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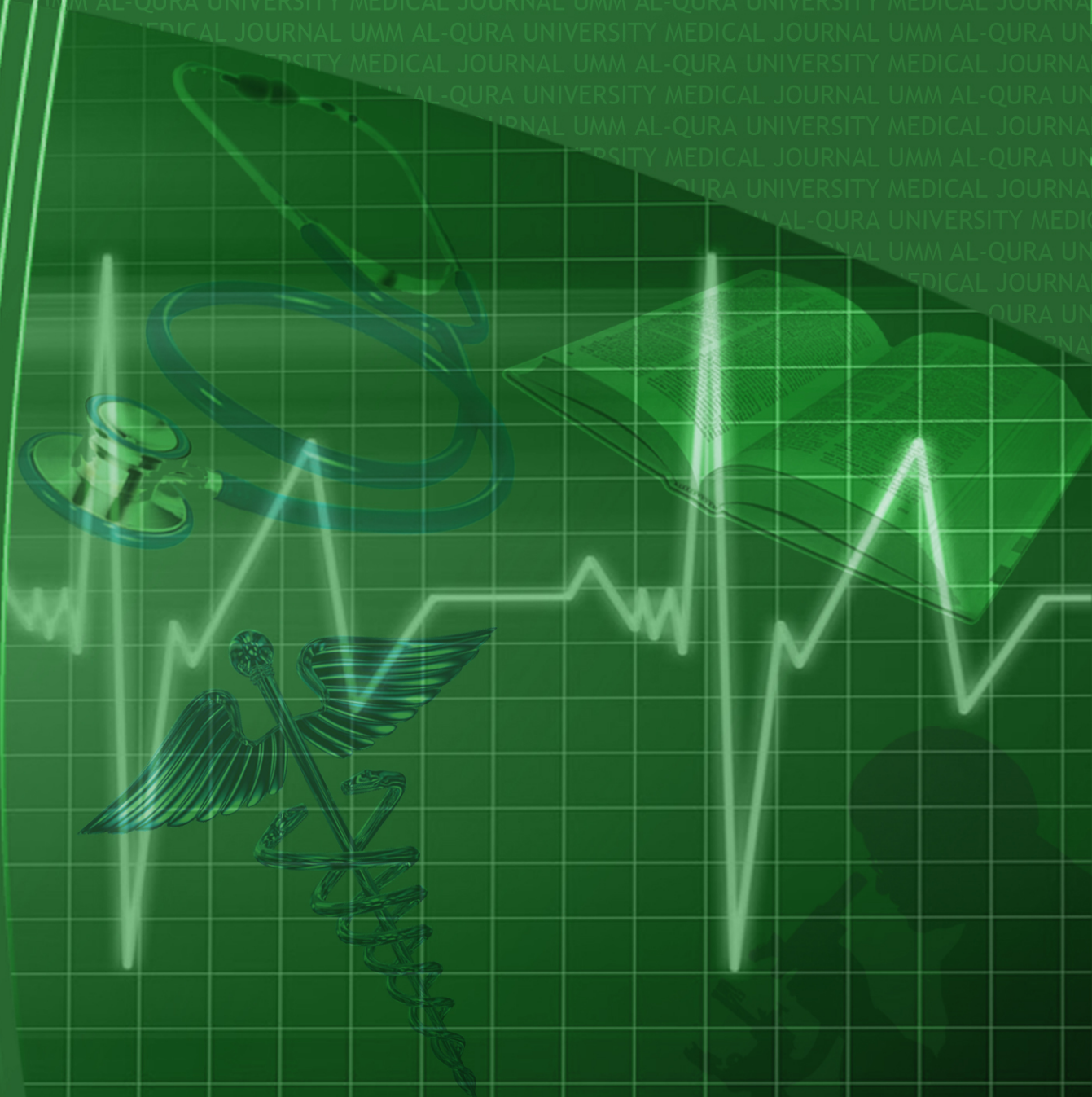

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UQU Medical Journal

Original Article

Ultrasound of knee osteoarthritis

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إستخدام الموجات الصوتية في تشخيص خشونة مفصل الركبة الرومتيزمي

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الملخص

خلفية البحث وأهدافه : الصور الأشعاعية هي تقنية التصوير الرئيسية في الممارسة السريرية اليومية لتقييم مرضى خشونة مفصل الركبة الرومتيزمي وذلك نظرا لسهولة عملها وقلة تكالفيها باضافة إلي إمكانية مقارنة نتائجها. وللموجات فوق الصوتية ميزتها الفريدة كونها لا تعرض المريض إلي الإشعاع مع سهولة إستخدامها وإمكانية معاينة وفحص الغضاريف والانسجة اللينة والعضلات.و بالرغم من ذلك,فان استخدام الموجات فوق الصوتية في المملكة العربية السعودية لمثل هذة الحالات محدود.تهدف هذه الدراسة إلي استخدام الموجات فوق الصوتية لمعاينة الملامح المختلفة لخشونة مفصل الركبة الرومتيزمي ومقارنتها بالصور الاشعاعية.

الطريقة: تم دراسة ستين مريضا يعانون من خشونة مفصل الركبة الرومتيزمي ووجد أن 47 مريضا من ستين يعانون من ضيق في مفصل الركبة حسب نتائج الصور الإشعاعية، بينما تم إكتشاف جميع المرضى بالموجات فوق الصوتية حيث وجد تهالك في الغضروف المفصلي في جميع المرضى. تم اكتشاف وجود سائل مفصلي في 17 مريض بينما تم اكتشاف خمس حالات فقط بالصور فوق الأشعاعية.كما تم اكتشاف تورم الغشاء المفصلي السميك بالموجات فوق الصوتية في 7 حالات بينما لم يتم إكتشاف اي من هذة الحالات بالصور الاشعاعية.

اكتشفت الصور الاشعاعية 54 حالة من الزوائد العظمية المصاحبة لمرض خشونة مفصل الركبة الرومتيزمي بينما تم اكتشاف 52 حالة. وجدت الموجات فوق الصوتية تحسنا في تجمع السائل المفصلي في 8 حالات من عشرة تم علاجها بواسطة العقاقير المضادة للالتهاب غير الستيرويدية بينما اختفى السائل المفصلي تماما في حالة واحدة ولوحظ عدم تحسن في حالة واحدة فقط.

الخلاصة:

الموجات فوق الصوتية مفيدة جدا في الفحص المبكر لمرضي خشونة مفصل الركبة الرومتيزمي حيث أنها تستطيع المساعدة في الاكتشاف المبكر للمرض وذلك بمعانية الغضروف المتمفصل وزيادة سائل مفصل الركبة وكذلك معاينة التورم الناتج عن المرض في الغشاء المفصلي السميك و إمكانية معاينة الزوائد العظمية. كل ذلك بالاضافه الى سهولة عملها وعدم وجود الاشعاع الذي قد يضر بالمرضى, مما يؤهل هذا الفحص ليكون من الفحوص الاولية التى تجرى لمرضى خشونة مفصل الركبة الرومتيزمي.

ABSTRACT

Background: Radiography is the main imaging technique in daily clinical practice for the evaluation of patients with osteoarthritis (OA), owing to its accessibility, low cost and reproducibility. Ultrasound (US) imaging has unique advantages in that it involves no ionizing radiation, is easy to use and visualizes soft tissue structures. However, musculoskeletal US is relatively underused in Saudi Arabia. The aim of this study was to use US imaging in the detection of different features of knee OA.

Methods: In sixty patients with OA, clinical assessment of both knees was performed by the rheumatologist. Weight-bearing anteroposterior and lateral knee radiographs were done. US examination of the knees was done for all patients under study. Comparison between the US and plain radiographs was performed. US follow-up after three months on patients with acute flare of their OA after management with NSAIDs was also performed and compared with their prior US.

Results: Sixty patients with degenerative OA were studied; **47/60** showed narrowing of femero-tibial (FT) articulations seen by X-ray, while all were detected by US as articular cartilage destruction. **Seventeen** cases had synovial effusion elicited by US, while only five were seen by plain radiography. Seven cases showed synovial thickening, while none was identified on plain radiography. However, as regards osteophytes, radiographs detected **54** cases while US elicited **52** cases. Ten patients were treated with NSAIDs for three months, eight of whom showed significant improvement to minimal effusion, **one case** fully resolved, while one case showed no improvement.

Conclusion: Ultrasound is a useful tool that has been demonstrated to be more sensitive than clinical examination and radiography. Ultrasound also allows broad assessment of structural damage and lesions. It is able to detect the presence of inflammation within the joints and at the peri-articular soft-tissue level. Substantial agreement was observed between ultrasound and radiographs for presence of osteophytes.

INTRODUCTION

Osteoarthritis (OA) is a degenerative and progressive joint disease that causes physical inactivity and impaired quality of life and whose frequency is increasing. OA most commonly affects the elderly population, where 70% of those affected are over 65 years of age. OA is considered a multifactorial disease in which numerous risk factors are involved, including advanced age, female gender and mechanical factors (trauma, overuse, articular malposition or malformation, joint instability, occupational and sport activities). Genetic predisposition, inflammation, obesity and endocrine disorders (diabetes, hyperuricemia) are also included. In particular, the increased prevalence of obesity is associated with the rise of OA, especially knee OA in women. The typically affected joints are the knees, hips, lumbosacral spine, neck, feet and hands. Clinically, OA is characterized by pain, morning stiffness (lasting less than 30 minutes), functional limitation and crackles. The joint structures involved are articular

cartilages, bone and the synovium. Most commonly, abnormalities are represented by articular cartilage breakdown, osteophytes at the joint margins, subchondral sclerosis and subchondral cysts, ligamentous contractures and relaxation, muscle atrophy and spasm, in addition to morphological alterations of the synovium[1].

However, OA remains a poorly understood disease. Over the last few years, imaging techniques have become more sophisticated, especially with advances in magnetic resonance imaging (MRI) and ultrasound technologies. Although the use of MRI and other imaging techniques allows the detection of early cartilage fibrillation and defects not seen on conventional radiography (X-ray), several studies have demonstrated that X-ray remains the mainstay of imaging in OA owing to its accessibility, low cost and reproducibility [6,9].

Ultrasound examination may be considered useful in OA assessment owing to its low cost, short duration of examination, and the possibility of performing a multiregional joint evaluation in the same scanning session. This technique allows various anatomical structures to be depicted in fine detail, thus it is considered a promising imaging technique for OA evaluation. Ultrasound has the advantage over MRI in that it is cheaper, convenient, easier to use, dynamic and has no contra-indications to its use [2]. Ultrasound involves no radiation and can obtain views in multiple planes. It can also visualize soft tissue structures like the menisci and cartilages, which are known to be involved in the pathophysiology and progression of OA [3].

OBJECTIVE

The aim of this work is to demonstrate the role of ultrasound in the detection of different features of knee OA.

MATERIAL AND METHODS

This current study was carried out at the departments of radiology and orthopedic surgery Umm Al-Qura University (UQU). This study included 60 patients. All patients attended the outpatient rheumatology clinic of UQU . There were 35 women and 25 men, all with a history of OA. with a mean age of 52 year. A written informed consent was obtained from each patient before participation. Clinical assessment of both knees was performed by the rheumatologist. Weight-bearing anteroposterior (AP) and lateral knee radiographs were done. US examination prior to treatment with NSAIDs was compared to the knee radiographs for each patient involved in the study. Ten patients, who were in severe acute flare and were treated with NSAIDs for three month, underwent US examination of their affected knees at the end of treatment.

All patients were subjected to the following:

Clinical assessment

A- History taking including patient age, occupation (staff, students, or employee), and complaints such as pain, swelling, locking….etc.

B- Local examination for the diseased knee by referring physicians.

Radiographic assessment

Weight-bearing anteroposterior (AP) and lateral knee radiographs were done for all patients.

US assessment

All patients underwent US examination of the knees within 5 days of clinical evaluation usinga commercially available ultrasound real-time scanner (AU5; ESAOTE, Genoa, Italy) with a multi-frequency linear transducer (7–10MHz). The patient lay in supine position on the examining table exposing both knees for comparison.

Anterior approach: The examination of the knee started on the suprapatellar area, with the knee flexed 30°. Longitudinal and transverse scans of the quadriceps tendon, suprapatellar bursa and prepatellar bursa were performed. In the infrapatellar anterior knee, the patellar tendon and infrapatellar superficial and deep bursae were scanned longitudinally and transversely, with the patient supine and the knee flexed 45°.

Medial approach: The patient was in the supine position, with external rotation of the leg and the knee flexed 10° with mild valgus stress. Longitudinal and transverse scans of the medial collateral ligament (MCL) and the anterior horn of the medial meniscus were performed

Lateral approach: Longitudinal and transverse scans of the lateral collateral ligament, anterior horn of the lateral meniscus, iliotibial band and biceps femoris tendon were performed in the lateral aspect of the knee. Thehe patient lay supine, with internal rotation of the leg, and the knee flexed 10° with mild varus stress.

Posterior Approach: The examination of the posterior aspect of the knee was performed with the patient prone and the knee in full extension. Examination included longitudinal and transverse scans of the gastrocnemiussemimembranosus bursa, posterior meniscal horns and posterior cruciate ligament.

The presence or absence of osteophytes was assessed in the tibial and femoral sites of both knees, with 30 degrees of knee flexion. Osteophytes were defined as cortical protrusions at the joint margin seen in two planes [4]. Femoral and tibial osteophytes were assessed in the medial and lateral compartments using medial and lateral longitudinal scan positions, respectively. Flexion of the knees at 30^{o} was standardized by using the same wedge for all ultrasound assessments.

Synovial effusion was defined as an abnormal anechoic or hypoechoic area in the joint that was displaceable,compressible, and lacks Doppler signal [5]. The size of effusions was measured in the longitudinal supra-patellar position, with the knee in 30 degrees flexion. The maximum diameter of the effusion in the longitudinal view was used to quantify it. Joint effusion was defined by using a cut off of ≥4 mm effusion depth, as seen in a previous multicentre European study [6]. Normal MCL was seen hyperechoic covering the medial femoral condyle, the outer margin of the medial meniscus and the medial tibial plateau [7, 8]. Distances were measured using electronic calipers.

Protrusion of the menisci was defined as the distance between the peripheral border of the meniscus and the outline of the tibial plateau greater than 2 mm. The measurement of meniscal protrusion was also recorded in this study.

RESULTS

Among the sixty patients studied, there were 35 women and 25 men, with a mean age of 52 years. Degenerative OA was diagnosed by clinical and conventional knee radiographs taken in the standing position. **Forty-seven** of the sixty patients revealed narrowing of the medial compartments of the femero-tibial (FT) articulations by plain radiography subsequent to articular cartilage destruction.

On sonography, there was thinning out of the articular cartilage of all **60** cases over the medial femoral condyle, associated with clouding and loss of the sharp anterior and posterior edges. Irregularity of the bony surfaces and calcification of the menisci were also noted in some cases (Fig. 1A, B, C & D).

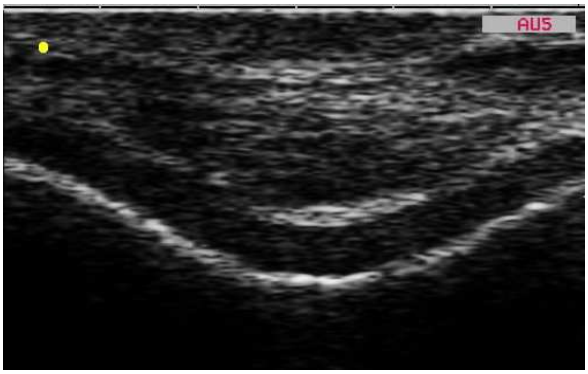

Fig.1A: Normal articular cartilage with sharp edges and homogenous hypoechogenicity.

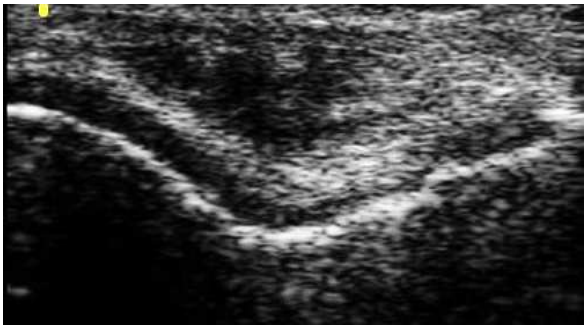

Fig.1B: Irregular thinned out articular cartilage in a patient with knee OA.

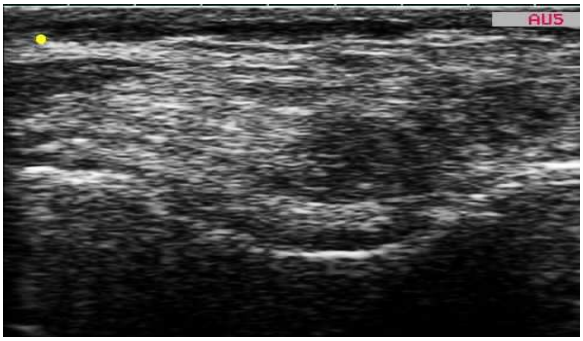

Fig.1C : Irregularities of the bony surface with destroyed articular cartilage.

Fig.1D : Calcified extruded fragments of the meniscus

Conventional knee radiographs showed **54** patients with *osteophytes*. In 52 patients, *osteophytic lipping* was seen by US as dense echoic projections from the bone margins, and was associated with extrusion of the medial menisci in **16** cases. This was also associated with the medial collateral ligament (MCL) bowed or stretched over the extruded menisci. **Three** meniscal cysts were also seen (Fig. 2).

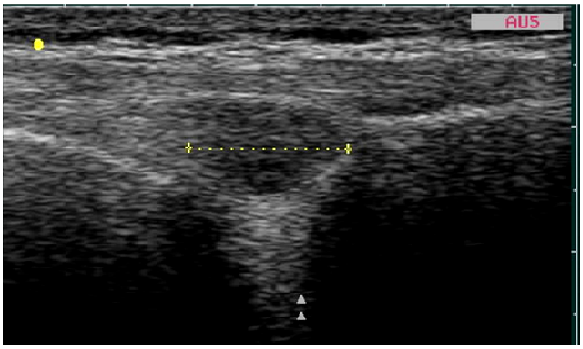

Fig.2: Posterior lateral meniscus with a tear and a meniscal cyst near the outer surface (ice cream cone).

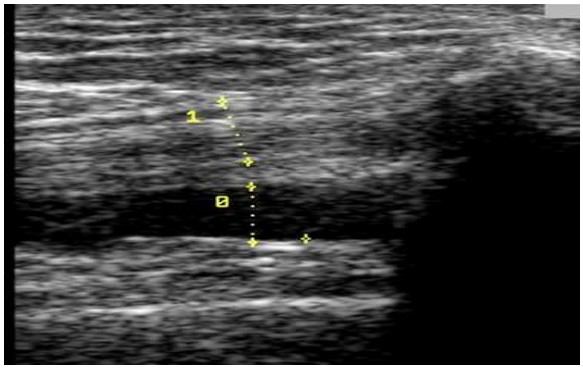

Fig.3 : Moderate suprapatellar effusion deep to the quadriceps tendon.

Fluid collections appeared anechoic on US (Fig. 3), seen as suprapatellar recess *effusion* in **17**cases, Baker's cysts in **4** cases, as well as a prepatellar bursa and a small pes anserine bursa in one case for each. Only **5/17** of these suprapatellar effusions were seen radiographically. None of the Baker's cysts or the fluid collections seen in the prepatellar bursa or the pes anserine bursa was seen radiographically.

Synovial thickening was seen in **7** cases within the suprapatellar recesses (Fig.4). One of them showed mild increase of vascularity by power Doppler sonography (PDS).

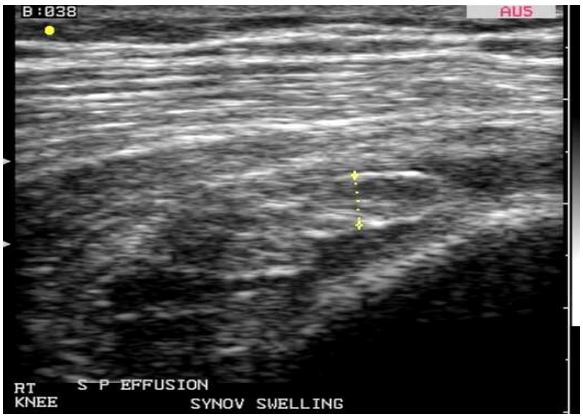

Fig.4: Synovial swelling in the lateral recess of the right knee

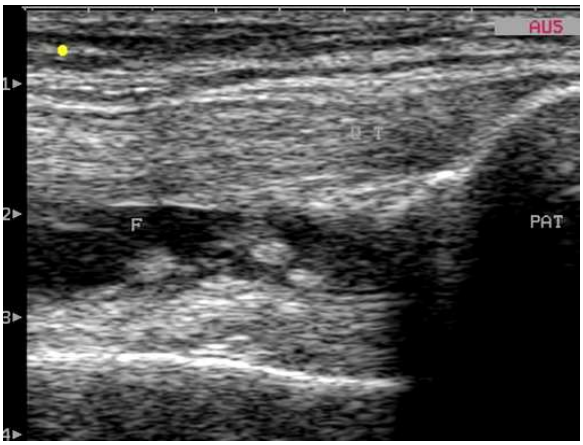

Fig.5A:Suprapatellar effusion with osteochondral fragments

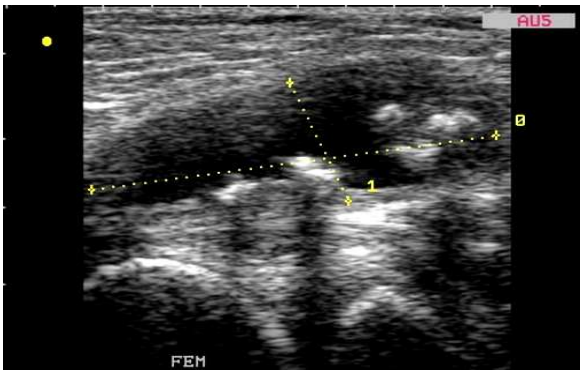

Fig.5B : Baker's cyst with osteochondral fragments

*Loose bodies (*osteochondral fragments) were seen. One was seen within a Baker's cyst (Fig 5A), and two were identified in the suprapatellar effusion (Fig.5B). They appeared as hyperechoic foci with acoustic back shadows within the anechoic fluids.

In **10** patients with acute flare of their symptoms and who were treated with non-steroidal anti-inflammatory drugs (NSAIDs) and followed up subsequently after 3 months, **8** effusions diminished, 1 did not improve, and **1** showed absence of effusion.

One case of pre-patellar bursitis and one case of pes anserine bursitis were identified on US but were not seen radiographically.

Table 1: **Sonographic findings**

Sonographic findings	***No***	Knee radiographs	***No***
Articular cartilage destruction	47	*Narrowing of(FT) articulations*	47
Osteophytes	52	***Osteophytic lipping***	54
Suprapatellar effusion	17	*Suprapatellar effusion*	5
Synovial thickening	7	*Synovial thickening*	0
Bursae *Baker cyst* *Pre-patellar bursitis* *Pes Anserine bursitis*	 4 1 1	*Bursae* *Baker cyst* *Pre-patellar bursitis* *Pes Anserine bursitis*	 0 0 0
Loose bodies	3	*Loose bodies*	7

DISCUSSION

Ultrasound assessment of osteoarthritis is based on measurements of cartilage thickness and detection of osteophytes [9]. The sonographic feature of an osteoarthritic cartilage is loss of the normal sharpness of the synovial space-cartilage interface, where it appears blurred with poor visualization of

the outer cartilaginous margin. Loss of cartilage transparency is an early sonographic feature of osteoarthritis. The increased echogenicity may reflect structural alteration such as fibrillation of cartilage and cleft formation [10].

Major changes of echogenicity of the cartilage are clearly evident in patients with advanced osteoarthritis. Narrowing of the articular cartilage and even its complete absence can be observed in patients with osteoarthritis. Loss of articular cartilage resulting in asymmetric narrowing of the inter-bone distance, with increased intensity of the posterior bone cartilage interface and loss of continuity of the bone profile can be also detected [11]. Osteochondral fragments may be detected within the joint fluid located in the suprapatellar pouch deep to the quadriceps tendon, or posteriorly within a baker's cyst [12]. Joint space narrowing is a primary radiographic feature of OA.

Studies have shown that menisci can contribute to joint space width.Meniscal protrusion, or displacement away from their normal anatomic location, may cause radiographic FT space narrowing independent of cartilage thinning in knee OA. In this study, the sonographic findings in 47/60 patients with degenerative arthritis showed comparable results.

Sonographic assessment of the extent of cartilage damage in patients with OA is important in the early diagnosis and monitoring of therapy in osteo-arthritis [11]. The hyaline articular cartilage in the intercondylar notch can be used as a marker of activity of inflammatory arthropathy [13].

Although cartilage evaluation by US seems reliable, the clinical value is limited in active inflammation because the weight bearing areas are inaccessible [14)]. In patients affected by OA, the typical bone changes are osteophytes, which appear as hyperechoic signals at the joint margins. There is optimal correlation between ultrasound and plain radiography in detecting the presence of osteophytosis.Recently, ultrasound has been demonstrated to be more sensitive than X-ray in the detection of osteophytes in patients with hand OA [6]. Ultrasound is able to detect, with higher sensitivity than clinical examination, the presence of joint effusion, correlating well with MRI, arthroscopic findings and pain in knee OA [16, 17]. Usually, the fluid is anechoic, but in OA it may appear inhomogeneous with particulate matter, possibly due to proteinaceous material, debris or calcified fragments. Moreover, by using color Doppler and power Doppler, it is possible to show hyperaemia due to raised synovial vascularity, correlating with histological findings in patients with OA [18, 19]. Moreover, by using ultrasound, it is possible to evaluate the pathology of the adjacent soft tissues, such as Baker's cysts, which are frequently involved in OA.

Ultrasound is also useful and safe as a guide for joint injections[15]. Therefore, by using ultrasound, it is possible to image the structural damage and the inflammatory state of the OA. Since ultrasound can detect minimal synovitis, this technique can identify patients with a higher risk of progression and can be used to monitor the progression of the disease [19]. In this work, marked synovial thickening with increased vascularity are seen as signs of inflamed synovium and detected in some patients with acute flare of OA.

In this study, sonographic examination in patients with bursitis showed hypoechoic fluid collection with coarse internal echoes in the superficial and deep infra-patellar bursae. This is in agreement with Acebes et al[20], who reported that bursae adjacent to joints with irregular bony contours and hypertrophic tendon insertions were predisposed to the development of frictional bursitis. Bursae of the knee most commonly involved are the pre-patellar as well as infra-patellar bursae. In chronic bursitis due to impingement or overuse, the bursa is

distended with anechoic fluid. More frequently, there is just bursal thickening evidenced by bands of moderate echogenicity with echogenic debris.

CONCLUSIONS

This study has shown several advantages of ultrasonography, including absence of hazardous ionizing radiation, accessibility, low price, noninvasiveness, quick and precise evaluation of the entire knee soft tissue structures which are all frequently involved in knee OA, as well as the possibility of frequent repetitions.

The US technique is done within 15 minutes for bilateral knee joints, which is a short time compared to another advanced imaging modality, i.e. MRI, which would take 30 minutes for one knee examination, not taking in consideration the reading time required afterwards.

Ultrasound can be used efficiently to follow up diagnosed osteoarthritic patients.

The quality of ultrasound examination depends on technical equipment and the doctor's experience.

This study recommends the use of ultrasonography as a routine and fundamental method in contemporary rheumatological practice, and as a complement to clinical examination.

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Original Article

Mouse model developed to study the impact of B cell depletion therapy on Atherosclerosis

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نموذج الفأر المطور لدراسة تأثير انخفاض خلايا بي اللمفاوية كعلاج لتصلب الشرايين

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الملخص

الأهداف : مرضى التهاب المفاصل الروماتيزمي لديهم قابليةعالية للإصابة بأمراض القلب. من المثير للإهتمام أن خلايا بي اللمفاوية لديها طريقة معاكسة في التكوين المرضي لمرض التهاب المفاصل الروماتيزمي ومرض تصلب الشرايين .الهدف من هذه الدراسة هو فحص فعالية العلاج بعقار خافض خلايا بي على المجموعات الفرعية للخلايا بي وتصلب الشرايين في الفئران.

الطريقة :قمنا بتحضيرنموذج معملي من الفئران مشابه لمرض تصلب الشرايين من نوع -/- Apo / $huCD20^{+}$ وقد تم علاج الفئران بواسطة دواء مخفض لخلايا بي وهو ريتوكسي ماب وَ قياس نسبة خلايا بي قبل وبعد كل علاج ،وفى نهاية فترة العلاج تم فحص الشرايين التاجية لتقييم حالة التصلب بها.

النتائج : خلال فترة الدراسة , أدى العلاج الأولى بريتوكسي ماب إلى انخفاض كبير (أكبر من 90 %) في نسبة خلايا بي . بينما أظهرت خلايا بي في الطحال والعقد اللمفاوية التى تم حصدها في نهاية الدراسة مقاومة للعلاج بواسطة ريتوكسي ماب. أما بالنسبة للشريان التاجى، فقد تقلص حجم التصلب ضعفين مقارنة بالمجموعة الضابطة والتى تم علاجها بواسطة الاجسام المضادة IgG.

الخلاصة : تم فى هذه الدراسة تجهيز نموذج من الفئران مشابه لمرض تصلب الشرايين، وقد أظهرت المعطيات الأولية تقلصا فى تصلب الشرايين عند استخدام علاج خافض للخلايا بي .

ABSTRACT

Objective
Rheumatoid Arthritis patients have an increased risk of developing co-morbid cardiovascular disease (CVD). Interestingly, B-lymphocytes have an opposite role in the pathogenesis of RA and atherosclerosis. The aim of this study was to investigate the impact of B cell depletion treatment on B cell subsets and atherosclerosis in mice.
Method
We established an experimental model to mimic atherosclerosis and thus raised huCD20^{+}/ApoE$^{-/-}$ mice. These mice were treated with the B cell depleting agent Rituximab, and B cell percentage was examined before and after every treatment. At the termination of the study, aortas were explored for atherosclerotic lesions.
Results
During the course of the study, first treatment with rituximab resulted in a massive reduction (>90%) in B cell percentage. Moreover, B cells of spleen and lymph nodes harvested at the end of study-exhibited resistance to Rituximab treatment. However, the aorta showed almost a 2-fold reduction in lesion size in response to rituximab treatment in comparison with the IgG treated control mice.
Conclusion
This study established a mouse model and the preliminary data is suggestive of reduction in atherosclerotic plaques with B cell depletion therapy.

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease that primarily affects the joints and is characterised by bone and cartilage erosion. RA patients show strong susceptibility to cardiovascular diseases leading to morbidity and mortality (1-3). They require sequential immune modulatory therapeutics(4). Patients refractory to treatment with anti TNF can respond effectively to B cell depletion therapy (5).

The only FDA approved B cell depleting agent is Rituximab, a chimeric monoclonal antibody to CD20, which is specifically expressed on human B cells (6-8), which have a transmembrane protein with 4 domains. The antibody started out as a murine antibody and was then engineered to contain parts of the human antibody. This resulted in a chimeric antibody, a combination of a constant region from humans and an antigen binding variable portion of a murine origin. The cardiovascular complications seen in RA patients are the result of atherosclerosis, a gradually advancing, and chronic inflammatory disease seen as asymmetrical intimal thickening of large arteries. (9)
The functional role of B-lymphocytes in atherosclerosis seems very

interesting. In the past, numerous investigators substantiated a protective role for B cells in atherosclerosis (10). Recently, different B cell subsets have been shown to have an opposite role in the course of atherosclerosis. The B2 cells have been shown to have atherogenic character (11), whereas the natural IgM antibody producing serosal B1a cells are atheroprotective (12). The B1a cells produce their atheroprotective effects not only through natural antibodies, but also though the anti-inflammatory cytokine IL-10 (12). This functional dichotomy in B cell subsets in atherosclerosis is intriguing.

Rituximab therapy in patients results in more than 95% reduction of detectable circulating B-lymphocytes (13). Clinical responses suggest a pro-inflammatory role of B cells in RA pathogenesis. Importantly, RA patients are strongly linked with cardiovascular morbidity and mortality and studies suggest that B cells have an anti-inflammatory role in atherosclerosis (14). Keeping this in view, it becomes very important to address the implications of B cell depletion therapy on atherosclerosis, especially when Rituximab is used in refractory cases of RA. This group has in any case a higher than expected incident rate of vascular events and thus subtle risk factor modulation may be of clinical significance. Therefore, it is important to examine the effect of Rituximab therapy on B1a and B2 cells in the circulation and other lymphoid organs, in addition to implications on the course of atherosclerosis.

To investigate this, we decided to use the ApoE-/- murine model of atherosclerosis. These mice develop atherosclerosis as they age; however, if these mice are given a high fat diet, the process of atherosclerosis is accelerated (15-17). Human CD20 transgenic mice express the human CD20 receptor and are, therefore, susceptible to Rituximab-induced B cell depletion (18,19). We crossed these two murine strains to generate the huCD20^{+}/ApoE$^{-/-}$ murine line. These mice were fed on a high fat diet (HFD) and treated with Rituximab to deplete B cell.

The aim of this study was to investigate the impact of B cell depletion therapy on different B cell subsets and, in turn, on plaque formation in atherosclerosis- prone mice.

MATERIAL AND METHODS

A. Modified Mouse Model of Atherosclerosis

Human CD20 (huCD20+) transgenic mice were kindly provided by Professor Mark J Shlomchick (Yale University, New Haven) (18). These mice were crossed with Apolipoprotein E knockout mice (ApoE-/-) (Jackson laboratory) to produce "huCD20+/ApoE-/- mice". These mice were given 100µl of 100µg intravenous (iv) injections of Rituximab (Rituxan) for the study group, or chromopure human IgG (Jackson Immunochemicals) for the control group, every 4 weeks. To monitor B cell depletion in these mice, they were bled a week before and after each systemic treatment. Mice were weighed every time they were injected or bled. The model was set up to sacrifice mice after 4 treatments around the age of 22 weeks (16 weeks on HFD). At the end of the study, heart and aortas were to be examined for lesions. Spleen, lymph nodes, bone marrow and blood were harvested to examine B cells and their subsets.

B. Peripheral blood mononuclear cells staining (PBMCs)

PBMCs from huCD20+/ApoE-/- were stained as per manufacturer guidelines for different cell surface antigens; CD19-APC (ID3, BD Pharmingen), CD3-PE (145-2c11, BD Pharmingen), B220-PerCP (RA3-6B2, BD Pharmingen), CD21-FITC (7G6, BD Pharmingen), CD23-PE (2G8, Southern Biotech), CD24-PE (BD Pharmingen, M1.69), IgM-PE (BD Pharmingen),

CD11b-PerCP (BD Pharmingen, M1.70), IgM-FITC (BD harmingen, II/41), IgD-FITC (Bioscience, 11-26c), CD43-FITC (BD Pharmingen, S7) and huCD20-FITC (L-27, BD bioscience). Cells were fixed and permeablized using buffer (BD Bioscience). The resulting data were analyzed using Flowjo (Treestar).

C. Flow cytometry

After sacrificing the mice, their organs (spleen, lymph nodes and bone marrow) were harvested and single cell suspensions were stained for different surface antigens; CD19-APC (ID3, BD Pharmingen), CD3-PE (145 2c11, BD Pharmingen), B220-PerCP (RA3-6B2, BD Pharmingen), CD21-FITC (7G6, BD Pharmingen), CD23-PE (2G8, Southern Biotech), CD24-PE (BD pharmingen, M1.69), IgM-PE (BD Pharmingen), IgM-FITC (BD Pharmingen, II/41), IgD-FITC (Bioscience, 11-26c), CD43-FITC (BD Pharmingen, S7) and huCD20-FITC (L-27, BD Bioscience). The staining was performed as per manufacturer guidelines.

D. Haematoxylin and Eosin Staining of aortic lesions

Aortic sections stained with hematoxylin and Eosin (H & E) were analysed using a light microscope (Carl Zeiss). Morphometric analysis of the lesions was performed on cross sections through the aortic lesion using an image analysis software (Axio vision 4.4). The aortic lumen and lesion area measurements from 5 sections were then used to calculate the percentage of luminal area obliterated by the lesion.

E. Statistical analysis

Quantitative data were described in the form of mean ± SD and the statistical analysis of the study was done using Graphpad prism version 4 for Mac (Graphpad software).

RESULTS

Rapid depletion of circulating B-lymphocytes with Rituximab treatment

To determine the baseline level of B-lymphocytes in the blood, PBMCs were extracted from the blood at week (0) and were stained for CD19 and human CD20. FACS analysis showed similar B cell percentage, i.e. Rituximab- treated mice (n=2) had a mean of 44.6% ± 0.3 huCD20 positive B cells, while human IgG treated mice (n=2) had a mean of 43.4% ± 7.3.

One week after systemic treatment of all the mice (n=4) they were bled again and the percentage of B cells present in the blood were analysed by FACS. The analysis showed significant depletion of B cells in Rituximab treated mice. In specific, Rituximab-treated mice had 0.45% ± 0.4 (mean ± SD) B cells, representing a 98% reduction (Figure 1, A, B). The huCD20 positive cells were not affected by the treatment (100µg, IgG) and the B cells in the control mice were 45.6% ± 1 (mean ± SD) of the gated lymphocytes (Figure 1, C, D)

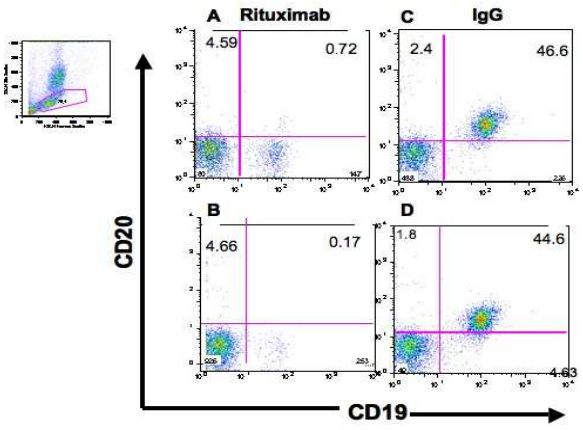

Figure 1. Circulating B cells (huCD20^{+}) one week after systemic treatment

Mice were bled one week after first treatment. (A & B) are Rituximab-treated

mice, (C & D) are the control mice; PBMCs were isolated from the blood and stained for 4-colour flow cytometric analysis. Pseudocolour dot plots were gated on lymphocytes as shown in the smaller panel. (CD19 vs. CD20) showed a 98% reduction in $CD20^+$ B cells in the Rituximab-treated mice, whereasIgG treatment did not affect the CD20 expressing population. The percentages are shown in each quadrant.

Thereafter, the mice were bled again a week before the second treatment to see if the huCD20 positive cells were replenished in the Rituximab-treated mice (n=2) during the two-week time. There was a rapid recovery of huCD20 positive B cells in Rituximab-treated mice as a 77% increase was observed evident from B cell percentages (34.7% ± 5.2). In fact, the mean B cell percentage increased further in the IgG treated mice (n=2), (51.75% ± 4.35).)

However, a week after the second treatment with Rituximab, a modest depletion of 9% was observed in the peripheral blood in these mice; whereas, a week after the second treatment with IgG, the mice had a further 15% increase in there circulating B cells. Moreover, one week after the third treatment, the Rituximab-treated mice had a modest drop of 20% in the circulating B cells, while the IgG-treated mice had steady levels of circulating B cells.

B cell directed therapy did not affect lymphocytes of spleen and lymph nodes

Having established that depletion of circulating B cells was massive (98%) after the first treatment and later on they resisted depletion, even as small as 9% depletion was seen in these mice as compared to their B cell levels that were replenished in 3 weeks' time prior to treatment. Mice were sacrificed and aorta, spleen, bone marrow, lymph nodes and blood were all harvested from the mice. Aortas were examined for atherosclerotic lesions. Bone marrow and secondary lymphoid organs were assessed for B cell depletion.

The ratios of B to T lymphocytes in the spleen of Rituximab- vs. IgG-treated mice were 1.85 and 1.6, respectively. On the other hand, the ratios of lymphocytes (B and T) in the lymph nodes of Rituximab- and IgG-treated mice were 0.58 and 0.68, respectively. This showed that both spleen and lymph nodes had similar ratios of lymphocytes, so the depletion therapy did not affect the huCD20 positive B cells in these organs (Figure 2).

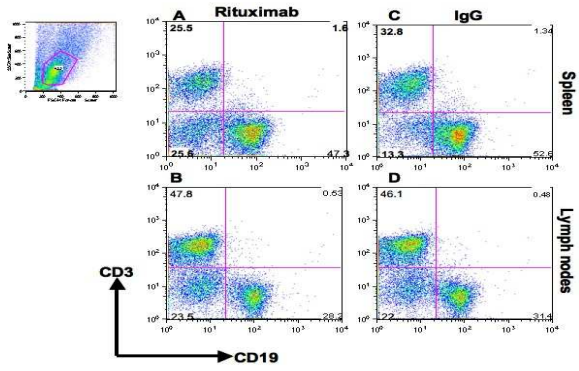

Figure 2. Depletion therapy and lymphocytes in spleen and lymph nodes

Single cell suspensions of lymphocytes were extracted from spleen (A,C) and lymph nodes (B,D). Pseudocolour dot plots were gated on lymphocytes as shown in the smaller panel in the left corner. B and T lymphocyte percentages in spleen of Rituximab-treated mice were 47.3% and 25.5%, and in lymph nodes 28.2% and 47.8%, respectively. On the other hand, B and T lymphocyte percentages in spleen of IgG- treated mice were 52.6% and 32.8%, and in lymph nodes 31.4% and 46.1%, respectively. The percentages are indicated in corner of each quadrant.

Effect of Rituximab on B cell subsets in spleen

Rituximab treatment in $huCD20^+/ApoE^{-/-}$ mice demonstrated no depletion of B cells in spleen and lymph nodes. We also wanted to validate if the treatment affected different B cells subsets in secondary

lymphoid organs. Harvested spleen cells were stained for different B cells subsets. The identification of transitional (T2), marginal zone (Mz) and follicular (Fo) B cells in the spleen was possible through combination of several markers, which are expressed during development. The combination included CD19, CD21 and CD23; a plot of forward scatter (FSC) vs. CD19 can be used to separate ($CD21^+CD23^+$) cells. This population was subdivided into Fo ($CD21^+CD23^+$lo), T2 ($CD21^+CD23^+$hi) and Mz ($CD21^+CD23^+$dull) B cells. There was a difference noted in marginal zone B cells between Rituximab-treated (4.18%) and control mice (2.84%). This altered representation of B cell subset percentage could be a response of decreased follicular B cells (Figure 3).

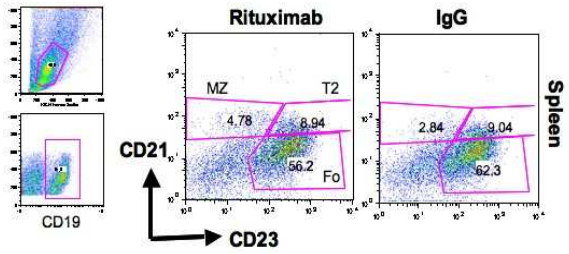

Figure 3. Marginal zone (MZ), follicular (Fo) and transitional type 2 (T2) B cells

The single cell suspension was isolated from Rituximab- and IgG-treated mice. These cells were stained for FACS analysis. A plot of forward scatter (FSC) was used to separate out lymphocytes as shown in the top small panel on the left. These cells were further gated on to $CD19^+$ cells to separate $CD21^+CD23^+$ B cells. The $CD21^+CD23^+$ fraction was further subdivided into $CD21^+CD23^+$lo Fo cells and $CD21^+CD23^+$hi T2 and Mz B cells. The percentages of Fo, T2 and Mz cells are written beside the gated factions**.**

Rituximab seems to increase transitional type 1 B cells in spleen

Harvested cells from spleen and lymph nodes were stained for T1, T2, Mz and Fo B cells. This was possible through combination of several markers, which are expressed during development. The combination included CD19, CD21 and CD24; a plot of forward scatter (FSC) vs. CD19 was used to separate $CD21^+$ and $CD24^+$ cells. This population was subdivided into T 1 ($CD21^+CD24^+$lo), T2, Mz ($CD21^+CD24^+$hi), but this did not allow the discrimination of Mz and T2 cells, while Fo cells were an intermediate population ($CD21^+CD24^+$). The response of Rituximab treatment on splenic B cells (T1, Mz and Fo) was 31.5%, 8.01%, 49.6% vs. IgG treatment 16.3%, 5.56%, 63.6%, respectively. These demonstrate that Rituximab resulted in an increase in the T1 subset (31.5%) compared to IgG treatment, which resulted in a 16.3% increase in the same subset (Figure 4).

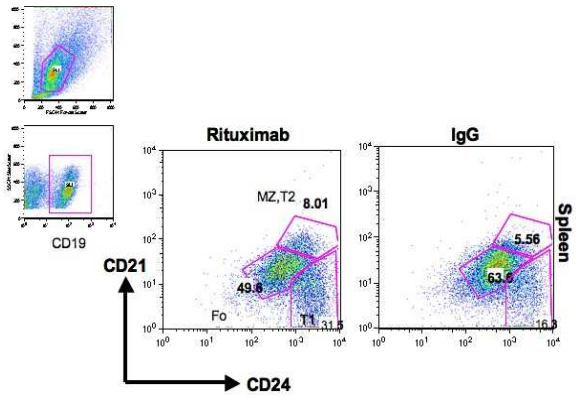

Figure 4. B cells subsets in spleen

Single cell suspensions of spleen and lymph node was isolated from Rituximab- and IgG-treated mice. A plot of forward scatter (FSC) was used to separate out lymphocytes as shown in the top small panel on the left. A plot of forward scatter vs. CD19 was used to separate ($CD21^+CD24^+$) B cells. The $CD21^+CD24^+$ fraction can be further subdivided into T 1 ($CD21^+CD24^+$lo), the T2+Mz ($CD21^+CD24^+$hi) and Fo ($CD21^+CD24^+$ intermediate population). The CD21 and CD24 staining did not allow discrimination of MZ & T2 cells. The percentage in Rituximab treated mice in spleen was compared to control mice.

B1a cells in spleen and lymph nodes resist depletion

Previous studies have shown that generation of natural antibodies IgM (T15) can be atheroprotective, which implies a role for B1 cells in atherosclerosis (10,12,20). Therefore we estimated the percentages of B1 cells in spleen and lymph nodes of treated mice (n=3). Harvested cells from spleen and lymph nodes were stained for flow cytometric analysis of the B cell subset (B1a). A plot of forward scatter (FSC) vs. side scatter was used to gate lymphocytes. This was then used to gate $CD19^{+}IgD^{+}$ intermediate population. This population was used to separate ($CD5^{+}CD43^{+}$ Hi) population recognised as B1a cells. The response of the Rituximab treatment on the percentage of the gated B cell population, i.e. B1a cells was 4.51% whereas in the IgG-treated mice it was 6.64%, with no significant difference in the statistical form. In fact, a similar observation was made for the percentage of B1a subset in the lymph nodes of Rituximab-treated mice (14.1%) compared to IgG-treated mice (11.6%) as shown (Figure 5).

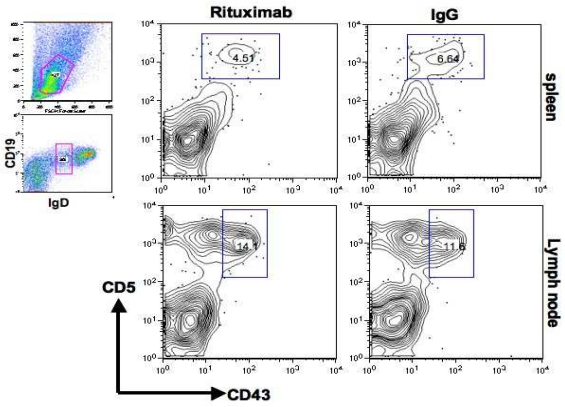

Figure 5. B1a cells in spleen and lymph nodes

Single cell suspensions of spleen and lymph nodes were isolated from Rituximab- and IgG-treated mice. A plot of forward scatter (FSC) was used to separate out lymphocytes as shown in the top small panel on the left. These cells were further gated on to ($CD19^{+}$ IgD^{+}) intermediate population to separate ($CD43^{+}CD5^{+}$)^{Hi} B1a cells.

Rituximab treatment reduced atherosclerotic lesions

The H and E stained sections demonstrate atherosclerotic lesions in the aorta of the tested mice. The lesions seen in the Rituximab-treated mice were small as compared to the lesions in control mice. The cholesterol cleft can be seen as white holes or clefts in the areas of maximum elevation of the lesion into the lumen (Figure 6 A & B).

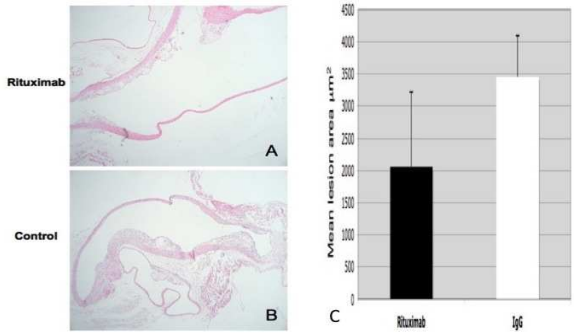

Figure 6. Aortic lesions in huCD20^{+}/ApoE$^{-/-}$ mice

Mice were given a high fat diet (HFD), treated every four weeks with IV Rituximab or IgG (control), and were sacrificed around 9 weeks. The aortic lesions were examined by H & E staining. As shown in figure 6, the Rituximab-treated mouse (A) had small lesions, whereas the IgG-treated mouse (B) had much larger lesions that covered a larger area of the lining layer. The average lesion size in cross section through the aortic origin is indicated in μm^2. The Rituximab-treated mice(black bar) had almost half the lesion area as compared to IgG-treated mice (white bar) (C).

The aortic lesions and the luminal area were measured in μm^2 using the imaging software (Axiovision version 4). The mean lesion area was calculated for 5 sections, every section 7µm thick and each section 7µm apart. The average lesion size was

measured for both Rituximab-treated mice and IgG-treated controls as shown in table 1. This showed an almost 2-fold reduction in lesion area in Rituximab-treated mice. As the sections used for measuring the lesions size were from 5 consecutive slides, this means the lesions extended longitudinally over 70μm from the proximal aorta.

Table 1 Effect of treatment on atherosclerotic lesions in huCD20^{+}/ApoE$^{-/-}$ mice

	Rituximab 1		Rituximab 2		IgG 1	IgG 2
Average lesion size (μm^2 ± SD)	2058 1158.5	±	1893 1146	±	3982 ± 638	2932 ± 694.3
Average aortic lumen	28522 11858	±	30939 7440	±	20772 ± 1336	1611 ± 2549
Percentage occlusion of lumen	5.58 2.88%	±	5.57 2.68%	±	19.3 ± 5.15 %	18.17 ± 3.91 %

We observed a variation in size of the aorta between these mice, so to ensure that the results reflected the absolute lesion area compared to vessel size, we determined the percentage area of the lesion relative to luminal area. We calculated the percentage of aortic lumen occluded for all 5 sections per mouse by (lesion area / luminal area × 100) for each section of the tested mice (n=4) as previously described (21), which revealed the percentage of aortic lumen obliterated with lesion. There was reduction in the percentage area of aortic lumen obliterated with lesion in the Rituximab-treated compared to IgG treated control mice (n=2) as shown in table 1. The lesion of the Rituximab- treated mouse had small plaques on 1-3 sections. In fact, the last 2 sections had no lesions at all. On the other hand, the IgG- treated mice had lesions bigger than the Rituximab-treated mouse.

DISCUSSION

This result defines an approach that now requires to be expanded to yield truly informative data. Initial observations demonstrate proof of principle that the methodologies are sound and can generate data of a meaningful nature. RA patients are vulnerable to cardiovascular morbidity and mortality and we hypothesised that depletion of B-lymphocytes (atheroprotective cells) (14) in the experimental model of atherosclerosis might result in aggravation of lesion formation in the mice. However, this preliminary data from a limited number of mice (n=4) gives us the clue what to expect from a full study with a reasonable number of huCD20^{+}/ApoE$^{-/-}$ mice and is in fact reassuring.

The current data show a 2-fold reduction in lesion size in response to Rituximab treatment in comparison with the IgG-treated control mice. Variation was observed in size of aortic lumen and arterial wall thickness in these genetically engineered mice. Therefore not only was the aortic lesion area compared, but we also calculated the percentage area of the aortic lumen obliterated. Importantly, the measures of aortic lesion area and percentage area of the aortic lumen obliterated have both shown that B cell depletion resulted in at least 2-fold reduction in atherosclerotic lesions. Importantly, these lesions extended vertically from root of aorta towards the ascending aorta. However, the overall reduction in arterial wall thickness of these huCD20^{+}/ApoE$^{-/-}$ mice needs to be validated in future studies.

B cell depletion every four weeks with Rituximab (100μg) was monitored throughout the course of the study, and a massive (>90%) reduction was observed in the B cell percentage after the first treatment, which was followed by rapid recovery of the B-lymphocytes in a three weeks' time. Interestingly, the systemic

treatments (second and third) resulted in modest depletion of B cells (9-20%). In one study, Rituximab (type I) has been shown to be 5 times less potent then tositumomab (type II). The return of B cells was reported 30-35 days following treatment (16). In addition, comparison of B cell depletion with a single dose of Rituximab (250µg) in two different strains of mice was performed, and it was demonstrated that C57BL/6 mice were more resistant than BALB/c. In fact, the analysis of B cell depletion in peripheral lymphoid organs (bone marrow and lymph nodes) was resistant to Rituximab therapy (22). Although in the present study the Rituximab dose (100µg) is less than half the dose used in the study mentioned, a massive depletion was confirmed in our mice on C57BL/6 background. However, the spleen and lymph nodes harvested at the end of the study did show resistance to rituximab therapy.

Mz and B1 B cells are potent responders to TLR activation, which has resulted in them being referred to as innate B cells (23-25). Moreover, pneumococcal vaccination in $Ldlr^{-/-}$ mouse has been demonstrated to reduce the atherosclerotic burden in mice, which was shown to be a result of oxLDL specific IgM antibodies produced by splenic B cells (26). In the present study, we observed an increase in the T1 B cells in the spleens of Rituximab-treated mice. Even though this subpopulation is small, but there is a fold increase in this population, which might be because they escape depletion or because of some stimulatory response. Moreover, the B1 B cells are mainly found in the peritoneal cavity (27). A modest population of B1 B cells was identified in the spleen and lymph nodes, which was not affected by Rituximab treatment. It is very important to confirm if this $CD20^{+}$/$ApoE^{-/-}$ mouse model has a normal lipid profile to confirm that the effects observed were of B cell-directed therapy (Rituximab) rather than as a result of changes in serum lipids.

CONCLUSIONS

The present preliminary study demonstrates that this is a feasible mouse model to estimate the effects of Rituximab treatment on vascular disease, since it is unlikely that sufficient numbers of RA patients will be treated in the short to medium term to generate reliable vascular outcome data. Therefore, as this current study is extended, it will likely generate helpful information for future translation to the clinic. Moreover, the model will offer a rich potential for mechanistic testing and to evaluate formally the role for B cells in atherosclerosis progression.

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Original Article

The Effect of Assertiveness and Conflict Resolution Skills Utilized by Nurses on Nursing Care Productivity in Different Health Care Sectors at Menofia Governorate, Egypt

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تأثير التواصل الايجابي وأسلوب فض الصراع المتبع على إنتاجية الرعاية التمريضية فى قطاعات الرعاية الصحية المختلفة بمحافظة المنوفية/ مصر

الملخص

مقدمة

التواصل الايجابي هو إحدى المهارات الضرورية للاتصال الفعال فى بيئة العمل التمريضية الحديثة. وهو أولى الخطوات تجاه النجاح فى العمل , وسمة ضرورية تصف ممرضة/ممرض القرن الحادى والعشربين الناجحة. وهو سلوك يعنى القدرة على تعبير عن الذات والمحافظة على حقوق الفرد الشخصية دون التعدي على حقوق الآخرين. كما يجب ان يتسم بها القائد لتحقيق الأهداف المنشودة فى العمل من حيث زيادة جودة وإنتاجية الرعاية التمريضية فى حدود الإمكانيات الكمية والكيفية المتاحة .كما يمثل الصراع فى المستشفيات إحدى القضايا الهامة التى تواجه رئيساتالتمريض ويستحوذ على 25% من أوقاتهن لفض احد أشكال هذا الصراع. أوضحت الدراسات ان المهارة الإدارية فى معالجة الصراع مؤشر رئيسي للتنبؤ بنجاح وفعالية الإدارة , ويعرف الصراع بأنة "الموقف الذى يوجد فيه أهداف او مدركات او مشاعر غير متوافقة داخل او بين الأفراد او الجماعات او المؤسسات مما يتسبب فى حدوث التعارض او التفاعل العدواني بينهم". لذا يجب على الهيئات والمنظمات الحكومية الصحية ان توفر لرئيسات التمريض الفرص لتنمية مهارات الاتصال الايجابي ومهارات فض الصراع عن طريق عمل ورش العمل والمؤتمرات لما لها من تأثير بشكل فعال وايجابي على رفع الجودة والإنتاجية التمريضية لدى هيئة التمريض . كما ان الكفاءة الإنتاجية التمريضية والتي تعرف بشكل عام بمدى قدرة المؤسسة على الاستفادة والاستغلال الأمثل للموارد المتاحة من اجل الحصول على أفضل النتائج المطلوبة واكبر عائد بأقل تكلفة .وتقاس الكفاءة الإنتاجية التمريضية بنسبة الإنتاج (المخرجات) الى الموارد (المدخلات) المستخدمة فى تحقيق هذه المخرجات .

هدف الدراسة:تهدف هذه الدراسة الى استكشاف تأثير التواصل الايجابي وأسلوب فض الصراع المتبع على إنتاجية الرعاية التمريضية فى قطاعات الرعاية الصحية المختلفة بمحافظة المنوفية.

عينة الدراسة: أجريت هذه الدراسة على مجموعتين من أعضاء هيئة التمريض, اشتملت المجموعة الأولى على 140 ممرض و ممرضة(50 من مستشفى شبين الكوم الجامعي و50 من مستشفى شبين الكوم التعليمي و40 من مستشفى الهلال للتامين الصحي) و اشتملت المجموعة الثانية علي ٣٠رئيسة وحدة تمريضية (10من كل مستشفى)

أدوات جمع البيانات:1- استمارة استبيان لتحديد مدى إتباع التواصل الايجابي لدى الممرضات بالقطاعات الصحية المختلفة بمحافظة المنوفية.

2- استمارة استبيان لتحديد مهارات فض النزاع.

3- استمارة استبيان لقياس الإنتاجية المهنية.

نتائج الدراسة: - أثبتت الدراسة أن النسبة المئوية الأعلى من الممرضيين ا يقدمن خدمة مباشرة للمرضى 49.3% كانت لديهم درجة عالية من التواصل الايجابي، كما وجد ان النسبة المئوية الأعلى من مشرفي الوحدات 53.3% كانت لديهم درجة متوسطة من التواصل الايجابي. كما وجد ان النسبة المئوية الأعلى من مشرفي الوحدات 73.3% كانت لديهم أيضا مهارات متوسطة من مهارات فض الصراع. وأيضا عند دراسة العلاقة بين درجة التواصل الايجابي و مهارات فض الصراع و معايير قياس الإنتاجية التمريضية بين ممرضات عينة البحث الكلية وجد ان الفارق بين درجة التواصل الايجابي ومهارات فض الصراع و معايير قياس الإنتاجية التمريضية ذو دلالة إحصائية. بالنسبة لانماط الحلول المستخدمة فى ادارة الصراعات بين الممرضيين، اوضحت نتائج الدراسة ان استخدام الحل التعاونى نمط مشاركة اطراف الصراع (74%) و استخدام الحل التوفيقى (36%) على التوالى لادارة الصراعات هما اكثر الانماط استخداما فى حل الصراعات بين الممرضيين. بينما ثبت أن استخدام الحل الوسط نمط الاتفاق الودى بين اطراف الصراع (5.9%) هو اقل الانماط استخداما فى حل الصراعات بين الممرضيين ، وقد تبين عدم وجود فرق ذى دلالة احصائية بين الممرضات فيما يتعلق باستخدام الحل التعاونى والتفادى فى حل الصراعات .

التوصيات:في ضوء النتائج التي توصلت إليها الدراسة يوصى بالآتي:

1- تنفيذ برنامج تعليمي مستمر من قبل إدارة المستشفى يركز على تعليم الممرضيين مهارات التواصل الايجابي و مهارات فض الصراع وذلك لتحسين علاقتهم مع بعضهم البعض ومع المرضى .
2- الإبقاء على خطوط الاتصال مفتوحة بين الممرضيين والإدارة بالمستشفى وذلك بعقد اجتماعات دورية مع الممرضيين لإعطائهن الفرصة للمشاركة فى صنع القرارات الخاصة بهم .

ABSTRACT

Background: Assertiveness is a term used to describe behaviors that a person can use to stand up for himself and his rights without violating the rights of others. Conflict is defined as a clash that occurs when the balance among feelings, thoughts, values, needs, priorities, desires and behaviors is threatened. This disturbance results is incompatible behavior that interferes with goal attainment**.** Nursing productivity is defined as converting resources into products and services efficiently, effectively and with optimum utilization of human capital and physical resources for the benefit of society, the economy and the environment.

Aim: To explore the effect of assertiveness and conflict resolution skills utilized on nursing care productivity in different health care sectors at Menofia Governorate.

Design: descriptive correlation design.

Setting: The present study was conducted in three health care sectors at Shebin El-Kom, Menofia governorate-Egypt.

Subjects: A simple random sample was used to collect data from 140 staff nurses, and 30 nurse managers.

Tools: Three different tools were used in this study, namely: 1-assertiveness questionnaire 2-conflict resolution inventory, and 3-professional productivity checklist.

Results: (1) The majority of staff nurses at the threeselected health sectors had moderate to high assertiveness degree. (2) There was a statistically significant difference between assertiveness, conflict resolution skills and total productivity among the total studied sample. (3) The higher percentage of the total studied sample had moderate conflict resolution skills. (4) Thetotal studied sample reported collaboration style which is the most common style utilized followed by accommodating style.

Recommendation: Hospital managements are advised to encourage nurses to know their rights and responsibilities to help them in the application of assertive communication processes.

Key words: *Assertiveness, Conflict Resolution Skills, Nursing Care Productivity.*

INTRODUCTION

Nursing takes place within an organization requiring effective communication skills that a nurse needs to provide a safe practice and good standard of care. These skills include using assertive communication, which is one of the essential skills in the modern working environment. Assertiveness is a term used to describe behaviors that a person can use to stand up for himself and his rights without violating the rights of others.[1]

Assertiveness is not a talent. It is a healthy behavior and skill that is developed through practice. No one is born knowing how to be assertive. Having knowledge of assertiveness is essential. Assertiveness is a tool for nurses that enables her to act forpatient advocacy. As a nurse works within a professional team, using assertiveness skills is an essential component of working in a professional manner.[2]

There are a number of key principles that describe the concept of assertiveness. Essentially, these principles identify types of behavior, attitudes and feelings that influence how we interact with other individuals. Assertiveness is a way of communication that allows individuals to express themselves in direct, honest, and appropriate ways that donot infringe upon other people's rights.[3]

Hein & Albert[4] have mentioned that there are many benefits of being assertive, such asbeing a better time manger, increasing self–esteem, and having the ability to negotiate more effectively. Assertiveness enables nurses to move towards professionalization and respect the rights of others. Most nurse educators prepare nurses to develop more nursing skills and teach them how to assert themselves as skill practitioners. People who learn assertive communication report a decrease in somatic symptoms such as headache, abdominal distress, and it seems reasonable to assume that an honest expression of feelings would reduce a great deal of internal stress.[5]

Conflict is a natural phenomenon that strengthens an organization. It is an inevitable part of today's health care environment. It is often a prerequisite to change in people and organization. A certain degree of conflict is beneficial to an organization. Conflict can increase creativity by acting as a stimulus for developing new ideas or identifying methods for solving problems.onflict serves as a powerful motivator to improve performance, effectiveness and satisfaction.[6] Also Connie[7] added that, resolving conflicts in a professional manner is incredibly important and there are a variety of strategies that can help manage conflicts and one important tool is clear communication.

According to Marquis& Huston[2], conflict occurs in four categories, intrapersonal within one individual, interpersonal between two or more individuals, intragroup within one group, and intergroup conflict between two or more groups. William[8] has described five conflict approaches,avoiding, accommodating, competing, compromising, and collaborating. On the other hand, Lewis[9] has described five conflict handling modes in terms of two underling dimensions, assertiveness and cooperativeness. Assertiveness is the extent to which the individual attempts to satisfy one own concern without neglecting concerns of others. Cooperativeness is the extent to which the individual attempts to satisfy the other person's concerns.[6]

Productivity has become a day-to-day concern for managers, because productivity indicates the overall efficiency of their organizations. It is very important to know all about productivity to reach the maximum quality in our health organizations. Nursing productivity refers to effectiveness of nursing care, which relates to itsquality,appropriateness, and efficiency.[10] Nursing productivity has been defined as the ratio of patient care hours per patient day to

salary and benefit costs paid out to staff by the organization. Nursing productivity models should take into account patients' needs, nursing competencies, the availability of material resources, and services provided. Nursing workload is a direct reflection of these variables and affects the delivery of patient care, patient safety, as well as satisfaction of nurses and of patients and their family members[11]. Evidence is rapidly accumulated to report that staff productivity and effectiveness increase by improving assertiveness, interpersonal communication skills, as well as conflict management skills and effective team work. There are characteristics of a highly performing system, such asclarity of the purposes and objectives, commitment to these purposes, team work is focused on the task, and leadership is strong and clear.[12]

King[13] has reported that assertiveness and productivity are essential characteristics of successful 21century nurses, while conflict destroys productivity and morale. Assertiveness training has the benefit of increasing productivity through more effective communication, reduced interruptions at work, and increased work effectiveness.

Significance of the Study

Based on review of literature and clinical practice, it is found that lack of assertiveness leads to lowered job productivity.Nurse managers can increase productivity through an assertive communication style. In addition, the previous studies done by Bennett[13] revealed that one of the most frequently described barriers to productivity is conflict. So, it is illustrated that the effect of assertiveness and conflict resolution on productivity is an important factor in improving quality of patient care. Therefore, the present study aims to explore the effect of assertiveness and conflict resolution skills utilized on nursing care productivity in different health care sectors at Menofia Governorate, Egypt.

Aim of the study: The aim of the present study is to explore the effect of assertiveness and conflict resolution skills on nursing care productivity in different health care sectors at Menofia Governorate, Egypt.

This aim should be fulfilled through the following objectives

1- Assess the assertiveness of nurses in different health care sectors at Menofia Governorate.
2-Assess conflict resolution skills of nurses in different health care sectors at Menoufia Governorate.
3-Explore the correlation between assertiveness, conflict resolution, and nursing care productivity in different health care sectors at Menofia Governorate.

Subjects and methods

Research design: A descriptive correlation design was used for this study. Correlation is a procedure for quantifying the relationship between two or more variables. It measures the strength and indicates the direction of the relationship.[15]

Setting: The present study was conducted in three health care sectors at Shebin El-Kom, Menofia Governorate, Egypt. The first setting is Menofia University Hospital,which is affiliated to the university sector. Its bed capacity is 700 beds, and employs 790 nursing personnel, their qualifications ranging from diploma, bachelor, to master'sdegree in nursing. The second setting is Shebin El-Kom Teaching Hospital, which affiliates to Ministry of Health and Population MOHP. The nursing staff consists of 625 nurses. Their qualifications range from diploma to bachelor degree in nursing. The third setting is El Helal Hospital which is affiliated to the health insurance sector. The nursing staff, consists of 140 nurses classified into categories. The first category includesa minority of nurses with bachelor degree.. The second category comprises the majority of nurses with diploma in nursing.

Subjects: The total subjects included in the present study were 170 nurses and consisted of two groups: nurse managers and staff nurses group.

Nurse managers: this group consisted of 30 nurse managers of different wards/units, haemodialysis, orthopedics, urology, operations, premature, obstetrics, emergency, medicine, surgery and intensive care who were working in these departments during the period of data collection. A nurse manager sample consisted of 10 nurse managers from each of the selected hospitals, namely Menofia University, Teaching and El Helal hospital.

Staff nurses: Asimplerandom sample of 140 staff nurses was selected to constitute the present study subjects from different wards/units,haemodialysis ,orthopedics, urology, operations, premature, obstetrics, emergency, medicine, surgery and intensive care in the three selected hospitals, in addition to the oncology ward in Menofia University. This group consisted of the staff nurses whose qualifications ranaged from diploma, diploma with specialty, techniccal institute, or bachelor degree in nursing, and had the responsibility of direct patient care and who were working in the study settings during the period of data collection and agreed to be included in the study. The sample consisted of 50 staff nurses from each of the University and Teaching hospitals and 40 from El Helal hospital.

Tools of data collection: In order to fulfill the research objectives of this study, three tools were used to collect data. *The first tool:part one:* it was concerned with the socio-demographic data of nurses, such as hospital name, age, marital status, residence, and job related data, including qualification, years of experience and attendance of assertiveness course.

Part two: Assertive behavior inventory tools (ABIT) developed by Clarck & Shea [16], which was used before in Egypt by EL Molla [17], Bakr [18] and Safey EL-Din [19].The scale aimed to measure assertive behavior after being translated into Arabic in order to accommodate our community.It was reviewed by three experts of psychiatric nursing and three experts of nursing administration. The questionnaire consisted of 46 questions constructed to collect data on verbal and non-verbal communication style, control of anxiety and fear, active orientation, work habits, questions related to co-workers and negotiating the system.

*Scoring system:*The five possible responses of each item in the scale were“never", “rarely", “sometimes" “often", and “always". They were scored 1, 2, 3, 4, and 5, respectively. This tool can be categorized as low, moderate, and high levels of assertiveness. The score which was less than 90 wasconsidered a low level of assertiveness, the score which ranged from 90 to135 was considered a moderate level , while the score which more than 135 was considered a high level of assertive.

The second tool: *Conflict resolution inventory:* This inventory was developed by Hurt & Kinney[20], and was used and validated in Egypt by Ismail [21] and Mohamed [22],and was directed toboth nurse managers and their staff nurses to identify conflict resolution styles as self-perceived and as perceived by their staff nurses. It included 29 items which represented five basic conflict management styles that cover all the effective ways of dealing with conflict, namely collaborating style (6 items), compromising style (6 items), accommodating style (6 items), competing style (6 items), and avoiding style (5 items).

*Scoring system :*the five possible responses of each item in the scale were “never", “rarely", “sometimes" , “often", and “always". They were scored 1, 2, 3, 4, and 5, respectively. The scores of the items for each domain were summedup and the total score was divided by the number of the

items giving the average score of this domain. These scores were converted into a percent score to facilitate the comparing across domains.

The third tool: *Professional productivity checklist:* It was developed by Curtin [23] and was directed toboth nurse managerss and their staff nurses. This instrument was designed to measure productivity by the following means

1- Objective measures of efficacy which included information about qualification, certificatesoftraining and skill courses, and years of experience in nursing,

2- Objective measures of effectivenesswhich includeddemonstrating the ability to execute job-related procedures, correctly prioritized activities, performance according to professional and legal standards, clear and concise recording of appropriate information, and cooperative working with others, 3-Objective measures of efficiency which includedpromptness, attendance, reliability, adaptability, and economic disposition of resources.

Scoring system: the responses "not done (No)" and "done (Yes)" were scored "0"and "1", respectively. The researcher made three observations of the performance for each nurse and head nurse related to objective measures of effectiveness and efficiency, and scored each item as “done (yes)” if two of the three incidences met the criteria, and as "not done (no)" if only done once or not at all. All scores were expressed as percentages. The performance was considered adequate if the percent score was 60% or more, and inadequate if less than 60%.

Pilot study

After revision of the questionnaire by experts and its approval, a pilot study was carried out before starting the actual data collection. The purpose of the pilot study was to ascertain the clarity and applicability of the study tools, and to identify the obstacles and problems that may be encountered during data collection. It also helped to estimate the time needed to fill in the questionnaire. Based on the results of the pilot study, modifications, clarifications, omissions, and rearrangement of some questions were done. The pilot study was done on 20 staff nurses and 6 unit managers working in different departments of the selected study hospitals, and these were not included in the total sample of the research to ensure stability of the answers.

Ethical considerations and procedure

Before any attempt to collect data, a formal letter was issued from the Faculty of nursing, Menofia University, to obtain an official approval from the administrators of the hospitals where the data were collected to conduct the study. The letter identified the researcher, the title, and the aim of the research. The data collection phase of the study was carried out over a three-month period, starting from January 2008 to the end of March 2008. The researcher introduced herself to the respondents, and explained the aim and objectives of the study to the nurses in the study setting. Each participant was notified about the right to refuse to participate in the study before taking her verbal consent. Anonymity and confidentiality of the information gathered was ensured. Then, the study tools were distributed among participants, during both morning and night shifts for three daysa week, with instructions about their filling, and were collected on the same day or the following day. This was repeated in each unit/ward of the study hospitals. The researcher was present most of the time to clarify any ambiguity. For observation of productivity measures, the procedure was repeated three times. The result was considered negative if two observations were negative and the third was positive. Conversely, the result was considered positive if two observations were positive and the third was negative. The time taken for every questionnaire to be completed was about 20-25 minutes for each nurse. Head nurses from selected units helped as research

assistants. They were excluded from the study sample. . On the other hand, bachelor nurses observed professional productivity of staff nurses, while nurse managers utilized the professional productivity checklist.

Data management and statistical analysis: data entry and analysis were done using Statistical Package for the Social Sciences "SPSS" program, version 13. Data were represented using descriptive statistics in the form of frequencies and percentages for qualitative variables and means and standard deviations for quantitative variables. Pearson correlation analysis was used for assessment of the relationships among quantitative variables, while the Chi-square test was used for qualitative data. Statistical significance was considered at p-value ≤0.05.

RESULTS

Table 1 demonstrates the socio-demographic characteristics of nurses under study at different health sectors. Concerning age, more than half of the total sample of nurses (53.5%) were 25 years to less than 30 years old. The majority of nurses (92.9%) were females. As for nursing qualifications, half of the nurses (50%) had nursing diplomas. Regarding the occupation of nurses.More than three quarters (82.4%) were staff nurses. Most of them (71.2 %) were married. More than half (54.1%) were from rural areas.

The degree of assertiveness of the studied sample of nurses distributed by their different health sectors is illustrated in table (2). It indicates that nearly half of the staff nurses (49.3%) were highly assertive,compared to 53.3% of nurse managers who were moderately assertive. There was a statistically significant association between health sectors regarding the degree of assertiveness among staff nurses (p = 0.0001) but not among nurse managers. However, there was no statistically significant association between the total degree of assertiveness among staff nurses and nurse managers in different health sectors (p = 0.67).

In table (3), it is evident that more than one half of staff nurses (58.5%) had moderate conflict resolution skills, compared to 73.3% of nurse managers. However, there was astatistically significant difference between staff nurses and nurse managers at health sectors regarding conflict resolution skills (p =0.05).

Table (4) shows thatthe collaboration style was the most common style utilized by nurses in conflict management skills (43.5%), followed by the accommodating style (21.1%), while the compromising style was the least used (5.9%). A statistically significant difference was observed among studied nurses in different health sectors regarding the utilization of competing, compromising and accommodating styles in conflict management (p=0.001,0.04,and 0.05, respectively).

Table (5)shows that there was a statistically significant difference between conflict resolution skills andthe item "demonstrated ability to execute job-related procedures" (p = 0.001). Also, there was a statistically significant difference between assertiveness andthe items "demonstrated ability to execute job-related procedures", "performance according to professional and legal standards", "reliability", and "economic disposition of resources", (p =0.017, 0.031,0.011 and 0.041, respectively). There was a statistically significant difference between the total scores of assertiveness and total nursing care

productivity, where p =0.02. Also, there was a statistically significant difference between the total scores of conflict resolution skills and total nursing care productivity, where p = 0.04.

Table (1): Distribution of nursesaccording to their demographic characteristics in different health sectors (n=170).

Demographic data		Health sectors: University hospital No	%	Teaching hospital No	%	E L-Helal hospital No	%	Total No	%	p-value
Age (years)	20-<25	17	28.3	13	21.7	19	38	49	28.8	χ^2 =9.26 p =0.06
	25-<30	36	60	30	50	25	50	91	53.5	
	>30	7	11.7	17	28.3	6	12	30	17.7	
Gender :										χ^2 =0.60 p =0.73
	Male	5	8.3	3	5	4	8	12	7.1	
	Femal e	55	91.7	57	95	46	92	158	92.9	
	Total	60	100	60	100	50	100	170	100	
Nursing qualification:										χ^2 =57.4 p =0.000
Nursing Bachelor		31	51.7	8	13.3	10	20	49	28.8	
Health technical institute		6	10	5	8.3	2	4	13	7.6	
Associated Degree		0	0	21	35	2	4	23	13.6	
Nursing Diploma		23	38.3	26	43.4	36	72	85	50	
Occupation:										χ^2 =32.6 p =0.000
Staff nurses		50	83.3	50	83.3	40	80	140	82.4	
Nurse manager		10	16.7	10	16.7	10	20	30	17.6	
Total		60	35.2	60	35.2	50	29.4	170	100	
Marital status:										χ^2 =5.3 p =0.50
Single		16	26.7	13	21.7	16	32	45	26.5	
Married		42	70	46	76.7	33	66	121	71.2	
Divorce		0	0	1	1.7	0	0	1	0.5	
widow		2	3.3	0	0	1	2	3	1.76	
Residence:										χ^2 =1.32 p =0.51
Urban		24	40	29	48.3	25	50	78	45.9	
Rural		36	60	31	51.7	25	50	92	54.1	
Mean nursing educational years ± SD		3.4 ± 0.64		3.3 ± 0.69		3.2 ±.46		3.3 ± 0.62		p = 0.07
Total		60	100	60	100	50	100	170	100	

Table (2): Distribution of nurses according to their degree of assertiveness in different health sectors.

Assertiveness degree	Health care sectors: University hospital No	%	Teaching hospital No	%	EL-helal hospital No	%	Total No	%	p-value
Staff nurses :									
Low assertive	0	0	0	0	3	7.5	3	2.1	χ^2 =43.0 p =0.0001
Moderate assertive	38	76	9	18	21	52.5	68	48.6	
High assertive	12	24	41	82	16	40	69	49.3	
Subtotal	50	100	50	100	40	100	140	100	
Nurse managers :									
Low assertive	0	0	0	0	0	0	0	0	χ^2 =4.2 p = 0.11
Moderate assertive	4	40	8	80	4	40	16	53.3	
High assertive	6	60	2	20	6	60	14	46.7	
Subtotal	10	100	10	100	10	100	30	100	
Total	60	100 %	60	100 %	50	100 %	170	100 %	

* Comparison between the total degree of assertiveness among staff nurses and nurse manager: χ^2 = 0.79, p = 0.67

Table (3): Conflict resolution skills among nurses in different health sectors (n=170).

Conflict resolution skills	Health sectors: University hospital No	%	Teaching hospital No	%	EL-helal hospital No	%	* Total No	%
Staff nurses : Low conflict resolution skills	5	10	10	20	9	22.5	24	17.1
Moderate conflict resolution skills	37	74	23	46	22	55	82	58.6
High conflict resolution skills	8	16	17	34	9	22.5	34	24.3
Subtotal	50	100	50	100	40	100	140	100
Nurse manager Low conflict resolution skills	0	0	2	20	0	0	2	6.7
Moderate conflict resolution skills	9	90	5	50	8	80	22	73.3
High conflict resolution skills	1	10	3	30	2	20	6	20
Subtotal	10	100	10	100	10	100	30	100
Total	60	100	60	100	50	100	170	100

* Chi square test = 9.27, p≤ 0.05 means a significant difference

Table (4): Conflict management skills (styles) among nurses in different health sectors.

Conflict resolution skills	University hospital		Teachinghospital		EL-helal hospital		Total		p-value
	No	%	No	%	No	%	No	%	
Avoiding: Never used Sometimes used Always used	6 53 1	10 88.3 1.7	9 44 7	15 73.3 11.7	8 38 4	16 76 8	23 135 12	13.5 79.4 7.1	χ^2 =6.2 p =0.18
Collaborating: Never used Sometimes used Always used	1 32 27	1.7 53.3 45	7 25 28	11.6 41.6 46.6	3 28 19	6 56 38	10 85 74	6.5 50.0 43.5	χ^2 =8.7 p =0.06
Competing : Never used Sometimes used Always used	0 57 3	0 95 5	7 42 11	11.7 70 18.3	0 47 3	0 94 6	7 146 17	4.1 85.9 10	χ^2 =22 p =0.001
Compromising : Never used Sometimes used Always used	16 43 1	26.7 71.7 1.6	19 36 5	31.7 60 8.3	24 22 4	48 44 8	59 101 10	34.7 59.4 5.9	χ^2 =10.1 p =0.04
Accommodating Never used Sometimes used Always used	11 41 8	18.3 68.3 13.4	15 31 14	25 51.6 23.3	16 20 14	32 40 28	42 92 36	24.7 54.1 21.1	χ^2 =9.2 p =0.05
Total	60	100	60	100	50	100	170	100	

Table (5): Correlation coefficient (r) betweentotal scores of the degree of assertiveness, total scores of conflict resolution skills, and nursing care productivity among all nurses under study (n=170).

Variables	Assertiveness		conflict	
	r	p	r	p
PQ1: Demonstrated ability to execute job-related procedures.	.183*	.017	.257**	.001
PQ2: correctly prioritized activities.	.090	.244	.076	.324
PQ3: Performance according to professional and legal standards.	.166*	.031	.073	.346
PQ4: Appropriate information clearly concisely recorded, cooperative working with others.	.133	.085	-.122	.113
PQ5: promptness.	.131	.089	-.108	.162
PQ6: Attendance.	.097	.209	-.090	.243
pQ7: Reliability.	.195*	.011	-.061	.432
PQ8: Adaptability.	.105	.174	-.006	.936
PQ9: Economically disposition of resources.	.157*	.041	-.029	.705
Total productivity	0.25*	0.02	0.15*	0.04

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed)

DISCUSSION

Assertiveness is developed over time. Like a good physical workout, the results of being assertive are cumulative. Your body feels better and your sense of self-value improves. Communication is the key to assertive behavior. Communication includes a sender, a message and a receiver. The sender must put out a clear message. If the message is clear and assertive, the receiver will have an easier time responding in a similar manner. Assertiveness is enriching. It allows you to show genuine concern for others' rights because your own have been met[24]. Being assertive is a core communication skill. Being assertive means that you express yourself effectively and stand up for your point of view, while also respecting the rights and beliefs of others. Being assertive can also help improve your self-esteem and earn others' respect. Because assertiveness is based on mutual respect, it's an effective and diplomatic communication style. Being assertive shows that you respect yourself, because you're willing to stand up for your interests and express your thoughts and feelings. It also demonstrates that you're aware of the rights of others and are willing to work on resolving conflicts[25].

The present study findings revealed that half of the nurses in the study had diploma degrees.This may be because the nursing diploma program was the only one available at Menofia Governorate until the establishment of the Faculty of Nursing at Shebin El-Kom in 1992.

Menofia University Hospital had a higher percentage of nurses (51.7%) with bachelor degrees, but with less years of clinical experience compared to Shebin El-Kom Teaching Hospital. This may be due to

the existence of the Health Technical Institute and Faculty of Nursing in Menofia University, which are responsible for the graduation of younger and less experienced nurses each year, and who enter the workforce and are mostly attracted to the newly established University Hospital.

The high percentages of the nurses were married, so they had more responsibilities in general life which could affect their work responsibility. The findings of the present study indicated that the majority of the sample nurses were moderately to highly assertive. This might be attributed to the age of the subject, where younger ages were more enthusiastic, more productive and assertive.

These findingsare on the same line with Safey El-Din [19],who studied factors affecting assertive behavior of nurses working in different units in Cairo University Hospitals.His study indicated that the majority of the sample nurses were moderately to highly assertive.

The result of the present study is in disagreement with Ehninger [26], who pointed out that many nurses were faced with societal and professional sanctions against assertiveness, such as perceiving themselves as powerless to change their situation. This was due to the presence of three factors, helplessness, powerlessnessand unrecognition.All of these factors lead to depression which interferes with their motivation to assert themselves. Conversely, the opposite situation occurs in head nurses who possess the authority to change.

It is evident from the results of the present study that there was a statistically significant differencebetween total assertiveness, objective measures of effectiveness, and efficiency of productivity among the three settings of the study.This may be due to the style of hospital management which can give the nursing staff a chance that enables them to control over work activities and the respect from doctors with whom they work.

Participants in the present study have mentioned some factors that can improve their job environment to achieve quality of care. These factors are good doctor-nurse relationship, involvement in decision-making, taking feedback from supervisors regarding job performance, meeting the perceived demands of immediate supervisors,absence ofconflict with other healthcare providers, adequate job policies, opportunity to advance, adequate facilities, and financial resources, in addition to absence oftime pressure and low salary.

The present study revealed that the higher percentage of staff nurses and nurse managers had moderate conflict resolution skills, and there was astatistically significant difference between them. The present study contradicted with the findings of the study done by Mohammed [22] and Abd Elgheny [27]. Their findings showed that nurse managers reported high conflict resolution skills compared to staff nurses upon the utilization of appropriate conflict resolution skills.This might be related to difference in the nursing educational level between staff nurses and nurse managers that reflected on differing views of expectation of inherent conflict resolution skills.

Analysis of the results of the present study indicated that there was no appropriate or inappropriate management style to deal with conflict. However, detecting initial symptoms of conflict and adopting the most effective behavior to conflict resolution is essential in nursing units [28]. In this respect, the present study revealed that collaborating

was the most frequently style utilized by nurses in managing conflict, followed by accommodating, competing, avoiding and compromising. This result was in total agreement with Cox [29] who found a greater preference for non-confrontation, and more comfortable and often less effective choices of accommodation, and compromising for conflict management than more assertive and dominating styles of collaborating and competing styles.

Also, this result was in total agreement with that of many similar research studies [22,27,30,31]. On the contrary, results by Hendel et al [32] showed that head nurses viewed themselves as transformational leaders as opposed to transactional leaders.Thecompromise strategy was the most common strategy used in conflict resolution.

The present study revealed that there was astatistically significantcorrelation coefficient between total scores of assertiveness and total scores of conflict among the whole studied sample. This result is supported by the work of Davies [33]. Moreover, Jundt [34] mentioned that assertiveness was one mode for handling conflict, where nurse managers' communication often centers on conflict which consumes as much as 25% of theirtime.

Regarding the relationship between assertiveness and nursing care productivity, the present study findings show thatthere was astatistically significant relation between assertiveness and nursing care productivity among the whole studied sample.This result is on the same line with Fabra & Stewart[32], who added thatthe non-assertive behavior affected the work group as evidenced by decreased productivity and negativejob feeling.

Also, the present study revealed that there was astatistically significant relationship between conflict and productivity among the whole studied sample.This result is on line with the results of [36],who mentioned that the conflict can lead to job dissatisfaction, absenteeism and turnover which are all considered as symptoms of low productivity.

CONCLUSION

In the light of the present study findings, it may beconcluded that the majority of staff nurses at the University Hospital, Shibin El kom Teaching Hospitalm and El -Helal Hospital had high degrees of assertiveness, whilethe majority of nurse managers had moderate degrees of assertiveness, but there was no statistically significant difference between the total degrees of assertiveness among nurse managers in different health sectors.There was astatistically significant difference between staff nurses and nurse managers regarding conflict resolution skills.Also, the higher percentage of staff nurses and nurse managers in the studied sample had moderate conflict resolution skills. Nurses reported thatthe collaboration style was the most common style utilized, followed by the accommodating and competing styles. A statistically significant difference was notedamong the studied nurses in different health sectors regarding the utilization of competing, compromising and accommodating styles in conflict management. However, there was no statistically significant difference amongother styles.There was a statistically significant difference between assertiveness, conflict resolution skills and total productivity among the total studied sample of nurses.

RECOMMENDATIONS

Based on the literature review and the findings of this study, the following recommendations are proposed:

1-Periodical assessment of the assertiveness status of nurses to identify the aspectsof weakness in their behavioral communication attitudes.

2- Encourage nurses to know their rights and responsibilities to help them in the application of assertive communication processes.

3- Staff development programs should be conducted for nursing personnel focusing on assertive communication and conflict resolutions skills to learn how to react effectively and positively with them.

4- Further studies should be done regarding staff development programs conducted for nursing personnel and focusing on assertive communication and conflict resolutions skills to learn how to react effectively and positively with them.

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Original Article

Prevalence of Asymptomatic Urinary Abnormalities Among Primary School Children in Damietta Governorate

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معدل الإنتشار لمشاكل الجهاز البولى الغير ظاهرة بين أطفال مدارس التعليم الأساسى فى محافظة دمياط

محمد أسامة نور[1] ، على السيد منصور[1] ، أحمد على غندور[1] ، عمر عمر زيدان[1] ، محمود فرج[2]
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الملخص

يفيد إجراء عملية المسح لمشاكل الجهاز البولى الغير ظاهرة فى الإكتشاف المبكر لأمراض الكلى ولتحسين كفاءتها الوظيفية . وتعتبر طريقة الغمر العصوى من أكثر طرق المسح شيوعا للإكتشاف المبكر لمشاكل الجهاز البولى الغير ظاهرة. وقد اجريت هذه الدراسة لتحديد معدل الإنتشار لمشاكل الجهاز البولى الغير ظاهرة بين أطفال مدارس التعليم الأساسى فى دمياط ولرفع وعيهم تجاه هذه المشاكل .

وقد تم اجراء دراسة مقطعية على 2873 من الأطفال الأصحاء من 22 مدرسة تعليم أساسى وتم استخدام طريقة الغمر العصوى لإجراء المسح البولى وتبع ذلك إجراء تثقيف صحى للأطفال .

وقد وجد بعد اجراء المسح الأول أن 64 طفلا (2.2%) يعانون من مشاكل بولية منهم 35 طفلا فقط (1.2%) مازال عندهم مشاكل بولية مستمرة بعد الفحص الثانى مع وجود فروق ذات دلالة احصائية بين الأولاد والبنات وبين أطفال الريف والحضر وكذلك بين أطفال المدارس الحكومية والخاصة . ومن بين الخمسة والثلاثين طفلا الذين يعانون من مشاكل بولية مستمرة وجد أن منهم 7 أطفال (0.24%) يعانون من وجود دم بالبول و 5 أطفال (0.17%) يعانون من وجود بروتين بالبول و 6 أطفال (0.21%) يعانون من وجود خليط من الدم والبروتين بالبول و7 أطفال (0.24%) يعانون من وجود صديد بالبول و 4 أطفال (0.14 %) يعانون من وجود سكر بالبول و 6 أطفال (0.21%) يعانون من وجود أملاح بالبول.

كما وجد انه من بين 18 طفلا يعانون من الوجود المستمر للدم أو للبروتين أو كليهما بالبول ، هناك 5 منهم (27.8%) يعانون من وجود إلتهابات الكلى . وقد أظهرت النتائج الدلالة العالية لطريقة الغمر العصوى فى اجراء المسح لمشاكل الجهاز البولى الغير ظاهرة.

وقد اظهر هذا البحث أن مشاكل الجهاز البولى الغير ظاهرة تمثل نسبة بسيطة من أطفال مدارس التعليم الأساسى فى دمياط، وأن التهابات الكلى الحادة التى تلى الإصابة بالميكروب السبحى من أهم أسباب هذه المشاكل، ويعتبر الغمر العصوى طريقة مقبولة عند إجراء المسح البولى والذى يساهم فى الإكتشاف المبكر لأمراض الجهاز البولى. و يجب تقدير نسبة التكلفة والمنافع لفئات بعينها قبل اجراء مثل هذه البرامج.

ABSTRACT

Background: Screening for asymptomatic urinary abnormalities is useful for early detection of renal diseases and to improve its outcome.Dipstick method is the most common screening procedure for early detection of asymptomatic urinary abnormalities. This study was undertaken to determine the prevalence of silent urinary abnormalities among primary school children in Damietta and to raise their awareness. A cross section study was conducted on 2873 healthy children from 22 primary schools. Dipstick method was used for urinary screening. Health education was conducted to children after screening. At the first screening, 64 children (2.2%) had urinary abnormalities and only 35 (1.2%) of them had persistent abnormalities at the second screening with significant difference between boys and girls, rural and urban children, and between children of public and private schools. Of the 35 children with persistent urinary abnormalities; 7 (0.24%) had isolated hematuria (IH), 5 (0.17%) had isolated proteinuria (IP), 6 (0.21%) had combined hematuria and proteinuria (CHP), 7 (0.24%) had pyuria, 4 (0.14%) had glycosuria, and 6 (0.21%) had crystalluria. Of the 18 children with persistent hematuria and/or proteinuria, 5 (27.8%) had evidence of glomerulonephritis (GN). Screening of asymptomatic urinary abnormalities by dipstick method showed high validity.

Conclusion: Asymptomatic urinary abnormalities were detected in a small number of primary school children in Damietta. Acute poststreptococcal glomerulonephritis (APSGN) was the leading cause for these abnormalities. Dipstick test is accepted in mass urinary screening to allow early detection of urinary diseases. The cost-benefit ratio for specific populations should be determined before the implementation of such programs.

Key words: *Asymptomatic urinary abnormalities, Dipstick method, Primary school children, Hematuria, Proteinuria, Health education.*

INTRODUCTION

The increasing incidence of chronic renal diseases among both children and adults is a global health problem [1]. Screening for asymptomatic urinary abnormalities (AUA) is useful for early detection of renal diseases and asymptomatic infections, particularly among children [2]. Because of its simplicity, urine analysis using the dipstick method is the most common screening procedure for early detection of AUA at a relatively low cost. It can be a guide for further evaluation of renal diseases and may help to avoid unnecessary investigations [3]. The justification for screening of AUA of childhood remains questionable given their relative relation with acute renal diseases, which may help to prevent progression into chronic renal illness and renal failure [4]. This study was conducted to determine the prevalence of AUA among apparently healthy primary school children in Damietta and to raise their awareness regarding specific hygienic protective measures through health education.

MATERIAL AND METHODS

This cross section study was carried out from November 2011 to July 2012 on 2873 apparently healthy primary school children from Damietta governorate in the northeast part of Egypt. The children were selected, by simple random sampling, from 22 primary schools. In each school, children were recruited from all grades, by stratified random sampling, with a total number ranging from 110 – 140 children per school. The study was approved by the local Institutional Ethics Committee and informed consent was obtained from the children's parents or caregivers and school directors.

Participants were instructed to void a clean catch mid stream urine specimen into a 200 ml sterile vessel, which was sent to a clinical pathology laboratory. A dipstick test (Multistix, Bayer Diagnostics, Miles Inc., USA) was performed on the urine specimen by trained laboratory technicians, with the reagent strip designed to react progressively producing color changes in given intervals. The results were decided by visual comparison of the test strip with a color chart provided on the bottle label. Urine samples were then prepared for microscopic analysis.

After screening, simple hygienic recommendations were conducted to primary school children and school staff through a health education session.

Abnormal urine findings were considered if one or more of the following were detected: hematuria (a red blood cell count of 5 or more per high power field), proteinuria {protein 1+ (30 mg/dL), 2+ (100 mg/dL), 3+ (300 mg/dL), and 4+ (1000–2000 mg/dL)}, pyuria (presence of more than 3 to 5 white blood cells per high-power field), glycosuria, and crystalluria. Children with positive results received a second urinary screening 10-15 days later and those with persistent abnormal findings were subjected to further evaluation then prepared to referral to a nephrologist. In case of hematuria, acute poststreptococcal glomerulonephritis (APSGN) was confirmed by presence of urinary red cell casts, low serum C3 level, and evidence of recent streptococcal infection by elevated antistreptolysin O titer. In case of proteinuria, fixed proteinuria, suggesting glomerular or tubular renal disorders, was confirmed by protein/creatinine ratio > 0.2. In case of pyuria, asymptomatic urinary tract infection (asymptomatic bacteriuria) was confirmed by a positive urine culture that showed >100,000 colonies of a single pathogen. In case of glycosuria, hyperglycemia was confirmed by random blood glucose greater than 200 mg/dL (11.1 mmol/L). In case of crystalluria, hypercalciuria, suggesting liability to renal stones, was confirmed by a calcium/ creatinine ratio ≥ 0.2.

Statistical analysis Statistical analysis was carried out using the SPSS computer package version 17.0 (SPSS Inc., Chicago, IL, USA). Qualitative data were expressed in the form of numbers and percentages. In order to assess the differences in frequency of qualitative variables, Chi-square test was used.

A *P*- value $\leq$ 0.05 was considered statistically significant.

RESULTS

The total number of primary school children in Damietta governorate was 149312, 56% lived in rural areas and 55% were boys. The children were selected by simple random sampling from 22 primary schools: 12 public schools in rural areas and 10 in urban areas (5 private and 5 public schools).Of the selected 2873 children, 1635 (56.9%) were from rural areas, whereas 1238 (43.1%) were from urban areas. Among them, 1663 were boys (57.9%) and 1210 girls (42.1%). Their ages ranged from 6 to 13 years (Table 1).

Table (1): General characteristics of the studied children.

Parameters \ Children		No.	%
Location of Schools (n= 22)	Rural	12	54.6
	Urban (Public)	5	22.7
	Urban (Private)	5	22.7
Residence of children (n= 2873)	Rural	1635	56.9
	Urban	1238	43.1
Gender of children (n= 2873)	Boys	1663	57.9
	Girls	1210	42.1
Age of children (years)	Mean $\pm$ SD	8.4 $\pm$ 1.2	
	Minimum - maximum	6 – 13	

At the first screening, 64 children (2.2%) had urinary abnormalities. However, only 35 (1.2%) of them had persistent urinary abnormalities at the second screening. Significant difference was observed in the prevalence of urinary abnormalities between boys and girls, between rural and urban children, and between children of public and private schools. However, no significant difference was observed between older and younger children (Table 2).

Table (2): Characteristics of the studied children according to urinary abnormalities.

Characteristics \ Abnormalities		Positive (N=35)		Negative (N=2838)		Total (N=2873)		*P*-value
		No.	%	No.	%	No.	%	
Gender	**Males**	14	0.49	1649	57.40	1663	57.9	0.038 *
	Females	21	0.73	1189	41.38	1210	42.1	
Age	**<10y**	16	0.56	1710	59.52	1726	60.1	0.085
	≥10y	19	0.66	1128	39.26	1147	39.9	
Residence	**Rural**	26	0.90	1609	56.00	1635	56.9	0.040 *
	Urban	9	0.31	1229	42.78	1238	43.1	
School	**Public**	22	0.77	2252	78.38	2274	79.2	0.033 *
	Private	13	0.45	586	20.39	599	20.8	

Values presented as numbers and percentage and analyzed by Fisher's Exact test. *: Significant.

Of the 35 children with persistent urinary abnormalities; 7 children (0.24%) had isolated hematuria (IH) [2 children (0.07%) were confirmed to have APSGN and 2 children (0.07%) were confirmed to have hypercalciuria], 5 children (0.17%) had isolated proteinuria (IP) [3 children (0.10%) were confirmed to have fixed proteinuria and one child (0.03%) with orthostatic proteinuria] and 6 children (0.21%) had combined hematuria and proteinuria (CHP) [3 children (0.10%) were confirmed to have APSGN and one child (0.03%) with orthostatic proteinuria] (Table 3), 7 children (0.24%) had pyuria of which 5 children

(0.17%) were confirmed to have asymptomatic UTI (3 with E coli, one with enterococci, and one with staphylococcusaureus) (Figure 1), 4 children (0.14%) had glycosuria of which only one child (0.03%) was confirmed to have hyperglycemia, and 6 children (0.21%) had crystalluria of which 2 children (0.07%) were confirmed to have hypercalciuria and liability to renal stones (Table 4). The remaining was considered undetermined causes that need further investigations.

Table (3): The patterns of renal diseases in children with persistent hematuria and/or proteinuria.

Symptoms / Patterns	IH (N=7)	IP (N=5)	CHP (N=6)
APSGN	2 (0.07%)	-	3 (0.10%)
Fixed proteinuria	-	3 (0.10%)	-
Orthostatic proteinuria	-	1 (0.03%)	1 (0.03%)
Hypercalciuria	2 (0.07%)	-	-
Undetermined causes *	3 (0.10%)	1 (0.03%)	2 (0.07%)

IH: isolated hematuria; IP: isolated proteinuria; CHP: combined hematuria and proteinuria;

* Undetermined causes may include: other types of glomerulonephritis and IgA nephropathy that should be confirmed by renal biopsy.

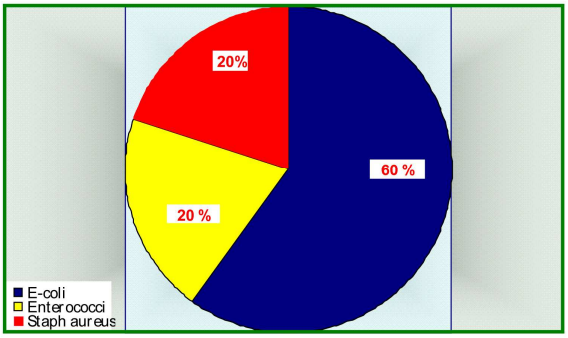

Figure (1): Isolated microorganisms among children with asymptomatic UTI.

Table (4): Distribution of renal diseases among children with persistent urinary abnormalities.

Urinary screening (N = 35) / Abnormalities		No.	% (n= 2873)
Isolated hematuria (n= 7)	**APSGN**	2	0.07
	Hypercalcinuria	2	0.07
	Undetermined causes	4	0.14
Isolated proteinuria (n= 5)	**Fixed**	3	0.10
	Orthostatic	1	0.03
	Undetermined causes	1	0.03
Compound Hematuria & Proteinuria (n= 6)	**APSGN**	3	0.10
	Orthostatic	1	0.03
	Undetermined causes	2	0.07
Pyuria (n= 7)	**Asymptom. UTI**	5	0.17
	Undetermined causes	2	0.07
Glycosuria (n= 4)	**Hyperglycemia**	1	0.03
	No Hyperglycemia	3	0.10
Crystalluria (n= 6)	**Hypercalciuria**	2	0.07
	Undetermined causes	4	0.14

Hematuria detected by dipstick method (isolated and combined) was confirmed by microscopic detection of RBCs with sensitivity of 84.6 %, specificity of 90.9 %, and accuracy of 88.6% (Table 5).

Table (5): Validity of dipstick test in diagnosis of hematuria.

Microscopic RBCs detection / Dipstick method	Hematuria	No Hematuria
Positive test	11 (True +ve)	2 (False +ve)
Negative test	2 (False –ve)	20 (True –ve)
Total	13	22

Pyuria detected by dipstick method was confirmed by urine culture with sensitivity of 100.0 %, specificity of 93.3 %, and accuracy of 94.3% (Table 6).

Table (6): Validity of dipstick test in diagnosis of pyuria.

Urine culture / Dipstick method	Pyuria	No Pyuria
Positive test	5 (True +ve)	2 (False +ve)
Negative test	0 (False –ve)	28 (True –ve)
Total	5	30

DISCUSSION

Routine urinalysis of asymptomatic patients has been shown to detect a variety of urinary tract disorders [5]. Prevalence studies have shown that asymptomatic urinary abnormalities may often be missed on history and physical examination, and the decision for screening must balance the risk for missed infections with the cost and inconvenience of testing [6]. Reports on the prevalence of asymptomatic urinary abnormalities among children in Egypt are generally lacking. Only 2.2% of the screened children had urinary abnormalities at the first screening that persisted in 1.2% at the second screening. Bakr et al screened 1670 Egyptian children from Dakahlia governorate where only 22 children (1.3%) had urinary abnormalities at the first screening that persisted in 12 children (0.72%) at the second screening [7]. In a Bolivian study, screening of 14082 subjects revealed urine abnormalities in 4261 subjects (30.3%) at the first screening and in only 1019 (7.2%) subjects at the second screening [8]. Zainal et al screened 45149 primary school children for proteinuria and hematuria and reported that 1.9% had positive results, but only 0.12% were found to be positive on further evaluation [9]. Other studies from Japan [10], Taiwan [11] and Nigeria [12] reported urinary abnormalities in 0.62%, 0.3%, and 9.6%, respectively, among elementary school children. This variance in prevalence rates during childhood may refer to differences in age, gender, and other factors such as uncircumcision [13], genitourinary tract abnormalities [14], abnormal voiding habits [15], and genetic tendencies such as lack of secretion of carbohydrates that protect against bacterial adherence in the urinary tract [16].

Our results showed that the prevalence of urinary abnormalities was significantly higher among females, among those living in rural areas, and among subjects in public schools (P= 0.038, 0.040, and 0.033, respectively). However, age had no impact on the prevalence of urinary abnormalities. On the other hand, Bakr et al found that gender, age or socioeconomic status had no impact on the prevalence of urinary abnormalities [7]. Similarly, Vehaskari et al found that the prevalence of urinary abnormalities was not age- or sex-dependent [17]. However, Oviasu and Oviasu showed that microscopic urinary abnormalities were more common in girls than in boys in Nigeria [18]. Also, Hajar et al found that urinary abnormalities were more common in girls than in boys in Lebanon [19]. The relatively higher prevalence among girls may be due to the shorter length of the female urethra so the periurethral area is colonized by both anaerobic and aerobic bacteria [20]. Other contributing factors may include bubble baths, tight-fitting clothes or wiping from back (near the anus) to front after going to the bathroom. In girls, this can bring bacteria to the urethral orifice [21].

Among children with urinary abnormalities, the male to female ratio was 0.67:1. Bakr et al reported a relatively similar male to female ratio of 0.71:1 among Egyptian children in Dakahlia governorate [7]. Lin et al reported a male to female ratio of 1.08:1 in Taiwan children [22]. A ratio of 0.94:1 was reported in Korean children [11].

Our results revealed that IH and pyuria were the most common urinary abnormalities (each of 0.24%) of the screened children while IP and CHP were found in 0.17% and 0.21%, respectively. In their study, Bakr et al found that IH was found in 0.36% of the screened children while IP and CHP were found in 0.12% and 0.24%, respectively [7]. Among primary school children in

Malaysia, urinary screening demonstrated that IP was the most common urinary abnormality (0.12%), followed by IH (0.03%) and CHP (0.02%) [9]. Among elementary school children in Korea [23] and Japan [10], the prevalence of IH and IP was 0.54% and 0.05%, and 0.64% and 0.48%, respectively. The highest prevalence of IH (46.4%) and CHP (14.3%) were reported by Lin et al after screening of 573 Taiwanese children with silent urinary abnormalities [22].

Yap et al discussed the role of urinary screening programs in prevention of chronic kidney disease among school children in Singapore. On the first urinary screening of 2325 twelve-year-old school children, IH, IP and CHP were positive in 6.8%, 1.2% and 2.3% of the children respectively [24].

APSGN is prevalent in Egypt as infection by β-hemolytic streptococci is still endemic. Of the 18 children with persistent hematuria and/or proteinuria, 5 (27.8%) had evidence of GN with possibility of other cases if renal biopsy was done. Hypercalciuria, renal stone, fixed and orthostatic proteinuria were the other underlying causes. No obvious causes were identified in 6 children. Results reported by Bakr et al showed that glomerulonephritis (GN) was the most common responsible underlying cause of persistent urinary abnormalities as 8 out of 12 children with persistent urinary changes (66.7%) had evidence of GN after renal biopsy [7].

In the same context, other several studies have confirmed that GN is the major cause of urinary abnormalities [11, 22, 25]. However, no cause was discovered by Bergstein et al in about 80% of children with microscopic hematuria and the most common cause of the disease was hypercalciuria (16%) [26]. Similarly, Chander et al reported that 52.1% of children with silent urinary abnormalities had no definite diagnosis, but hypercalciuria and organic renal diseases accounted for 14.4% and 14.9%, respectively [27].

An extensive evaluation is usually not necessary among children and adolescents with silent hematuria as favorable prognosis is usually predicted [24]. However, follow up is required after careful evaluation to exclude UTI, hypercalciuria, APSGN, and structural urinary abnormalities [28].

Proteinuria is a strong predictor and risk factor of End Stage Renal Disease (ESRD). Therefore, asymptomatic proteinuria warrants further work up and intervention to reduce the incidence of ESRD [29]. The most common causes of persistent pathological proteinuria in children include focal segmental glomerulosclerosis, IgA nephropathy, and membranoproliferative GN confirmed by renal biopsy [30]. Patients with CHP usually have more pathological changes than in those with IH or IP [11] that is correlated well with the severity of morphological alterations of glomeruli in the school age children [31].

Our results revealed that pyuria was present in 0.24% and glycosuria in 0.14% (glycosuria in the absence of hyperglycemia suggests renal glycosuria or proximal tubular disease). These results were comparable to some other studies. In their study of urinalysis in primary health care centers in Saudi Arabia, Al-Homrany et al found that glycosuria was present in 4.7% and pyuria in 10.6% of patients [32].

Our results agreed with the literature in that E. coli was the most common encountered microorganism among children with asymptomatic UTI [33, 34, 35].

Our results showed high validity of the dipstick method in screening of asymptomatic urinary abnormalities with high sensitivity and specificity.

In conclusion, asymptomatic urinary abnormalities are not prevalent in considerable percentage among primary school children in Damietta, and APSGN is the leading cause for these abnormalities. Dipstick test is valid in mass urinary screening. The cost-benefit ratio for specific populations should be determined before the implementation of such programs.

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Original Article

Knowledge of Diabetic Retinopathy Among Saudi Population in Makkah City

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مدى معرفة سكان مكة المكرمة السعوديين بمرض اعتلال الشبكية السكري، دراسة تشمل المراكز الصحية الأولية

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الملخص

المقدمة: يعد اعتلال الشبكية السكري أحد الأسباب التي تؤثر على الإبصار بسبب تغييرات السكري على العين. وتشمل تأثيرات مرض السكري على العين: الاعتلالات التي لا تسبب زيادة في الشعيرات الدموية في الشبكية مثل الارتشاح في مركز الإبصار والاعتلالات التي تسبب زيادة في الشعيرات الدموية في الشبكية.

الأهداف : قياس مدى وعي سكان مكة المكرمة السعوديين حول هذا المرض.
منهج البحث : تم توزيع استبيانات تختوي على مجموعة أسئلة لقياس مدى وعي الناس بمرض اعتلال الشبكية السكري على ٣٨٧ من المراجعين لدى المراكز الصحية الأولية بمكة من هم فوق عمر ال٤٠ عاما. وتم تحليل البيانات عن طريق الإحصاء الوصفي.

النتائج : لم يعرف ٥٢.٧٪ من سكان مكة المكرمة السعوديين أن اعتلال الشبكية السكري يؤثر على البصر. ٧٢.٧٪ لم يعرفوا أن هذا المرض يمكن أن يؤدي إلى العمى الكلي. ٥٢.٢٪ لم يعرفوا أنهم يحتاجون إلى مراجعات منتظمة في عيادات العيون . ٦٨.٧٪ لم يعرفوا أن هذا المرض يمكن علاجه جراحيا بينما لم يعرف ٥٨.٩٪ أن هذا المرض يمكن علاجه عن طريق الليزر.

الخاتمة: معرفة سكان مكة المكرمة من السعوديين عن مرض اعتلال الشبكية السكري تعد ضئيلة ويجب بذل المزيد من الجهد لزيادة معرفتهم بهذا المرض.

ABSTRACT

Background: Diabetic retinopathy causes vision loss due to various diabetes-related changes in the eye. These changes include non proliferative retinopathy, proliferative retinopathy, macular edema and complete visual loss. The progression of diabetic retinopathy
Purpose : Purpose : To assess the knowledge of Saudi population in Makkah city about diabetic retinopathy.
Methods : Questionnaires consisting of items assessing knowledge of diabetic retinopathy were administered to 387 persons aged 40 years or above years. The participants were attending Primary Health Care Centers in Makkah city. Descriptive statistics were used to analyze the data.
Results : 52.7% didn't know that diabetic retinopathy causes blurring of vision, 72.7% didn't know that it can lead to blindness and 52.2% didn't know that they need regular visits to the ophthalmology clinic for follow up. 68.7% didn't know that diabetic retinopathy can be treated by surgery and 58.9% didn't know that diabetic retinopathy can be treated by laser.
Coclusion : : Saudi population in Makkah city 40 years old or above have poor knowledge about cataract and efforts should be done to increase the knowledge and awareness of the disease.
Keywords : *Knowledge, Diabetic Retinopathy*

INTRODUCTION

Osteoarthritis Diabetes Mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to an absolute or relative deficiency of insulin [1, 2] . Insulin deficiency may arise in various ways such as destruction of β– cells of the pancreas, an organ responsible for the production of insulin [2]. Insulin deficiency affects the metabolism of carbohydrates, proteins, fats, electrolytes and water leading to major organ function disorders throughout the body [2]. DM may be broadly divided into two main groups, each with differences in pathogenesis, clinical appearance, management and treatment [3]. Insulin Dependent Diabetes Mellitus (IDDM) or Type 1 DM, is due to lack of insulin and has a peak incidence at 10-20 years [3]. It is less common and estimated to account for 5 to 10% of all diagnosed cases of DM worldwide [3]. About 171 million people worldwide suffer from DM with 3.8 million deaths reported annually from complications of the disease [4]. It is projected that the number of people with DM will rise to 366 million by the year 2030 [4, 17]. The ocular manifestations of DM have been well documented [6-15]. Ocular changes such as diabetic retinopathy and macular edema are leading causes of blindness amongst diabetic patients [12-14]. Gender (males), race, control of diabetes, as well as pregnancy have been identified as risk factors for diabetic retinopathy [2,5]. The early phase of diabetic retinopathy (non-proliferative) is characterized by weakened vessels that leak forming haemorrhages [12-14]. Cotton wool spots (micro-infarctions in the nerve cell layer), hard exudates and venous dilatation are also common features of diabetic retinopathy [12-14]. The late phase (proliferative stage) is characterized by retinal detachment which results from retinal traction by scar tissue, often in the wake of haemorrhages after rupture of fragile new vessels (neovascularization) [12-14]. Other visual and ocular complications include higher prevalence of cataracts, secondary glaucoma, tritan colour vision deficiencies

and reduced corneal sensitivity et cetera [15]. Studies have suggested that up to 25% of all Type 2 diabetics show some degree of diabetic retinopathy when they are first diagnosed and 60-80% of these patients show evidence of diabetic retinopathy after 15 years from the onset of diagnosis [16]. Early detection and treatment of DM may therefore reduce the risk of severe vision loss from diabetic retinopathy. It has been recommended that patients diagnosed with mild to moderate non-proliferative retinopathy require annual eye assessments, and those with severe non-proliferative retinopathy need 3 to 6 month ocular assessments [16]. The proliferative stage requires urgent referral to an ophthalmologist (within two to four weeks) as well as follow up monitoring within 2 to 3 months of the specialist visit [16]. An estimated 12 000 to 24 000 diabetic sufferers lose their sight every year, making it one of the leading causes of blindness in adults between the ages of 20 and 74 years [17]. Studies have been undertaken to investigate the consequences of DM and the knowledge that the public and diabetic sufferers have of the disease [18-31].

The prevalence of diabetes in Saudi Arabia is 16.7% [32]. 31% of diabetics in Saudi Arabia have diabetic retinopathy [33].

MATERIAL AND METHODS

This The study was conducted in Makkah city of Saudi Arabia , between April 2011 and September 2011. It is a cross sectional study which includes all the Saudi population in Makkah city who are 40 years old or older and according to the latest officially announced census. . The Saudi population in Makkah who are 40 years old or above according to the last census was 805206 and by calculating the sample size using (Roasoft) program at margin of error 5% and level of confidence 95% was 384 as the minimum recommended size for this survey. A questionnaire was structured to assess knowledge about cataract. Questions were developed by the researchers and subsequently scrutinized by a panel of experts to establish content validity. The questionnaire was pretested on a volunteer sample of 20 persons aged above 40 to assess questionnaire comprehension. To assess reliability of the questionnaire, 50 persons aged above 40 years volunteered to complete the questionnaire twice within a 1-week time frame. Test-retest reliability for the knowledge section was as follows for the two trials: knowledge about diabetic retinopathy and its treatment (r = 0.87) and for best sources to get information about diabetes (r = 0.83). Given these findings, the questionnaire was considered to be a reliable instrument. The questionnaires were then distributed and administered from 384 participants by the researchers at primary health care centers in Makkah city. Data entry and analysis was done by using SPSS version 17 . Data were presented using descriptive statistics in the form of frequencies and percentages. Statistical significance was considered at p-value = 0.05

RESULTS

The total number of participants was 387. 79.8% were males and 20.2% females. 4.2% were of elementary education, 4.4% of intermediate education, 22.9% of high education, 64.4% of university education and 4.4% of higher education.19.9% of population thought that they know about diabetic retinopathy, 68.8% have got information from other friends and 62.3% from the television. 52.7% didn't know that diabetic retinopathy causes blurring of vision, 72.7% didn't know that it can lead to blindness and 52.2% didn't know that they need regular visits to the ophthalmology clinic for follow up. 68.7% didn't know that diabetic retinopathy can be treated by surgery and 58.9% didn't know that diabetic retinopathy can be treated by laser. Previous diagnosis of diabetic retinopathy increased the knowledge of population about the disease but previous diagnosis of diabetes didn't. 24.5% of population were diagnosed

as diabetics, 43.9% of them had dilated eye exam before 5-6 months and 37.8% had dilated eye exam before 7-12 months. 43.9% were following up at the ophthalmology clinic every 7-12 months, 25.6% every 5-6 months and 23.2% every 3-4 months. 82.4% of population wanted to know more about diabetic retinopathy. 93.2% thought that they could get more information from the media, 90.2% from campaigns and 85.9% from the internet. 82.4% of population wanted to know more about diabetic retinopathy.

DISCUSSION

A 19.9% is considered to be a very low number as a percentage of population who thought that they have had previous information about diabetic retinopathy. The results showed that vast majority of Makkah population above 40 years old know that diabetis retinopathy is a disease, but other than that, their knowledge of diabetic retinopathy and its treatment is poor. It was expected that diabetic retinopathy patients were having more information about diabetic retinopathy than other persons in the population. It was expected that the population needs more information which has been proven subjectively as 82.4% of population wanted to know more about diabetic retinopathy. The media, educatory campaigns and internet should be stressed to be a source of information for the population about diabetic retinopathy in the future.

CONCLUSIONS

Saudi population in Makkah city 40 years old or above have poor knowledge about diabetic retinopathy and efforts should be done to increase the knowledge and awareness of the disease.

The researchers have not found any educatory programs in Makkah city for Saudi population about diabetic retinopathy. From that point and since that there are no educatory programs in Makkah city about diabetic retinopathy, the idea of the research comes aiming to know the knowledge of Saudi population about this disease.

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A case report

Allergen Injection Immunotherapy for Seasonal Allergic Rhino-Conjunctivitis with Co-morbid Asthma: A case report

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العلاج المناعي لحساسية الأنف الموسمية وإلتهاب الملتحمة مع الربو: تقرير حالة

الملخص
بالرغم من ثبوت ارتباط في الاعتلال الوظيفي بين حساسية الأنف والملتحمة والربو ، إلا أن الدراسات السريرية في علاج هذه الامراض باستخدام حقن العلاج المناعي ليست كافيه. والدراسة الحالية هي حالة انثى سعوديه عمرها 33 سنة لديها نوبات من العطس واحتقان وسيلان الأنف، وتستيل أنفي خلفي، مع حكة في العينين منذ سن 18 عاما، مع تكرار هذه الأعراض فى أوائل الربيع ومواسم الصيف. وقد ازدادت هذه الأعراض سوءا تدريجيا مع اضطراب في أداء العمل والنوم والأنشطة اليومية. وكان اختبار وخز الجلد لمسببات الحساسية المستنشقه الشائعه لهذه المريضه ايجابيا وخصوصا طلع شجرة المسكيت. وقد أكدت الأعراض الموسمية والنتائج السريرية واختبار الحساسية تشخيص حساسية الأنف الموسمية والتهاب الملتحمة مع الربو كما يلي: كانت المريضه تستفيد جزئيا لمضادات الهيستامين والكورتيزون المستنشق، علاوة على ذلك تلقت المريضه دورات متكررة من الكورتيزون عن طريق الفم للسيطرة على الربو خلال التفاقم ، وأخيرا،فقد لاحظت المريضة تحسنا كبيرا فى أعراض الحساسية المزعجة ونوعية الحياة بعد بدء العلاج المناعي.

ABSTRACT

A pathophysiologic connection between allergic rhinitis, rhino-conjunctivitis, and asthma has been proposed. However, there are insufficient clinical studies of Allergen Injection Immunotherapy on these comorbid conditions. This is a case study on 33-year-old Saudi female experiencing episodes of sneezing, nasal congestion, runny nose, and post-nasal drip with itchy watery eyes, since the age of 18 years that occur frequently in early spring and summer seasons. Her symptoms have been progressively worsening in severity with significant disruption in work performance, sleep, and daily activities. In vivo skin prick testing to common inhalant allergens was positive mainly to Prosopis Juliflora (mesquite) pollens. Seasonality of symptoms, clinical findings, and allergy testing have established the diagnosis of seasonal allergic rhino-conjunctivitis with comorbid asthma as follows: the patient had partial benefit to antihistamines and inhaled steroids; moreover, the patient received repeated courses of oral steroids to control asthma exacerbations; finally, the patient noticed alleviation of troublesome allergy symptoms and dramatic improvement in quality of life after commencing immunotherapy.

INTRODUCTION

Seasonal allergic rhinitis (SAR), also known as hay fever, is an inflammatory condition of the upper airways that occurs in response to exposure to airborne allergens (typically tree, grass, and weed pollens) in sensitized individuals. SAR is distinguished from perennial allergic rhinitis (PAR), which is triggered by continuous exposure to house dust mites, animal dander, and other allergens generally found in an individual's indoor environment. Patients may have either SAR, PAR, or both (i.e., PAR with seasonal exacerbations).

In recent times, the incidence of allergic diseases, particularly allergic rhinitis (AR), has been increasing worldwide. It affects approximately 30 percent of adults and up to 40 percent of children in industrialized societies.[1] In developing countries, the International Study of Asthma and Allergies in Childhood (ISAAC) showed that 50% of adolescents are affected.[2] It is estimated the minimum prevalence of AR to be 8.8 percent in the United States[3], and 24 percent in UK population[4], while the reported prevalence in Saudi population is 26.5%.[5]

Medications used to treat SAR target biochemical pathways that cause characteristic symptoms. SAR results from the binding of an inhaled aeroallergen to immunoglobulin E (IgE) on the surface of mast cells in the nasal mucosa. An early phase allergic response follows: mast cell degranulation releases preformed inflammatory mediators, such as histamine, tryptase, leukotrienes and prostaglandins, which produce immediate nasal itching and sneezing. Histamine stimulation of the histamine-1 (H1) receptors on sensory nerves causes vascular dilation and increased plasma leakage. Stimulation of parasympathetic (cholinergic) nerve fibers by leukotrienes and other mediators causes mucus secretion from nasal glands. Leukotrienes also increase vascular permeability. The result is nasal discharge and congestion, which is maximal at 15 to 30 minutes. Four to 12 hours after allergen exposure, a late-phase allergic response may occur. The late-phase response consists primarily of nasal congestion and is mediated by the influx and activation of inflammatory T-cells and eosinophils.[2,6,7] Ongoing, prolonged allergen exposure and repeated late-phase responses lead to

progressive inflammation of the nasal mucosa and increased allergen sensitivity. The amount of allergen capable of eliciting an allergic response lessens over time, an effect termed priming. The priming effect is thought to explain the development of mucosal hyper-responsiveness to nonallergen triggers, such as strong odors, cigarette smoke, and cold temperatures.[7,8] It also provides the rationale for initiating effective rhinitis therapies prophylactically before the commencement of pollen season.[9,10]

The diagnosis of AR is based mainly on the history and physical examination.[10] The cardinal symptoms are nasal discharge (rhinorrhea), nasal itching, sneezing, and/or nasal congestion. Many patients also experience symptoms of allergic conjunctivitis, such as itchy and watery eyes.[11] The history of seasonality of symptoms with clear exacerbations, in relation to allergen exposure, help establish a diagnosis of seasonal rhino-conjunctivitis (SARC).

Normally, very low levels of IgE are present in the serum. High serum levels have been detected in as many as 30-60% of patients with AR.[12] Antigen-specific IgE antibodies are the most important *in-vitro* allergy tests in establishing the diagnosis of inhalant allergy.[13] Treatments for AR comprise allergen avoidance and triggering factors, use of appropriate pharmacotherapy, immunotherapy, patient education and follow-up.[14]

CASE HISTORY

In February 2010, a 33-year-old Saudi female mathematics teacher visited her general practitioner and reported suffering from repetitive sneezing, nasal blockage, itching of the nose, watery nasal discharge and a tickling sensation at the back of the throat. These symptoms, she reported, dated back to 8 weeks prior to her visit. She suffered from red, itchy and watery eyes. She also felt dizzy and fatigued. The patient recounted that these symptoms have been reoccurring frequently in early spring and summer since she was in high school, but have been progressively worsening in recent years. Three years earlier, she developed repeated episodes of cough, wheezing and chest tightness. Over the previous three months, she developed two episodes of acute asthma exacerbation and was hospitalized at the emergency department, where she received repeated short-rescue courses of oral steroids.

The symptoms were getting worse, however. The patient complained that her daily activities were disrupted by frequent absences from work and that she was socially embarrassed in the presence of her students and colleagues. Her relationship with her husband, as well as her daily activities, were also disturbed due to these respiratory symptoms. The patient reported that she had no pets at home and that her symptoms were triggered by cold air, tobacco smoke and being outdoors early in the morning. Her husband is a smoker, but she denied history of smoking.

Antihistamine chlorphenamine (Piriton®) tablets, prescribed to her many years ago, were helpful but induced sleep by day. She had used Sodium Cromoglicate (Rynacrom®) 4% nasal spray intermittently and also nasal spray (Otrivine®), with partial response. For chest tightness and wheezing, she used Fluticasone (Flixotide®) inhaler, intermittently, and Salbutamol (Ventolin®) inhaler, when needed. Family history revealed atopic eczema and asthma in her elder child and mother. She resides in Abha city south of Saudi Arabia, a mountainous high altitude city with wide agricultural lands and farms.

On examination, she appeared to be uncomfortable and distressed. Her nasopharynx was congested. Nasal examination showed pale boggy mucous

membranes but no polyps or post nasal discharges were found. The conjunctivae appeared congested and edematous with watery discharge. In addition, the tympanic membranes showed a middle ear effusion. On auscultation, the lungs were wheezy on both sides. Peak expiratory flow rate (PEFR) was 50% of the predicted value.

The result of the Skin Prick Test (SPT) with common inhalant allergens was positive to pollens as follows: Prosopis Juliflora 8 millimeters, Bermuda 4 millimeters, Mugwort 3 millimeters and Timothy 3 millimeters. Total IgE level was high (352.6 IU/ml), and serum specific IgE (sIgE) to Prosopis Juliflora and Bermuda grass was 54.27 IU/ml and 23.44 IU/ml, respectively. Peripheral blood eosinophil count was normal.

Mometasone furoate (Nasonex®) nasal spray was prescribed, 100 micrograms in each nostril once daily. To achieve the maximum benefit, the patient was instructed to avoid the septum when spraying, and to use the medication on a regular basis rather than as needed. Inhaled Fluticasone in a dose of 250 micrograms combined with the long acting bronchodilator Salmetrol 50 micrograms (Seretide®) twice daily was prescribed for 3 months. Cetirizine hydrochloride (Zyretic®) once daily to control nasal symptoms, and Olopatadine (Opatanol®) two drops in both eyes twice daily for control of her ocular symptoms were added to the management plan. She was advised to start treatment two weeks before and to continue therapy through the pollen season. She was advised to discontinue over the counter (OTC) medication and Sodium Cromoglicate spray.

The patient was instructed on the importance of spending as much time as possible indoors with air conditioning during the seasons of spring, summer and fall, and spending as little time as possible outdoors, particularly in the early morning when the pollen count was high.

During follow-up visits, the patient expressed her concerns of using inhaled medications, and fears of developing dependence on them. She expressed her concern over the frequency of her absence from work and the overuse of OTC medications without improvement. These concerns were addressed and the patient was educated about her safety and the importance of compliance to medications.

On her following visit, she did not improve and looked unwell. She expressed concern over the difficulties she encountered in conducting her teaching sessions due to fatigue and lack of concentration. She was compliant on drugs but rhinitis symptoms did not improve. The patient was prescribed an oral Prednisolone course of 25 milligrams daily for 3 days, which was reduced by 5 milligrams per day, and was advised to continue oral antihistamine and inhaled medications.

Because partial clinical improvement was achieved, we opted for specific immunotherapy. Referral to an allergist at the regional hospital was arranged for the patient. After counseling for the pros and cons, the patient was started on sublingual immunotherapy (SLIT) four months before the pollen season, and stopped at the end of the pollen season. The build-up phase was done over six weeks and a maintenance phase protocol was followed with no dose reduction during the pollen season.

The percentage of pollen allergen extract in SLIT solution was as follows: mesquite 40%, Bermuda 20%, Mugwort 20% and Timothy 20%. An allergen extract was prepared in separate vials at different and increasing concentrations of 10, 100 and 300 IR (Index of reactivity).

The patient was followed up for three years. She noticed dramatic improvement of the troublesome allergy symptoms. Work performance, tolerance to daily activities

and sleep significantly improved. Inhaled medications were reduced gradually with antihistamines used intermittently. No oral steroids were required during immunotherapy. She continued SLIT for three years with no recurrence of the symptoms after cessation of treatment.

CASE DISCUSSION

Airway allergic disorders are attributed to aeroallergen exposure. In recent decades, researchers have put forth allergen exposure as a major cause of rhinitis and asthma [15-18], and hence the global increase in exposure to aeroallergens is labeled responsible for the disease[17].

Mesquite (*Prosopis juliflora*) is primarily associated with allergic disease in southwestern United States [19,20], Mexico [21], Saudi Arabia [22], South Africa[23], Kuwait [24], United Arab Emirates (UAE) [25], and India [26]. The legume *Prosopis juliflora* has several varieties [20], and is used for the restoration of desert land and as a wood resource. [22,26] It is found to be a rich and significant source of allergens [23]. In UAE, patients sensitive to prosopis were found to be around forty-five percent[25]. Al-Frayh et al. reported the role of Prosopis pollens as a sensitizing factor in Saudi Arabia [22].

Asthma and allergic rhinitis (AR) co-morbidity refers to the association between asthma and AR. This is due to their physiopathological, epidemiological, and clinical similarities[27-31]. The impact of rhinitis with co-morbid asthma on quality of life is significant. In one study, concomitant asthma with rhinitis caused more physical limitations, higher rate of asthma attacks, more emergency room and GP visits than AR alone did to patients.[7]

In the Allergic Rhinitis and its Impact on Asthma (ARIA) classification, intermittent and persistent rhinitis were proposed to replace seasonal and perennial allergic rhinitis (AR). Our patient was categorized as moderate to severe intermittent AR. The global assessment of the patient's nasal and non-nasal symptom severity score was five. This score was measured with a modified 7-point visual analog scale (score seven indicates unbearably severe symptoms).[32]

Nasal antihistamines are similar in efficacy to oral antihistamines. Combined topical ocular antihistamines, non-steroidal anti-inflammatory drugs, and mast cell stabilizers should be used for associated allergic conjunctivitis, as they significantly reduce ocular symptoms.[33,34]

Intranasal corticosteroid therapy is the most effective medication for treating seasonal allergic rhinitis. Patients should start intranasal corticosteroid two to four weeks before the beginning of the pollen season for the prevention of nasal symptoms of seasonal allergies.[11] Sensory attributes of the nasal spray, e.g. smell and taste, might affect patient compliance.[35] Combination therapy of intranasal corticosteroid and oral antihistamines is beneficial to control severe symptoms; an attempt is made to discontinue one of the agents when symptoms have abated.[36,37] In patients with severe symptoms despite treatment with topical corticosteroids and antihistamines, a better alternative is the occasional, intermittent use of oral prednisolone (0.1-0.2 mg/kg) in the morning of days when the pollen count is high.[37] Leukotriene receptor antagonists are indicated as an adjunct to treatment if the patient showed inadequate response to intranasal corticosteroid and antihistamines.

The mainstay of allergen-specific immunotherapy is inducing tolerance to the causative allergen. The key factor is the anti-inflammatory effect of immunotherapy and is based on switching T cell phenotype which, in allergic subjects, is categorized by a prevalence of the Th2 type and the release of IL-4, IL-5, IL-17, IL-13 and IL-32 cytokines.[38] Immunotherapy results in a Th1-phenotype characterized by increased

IFN-gamma and IL-2 release or by a suppressed Th2 response, through a mechanism of anergy or tolerance. It is now recognized that T-cell tolerance is described by the production of allergen-specific T regulatory (Treg) cells, which generate cytokines, such as IL-10 and TGF-beta with immunosuppressant or immunoregulatory activity. [39,40] The dendritic cells and regulatory T cells promote tolerance by suppressing inflammatory cells and inducing isotype switching of antibodies from IgE to IgG, mainly IgG4, which then block the allergens from binding to IgE located on the surface of mast cells and basophils, thus preventing cell degranulation.[41]

Multiple studies have found the ability of immunotherapy to prevent progression of allergic disease, but more research is needed to confirm the positive preventive role of immunotherapy in allergic diseases.[42]

Immunotherapy based on allergen, in its old-fashioned subcutaneous form, has ample verification of efficacy in allergic asthma, as established by a meta-analysis of 67 double-blind, placebo-controlled studies.[43] However, subcutaneous immunotherapy (SCIT) has a major flaw, specifically seen as a systemic reaction resembling anaphylaxis, that is quite exceptional but may be life-threatening and even lethal.[44] There are other problems of SCIT, which includes the irritation of frequent injections and insecurity concerning the optimal strength of extracts and the stability of allergen mixtures. This encouraged the pursuit for safer ways of administration of allergen extracts. Sublingual immunotherapy (SLIT), which was initiated in the 1990s, ultimately encountered such need while providing a clinical efficacy equivalent to SCIT. [45]

Meta-analyses have made it evident that SLIT is effective in allergic rhinitis by expressively reducing the clinical symptoms; [46-50] however, the efficacy in allergic asthma is still questioned. In fact, in the first meta-analysis, there were inadequate data from patients with asthma, [46] and ensuing analyses gave conflicting results, some even advocating negative conclusions. [48,51]

In conventional SCIT, gradually ascending dosages of the allergen extracts are injected subcutaneously in weekly intervals (up-dose period) until the individual maximum dose is reached (dose-maintenance period). Despite the clear benefits of SCIT in allergic rhinoconjunctivitis and (allergic) bronchial asthma, only a few allergic patients subscribe to this treatment. [52-54] Inconvenience is likely the most common reason for not beginning, or discontinuing, the conventional form of SCIT. [52]

In accelerated SCIT protocols, two to three injections are administered per treatment day with an interval of 30 minutes between the injections in weekly intervals. Accelerated SCIT schedules saves time with the cost of a slightly increased frequency of side effects.[55] However, recent studies have suggested similar safety profile as conventional schedules.[52]

SLIT also requires tolerance of the mouth itching that may occur for a few weeks to months at the onset of treatment. Contraindications for SLIT are mainly the same as for SCIT, including lack of compliance, pregnancy, uncontrolled asthma, immunodeficiency, and autoimmune diseases. For SLIT additionally, oral mucosal diseases can be contraindications if immunotherapy irritates the mucosa.[56]

SCIT can be used by non-modified ("native") extracts with unchanged allergen conformation and chemically modified (polymerized) extracts (so-called allergoids). Allergoids are equivalent in efficacy to that of standard SCIT with low rate of systemic reaction.

The major advantages of allergoids are the low number of injections required to reach

the maximal allergen dose (six injections in the majority of patients) given at 1-week intervals, followed by three additional doses at intervals of 2 weeks. There are few commercially available allergen-specific immunotherapy (SIT) products based on allergoids, whether for subcutaneous injection or as sublingual formulations. Conclusions on the efficacy of allergoid preparations are limited by the amount of published data. Further research is needed to increase the level of evidence for these preparations in SIT.[57-59]

Education is required to increase the patient's knowledge about immunotherapy and compliance. Immunotherapy, in general, is usually not more costly than traditional allergy medications over the projected course of treatment. SLIT, however, has been shown to be more cost effective than SCIT from all perspectives.

CONCLUSIONS

SIT can significantly improve the management, outcome, and quality of life in moderately severe SARC with asthma partially controlled with conventional therapy. Characteristic allergy symptoms with seasonal exposure to pollens and associated clinical features, supported with allergy testing, help establish diagnosis.

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