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From the Editor



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This is the third issue for 2007 and with it we are starting Child Watch - a project to monitor at risk children around the world and to provide and disseminate educational strategies to reduce and eliminate these risks.

In this issue a study from Jordan looks at the clinical features and prognostic factors of breast cancer. The aim of the author is to analyze the clinical presentation and outcome of Jordanian patients with breast cancer. Data from 184 patients registered and treated at different Royal Medical Services Hospitals in Jordan, from January 2002 to December 2005 were analyzed. The study's results indicated that breast cancer prognosis in Jordan remains poor, primarily due to late diagnosis. The authors stressed that that future studies of survival of node-negative patients should include information on co-morbidity and treatment.

Prof Abdul Rahman Al-ajlan, studied the incidence of hyperkalemia among diabetic patients. He studied a total of 362 patients and 158 non-diabetic control subjects. He observed that there is a strong association between hyperglycemia and hyperkalemia in Saudi diabetes mellitus patients of type 1 and type 2. The elderly uncontrolled diabetics are at a higher risk of hyperkalemia. Hyperkalemia in uncontrolled diabetics can lead to kidney and liver damage and cardiac arrest. The physicians, while prescribing ACE inhibitors to diabetics, must take precautions to avoid complications of hyperkalemia.

A study from Basrah was presented on the prevalence of metabolic syndrome among diabetic patients with type 2 diabetes mellitus (DM). This was a cross sectional hospital based study of patients. Highest prevalence of MetS was reported in this study which includes diabetic patients only, although this high figure may be due to a different definition and population studied with selection bias. The main stay of management of MetS is dietary modification and weight reduction which may delay the development of DM, and improves the control of established DM and decreases morbidity and mortality associated with this syndrome.

A two-stage prospective study from Saudi Arabia was performed in an IVF unit in the eastern province. The first stage compared the fertilization and pregnancy outcomes in patients with Polycystic Ovary (PCO) Syndrome and patients with poor response to recombinant Follicular Stimulation Hormone

(rFSH). The second study compared these outcomes according to follicular size. The authors concluded that concentrations higher than 0.075 IU ml in culture media for IVM are not necessarily associated with a better outcome. Larger Follicular size produces better fertilization and pregnancy rates. In both PCO and poor responders, cycle irregularity is associated with poorer outcomes.

Dr Magableh S and Bataineh HA studied the prevalence of childhood brucellosis among patients attending the pediatric department at Prince Rashed Hospital (PRH). In their series, pediatric brucellosis is quite common since this area is endemic to *B. melitensis* where a strong clinical suspicion or laboratory routine screening has to be done to diagnose and institute specific therapy.

A paper from Tehran investigated the relationship between social and family factors and the idea of committing suicide, among university students in Iran. 100 university students (50 male, 50 female) from the University of Welfare and Rehabilitation Sciences were randomly selected and participated in the study.

It was found that the singles were more inclined to commit suicide than the married students. Divorce, failure in education, and family background also increase the likelihood. Among the other increasing factors old age and female sex should was indicated.

A well rounded study evaluated the relationships between health behaviors, some medical conditions and health related quality of life in an east Mediterranean community sample. The study population consisted of 327 adult Datca-Knidos county residents. Participants filled out a questionnaire regarding health behaviors, medical history and an extensive health related quality of life (HRQOL) measurement short form questionnaire (SF-36v2).

In this issue Dr Thamer Al Hilfy discusses the concept of total quality management (TQM) which is defined as controlling every thing about what is actually done to create a product, in this case better quality of education and better quality of graduates related to one of Iraqi colleges (Tikrit College of medicine/ University Tikrit/Iraq).

Total quality management and accreditation in Iraq

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Introduction

Total quality management (TQM) is defined as controlling every thing about what is actually done to create a product (e.g. better quality of education and better quality of graduates related to one of Iraqi colleges (Tikrit College of medicine/university tikrit/Iraq). The issue of education, research and development, developing the role of the health services in education, research and development in partnership with other organizations and agencies focusing on health services research, are among many concerns and responsibilities of this college.

The MOHE in Iraq recently (2 months prior to writing this paper) held a conference about the concept of total quality management and quality approach. The attendants were teachers and medical staff of all Iraqi universities and medical staff of both the MOHE and MOH. The intention of this conference was to review the recent quality revolution and reasons behind the need for increase in quality consciousness of our universities as well as to highlight the dimensions of quality in relation to structure, process and outcome (Donabedian). The conference highlighted to the attendees approaches to managing quality, and the difference between traditional, problem solving and total quality approach.

The college, teachers and staff members were involved in this conference in the hope of applying these new concepts (as far as our Iraqi colleges are concerned) to achieve better quality by following the true total quality processes with its 3 fundamental bases (Student and community focus, continuous improvement and employee involvement).

Unfortunately this conference and the associated recommendations that were followed did not find a basis for a starting point due to the current situation of the country and the instability regarding security conditions.

What was interesting mainly in this conference and the further meetings that followed, is the confusion that involved most of the participants in the way of differentiation between concepts related to TQM and quality assurance, appraisal and accreditation, evaluation and monitoring.

We do believe that a lot of work is needed in this field regarding proper application of TQM in Iraqi universities related to education, research and development.

Unfortunately this conference was not followed by any further steps of a practical nature.

Attempts to apply total quality management principles in Iraq:

The 1st scientific attempt in Iraq was started by the implementation of the National system of accreditation in 1993. Tikrit College of medicine was part of this attempt.

Three components did comprise this implementation:

1. The systematic questionnaire component: This was conducted centrally by a special unit in the MOHE and scientific research called, performance evaluation unit. This component comprises comprehensive and detailed check lists which involve seven domains. These cover the following topics : goal, objectives, departmental structure - which includes all data available on departments of our college, the scientific units connected with our college, the number and qualifications and experience of available human resources including administrators, technicians, workers and faculty staff members and relevant information concerning their academic qualifications and titles, resources (human, financial and physical) including services and equipment that are already available in the college for students and staff, like transportation, library and technology services, information .Professional and social services, number of students (Iraqi and non Iraqi at that time) including success and attrition rates, research and dissertations. Teaching staff including academic ranked differences, qualifications and teaching experience and load if any. Curriculum and methodologies being the only college in Iraq that follows the PBL approach and strategies that should be defended to face the classical colleges accusations, exploring teaching and learning strategies and approaches, educational training opportunities, resources available for teaching regarding classrooms, halls, datashow, overhead slide projectors, etc. scientific activities, research, cultural exchange and external cooperation.

Published research and books are evaluated also according to impact and usability of services. In addition to the number of conferences and symposiums held by the college.

This system is supposed to be designed to cover and fulfill agreed standards; feedback mechanism is supposed to be provided regarding the input data, processes and outcomes.

The unit of performance is responsible for analyzing these almost quantitative data to end with an evaluation of and feedback on, quantitative and qualitative bases together.

To comment on this component and in spite of the fact that this activity does not exist for the time being, and that there is no clear picture whether this unit will be activated or replaced

by a further unit like implementing TQM approach in a more scientific way. One point that characterizes this unit is that it did follow the traditional quality approach regarding managing quality. It emphasizes quality assurance, quality control to some extent and to lesser extents, statistical quality techniques based on random sampling from data related to our college.

No team problem solving in its technique were available to induct remedies. On the contrary it seems that the evaluation was done on a traditional approach and prescriptions provided in the same manner.

The goal was somehow, to preventing failure rather than to improve it continuously. The second comment on this evaluation is that it takes the number of activities, rather than the content of such activities, which makes the activities more like slogans or banners, rather than a scientific approach, and this includes also the type of research and other activities.

2. The second component: is to evaluate the outcome of learning processes in the form of the central student examination (CSE): Written multiple choice question examinations are conducted by central national boards and randomly selected (1-2) papers in each year will account for 50% of the total mark, in the selected topic.

We faced many problems regarding this issue as the main concentration and balance was on the knowledge domain focusing more on that issue, and neglecting the practical skills as another major domain which should be taken into consideration. Being a PBL College, this added more obstacles in relation to successful quality improvement in the education process.

3. The third component deals with what is called Annual performance evaluation of the teaching staff, following several domains and scoring systems. One important issue regarding this component is that this evaluation is directly linked to

promotion and increments of faculty staff. It is supposed that direct and face to face feedback is conducted with those to achieve highest marks and those who fail to achieve the minimum marks.

The main comment on this component is really related to absence of scientific standards (related to quality management), absence of certain specifications, and categories lead the component to more subjective outcomes than objective outcomes.

On the ground there is no face to face evaluation and the process is subjected to many interferences from the Dean and other power units in the college.

Conclusion

Vital attempts and great efforts were spent toward achieving the goal of total quality management and better quality of graduates. On the other hand, absence of constancy for improving the educational services, no clear philosophy attempted regarding quality and accreditation, dependence on some aspects of inspection, deficiency in training on the job programs, lack of trust between staff members and higher authorities regarding evaluation were revealed.

Confusion related to topics like total quality approach, Quality control and assurance, also lack of distinction between appraisal and accreditation, and lastly evaluation and monitoring. All these topics need to be addressed thoroughly for the sake of better quality education and better quality of graduates.

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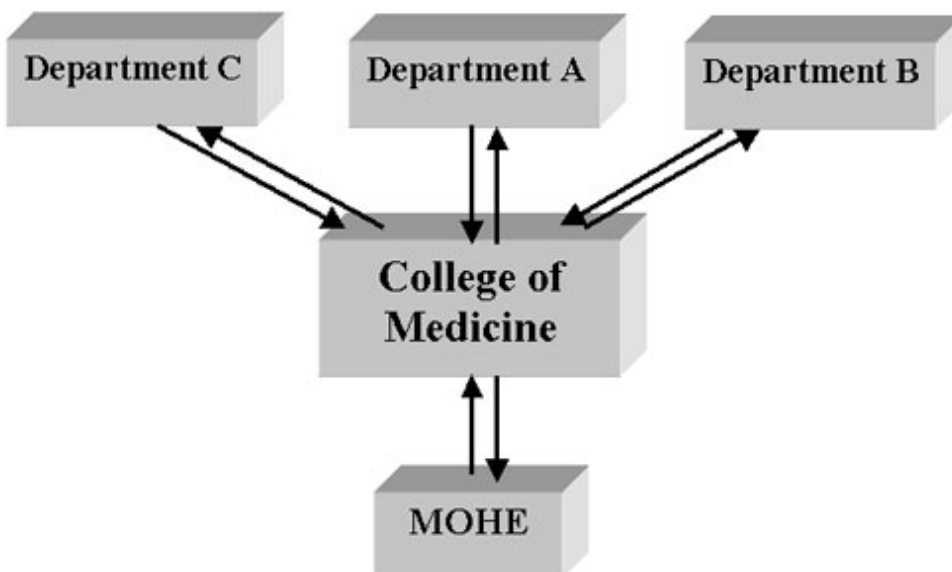


Figure 1. Iraqi Medical School (Systematic Accreditation)

Clinical features and prognostic factors of breast cancer at Jordan

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Abstract

Background: Data on the clinical profile of breast cancer from Jordan is scant, due to different factors such as lack of proper statistical centers, different lifestyle, and different socio-demographic structures.

Aims: To analyze the clinical presentation and outcome of Jordanian patients with breast cancer.

Materials and methods: Data from 184 patients registered and treated at different Royal Medical Services Hospitals in Jordan from January 2002 to December 2005 were analyzed. The analysis concentrates on age, site, lymph nodes status, grade and type of the breast cancer found in Jordanian patients.

Results: The median age was 52.5 years and 54% of patients were pre-menopausal. Ninety-six per cent (177) patients presented with a lump. Stages 1 (14/184), Stage 2 (111/184), and Stage 3 comprised (59/184). Right breast involved in breast cancer was (93 /184), left breast involvement (90/184) and one case had a bilateral involvement. Most patients who needed chemotherapy were prescribed Tamoxifen for 5 years. The majority (86.4%) had a lump size > two cm.

Conclusions: The study's results indicated that breast cancer prognosis in Jordan remains poor, primarily due to late diagnosis. Since breast conservation protocols yield results similar to mastectomy, its use should be extended. Search for biological prognostic indicators should continue for their potential use as guides for treatment decisions. Tumor size, grade and year of diagnosis all have significant constant effects on disease-specific survival in breast cancer, while the effects of age at diagnosis and disease stage have significant effects that vary over time. The histologic type is important to consider in the prognosis and treatment of women diagnosed with breast cancer. Future studies of survival of node-negative patients should include information on co-morbidity and treatment.

Introduction

Breast cancer is the most common cancer and the second leading cause of cancer death among women in general; annual breast cancer deaths are exceeded only by those for lung cancer.¹

The traditional diagnostic approach to breast lumps include physical examination, ultrasound and a mammogram screening procedure. These diagnostic procedures have a relatively low sensitivity regarding definite malignant small breast lumps and have largely been replaced by cytological lump evaluation. Breast cancer is one of the most common malignancies in women and the incidence has been increasing. Cytology play an important role not only in the diagnosis of breast lesions, but also in keeping the benign - to - malignant biopsy ratio low, so that unnecessary surgery is not performed. However, breast carcinomas do not always show every feature of malignancy. The well- differentiated or low-grade carcinomas are often difficult to differentiate from benign cells .It may be helpful to consider the clinical and radiological findings.

Conservative treatment of multifocal breast cancers, which can be completely removed by a single lumpectomy, seems, when technically feasible, an alternative to mastectomy. The increasing prevalence of breast cancer in our society has produced an ever-greater demand for new diagnostic and therapeutic technologies. Today, patients ask not only that these new technolo-

gies offer improved diagnostic and treatment capabilities but also that the procedures are convenient, cost-effective, and less invasive than before. Other diagnostic tools, such as sonography, mammography, magnetic resonance imaging and scintimammography, are now available .The additional information afforded by these technologies is intended to limit the number of patients who need further evaluation with breast biopsy. Early-onset breast cancer may differ with respect to etiology, clinical features and outcome compared with breast cancer in older women.

Clinically most of the patients with malignant breast lump had a palpable mass, which signifies the role of routine self-examination and screening programs.

Late diagnosis is a major factor for increased mortality as the majority of the patients present in advanced or metastatic stage. This is primarily attributed to lack of access to medical facilities, virtually non-existent breast cancer screening programs, lack of awareness and social-cultural attitudes. . A recent meta-analysis of the breast cancer screening trials indicates that screening reduces the mortality rate by approximately 25%².

Materials and Methods

Data from 184 patients registered and treated at different Royal Medical Services Hospitals in Jordan from 2002 through 2005 were analyzed. The analysis concentrated on age, site, lymph nodes status, grade and type of the breast cancer, found in Jordanian patients.

Case records of all the female patients presented at the surgical Clinic in the Royal Medical Services Hospitals over a four-year period from January 2002 to December 2005, were retrieved. EBC (Early Breast Cancer) was defined as tumors of less than five centimeters (T1, T2), with either impalpable (N0) or palpable (N1) but not fixed lymph nodes, with no evidence of distant metastases (M0), corresponding to Stages I. Patients with tumors more than five cm (T3) were included if they had N0 M0 disease; Stage IIb. All EBC cases with pathological confirmation either by fine needle aspiration cytology or core biopsy and who had been treated by at least one mode of treatment (surgery, chemotherapy or radiotherapy) were included in the analysis. (Table 1.). Data from 184 patients was thus analyzed. All patients were followed up every three months after discharge from the hospital, following the initial treatment.

Results

The median age was 52.5 years and 54% of patients were premenopausal. 5% have unknown menopausal status and 41% had a post menopausal status. Ninety-six per cent (177) patients presented with a lump. Stages 1 (14/184), Stage 2 (111/184), and Stage 3 comprised (59/184). Right breast involved in breast cancer was (93 /184), left breast involvement (90/184) and one case had a bilateral involvement. Most patients who needed chemotherapy were prescribed Tamoxifen for 5 years.

Median ages at menarche and menopause were 14 years (range 12-17 years) and 46 years (36-56 years), respectively. 177 (96%) patients presented with breast lump. The majority (86.4%) had a lump size > two cm. 77 (15.8%) had pain and 24 (4.9%) additionally had nipple discharge.

All patients underwent surgery; either a breast-conserving surgery (BCS) was carried out or simple mastectomy with axillary clearance was performed. Invasive ductal carcinoma was the commonest histology in 151 (82.1%) patients followed by invasive lobular carcinoma in 18 (9.7%), mixed type 12(6.5%) and medullary carcinoma in three (1.6%).

Adjuvant radiotherapy was given to some patients; indications included T3 tumor size, ≥ 4 positive axillary nodes, (Table 2), positive margins, and BCS. Chemotherapy was administered to other women. Most of the patients were given CMF regimen at the oncology clinic.

Discussion

Breast cancer is a major cause of cancer deaths in women and is increasing in incidence. There appears to be a leveling off in the incidence of breast cancer; previously the incidence had been increasing. A typical pathology report should indicate the type of breast cancer, the histologic grade, the size, and a comment on the surgical margins. In addition, depending upon the case, ancillary studies examining for estrogen and progesterone receptors may be ordered. The age-specific incidence rate curve for breast carcinoma overall increases rapidly until age of about 52 years, and then continues to increase at a slower rate for older women.

Breast cancer clinical research

An important goal is to analyze how factors are seen to affect the disease process. Meanwhile, the disease progression is not fully modeled using standard analysis since transitions between intermediate events such as local-regional recurrences or metachronous contra lateral breast cancer are not considered.

In the present study.

Breast cancer was usually self-diagnosed and tumors were > 2 cm at presentation in some of the cases, suggesting the possibilities of a delay in diagnosis, more aggressive tumors or both. Menopause did not seem to have any effect on Breast carcinoma as evidenced by steadily rising rates at all ages.

The 3 known causes of human breast cancer, ionizing radiation, exogenous ovarian hormones and beverage alcohol, offer some preventive possibilities but do little to explain the epidemiologic features of the majority of cases of the disease that occur in their absence ³

There is no evidence that detection bias plays a major role, and although the right breast is slightly larger, on average, than the left, there is little evidence that breast size is associated with breast cancer risk. The reason for the right-sided excess among women in our study remains unclear.

Breast carcinoma is an unpredictable disease in the sense that some patients may present with relatively early disease and die of widespread metastases within six months to one year, while others present with fairly advanced disease and yet survive longer ⁴. The various histologic types of breast cancer exhibit differences in regard to relative frequency, site pattern within the breast, and patient survival.

Young patients with breast cancer had the worst histopathological features and the worst survival rate compared to their older counterparts. Age was an independent significant prognostic factor for relapse.⁵ Tumor size, grade, race of patient, and year of diagnosis all have significant constant effects on disease-specific survival in breast cancer, while the effects of age at diagnosis and disease stage have significant effects that vary over time. ⁶

Younger patients as a group have more aggressive and advanced breast cancer at presentation compared with older patients. Considered in a multivariate model, together with other variables, age does not provide independent prognostic information and should not be used alone for management decisions ⁷. Young breast cancer patients have poorer outcomes, which are in part attributed to later stage disease, more aggressive tumors, and less favorable receptor status. There still appears to be other important factors that are contributing to the worse outcomes for these young patients, such as socio-economic status. Physicians need to have heightened awareness when evaluating this population, and increasingly efficacious adjuvant therapies need to be developed.

The outcome of these patients may be improved by patient education and availability of better health care facilities

Axillary ultrasonography is increasingly being used to improve the staging of breast cancer patients who have negative axillary lymph nodes on physical examination.⁸ This approach has a number of advantages. First, node-positive patients identified with ultrasonography can be referred for axillary dissection, without the need for sentinel lymph node (SLN) staging.⁹ The probability of death from breast cancer exceeded that from all other causes for patients diagnosed with localized disease before age 50 years, with regional disease before age 60 years, and with distant disease at any age.¹⁰ There is little evidence that breast size is associated with breast cancer risk.¹¹

Patient care decisions occur in the context of breast cancer and other age-related conditions. Co-morbidity in older patients

may limit the ability to obtain prognostic information (i.e., axillary lymph node dissection), tends to minimize treatment options (e.g., breast-conserving therapy), and increases the risk of death from causes other than breast cancer.¹² In general breast cancer is a major public health problem in Jordan. Late presentation is a major concern, as large numbers of early breast cancer patients are still diagnosed in clinical Stage II. Patient preference for mastectomy is an important reason for the underutilization of breast conservation therapy. Education/awareness campaigns, improvement of socio-economic conditions, better access to diagnostic resources, availability of higher standards of health care, use of breast self-examination, and screening mammography if implemented nationally would go a long way towards increasing early diagnosis and improved survival with a consequent possible rise in incidence of early cases as is happening in the West.

Conclusion

In our study there was no impact on recurrence of breast cancer with regard to size, age, menopausal status, nodal status, histologic subtype, adjuvant therapy, or extent of surgery.

- The study's results indicated that breast cancer prognosis in Jordan remains poor primarily due to late diagnosis.
- Since breast conservation protocols yield results similar to mastectomy, its use should be extended. Search for biological prognostic indicators should continue for their potential use as guides for treatment decisions.
- Mammogram is a valuable tool in early detection of breast cancer; this is especially in bilateral breast cancer, which is invariably advanced when diagnosed.
- Tumor size, grade and year of diagnosis all have significant constant effects on disease-specific survival in breast cancer, while the effects of age at diagnosis and disease stage have significant effects that vary over time.
- Future studies of survival of node-negative patients should include information on co morbidity and treatment.
- We conclude that histologic type is important to consider in the prognosis and treatment of women diagnosed with breast cancer.

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Table 1. Patient and tumor characteristics

Characteristic	No. (%) of patients
Age, mean (range)	52.5y
Primary tumor stage	
Tx	1
Tis (± microinvasion)	11
T1	78
T2	55
T3	23
T4	16
Pathologic nodal stage	
N0	64
N1	120
No. Of nodes recovered, mean (range) a	18 nodes
Method of diagnosis	
Fine-needle aspiration	29
Core needle biopsy	140
Excisional biopsy	21
Incisional biopsy	4
Interval between Breast and axillary ultrasonography+/-mammography and surgery	
<1 mo	164
1 < 3 mo	13
3 < 6 mo	7
A Data from 184 patients with complete axillary dissection.	

Table 2. Lymph Nodes Status in patients with breast cancer

Years	2002	2003	2004	2005	Total
Positive LN	22	33	42	23	120
Negative LN	9	20	17	18	64

Impact of Mediterranean lifestyle on quality of life - A sample of East Mediterranean community

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Abstract

Aim: The aim of the present study was to evaluate relationships between health behaviors, some medical conditions and health related quality of life in an east Mediterranean community sample.

Method: Study population consisted of 327 adult Datca-Knidos county residents. Participants filled out a questionnaire regarding health behaviors, medical history and an extensive health related quality of life (HRQOL) measurement short form questionnaire (SF-36v2).

Results: The majority of participants were born in Datca (Turkey). Mean age was 50.3±12.0. Mediterranean diet, at least moderate physical activity and regular swimming were associated with better outcomes on most scales of health related quality of life (HRQOL). Mental and physical dimensions of SF-36v2 were adversely affected by coronary heart disease (CHD), hypertension (HT), diabetes mellitus type 2 (DM) and age over 40.

Conclusion: Mediterranean diet, physical activity and regular swimming are associated with better outcomes on HRQOL in an east Mediterranean community sample. Overall quality of life declines in the presence of chronic diseases and advanced age.

Key words: Health related quality of life, Mediterranean diet, east Mediterranean community.

Introduction

Quality of life is a multidimensional construct including individuals' overall satisfaction with life assessing functional status in physical, emotional and social dimensions¹

Chronic diseases alter well-being and health related quality of life (HRQOL)^{2,3,4,7}

The relationship between health measurements and chronic conditions are well studied in a variety of age groups including the elderly and HRQOL found declining with chronic disease presence such as coronary heart disease, hypertension, diabetes^{2,3,5,6,7,8,9}. Several hospital-based studies have previously addressed impact of medical or surgical treatment of chronic conditions on HRQOL^{3,4,5,7,8,9}. However relatively fewer studies have evaluated HRQOL and its relationship with dietary habits and physical activity which are currently not very well addressed^{2,5}

In the present study, we aimed to verify the relationship between quality of life and health behaviors such as dietary habits, physical activity and frequently seen chronic diseases.

Method

The current study is based on a sample from the registered residents in the county of Datca, ancient name known as Knidos. Datca is a semi-urban, partly agricultural west Anatolian county located on the east Mediterranean coast, with an adult

population of around 3000. The study was announced to adults living in Datca by mail, hand-outs and loudspeaker announcement system via local municipal organizations. Volunteers were interviewed face to face by trained physicians. Approval consent was taken from each participant. 108 men and 219 women completed a questionnaire and Turkish version of SF-36v2 form.

SF-36v2 Form:

Short form 36 version 2 (SF-36v2) is a widely used as an extensive health related quality of life measurement. The major domains of SF-36v2 form are physical functioning (PF), social functioning (SF), role-emotional (RE), role-physical (RP), bodily pain (BP), vitality (VT), mental health (MH) and general health perception (GH). The calculated score of each scale was transformed to have a mean of 50 and standard deviation of 10 in general population, with higher scores indicating a better state of health(10). A Turkish version of SF-36v2 was used with permission of the Medical Outcome Trust.

Questionnaire:

Elements of the questionnaire consisted of demographics, chronic disease history, physical activity and dietary habits.

Age, gender and smoking habits were integrated in the demographics section of the questionnaire.

Four categories were included in the physical activity part of the questionnaire.

1. Sedentary, mostly sitting during the day.
2. Mild activity such as walking at least 20 minutes at a time and 3 days a week.
3. Moderate activity such as biking or running at least 20 minutes at a time and 3 days a week.
4. Vigorous activity such as weight lifting or hoeing in the garden at least 20 minutes at a time and 3 days a week.

For each category, time spent for the addressed physical activity was asked. Swimming 30 minutes at a time 3 days a week was considered as regular swimming. Swimming period of months in a year were asked separately in the physical activity part of the questionnaire.

Presence of coronary heart disease (CHD), hypertension (HT), type 2 Diabetes Mellitus (DM), and family history of these chronic diseases were questioned in the chronic disease part of the questionnaire.

Dietary habits were questioned in 5 categories and in a scale of 5. The five categories questioned were red meat, fish, fruit, olive oil and vegetables (raw and cooked) consumption. Scale One signified consuming every day; scale Two, ≥ 3 times/week; scale Three, 1-3 times/week; scale Four: <once/week; scale Five, <once/month or never eaten.

All participants reported olive oil preference in their daily cooking. Participants consuming vegetable and fruit everyday, fish, equal or more than once a week and red meat less than once a week and preferring olive oil rather than butter, were considered as using a Mediterranean diet.

Height and weight of each participant was measured using a standard procedure. BMI was calculated as weight in kilograms divided by the square of the height in meters [weight (kg) / height (m)²] and participants were grouped as normal, overweight and obese according to their BMI values¹¹.

Blood pressure was measured after 20 minute of resting.

Statistical Analysis:

Data were analyzed using the Statistical Package for the Social Sciences program (SPSS 10.0). Values are expressed as mean \pm S.D. Pearson χ^2 - test was used to analyze differences between demographic factors and chronic diseases. Correlation between quality of life dimensions, demographic, medical and health behavior indices were analyzed by Spearman's rank correlation coefficient. In order to study association between eight major domains of SF-36 questionnaire and certain categorical variables such as age, gender, health behaviors and chronic diseases, multiple linear regression analysis was carried out.

Results

Demographics: The majority of the participants were born in Datca. Mean age of the total group was 50.3 ± 12.0 . Mean BMI was 27.5 ± 4.6 . Participants who were active swimmers were swimming in an average of 2.3 months in a year. One in five participants had co-morbidity of the chronic disease that was included in the questionnaire. Demographic features are shown in Table 1.

Physical function, role physical, role emotional, mental health, vitality and general health perception domains of SF-36 were negatively affected by advanced age. Men rated higher scores on social function, mental health and vitality. Non-smokers rated high on physical function and role physical scale of the

SF-36. (Table 2 and Table 3).

Number of chronic diseases ($r=0.348$ $p<0.001$), BMI ($r=0.260$ $p<0.001$), systolic blood pressure ($r=0.527$ $p<0.001$) and diastolic blood pressure ($r=0.393$ $p<0.001$) were seen to be increasing with age. Smoking years were positively associated with number of chronic diseases ($r=0.131$ $p=0.02$).

Chronic Conditions:

Both mental and physical dimensions of SF-36v2 were affected by CHD, HT and DM. Scores in the physical function dimension of SF-36v2 were lower for those with CHD and HT whereas both RP and RE were affected in DM. On the contrary, mental health was not affected by any of the chronic diseases (Table 2).

Co-morbidity was more common in sedentary (OR:1,955 $p=0.01$), non-swimmer (OR:4,340 $p<0.001$), overweight and obese (OR: 9,450 $p<0.001$) participants.

Overweight was associated with HT (OR: 9.404 $p<0.001$), CHD (OR: 2.706 $p=0.001$) and DM (OR: 7.714 $p<0.001$).

Physical Activity:

Sedentary or mildly active participants had significantly lower scores in PF, SF, VT, BP and GH scales of the HRQOL (Table 2 and Table 3).

BMI ($r= - 0.188$ $p=0.001$) inversely, physical function ($r = 0.274$ $p<0.001$), social function ($r=0.192$ $p<0.001$) and bodily pain ($r= 0.143$ $p=0.01$) directly correlated with increased physical activity.

Swimming was seen to have a positive effect on both mental and physical components of HRQOL. Regular swimmers had higher scores in PF, RE, and GH scales of the SF-36v2.

Dietary Habits:

Scores in many dimensions of the SF-36v2 were higher for those having Mediterranean style of diet. Non-obese participants rated higher scores on SF, RP, and VT scales of the SF-36v2 (Table 2 and Table 3).

It is remarkable that higher consumption of raw vegetables ($r=0.230$ $p<0.001$) and fruit ($r=0.126$ $p=0.02$), increased physical activity ($r=0.179$ $p=0.001$) and swimming period in a year ($r=0.219$ $p=0.001$) were positively correlated with overall quality of life. On the contrary, BMI ($r=-0.147$ $p=0.01$), systolic blood pressure ($r=-0.173$ $p=0.005$) and diastolic blood pressure ($r=-0.179$ $p=0.003$) were negatively correlated with overall quality of life. Furthermore, higher BMI was associated with increased red meat consumption ($r=0.130$ $p=0.02$).

Mediterranean diet, at least moderate physical activity and regular swimming more than 3 months in a year have better impact on general health perception. However, general health perception declines in the presence of CHD, and over 40 years of age.

Discussion

In the present study, HRQOL have been analyzed in a sample of semi-urban east Mediterranean community with a multivariate approach to identify associations with health behavior along with some chronic diseases.

Several studies have shown that older age results in worse

HRQOL, reflecting physical health but not in scales reflecting mental health. (12,13). However, in our study population, age affected both physical and mental parameters.

There is a strong correlation with obesity and anxiety, depression, personal dissatisfaction and disturbed eating attitude¹⁴. Additionally, poor perceived health status and increased chronic disease risk factors are reported more prevalently in obese people¹⁵. In our study mental and physical component of HRQOL was better in non-obese participants.

It must be pointed out that, HT, DM and myocardial infarction adversely affect HRQOL². It is remarkable that chronic diseases affect quality of life not only by physical means but emotionally as well. It has been reported that anxiety, depression and negative beliefs about DM were related to lower physical and mental functioning in diabetics³. Participants in our study, with CHD, HT and DM rated lower scores in some of the physical and mental components of SF-36v2.

Moreover, low HRQOL can be a risk factor for cardiovascular events or complications which might result in increased mortality rate^{2,16}. Several studies report lower scores on most dimensions in HRQOL with general health perception being the most influenced domain^{2,5}. On a lighter note, GH is assumed to reflect both physical and mental health. Related to this is that a low general health perception indicates a belief that health is likely to get worse whereas psychosocial factors such as labeling effect might affect HRQOL among hypertensives². However, there is conflicting data about HT in relation to lower scores both in PCS and MCS^{2,17}. Our study results show that both physical function and role emotional, were affected in hypertensive participants.

Many studies address relationship between increased levels of exercise and improved health status. Sedentary people reported lowest scores on physical health¹⁸. Besides daily physical activity, we have questioned swimming separately and evaluated if it has a unique affect on HRQOL. We have found that regular swimming, more than 3 months in a year, is associated with better outcomes on both physical and mental components and general health perception of HRQOL.

Dietary habits are linked to socioeconomic conditions and lifestyle, possibly reflecting cultural development of past habits and may be influenced by diseases¹⁹. High intake of fat, sugar and milk products and low intake of vegetables and fruits are considered to be related to cardiovascular disease¹⁶. Furthermore, fish consumption had been linked to a decrease of coronary heart disease in women^{20,21}. As it was pointed out previously, higher intake of fruits, vegetables, fish and preference of olive oil and lower intake of red meat and fat are characteristics of Mediterranean diet. Mediterranean life style programs produced significant improvement on behavioral risk factors of coronary heart disease such as eating patterns and physical activity and improvement in quality of life was also significant²⁰. As a result, in our study, better scores on HRQOL were obtained by participants with Mediterranean dietary habits, which include regular fish consumption.

Limitations of our study are the relatively small number of participants for general population studies and lack of detailed energy intake information. Nevertheless, we designed our study on a voluntary basis and Datca-Knidos is a well preserved typical east Mediterranean county. In addition, information bias is a possibility in self-reported studies. We believe inclusion of biological outcomes assessment and detailed dietary informa-

tion should be a focus of further research.

Conclusion

Consequently, the present study focuses on related factors on quality of life in a group of people living in east Mediterranean. Mediterranean diet, at least moderate physical activity and regular swimming are associated with better outcomes on HRQOL.

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Table 1. Demographic features of 327 participants

	Women (n=219) n (%)	Men (n=108) n (%)	Total (n=327) n (%)
Age:			
< 40 years old	39 (12.1%)	18 (5.5%)	57 (17.4%)
40-54 years old	128 (39.4%)	42 (12.8%)	170 (52.3%)
55-64 years old	30 (9.2%)	27 (8.3%)	58 (17.5%)
≥ 65 years old	21(6.4%)	21 (6.4%)	42 (12.8%)
Born in Datca	156 (71.2%)	57 (52.8%)	213 (65.1%)
Smoker	99 (45.2%)	93 (86.1%)	192 (58.7%)
Coronary Artery Disease	69 (31.5%)	36 (33.3%)	105 (32.1%)
Hypertension	78 (35.6%)	30 (27.8%)	108 (33.0%)
DM Type 2	36 (16.4%)	21 (19.4%)	57 (17.4%)
Dietary Habits			
Red meat (< once/week)			
Fish (≥3 times/week)	117 (53.4%)	63 (58.3%)	180 (55.0%)
Fruit (everyday)	28 (12.8%)	15 (13.9%)	43 (13.1%)
Vegetable (everyday)	171 (78.1%)	57 (52.8%)	228 (69.7%)
Raw	111 (50.7%)	57 (52.8%)	168 (51.4%)
Cooked	90 (41.1%)	18 (16.7%)	108 (33.0%)
Physical Activity			
I Sedentary	27 (12.3%)	15 (13.9%)	42 (12.8%)
II Mild	54 (24.6%)	21 (19.4%)	75 (22.9%)
III Moderate	108 (49.3%)	42 (38.9%)	150 (45.8%)
IV Vigorous	30 (13.7%)	30 (27.8%)	60 (18.3%)
Regular swimmers	138 (63.0%)	72 (66.7%)	210 (64.2%)
Obesity	75 (34.2%)	21(19.4%)	96 (29.4%)

Table 2. Results of linear regression analysis of SF-36v2 scores, Physical Function (PF), Social Function (SF), Role physical (RP), Role Emotional (RE)

Variables	PF β	SF β	RP β	RE β
Age ≥41 years	-4,896*	1,608	-3,653	-6,764**
Male gender	3,312	5,032**	-3,133	2,109
Non-smoker	5,848**	-0,563	6,905***	2,314
Coronary Artery Disease	-10,848***	-4,261*	-2,210	0,522
Hypertension	-4,899*	-2,518	0,180	-6,468**
DM Type 2	-1,641	-0,713	-3,540*	-6,598**
Mediterranean Diet	10,031**	4,764	2,428	9,444**
Sedentary or mildly active	-4,189*	-7,032***	-0,706	0,103
Swimming > 3 months/year	5,082**	0,768	2,183	6,277**
Non-obese	2,289	4,770*	5,087**	1,430
Adjusted R ²	0,309	0,097	0,076	0,088
Significance	<0.001	<0.001	<0.001	<0.001

* p<0.05 **p<0.01 ***p<0.001

Table 3. Results of linear regression analysis of SF-36v2 scores Mental Health (MH), Vitality (VT), Bodily Pain (BP), and General Health (GH)

Variables	MH β	VT β	BP β	GH β
Age ≥41 years	-10,146***	-7,776***	-3,263	
Male gender	3,692**	3,121**	-0,685	-1,740
Non-smoker	-1,393	-0,684	3,652	-0,687
Coronary Artery Disease	-1,851	0,508	-10,182***	-4,977**
Hypertension	-0,770	-1,239	2,343	-0,680
DM Type 2	-2,298	-3,221*	2,137	-3,561
Mediterranean Diet	10,286***	9,119***	6,050	7,124**
Sedentary or mildly active	-0,780	-2,686*	-4,167*	
Swimming > 3 months/year	0,520	0,826	3,450	4,106**
Non-obese	-0,239	2,715*	-0,108	1,574
Adjusted R ²	0,219	0,172	0,110	0,230
Significance	<0.001	<0.001	<0.001	<0.001

*p<0.05 **p<0.01 ***p<0.001

In vitro maturation in polycystic ovary syndrome and poor responders - Effect of follicular size and FSH concentration in culture media

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Abstract

Objectives:

- To determine the effect of recombinant Follicle Stimulating Hormone (r-FSH) concentration in culture media on in vitro maturation outcomes.
- To determine the effect of the follicle size on in vitro maturation outcomes.
- To determine the in vitro maturation outcomes of immature oocytes recovered from infertile patients with polycystic ovaries (PCO) and poor responders.

Design & Methods: Two-stage prospective study was performed in an IVF unit in the eastern province of Saudi Arabia. The first stage compared the fertilization and pregnancy outcomes in patients with Polycystic Ovary (PCO) Syndrome and patients with poor response to recombinant Follicular Stimulation Hormone (rFSH). The second compared these outcomes according to follicular size.

Oocytes retrieved after 5 days rFSH course were divided into two groups according to follicular size (8-10mm and 11-13mm) and were cultured in a 0.075 IU/ml medium. The effect of follicular size on oocytes-maturation, fertilization, embryo cleavage, and pregnancy rate was assessed in the two groups and in those with PCO and poor responders.

Results: There was no difference in the main outcome measures between oocytes cultured in the two concentrations of FSH. Oocytes retrieved from 11-13 mm follicles showed higher rates of maturation, fertilization and pregnancy, than those retrieved from 8-10 mm follicles. In both PCO and poor responders patients embryos produced from regularly cycling patients had a significantly higher embryo development ratio, even though cleavage was not significantly different.

Conclusion: Concentrations higher than 0.075 IU ml in culture media for IVM are not necessarily associated with better outcomes. Larger follicular size produces better fertilization and pregnancy rates. In both PCO and poor responders, cycle irregularity is associated with poorer outcomes.

Introduction

Since the first successful human pregnancy from in-vitro fertilization (IVF) was achieved (Stephoe and Edwards, 1978), assisted reproductive technology has become the frontier of birth infertility treatment and research. There have been continuous improvements in the pregnancy and birth rates with IVF.

These improvements have been directly attributed to advances in the hormonal stimulation of patients with various controlled ovarian hyperstimulation (COH) protocols and improved culture media and culture systems for oocytes, sperm, and embryos. However, through all these improvements with stimulated cycles, there has been continued development with natural, unstimulated, or limited-stimulation cycles followed by in vitro maturation (IVM) of oocytes. Any protocol that would decrease the amount and duration of hormonal stimulation before oocyte retrieval would have an advantage over the more common COH/IVF protocols if the resulting pregnancy rates were the same or improved (Cha K. et al, 1991). Research in in-vitro maturation (IVM) of the human oocyte has shown significant

progress and provided hope for certain groups of patients who have either poor response or have a high risk of developing ovarian hyperstimulation. Human oocytes recovered from immature follicles, following retrieval can resume and complete meiosis in-vitro when cultured in media supplemented with recombinant follicle Stimulating Hormone (r-FSH) and Human Chorionic Gonadotrophin (hCG) .

Several reports showed that in-vitro matured oocytes could be fertilized, and result in pregnancy (Jaroudi K., et al, 1999), and birth of healthy babies (Chian R., et al, 2001, Suikkari A. et al, 2005). Despite the clinical utilization of IVM in the field of human reproduction, its pregnancy and birth rates remain low compared to in-vivo matured oocytes (Lui J., et al, 2003, Lin Y., et al, 2003).

Objectives

This study aims to study the effect of the follicles' size on oocyte maturation, fertilization and cleavage, and to compare the outcomes of in-vitro maturation of immature oocytes re-

covered in situ from infertile women with polycystic ovaries, versus poor responders.

- To determine the effect of recombinant follicle stimulating hormone (r-FSH) concentration in culture media on in vitro maturation outcomes.
- To determine the effect of the follicle size on in vitro maturation outcomes.
- To determine the in vitro maturation outcomes of immature oocytes recovered from infertile patients with polycystic ovaries (PCO) and poor responders.

Methods

This study was conducted during the period from April 2000 to December 2004. The results of this study were collected and evaluated from the Assisted Reproduction Unit at Almana General Hospital, Dammam, Eastern Province of the Kingdom of Saudi Arabia and incorporation with the department of Obstetrics and Gynecology, Campus Benjamin Franklin, Charité, Homboldt University. The study was approved by the research ethics board of the hospital. A written informed consent was obtained from all patients. To decide which concentration to use in the culture medium, a preliminary experiment was performed to compare 2 concentrations (7.5 IU/ml and 0.075 IU/ml) and compared to a medium with no FSH.

(A) The effect of r-FSH concentration in the culture media on in-vitro maturation of oocytes

Recombinant FSH in the culture media was used in two concentrations of 0.075, 7.5 IU/ml and none as a control.

This experiment was performed on patients producing more than 15 germinal vesicles (GV) oocytes. Immediately after collection, the oocytes were equally distributed in three groups of 5 oocytes each in three center-well dishes containing 3ml Ham's F10 media.

Two r-FSH concentrations of 0.075, 7.5 IU/ml were added in two dishes and none as control, respectively. Oocytes maturation was evaluated 30 hours after incubation. Oocytes maturation, fertilization, cleavage and pregnancy rates were assessed.

(B) The effect of follicular size on the rate of oocyte maturation

In this experiment, oocytes were collected from 50 PCO patients (Group 2) who were stimulated with a daily dose of 300 IU (Purgeon, Organon, Holland) for 5 days, starting on day 2 of the menstrual cycle until day 6 when a transvaginal ultrasound scan was performed. The scan showed follicular size ranging between 8-13 mm. The PCO patients were divided into two subgroups according to follicular size on the day of hCG injection; Group 2I had a follicular size of 8-10 mm and Group 2II had a size of 11-13 mm. The oocytes retrieved from these patients were incubated for 30 hours in Ham's F10 supplemented with 0.075 IU r-FSH/ml. Oocyte maturation, fertilization, cleavage, and pregnancy rates were then assessed.

(C) In vitro maturation outcomes of immature oocytes recovered in-situ from infertile patients with polycystic ovaries (PCO) and poor Responders

This part of the study was conducted on 40 infertile women (Group 3). This group was further divided into two subgroups, 20 infertile women with polycystic ovaries (Group 3I) and 20 poor responder infertile women (Group 3II). The timing of the start of treatment was random, as most of the patients had an irregular menstrual cycle.

Patients' criteria

Infertile women with polycystic ovaries and poor responders were included in this study during their schedule for ICSI in the IVF program. The patients were recruited at random. It was fully explained to each patient that the procedures related to the study were not part of the routine diagnostic procedures required for their infertility assessment.

Patients were recruited after PCO was identified by:

- i) Pelvic ultrasound (the ultrasonic criteria of PCO were essential for the diagnosis. It included the presence of more than 8 small follicles of 2-8 mm in diameter around a dense core of stroma and a dense ovarian capsule),
- ii) Their endocrine and clinical features varied between regular and irregular cycles,
- iii) Anovulatory polycystic ovarian syndrome patients had characteristically elevated androgen level, LH: FSH ratio >2, and frequently, the clinical features of hirsutism and increased body weight (Adams J. et al., 1985; Hershlag A. et al, 1996).

Poor responders are patients who fulfilled one or more of the following criteria:

1. Failed to achieve estradiol concentration above the level of 200 pg/ml on the day of hCG (Garcia J. et al, 1983).
2. Produced less than three mature follicles during the previous stimulation attempts (Serafini P. et al, 1988).
3. Failure and/or cancellation of previous IVF cycles due to low quality of oocytes retrieved in previous stimulations (Rienzi L. et al, 2002).

Oocytes retrieval and IVM Procedure

Transvaginal ultrasound guided oocytes collection was performed using a specially designed 17-G single-lumen aspiration needle (Casmed, UK) with a reduced aspiration pressure of 7.5 kpa. Aspiration of the follicles was performed under general anesthesia for all patients. All patients received an antibiotic cover of a single dose of 500 mg of metronidazole intravenously during the procedure.

Oocytes were collected in culture tubes containing warm Earl's balanced salt solution with 5000 IU/ml heparin. Immature oocytes were incubated in a culture dish containing 1ml of 3M (Medicult) medium supplemented with r-FSH (Puregon, Organon) (according to the stage of the study) and 5.00 IU/ml hCG (Pregnyl, Organon) at a temperature of 37°C in an atmosphere of 5% CO₂ and 95% air with high humidity. After culture, the maturity of the oocytes was determined under the stereomicroscope at 30 hours post collection. Oocytes were denuded of cumulus and maturity was determined by the presence of the first polar body. Suitable oocytes were injected with single sperma-

tozoa by micromanipulation (Research Instrument, UK). Following ICSI, each oocyte was transferred into 1ml of Medi-cult IVF medium in a tissue culture dish. Fertilization was assessed 18 hours after ICSI for the appearance of two distinct pronuclei and two polar bodies. Oocytes with two pronuclei were further cultured in Medi-cult IVF medium. Embryos were transferred on day 2 or 3 after ICSI.

Statistical analysis was done by the student's t - test. Frequency data were analyzed by χ^2 contingency tests. Embryo development ratio data were analyzed by analysis of variance. Values were considered significant when $P < 0.05$. Since the oocytes were not matured and inseminated at the same time following maturation in culture; the development stages of embryos were variable both within and between patients.

Results

The results of the present study were based on data generated from the two experiments. The mean duration of infertility was 12.3 ± 4.6 years for all patients of the study groups. All patients were under 45 years of age with a range of 21 – 44 years (mean 35.1 ± 5.3 years).

Results of the First experiment (FSH Concentration)

The first experiment was designed to define the optimum r-FSH concentration. Our data showed that 0.075 IU/ml was the optimum concentration that provided higher maturation, fertilization and pregnancy rates compared to 7.5 IU/ml and the control. Details regarding the number of oocytes collected, maturation, fertilization and pregnancy rates after in vitro maturation in media containing different concentrations of r-FSH are shown in table 1. Recombinant FSH concentration had significantly ($p < 0.05$) increased the rate of oocyte maturation from 47% at 0 concentration to 81% and 83% at 0.075 and 7.5 IU/ml, respectively. Fertilization, cleavage, and clinical pregnancy rates showed a similar trend and significantly increased from 45% to 83% and 80%; from 32% to 80% and 77% and from 0% to 17% and 14% at the three concentrations, respectively. The results however showed that increasing r-FSH concentration to levels more than 0.075 IU did not further improve maturation, fertilization, cleavage and pregnancy rates even when the concentration was increased up to 100 folds. Our data showed that 0.075 IU/ml was the optimum concentration that provided higher maturation, fertilization and pregnancy rates compared to 7.5 IU/ml and the control.

Table 1. The effect of different r-FSH concentrations (in IU) on oocytes maturation, fertilization, embryo cleavage and pregnancy rate.

Parameters	(0.00)	(0.075 IU)	(7.5 IU)
GV collected	225	219	230
Matured oocyte	105 (47%)	178 (81%)	186 (83%)
Fertilized oocyte	47 (45%)	147 (83%)	149 (80%)
Cleaved embryos	15 (3%)	119 (80%)	116 (77%)
Transferred embryos	12 (2/ET)	55 (1.4ET)	60 (1.7/ET)
Clinical Pregnancy	0.00	6 (17%)	5 (14%)
No of patients who had ET	6	39	35

Results of the Second experiment (Follicular Size)

Based on the optimum rFSH concentration as decided from the first experiment, the second experiment was designed to study the effect of the follicle size on oocytes maturation, fertilization and developmental competence.

The concentration of rFSH chosen was 0.075 IU.

The results of two different follicle sizes (group 2) are shown in table 2. Oocytes retrieved from 11-13 mm follicles showed higher rates of maturation, fertilization and pregnancy, than those retrieved from 8-10 mm follicles. The above parameters increased from 48 to 70%; from 54 to 76% and from 11 to 22.5%, in the two follicle sizes, respectively. In the first subgroup study (group 2I), the 6 and 5 pregnancies resulting from oocyte cultured in media containing 0.075 and 7.5 IU/ml all ended in delivery of healthy children. On the other hand, in the second subgroup (group 2II), the two pregnancies resulting from 8-10 mm follicles size completed full term, whereas two of the nine pregnancies in the 10-12 mm follicle size subgroup ended in miscarriage and the remaining seven pregnancies ended in delivery of healthy babies. Follicular size showed significant ($P < 0.05$) effect on the assessment parameters.

Table 2. The effect of follicular size on oocytes-maturation, fertilization, embryo cleavage, and pregnancy rate.

Parameters	Follicular size (mm)	
	8-10	11-13
GV collected	250	250
Matured oocyte	120 (48%)a	177 (70%) b
Fertilized oocyte	65 (54%) a	138 (76%) b
Cleaved embryos	42 (64%) a	94 (68%) b
Transferred embryos	33 (1.9/ET)	60 (1.7 ET)
Clinical pregnancy	2 (11%) a	9 (22.5%) b
No of patients who had ET	17	40

Results of the Third experiment (PCO and Poor responders)

The mean age of group 3 patients was 32.3 ± 5.8 for PCO patients and 36.4 ± 7.1 for the group of poor responders. The means of parity, abortion, and Hb% were also comparable between the two sub groups. Both the body mass index (29.7 ± 2.3 vs. 27.1 ± 1.6) and the duration of the cycles (53.2 ± 21.3 vs. 30.3 ± 8.6) were higher in group 3I (table 3). There was however no difference between the two subgroups (group 3I and group 3II) in the concentrations of estradiol, progesterone, FSH, and LH on day 2 and on the day of oocytes retrieval (tables 2).

Table 3. Patients Criteria

Variable	G3	G3	P-value
Age (years)	32.3 ± 5.8	36.4 ± 7.1	0.496 Not Significant
Parity	0.63 ± 1.2	0.94 ± 1.8	0.251 Not Significant
Duration of cycle (Days)	53.2 ± 21.3	30.3 ± 8.6	< 0.001 Significant
BMI	29.7 ± 2.3	27.1 ± 1.6	0.038 Significant
Hb g%	13.0 ± 0.7	12.5 ± 1.0	0.126 Not Significant

From 20 PCO women (Group 3I), the mean number of oocytes recovered, matured in vitro, fertilized after insemination, and cleaved in culture was 23.5, 16.1, 7.3, and 4.7 respectively. From 12 irregular PCO women (G3Ia), the mean numbers of

oocytes recovered, matured in vitro, and fertilized after insemination, and cleaved in culture were 18.1, 11.7, 4.2, and 3.1, respectively. The mean numbers of oocytes recovered, matured, fertilized and cleaved from 8 regular cycling PCO women (G3Ib) were 5.4, 4.4, 3.1 and 1.6, respectively. Oocytes recovered from regularly cycling patients had a higher developmental potential when compared with irregular and anovulatory patients with significantly ($P < 0.05$) including higher maturation and fertilization rates (table 4). Cleavage was not significantly different between the two subgroups, although there was a trend to increased cleavage of embryos in the regular cycling group. Moreover, embryos produced from regularly cycling patients had a significantly higher embryo development ratio ($P < 0.05$), indicating the faster cleavage rate of embryos produced from this group of patients. Embryo development ratio is defined as the observed cleavage stage/ the expected cleavage stage \times 100. Three pregnancies were obtained, one has delivered a pre-term at 36 weeks and two miscarried at 8 and 10 weeks.

Table 4. Oocytes maturation, fertilization and cleavage in vitro in study group 3 (G3)

Patient group (G3)	Oocytes cultured	Oocytes matured	Oocytes fertilized	Oocytes cleaved	Embryo
PCO patients (G3)	250	170 (68%)	56 (22.4%)	45 (18%)	74.2 \pm 2.6
Poor	200	140 (70%)	60 (30%)	35 (17.5%)	63.4 \pm 2.6
P-value	0.251	0.125	0.046	0.223	0.049

From 20 poor responder women (Group 3II), the mean numbers of oocytes recovered, matured in vitro, fertilized after insemination, and cleaved in culture were 18.1, 14.5, 5.1 and 3.4 respectively (table 5). The embryo development ratio was 63.4 \pm 2.6. One pregnancy was obtained with the delivery of a full term female baby.

Table 5. Oocytes maturation, fertilization and cleavage in vitro in study group 3 (G3)

Patient group (G3)	oocytes cultured	oocytes matured	oocytes fertilized	oocytes cleaved	Embryo development ratio
Irregular anovulatory (G3a) (12 patients)	175	112 (64%)	31 (27.9%)	27 (14.1%)	66.7 \pm 3.1
Regular cycle (G3b) (8 patients)	75	58 (74%)	25 (33%)	18 (18%)	81.5 \pm 3.4
Total	250	170 (68%)	56 (22.4%)	45 (18%)	74.2 \pm 2.6
P-value	0.046	0.016	0.038	0.049	0.028

Discussion

The feasibility of obtaining full-term pregnancies from in vitro-matured immature oocytes obtained from stimulated and non-stimulated ovaries is well established (Veek L. et al, 1983; Cha K. et al, 1991). The scarcity of subsequent reports points to the fact that the procedure is not even close to being transferred into daily clinical work. The impossibility of judging ooplasmic maturation forces the use of nuclear maturation as the basis for classification of female gametes. The present study showed that in-vitro matured oocytes retrieved from PCOS patients had the potential to undergo suc-

cessful maturation, fertilization and the resultant embryos and showed good developmental competence. Following the IVM procedure, embryo transfer culminated in clinical pregnancies and birth of healthy children. All the oocytes retrieved in this study were at the germinal vesicle (GV) stage. The latter is defined as the stage that represents oocytes arrested at prophase of meiosis-1 with prominent discernable germinal vesicle nucleus.

There are various factors that affect oocyte in-vitro maturation. The most important among these factors are: the exposure of the immature oocyte to gonadotrophins in the culture media, and the follicle size at which the oocyte was retrieved. r-FSH, LH, and hCG (Hreinsson J. et al, 2003), and purified gonadotrophins (Mikkelsen A.L. et al, 2001) were used to induce oocyte maturation in vitro. In this study the effect of both factors on oocyte maturation, fertilization, cleavage, and pregnancy rates were investigated.

Cha et al, reported a pregnancy rate of 27.1% after IVM and IVF-ET in patients with PCOS. They also reported that the combined ET (ZIFT + uterine ET) yielded a significantly higher pregnancy rate than either ZIFT alone or uterine ET alone (Cha K., et al, 2000). Previously, other studies have shown that the pregnancy rate of conventional IVF in PCOS patients was similar to that of conventional IVF in non-PCOS (MacDougall M., et al, 1993). A possible mechanism suggested for the lower pregnancy rate of IVM is that some of the oocytes undergoing nuclear maturation after IVM are incapable of undergoing cytoplasmic maturation, thus resulting in poor embryo quality and a higher incidence of pregnancy failure. A number of other factors might lead to a lower success rate of IVM, including sub-optimal culture conditions, advancing maternal age, an endocrine disturbance, previous IVF failures, and sub-optimal timing of insemination (Picton H., 2002). Table 6 compares different oocyte in-vitro maturation rates obtained from various studies to the rate obtained in our study.

Table 6. Maturation rates obtained from this study compared with other recent studies

Study	Rate
Our present study	81%
Barnes F., et al, 1996	62%
Hwu Y., et al, 1998	67%
Jaroudi K. et al, 1999	71%
Child T., et al, 2001	61%
Combelles C., et al, 2002	66%
Gaspard O., et al, 2003	58%
Hreinsson J., et al, 2003	55.9%

The variations in maturation rates between the present study and those mentioned in table 6 may be due to the composition of the culture medium used and protein supplement. In the present study our optimum culture time (30h) was comparable with other studies (Cha K.Y. et al, 1998). Inadequacies of cultured media could not be ruled out as a possible cause for low IVM success (Combelles C.M. et al, 2002). There is evidence suggesting that culture media used for IVM adequately support nuclear maturation, but failed to produce oocyte with cytoplasmic maturation. While we used synthetic serum supplement as a sources of proteins, in other studies fetal bovine serum (FBS)

was used. FBS was considered more crucial for bovine oocyte maturation than human. In addition, our base medium used was Hams F10, which is designed to meet the nutritional and maturational needs of human oocyte.

On the other hand the effect of follicle size on the above parameters showed some interesting results. Our data showed that oocyte maturation rate and developmental competence has significantly increased with increase in follicle size. Eppig J.J. et al, (1992), concluded that developmental competence of oocytes depends on the follicle and oocyte size. The growth in size is due to the fact that oocyte synthesizes and stores mRNA and proteins that are essential for the completion of maturation and for the subsequent acquisition of embryo developmental competence (Gosden R. et al, 1995). This probably explains the relatively higher maturation, fertilization, cleavage, and pregnancy rate in oocyte obtained from follicle with 11-13 mm size rather than 8-10 mm. While in the present study pregnancy rate increased with follicle size, other reports found that implantation, pregnancy, and birth rates were independent of follicular size (Wittmaack F. et al, 1994; Salha O. et al, 1998). Our data suggested that when oocytes were cultured in IVM media containing 0.075 IU r-FSH or retrieved from follicle size exceeding 10mm, a comparable or even better maturation rates and developmental competence than results shown in several recent reports were obtained.

Also, the results indicate that in vitro maturation of oocytes recovered from PCO patients exhibit developmental competence more than the oocytes recovered from poor responder patients. The explanation of this finding might be related to the age of the patients where most of the poor responders are older than PCO patients with the contribution of other factors like the male factor, whereas PCO patients are younger and their main problem was the competency of in vivo oocytes maturation. In studying the effect of the male factor, all males in PCO patients had normal sperm count and viability. In poor responders, only 1 case showed subnormal sperm count. The effect of the male factor could be omitted in our study due to the low number of cases and the inability of any statistical evaluation.

Conclusion

IVM is a useful treatment option for women with PCOS or who are resistant to FSH with less risk of Ovarian Hyperstimulation. As this group of patients are resistant to gonadotropin stimulation for various reasons and as they require prolonged and higher doses of gonadotrophin stimulation protocols, IVM provides a different approach to a safer and cheaper treatment modality. In addition, natural-cycle IVF combined with IVM might provide more efficient treatment for poor responder infertile women. Oocyte maturation and embryo development are less in women with irregular menstrual cycles.

In the present study factors affecting immature oocyte maturation and developmental competence are not fully explored. There are many gaps that need to be bridged and other factors need to be closely investigated. The effect of growth hormone in culture media during oocyte maturation, chromosomal anomalies as well as the effect of anesthesia is a worthwhile thorough investigation.

Appendix. Components of culture media - Nutrients Mixture Ham's F-10

Old Cat. No. New Cat. No.	041-02390 22390 IX Liquid
Component	Mg/L
INORGANIC SALTS:	
CaCl ₂ (anhyd.)	-
CaCl ₂ *2 H ₂ O	44.00
CuSO ₄ *5 H ₂ O	0.0025
FeSO ₄ *7H ₂ O	0.834
KCl	285.00
KH ₂ PO ₄	83.00
MgSO ₄ (anhyd.)	-
MgSO ₄ *7 H ₂ O	153.00
NaCl	6900.00
NaHCO ₃	1200.00
Na ₂ HPO ₄ (anhyd.)	154.50
ZnSO ₄ *7 H ₂ O	0.0288
OTHER COMPONENTS:	
D-Glucose	1100.00
HEPES	5958.00
Hypoxanthine	4.08
Hypoxanthine (sodium salt)	-
DL-68-Thioctic Acid	0.20
Phenol Red	1.20
Sodium Pyruvate	110.00
Thymidine	0.73
AMINO ACIDS:	
L-Alanine	8.92
L-Arginine *HCl	211.00
L-Asparagine	12.98
L-Aspartic Acid	13.30
L-Cysteine	25.00
L-Glutamic Acid	14.70
L-Glutamine	146.00
L-Alanyl – L-Glutamine	-
L-Glycine	7.52
L-Histidine HCl * H ₂ O	23.00
L-Isoleucine	2.60
L-Leucine	13.10
L-Lysine * HCl	29.30
L-Methionine	4.48
L-Phenylalanine	4.96
L-Proline	11.50
L-Serine	10.50
L-Threonine	3.58
L-Tryptophan	0.60
L-Tyrosine	1.81
L-Tyrosine (disodium salt)	-
L-Valine	3.50
VITAMINS:	
Biotin	0.024
D-Ca Pantothenate	0.72
Choline Chloride	0.70
Folic Acid	1.31
i-Inositol	0.54
Niacinamide	0.62
Pyridoxal HCl	0.21
Riboflavin	0.38
Thiamine HCl	1.01
Vitamin B12	1.36

Clinical Study of Childhood Brucellosis in Jordan

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Abstract:

Objective: The present study was carried out to obtain the prevalence of childhood brucellosis among patients attending the pediatric department at PRH.

Material and Methods: A total of 5726 blood specimens (from children aged 14 years and younger) were studied for the serological evidence of brucellosis.

Results: Ninety-three (1.6 per cent) showed diagnostic agglutinin titres. Forty-three (59.7 per cent) blood specimens yielded the growth of *Brucella melitensis*. Thirty-nine patients (41.93 per cent) were shepherds. More than 60 per cent of the patients had a history of both consumption of fresh goat's milk and close animal contact. Seventy-three (78.49 per cent) were males and 20 (21.51 per cent) were females, with a male to female ratio of 3:1. The disease occurred mainly in the school age group (mean age 10.3 years). All the patients had an acute history of less than 2 months. Forty-nine (52.68 per cent) patients presented with persistent fever, 19 (20.43 per cent) with joint pain. Pityriasis Alba was the consistent physical finding, with fever in the majority of the patients. The major joint found to be involved was the knee (52.77 per cent). Eight patients presented with complications. In 15 cases (16.13 per cent) brucellosis was suspected clinically whereas 78 (83.87 per cent) cases, only serological evidence of brucellosis confirmed the diagnosis. None of the cases relapsed. In our experience an initial combination therapy two-drug regimen for a minimum of 6 weeks was given.

Conclusion: In our series, pediatric brucellosis is quite common since this area is endemic to *B. melitensis* where a strong clinical suspicion or laboratory routine screening has to be done to diagnose and institute specific therapy.

Keywords: prevalence, brucellosis.

Introduction

Brucellosis constitutes a major health and economic problem in many parts of the world, including countries of the Mediterranean Basin, the Middle East and the Arabian Gulf.^{1,2} It remains an uncontrolled problem in regions of high endemicity such as the Mediterranean, Middle East, Africa, Latin America and parts of Asia.^{3,4}

Humans are infected accidentally by close animal contact or consumption of animal products infected by bacteria of the genus *Brucella*.⁵ Six species are recognized, and four are well-established human pathogens. Human infection can occur through consumption of infected raw milk, raw milk products, or raw meat.⁶ Other means of infection include skin abrasions⁷ or inhalation of airborne animal manure particles.⁸ Brucellosis can affect any age including children. The incidence of childhood brucellosis varies. Some authors have concluded that brucellosis in children is rare.⁹

Brucellosis is an endemic disease in Jordan as evidenced by a marked increase in the number of reported cases by the Jordanian Ministry of Health.^{10,11} Brucellosis, especially related to *Brucella abortus* is not frequent in children.¹² In endemic *B. melitensis* areas; children represent 20–25 per cent of cases.¹³ The present study was carried out to obtain the prevalence of childhood brucellosis among patients attending PRH for clinical profile determination.

Material and Methods

During the period from August 1996 to September 2006, all 5726 serum samples referred to the microbiology laboratory were examined for evidence of brucellosis. All the sera were screened for *B. agglutinins* by slide agglutination test using *B. abortus* colored antigen. The positive samples (97) found with the slide method, were analysed further for the levels of antibodies by standard tube agglutination employing *B. abortus*-plain antigen. Of the 93 blood specimens' positive for diagnostic titres (160), blood cultures were carried out in 72 cases. The blood specimens were inoculated onto two Castaneda's biphasic media consisting of trypticase soy agar and broth. The media were incubated at 37°C with and without CO₂ for 1 month. The slide agglutination test was performed using *B. abortus* and *B. melitensis* monospecific antisera.

The tube agglutination test, with the help of same antisera, was also carried out wherever it was indicated. The antisera were obtained from Murex Biotech Ltd, Dartford, England.

The synovial fluid and CSF specimens were also subjected for *B. agglutinins* demonstration with both slide and tube tests as mentioned above. Additional specimens such as synovial fluid, CSF, and skin were cultured using the above techniques. A detailed clinical history including epidemiological features and examination findings were recorded and analysed.

Results

Of the 5726 serum samples studied, 93 (1.6 per cent) demonstrated *B. agglutinins* in diagnostic titres. The titres ranged between 160 and 5120, (Table 1). Forty-three blood specimens (59 per cent) grew *B. melitensis*; 42 were biotype 1 and one isolate was biotype 3. Shepherds (39 patients) were the major occupational group affected in the present study. Of the 93 patients, 58 gave a history of both animal contact and raw milk ingestion. Males (73 patients) were predominant in our study with a male to female ratio of 3:1 (Table 2). The major age group affected was 11–14 years, followed by 6–10 years (Table 2). The youngest age recorded with brucellosis was 33 months, a female child who had a history of raw milk ingestion. The patients presented with fever, joint pain, and low backache; fever being the main presentation (Table 3). One patient had involuntary movements of limbs alone and one presented with burning feet only. Pityriasis Alba was the consistent physical finding, with fever in the majority of patients. Hepatosplenomegaly was noticed in 48 patients, splenomegaly alone in nine, and hepatomegaly alone in five patients. Single joint involvement was found in 29 patients, the knee joint (19 patients) being the major joint affected (Table 4). Successful isolation of *B. melitensis* was possible in knee joint synovial fluid of three out of five patients attempted. Two joints were affected in four patients and three patients showed involvement of three joints.

Eight patients presented with complications that included papular skin lesions (3), carditis (2), chorea (1), meningitis (1), and peripheral neuritis (1) (Table 5).

Discussion

The prevalence of brucellosis in the present study was 1.6 per cent (93 children), which is much higher than the reports of Spink⁵ and Cucullu.⁹

Pediatric brucellosis is uncommon where *B. abortus* is endemic.¹² However, in areas where *B. melitensis* is endemic, pediatric cases are seen¹⁴⁻¹⁷ in endemic *B. melitensis* areas, children represent 20–25 per cent of the cases.¹³

In the present study, 93 (19.1 per cent) children out of 485 cases were diagnosed as having brucellosis during a period from 1996 to 2006. This finding is similar to the data obtained from the Middle East countries,¹⁴⁻¹⁷ although lower figures have been quoted by Dalrymple-Champney¹⁸ from England. The high prevalence of childhood brucellosis in the present series can be attributed to the endemicity of this area for *B. melitensis*. The isolation of only *B. melitensis* species supported this fact. All the 73 patients, including 32 children with brucellosis, were due to *B. melitensis* in Israel¹⁶ and *B. melitensis* remains the principal cause of human brucellosis¹⁹

The vehicle of transmission in most of the cases in the present study was the consumption of raw milk. Like that based on the findings of our study, we conclude that the main risk factor for brucellosis is consumption of fresh, unpasteurized dairy produce.²⁰

The studies from Saudi Arabia,^{21, 22} Iran,²³ and Spain²⁴ report that raw milk ingestion is an important factor in disease transmission. This finding may also be the reason for our cases showing predominance in school-aged children. These children may consume raw milk while tending the flock in their spare time. Children younger than 5 years had the least infection, and this has also been reported in literature.²⁵⁻²⁸

Human brucellosis usually manifests as an acute or sub acute febrile illness, which may persist, and progress to a chronically incapacitating disease with severe complications.²⁹ In the present study; only 15 cases (16.13 per cent) were suspected of having brucellosis, showing

that the disease awareness in an endemic area is important to arrive at a clinical diagnosis like Al-Shamahy et al in which: "If clinicians are made more aware of the presenting features of brucellosis and that it should come into the differential diagnosis of fever associated with enlarged liver, spleen and lymph nodes, it will lead to an increasing index of suspicion for this infection".³⁰

In the present series, 78 cases (83.87 per cent) on admission were classified as enteric fever, malaria, pyrexia of unknown origin, and rheumatoid arthritis, showing the protean manifestations of brucellosis and necessitating collaboration between clinician and microbiologist even in endemic areas for the diagnosis of brucellosis. So: Brucellosis should be suspected and investigated for, in any case of pyrexia of unknown origin.³¹

The main clinical presentation of brucellosis in children is fever, but the skeletal manifestations of the disease are also significant.²³ Fever was the commonest complaint in the present study and it is worth mentioning the joint pain, which was the only complaint in 19 patients. Fever and pityriasis Alba were a common association in the present series as ; In a prospective study in Jordan, fever (88%) was the most common clinical feature encountered, followed by sweating, arthralgia and general weakness.³² and as that in Japan in which: Fever, arthritis or arthralgia, hepatomegaly and splenomegaly were the main findings.³³

Monoarticular arthritis of the knee is the most frequent reported form,^{14, 15, 34} which was observed in 19 patients in the present series.

Skin lesions are an uncommon feature of brucellosis.^{5, 35-38} All three patients with skin lesions in the present series had papules. To our knowledge, ours is the fourth report of bacteriologically confirmed skin lesions in brucellosis in the world. The skin lesions disappeared within 8-10 days of the start of antibiotic therapy. Neurological manifestations of brucellar origin although reported, have not documented chorea as a symptom in the world literature. One patient had brucellar chorea that was successfully treated. Brucellar meningitis reported in the present series received successful treatment. Relapse was not recorded in any of the cases. In our experience combination therapy with a minimum of two drugs and extending treatment for at least 6 weeks with two drugs seems warranted to improve outcome and prevent relapses like in Henk et al: The standard treatment of uncomplicated cases in adults and children 8 years of age and older is 100 mg doxycycline twice a day for 6 weeks plus 1 g streptomycin daily for 2 to 3 weeks. Instead of streptomycin, rifampicin may be given in combination with doxycycline (200 mg/day orally for 6 weeks) at a dose of 600-900 mg for 6 weeks.³⁹ In our series, pediatric brucellosis is quite common since this area is endemic to *B. melitensis* where a strong clinical suspicion or laboratory routine screening has to be done to diagnose and institute specific therapy. Similar to Issa H et al In 1999 in south of Jordan "Brucella agglutination test and titer in association with a suggestive clinical picture was more sensitive than blood culture in the diagnosis of brucellosis".⁴⁰

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Table 1. Antibody profile and culture status

Titre	Number positive	Number culture done	Culture positive
160	37	24	15
320	23	19	08
640	10	10	07
1280	15	15	09
2560	04	02	02
5120	04	02	02
Total	93	72	43

Table 2. Age and sex distribution of 93 patients

Age (years)	Male	Female	Total
0-5	02	01	03
6-10	24	08	32
11-14	47	11	58
Total	73 (78.49%)	20 (21.5%)	93

Table 3. Clinical profile of 93 patients

Clinical presentation	No. of patients	% of patients
Fever	49	52.68
Joint pain	19	20.43
Fever, joint pain and low backache	03	3.2
Fever and joint pain	14	15.05
Fever and low backache	06	06.43
Jerky movements of limbs	01	01.07
Burning feet	01	01.07
Splenomegaly	09	09.67
Hepatomegaly	05	05.37
Hepatosplenomegaly	48	51.61

Table 4. Involvement of joints

Joint(s)	No. of patients	% of patients
Knee	19	52.77
Hip	07	19.4
Shoulder	01	02.7
Ankle	02	05.5
Knee and elbow	01	02.7
Knee and hip	03	8.3
More than 2	03	8.3

Table 5. Complications of brucellosis

Complication	No. of patients
Skin lesions	03
Carditis	02
Chorea	01
Meningitis	01
Peripheral neuritis	01
Total	08

The prevalence of metabolic syndrome among patients with type 2 diabetes mellitus in Basrah

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Abstract

Background: Metabolic syndrome (MetS) is a cluster of multiple metabolic abnormalities that increase the risk of cardiovascular morbidity and mortality. The aim of this study is to assess the prevalence of MetS in patients with type 2 diabetes mellitus (DM).

Methods: This was a cross sectional hospital based study of patients with type 2 DM. MetS diagnosis was based on the presence of 2 of 4 metabolic abnormalities, which are hypertension, visceral obesity, high triglyceride and low high density lipoprotein.

Results: Total number of patients was 200. Of these there were 145 males and 55 females. Age range was 28-88 years, and mean age 51.9 ± 10.6 year. Over all MetS seen in 86% (82.7% of males and 94.5% of females).

Conclusion: Highest prevalence of MetS was reported in this study which includes diabetic patients only, although this high figure may be due to a different definition and population studied with selection bias. The main stay of management of MetS is dietary modification and weight reduction which may delay the development of DM, improves the control of established DM and decreases morbidity and mortality associated with this syndrome.

Key words: diabetes mellitus, metabolism, cross sectional studies, metabolic syndrome.

Introduction

According to the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults in USA. Adult Treatment Panel III (ATP III), MetS (formerly called syndrome X, insulin resistance syndrome, dysmetabolic syndrome, cardiovascular multiple metabolic syndrome, multiple metabolic syndrome or cardio-metabolic syndrome) was defined, as when three or more of the following abnormalities are present, which are: abdominal obesity (AO) with waist circumference for men >102 cm and women >88 cm, serum triglycerides (TG) ≥ 150 mg/dl (≥ 1.7 mmol/l), high density lipoprotein (HDL) cholesterol for men <40 mg/dl (< 0.9 mmol/l), and for women <50 mg/dl (< 1.0 mmol/l), blood pressure $\geq 130/85$ mmHg, and fasting plasma glucose ≥ 110 mg/dL (6.1 mmol/l).

The syndrome is not new, having been already observed in 1923 by Kylin, who described the clustering of hypertension, hyperglycemia, and gout as a syndrome.³

MetS increases the risk for coronary heart disease and stroke by three fold with marked increase in cardiovascular mortality.⁴

The aim of the study is to assess the prevalence of MetS in patients with type 2 diabetes mellitus (DM) according to the definition of the ATP III report.

Methods

This was a cross sectional hospital based study of patients with type 2 DM. It includes patients with type 2 DM seen in the in-patient and out-patient clinic of the Basrah Military hospital over a period from Jan 2002 to October 2002. All patients with type 2 DM, regardless of the duration of DM, were included if they agreed to participate in this study.

The new type 2 DM was diagnosed according to the American Diabetic Association (ADA) recommendations in 2002.⁵ Patients who were currently on drug treatment for diabetes and hypertension were considered hypertensive and diabetic respectively. For blood pressure, the average of second and third blood pressure measurements in the office were considered. Two blood pressure recordings were obtained from the right arm of patients in a sitting position after 30 minutes of rest at 5-min intervals, and their mean value was calculated.

The women were non-pregnant, and the blood estimation of lipoprotein was taken after at least an 8 hour fast. Diabetes duration ranged from a few days to 30 years.

Since all of our patients were diabetics, the presence of 2 metabolic abnormalities other than DM, is enough to establish the diagnosis of MetS.

The waist circumference was measured with a soft tape on standing subjects, midway between the lowest rib and the iliac crest.¹

Results

Total number of patients was 200. Of these 145 were males and 55 females. Age range was 28-88 years, and mean age 51.9±10.6 years. Overall MetS (Table-1) was seen in 86% (82.7% of males and 94.5% of females).

Prevalence of different metabolic abnormalities are presented in Table 2. At least 2 metabolic abnormalities were seen in 32.5% of patients.

In Table 3, hypertension was the commonest metabolic abnormality (76.5%) followed by high TG (69%).

The commonest combinations that constitute the MetS with diabetes (table 4) were Hypertension, abdominal obesity, low HDL and High TG in 26.5%.

Discussion

An array of metabolic, hemodynamic, and renal abnormalities constitutes the cardiometabolic syndrome. A hallmark of this syndrome is visceral obesity and associated insulin resistance/hyperinsulinemia. The syndrome is also associated with essential hypertension, abnormalities in the circadian rhythm of blood pressure and heart rate, the diabetic dyslipidemic syndrome, hypercoagulability, hyperuricemia, increased cardiovascular inflammation, and microalbuminuria, all of which contribute to an increased risk of cardiovascular disease morbidity and mortality.^{2,6-8}

Insulin resistance may be the underlying feature of MetS.⁹ The World Health Organization (WHO) definition of MetS in 1998¹⁰ is different from that of AHA and ATP III¹¹, where the WHO defined the MetS as presence of at least two of the following 1) hypertension, defined as antihypertensive treatment and/or elevated blood pressure (> 160 mmHg systolic or > 90 mmHg diastolic); 2) dyslipidemia, defined as elevated plasma triglyceride { ≥ 1.7 mmol/l (150 mg/dl)} and/or low HDL cholesterol {< 0.9 mmol/l in men (40 mg/dl), < 1.0 (50 mg/dl) mmol/l in women} concentrations; 3) obesity, defined as a high BMI (≥ 30 kg/m²) and/or a high WHR ratio (> 0.90 in men, > 0.85 in women); and 4) microalbuminuria (urinary albumin ≥ 20 μ g/min). We chose the ATP III definition, because it is easier as we have difficulty in measuring microalbuminuria in our area and even some questioned the value of the last WHO criteria because of its rarity.^{11,12}

In this study we reported the highest prevalence of MetS reported in literature, which was 86% (82.7% of males and 94.5% of females). The prevalence of MetS among patients with type 2 DM according to WHO definition for women and men respectively was 84% and 78%, in Botnia study (~ 80% for both sexes) in Finland and Sweden.⁴ In USA, MetS among adults was seen in 6.7% to 42% according to age (increase with age), with an age adjusted rate of 23.7%.¹³ In Saudi patients MetS is seen in 56% of patients with Type 2 DM and the commonest component of the syndrome was hypertension.¹⁴

For all studies MetS was more common in females than males. In this study, hypertension is again the common-

est metabolic abnormality and the commonest constellation of metabolic abnormalities were hypertension, abdominal obesity, low HDL and high TG. One explanation of this high rate of MetS in this study is adoption of Western lifestyle in our society with overweight, physical inactivity, sedentary behaviour, and unhealthy dietary habits (non healthier lifestyle).

The prevalence of the MetS and its components is strongly dependent on the definition of the different components of the syndrome, which is still not accepted for all globally.^{2,4,11,13,15}

In conclusion the highest prevalence of MetS was reported in this study, which includes diabetic patients only, although this high figure may be due to different definitions and population studied with selection bias.¹³ These figures seem alarming if no prevention protocol is adopted. The mainstay of management of MetS is dietary modification and weight reduction which may delay the development of DM, improves the control of established DM and decreases morbidity and mortality associated with this syndrome.¹ Further studies including all people whether diabetic or not, is mandatory to estimate the prevalence of MetS.

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Table 1. Prevalence of MetS according to sex.

	Number	%
Metabolic syndrome in all patients	172	86%
Metabolic syndrome in males	120	82.7%
Metabolic syndrome in females	52	94.5%

Table 2. Prevalence of metabolic abnormalities among study group according to sex.

Number of metabolic abnormalities	Men	Women	Total (%)
4	32	21	53(26.5%)
3	35	19	54(27%)
2	53	12	65(32.5%)
1	21	3	24(12%)
0*	4	0	4(2%)
Total	145	55	200

*They have only one metabolic abnormality, which is diabetes.

Table 3. Prevalence of the different components of MetS among patients according to sex.

Metabolic abnormalities	Men	Women	Total N (%)
Hypertension	106	47	153(76.5%)
High TG	105	33	138(69%)
Abdominal obesity	83	50	133(66.5%)
Low HDL	56	34	90(45%)

Table 4. Prevalence of different combinations of the individual component of MetS among patients of both sexes of type 2 DM.

Metabolic abnormalities	Men	Women	Total
Hypertension+ abdominal obesity+low HDL+High TG	33	20	53(26.5%)
Hypertension+Abdominal obesity +high TG	23	9	32(16%)
Hypertension+High TG	25	0	25(12.5%)
Hypertension+ abdominal obesity	12	8	20(10%)
Hypertension+ abdominal obesity+low HDL	6	8	14(7%)
Abdominal obesity +high TG	6	2	8(4%)
Low HDL+High TG	6	0	6(3%)
Hypertension+high TG+low HDL	5	1	6(3%)
Low HDL +hypertension	4	1	5(2.5%)
Abdominal obesity +high TG+low HDL	1	1	2(1%)
Abdominal obesity+ low HDL	0	1	1(0.5%)
Abdominal obesity+low HDL+High TG	0	0	0

Effect of Social and family factors on committing suicide among university students in Iran

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Abstract

In all societies people of different ages and races commit suicide, and it is considered as one of the first ten causes of death. There may be several reasons for suicide and their recognition has always been of great importance for the authorities who are supposed to control it.

In fact, committing suicide among the young people, especially university students is a great social problem. It is also a matter of concern for mental health specialists. The aim of this study is to investigate the relationship between social and family factors and the idea of committing suicide among university students in Iran. 100 university students (50 male, 50 female) from University of Welfare and Rehabilitation sciences were randomly selected and participated in the study.

A 59 question demographic questionnaire about family situation, personal features and the idea of committing suicide and also a Beck questionnaire about depression and disappointment. The questionnaires are filled out in a private interview.

The samples were taken randomly. So it was found out that the singles were more inclined to commit suicide than the married ones. Divorce, failure in education, and family background also increase it. Among the other increasing factors old age and female sex should be indicated.

Key words: Social and family factors, suicidal idea and attempt, university students.

Introduction

The word suicide is a French word that consists of two parts: sui the means self and cide that means Killing (Dorckhime, 1999). .Piere Mourn indicates that Suicide is an intentional work either consciously or unconsciously in order to destroy someone's self (Moron,1997) Aristotle believes that suicide is different from sacrifice (Azkia,1985) Freud believes that sexual relationship with the others is an important factor (Roiters,1994) According to Eric From the disintegration of social and traditional beliefs is an effective factor (khosravi,1960) This theory is confirmed by Hallbwachs (Shabani Fard Jahromi) Dorkhime claims that economical welfare decreases suicide (Halbwachs,1930)Henry and Short confirm this idea with and emphasis on aggression (Henry,1965)Gibbs and Martin emphasize the contrast of roles (Gibbs,1965)some people believe that social vacancy surrounding a person is the only cause of his suicide (AlecRay)sometimes suicides finds an elevated value in the society (Heidary,1997)of course in this respect, the amount of suicides in the society and the social position of the people should be considered as determining factors (Jahan Pajuhesh) Even there are a lot of praising and glorious example of suicide in literature such as the examples in Shakespeare's Works including the suicide of Juliet in Romeo and Juliet, that of Ophilia in Hamlet and that of Cleopatra in Antony and Cleopatra and also suicide in the works written by Victor Hugo.

We can see even the suicide of some famous people such as Ernest Hemingway. It is estimated that 6% to 14% of people have the idea of suicide, and 10% to 14% of those with the same idea finally

committed suicide. Statistices shows that it is increasing specially among young people all over the world (Mohseni ,1987)Researches show that the number of women who have to stay in hospital because of suicide is more than that of men (Burke,1978,7-11) and concerning the seasonal effects, it increases a bit in spring and autumn and decreases in Winter.

Suicide is a great social pathology and also a matter of concern for those who deal with mental health. This problem is worse specially when it is about Young people and university students who are the hope of our future. (Shopfropfer 2001) .

The people of all different ages, races, and social classes may commit suicide. (Jilianeh and Jeifer 1993) . When the number of young people increases in a society, the number of suicides increases too. For example after the second world war with the large number of children the problem was that a lot of young people committed suicide (Caplan and Sadud 2000, Merk 2002) .

It seems that the increase of suicide is the result of different factors including social environment, a change in the way we look at suicide, and availability of its tools (Hawthon and Kate 1997)

Among the other causes of suicide we can refer to great depression, misuse of drugs, and criminal behaviors (Caplan and Saduk 2000, and Merk 2002) and (Sarason,1994)In this respect there are two groups of causes: those that make the victim inclined and those that make his tendency evident. In the first group we can refer to family background, mental disorders, physical problems

and also tendency to attempt suicide in the family, specially the parents. In the second group the crises of conformity, quarrel with parents, friends, and classmates, joblessness, divorce or separation, bereavement, and also all the stressful events of life. (Caplan, Saduk and Gereb, 1996). Men are more successful in suicide than women. In this respect China is an exception. Iran is the 58th country in the world in which out of each 100000 people 6 ones attempt suicide (Table 1 shows the rate of suicide in some countries for the two sexes)

It is reported that in 2001 there were 3000 suicides in Iran (%65 men, %35 women) that is about %1 of total deaths. In developed countries this rate changes to %1 to %2 of total deaths. (Ganil, 2000). The number of suicidal attempts is more than successful suicides. For example in our country it is reported about 2 to 50 times more and this number changes in different provinces. In different countries women usually attempt suicide 3 to 4 times more than men but men have successful suicides 3 times more than women (Caplan and Saduk, 2000).

In Iran men usually have successful suicides 2 times more than women. But in some provinces such as Ilam, Bushehr, Khuzestati, Kohgiluyeh and Boyer-Ahmad, Fars, and Kerman the number of women who commit suicide is more than men. It is reported that the highest rate of successful suicide is in Ilam (26 in 100000) and in Kermanshah (23 in 100000) and the lowest rate is in Tehran and Sistan and Baluchestan. The oldest statistics about suicide in Iran can be taken from an article written by Dr. Mirsepassi in 1970 and published in a magazine about psychology. Manoochehr Mohseni 1884 in which he announced 229 cases of suicide in Iran (1.3 in 100000). In a research made by Dr. Naghavi in 1994 it is reported that among the population of villagers, the rate of suicide is 5 in 100000. Killing by fire is one of the most frequent ways of suicide among women in some provinces. According to the study of Kamalzadeh and his colleagues the rate of suicide in Tehran has gone up three times higher in comparison with the last decade. Based on a research in Kerman it is observed that the attempt women for suicide is 1.5 times more than men but successful suicide among men is 1.5 times more than woman (Abbasizadeh, 1999). Studies about this matter are so expanded that it is not possible to deal with all different aspects and texts, so some of the outstanding points will be given as follows: Although the rate of suicide normally increases among the middle-aged and old people (men after 45 and woman after 55), it is also increasing very rapidly among the young people specially boys between 15-24 years old (Tehran University, 1996). Depression and Schizophrenia are the two main causes of suicide, and the background of its attempt shows how serious it might be (Caplan and saduk, 1999). The idea of suicide is more common among men, old people, and single or divorced people (Caplan and saduk, 1999). Suicide is more common in urban and industrial areas in contrast with rural and non-industrial areas (Sheibani, 1973). The matter of suicide is rarely observed among children only in urban areas (Mohseni, 1967, 9-11). Higher social position and descending in social rank are two other causes of suicide (Caplan and saduk, 1999). The other cause is social disorder that leads to personal disorder (Caran, 1965). Suicide is very common among the medicine Doctors, specially female doctors and its main causes are depression and addiction. Psychiatrists and then ophthalmologist and anesthetists in contrast with the other specialists have greater tendency to commit suicide. The unemployed people have more tendency to do this work (Caplan and saduk, 1999). And in general in high and low positions it is more popular than in average positions (Mohseni, 1987). The rate of suicide among the whites is more than the blacks (Caplan and saduk, 1999). The acceptance of a person in the family is the cause of his physical and moral health and as a result in de-

creases the danger of suicide (Mohagheghi, 1985). Marriage and having children decrease the rate of suicide enormously. It is observed that suicide among the singles is two times more than the married people and also among the divorced people is two times more than the singles (Caplan and saduk, 1999). Disintegrated families increase the rate of suicide especially among girls (Ministry of the Interior, Iran, 1990). The Jews and Protestants commit suicide more than the Catholics and the Moslems less than the others (Mohseni, 1987). Porterfield believes that impiety is closely related to suicide (Caran, 1965). Regardless of ethical, religious, and philosophical matters, psychologists investigated the subject of suicide based on clinical cases and their attempt to understand the reality of suicide (Caplan and saduk, 1999). There is a close relationship between physical health, sickness, and suicide (%12 to %15 of suicides) (Mohseni, 1987). Women are more likely to commit suicide during their monthly period, specially on the first day (Hassanpur, Mashhad and Beka and colleagues, Spanish). But it rarely happens during their pregnancy (Abbasizadeh, 1999). Having children is one of the factors that immunize women more than men against suicide (31). Imitation is one of the increasing factors but for a limited time (Dorckhime, 1999). About educational: collegians and students, according to the studies of Dr. Mohseni in 1973-76 in Tehran, it is observed that %17.5 of suicides were related to the collegians and students. Failure in educational matters, specially in exams, increases the rate of suicide among university students (Alishiri, 1991). Revolution doesn't affect the rate of suicide, but war decreases it (Eslami Nasab, 1992). Social complications increase it (Eslami Nasab, 1992). When the rate of homicide increases in a country, the rate of suicide decreases consequently (Eslami Nasab, 1992). Availability of the device is very important in determining the type of suicide, for example in America gun is a very common device. In winter, suffocation by gas, and in summer drowning in water are very common (Elahi, 1987). There are some other factors that increase the danger of suicide including social forces, sudden strong stresses, family problems and crises, death of a close relative, dismissal, the sense of failure, and also strong criticism by others (Ghaem Magham, 1985). Addiction to alcohol and drugs can be added to the list (Oryan, 1998). The common people suppose that poverty increases the risk of suicide, but the fact is exactly in contrast (Dorckhime, 1999). Of course in some countries such as India and Uzbekistan, it is observed that there is a close relationship between economic crisis and poverty with suicide (Sotudeh, 1994). Studies confirm the same point even in Iran (The Entekhab newspaper). Although the relationship between modernity and suicide has not been proved (Sotudeh, 1994). Old studies and statistics express the point that the movement of society toward modernity increase the rate of suicide (Shabani Fard Jahromi). In Iran increasing of the immigration of villagers to cities is considered as another cause (Hesamian, 1984).

Finally we are going to have a look at different causes of suicide in Iran: in Lorestan, addiction and poverty; in Ilam, depression, poverty, and accusation of someone's chastity; in Gilanharb, sexual privation, limitations, and chastity affairs (Hesamian, 1994). In Kermanshah, family problems, and psychological and mental problems (Province council of Kermanshah, 1997) in Mazandaran, family conflicts (Province council of Mazandaran, 1997) and in Kerman, family problems, and cultural poverty (Province council of Kerman, 1997). Based on the studies about women, we can classify some of the causes of suicide among women in this way: husband's addiction, great difference between the ages, maladjustment, the existence of several wives for a man, lack of ability to make decision, the interference of others in the family affairs, marriage in the early ages, and also considering divorce as a very undesirable work (Asgari, 1997). It is interesting to

know that in Iran suicide is very popular among the young married women while in western countries it is popular among the old unmarried men. (Asgari, 1997). There are several researches about different causes of suicide in Iran: according to a research made in 1994, the causes are mentioned respectively as loneliness, age, irremediable disease, and failure in life and love (Gudarzi, 1994). In another research, the causes are pointed out as marital problems, undesirable condition of family life, psychological problems, failure in love, mental and personal disorders, poverty, joblessness, addiction, urban and industrial life and disintegration of social groups (Sotudeh, 1994). Based on another research the factors are mentioned respectively as marital problems, undesirable condition of family life, poverty, joblessness, addiction, psychological problems, personal and mental disorders, failure in love, and urban and industrial life (Mohseni, 1987).

Material and Method

The students of bachelor level at the university of Welfare and Rehabilitation in Tehran make the society of statistical research. A sample group of 100 people (50 male, 50 female) were taken randomly from the same society.

The device of measurement:

Demographic questionnaire about information and two Beck questionnaires about hopelessness and depression which were filled out respectively in a private and face - to - face situation. At the same time all the questions of the samples were answered. The type of research: This is a kind of retrospective research

The variables of research:

The independent variables are social and family factors and the dependant variable is suicide.

Statistical methods:

The software SPSS (9.5) is used in this research and then the method of one sample T test is used in which the relationship between the main variables and those that affect the number and rate of depression (which determines the rate of suicidal thought) is considered. The important point is the meaningful level that is about 0.0005 in the four case of divorce, failure in education, marital status, and family background.

Results

50 men and 50 women took part in this test. Their ages were between 17 and 26 and the highest percent belonged to the age of 22 that was %23 of the whole. %15 of the samples were married, %58 stayed at the dormitories and %42 lived at home. %8 of the samples had experienced failure during their education. %32 of the samples had the idea of suicide and %6 attempted unsuccessful suicides. %28 had experienced the lose of a close relative in the last 6 months. In the family of two of them there was a background for suicide. Among the samples, there was a significant relationship between depression and divorce, failure in education, marital status, and family background. Of course the relationship between depression and family background was stronger than the others (Table 2). About the marks of hopelessness we can conclude that they took from 1 to 15. Most of them were between 2 and 8. The highest percents were for mark 3 by %17, mark 2 by %16, and mark 5 by %10.

Discussion and conclusion

For many years in Iran nobody paid attention to comprehensive research about suicide (Mohseni ,1987) and about the students

rarely made such researches. Studies about educational matters in America and specially at some universities such as Yale, Kernel, and Harvard support the fact that in these cities the university students commit suicide more than the other groups of people. According to the research of Dr. Mohseni about suicide in Tehran (1973-74), it is observed that %17.5 of suicides were related to collegians and students that supports the above- mentioned point. In this research, some factors such as failure in exams, lack of educational success, and family conditions are considered as the main causes of suicide (Alishiri ,1991). Based on a research in Kermanshah (97-98) %3 of suicides were because of failure in education (Province council of Kermanshah ,1997). In our sample test 8 people had experienced the some failure and two of them had thought of suicide . Separation from family is another cause of the same thought, specially among girls , the reason is that they are dependant of their families for social, economical , and emotional matters (Ministry of the Interior, Iran , 1990). A research in Tabriz (1978-79) shows that the death of close relatives is the main cause of suicide (Karbasi) and another research made in 1994 supports the same point in the whole country (Gudarzi ,1994). In our test , 28 people had experienced the separation of a close relative in the last 6 months and 19 of them had thought of suicide and 3 of them committed suicide . Among the samples there were also 58 students who lived in the dormitories far from their families from which 21 students had thought of suicide. Researches show that the rate of suicide among the unmarried people is two times the married ones (Caplan and saduk, 1999). In our research there were 85 singles and 15 married ones, and 30 of the singles (%35) and 2 of the married ones (%13) had thought of suicide. Also from the 6 students who committed suicide 5 ones were single. Of course in Iran marriage can be considered as a controlling factor especially for men (Asgari, 1997) and as a result, marriage decreases the amount of suicide (Mohagheghi, 1985). Researches show that suicide has increased in extended families in comparison with the nuclear families (Ministry of the Interior, Iran, 1990). In our test, there were suicide background only in the family of 2 samples, but neither of them had tendency to the same work. Of course the problem is that our statistical society is limited. Most of the researches confirm that family problems are the main causes in Iran (between %54 and %80) (Mohseni ,1987, Province council of Kermanshah ,1997 , Malek ,1994) . The immunity of women against suicide is more than men (Malek, 1978). According to the old researches women committed suicide more than men in Iran (Asgari ,1997) but new researches show the opposite situation (Asgari ,2004) In our recent study 32 people out of 100 had though of suicide (19 women and 13 men) and of course 6 of them committed suicide (4 women and 2 men) .Increasing age is also an important factor (Tehran University, 1996) Suicide is increasing very fast among the men of 15 to 24 years old (Tehran University, 1996). In our recent study we observed that there is a direct relationship between increasing age and suicidal thought. The results of this study proved all our hypotheses: there is a significant relationship between suicide (thought and attempt) and divorce, failure in education, marital status, and family background. Age and sex also have a significant relationship with suicide (thought and attempt).

Limitations :

- 1- Lack of ability to apply this research to the whole society because the selected people may not represent the society.
- 2- Limitation and small size of the selected society that is considered as a pilot study .

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Table 1. The rate of suicide in different countries for the two sexes (in 100,000 people)

Number	Country	Suicide rate women	Suicide rate men
1	Canada	5.4	21.5
2	Norway	6.9	17.7
3	The United States	4.5	19.8
4	Sweden	9.2	21.5
5	Australia	4.7	21
6	France	10.7	31.5
7	Finland	11.8	43.4
8	Germany	8.7	32.2
9	Denmark	11.2	42.2
10	Italy	4	12.7
11	Spain	3.7	12.7
12	Chile	1.4	10.2
13	Costa Rica	1.8	8
14	Poland	16.7	50.6
15	Venezuela	1.9	8.3
16	Mexico	1	5.4
17	Colombia	1.5	5.5
18	Cuba	14.9	25.6
19	Latvia	15.6	79.1
20	Thailand	2.4	5.6
21	Iran	3.4	3.8

Source: the report of human expansion 1999 (undp)

Table 2. The rate of correlation between depression and the four Hypotheses:

	Number	Correlation	Meaningful level	average	Standard marks	Meaningful level 2- Tailed
1. divorce and depression	100	- 0.10	0.31	1.46	0.78	0.000
2. Failure in education and depression	100	- 0.29	0.01	1.66	0.71	0.000
3. Marital status and depression	100	- 0.42	0.67	0.89	0.70	0.000
4. Family background and depression	100	- 0.003	0.97	1.7	0.64	0.000

In this table the variables are considered in pair and there is a significant relationship between depression and the four hypotheses. The important point in this table is the positive correlation between depression and family.

1-The relationship is significant. 2-The relationship is significant. 3- The relationship is significant. 4- The relationship is significant.

Incidence of hyperkalemia in patients of type 1 and type 2 diabetes mellitus in Saudi Arabia

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Abstract

Background & Objective: The objective of this study is to determine the level of hyperkalemia in Saudi patients of Type 1 and Type 2 diabetes mellitus, since the patients of diabetes mellitus with hyperkalemia are at a higher risk.

Methods: In the present study, 362 male and female known diabetic patients of Type 1 and Type 2 and 158 non diabetic control subjects visiting Al Iman General and Prince Salman hospitals of Riyadh were studied from October 2003 to August 2005. The diabetics were classified into Type 1 and Type 2 on the latest criteria laid down by the International expert committee on Diabetes Mellitus. None of the diabetics included in our study had shown signs of renal failure. Both types of diabetics were subdivided on the basis of their fasting plasma glucose levels (FPG) in three groups, group 1 (7.1 -10.0) group 2 (10.1 -20.0) and group 3 (>20.0) mmol / L and their serum potassium levels were estimated.

In the control and test groups the plasma glucose level (FPG) and the serum potassium level were measured after twelve hours of night fasting.

Results: Hyperkalemia was not detected in the group 1 diabetics of Type 1 and females of Type 2. The group 2 diabetics of Type 1 and Type 2 showed serum potassium levels of 5.9 ± 1.1 and 7.2 ± 1.4 mmol /L ($P < 0.001$). The serum potassium levels in the group 3 of Type 1 and Type 2 diabetics carrying a FPG of > 20 mmol /L were 6.8 ± 1.2 ($r = 0.56$) and 8.1 ± 1.7 mmol /L ($r = 0.68$) $P < 0.05$.

Conclusion: It was observed that there is a strong association between hyperglycemia and hyperkalemia in Saudi diabetes mellitus patients of Type 1 and Type 2. The elderly uncontrolled diabetics are at a higher risk of hyperkalemia. Hyperkalemia in uncontrolled diabetics can lead to kidney and liver damage and cardiac arrest. The physicians, while prescribing ACE inhibitors to diabetics, must take precautions to avoid complications of hyperkalemia.

Key Words: Diabetes Mellitus, Hyperkalemia, Saudi Arabia

Introduction

Potassium is the most abundant cation in the body. 98% of the total 4000 mmol is in the intracellular fluid compartment; with only 60 mmol being in the extracellular fluid of an adult. The kidneys regulate long term balance of potassium.¹ Cellular uptake of potassium is regulated by insulin, acid base status aldosterone and adrenergic activity. Hyperkalemia is caused by redistribution of potassium from the intracellular to the extracellular fluid compartment due to the factors leading to impaired cellular uptake, like insulin insufficiency². Decreased renal excretion adds to further retention of potassium.^{2,3}

Hyperkalemia is a life threatening emergency and warrants immediate treatment because of its deleterious cardiac consequences⁴. In general physiological and pathological changes that occur in patients as they grow older may result in distal renal tubular dysfunction, as well as decreased level of plasma aldosterone. Such alterations result in a tendency toward hyperkalemia.⁵⁻⁷ Abnormalities of potassium homeostasis in diabetes are probably related to insulin and mineral corticoid deficiency.⁸

Chronic hyperkalemia in elderly diabetics is most often attributable to hyporeninemic hypoaldosteronism⁹. In the diabetic with ketoacidosis hyperkalemia in the face of potassium depletion may be attributed to reduced renal function, acidosis and release of potassium from cells due to glycogenolysis.⁹

Generally diabetes is considered as an independent cause of hyperkalemia¹⁰. Studies have shown that hyperglycemia alone and not insulin or epinephrine or glucagon is a direct determinant of plasma potassium. The hyperkalemia may be intermittent or persistent.^{11,12}

Physicians treating patients with diabetes should be aware of the dangers of precipitating life threatening hyperkalemia whenever prescribing for their patients. Dangerous hyperkalemia during use of ACE inhibitors and potassium-sparing diuretics have been reported in diabetic patients.¹³⁻¹⁶

Hyperkalemia is a common and potentially lethal clinical problem. The efficacy of intravenous insulin in cases of hyperkalemia in end stage kidney disease is reported¹⁷.

Our objective is to draw attention to the fact that hyperglycemia induces severe hyperkalemia especially in the setting of insulin absence or reduced insulin responsiveness. The risk factors for hyperkalemia include advanced age, significant prematurity, and the presence of renal failure, diabetes mellitus, and heart failure. Polypharmacy, particularly the use of potassium supplements and potassium-sparing diuretics, in patients underlying renal insufficiency contributed to hyperkalemia in almost one half of the cases.^{13,17} The data are not available about the incidence of hyperkalemia in diabetics in Saudi Arabia. Our study is the first of its kind in this region.

Methods

In this study 362 diabetic patients and 158 control non-diabetics were studied from September 2003 to August 2005 at Al Iman general hospital and prince Salman hospitals of Riyadh, Saudi Arabia.

The average age of the male and female control subjects was 19.5 (6-25) years and 18 (5 – 24) years while the mean age of Type 1 male diabetics was 17 (4-25) years and female was 18 (5- 23) years of age. Similarly the male and female control subjects included in the study of Type 2 diabetes were 45 (26-75) and 46 (26- 79) years of age. The average age of the diabetic Type 2 male and female patients was 47 (32 – 80) and 45 (35 -72) years respectively.

The patients were classified in Type 1 and Type 2 diabetes mellitus on the basis of classification of diabetes of 1997 given by the “International expert committee on the diagnosis and classification of diabetes mellitus”.¹⁸ We found 119 patients were diagnosed as Type 1 and 243 as Type 2 diabetes mellitus.

The Type 1 and Type 2 diabetics were subdivided into three study groups based on their fasting plasma glucose (FPG) levels as Group -1 (7.1- 10 mmol/L), group-2 (10.1- 20 mmol/L) and Group -3 (> 20 mmol/ L). The non diabetic control group having a FPG level of < 7.0 mmol /L and corresponding to the age group of less than 25 years and more than 25 years for Type 1 and Type 2 diabetes mellitus were selected randomly from the out-patients of the hospitals under study.

The serum potassium levels of >5.0 mmol/ L was considered as hyperkalemia.¹¹

In each group of normal control subjects and diabetic patients, a blood sample of 10 ml was withdrawn after twelve hours of fasting in fluoride and plain vials, and subjected to measurement of plasma glucose level and serum potassium ion. Samples were stored at 4°C for not more than 2 hours. The plasma was carefully separated by centrifugation at 3000 rpm for 10 minutes. Fasting plasma glucose was measured by glucoxidase peroxidase (God Pod) method on Dade-Behring, Dimension AR analyzer. The estimation of serum potassium was carried out by spectrophotometry.

All the subjects under study had undergone a thorough examination and tests for renal functions and significantly none of our diabetic patients had shown signs of renal failure.

Statistical Analysis

Comparison of continuous variables was carried out by student t test. The value of $p < 0.05$ for different variables was considered significant. Analysis of variance was used to test differences between the potassium ion concentration and the duration of hyperkalemia. Pearson’s correlation coefficient was applied to correlate the levels of FPG with serum potassium.

Results

It was observed that mostly older patients with a mean age of 60 had FPG level of > 20 mmol/L and fell in the group 3. The females with Type 2 diabetes in group 2 with FPG level between 10.1 and 20.0 mmol/L were the oldest with an average age of 58 years.

There was no significant difference in the mean FPG levels of male and female control subjects studied with Type 1 and Type 2 diabetes mellitus patients. The FPG level ranged between 4.05 to 5.03 mmol/L.

The mean serum potassium level in the controls of Type 2 diabetes was a little higher (4.1+ 0.6 vs 3.9 + 0.11 mmol /L) than Type 1 controls ($p < 0.05$).

Table1: shows the mean and SD of the levels of serum potassium in three study groups of Type 1 diabetes mellitus patients.

Table 2: shows the mean and SD of the levels of serum potassium in the patients of three study groups of diabetes mellitus Type 2.

No significant sex bias was noticed in the serum potassium levels in the Type 1 diabetes mellitus patients, while in Type 2 diabetes the male patients in group 2 and 3 had higher levels of serum potassium.

The most significant finding common to both Type 1 and Type 2 diabetes mellitus was a proportionate rise in the levels of serum potassium with the increasing levels of FPG. The highest levels of 8.1+ 1.7 ($r = 0.68$) of serum potassium was found in the males of group 3 (>20 FPG) of Type 2 diabetics. In the Type 1 diabetes the marked rise in s.potassium level was observed in group 3 patients while in Type 2 patients there was a noticeable rise even in group 2.

Discussion

In this study, which is first of its kind in Saudi Arabia, we had tried to find the incidence of hyperkalemia in Type 1 and 2 diabetes mellitus patients. 362 diabetes mellitus patients of which 119 were Type 1 and 243 Type 2 and 158 healthy control subjects were included in this study. For classification of diabetes mellitus we have followed the established criteria of the International expert committee¹⁸. The cut off upper limit for fasting plasma glucose (FPG) level in normal controls was taken as <7.0 mmol/ L. Hyperkalemia was declared in patients having a serum potassium level of > 5.0 mmol / L ¹¹.

As observed earlier by other authors we too did not find a significant difference in the levels of serum potassium in males and females.^{13,20}

In accordance with most of the previous studies we observed that there was a rise in serum potassium levels with increasing FPG levels in Type 1 and Type 2 diabetes mellitus patients⁸⁻¹³

Hyperkalemia is known to be relatively common in diabetic patients reflecting the role of insulin in potassium homeostasis. The unreported feature is the independent effect of diabetes in attenuating the early dip in serum potassium concentration and its later recovery. In these respects, patients with diabetes behaved remarkably like patients pretreated with β Blockers, making sympathetic nerve dysfunction, the most plausible explanation for the effects on potassium.²⁰

The higher levels of serum potassium in Type 2 diabetics having FPG level of > 20 mmol/L may be attributed to the fact that most of the patients in this group were elderly.^{5,6} Physiological and pathological events that occur in patients as they grow older may result in distal renal dysfunction, as well as decreased levels of plasma renin activity and plasma aldosterone. A syndrome termed hyporeninemic hypoaldosteronism, associated with hyperkalemia, has been frequently described in elderly patients.^{5,6}

The common occurrence of hyperkalemia in the elderly may be aggravated by the use of drugs that either further suppress renin and/or aldosterone or interfere with distal tubular potassium excretion.

Insulin resistance may also have had a role in preventing the early dip in serum potassium in diabetes by attenuating intracellular ionic flux early after the onset of symptoms, although the experimental finding of Brown and colleagues indicates that insulin does not contribute significantly to adrenergically driven changes in serum potassium.

We conclude that there appears a strong association between the hyperglycemia and hyperkalemia in both types of diabetes mellitus.^{8-11,21} Specially in uncontrolled elderly Type 2 diabetics, having a FPG level of > 20 mmol/L, the hyperkalemia is marked and may lead to cardiac emergencies⁴

Physicians while prescribing ACE inhibitors to their diabetic patients must be careful because a combination of uncontrolled hyperglycemia and use of ACE inhibitors may lead to severe hyperkalemia and may precipitate cardiac arrest.¹³⁻¹⁵

Table 1: Mean and SD of serum potassium levels in different study groups of type 1 diabetes mellitus patients.

Study groups	FPG level mmol / L	S. potassium level (Mean & SD) mmol / L	
		M (n=94)	F (n=61)
Control (n= 36)	< 7.0-7.0	4.0 + 0.52	3.9 + 0.11
Group 1 (n=27)	7.1 – 10.	4.7 + 1.01	4.5 + 0.98
Group 2 (n= 74)	10-20	5.9 + 1.1	5.8 + 1.3
Group 3 (n=13)	> 20	6.8 + 1.2	6.3 + 1.1

n= number , FPG = Fasting Plasma Glucose, SD = Standard deviation, M= Male, F= Female

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Table 2: Mean and SD of serum potassium level in different study groups in type 2 diabetes mellitus patients

Study groups	FPG level mmol/ L	S. potassium level (Mean & SD) mmol / L	
		M (n=215)	F (n=150)
Control (n=122)	< 7.0-7.0	4.3 + 0.8	4.1 + 0.6
Group 1 (n=78)	7.1 – 10.	5.5 + 1.4	4.9 + 1.2
Group 2 (n=130)	10 - 20	7.2 + 1.4	6.6 + 1.05
Group 3 (n=35)	> 20	8.1 + 1.7	8.0 + 1.09

n= number , FPG = Fasting Plasma Glucose, SD = Standard deviation, M= Male, F= Female

The health and social needs of children in impoverished areas

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Despite living in close vicinity to Islamabad, the children of Shamsabad face many health problems. The under-5 morbidity and mortality is very high in this community. The main reasons for this are:

1. Inadequate health care facilities for this age group
2. Inability of parents to access available health care facilities, due to poverty and ignorance
3. Inavailability of school health services in the community.

Impairment of visual acuity, chronic ear discharge, chronic diarrhoea, recurrent chest infections and malnutrition are very common in impoverished communities like ours. The Child Health sector of Shamsabad Mother Child Health Program especially concentrates on health of deprived children in orphanages and community schools, both regular and those meant for Special children.

Our focus of this article is on preventive aspects of Child Health. Our health workers have dedicated their efforts towards improving the personal hygiene and prevention of blindness, deafness, and malnutrition in the region.

About 75% of the blindness occurring in developing countries is avoidable, i.e. it is either treatable or preventable [1, 2]. According to the population-based survey 1987-1990, conducted by the Ministry of Health of Pakistan and the World Health Organization (WHO), a prevalence of blindness of 1.78% was found in Pakistan. The major causes of blindness are cataract, corneal opacities, uncorrected refractive errors and glaucoma. [3].

Inadequate intake of protein, calories, iron, and other nutrients make up the different types of malnutrition. As many as 800 million persons worldwide are affected by malnutrition. More than half the childhood deaths in developing countries are related to malnutrition [4]. If the body does not receive the energy it needs in the form of food, weight loss will occur. Children with malnutrition have inadequate fat stores and very little muscle. Their bones are prominent and they often have disproportionately large abdomens. Brain development can be impaired, and these children have a high incidence of disease because their bodies cannot fight infection. Malnutrition contributes to the high death rate among children in developing countries. [4]. The body requires micronutrients from diet because the body does not make all the products it needs for optimum function. Micronutrients include vitamins A, B, and C, folate, zinc, calcium, iodine, and iron. The 3 major micronutrient deficiencies in the developing world are iron (anaemia), iodine (deficiency can cause goiter and can lead to death or mental retardation for a developing fetus), and vitamin A. Vitamin A deficiency is a serious worldwide medical problem because it is the leading cause of preventable blindness in children. [4].

Worldwide, iron deficiency is the most common form of malnutrition. As many as 4 billion individuals may lack enough iron in their diet. Malaria and parasitic infections are common contributing causes. Iron deficiency causes anaemia (low red blood cell count). Anaemia causes fatigue, may cause heart failure in severe cases, and may also affect brain function. Preventing iron deficiency requires an adequate diet including

iron-rich foods such as leafy green vegetables, beans, and red meats. [4].

To summarize, the following are the common Medical Problems in our community:

- Anaemia
- Poor Oral Health
- Slow Development
- Eczema and Scabies
- Hearing deficiencies
- Visual deficiencies
- Iodine Deficiency
- Parasitic and Bacterial Intestinal Infections
- Malnutrition, Growth Failure and Rickets
- Asthma
- Tuberculosis
- Inadequate vaccine facilities

Social Problems of Special Schools [Blind girls]

Many of the blind girls have been unable to get even primary education in the wake of non-existence of special educational institutions for them, interviews with blind girls in Peshawar revealed. [5] The problem is exacerbated by the fact that those wanting to get education have to leave home and face a number of problems.

The girls are provided education only up to primary level and after completing five years they have to either leave their studies incomplete or go to a middle school in Islamabad for further studies. [5]. The examination system does not provide much relief to the blind candidates. Blind candidates are supposed to attempt the same paper and are given only 45 minutes additional time along with the three hours to solve a question paper. The blind candidates who appear with the normal candidates in examination are provided with a one class junior writer. [5].

Many parents of the blind girls are already afraid to send their daughters to the far off educational institutes as the biggest problem is to pick up and drop them. Many districts have institutes for the blind boys but the parents could not send their blind daughters to the mixed environment. Many blind girls remain deprived of the enlightenment due to the lack of facilities for special persons. [5]

Some Specific Medical Problems of Blind Girls

Our health workers are working to solve health problems of blind girls in a school which is situated in Shamsabad. [6] We have determined that in addition to medical problems mentioned above, they have difficulties in maintaining personal hygiene. The most important in this regard is care during menses. They have a free treatment facility at Rawalpindi General Hospital but they cannot go there, especially at night, because no body is free enough to take them to that hospital.

Our Strategy for these girls

1. We are already providing them treatment at low cost.
2. We have started health education especially in personal hygiene, care and protection during menses plus oral care.

Our team visits them regularly to provide them this education, training and essentials of personal life like soap, toothbrush, toothpaste, shampoos, detergents, accessories used during menses.

- To help these girls, we have to have an exact understanding of their usual habits. Towards, this end, we did various surveys.
- We have established a small first aid dispensary in this school to cater emergency first aid medicines, for example, analgesics, anti-emetics, anti-diarrhoeals, etc.

To make this dispensary useful and safe, we have selected their Hostel warden for training as a Health Worker. Ms. Fauzia Khanum, who is also their senior school teacher, daily attended our clinic at evening [her free time from school] for 6-weeks to learn the basics.

Community Based School Health Service is our main Strategy to address these problems. We are striving;

- To train health workers in school health services
- To train health workers in record keeping and reporting
- To identify preventable diseases in under-5 children
- To identify communicable diseases in under-5 children
- To identify anaemic and grossly malnourished under-5 children
- To treat anaemic and grossly malnourished under-5 children from our clinic's own resources
- To inform parents of suffering children, about early management of diagnosed problems.
- To establish a referral to experts system for the sufferers
- To assess and record general health status of under-5 children of the community

How Our Health Team Works:

The trained health workers have been divided into two groups. A smaller group deals with all under-5 children coming to our clinic for any reason. A bigger group visits all schools of Shamsabad.

The health workers examine and record the general physical examination and systemic examination with special attention to common diseases of this age group. They screen out the sufferers and arrange their check-up with a GP. The children who can be managed in the clinic are given full assistance and guidance. The very poor are given free treatment and those who can afford are given treatment at small cost. The difficult to treat cases are referred to experts for investigation and care.

Main Activities of our Community Based School Health Service

- Training of Blind girls in oral care. [6]
- Training of Blind girls in Special care during menses. [6]
- Screening of eye problems, with special attention to Visual Acuity, night blindness, problems of cornea, conjunctiva, and sclera [7]
- Screening of ear problems, with special attention to ear drums, difficulty in hearing [7]
- Screening of malnourished children, with special attention to growth retardation, chronic diarrhoea, repeated chest infections, anaemia, Rickets [7]

Community Surveys

The Blind Girl's School, Shamsabad, Rawalpindi

Dated: 08-03-2006. [6]

Activity executed by:

Project Team Leader---Mrs. Rahila Manzoor
Team Members: Ms. Sajida [Senior Community Volunteer & School Teacher], Mrs. Afshan Munir [Junior Community Volunteer & House-Wife], Mr. Mumtaz Bhatti [Senior Community Health Worker as Support Person]

1-Personal Hygiene survey - Oral Care

Total girls in the school hostel ----- 75

Total girls present during visit-----61

Total girls interviewed: ----- 61

Question-1:

What methods do you use for cleaning your teeth?

Miswak	Bark of tree (Dandasa)	Brushing of teeth	Others - Coal, ash
6 [9.83%]	10 [16.39%]	43 [70.49%]	2 [3.27%]

Question-2:

If you brush your teeth, what materials do you use? [43 out of 61]

Toothpaste	Toothpowder
35 [81.39%]	8 [18.60%]

Question-3:

Whatever the method & material, how many times do you clean your teeth?

Once daily	Twice daily	Thrice daily
37 [60.65%]	24 [39.34%]	-

Question-4:

When do you clean your teeth?

Before breakfast	Before every meal	After every meal
55 [90.16%]	6 [9.83%]	-

Question-5:

Do you have bleeding from your teeth?

Yes	No	I do not know
11 [18.03]	40 [65.57]	10 [16.39]

Question-6:

Do you have bad odour from your mouth?

Yes	No	I do not know
35 [57.37]	19 [31.14%]	7 [11.45]

Question-7:

Did you understand the information that we have conveyed to you?

Yes	No	I do not know
61 [100%]	-	-

Question-8

Are you now convinced that we should regularly brush our teeth with an adequate toothpaste at least twice a day, once after breakfast and secondly before going to bed at night?

Yes	No	I do not know
61 [100%]	-	-

Activity: provide toothpaste, brushes

2. Menstruation & Feminine Care

Total girls in the school hostel ----- 75
 Total girls present during the visit-----61
 Total girls who have periods-----20 [others are of younger age group]
 Total girls interviewed: ----- 20

Question-1:

Do you bathe during menses?

Yes	No	I do not know
-	20 [100%]	-

Question-2

What do you think about menses----is it a natural process or a disease?

A natural process	A disease	I do not know
18 [90%]	2 [10%]	-

Question-3:

Should a girl/woman continue normal activities & games during menses?

Yes	No	I do not know
16 [80%]	1 [5%]	3 [15%]

Question-4:

What material do you use during menses?

Sanitary Pads	Cotton with underwear	Only Cotton	Old used clothes/cotton with string
3 [15%]	1 [5%]	-	16 [80%]

Question-5

Did you understand the information that we have conveyed to you?

Yes	No	I do not know
20 [100]	-	-

Question-6

Are you now convinced that girls/women should regularly bathe and continue work and games during menses because menses is a natural process and not any disease?

Yes	No	I do not know
20 [100%]	-	-

Activity: Teaching the girls how to do feminine care - provide soap, cotton, underwear and cloth for making pads

Images

Screening of Eye Problems: with special attention to Visual Acuity, night blindness, problems of cornea, conjunctiva, and sclera



Screening of Ear Problems: with special attention to discharge, ear drums, difficulty in hearing



Screening of Malnourished children: with special attention to growth retardation, chronic diarrhoea, repeated chest infections, anaemia, Rickets



Health workers are questioning the girls about their various problems



Mrs. Rahila Manzoor is training teachers of blind school on how to make sanitary pads and about personal hygiene. These teachers in turn train the blind girls in this knowledge and skills.



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Global Launch of Child Watch



Child Watch is an initiative of the Middle East Journal of Family Medicine and was originally formed to assist Iraqi children who are suffering greatly from lack of medical resources and child size devices, as well as the psychological aspects of prolonged warfare.

Since then we find that many of the problems extend to the rest of the Middle East region and indeed the world. There is also a lack of focus globally on child-specific aspects of many medical conditions.

We are taking therefore both an academic and a practical approach to child health. We welcome articles on any topic related to aspects of child health and we also hope to provide practical assistance where possible.

Our first donation has been received from Mr Andrew Currie, of Melbourne, Australia, specifically to assist institutionalized blind girls of Rawalpindi, Pakistan, and we thank Mr Currie for his own initiative.

Please send articles or assistance, to publisher@mejfm.com.

We also welcome your ideas and your advice about effective programs in your own country or region.

I thank you all for supporting this initiative.

Lesley Pocock
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