which produces a cellular suspension of freshly exfoliated epithelial cells. This specimen is collected before any biopsy sampling. The chief advantages of bladder washings over voided urine are: better cellular preservation, greater cellularity, and less chance of contamination by background debris ⁽¹⁾.

Voided specimens are known to be more specific, and slightly less sensitive, than instrumented specimens. This higher degree of specificity could be explained partly by the absence of the instrumentation-induced reactive changes with the resulting cell clustering, making the interpretation of the cytological findings in voided urine more straightforward ⁽³⁾.

Generally, the specificity of cytology is greater than 90%. The sensitivity for high-grade malignancies of the entire urinary tract and CIS can be as high as 80 to 90% ,while the sensitivity of voided urinary cytology is anywhere between 20 to 50% for low-grade papillary tumors ⁽⁴⁾. There are two main reasons for such low sensitivity: tumor cells of low-grade are not routinely shed into the urine because of their cohesive nature and, probably more importantly, is the fact that low-grade tumor cells may have similar cytomorphology to normal urothelial cells microscopically ⁽⁴⁾.

Bladder cancer is a common adult malignancy at Gezira State, central Sudan, where searching for accurate, non-invasive and cost-effective tests for diagnosis of both primary tumors and recurrences is increasing. The aim of this study was to evaluate the difference of urine collection methods (voided vs. washed) in relation to the urine cytology findings of patients suspected to have bladder cancer at Gezira Hospital for Renal Diseases and Surgery (GHRDS).

Methodology:

1.1. Patients: Samples were obtained from patients who were referred to Gezira Hospital for Renal Diseases and Surgery (GHRDS) with suspicion of bladder tumors and planned for cystoscopy and +/- transurethral resection of bladder tumor (TURBT). Both a voided urine sample and bladder wash-out samples were obtained under aseptic conditions just before and during cystoscopy, respectively. Age, gender and history of smoking were recorded. The cytological findings were registered within the following four categories: atypical or suspicious cells, grade II cells, grade III cells or negative. All the study subjects were notified of the study purposes and objectives and a written informed consent was obtained from study subjects. The study was approved by the Ethical Committee at the Faculty of Medicine, University of Gezira. Subsequently, the proposal was reviewed by the Division of Urology Research Committee for feedback from urologists treating the potential participants. All data were collected anonymously. Each urine and bladder washings

were examined microscopically, and a test is considered positive if cells are malignant or suspicious.

1.2. Voided urine samples: Freshly voided urine samples were obtained upon arrival of patients to the outpatient clinic. The samples were transferred within 30 minutes to the Histopathology Department at Medical Laboratory, University of Gezira, Faculty of Medicine, where the samples were spun, stained with Haematoxylin and Eosin (H&E) and assessed by an expert pathologist. Other smears were air dried and stained with Diff-Quik and MGG stains (Diagnostics GmbH, Germany).

Bladder wash-out samples: Bladder wash-out material was obtained by rinsing the bladder at least twice with 100 ml of saline solution through the flexible cystoscope; the first 15 to 20 ml being discarded, then 25 to 45 ml was collected in sterile container. For uniformity of interpretation, all specimens were assessed by a single pathologist. Staging and grading were done according to the WHO Guidelines, 1973 ⁽⁵⁾.

2.3. Data analysis: The data was coded and entered in an Excel (Microsoft) and then analyzed by using SPSS version 20. The sensitivity of a urine cytology is defined as the percentage of patients with positive tissue specimens obtained via TURBT for whom the urine test was positive (i.e., the "true positives," those who tested positive on the urine cytology divided by those with evidence of disease at tissue specimens). Specificity is defined as the percentage of patients with negative tissue specimens obtained via TURBT in whom the test is also negative (i.e., the "true negatives," those who tested negative on the urine cytology divided by those with no evidence of disease at tissue specimens). P value less than 0.05 was considered significant. The sensitivity and specificity and positive predictive value were calculated by using the formulae:

$$\text{Sensitivity} = \frac{TP}{TP+FN},$$

$$\text{Specificity} = \frac{TN}{FP+TN},$$

Positive predictive value= TP/TP+FP

TP = True positive, FN = False negative, TN = True negative, FP = False positive

Results:

The study included a total of 86 patients confirmed as having bladder tumors, who had both voided urine and bladder washing cytology collected. Their ages ranged between 25-95 years and 62 (72.1%) of the patients were male with a ratio of 2.5:1. The majority of the study subjects are resident in Gezira State, followed by patients coming from Sinnar and the adjacent states. Of the included patients, 90.7% had hematuria, and 55.8% have presented with LUTS and UTI (Table 1).

Cystoscopic examinations were prompted by history of hematuria and/or bladder mass on imaging in patients. All patients had U/S abdomen& pelvis while only three patients had CT abdomen& pelvis. Findings of imaging studies are shown in Table 2.

Cystoscopy and TURBT were performed for all cases (100%). Distribution of the cases according to tumors location on cystoscopy examinations are shown in Table 3. Thirty-one (72.1%) specimens obtained via TURBT were positive for malignancy, while twelve (27.9%) specimens showed benign changes on histopathological examination. Of these, 90.3% of study cases were having transitional cell carcinoma (TCC) according to the histopathology findings (Figure 1). The majority of the tumors detected (64.5%) were high-grade urothelial cancers (2 or 3). The number and percentage of the patients with different tumor grades are shown in Table 4.

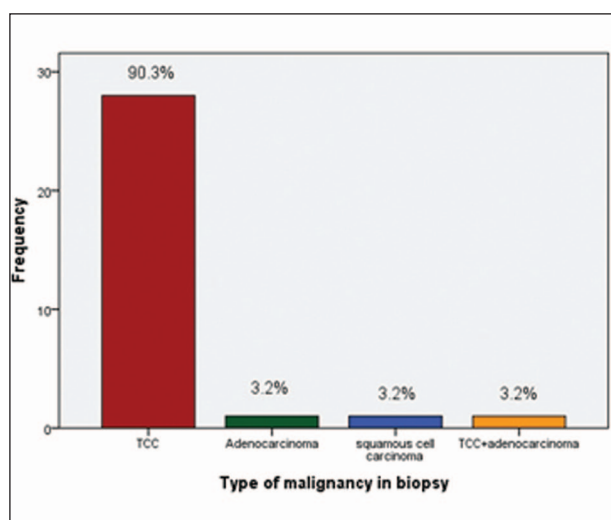
The sensitivity of both voided and washed urine cytology in the study was 93.5%; specificity 100%. Positive predictive value of the test was 100%. In 79.1% of bladder wash-out specimens had an excellent quality with more cellularity and preservation of cells observed in cytological smears, while only 30.2% of voided urine had an excellent quality.

Table 1: Demographic characteristics of patient

Age	Patients (%)	
< 35	24 (27.9)	
35-55	12 (14.0)	
56-75	46 (53.5)	
76-95	4 (4.6)	
Gender		
Male	62 (72.1)	
Female	24 (27.9)	
Residency	Gezira	52 (60.5)
	Sinnar	10 (11.6)
	Gadarif	8 (9.3)
	Khartoum	4 (4.7)
	Aldamazin	4 (4.7)
	Kassala	8 (9.3)
Occupation	House wife	24 (27.9)
	Casual workers	18 (20.9)
	Retired	16 (18.6)
	Farmers	10 (11.6)
	Others	18 (21.0)
Hematuria		
Yes	78 (90.7)	
No	6 (9.3)	
Presence of LUTS		
Yes	48 (55.8)	
No	38 (44.2)	
History of recurrent UTI		
Yes	48 (55.8)	
No	38 (44.2)	

Table 2: Distribution of patients according to findings of imaging studies

Imaging modality	Patients (%)
U/S abdomen& pelvis	
Bladder mass	54 (62.8)
No bladder mass	32 (41.9)
CT Abdomen& pelvis	
Bladder mass	6 (7.0)
No Bladder mass	0
Not done	80 (93.0)

**Fig 1:** Voided versus washed urine cytology in diagnosis of bladder cancer. Types of malignancy in biopsies**Table 3:** Variable sites of masses seen in cystoscopy

Site of mass	Frequency	Percent
Right lateral	2	2.3
Left lateral	22	25.6
Posterior	10	11.6
Dome of the bladder	2	2.3
Anterior	8	9.3
Trigone	4	4.7
Multiple sites	38	44.2
Total	86	100.0

Table 4: The number and percentages of the patients with different tumor grades

Grade	Frequency	Percent
Grade 1 (well-differentiated)	32	37.2
Grade 2 (moderately-differentiation)	18	20.9
Grade 3 (poorly-differentiated)	36	41.9
Total	86	100.0

Discussion:

Urothelial carcinoma (UCa) of the bladder is the most common malignancy of the urinary tract. Urine cytology is widely used in the diagnostic evaluation and surveillance of UCa. The objective of the current study was to evaluate the diagnostic value of voided urine cytology and washed urine cytology in detecting bladder cancers.

Age is the known common risk factor for bladder cancer and a previous study done in Egypt investigated the utility of urine cytology in patients having bladder cancer found that most of them were above 50 years with males affected more than females with no correlation between patients' age and the disease⁽⁶⁾. In this study, 53.5% of study population were above 55 years of age with male being affected more than females.

According to radiological imaging, which helps in detection of bladder tumors, previous studies investigated the utility of urine cytology in patients with high- or low-risk for bladder cancer, showed positive cytology in all patients who had ultra-sonographically suspected bladder lesions. This study showed that 62.8% of all patients had suspected bladder masses detected by ultrasound; 37.8% presented with haematuria with no obvious bladder mass detected by ultrasound. In three cases, CT scan was requested and revealed bladder mass. The accuracy of CT scan was higher in detection of tumor recurrence especially when combined with urine cytology^(2, 6).

In this study, cystoscopic examination revealed bladder mass in all cases. In 31 out of 42 patients (67.4%) had positive urine cytology for malignancy, and confirmed by histopathological examinations. Four percent of the patients who had positive cytology were newly diagnosed and two cases were known patients with bladder cancer on follow-up. Most of the previous studies concentrated on the value of urine cytology in combination with cystoscopy only for follow-up of superficial bladder TCC with high sensitivity of cystoscopy in detection of recurrence ⁽⁷⁻⁹⁾.

In the current study, cystoscopic examinations showed that in the majority of cases tumors were found in multiple sites. Considering the importance of the sites in which bladder masses grow, a previous study found that the percentage of positive cytology was highest in patients with posterior wall lesions, followed by multi-centric lesions ⁽⁶⁾. In contrast, this study showed that 44.2% of patients had multi-centric foci of bladder tumors, most of them had positive cytology and histopathology for transitional cell carcinoma, and it was the commonest site seen by cystoscopy, followed by left lateral and posterior wall lesions.

Ultimately, sensitivity and specificity of urine cytology should be determined as well as positive predictive value. Many studies showed the sensitivity of urine cytology ranged from 29.6-69 % and specificity ranged from 49.2-85% depending on which threshold was used to consider a cytological result as positive ⁽³⁾. A study conducted by Planz et al to evaluate the role of urine cytology for detection of bladder cancers, revealed a sensitivity of 38% and a specificity of 98.3% with a positive predictive value of 90.6% ⁽¹²⁾. Mythri and colleagues evaluated cytological findings in routine voided urine samples with hematuria from a tertiary care center in South India and found that the sensitivity and specificity of voided urine cytology were 98.5% and 74.5% respectively ⁽¹³⁾. The sensitivity of both voided urine and bladder wash-out cytology in this study was 93.5%, and the specificity was 100% and positive predictive value was 100%. The high

sensitivity of urine cytology could be explained by the large number of true positive results and the low number of false negative results. The high specificity was affected by the high number of true negative results with no false positive results, depending on histopathological positivity as the gold standard through which the cytological results are confirmed. Also, the results were affected by the small number of patients selected in the study; they were highly suspected to have bladder cancer.

TCC is the most common histopathological types of bladder cancer in studies carried out in USA and Europe ^(10,11). Other studies reported squamous cell carcinoma of urinary bladder cytologically with more positive results in advanced stages ⁽⁶⁾. Most of the cases of positive cytology in the study were TCC with the same result in histopathology.

The cytology was sensitive in detection of mucinous adenocarcinoma. Conversely, the squamous cell carcinoma which was diagnosed by biopsy, its cytology was negative and only reactive/inflammatory changes appeared in cytological smears. Most probably the severe inflammation obscured the squamoid features and affected the cytology result.

The histological grading of urothelial carcinomas is as important in prognosis and efficacy of treatment. Previous studies utilized cytomorphological characteristics to grade urothelial carcinomas in urine samples and found that cytology was sensitive in both high (G3) and low grade (G1) urothelial carcinoma; highly specific in G3 but not specific in G1. Although failure to identify low- or high-grade malignant cells can occur due to low specimen cellularity, inflammation and blood ^(10, 11).

Urine cytology was highly sensitive in G3 tumors, which represented 38.7% of malignancy in this study. Approximately half of malignant cytological specimens in the study were G1 transitional cell carcinoma. One of these G1 urothelial carcinoma had features of high-grade tumor in cytology; this can be explained by the degree of atypia and the existence of post-inflammatory squamous metaplasia.

Staging of urothelial carcinomas is critical in the assessment of bladder neoplasms and also in the treatment. Studies showed high sensitivity of urine cytology in invasive urothelial carcinomas reaching 100%, with increased sensitivity for non-muscle invasive or early invasive tumors by using FISH test ^(2,11). In this study, urine cytology detected both superficial and invasive carcinoma: 51.6% of positive histological specimens showed muscle invasion. In most of them muscle and lamina propria invasive tumors were detected in cytology.

The method of urine collection had a great effect on accuracy of urine cytology. A study in Germany which aimed at testing the value of urine cytology in diagnosis of bladder cancers, found that there were no significant difference between the sensitivity and specificity of voided and washed urine samples ⁽⁷⁾. Voided urine and bladder wash-out cytology specimens were performed in all patients. In 30.2% of voided urine, specimens had an excellent quality while 79.1% of bladder wash-out specimens had an excellent quality with more cellularity and preservation of cells observed in cytological smears whatever the diagnosis; and it was more sensitive in G1 as well as G3.

Conclusions: The sensitivity and specificity of voided and washed urine were similar. Bladder wash-out specimens had an excellent quality with more cellularity and preservation of cells in the cytological smears.

Limitations:

- Small sample size.
- Histopathology was done in different labs.

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The authors are entirely responsible for the accuracy of all statements and data contained in the manuscript

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Audit in surgery

An Audit on pediatric surgery services at Sinnar Teaching Hospital: outcome and challenges

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مستخلص:

خلفية: المراجعة أمر بالغ الأهمية لتحسين جودة الخدمات الصحية، وكذلك توفير بيانات قيمة للسلطات الصحية. تهدف هذه الدراسة لعكس حجم العمل ونتائجه في وحدة جراحة الأطفال بمستشفى سنار التعليمي كما تلقي بعض الضوء على التحديات والعقبات التي تواجه خدمات جراحة الأطفال خارج العاصمة.

طرق البحث: هذه دراسة وصفية رجعية شملت جميع المرضى الذين حضروا إلى وحدة جراحة الأطفال في مستشفى سنار التعليمي وخضعوا لجراحات طارئة أو باردة في الفترة من يناير ٢٠٠٩ إلى ديسمبر ٢٠١٢.

النتائج: شوهد عدد ٢٤٠٠ مريضاً في الوحدة على مدى أربع سنوات. معلومات خضع نصفهم ١٢١٠ (٥٠,٤٪) لجراحة طارئة أو باردة. حالات الفتاق الأربي وكيس الصفن هي أكثر العمليات الباردة التي أجريت ٤٥٠ (٣٧٪). (استئصال الزائدة الدودية الأكثر شيوعاً في عمليات الطوارئ ١٦٩ (١٤٪). (أربعة وأربعون مريضاً (٢٪) تمت إحالتهم لولايي الجزيرة أو الخرطوم لمزيد من الفحوصات أو للرعاية المتقدمة وكانت الغالبية العظمى من الحالات المشار إليها ممن تستدعي حالتهم خدمات أكثر تخصصاً كطب الأورام أو جراحة المخ والأعصاب، بالإضافة إلى بعض المرضى الذين يحتاجون لتدخلات غير جراحية (كتفتيت الحصى بالليزر على سبيل المثال) أو تلك التي تحتاج إلى تخصصات دقيقة متعددة (المثانة الخارج البطن، إصلاح مجاري البول الدانية). كان معدل الوفيات الإجمالي ٢,٤٪ (٥٢) لوحظ أعلى معدل وفيات في جراحات حديثي الولادة حيث مثلت ٢٠٪ من جميع الوفيات (١٠) وذلك بسبب عدم وجود أطباء التخدير المدربين و وحدة العناية المركزة للأطفال وتأخر عرض بعض الحالات.

الخلاصة: تقديم خدمة جراحة الأطفال خارج العاصمة هو أمر صعب ويواجه عقبات مختلفة، ولكن ممكن مع نتائج معقولة. توجد حالات جراحية (طارئة أو باردة) متعددة ويمكن أن تعالج الغالبية منهم بشكل جيد على مستوى مستشفى الولاية. توفر أطباء التخدير وغرف الرعاية المركزة للأطفال مع تواجد طاقم تمريض مؤهل هو حجر الزاوية لخدمات ذات جودة أفضل مع الحد الأدنى من معدلات المضاعفات والوفيات. إنشاء خدمات جراحة الأطفال في الولايات يقلل دائماً من الازدحام المركزي والإحالة إلى مستشفيات العاصمة، كما أنه يقلل الانفاق غير المبرر والتكلفة على الحالة خاصة بالنسبة للأسر منخفضة ومتوسطة الدخل.

Abstract

Background: Auditing is crucial for improving the quality of health services, as well as providing a valuable data for health authorities. The aim of this study was to reflect the burden and outcome of one pediatric surgery unit at Sinnar Teaching Hospital (STH). It also throws some light into challenges and obstacles that face running of pediatric surgery services outside of the capital.

Methods: This was a retrospective, descriptive review. It included all the patients who presented to the Pediatric Surgery Unit at Sinnar Teaching Hospital (STH) and underwent emergency or elective operations during the period from January 2009 to December 2012.

Results: A total number of 2400 patients were seen at the unit over four years. About half of them (1210) (50.4%) underwent emergency or elective operations. Inguinoscrotal conditions were the most frequently performed elective operations 450 (37%). Appendectomy was the commonest

emergency operation: 169 (14%). Forty four (2%) were referred to Al-Jazeera or Khartoum States for further work-up or advanced care. The majority of the referred cases were those who required more specialized oncological or neurosurgical services, in addition to some patients who needed non-invasive interventions (like ESWL for instance) or multidisciplinary management (bladder exostrophy and proximal hypospadias). The overall mortality rate was 2.4% (n=52) with higher mortality rate noticed among neonatal conditions: 20% of it (n=10) due to lack of trained anesthetists, pediatric intensive care unit facilities, and delayed presentation.

Conclusion: Conduction of a pediatric surgery service outside of the capital is challenging and faces various obstacles, but it is possible with a reasonable outcome. A wide variety of emergency and elective pediatric surgical conditions are seen and the majority of them could be managed properly at a state hospital level. Availability of well-established anesthetic and pediatric intensive care facilities, with trained nursing staff is the cornerstone for better quality services with minimum morbidity and mortality rates. Establishment of pediatric surgery services in the states would invariably decrease the central congestion and referral to capital hospitals. It can also minimize the unnecessary, and indeed, costly expenditure on referral, especially for low- and middle-income families.

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Introduction:

Sinnar State is located on the west bank of the Blue Nile (about 400 km south from Khartoum State). It is bounded from the north by Al-Jazeera State, from the south by the Blue Nile State, from the east by Gadaref State and from the west by the White Nile State. The general surgery services have been provided for decades at the State Teaching Hospital, but the pediatric surgery service was launched in the year 2006. The pediatric surgery unit had started as part of the general surgery department (which has a capacity of 90 beds) and consists of a single surgeon, one or two surgical registrars, two medical officers and eight to ten house officers. The unit's activities consist: of weekly referred clinic, operative theatre, major round, discharge clinic and twice weekly morning sessions. These activities are attended by all unit's staff as well as final year's medical students of Sinnar Medical School. The pediatric surgery unit receives patients referred by pediatricians, general surgeons and medical officers from all over Sinnar State, as well as patients from nearby states: White Nile, Blue Nile States and Upper Nile State (before independence of South Sudan in July 2011). So, it covers a large number of populations from a widespread catchment area. Both emergency and elective services are offered at the unit.

The bulk of the work in auditing surgical services in Sudan was carried out at major teaching, university and tertiary hospitals in the capital with very few published reports which described the surgical services and pattern of operations performed at State's hospitals ^(1, 2). This audit describes the patterns of pediatric surgery conditions at Sinnar Teaching Hospital over a period of 4 years and it also throws some light into challenges and obstacles that face pediatric surgery services outside of the capital. The pattern of these conditions could give a clue to the varieties of pediatric surgery cases in Sudan.

Patients and Methods: This was a retrospective, descriptive, hospital-based review that included all patients who presented to the pediatric surgery unit at Sinnar Teaching Hospital (STH) and underwent emergency or elective operations during the period from January 2009 to December 2012. The referred cases were summarized and the causes of the referrals were reported. Major morbidities and the overall mortality rates were estimated. The statistical analysis was performed by Statistical Package for Social Science (SPSS) version 21.

Results:

A total number of 2400 patients were seen at the unit over four years period. About half of them: 1210 (50.4%) underwent emergency or elective operations (Table 1). The age of patients ranged between 2 days to 18 years with a peak incidence (64%) between 3 months-2 years. Male to female ratio was 1.4:1.

Inguino-scrotal conditions were the most frequently performed operations 450 (37%) (Table 2). Acute scrotal conditions presented as an emergency and represented about 4% (n=14)..

A wide variety of gastrointestinal conditions were seen among various age groups with different presentations. Appendectomies were the most common GI operation 56.3% (n=169) performed. The main associated morbidities after appendectomies were surgical site infection (SSI) in thirty patients (17%) and fecal fistula in two patients). Other GI operations included: colostomies for congenital ano-rectal malformations (ARM) 15.6% (n=47) and Hirschsprung's disease 9.6% (n=29) followed by neonatal intestinal obstruction 12.3% (n=37) and intussusception 6% (n=18). Ano-rectal malformations were observed slightly more among females; although this association was not statistically significant ($P > 0.05$) (Table 3). Neonatal GI surgeries included: laparotomies for atresia, midgut volvulus with mal-rotation and omphalocele repair. Neonatal atresia (n=21), with the jejunum the most common site of atresia (n=10) followed by ileum (n=6) and then duodenum (n=5). A significantly higher mortality rate 27% (n=10) is encountered among neonatal surgeries. Ano-rectal conditions contributed to 6.2% (n=76) of operations (Table 4). The most common was: rectal polyps that were treated by examination under anesthesia (EAU) and excision. Rectal prolapse cases were treated conservatively primarily, or with injection sclerotherapy using hypertonic saline.

Urological operations accounted for 8% (n=97), half of them 51% (n=49) were circumcisions.

Lithotomies for stone disease were the second common pediatric urological operations, followed by distal hypospadias repair (Table 5). Cases of proximal hypospadias, bladder exostrophy and some stones that were candidates for ESWL were referred to Khartoum.

Various congenital or acquired head and neck conditions were also seen and managed 6% (n=73). The cleft lip with/ without palate defects were the most frequent ones followed by dermoid cysts and hemangiomas. Abdominal wall defects were also encountered and constituted about 5% (n=60). Neurosurgery accounted for 3% (n=37) and included spina bifida, hydrocephalus or both. Mycetoma excision was performed also in 5% of all operations (n=60). Other operations included some elective and emergencies conditions are shown in Table 6.

Forty four of patients (2%) were referred to Al-Jazeera or Khartoum States for further work-up or advanced care. The referred cases required more specialized oncological or neurosurgical services, in addition to some patients who needed non-invasive approaches (like ESWL for instance) or multidisciplinary management (ectopic bladder, proximal hypospadias).

The overall mortality rate was 2.4% (n= 52), about one- fifth of them occurred in neonatal surgeries 20% (n=10). These mortalities were due to lack of well-equipped theatres, intensive care services and delayed presentation in some cases.

Table 1. Pattern of operations performed at pediatric surgery unit in Sinnar Teaching Hospital (2009-2012)

Conditions	Frequency	Percentage (%)
Inguinoscrotal	447	37
GIT	300	24.9
Ano-rectal conditions	76	6.2
Urology	97	8
Head and neck surgery	72	6
Abdominal wall defects	60	5
Mycetoma	60	5
Neurosurgery	36	3
Abdominal mass for exploration	12	1
Miscellaneous	48	4
Total	1210	100

Table 2. Types of inguinoscrotal conditions (n=447)

Condition	Frequency	Percentage
Inguinal hernia	161	36.2
Hydrocele	134	30.9
Undescended testis	118	29.6
Acute Scrotum	14	3.3
Total	447	100

Table 3. Sex distribution of the types of anorectal malformations

Anorectal Malformation type *	Male	Female
High	11	17
Low	8	7
Total	19	24

*P>0.05

Table 4. Anorectal conditions

Condition	Frequency	Percentage
Rectal polyp	46	61
Rectal prolapse	17	22
Anal fistula	10	13
Anal fissure	3	4
Total	76	100

Table 5. Pattern of pediatric urological operations

Operation	Frequency	Percentage
Circumcision	50	51
Stone disease	26	27
Hypospadias	13	14
Posterior urethral valve	3	3
Nephrectomy	3	3
Ectopic bladder	2	2
Total	97	100

Table 6. Miscellaneous operations performed

Condition	Frequency	Percentage
Umbilical polyps	19	39
Talipes-Equine Varus (TEV)	12	26
Burn contractures	5	10
Osteomyelitis	5	10
Diaphragmatic hernia	7	15
Total	48	100

Discussion:

There is still paucity in records regarding the magnitude of both general and specialized surgery activities performed outside the center with few reports from Gadarif ⁽¹⁾ and El-Obied ⁽²⁾. Although pediatric surgery services had started early in Sudan, they remain highly centralized and far from the reach of district states. This pattern of pediatric surgery service's distribution is typical of the African continent ⁽³⁾, where more than two-thirds of the populations live in rural areas; families and children with surgical diseases may have to travel long distances to be able to access the services of trained pediatric surgeons ⁽³⁾. Lohfa et al found that more than 90% of pediatric surgeons are practising in tertiary hospitals or centers in major cities ⁽⁴⁾. Moreover, in Sudan, a considerable load of surgical subspecialties in the state/district hospitals is handled by general surgeons ⁽¹⁾. In Gadarif State, about 18.75 % of the total emergency and elective operations were pediatric surgical conditions ⁽⁵⁾.

The pattern of surgical conditions observed in this audit is comparable to the burden of other pediatric surgery units with inguino-scrotal conditions as the commonest elective operations that are usually performed as day-case surgeries ⁽⁶⁾. These multiple varieties of elective and emergency conditions would be extremely valuable with regard to teaching of medical

students and training of surgical residents and nursing staff in both general and pediatric surgery disciplines, completing the borders of the well-proposed "Integrated Triangle" model of health service ⁽⁷⁾. In addition, this large workload was covered by one unit only with a single-handed pediatric surgeon; therefore, augmenting the existing staff with more trained surgeons and anesthetists would help to address the current shortage in manpower.

A relatively high mortality rate among neonatal surgeries (27%) was encountered in this review. The causes could be attributed to many factors. Firstly the lack of standard perioperative settings (most notably competent anesthetists as the conduction and supervision of regional and general anesthesia in our setting - even for difficult neonatal operations - was performed by assistant anaesthetists only) as well as pediatric intensive care units (PICU). Postoperatively, critically- ill patients were discharged into a high-dependency unit that was designed for adult's care where the pediatric care and follow-up were insufficient and greatly compromised. This setting is quite comparable to other African countries where PICUs are non-existent, not only in peripheral state hospitals, but even in major cities' centers ⁽⁸⁾. This lack of PICUs coupled with shortage of appropriate-sized instruments in the operating rooms rendered the achievement of good outcomes challenging ⁽⁸⁾. Additionally, it is well-established that anesthetic deaths are more common in infants and children compared to adults ⁽⁹⁾. Dubowitz et al confirmed the paucity of trained anesthesiologists in low- and middle-income countries in the developing regions ⁽¹⁰⁾. This actually renders major pediatric surgeries that are performed under general anesthesia largely unsafe procedures, especially for neonates ⁽¹¹⁾. Additionally, the delayed recovery from anesthesia in neonates can be associated with hypoxic brain damage with serious long-term consequences. The late presentation to the hospital, particularly for those coming from distant and remote rural areas, was also a significant contributor to this higher neonatal mortality rate. This is fairly similar to other regional countries where the late presentation is

another major challenge facing the delivery of pediatric surgery services, especially neonatal ones, to children in Africa⁽⁸⁾. In fact, more than 95% of births in many parts of Africa take place at home, mostly attended by traditional midwives⁽¹²⁾, who do not usually recognize signs of many life-threatening neonatal conditions. As a result of that, many patients are brought to hospitals several days (or sometimes weeks) with severe fluid and electrolyte deficits, anemia, and sometimes sepsis⁽¹²⁾. In addition, poor transportation means in vast district areas in Sudan worsens the condition.

Although the majority of cases were handled and managed at the state hospital level, some cases were referred for further work-up or for advanced care. The referred cases were those requiring more specialized oncological or neurosurgical services, in addition to some patients who needed minimally-invasive or non-invasive approaches (like ESWL for instance) or multidisciplinary management (i.e. ectopic bladder and DSD).

In conclusion, conduction of a pediatric surgery service outside of the capital is challenging and faces various obstacles, but it is still quite possible with a reasonable outcome. A wide variety of both emergency and elective pediatric surgery conditions are seen and the majority of them could be properly managed at a state hospital level. Availability of well-established anesthetic and pediatric intensive care facilities with trained nurse staff is the cornerstone for better quality services with minimum morbidity and mortality.

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Complementary and alternative therapies for premenstrual syndrome: an exploratory study

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Abstract

Background: Data related to the use of complementary and alternative therapies (CAT) for premenstrual syndrome in the communities is scarce. There is very limited information about complementary and alternative therapies practice among nursing students in Dakahlia governorate, Egypt.

Methods: A descriptive exploratory design was conducted in Dakahlia governorate, Egypt, on all secondary technical nursing schools students to explore the use of complementary and alternative therapies to relieve premenstrual syndrome.

A sample of 1120 students was included. A structured self-administered questionnaire (Arabic language) was used for data collection in the period of March to May, 2014.

Results: Most of the study subjects (87.0%) used CAT to minimize symptoms of premenstrual syndrome. Herbal therapy was the most commonly used as CAT followed by hydrotherapy, changing food types, massage and exercise.

Conclusion: The majority of girls used CAT to minimize PMS. The greater part of students used herbal therapy to relieve their symptoms, followed by hydrotherapy; food Change; massage; and exercise.

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Introduction

Premenstrual syndrome (PMS) can be defined as a recurrent disorder that occurs every month in the luteal phase of the menstrual cycle, and remits with the onset of menstruation. It is characterized by a complex set of symptoms, which include physical, psychological and behavioral changes of varying severity. This can interfere with the lives of girls, as well as their interpersonal relationships⁽¹⁾.

The National Center for Complementary and Alternative Medicine (NCCAM) stated that, "complementary and alternative medicine is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional

medicine". NCCAM categories and examples of these types of therapies have been reported in the literature. Some of these procedures have been widely used and researched, whereas others are relatively unknown in the United States⁽²⁾.

A systematic review was designed by Stevinson, and Ernst to determine whether the use of such therapies was supported by evidence of effectiveness from rigorous clinical trials. Twenty seven randomized controlled trials investigated various complementary and alternative therapies in women with PMS. These included herbal medicine, homeopathy ,dietary supplements , relaxation , massage ,

reflexology ,chiropractic , and bio-feedback . Despite some positive findings, the evidence was not compelling for any of these therapies, due to various methodological limitations. So, no complementary and alternative therapies can be recommended as a definitive treatment for PMS⁽³⁾.

On the other hand, Ghanbari et al conducted a quasi- experimental study to evaluate the effect of aerobic exercises on the severity of PMS in Tehran University of Medical Sciences on 91 volunteer women aged 16-48 years old, with regular menstrual cycle, and without any medical disease, reported that three months of regular aerobic exercises effectively reduced the severity of PMS symptoms⁽⁴⁾. Many girls seek alternative therapies including: herbs, botanical dietary supplements, vitamins and minerals because conventional therapies don't help them, or because they want to avoid the risk of side-effects of hormonal or psychotropic drugs^(5,6).

Maternity nurses play a crucial role as educators and counsellors, especially regarding PMS management.

The aim of this study was to explore complementary and alternative therapies used by nursing technical school students to minimize PMS in Dakhalia, Egypt.

Material and Methods:

Research design:

An exploratory design was used to meet the purpose of the study. The study was conducted at all secondary technical nursing schools (fifteen schools), which are present in Dakahlia governorate, Egypt.

Participants:

All student girls at the fifteen schools with an age range from 14 – 18 years; a pilot study was carried out on 10% of the total sample (124). The researchers selected 10.0% from each school and did not include them in the actual study sample. The total number of students who had PMS was 822 girls. Students who got

married and/or those who suffered from any systemic health problems were excluded.

Data collection:

A self-administered structured questionnaire was used as a tool for data collection. The questionnaire was developed by the researchers (in Arabic language) after review of the relevant literature and Modified Version of Menstrual Distress Questionnaire (MMDQ), designed by Moss⁽⁷⁾ and modified by the researchers and used to assess symptoms that participants experienced in the week before their period.

Content validity for the questionnaire was tested by a group of experts (five experts in nursing academic field). The questionnaire was modified according to the experts' comments and recommendations.

Ethical Consideration:

Ethical approval to conduct the study was obtained from the Faculty of Nursing, Port-Said University. Official permission was obtained from the headmaster of each institute included in the study. Oral consents were obtained from participants after explanation of the purpose of the study.

Data analysis:

The statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 20.0. Qualitative data were described using number and percent. Quantitative data were described using minimum and maximum, mean and standard deviation. Level of significance was at 5.0%. Data were presented using descriptive statistics in the form of frequencies and percentages for qualitative variables, and means and standard deviations for quantitative variables.

Results:

Most of the studied students' (87.0%) used complementary and alternative therapies to minimize premenstrual syndrome. The greater part of the students (97.5%) reported that the herbal therapy was the main CAT they used

to minimize PMS followed by hydrotherapy (75.5%), food change (60.1%), massage (49.7%), exercise (43%), fixed oils (5.7%), prayers (4.2%), aromatherapy (3.1%), and others (rest / sleep and hot apostasy) (0.6%).

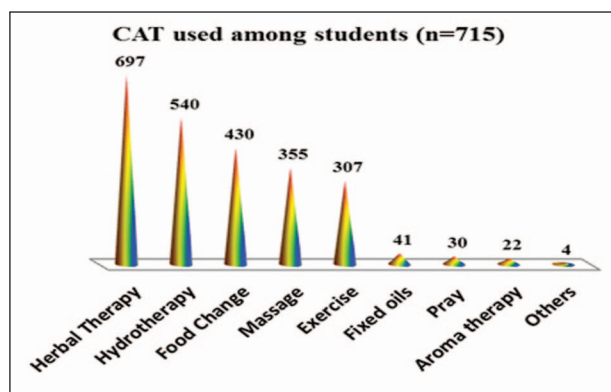


Fig 1. The different CAT used by students to reduce PMS symptoms (n = 715)

Table 1. Common types of CAT used by nursing students to reduce PMS symptoms (n= 715)

Types of CAT No.	Nursing students =715	
	No.	%
Herbal Therapy*	697	97.5
Aniseed	475	68.1
Tea	218	31.3
Cinnamon	182	26.1
Fenugreek	299	43.0
Orchid	63	9.1
Peppermint	370	53.1
Treatment using Fixed oils*	41	5.7
Corn oil	8	19.5
Olive oil	28	68.3
Sesame oil	3	7.3
Hydrotherapy*	540	75.5
Warm bath	479	88.7
Warm water on lower abdomen/ lower back	102	18.9
Cold bath	26	4.8
Food change*	430	60.1

Low intake of food and beverages containing caffeine, cola, and chocolate	311	72.3
Low intake of sweets	157	36.5
Limitation of salty food	179	41.6
Green leafy vegetables and foods containing vitamin B6	236	54.9
Exercise*	367	51.2
Abdominal exercises	76	20.7
Back exercises	26	7.1
Breathing exercises	58	15.8
Walking exercises	218	59.4
Massage*	355	49.6
Abdominal massage	316	89.0
Back massage	71	20.0

*More than one answer

Table 2. Time during which students used a CAT, reasons and its effects on PMS relief (n= 715).

Items	Nursing students (715)	
	No.	%
Time of use (n = 715)		
Pre-menstruation	16	2.2
During menstruation	450	63.0
Pre & during menstruation together	249	34.8
Reason for using *		
Available at home	330	46.2
Cheap	47	6.6
Better than pharmacological	316	44.2
Effective	333	46.6
No side effects	293	41.0
Effect of its use*		
Overall improvement	661	92.4
No improvement	54	7.6

*More than one answer

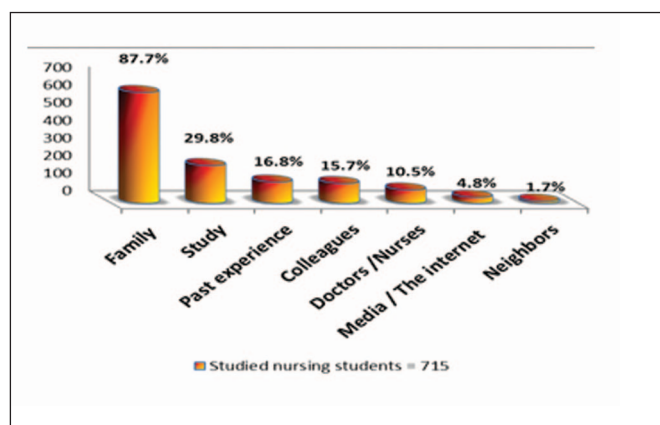


Fig 2. Sources of knowledge for the use of CAT

Table 3. Degree of PMS and types of CAT (n = 715)

Types of CAT	Degree of PMS				X ²	MCP
	Mild PMS	Moderate PMS	Strong PMS	Severe PMS		
	(n = 386)	(n = 250)	(n = 77)	(n = 2)		
	%	%	%	%		
Herbal Therapy	97.4	97.6	98.7	50.0	7.322	0.074
Fixed oil	3.5	6.0	10.1	0.0	7.443*	0.049*
Hydrotherapy	74.6	76.0	79.2	50.0	1.851	0.575
Food Change	59.3	60.0	64.9	50.0	1.192	0.800
Exercise	39.9	43.6	57.1	0.0	8.879*	0.023*
Massage	47.7	51.2	54.5	50.0	1.826	0.684

#others (rest/sleep and hot apostasy) X²: value for Chi square MC: Monte Carlo test *:

Statistically significant at $p \leq 0.05$

Discussion:

The aim of this study was to explore complementary and alternative therapies used by nursing technical school students to minimize PMS. In this study, the prevalence of PMS was 73.4% as measured by (MMDQ). This is in agreement with Seedhom et al., who reported that the prevalence of PMS was 80.2% among 253 unmarried female students at El-Minia University ⁽⁸⁾. Also, the results of the current study is in agreement with Mohamed et al., who found that the prevalence of premenstrual syndrome among females in the child bearing period in Alganaen Village (Suez Canal), Egypt,

was 80.8% ⁽⁹⁾. Moreover, the current results are close to the findings of Ibrahim et al. who reported that 80.0% of students suffer from PMS at the Faculty of Nursing, Ain Shams University ⁽¹⁰⁾.

Most of the students (87.0%) who participated in the current study, and were suffering from PMS, used complementary and alternative therapy to minimize premenstrual syndrome. The same findings were reported by Yassin, who stated that more than three quarters of the study subjects had experienced PMS; of these, 72.7% of them used herbal remedy for treatment of PMS ⁽¹¹⁾.

The current study finding is not in line with those reported by Ibrahim et al. who indicated that the most previous methods used to relieve PMS were analgesic drugs with music, antispasmodics with light therapy, and light therapy with calcium (28.1%, 21.3%, & 19.2%) respectively ⁽¹⁰⁾.

In the present study, the majority of students used herbal therapy (97.5%) to minimize premenstrual syndrome symptoms. The most common herbs used were: aniseed (68.1%), peppermint (53.1%), and fenugreek (43.0%). According to Howland, herbal remedies are one of the most prominent forms of complementary and alternative treatment used in the treatment of depression and anxiety, as well as sleep disorders ⁽¹²⁾.

Other workers reported that fenugreek was the most common herbs used to manage menstrual disorders followed by peppermint and aniseed ^(11, 13).

Das stated that, systemic symptoms of dysmenorrhea (fatigue, headache, nausea, vomiting, lack of energy) improved in the fenugreek seed group ($p < 0.05$). No side effects were reported in the fenugreek group. Also, due to its estrogen-like properties, fenugreek helps to lessen the effect of hot flushes, mood fluctuations which are common symptoms of PMS ⁽¹⁴⁾.

In the present study, the results showed that 4.3% of students used ginger to minimize PMS. Khayat et al. evaluated the effect of ginger on the severity of symptoms of PMS. They reported that, ginger was effective in reducing the severity of the physical and behavioral symptoms of PMS and they recommended its use as treatment for PMS ⁽¹⁵⁾.

Studies are very scanty in this field. Further studies should be conducted to determine the efficacy of different types of herbal therapy on PMS.

Conclusions:

The majority of girls used CAT to minimize PMS. The majority of students used herbal therapy to relieve their symptoms, followed by hydrotherapy; food Change; massage; exercise; fixed oils; and aromatherapy. The main sources of the girls' information about CATs were: their family.

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Case report

Post-malaria Myasthenia Gravis:

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Abstract:

We report a nine-year-old girl who presented with complete drooping of the left eyelid and restriction of medial gaze following an attack of febrile illness. The child was admitted into a rural hospital where she was misdiagnosed and managed as a case of meningitis. She was referred to a tertiary children hospital when her condition was not improving and where she developed the eye signs. She was diagnosed as a case of severe malaria which responded well to quinine therapy. In our neurophysiology clinic, examination revealed partial unilateral left eye ptosis, weak frontalis, neck flexors, fingers extensors & knee flexors. Her investigations revealed positive neostigmine test, decremental response to repetitive nerve stimulation (-15.6%, nasalis), increased jitter in single-fibre electromyography (left frontalis & extensor-digitorum communis) and negative serology for myasthenia gravis antibodies. She showed remarkable improvement after pyridostigmine therapy which continued for three months. Regular follow-up showed no recurrence of her symptoms.

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Introduction:

Myasthenia gravis (MG) is an autoimmune syndrome caused by failure of neuromuscular transmission, resulting from binding of autoantibodies to neuromuscular junction (NMJ) signaling proteins which include the nicotinic acetyl choline receptor or, less frequently, a muscle-specific tyrosine kinase, LRP4 and agrin.⁽¹⁻³⁾ The hypothesis of molecular mimicry has been proposed as a pathogenic mechanism to explain possible connection between infections and immune-mediated diseases.⁽⁴⁻⁸⁾

Extensive review of the literature revealed cases of MG following viral infections.⁽⁹⁻¹⁵⁾ This case, to the best of our knowledge, is the first reported case of MG following malaria infection.

Case History:

We report on a nine-years-girl admitted to a rural hospital with high grade fever, headache and mild neck stiffness. There was no photophobia or signs of increased intracranial pressure (ICP), no convulsions or loss of consciousness. She has been treated there empirically for the

suspicion of meningitis. She was then referred to a specialized tertiary children hospital in the capital city Khartoum when her condition showed no improvement. She was properly investigated and the diagnosis of meningitis was excluded. She was diagnosed as a case of severe malaria infection which was confirmed by a positive blood film for plasmodium falciparum malaria with heavy parasitaemia and positive immune-chromatographic test (ICT). Complete blood count (CBC) was normal, showing normal total and differential WBC counts. During her stay in hospital, she developed complete drooping of the left eyelid with restriction of the gaze medially. No generalized fatigue, limb weakness or bulbar involvement. There was no history suggestive of recent viral infections or immunization. She responded very well to quinine therapy, but her eye signs improved partially. When she was referred to our neurophysiology clinic, re-examination revealed no papilledema, partial unilateral left eye ptosis (positive fatigable ptosis), weak frontalis, strong orbicularis oculi

& no ophthalmoplegia. Limb muscle bulk, strength and reflexes were normal except for mild weakness of neck flexors, fingers extensors & knee flexors (power grade 4). She showed dramatic complete response to intramuscular neostigmine. Repetitive nerve stimulation (RNS) studies at three Hz of the left facial nerve/nasalis showed decremental response of (-15.6%) as shown in figure 1. Single fibre electromyography (SFEMG) test was performed, using voluntary activation technique and concentric needle electrode. Mean jitter was increased in left frontalis (36 μ s) [figure 2] & left extensor digitorum communis/EDC (38 μ s) [figure 3] but normal in left Orbicularis Oculi (28 μ s). Acetylcholine receptor (AChR) & muscle-specific tyrosine kinase (MuSK) antibodies were negative. She has been treated with pyridostigmine 30 mg qds. Seven days later, she showed remarkable improvement. She was almost back to normal [figure 4]. She was doing well on regular follow-up for 6 months. There was no recurrence of her symptoms following discontinuation of pyridostigmine therapy.

Discussion:

MG can occur at any age. The male-to-female ratio in children with MG is 1:5.⁽¹⁶⁾ It is estimated that between 10%-15% of the cases of myasthenia occur in the pediatric population.⁽¹⁷⁾ Malaria is a common parasitic disease caused by a protozoan from the genus 'Plasmodium' of which there are four human species: *Plasmodium vivax*, *Plasmodium falciparum*, *Plasmodium ovale* and *Plasmodium malariae*. Several neurological complications are associated with complicated and severe *falciparum* malaria. Cerebral malaria is one of the most serious complications. Children are particularly more vulnerable to have this complication.⁽¹⁸⁾ *Falciparum* malaria affects both young and old persons, but children are particularly at risk.⁽¹⁹⁾ A wide spectrum of neurological complications have been described in some malaria cases including: spinal cord and peripheral nerve involvement (mono-neuritic syndromes, trigeminal neuralgia, retro-bulbar optic neuritis, involvement of ulnar, circumflex

& lateral popliteal nerves) as well as transient muscle paralysis resembling periodic paralysis.^(18,20) Some studies reported cases of Guillain-Barre-type polyneuropathy following *vivax* or *falciparum* malaria.⁽²¹⁻²³⁾

Our case was a nine-year-old female with *Plasmodium falciparum* malaria who developed symptoms and signs of MG, few weeks following malaria infection. Clinical examination and electrophysiological studies confirmed the diagnosis of myasthenia, which was not previously reported in *Plasmodium falciparum* malaria cases. Viruses are commonly cited as triggers for autoimmune diseases. A previous study raised the possibility of viral infection as etiological factor for myasthenia gravis and described five myasthenic patients, whose symptoms began a few weeks after a proven viral infection.⁽⁹⁾ In addition, two cases of post-infectious myasthenia gravis were reported by Felice and colleagues in 2005⁽¹⁰⁾; a five year old boy who developed oculo-bulbar weakness two weeks following a varicella-zoster infection and a four-year-old boy who developed facial diplegia and dysarthria several weeks following a viral pharyngitis. A third case was reported in 2007 by Saha et al representing the youngest, and second reported, case of post-varicella myasthenia gravis.⁽¹²⁾ Additional cases of anti-MuSK myasthenia gravis associated with Epstein-Barr virus⁽¹¹⁾ or HIV infections⁽¹³⁾ had been reported. Another recent report described a case of anti-MuSK myasthenia gravis associated with acute hepatitis E infection (HEV) in a young, immune-competent patient in France, suggesting a potential role of HEV infection as a trigger of autoimmune disorders.⁽¹⁴⁾ Another study reported six cases of seropositive myasthenia gravis (MG) developing several months after infection by West Nile Virus (WNV), all of them had elevated acetylcholine receptor (AChR) antibodies, and one had thymoma.⁽¹⁵⁾

The diagnostic sensitivity of the three laboratory tests [serum anti-acetylcholine receptor antibody (AChR-ab) assay, the RNS test, and the SFEMG] for MG, which was compared in 120 patients showed that SFEMG

was the most sensitive test, being abnormal in (92%) of cases, followed by the RNS test (77%) and the AChR-ab assay (73%).⁽²⁴⁾ The American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) has developed guidelines for electrodiagnostic testing for evaluation of MG.⁽¹⁾

Anti-AChR antibodies are detectable only in 80%–90% of generalized MG patients and 30%–50% of ocular MG patients.^(1,25,26) The Anti-MuSK autoantibody is positive in about 30–40% of patients with negative antibodies to the AChR. About 5% of MG patients have neither anti-AChR nor anti-MuSK antibodies⁽¹⁾, similar to the findings in our patient.

The amplitude of the compound muscle action potential (CMAP) elicited by repetitive nerve stimulation is normal or only slightly reduced in patients without MG; while the amplitude of the fourth or fifth response to a train of low frequency nerve stimuli falls at least 10% from the initial value in myasthenic patients. This decrementing response to RNS is seen more often in proximal muscles, such as the facial muscles, biceps, deltoid, and trapezius than in hand muscles.⁽²⁷⁾ The repetitive nerve stimulation is the most commonly used method in electrophysiological diagnosis of MG. The test sensitivity is (80%–90%) in generalized MG patients and (30%–50%) in ocular MG patients.

⁽¹⁾ SFEMG needs more patient cooperation and all of the methods (voluntary and axonal micro-stimulation) are technically demanding.⁽²⁷⁾ However, SFEMG has the highest sensitivity (95%–99%) and excludes the diagnosis of MG when it yields normal results.⁽¹⁾ It selectively records action potentials from a small number (usually two or three) of muscle fibers innervated by a single motor unit using either a standard single fiber electrode or a concentric needle EMG electrode with the smallest recording surface.⁽²⁷⁾ The amount of ACh released at the NMJ at different times has a small variability, resulting in comparable variations in the rise of end-plate potential (EPP) and the muscle fiber pair inter-potential intervals. This variability in successive inter-potential intervals is expressed

using the mean consecutive difference (MCD), referred to as the ‘jitter’, is highly sensitive to neuromuscular transmission abnormalities. When there is a disorder of the NMJ, this will affect the time taken to depolarize the muscle fiber and there will be an increased variability resulting in an increase in jitter. And if the disorder is severe, there might be a complete failure of transmission down one nerve branch of the pair under study and the impulse will be blocked. In competent hands it is very accurate and should, perhaps, be considered as the gold standard in the diagnosis of the disorders of the NMJ.⁽²⁸⁾

According to Myasthenia Gravis Foundation of America (MGFA) clinical classification⁽¹⁶⁾, our patient belonged to Class II which is a mild disease that is characterized by ocular muscle weakness of any severity, in addition to mild weakness affecting other than the ocular muscles (e.g. forearm extensors). In our patient, the decremental response of (–15.6%) in the amplitude of the fourth response (CMAP) compared to the initial value in the Nasalis muscle was highly diagnostic (>10% cut off value) and specific as RNS has very high specificity in the diagnosis of MG.⁽²⁹⁾ In addition, the results of the highly sensitive SFEMG test of increased jitter in Frontalis and EDC muscles, confirmed that the NMJ in this case was abnormal.

The dramatic response to pyridostigmine in our patient probably reflects a mild reversible pathology which resolved with treatment of the primary trigger. The excellent response to acetylcholine esterase inhibitors treatment was also noticed in other post-viral MG cases^(10, 12) suggesting that post-infectious MG is a relatively mild condition, and if diagnosed correctly, and treated promptly, the patient can lead a good quality life with self-recovery over a span of a few years.

Conclusions and Recommendations:

In our case, interpreting the clinical manifestations with the electrophysiological and laboratory investigations, confirmed

malaria as the predisposing factor for the development of MG. However, this case report necessitates further detailed immunological studies that would document sequence homology between proteins involved in signaling at the neuromuscular junction (e.g. AChR) and plasmodium parasites so as to support a possible connection between malaria and myasthenia gravis.

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Fig 1: Repetitive nerve stimulation (RNS) of left Nasalis Muscle

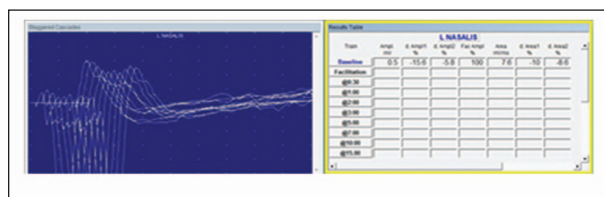


Fig 2: Voluntary-SFEMG of left Frontalis Muscle

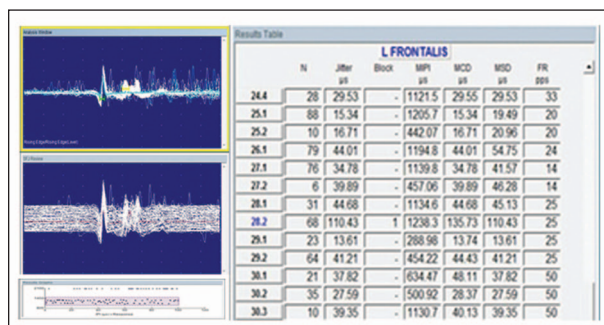


Fig 3: Voluntary-SFEMG of EDC Muscle

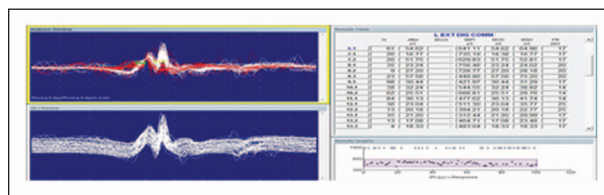


Fig 4: Photographic appearance of the patient's eye lids before and after treatment



Legends of the Figures

Fig 1: Repetitive nerve stimulation of the left Nasalis muscle showing a decremental response of -15.6%

Fig 2: Voluntary-SFEMG of left Frontalis muscle showing increased jitter

Fig 3: Voluntary-SFEMG of EDC muscle showing increased jitter

Fig 4: Partial left upper eye lid drooping before treatment with pyridostigmine

(a). Complete recovery of the left upper eye lid drooping one week after starting treatment with pyridostigmine

(b). Complete recovery of the left upper eye lid drooping one week after starting treatment with pyridostigmine

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

Reference on-line

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

Book on the Internet

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

Internet homepage/website

Cancer-Pain.org [homepage on the Internet]. New

York: Association of Cancer Online Resources, Inc.; c2000-01 [updated 2002 May 16; cited 2002 Jul 9]. Available from: <http://www.cancer-pain.org>.

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